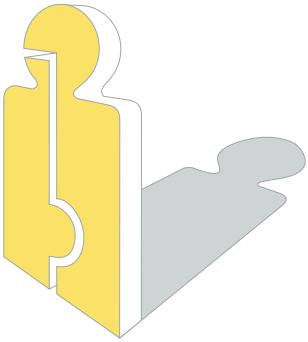
Programma Najaarscongres

NEDERLANDSE VERENIGING VOOR GASTRO-ENTEROLOGIE

voortzetting van de Vereniging van Nederlandse maag-darmartsen, opgericht 26 oktober 1913



6 en 7 oktober 2016

NH Conference Centre Koningshof

Veldhoven

NEDERLANDSE VERENIGING VOOR GASTRO-ENTEROLOGIE

NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

NEDERLANDSE VERENIGING VOOR GASTRO-INTESTINALE CHIRURGIE

NEDERLANDSE VERENIGING VAN MAAG-DARM-LEVERARTSEN

INHOUDSOPGAVE pag

Tijdstippen diverse ledenvergaderingen op donderdag:

Nederlandse Vereniging voor Gastroenterologie	6 oktober	11.30 uur – Brabantzaal
NVMDL i.o	6 oktober	12.00 uur – zaal 63/64
Nederlandse Vereniging voor Hepatologie	6 oktober	15.00 uur – Baroniezaal
Nederlandse Vereniging voor Gastrointestinale Chirurgie	6 oktober	14.15 uur – Auditorium

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Vrijdag 7 oktober 2016

Tijdstippen diverse ledenvergaderingen op vrijdag:

Nederlandse Vereniging van Maag-Darm-Leverartsen	7 oktober	08.00 uur – zaal 81-83
Sectie Gastrointestinale Oncologie (korte ledenvergadering)	7 oktober	11.00 uur – Parkzaal
Sectie Inflammatoire Darmziekten (IBD) (korte ledenvergadering)	7 oktober	13.00 uur – Baroniezaal

Belangrijke mededeling
over de aanwezigheid van farmaceutische industrieën

Aan alle deelnemers tijdens het najaarscongres op 6 en 7 oktober 2016

De Nederlandse Vereniging voor Gastroenterologie kent een jarenlange samenwerking met de farmaceutische industrie. De vereniging stelt de farmaceutische industrie in de gelegenheid aanwezig te zijn bij de wetenschappelijke vergaderingen met een stand. Mede hierdoor kan de vereniging haar wetenschappelijke bijeenkomsten organiseren.

De Geneesmiddelenwet zegt dat - onder strikte voorwaarden - de farmaceutische industrie alleen reclame mag maken voor receptgeneesmiddelen voor personen die bevoegd zijn om dergelijke geneesmiddelen voor te schrijven. Alle andere personen (inclusief bijvoorbeeld verpleegkundigen, endoscopie-assistenten en biochemici) worden beschouwd als “publiek”. De farmaceutische industrie mag geen reclame maken voor receptgeneesmiddelen voor publiek.
De Nederlandse Vereniging voor Gastroenterologie is een wetenschappelijke vereniging voor personen die beroepsmatig betrokken zijn bij zorg, onderwijs en onderzoek ten behoeve van patiënten met maag-, darm- en leveraandoeningen. Dat betekent dat ook personen die geen arts zijn, lid van de NVGE zijn.
De aanwezigheid van artsen, niet-artsen en farmaceutische industrieën tijdens het congres kan de NVGE ongewild in aanraking brengen met de inspectie voor de gezondheidszorg, sectie reclametoezicht, en daarmee in diskrediet worden gebracht. Dat willen wij uiteraard voorkomen.

In verband met de Gedragscode Geneesmiddelenreclame van de CGR en de aan het NVGE-congres verbonden expositie van farmaceutische producten, medische instrumenten en voedingsmiddelen, zal bij uw congresregistratie via de NVGE-website worden gevraagd naar uw bevoegdheid om medicijnen voor te schrijven.

Alle congresdeelnemers dragen verplicht een congresbadge waarop behalve de naam ook beroep/ functie staat aangegeven. Farmaceutische standhouders benaderen uitsluitend congresdeelnemers die de bevoegdheid hebben om receptgeneesmiddelen voor te schrijven of ter hand te stellen. Om dit extra te verduidelijken zal wederom worden gekozen voor verschillende kleuren congresbadges.

Uit het bovenstaande volgt dat aanwezige reclame-uitingen en merkproductinformatie van farmaceutische industrieën alleen gericht zijn op personen die bevoegd zijn om de betreffende geneesmiddelen voor te schrijven. Wij maken u erop attent dat het voor niet-artsen dan ook niet is toegestaan de stands van de aanwezige farmaceutische industrieën te bezoeken.

De NVGE en farmaceutische industrie (sponsoren) vertrouwen erop u met bovenstaande voldoende te hebben geïnformeerd.

Het bestuur van de NVGE

Voorwoord

Hierbij treft u het volledige programma aan van het najaarscongres dat gehouden wordt op 6 en 7 oktober a.s. in NH Conference Center Koningshof te Veldhoven. Zoals gebruikelijk wordt ons congres vooraf gegaan door het cursorisch onderwijs op woensdag 5 oktober, waarvan u het programma aantreft op bladzijde 8 en 9.

Traditioneel zijn er in het najaar veel klinische symposia, die dit najaar weer een doorlopend programma vormen parallel aan de abstractsessies. De klinische symposia zijn veelal multidisciplinair en georganiseerd door secties of specifieke werkgroepen.
Na de start op donderdagmorgen vroeg met een bijeenkomst over carrièreplanning, georganiseerd door de Juniorvereniging, is er op donderdag een doorlopend NVGIC- en een doorlopend NVH-programma met symposia en klinische abstracts. Vanaf 13.00 uur is er na het succes van vorig jaar weer een programma door en voor oudgedienden, met dank aan Joep Bartelsman en Henk Festen. Parallel daaraan een symposium over "Sedatie op de endoscopiekamer".
In de Brabantzaal wordt om 15.30 uur de MDL Kennisagenda gepresenteerd, en het rapport wordt officieel overhandigd aan de voorzitters van NVMDL, NVH en NVGE door commissievoorzitter Thijs Schwartz. De donderdag wordt afgesloten met de bekendmaking van de gesubsidieerde projecten, de President Select voordrachten en de uitreiking van de MLDS Award Daarna volgt de Presidential Lecture door de voormalige voorzitter van de ESGE richtlijnen commissie, Cesare Hassan uit Rome, gevolgd door een voordracht door Chris Mulder.

Op vrijdag aansluitend aan de ALV van de NVMDL de inmiddels traditionele videosessie van de Sectie Gastrointestinale Endoscopie, gevolgd door een minisymposium 'Let's talk about sex'. Ook op vrijdagmorgen symposia over de richtlijn HCC (benigne levertumoren) en door de sectie neurogastroenterologie en motiliteit: 'Invasive strategies for functional GI diseases'. De Netherlands Society of Parenteral and Enteral Nutrition verzorgt een symposium een zaal 80. Na de lunch in het Auditorium een symposium over het BVO colorectaal carcinoom. Vrijdag zijn er tevens in diverse zalen abstractsessies van de secties oncologie, IBD, endoscopie en voeding.
Ook zijn er tijdens het najaarscongres weer meet the expert sessies. U kunt zich inschrijven voor deze sessies die op donderdag worden gehouden, er is slechts beperkt plaats. In een kleine groep kunt u tijdens deze sessies interactief casuïstiek bespreken die door de experts is voorbereid. De collegae Beuers en De Knegt verzorgen een sessie over leverenzymstoornissen; de collegae Moons en Sanduleanu verzorgen een sessie over poliepherkenning en poliepectomie.

Tot ziens in Veldhoven!
Dr. J.J. Keller, secretaris NVGE

Programma donderdag 6 oktober 2016

Donderdag	Brabantzaal	Baroniezaal	Auditorium	Parkzaal
08.30 - 10.00	Ontvangst en koffie	Career Development Sessie voor aios MDL-Medisch Leiderschap *pagina 19*	Ontvangst en koffie	Ontvangst en koffie
10.00 – 11.30	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie *pagina 10*	Klinisch Symposium NVH - Complications of cirrhosis *pagina 19*	NVGIC Symposium I & II: "De helpende hand" tussen MDL-arts en bariatrisch chirurg/Upper GI-chirurg *(aanvang 09.30 uur)* *pagina 16*	Vrije voordrachten Nederlandse Vereniging voor Gastrointestinale Chirurgie *pagina 24*
11.30 - 12.00	Ledenvergadering NVGE	Geen programma i.v.m. Ledenvergadering NVGE	Geen programma i.v.m. Ledenvergadering NVGE	Geen programma i.v.m. Ledenvergadering
12.00 - 13.00	Lunch in expositiehal	Lunch in expositiehal	Lunch in expositiehal	Lunch in expositiehal
13.00 – 15.00	'Sedatie op de endoscopiekamer: Propofol voor iedereen?' *pagina 12*	Vrije voordrachten Nederlandse Vereniging voor Hepatologie *pagina 20*	NVGIC symposium III: DHCG en Werkgroep Leverchirurgie *pagina 17*	Vrije voordrachten Ned. Vereniging voor Gastrointestinale Chirurgie *pagina 26*
15.00 - 15.30	Theepauze	Theepauze + ALV NVH	Theepauze	Theepauze
15.30 - 17.00	Symposium kennis-agenda MDL *pagina 13*	Vrije voordrachten Nederlandse Vereniging voor Hepatologie *pagina 22*	NVGIC symposium IV: Pancreatitis Werkgroep Nederland en DPCG *pagina 18*	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie *pagina 28*
17.00 - 17.30	Voordrachten President Select - *pagina 13*			
17.30 – 17.40	Uitreiking MLDS Award 2016 – *pagina 14*			
17.40 – 18.10	State of the Art Lecture: Cesare Hassan *pagina 15*			
18.10 – 18.30	State of the Art Lecture Chris Mulder *pagina 15*			
18.30 - 19.30	Borrel in expositiehal			
19.30 - 22.00	Diner Genderzaal			
22.00 - 01.00	Borrel / Muziek in foyer			

Donderdag	Zaal 81 – Meet the expert - Leverenzym-afwijkingen	Zaal 82: Meet the expert - Poliepherkenning en poliepectomie
15.30 – 16.15 16.15 – 17.00	Groep 1 - volgeboekt Groep 2 – volgeboekt *pagina 30*	Groep 1 - volgeboekt Groep 2 – volgeboekt *pagina 30*

Donderdag	Seniorenprogramma
12.00 – 13.00 13.00 – 15.00	Lunch in de Uithof Lounge (gele zone) Programma zaal 65 - *pagina 31*

Programma vrijdag 7 oktober 2016

Vrijdag	Brabantzaal	Baroniezaal	Auditorium	Parkzaal
08.30 – 09.30	Ontvangst en koffie	Ontvangst en koffie	Ontvangst en koffie	Ontvangst en koffie
09.30 – 10.30	Ledenvergadering V&VN 09.30 uur Programma V&VN aanvang 10.00 uur *pagina 45*	Symposium Sectie Inflammatoire Darm-ziekten: Behandelen als richtlijnen tekort schieten. *pagina 35*	Videosessie Sectie Endoscopie pagina, gevolgd door mini symposium: 'Let's talk about seks' *pagina 32 - 33*	Vrije voordrachten Sectie Gastrointestinale Oncologie *pagina 40*
11.00 - 11.30	11.30 Koffiepauze expo	Koffiepauze expo	Koffiepauze expo	Koffiepauze expo
11.30 - 13.00	Programma V&VN *pagina 45*	Vrije voordrachten Sectie Inflammatoire Darmziekten *pagina 36*	Richtlijn HCC: symposium benigne levertumoren *pagina 33*	Motiliteitssymposium: Invasive strategies for functional GI diseases *pagina 42*
13.00 – 14.00	12.50 Lunch expositiehal	Lunch expositiehal	Lunch expositiehal	Lunch expositiehal
14.00 – 15.30	Middagprogramma Endoscopieverpleegkundigen in de Brabantzaal; IBD en Lever-verpleeg-kundigen in zaal 52 *pagina 46*	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie *pagina 38*	Symposium CRC *pagina 34*	

Programma vrijdag 7 oktober 2016
NESPEN en sectie Gastrointestinale Endoscopie

Vrijdag	Zaal 80
09.30 – 09.50	Sessie met vrije voordrachten NESPEN - *pagina 42*
09.50 – 11.00	Symposium NESPEN – Behandeling van high output fistel stomata en fistels - *pagina 43*
11.00 – 11.30	Koffiepauze in de expositiehal
11.30 – 13.00	Vrije voordrachten Sectie Gastrointestinale Endoscopie - *pagina 43*
13.00	Lunch in de expositiehal
	In de middag geen programma in deze zaal

Cursorisch onderwijs in maag-darm-leverziekten, 5 oktober 2016

Cursuscommissie
Prof. dr. U.H.W. Beuers, voorzitter, MDL-arts, AMC, Amsterdam
Mevr. dr. C.M. Bakker, MDL-arts, Atrium MC, Heerlen
Drs. K. van Hee, aios MDL, Radboud UMC, Nijmegen
Dr. J. Heisterkamp, chirurg, St. Elisabeth Ziekenhuis, Tilburg
Dr. M.A.J.M. Jacobs, MDL-arts, VUmc, Amsterdam
Mevr. dr. A.M.J. Langers, MDL-arts, LUMC, Leiden
Dr. B. Oldenburg, MDL-arts, UMCU, Utrecht
Mevr. dr. R.E. Pouw, aios MDL, AMC, Amsterdam
Dr. B.J. Veldt, MDL-arts, Reinier de Graaf Gasthuis, Delft
Mevr. dr. K. Verweij, Erasmus MC, Rotterdam

Onderwerp: IBD en coeliakie

IBD 1

Voorzitters: *Prof. dr. U.H.W. Beuers, Dr. K. Verweij*

14.30 – 14.35 Inleiding

14.35 – 14.55 Microscopische colitis: diagnostiek, kliniek en behandeling
Prof. dr. G. Bouma (MDL-arts, VUmc, Amsterdam)

15.00 – 15.20 Inductie- en onderhoudstherapie bij ziekte van Crohn
Dr. P.W.J. Maljaars (MDL-arts, LUMC, Leiden)

15.25 – 15.45 Fistelbehandeling bij ziekte van Crohn
Prof. dr. C.J. van der Woude (MDL-arts, Erasmus MC, Rotterdam)

15.50 – 16.10 Kliniek, diagnostiek en monitoring: ziekte van Crohn
Dr. A.E. van der Meulen (MDL-arts, LUMC, Leiden)

16.15 – 16.40 Pauze

De cursuscommissie verwacht van de MDL-artsen i.o. dat ze de Cursus Klinische Hepatologie (NVH) tijdens de Dutch Liver Week éénmaal bezoeken in het tweede deel van de MDL-opleiding (jaar vier tot zes).

Cursorisch onderwijs in maag-darm-leverziekten	**Auditorium**

IBD II

Voorzitters: *Dr. A.M.J. Langers, Drs. K. van Hee*

16.40 – 17.00 Diagnostiek en monitoring: Colitis ulcerosa
Dr. F. Hoentjen (MDL-arts, Radboudumc, Nijmegen)

17.05 – 17.25 Inductie- en onderhoudsbehandeling van colitis ulcerosa
Dr. B. Oldenburg (MDL-arts, UMCU, Utrecht)

17.30 – 17.50 Nieuwe middelen bij IBD
Prof. dr. G.R. van den Brink (MDL-arts, AMC, Amsterdam)

17.55 – 18.15 Timing van IBD chirurgie
Prof. dr. W.A. Bemelman (chirurg, AMC, Amsterdam)

18.20 – 18.45 Pauze

Coeliakie en microscopische colitis

Voorzitters: *Dr. M.A.J.M. Jacobs, Dr. R.E. Pouw*

18.45 – 19.05 Klinische aanpak van coeliakie
Prof. dr. C.J.J. Mulder (MDL-arts, VUmc, Amsterdam)

19.10 – 19.30 Extraïntestinale manifestaties bij ziekte van Crohn en colitis ulcerosa
Dr. C.Y. Ponsioen (MDL-arts, AMC, Amsterdam)

19.35 – 19.55 Voeding bij zieke darm: IBD, coeliakie, 'short bowel'
Dr. G.J.A. Wanten (MDL-arts, Radboudumc, Nijmegen)

20.00 Einde cursus, diner

Op het cursorisch onderwijs zijn conform de eisen van het Centraal Register Kort Beroepsonderwijs leveringsvoorwaarden van toepassing. Informatie vindt u op de onderwijspagina van www.mdl.nl en www.nvge.nl.

Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie **Brabantzaal**

Voorzitters: R.W.M. van der Hulst en V.M.C.W. Spaander

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

10.00 Endoscopically resectable colorectal cancer in a FIT-based screening population in the Netherlands: progress still to be made (p.48)

E Wieten, E. Wieten[1], E.J. Grobbee[1], E.J. Kuipers[1], P. Didden[1], M.J. Bruno[1], M.C.W. Spaander[1]. [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

10.10 Differences in quality indicators in colonoscopy performed by trainees and gastroenterologists (p.49)

P.C.J. ter Borg, P.C.J. ter Borg1, R.J.Th. Ouwendijk1, A.D. Koch2, E.J. Kuipers2, 1Dept of Gastroenterology, Ikazia Hospital, Rotterdam, 2Dept of Gastroenterology, Erasmus MC University Medical Center, Rotterdam, The Netherlands

10.20 Implementation of an Optical Diagnosis Strategy Saves Costs and Does Not Impair Clinical Outcomes of a FIT-based CRC Screening Programme (p.50)

J.L.A Vleugels[1], M.J.E. Greuter[2], Y. Hazewinkel[1], V.M.H. Coupé[2], E. Dekker[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [2]Dept of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands

10.30 Organized colorectal cancer screening programs and socioeconomic and ethnic inequalities in participation (p.51)

C.M. de Klerk1, S. Gupta2, E. Dekker1, M.L. Essink-Bot3, 1Dept of Gastroenterology and Hepatology, Academic Medical Center, University of Amsterdam, The Netherlands, 2Division of Gastroenterology, Dept of Internal Medicine, University of California San Diego, USA, [3]Dept of Public Health, Academic Medical Center, University of Amsterdam, The Netherlands

10.40 External validation of a clinically based staging system for perihilar cholangiocarcinoma (p.52)

T.A. Labeur, R.J.S. Coelen[1], M.P. Gaspersz[2], T.A. Labeur[3], J.L.A. van Vugt[2], S. van Dieren[1], H-J. Klümpen[3], B. Groot Koerkamp[2], T.M. van Gulik[1*] * these authors share senior authorship, [1]Dept of Surgery, Academic Medical Center, Amsterdam, [2]Dept of Surgery, Erasmus Medical Center, Rotterdam, [3]Dept of Medical Oncology, Academic Medical Center, Amsterdam, The Netherlands*

10.50 Online self-test identifies those at high risk for Lynch syndrome in population-based colorectal cancer screening without inducing anxiety or distress (p.53)

A van Erkelens[1], B.W.M. Spanier[2], A.S. Sie[1], M. van Kouwen[3], J.B. Prins[4], N. Hoogerbrugge[1], [1]Dept of Human Genetics, Radboud University Medical Center, Nijmegen, [2]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [3]Dept of Gastroenterology and Hepatology, Radboud university medical center, Nijmegen, [4]Dept of Medical Psychology, Radboud University Medical Center, Nijmegen, The Netherlands

11.00 Indications and consequences of MSI-analysis in colorectal cancer (p.54)

M.H.A. Lammertink[1], L. Leicher[1], J.W.B. de Groot[2], H.L. van Westreenen[3], S.R. Offerman[4], M.M. de Jong[5], H. Morreau[6], H.F.A. Vasen[7,8], W.H. de Vos tot Nederveen Cappel[1], [1]Dept of Gastroenterology and Hepatology, [2]Oncology, [3]Surgery, [4]Pathology, Isala Zwolle, [5]Dept of Human and Clinical Genetics, University Medical Center Groningen, Groningen, [6]Dept of Pathology, Leiden University Medical Center, Leiden, [7]Dept of Gastroenterology and Hepatology, Foundation for the Detection of Hereditary Tumors, [8]Leiden University Medical Center, Leiden, The Netherlands

11.10 A digital review platform for Barrett's esophagus: going national (p.55)

M.J. van der Wel[1,2], R.E. Pouw[2], C.A. Seldenrijk[3], G.J.A. Offerhaus[4], M. Visser[5], F.J. ten Kate[4], K. Biermann[6], M. Doukas[6], C. Huysentruyt[7], A. Karrenbeld[8], G. Kats-Ugurlu[8], J. van der Laan[9], I. van Lijnschoten[7], F. Moll[10], A. Ooms[11], H. van der Valk[11], J.G. Tijssen[12], J.J. Bergman[2], S.L. Meijer[1], [1]Dept of Pathology, Academic Medical Center, Amsterdam, [2]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [3]Dept of Pathology, St. Antonius Hospital, Nieuwegein, [4]Dept of Pathology, University Medical Center, Utrecht, [5]Dept of Pathology, Zaans Medical Center, [6]Dept of Pathology, Erasmus Medical Center, Rotterdam, [7]Dept of Pathology, Catharina Hospital, Eindhoven, [8]Dept of Pathology, Academic Medical Center Groningen, Groningen, [9]Dept of Pathology, Haga Hospital, The Hague, [10]Dept of Pathology, Isala Clinics, Zwolle, [11]Dept of Pathology, St. Fransiscus Hospital, Rotterdam, [12]Dept of Cardiology, Academic Medical Center, Amsterdam, The Netherlands*

11.20 The Natural Behavior of Small Colorectal Adenomas: a Systematic Literature Review (p.56)

J.L.A. Vleugels[1], Y. Hazewinkel[1], P. Fockens[1], E. Dekker[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands

11.30 Korte ledenvergadering Nederlandse Vereniging voor Gastroenterologie

12.00 Lunch in expositiehal

Sedatiesymposium **Brabantzaal**

Voorzitters: R.J. Robijn en B. Preckel

Symposium
Sedatie op de endoscopiekamer: Propofol voor iedereen

13.00 'Samenwerken': Propofol sedatie op de endoscopiekamer door SPS:
E. de Jong, SPS, PA anesthesiologie, Heerenveen
(lid van de sedatiecommissie)

13.20 Endoscopie bij kinderen en adolescenten onder propofol:
Prof. dr. J.C. Escher, kinderarts-MDL,
Erasmus MC-Sophia, Rotterdam

13.40 Complicaties na 2 jaar propofol op de endoscopiekamer.
Is er nog ruimte voor algehele narcose?
Prof. B. Preckel, anesthesist AMC

14.00 Knelpunten bij het gebruik van propofol op de endoscopiekamer:
Dr. M. Klemt-Kropp, MDL-arts, Alkmaar
(voorzitter sedatiecommissie)

14.20 Propofol op de endoscopiekamer in een ideale wereld:
Dr. R.J. Robijn, MDL-arts, Arnhem
(lid sedatiecommissie)

14.40 Propofol straks voor iedereen? Plenaire discussie.
Moderatoren: *B. Preckel, R.J. Robijn, E. de Jong,*
J.C. Escher, M. Klemt-Kropp

15.00 Theepauze expositiehal

Symposium NVMDL **Brabantzaal**

Voorzitters : A.A.M. Masclee en P.D. Siersema

Symposium Kennisagenda NVMDL

15.30 Opening door A.A.M. Masclee

15.35 Presentatie Kennisagenda NVMDL
Dr. M.P. Schwartz, namens de Commissie Kwaliteit van de NVMDL en aanbieden rapport aan voorzitters NVMDL, NVGE en NVH

16.10 'Van Kennisagenda tot NVOG-kwaliteitsregio's'
Dr. G.L. Bremer, gynaecoloog Orbis MC, Sittard

16.35 "Hoe impact van onderzoek te versterken? Het belang van kennisagenda's en participatie."
M. Snijders, programmacoördinator ZonMw

17.00 Einde programma

NVGE subsidies **Brabantzaal**

17.00 **Bekendmaking toegekende NVGE-subsidies**:

- Subsidies Gastrostart
- Subsidies voor multidisciplinaire en instelling-overstijgende onderzoeksinitiatieven of werkgroepen.

Voordrachten President Select **Brabantzaal**

Voorzitters: J.J. Keller en P.D. Siersema

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

17.05 Management of Eosinophilic Esophagitis in Daily Clinical Practice (p.57)

B.D. Vermeulen[1], A. Bogte[1], P.D. Siersema[1,2], [1]Dept of Gastroenterology and Hepatology, University Medical Center, Utrecht and [2]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands

17.15 Genomic and expression analysis identify WWOX as a disease modifier gene in fibrostenotic Crohn's disease (p.58)

M.C. Visschedijk[1,2], L.M. Spekhorst[1,2], S-C. Cheng[3], E.S. van Loo[4], B.H.D. Jansen[1], T. Blokzijl[1,5], H. Kil[6], D.J. de Jong[7^], M. Pierik[8^], A.E. van der Meulen-de Jong[9^], C.J. van der Woude[10^], A.A. van Bodegraven[11^], B. Oldenburg[12^], M. Lowenberg[13^], V.B. Nieuwenhuijs[14], F. Imhann[1,2], S. van Sommeren[1,2], R.J. Xavier[3], G. Dijkstra[1^], K.N. Faber[1,5], C.M. Aldaz[6], R.K. Weersma[#1^], E.A.M. Festen[#1,2], [1]Dept of Gastroenterology and Hepatology, University of Groningen and University Medical Centre Groningen, [2]Dept of Genetics, University of Groningen and University Medical Centre Groningen, The Netherlands, [3]Broad Institute of Harvard and MIT, Boston, USA, [4]Dept of Surgery, University of Groningen and University Medical Centre Groningen, [5]Dept of Laboratory Medicine, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands, [6]Dept of Epigenetics and Molecular Carcinogenesis, Science Park, The University of Texas M.D. Anderson Cancer Centre, Smithville, USA, [7]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, [8]Division of Gastroenterology and Hepatology, University Medical Centre Maastricht, Maastricht, [9]Dept of Gastroenterology and Hepatology, Leiden University Medical Centre, Leiden, [10]Dept of Gastroenterology and Hepatology, Erasmus Medical Centre, Rotterdam, [11]Dept of Gastroenterology and Hepatology, VU University Medical Centre, Amsterdam, [12]Dept of Gastroenterology and Hepatology, University Medical Centre Utrecht, Utrecht, [13]Dept of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, [14]Dept of Surgery, Isala Clinics, Zwolle, The Netherlands - ^ On behalf of the Dutch Initiative on Crohn and Colitis (ICC) and the IBD pearl of the Parelsnoer Institute

17.25 Transanal endoscopic microsurgery versus endoscopic mucosal resection for large rectal adenomas (TREND-study) (p.59)

R.M. Barendse[1], G.D. Musters[1], E.J.R. de Graaf[2], F.J.C. van den Broek[3], E.C.J. Consten[4], P.G. Doornebosch[2], J.C. Hardwick[5], I.H.J.T. de Hingh[6], Chr. Hoff[7], J.M. Jansen[8], A.W.M. van Milligen de Wit[9], G.P. van der Schelling[10], E.J. Schoon[11], M.P. Schwartz[12], B.L.A.M. Weusten[13], M.G. Dijkgraaf[14], P. Fockens[15], W.A. Bemelman[1] and E. Dekker[15] on behalf of the TREND study group, [1]Dept of Surgery, Academic Medical Center, Amsterdam, [2]Dept of Surgery, IJsselland Hospital, Capelle aan den IJssel, [3]Dept of Surgery, Máxima Medical Center, Eindhoven, [4]Dept of Surgery, Meander Medical Center, Amersfoort, [5]Dept of Gastroenterology, Leiden University Medical Center, Leiden, [6]Dept of Surgery, Catharina Hospital, Eindhoven, [7]Dept of Surgery, Medical Center Leeuwarden, Leeuwarden, [8]Dept of Gastroenterology, Onze Lieve Vrouwe Gasthuis, Amsterdam, [9]Dept of Gastroenterology, Amphia Hospital, Breda, [10]Dept of Surgery, Amphia Hospital, Breda, [11]Dept of Gastroenterology, Catharina Hospital, Eindhoven, [12]Dept of Gastroenterology, Meander Medical Center, Amersfoort, [13]Dept of Gastroenterology, St. Antonius Hospital, Nieuwegein, [14]Clinical Research Unit, Academic Medical Center, Amsterdam, [15]Dept of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands

Prijsuitreiking **Brabantzaal**

17.35 **Uitreiking MLDS-Award 2016 voor meest impactvolle artikel voor patiënten**
de uitreiking wordt gevolgd door een korte voordracht.

Uitreiking door Prof. dr. G. Kazemier (VUmc), lid jury MLDS Award en jhr. mr. J. Backer, voorzitter Raad van Toezicht MLDS

Winnaar MLDS Award 2016:
Floris Imhann, MD (UMCG)
Titel publicatie: Maagzuurremmers beïnvloeden de darmbacteriën

State of the art lectures **Brabantzaal**

Voorzitters: J.J. Keller en P.D. Siersema

17.45 **The Professional and Legal Role of Guidelines in Gastroenterology: Where Will it End**
Dr. Cesare Hassan, Chair Guideline Committee European Society of Gastrointestinal Endoscopy (ESGE), Department of Gastro-enterology, Nuovo Regina Margherita Hospital, Rome, Italy.

18.15 **35 jaar coeliakie**
Prof. dr. C.J.J. Mulder, MDL-arts, VU medisch centrum Amsterdam

18.35 Einde programma, congresborrel in expositiehal

20.00 Diner in Beneluxzaal

Symposium Ned. Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: n.t.b.

Symposium I: *"De helpende hand" tussen MDL-arts en bariatrisch chirurg.*

09.30 Postbariatrisch galsteenlijden.
Dr. Bert van Ramshorst, chirurg, St Antonius ziekenhuis, Nieuwegein

09.45 ERCP na gastric bypass.
Dr. S.D. Kuiken, MDL-arts OLVG, Amsterdam

10.00 Endoluminale behandeling van naadlekkage na sleeve gastrectomie.
Dr. L. Berk, MDL-arts St. Franciscus Gasthuis, Rotterdam

10.15 GEJ stenose: dilateren of reviseren

Symposium Ned. Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: M. Luyer en J. Stoot

Symposium II: *"De helpende hand" tussen MDL-arts en Upper-GI chirurg*

10.30 Chirurgische behandeling van GERD en complicaties
Prof. dr. N. Bouvy, chirurg, Maastricht UMC+

10.45 Behandeling van slokdarmcarcinoom door de MDL-arts.
Dr. W.L. Curvers, MDL-arts, Catherina Ziekenhuis, Eindhoven

11.00 Behandeling van complicaties na slokdarmresectie.
Dr. C.M. Bakker, MDL-arts, Zuyderland Ziekenhuis, Heerlen

11.15 Behandeling van oesophagusruptuur na endoscopie
Dr. S.M. Lagarde, chirurg, Erasmus MC, Rotterdam

Symposium Ned. Vereniging voor Gastrointestinale Chirurgie **Auditorium**

11.30 Korte ledenvergadering Nederlandse Vereniging voor Gastroenterologie

12.00 Lunch in expositiehal

Symposium Ned. Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: n.t.b.

Symposium III: DHCG en Werkgroep Leverchirurgie

13.00 Overview ongoing clinical trials DHCG; ASCO 2016 update,
Dr. H.J. Klümpen, internist oncoloog, AMC, Amsterdam

13.15 Peri-hilar cholangiocarcinoma; To drain or not to drain?
Dr. B. Groot Koerkamp, chirurg, Erasmus MC, Rotterdam

13.30 Classification of CC; histogenetic difference between intra- & extra hepatic CC?
Prof. dr. A.S.H. Gouw, patholoog, UMCG, Groningen

13.45 Bridge to transplant in HCC patients: improving the chance of surgical success?
Drs. M.C. Burgmans, radioloog, LUMC, Leiden

14.00 Fascilitating surgical resection in HCC patients: portal vein embolization versus radioembolization.
Prof. O.M. van Delden, radioloog, AMC, Amsterdam

14.15 Einde programma, gevolgd door ledenvergadering NVGIC en theepauze

Symposium Ned. Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: M.J. Bruno en C.H.C. Dejong

Symposium: IV : "de helpende hand" tussen MDL-arts, interventieradioloog en chirurg bij het oplossen complicaties
Pancreatitis Werkgroep Nederland en Dutch Pancreatic Cancer Group

15.30 Endoscopische behandeling complicaties pancreaschirurgie
Dr. F. Vleggaar, MDL-arts, UMC Utrecht

15.45 Preventie en behandeling gastroparese bij pancreaschirurgie/pancreatitis
Dr. A. Gerritsen, chirurg i.o., Gelre ziekenhuizen, Apeldoorn

16.00 Radiologisch-chirurgische behandeling duodenumperforaties
Dr. M.G.H. Besselink, chirurg, AMC Amsterdam

16.15 Post-ERCP pancreatitis: lering trekken uit 13 jaar PWN
Dr. E.J.M. van Geenen, MDL-arts, Radboudumc Nijmegen

16.30 Preventie van complicaties van galwegdrainage middels plastic/metalen stents
Dr. J.E. van Hooft, MDL-arts, AMC Amsterdam.

16.45 Plenair vervolgprogramma in de Brabantzaal

Career Development Sessie voor aios MDL **Baroniezaal**

Voorzitters: S. Onderwater, voorzitter NVMDLi.o.

Thema: Medisch Leiderschap

08.30 J. van Hooft, MDL-arts AMC, MBA
M. Spanier, specialist manager maatschap MDL Rijnstate
M. Westerman, promotie VUmc:
'Mind the gap; the transition to hospital consultant'

10.00 Einde bijeenkomst Career Development Sessie

Klinisch symposium Hepatologie **Baroniezaal**

Voorzitters: U.H.W. Beuers en H.J. Metselaar

Symposium
Complications of cirrhosis

10.00 Bèta blockers for varices - when indicated and when not?
Dr. M.J. Coenraad, Leiden University Medical Center

10.20 Hepatic encephalopathy - new insights in pathogenesis, diagnosis and treatment
Prof. dr. D. Häussinger, University of Düsseldorf

10.50 'Battle' for the Young Hepatologist Award 2016 (clinical research)

11.05 Kidney failure in cirrhosis: recent advances in pathophysiology and treatment
Prof. dr. H.J. Metselaar, Erasmus Medical Centre Rotterdam

11.30 End of symposium

12.00 Lunch in expositiehal

Voorzitters: S. Darwish Murad en J.M. Vrolijk

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

13.00 Durable Response in the Markers of Cholestasis through 18 Months of Open-Label Long-Term Safety Extension Study of Obeticholic Acid in Primary Biliary Cirrhosis (p.60)

J. Drenth, M. Trauner[1], F. Nevens[2], P. Andreone[3], G. Mazzella[3], S. Strasser[4], C. Bowlus[5], P. Invernizzi[6], J. Drenth[7], P. Pockros[8], J. Regula[9], A. Floreani[10], S. Hohenester[11], V. Luketic[12], M. Shiffman[13], K. van Erpecum[14], V. Vargas[15], C. Vincent[16], B. Hansen[17], L. MacConell[18], T. Marmon[18], D. Shapiro[18], [1]Medical University of Vienna, Vienna, Austria, [2]UZ Leuven, Leuven, Belgium, [3]Dipartimento di Scienze Mediche e Chirurgiche, University of Bologna, Bologna, Italy, [4]Royal Prince Alfred Hospital, Sydney, NSW, Australia, [5]University of California-Davis, Sacramento, CA, USA, [6]Humanitas Clinical and Research Center, Rozzano, Italy, [7]Radboudumc Nijmegen, The Netherlands, [8]Scripps Clinic, La Jolla, CA, USA, [9]Cancer Centre, Warsaw, Poland, [10]Università di Padova, Padova, Italy, [11]LMU University of Munich, Munich, Germany, [12]McGuire DVAMC and Virginia Commonwealth University School of Medicine, Richmond, VA, USA, [13]Liver Institute of Virginia, Newport News, VA, USA, [14]UMC Utrecht, Utrecht, The Netherlands; [15]Hospital Vall d'Hebron, Universitat Autònoma, CIBEREHD, Barcelona, Spain, [16]Centre Hospitalier Universitaire de l'Université de Montréal- St. Luc, Montréal, QC, Canada, [17]Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [18]Intercept Pharmaceuticals, Inc., San Diego, CA, USA

13.10 Patients with polycystic livers more than two times the normal size are likely to develop symptoms (p.61)

M.K. Neijenhuis[1], S.M.H. Verheesen[1], M.C. Hogan[2], J.A. Sloan[3], W. Kievit[4], T.J.G. Gevers[1], J.P.H. Drenth[1], [1]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen MC, Nijmegen, The Netherlands, [2]Division of Nephrology and Hypertension, Dept of Internal Medicine, Mayo Clinic, Rochester (MN), US, [3]Quality of Life Group, Dept of Health Sciences Research, Mayo Clinic, Rochester (MN), USA, [4]Radboud Institute for Health Sciences, Radboud University Nijmegen MC, Nijmegen, The Netherlands

13.20 IgG4-associated cholangitis in patients resected for presumed perihilar cholangiocarcinoma (p.62)

E. Roos, R.J.S. Coelen[1], L.M. Hubers[2*], E. Roos[1], J. Verheij[3], T.M. van Gulik[2°], U. Beuers[1°], [1]Dept of Surgery, Academic Medical Center, Amsterdam, [2]Dept of Gastroenterology & Hepatology and Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, [3]Dept of Pathology, Academic Medical Center, Amsterdam, The Netherlands * ° These authors contributed equally*

13.30 Post-transplant lymphoproliferative disease after adult liver transplantation and its prevention by pre-emptive strategy based on Epstein-Barr viral load monitoring. A single center study (p.63)

N. Francisco[1], A. Inderson[1*], R. Wolterbeek[2], J. Dubbeld[3], A. Vossen[4], B. van Hoek[1] *) These authors contributed equally to this manuscript, [1]Dept of Gastroenterology and Hepatology, [2]Dept of Medical Statistics, [3]Dept of Surgery, [4]Dept of Medical Microbiology, The Netherlands*

13.40 Mitochondrial reactive oxygen species production triggers hepatic ischemia/-reperfusion injury by inducing the release of high-mobility group box 1 (p.64)

R.F. van Golen[1], M.J. Reiniers[1], L.K. Alles[1], D.M. van Rooyen[3], G. Marsman[9,12], B. Petri[5,6], V.A. Van der Mark[1,10], A. van Beek[11], B. Meijer[11], M.A. Maas[1], B.M. Luken[9,12], J. Verheij[7], G.C. Farrell[3], S. Zeerleder[8,9,12], N.C. Teoh[3], T.M. van Gulik[1], M.P. Murphy[2], P. Kubes[4,5], M. Heger[1], [1]Dept of Experimental*

Surgery, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [2]Gastroenterology Unit, The Canberra Hospital, Canberra, Australia, [3]Medical Research Council Mitochondrial Biology Unit, Cambridge, United Kingdom, [4]Depts of Physiology & Pharmacology and Medicine, Snyder Institute for Chronic diseases, University of Calgary, Calgary, [5]Immunology Research Group, Snyder Institute for Chronic diseases, University of Calgary, Calgary, [6]Dept of Microbiology, Immunology, and Infectious Diseases, Snyder Institute for Chronic diseases, University of Calgary, Calgary, Canada, [7]Dept of Pathology, Academic Medical Center, University of Amsterdam, Amsterdam, [8]Dept of Hematology, Academic Medical Center, University of Amsterdam, Amsterdam, [9]Dept of Immunopathology, Sanquin Research, Amsterdam, [10]Tytgat Institute for Gastrointestinal and Liver Research, Academic Medical Center, University of Amsterdam, Amsterdam, [11]Gut Health and Food Safety, Institute of Food Research, Dept of Cell Biology and Immunology, Wageningen University, Wageningen, [12]Landsteiner Laboratory, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

13.50 Liver transplantation for cirrhosis secondary to non-alcoholic steatohepatitis is not perormed at the expense of major postoperative morbidity (p.65)

R.M. Douwes[1], E.H. van den Berg[1], V.E de Meijer[2], T.C.M.A Schreuder[1], J. Blokzijl[1], [1]Dept of Gastroenterology and Hepatology, University of Groningen and University Medical Center Groningen, Groningen and [2]Section of Hepatobiliary surgery and Liver Transplantation, Dept of surgery, University of Groningen and University Medical Center Groningen, Groningen, The Netherlands

14.00 The effectiveness of non-surgical interventions in biliary duct complications after liver transplantation (p.66)

F.J.M. Roos[1], J.W. Poley[1], B.E. Hansen[1], A. Moelker[2], W.G. Polak[3], H.J. Metselaar[1], [1]Dept of Gastroenterology and Hepatology, Erasmus Medical Center Rotterdam, Rotterdam, [2]Dept of Interventional Radiology, Erasmus Medical Center Rotterdam, Rotterdam, [3]Dept of Surgery, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

14.10 Bacterascites is associated with poor clinical outcome in decompensated cirrhosis (p.67)

R.C. Oey, H.R. van Buuren, B.E. Hansen, R.A. de Man, Dept of Gastroenterology and Hepatology, Erasmus MC University Hospital, Rotterdam, The Netherlands

14.20 Primary Biliary Cholangitis at a Young Age - Clinical Characteristics and Prognosis (p.68)

M.H. Harms[1], S. Dotti [2], A.C. Cheung[3], V. Ronca[4], M. Carbone[4], W.J. Lammers[1], P. Invernizzi[4,5], H.L. Janssen[3], P.M. Battezzati[2], B. E. Hansen[1], H.R. van Buuren[1] - on behalf of the Global PBC Study Group, [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands, [2]Dept of Health Sciences, Università degli Studi di Milano, Milan, Italy, [3]Toronto Centre for Liver disease, Francis Family Liver Clinic, Toronto General Hospital, Toronto, Canada, [4]Liver Unit and Center for Autoimmune Liver Diseases, Humanitas Clinical and Research Center, Rozzano, Italy, [5]Dept of Medicine and Surgery, University of Milan-Bicocca, Monza, Italy.

14.30 Differences in patient characteristics and long-term outcome between Asian and European patients treated with radiofrequency ablation for hepatocellular carcinoma (p.69)

J.C. Kerbert[1], M.C. Burgmans[2], C.W Too[3], M. Fiocco[4], J.J. Schaapman[1], A.R. van Erkel[2], M.J. Coenraad[1], B.S. Tan[3], [1]Dept of Gastroenterology and Hepatology, Leiden University Medical Centre, Leiden, [2]Dept of Radiology Leiden University Medical Centre, Leiden, The Netherlands, [3]Dept of Diagnostic Radiology, Singapore General Hospital, Singapore, [4]Dept of Medical Statistics and Bioinformatics Leiden University Medical Centre, The Netherlands

14.40 Patients' misconceptions about surveillance for hepatocellular carcinoma: Education is needed (p.70)

S. van Meer[1], F.I. Lieveld[1,2], K.J. van Erpecum[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht and [2]Dept of Internal Medicine and Infectious Diseases, University Medical Center Utrecht, Utrecht, The Netherlands

14.50 FXR agonist obeticholic acid induces liver growth but can transiently exacerbate biliary injury in rats with obstructive cholestasis (p.71)

R.F. van Golen[1#], P.B. Olthof[1#], D.A. Lionarons[1,2,3#], M.J. Reiniers[1], L.K. Alles[1], M.A. Maas[1], J.Verheij[5], P.L. Jansen[4], S.W. Olde Damink[4], F.G. Schaap[4], T.M. van Gulik[1], M. Heger[1], [1]Dept of Experimental Surgery, Academic Medical Center, University of Amsterdam, Amsterdam, [2]Tytgat Institute for Gastrointestinal and Liver Research, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [3]Dept of Signal Transduction, London Research Institute, Cancer Research UK, London, United Kingdom, [4]Dept of Surgery, NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht Univ., Maastricht, The Netherlands[5]. Dept of Pathology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands*

15.00 Theepauze en ledenvergadering NVH

Vrije voordrachten Nederlandse Vereniging voor Hepatologie — Baroniezaal

Voorzitters: M.J. Coenraad en J. de Bruijne

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

15.30 Coffee & herbal tea consumption is protective of liver stiffness in the general population: The Rotterdam Study (p.72)

L.J.M. Alferink[1], J. Fittipaldi[1,2], J.C. Kiefte-de Jong[2,3], J.D. Schoufour[2], P. Taimr[1], H.J. Metselaar[1], H.L.A. Janssen[1,4], O.H. Franco[2], S. Darwish Murad[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, [2]Dept of Epidemiology, Erasmus MC University Medical Center, Rotterdam, [3]Leiden University College, The Hague, The Netherlands, [4]Liver Centre, Toronto Western & General Hospital, University Health Network, Toronto, Canada

15.40 Under-reporting of complementary and alternative drug use in liver disease patients (p.73)

F.A.C. Berden[1], G.P.C.A. Netten[1], W. Kievit[2], J.P.H. Drenth[1], [1]Dept of Gastroenterology and Hepatology, Radboud university medical center, Nijmegen and [2]Dept for Health Evidence, Radboud University Medical Center, Nijmegen, The Netherlands

15.50 High rate of HBsAg loss after peginterferon based combination treatment for chronic hepatitis B patients: results after 5 years of follow-up (p.74)

F. Stelma[1], M. van der Ree[1], L. Jansen[1], M. Peters[1], A. de Niet[1], H.L.A. Janssen[2], H. Zaaijer[3], R. B. Takkenberg[1], H. W. Reesink[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [2]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands, [3]Toronto Centre for Liver Disease, Toronto Western & General Hospital, University Health Network, Toronto, Canada 3 Dept of Clinical Virology, Academic Medical Center, Amsterdam, The Netherlands

16.00 Addition of (pegylated) interferon to entecavir increases serological response in Hepatitis B e Antigen-positive, chronic hepatitis B patients (p.75)

K.S. Liem[1,2], W.P. Brouwer[2], H. Chi[2], Q. Xie[3], X. Qi[4], Q. Zhang[4], B.E. Hansen[2], H.L.A. Janssen[1,2], [1]Toronto Centre for Liver Disease, Toronto Western & General Hospital, University of Toronto, Toronto, Ontario, Canada, [2]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands, [3]Dept of Infectious Diseases, Ruijin Hospital, Jiaotong University, Shanghai, China, [4]Dept of Hepatitis Disease, Shanghai Public Health Clinical Center, Fudan University, Shanghai, China

16.10 Proton pump inhibitors decrease phlebotomy need in HFE-related haemochromatosis A double-blind randomized controlled trial - HE-PPI trial (p.76)

A. Vanclooster[1], van Deursen[2], Jaspers[2,3,4], D. Cassiman[1], G.H.Koek[4], [1]University Hospital Leuven, Belgium, [2]Zuyderland Medical Center Heerlen, [3]Laurentius hospital Roermond, [4]Maastricht UMC+, The Netherlands

16.20 Ribavirin plasma level is an independent predictor for sustained virologic response in difficult to treat hepatitis C-infected patients treated with direct-acting antivirals + ribavirin combination (p.77)

F.I. Lieveld[1,2], M. van Tilborg[3*], E.J. Smolders[4], J.E. Arends[2], A.S.M. Dofferhoff[6], J.P.H. Drenth[6], R. Maan[3], C.T.M.M. de Kanter[5], H. Blokzijl[7], M. Bijmolen[7], M. van der Valk[8], K.J. van Erpecum[1], R.J. de Knegt[3], D.M. Burger[4] *These authors share first co-authorship, [1]Dept Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Internal Medicine and Infectious Diseases, University Medical Center Utrecht, Utrecht, [3]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, [4]Dept of Pharmacy, Radboud University Medical Center, Nijmegen, The Netherlands [5]Dept of Pharmacy, University Medical Center Utrecht, Utrecht, the Netherlands [6]Dept Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, the Netherlands [7]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, the Netherlands [8]Dept of Internal Medicine and Infectious Diseases, Center for Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, The Netherlands*

16.30 Retrieval of chronic hepatitis B and C patients: collaboration between different healthcare professionals leads to the identification of patients lost to follow-up (p.78)

N. Beekmans and M. Klemt-Kropp, Dept of Gastroenterology and Hepatology, Northwestern Hospitalgroup, Alkmaar, The Netherlands

16.40 Point shear wave elastography has high diagnostic accuracy for staging of liver fibrosis in patients with chronic hepatitis B and C infection (p.79)

M van Tilborg[1], I. Sporea[2], N. Yousoufi[1], R. Mare[2], B.E. Hanssen[1], R.J. de Knegt[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands and [2]Dept of Gastroenterology and Hepatology, Timisoara, Romania

16.50 Free triiodothyronine as determinant of non-alcoholic fatty liver disease in euthyroid subjects: the LifeLines Cohort Study (p.80)

E.H. van den Berg[1], L.J.N. van Tienhoven-Wind[2], M. Amini[3], B.Z. Alizadeh[1,3], T.C.M.A. Schreuder[1], K.N. Faber[1], H. Blokzijl[1], R.P.F. Dullaart[2], [1]Dept of Gastroenterology and Hepatology, University of Groningen and University Medical Center Groningen, Groningen, [2]Dept of Internal Medicine (Endocrinology), University of Groningen and University Medical Center Groningen, Groningen, [3]Dept of Epidemiology, University of Groningen and University Medical Center Groningen, Groningen, The Netherlands

17.00 Einde abstractsessie, vervolg plenair programma in de Brabantzaal.

Vrije voordrachten Nederlandse Vereniging Gastrointestinale Chirurgie Parkzaal

Voorzitters: n.t.b.

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

10.00 Is nighttime really not the right time for a laparoscopic cholecystectomy? (p.81)

M.C. de Jong, J.W. Greve, M.N. Sosef, Dept of Surgery, Zuyderland Medical Center, Heerlen, The Netherlands

10.10 Conditional Survival After Surgical Resection of Gallbladder Carcinoma: A Multi- Institutional Analysis (p.82)

S. Buettner[1,11], G.A.M[1], Y. Kim[1], C.G. Ethun[2], S.K. Maithel[2], G. Poultsides[3], T. Tran[3], K. Idrees[4], C.A. Isom[4], R.C. Fields[5], B. Krasnick[5], S.M. Weber[6], A. Salem[6], R.C.G. Martin[7], C. Scoggins[7], P. Shen[8], H.D. Mogal[8], C. Schmidt[9], E. Beal[9], I. Hatzaras[10], R. Shenoy[10], T.M. Pawlik[1], [1]Division of Surgical Oncology, Dept of Surgery, The Johns Hopkins Hospital, Baltimore, MD, [2]Division of Surgical Oncology, Dept of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA, [3]Dept of Surgery, Stanford University Medical Center, Stanford, CA, [4]Division of Surgical Oncology, Dept of Surgery, Vanderbilt University Medical Center, Nashville, TN, [5]Dept of Surgery, Washington University School of Medicine, St Louis, MO, [6]Dept of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI, [7]Division of Surgical Oncology, Dept of Surgery, University of Louisville, Louisville, KY, [8]Dept of Surgery, Wake Forest University, Winston-Salem, NC, [9]Division of Surgical Oncology, The Ohio State University Comprehensive Cancer Center, Columbus, OH, [10]Dept of Surgery, New York University, New York, NY, USA, [11]Erasmus Medical Centre, Rotterdam, The Netherlands

10.20 A Comparison of Prognostic Schemes for Perihilar Cholangiocarcinoma (p.83)

S. Buettner[1,2], J.L.A. van Vugt[2], F. Gani[1], B. Groot Koerkamp[2], G.A. Margonis[1], C.G. Ethun[3], G. Poultsides[4], T. Tran[4], K. Idrees[5], C.A. Isom[5], R.C. Fields[6], B. Krasnick[6], S.M. Weber[7], A. Salem[7], R.C.G. Martin[8], C. Scoggins[8], P. Shen[9], H.D. Mogal[9], C. Schmidt[10], E. Beal[10], I. Hatzaras[11], R. Shenoy[11], S.K. Maithel[3], A. Guglielmi[12], J.N.M. IJzermans[2], T.M. Pawlik[1], [1]Dept of Surgery, Johns Hopkins Hospital, Baltimore, MD, USA, [2]Dept of Surgery, Erasmus Medical Centre, Rotterdam, The Netherlands, [3]Dept of Surgery, Emory University School of Medicine, Atlanta, GA, [4]Dept of Surgery, Stanford University Medical Center, Stanford, CA, [5]Dept of Surgery, Vanderbilt University Medical Center, Nashville, TN, [6]Dept of Surgery, Washington University School of Medicine, St Louis, MO, [7]Dept of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI, [8]Dept of Surgery, University of Louisville, Louisville, KY, [9]Dept of Surgery, Wake Forest University, Winston-Salem, NC, [10]Dept of Surgery, Ohio State University, Columbus, OH, [11]Dept of Surgery, New York University, New York, NY, USA, [12]Dept of Surgery, Verona University Medical Centre, Verona, Italy

10.30 Stereotactic body radiation therapy for colorectal liver metastases: is it equal to hepatic resection? A matched case-control study (p. 84)

R Poelstra[1], K. Muller[2], C.F.M. Klok[3], M.S.L. Liem[1], [1]Dept of Surgery, Division of gastro- intestinal Surgery and Surgical Oncology, Deventer Hospital, [2]Institute of Radiation Oncology, RISO, Deventer, [3]Dept of Radiology, Deventer Hospital, The Netherlands

10.40 RFA in locally advanced pancreatic cancer: CT-Findings 1 week after RFA and at follow-up (p. 85)

S.J.E. Rombouts[1], T.C. Derksen[1], I.Q. Molenaar[1], C.Y. Nio[2], M.S. van Leeuwen[3], [1]Dept of Surgery, University Medical Center Utrecht, [2]Dept of Radiology, Academic Medical Center Amsterdam, [3]Dept of Radiology, University Medical Center Utrecht, The Netherlands

10.50 Long-term quality of life after pancreatic surgery: do complications affect QoL? (p.86)

L. van Berkel[1], H.D. Heerkens[2], M. van Vulpen2, D.S.J. Tseng[3], H.C. van Santvoort[4], J. Hagendoorn[4], I.H.M. Borel Rinkes[4], I.M. Lips[5], I.Q. Molenaar[4], [1]Medical student participating in the Honours program of the Faculty of Medicine, University Medical Center Utrecht, Utrecht, [2]Dept of Radiation Oncology, University Medical Center Utrecht, Utrecht, [3]Dept of Radiation Oncology, Erasmus University Medical Center, Rotterdam, [4]Dept of Surgery, University Medical Center Utrecht, Utrecht, [5]Dept of Radiation Oncology, University Medical Center Utrecht, Utrecht, Dept of Radiation Oncology, Leiden University Medical Center, Leiden, The Netherlands

11.00 Worldwide survey on current use, value and safe implementation of minimally invasive pancreatic resection (p.87)

J van Hilst[1], T. de Rooij[1], M. Abu Hilal[2], H.J. Asbun[3], J. Barkun[4], U. Boggi[5], O.R. Busch[1], K.C. Conlon[6], M.G. Dijkgraaf[7], H. Han[8], P.D. Hansen[9], M.L. Kendrick[10], A.L. Montagnini[11], C. Palanivelu[12], B.I. Rosok[13], S.V. Shrikhande[14], G. Wakabayashi[15], H.J. Zeh[16], C.M. Vollmer[17], D.A. Kooby[18], M.G. Besselink[1] for the 2016 IHPBA state of the art conference on Minimally Invasive Pancreatic Resection, [1]Dept of surgery, Academic Medical Center, Amsterdam, The Netherlands, [2]Dept of surgery, Southampton University Hospital, Southampton, UK, [3]Dept of surgery, Mayo Clinic, Jacksonville, Florida, USA, [4]Dept of surgery, McGill University Health Center, Montreal, Canada, [5]Dept of surgery, University of Pisa, Pisa, Italy, [6]Dept of surgery, Trinity College Dublin, Dublin, Ireland, [7]Clinical research unit, Academic Medical Center, Amsterdam, The Netherlands, [8]Dept of surgery, Seoul National University Bundang Hospital, SeongNam si, Korea, [9]Dept of surgery, Portland Cancer Center, Orlando, USA, [10]Dept of surgery, Dept of Surgery, Mayo Clinic, Rochester, Minnesota, USA, [11]Dept of surgery, Hospital das clínicas, Sao Paulo, Brazil, [12]Dept of surgery, GEM Hospital & Research Center, Coimbatore, Tamil Nadu, India, [13]Dept of surgery, Oslo University Hospital, Oslo, Norway, [14]Dept of surgery, Tata Memorial Center, Parel, Mumbai, India, [15]Dept of surgery, Ageo Central General Hospital, Ageo city, Japan, [16]Dept of surgery, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA, [17]Dept of surgery, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA, [18]Dept of surgery, Emory University School of Medicine, Atlanta, Georgia, USA

11.10 Impact of a nationwide training program in minimally invasive distal pancreatectomy (LAELAPS) (p.88)

T. de Rooij[1], J. van Hilst[1], D. Boerma[2], P. van den Boezem[3], B. Bonsing[4], K. Bosscha[5], P-P. Coene[6], F. Daams[7], R. van Dam[8], C. Dejong[8], M. Dijkgraaf[9], C. van Eijck[10], J. Erdmann[11], S. Festen[12], M. Gerhards[12], B. Groot Koerkamp[10], E. van der Harst[6], I. de Hingh[13], G. Kazemier[7], J. Klaase[14], R. de Kleine[11], K. van Laarhoven[3], D. Lips[5], M. Luyer[13], Q. Molenaar[15], V. Nieuwenhuijs[16], G. Patijn[16], D. Roos[17], H. van Santvoort[2], J. Scheepers[17], G. van der Schelling[18], P. Steenvoorde[14], L. Welling[4], J. Wijsman[18], O. Busch[1], D. Gouma[1], M. Abu Hilal[19], M. Besselink[1], for the Dutch Pancreatic Cancer Group, [1]Dept of Surgery, Academic Medical Center, Amsterdam, [2]Dept of Surgery, St. Antonius Hospital, Nieuwegein, [3]Dept of surgery, Radboud University Medical Centre, Nijmegen, [4]Dept of surgery, Leiden University Medical Center, Leiden, [5]Dept of surgery, Jeroen Bosch Hospital, Den Bosch, [6]Dept of surgery, Maasstad Hospital, Rotterdam, [7]Dept of surgery, VU University Medical Center, Amsterdam, [8]Dept of surgery, Maastricht University Medical Center, Maastricht, [9]Clinical research unit, Academic Medical Center, Amsterdam, [10]Dept of surgery, Erasmus Medical Center, Rotterdam, [11]Dept of surgery, University Medical Center Groningen, Groningen, [12]Dept of surgery, Onze Lieve Vrouwe Gasthuis, Amsterdam, [13]Dept of surgery, Catharina Hospital, Eindhoven, [14]Dept of surgery, Medisch Spectrum Twente, Enschede, [15]Dept of surgery, University Medical Center Utrecht, Utrecht, [16]Dept of surgery, Isala Clincs, Zwolle,[17]Dept of surgery, Reinier de Graaf Gasthuis, Delft, [18]Dept of surgery, Amphia Hospital, Breda, The Netherlands, [19]Dept of surgery, Southampton University Hospital NHS Foundation Trust, Southampton, United Kingdom

11.20 Usefulness and reliability of upper gastro intestinal contrast studies in assessment of pouch size in patients with weight loss failure after Roux-en-Y gastric bypass (p.89)

M. Uittenbogaart[1], A.N. van der Linden[2], P. Smeele[1], A. Luijten[1], W. Leclercq[1], F. van Dielen[1], [1]Obesitas Centrum Máxima, Máxima Medisch Centrum, Eindhoven/Veldhoven and [2]Afdeling Radiologie, Máxima Medisch Centrum, Eindhoven/Veldhoven, The Netherlands

11.30 Einde programma
U kunt zich voor de NVGE ledenvergadering begeven naar de Brabantzaal

12.00 Lunch in expositiehal

Vrije voordrachten Ned. Vereniging voor Gastrointestinale Chirurgie — Parkzaal

Voorzitters: n.t.b.

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

13.00 Perineal wound complications after abdominoperineal resection for rectal cancer (p.90)
M.M. Deken, R.J.I. Bosker, M.S.L. Liem, Dept of Surgery, division of gastro-intestinal surgery and surgical oncology, Deventer Hospital, The Netherlands

13.10 Limited endoscopic assisted wedge resection for excision of colon polyps (p.91)
L.W. Leicher[1], W.H. de Vos tot Nederveen Cappel[1], H.L. van Westreenen[2], [1]Dept of Gastroenterology and Hepatology and [2]Dept of Surgery, Isala clinics, Zwolle, The Netherlands

13.20 The effect of preoperative optimization of nutritional status in patients with significant bowel obstruction (p.92)
N.L. de Boer, C.S. van Kessel, A.B. Smits, St Antonius Hospital, Nieuwegein, The Netherlands

13.30 Double-Blind Randomized Clinical Trial of Laparoscopic Toupet *versus* 180° Anterior Fundoplication for Gastroesophageal Reflux Disease (p.93)
J.E. Oor ,D.J. Roks[1], J.H. Koetje[2], J.A. Broeders[1], V.B. Nieuwenhuijs[2], E.J. Hazebroek[1], [1]St. Antonius Hospital Nieuwegein and [2]Isala, Zwolle, The Netherlands

13.40 Outcome of laparoscopic hiatal hernia repair: why use mesh? (p.94)
J.H. Koetje[1], J. Oor[2], L. De Wijkerslooth[3], E. Hazebroek[2], H.L. van Westreenen[1], V.B. Nieuwenhuijs[1], [1]Isala Zwolle, Chirurgie, [2]St. Antonius Nieuwegein, Chirurgie, [3]Isala Zwolle, MDL, The Netherlands

13.50 Diaphragmatic hernia following esophagectomy for cancer (p.95)
H.J.F. Brenkman[1], K. Parry[1,2], F. Noble[2], R. van Hillegersberg[1], D. Sharland[2], J. Kelly[2], J.P. Byrne[2], T.J. Underwood[2], J.P. Ruurda[1], [1]Dept of Surgery, University Medical Center Utrecht, Utrecht, The Netherlands and [2]Dept of Surgery, University Hospital Southampton, Southampton, United Kingdom

14.00 Costs of complications after esophagectomy for cancer (p.96)
L. Goense[1,2], J.P. Ruurda[1], W.A. van Dijk[3,4], R. van Hillegersberg[1], [1]Dept of Surgery, University Medical Center Utrecht, [2]Dept of Radiotherapy, University Medical Center Utrecht, [3]Performation, Bilthoven, [4]X-is, Delft, The Netherlands

14.10 Quality of life after neoadjuvant chemoradiation followed by surgery compared to surgery alone (p.97+98)

B.J. Noordman[1], M.G.E. Verdam[2], S.M. Lagarde[1], B.P.L. Wijnhoven[1], C.C.M. Hulshof[3], M.I. van Berge Henegouwen[4], A. van der Gaast[5], M.A.G. Sprangers[2], J.J.B. van Lanschot[1], for the CROSS study group, [1]Dept of Surgery, Erasmus MC – University Medical Center Rotterdam, Rotterdam, [2]Dept of Medical Psychology, Academic Medical Center, Amsterdam, [3]Dept of Radiation Oncology, Academic Medical Center, Amsterdam, [4]Dept of Surgery, Academic Medical Center, Amsterdam, [5]Dept of Medical Oncology, Erasmus MC – University Medical Center Rotterdam, Rotterdam, The Netherlands

14.20 Effects of different levels of vagotomy and nicotinic receptor agonists on the development of LPS induced lung injury in rats (p.99)

M.F.J. Seesing[1], T.J. Weijs[1], M.D.P. Luyer[2], J.P. Ruurda[1], G.A.P. Nieuwenhuijzen[2], R.L.A.W. Bleys[3], G. Folkerts[4], J. Garssen[4,5], v. Hillegersberg[1], [1]Dept of Surgical Oncology, UMC Utrecht, [2]Dept of Surgical Oncology, Catharina Hospital Eindhoven, [3]Dept of Anatomy, UMC Utrecht, [4]Faculty of Science, Dept of Pharmaceutical Sciences, Division of Pharmacology, Utrecht University, [5]Nutricia Research, Immunology, Utrecht, The Netherlands

14.30 The early introduction of minimally invasive gastrectomy in the Netherlands: short- term oncological outcomes comparable to open gastrectomy (p.100)

H.J.F. Brenkman[1], J.P. Ruurda[1], R.H.A. Verhoeven[2], R. van Hillegersberg[1], [1]Dept of Surgery, University Medical Center, Utrecht, [2]Netherlands Cancer Registry, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, The Netherlands*

14.40 Laparoscopic and open surgery for gastric cancer from a business intelligence viewpoint (p.101)

J.J.W. Tegels[1], F.E.N.M. Spauwen[1], S. Soudant[2], A.G.M. Hoofwijk[1], K.W.E. Hulsewé[1], J.H.M.B. Stoot[1], [1]Dept of Surgery, Zuyderland Medical Centre, Sittard and [2]Division of Industrial Engineering & Management, Hogeschool Zuyd, Heerlen, The Netherlands

14.50 Quality control of surgicopathological compliance in the CRITICS gastric cancer trial (p.102)

Y.H.M. Claassen[1], W.O. de Steur[1], H.H. Hartgrink[1], J.W. van Sandick[5], J.L. Dikken[1], E. Meershoek-Klein Kranenbarg[1], J.P.B.M. Braak[1], M. Duijm-de Carpentier[1], E.P.M. Jansen[2], N.C.T. van Grieken[3], H. Putter[4], A.K. Trip[2], H. Boot[6], A. Cats[6], K. Sikorska[7], H. van Tinteren[7], M. Verheij[2], C.J.H. Van de Velde[1], [1]Dept of Surgical Oncology, Leiden University Medical Center, [2]Dept of Radiation Oncology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, [3]Dept of Pathology, VU University Medical Center, Amsterdam, [4]Dept of Medical Statistics, Leiden University Medical Center, [5]Dept of Surgical Oncology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, [6]Dept of Gastroenterology and Hepatology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, [7]Dept of Biometrics, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

15.00 Theepauze in de expositiehal

Vrije voordrachten Ned. Vereniging voor Gastroenterologie **Parkzaal**

Voorzitters: J.C. Escher en S. van der Marel

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

15.30 **MLDS voordracht**
Endoscopic or surgical step-up approach for necrotizing pancreatitis, a multi-center randomized controlled trial (p.103)
S. van Brunschot on behalf of the Dutch Pancreatitis Study Group

15.40 **MLDS voordracht**
Next generation whole exome sequencing to discover genetic aberrations associated with poor outcome in untreated lymph node negative colon cancer (p.104)
R.R.J. Coebergh v.d. Braak[1], A.M. Sieuwerts[2,4], Z.S. Lalmahomed[1], M. Smid[2], V. de Weerd[2], A. van Galen[2], K. Biermann[3], J.A. Foekens[2], J.W.M. Martens[2,4], J.N.M. IJzermans[1], Dept of Surgery, Erasmus MC, Rotterdam, [2]Dept Medical Oncology, Erasmus MC Kankerinstituut, Rotterdam, [3]Dept Pathology, Erasmus MC, Rotterdam, [4]Cancer Genomics Center Nederland, Amsterdam, The Netherlands

15.50 Long term management and outcome of patients with hepatocellular adenoma presenting with massive bleeding (p.105)
A.J. Klompenhouwer[1], R.A. de Man[2], J.N.M. IJzermans[1], Depts of [1]Surgery and [2]Hepatology, Erasmus Medical Centre, Rotterdam, The Netherlands

16.00 ADHD and functional defecation disorders problems in childhood (p.106)
M.H. Vriesman[1], S. Kuizenga-Wessel[2], I.J.N. Koppen[2], M. van Dijk[3], M.L.R. Beelen[4], M. Groeneweg[4], R. Stoffelsen[5], M.A. Benninga[2], [1]University of Amsterdam, Academic Medical Center, Amsterdam, [2]Dept of pediatric Gastroenterology and Nutrition, Emma Children's Hospital, Academic Medical Center, Amsterdam, [3]Psychosocial Dept, Emma Children's Hospital, Academic Medical Center, Amsterdam, [4] Dept of Pediatrics, Maasstad Hospital, Rotterdam, [5]De Bascule, Academic Center for Child and Adolescent Psychiatry, Amsterdam, The Netherlands

16.10 The difference in endoscopic diagnostic yield in patients with either iron-deficiency anemia or anemia with normal ferritin (p.107)
J.A. Kwakman, E. Cleeren, C.J. van Oostveen, K. van Stralen, R.W.M. van der Hulst, Spaarne Gasthuis Haarlem, The Netherlands

16.20 Valvular heart disease, localization and number of angiodysplasias are predictors for symptomatic angiodysplasia bleeding (p.108)
K.V. Grooteman, M.C.P. van den Bemt, S. Dalloyaux, E.J.M. van Geenen, J.P.H. Drenth, Dept Radboudumc, Nijmegen, The Netherlands

16.30 Epidemiology of abdominal pain-related functional gastrointestinal disorders and the influence of biopsychosocial factors among adolescents in Curaçao (p.109)

J. Zeevenhooven[*1], *S. van der Heijden*[*1], *I. Gerstenbluth*[2], *N.M. Devanarayana*[3], *S. Rajindrajith*[3], *M.A. Benninga*[1] *Both authors contributed equally, [1]Dept of Pediatric Gastroenterology and Nutrition, Academic Medical Center, Amsterdam, The Netherlands, [2]Epidemiology & Research Unit, Ministry of Health, Environment & Nature of Curacao, [3]Dept of Physiology, Faculty of Medicine, University of Kelaniya, Sri Lanka*

16.40 Objectively diagnosing rumination syndrome in children using ambulatory 24 hour esophageal pH-impedance and manometry (p.110)

M.M.J. Singendonk[1], *J.M. Oors*[2], *A.J. Bredenoord*[2], *T.I. Omari*[3-5], *R.J. van der Pol*[1], *M.J. Smits*[1], *M.A. Benninga*[1], *M.P. van Wijk*[1,6], *[1]Dept of Pediatric Gastroenterology and Nutrition, Emma Children's Hospital AMC, Amsterdam, The Netherlands, [2]Dept of Gastroenterology and Hepatology, Academic Medical Center Amsterdam, Amsterdam, The Netherlands [3]Gastroenterology Unit, Women's and Children's Health Network, North Adelaide, SA, Australia [4]Translational Research Center for Gastrointestinal Diseases, University of Leuven, Leuven, Belgium 5School of Medicine, Flinders University, Bedford Park, SA, Australia 6Dept of Pediatric Gastroenterology, VU University Medical Center, Amsterdam, The Netherlands*

16.50 Excessive crying during infancy predisposes to behavioral problems in early childhood (p.111)

J. Zeevenhooven[1], *N. van Maasakker*[1], *F.E. de Bruin*[2], *A.M. Vlieger*[3], *M.A. Benninga*[1], *M.P. L'Hoir*[4], *B.E. van Sleuwen*[4], *[1]Dept of Pediatric Gastroenterology, Emma Children's Hospital/Academic Medical Center, Amsterdam, [2]Utrecht University, Faculty of Social and Behavioral Sciences, Utrecht, [3]Dept of Pediatrics, St. Antonius Hospital, Nieuwegein, [4]TNO Child Health, Leiden, The Netherlands*

17.00 Einde programma

Voor het plenaire programma kunt u zich begeven naar de Brabantzaal.

Meet the Expert Sessie **Zaal 81**

Leverenzym-afwijkingen

U.H.W. Beuers / R.J. de Knegt

groep 1: 15.30 – 16.15 uur
groep 2: 16.15 – 17.00 uur

** vanwege de grote belangstelling is deze sessie alleen toegankelijk voor deelnemers die zich hiervoor tevoren hebben ingeschreven*

Meet the Expert Sessie **Zaal 82**

Poliepherkenning en poliepectomie

L.M.G. Moons / S. Sanduleanu

groep 1: 15.30 – 16.15 uur
groep 2: 16.15 – 17.00 uur

** vanwege de grote belangstelling is deze sessie alleen toegankelijk voor deelnemers die zich hiervoor tevoren hebben ingeschreven*

Seniorenprogramma **Zaal 65**

12.00 Ontvangst en lunch tot 13.00 in de Uithof Lounge (gele zone)

Voorzitters: J.F.W.M. Bartelsman en H.P.M. Festen

13.00 'Kan biologie berekend worden? Eine deutsche Geschichte'
Prof. dr. P.L.M. Jansen

13.30 De Uniba-connectie
Prof. dr. G.P. van Berge Henegouwen

14.00 Voor de scopiërende pensionado: update coloscopie en poliepectomie
Prof. dr. E. Dekker

14.30 Ervaringen met de Levenseindekliniek
Dr. H.P.M. Festen en Prof. dr. J.F.W.M. Bartelsman

15.00 Theepauze

15.30 Vervolgprogramma in diverse zalen.

18.30 Borrel en diner

Videosessie Sectie Gastrointestinale Endoscopie **Auditorium**

Voorzitters: T.E.H. Römkens en R.C. Verdonk

09.30 **Programma met zonderlinge video's van eigen bodem**

Een bleke maag.
R.J.M. Ader, A. Alkhalaf. Isala klinieken, Zwolle

Single port ileo-pouch anale anastomose (IPAA)
B. Grotenhuis, E.J.R. de Graaf, P. Doornebosch, IJsselland Ziekenhuis Capelle aan den IJssel

Ubi pus ibi evacua
J. van der Kraan, A. Inderson, J. Boonstra, LUMC, Leiden

"De hoofdletter K".
I. Brands, Isala klinieken, Zwolle

Premaligne complicatie na een Coffey-procedure met een renaal staartje
K. van der Linden, MC Leeuwarden

TAMIS van een rectum hemangioom
E.J.R. de Graaf, IJsselland Ziekenhuis, Capelle aan den IJssel

Strange findings in the sigmoid colon
M. Kramer, Radboudumc, Nijmegen

Pancreaticolithiasis: Casus Intraductale Lithotripsie
P.J.F. de Jonge, J.W. Poley, Erasmus MC, Rotterdam.

Behandeling van parasiet wel of niet
R.J.M. Ader, D.J. Buurman, W.H. de Vos tot Nederveen Cappel, Isala klinieken, Zwolle

10.15 Einde Videosessie

Mini Symposium Sectie Gastrointestinale Endoscopie **Auditorium**

Voorzitters: Y. Keulemans en T. Römkens

"Let's talk about sex"

10.20 Verschillen tussen man en vrouw bij bevolkingsonderzoek naar darmkanker.
Prof. dr. E. Dekker, MDL-arts, Academisch Medisch Centrum Amsterdam

10.40 Genderverschillen bij sedatie op de endoscopiekamer.
Dr. M. Klemt-Kropp, MDL-arts,

11.00 Koffiepauze expositiehal

Symposium rond Richtlijn HCC – benigne levertumoren **Auditorium**

Voorzitters: R.A. de Man en J.N.M. IJzermans

Symposium Benigne Levertumoren

11.30 De noodzaak voor een richtlijn goedaardige levertumoren
Prof. dr. J.N.M. IJzermans, Erasmus MC, Rotterdam

11.40 Cysteuze leverafwijkingen
Prof. dr. J.P.H. Drenth, Radboudumc, Nijmegen

11.55 FNH en Adenoom
Dr. M. Broker, Reinier de Graaf Gasthuis, Delft

12.15 Radiologie
Dr. M. Thomeer, afd. Radiologie, Erasmus MC, Rotterdam

12.30 Pathologie
Dr. J. Verheij, afd. Pathologie, AMC, Amsterdam

12.50 Vragen en discussie

13.00 Lunch expositiehal

Symposium CRC **Auditorium**

Voorzitters: M.E. van Leerdam en W.H. de Vos tot Nederveen Cappel

14.00 Inleiding: BVO in Nederland: voorlopige resultaten, wat kan er nog beter?
Dr. M.E. van Leerdam, MDL-arts,
NKI Antoni van Leeuwenhoekhuis, Amsterdam

14.15 Serrated poliepen: handleiding voor de dagelijkse praktijk
Prof. dr. E. Dekker, MDL-arts,
Academisch Medisch Centrum Amsterdam

14.35 Erfeljike en familiair CRC & BVO
Prof. dr. N. Hoogerbrugge, hoogleraar erfelijke kanker,
Radboudumc, Nijmegen

14.50 Moeilijke poliepectomie: waar ligt de grens en door wie?
Prof. dr. P. Fockens, MDL-arts,
Academisch Medisch Centrum Amsterdam

15.10 Uitkomst van chirurgie in het kader van BVO
Dr. K.C.M.J. Peeters, chirurg, Leids Universitair Medisch Centrum

15.30 Behandeling van CRC bij de oudere patiënt
Dr. J. Portielje, oncoloog, Hagaziekenhuis, Den Haag

15.50 Einde programma

Symposium Sectie Inflammatoire Darmziekten **Baroniezaal**

Voorzitters: N. de Boer en C.J. van der Woude

Inflammatoire darmziekten: behandelen als richtlijnen tekort schieten.
Programma naar aanleiding van twee meest gestelde vragen aan het IBD expertpanel Nederland

09.30 Opening en korte inleiding door de voorzitters:
Prof. dr. C.J. van der Woude (Erasmus MC) en Dr. N. de Boer (VUmc)

De "beste behandelstrategie" bij een abces in de ileocecaal hoek?

09.40 Overzicht literatuur en richtlijnen: Dr. N. de Boer.

09.50 Panel discussie naar aanleiding van casus uit het Erasmus MC.
Panel: Prof. dr. G. d'Haens (MDL-arts) en Prof. dr L.P.S. Stassen (chirurg)
Casuspresentatie door Dr. V. de Jonge.

10.10 Prof. dr. G. d'Haens: de strategie in Nederland

Dysplasie in een colonbiopt, wat moet je ermee?

10.20 Overzicht literatuur en richtlijnen: Dr. N. de Boer.

10.30 Panel discussie naar aanleiding van casus uit het Radboudumc.
Panel: Dr. B. Oldenburg (MDL-arts) en drs. H.S. Hofker (chirurg)
Casuspresentatie door drs. L. Derikx

10.45 Dr. B. Oldenburg: de strategie in Nederland

10.55 Afsluiting symposium door voorzitter

11.00 Koffiepauze expositiehal

Vrije voordrachten Sectie Inflammatoire Darmziekten **Baroniezaal**

Voorzitters: D. van Leemreis en M. Pierik

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

11.30 The economic impact of the introduction of biosimilars in inflammatory bowel disease (p.112)

M. Severs[1], B. Oldenburg[1], A.A. van Bodegraven[2,3], P.D. Siersema[1,4], M-J.J. Mangen[5,6], on behalf of the initiative of Crohn's and Colitis, [1]Dept of Gastroenterology and Hepatology, University Medical Centre Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, VU University Medical Centre, Amsterdam, [3]Dept of Gastroenterology and Hepatology (Co-MIK), Zuyderland Medical Centre, Heerlen, Sittard, Geleen, [4]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, [5]Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, [6]Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands

11.40 Pharmacokinetics of golimumab in patients with moderate to severe ulcerative colitis (p.113)

S.E. Berends[1], A.S. Strik[2], P.S. van Egmond[1], J.F. Brandse[2], R.A.A. Mathôt[1], G.R. D'Haens[2], M. Löwenberg[2], [1]Dept Hospital Pharmacy, Academic Medical Center Amsterdam and [2]Dept of Gastroenterology, Academic Medical Center Amsterdam, The Netherlands

11.50 Disappearance of anti-drug antibodies to infliximab and adalimumab after addition of an immunomodulator in patients with inflammatory bowel disease (p.114)

A.S. Strik[1], G.R. van den Brink[1], C.I.J. Ponsioen[1], R.A.A. Mathot[2], M. Löwenberg[1], G.R. D'Haens[1], [1]Dept of Gastroenterology, Academic Medical Centre Amsterdam and [2]Dept Hospital Pharmacy, Academic Medical Centre Amsterdam, The Netherlands

12.00 Infliximab trough levels in inflammatory bowel disease patients: results of a prospective observational study from a Dutch peripheral hospital (p.115)

J. Strebus[1], R. Theeuwen[2], P.D. Knoester[3], M.K. Vu[2], [1]Dept of Gastroenterology & Hepatology, Noordwest Ziekenhuisgroep, Alkmaar, [2]Dept of Gastroenterology & Hepatology, Alrijne Ziekenhuisgroep, Leiderdorp, [3]Dept of Pharmacology, Alrijne Ziekenhuisgroep, Leiderdorp, The Netherlands

12.10 Anti-tumor necrosis factor alpha therapy is associated with modulation of extracellular matrix in Crohn's disease (p.``6)

J.R. de Bruyn[1,2], M.A. Becker[2], J. Steenkamer[2], M.E. Wildenberg[1,2], S.L. Meijer[3], C.J. Buskens[4], W.A. Bemelman[4], C.Y. Ponsioen[1], G.R. van den Brink[1,2], G.R. D'Haens[1], [1]Dept of Gastroenterology, [2]Tytgat Institute for Liver and Intestinal Research, [3]Dept of Pathology, [4]Dept of Surgery, Academic Medical Centre Amsterdam, The Netherlands

12.20 Tertiary lymphoid organ formation in gut mucosa of newly diagnosed, untreated Inflammatory Bowel Disease patients (p.117)

C.S. Horjus Talabur Horje[1], C. Smids[1*], J.W.R. Meijer[2], M.J. Groenen[1], M.K. Rijnders[2], E.G. van Lochem[3], P.J. Wahab[1] *Both authors contributed equally to this work, [1]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [2]Dept of Pathology, Rijnstate Hospital, Arnhem, [3]Dept of Microbiology and Immunology, Rijnstate Hospital, Arnhem, The Netherlands*

12.30 Pooled resequencing of 122 ulcerative colitis genes in a large Dutch cohort suggests population-specific associations of rare variants in MUC2 (p.118)

M.C. Visschedijk[1,2], R. Alberts[1], S. Mucha[3], P. Deelen[2], D.J. de Jong[4^], M. Pierik[5^], L.M. Spekhorst[1], F. Imhann[1], A.E. van der Meulen-de Jong[6^], C.J. van der Woude[7^], A.A. van Bodegraven[8^], B. Oldenburg[9^], M. Löwenberg[10^], G. Dijkstra[1^], D. Ellinghaus[3], S. Schreiber[11], C. Wijmenga[2], The Initiative on Crohn and Colitis, Parelsnoer Institute, M.A. Rivas[12], A. Franke[3], C.C. van Diemen[2&], R.K. Weersma[1&^], [1]Dept of Gastroenterology and Hepatology, University of Groningen, University Medical Centre Groningen, Groningen, [2]Dept of Genetics, University of Groningen, University Medical Centre Groningen, Groningen, The Netherlands, [3]Institute of Clinical Molecular Biology, Kiel University, Kiel, Germany, [4]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, [5]Division of Gastroenterology and Hepatology, Maastricht University Medical Centre, Maastricht, [6]Dept of Gastroenterology and Hepatology, Leiden University Medical Centre, Leiden, [7]Dept of Gastroenterology and Hepatology, Erasmus University Medical Centre, Rotterdam, [8]Dept of Gastroenterology and Hepatology, VU University Medical Centre, Amsterdam, [9]Dept of Gastroenterology and Hepatology, University Medical Centre Utrecht, Utrecht, [10]Dept of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands, [11]Dept of Internal Medicine I, University Medical Centre Schleswig-Holstein, Kiel, Kiel, Germany, [12]Centre for the Study of IBD (SCIBD) Genetics, The Broad Institute, Cambridge, Massachusetts, USA ^ On behalf of the Dutch Initiative on Crohn and Colitis (ICC) and the Dutch IBD Biobank of the Parelsnoer Institute & These authors contributed equally to this work*

12.40 Complications and disease recurrence after primary ileocecal resection in pediatric Crohn's disease: a multicenter cohort analysis (p.119)

K Diederen[1], L. de Ridder[2], P. van Rheenen[3], V.M. Wolters[4], M.L. Mearin[5], G.M. Damen[6], T.G. de Meij[7], H. van Wering[8], L.A. Tseng[1], M.W. Oomen[9], J.R. de Jong[9], M.A. Benninga[1], A. Kindermann[1], [1]Dept of Pediatric Gastroenterology and Nutrition, Academic Medical Center, Amsterdam, [2]Dept of Pediatric Gastroenterology, Erasmus MC-Sophia Children's Hospital, Rotterdam, [3]Dept of Pediatric Gastroenterology, University Medical Center Groningen, Groningen, [4]Dept of Pediatric Gastroenterology, University Medical Center Utrecht, Utrecht, [5]Dept of Pediatrics, Leids Universitair Medisch Centrum, Leiden, [6]Dept of Pediatric Gastroenterology, Radboud University Medical Center, Nijmegen, [7]Dept of Pediatric Gastroenterology, VU University Medical Center, Amsterdam, [8]Dept of Pediatrics, Amphia Hospital, Breda, [9]Dept of Pediatric Surgery, Academic Medical Center, Amsterdam, The Netherlands

12.50 Colorectal cancer risk in a nationwide inflammatory bowel disease cohort with low grade dysplasia (p.120)

L.A.A.P. Derikx[1,2], S.B. van Tilburg[1,2], I.D. Nagtegaal[3], L.H.C. Nissen[2], F. Hoentjen[1], [1]Inflammatory Bowel Disease Center, Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, [2]Dept of Gastroenterology and Hepatology, Jeroen Bosch hospital, 's-Hertogenbosch, [3]Dept of Pathology, Radboud University Medical Center, Nijmegen, The Netherlands

13.00 Korte ledenvergadering en aansluitend lunch in expositiehal

Vrije voordrachten NVGE / IBD **Baroniezaal**

Voorzitters: I.A.M. Gisbertz en M.W. Mundt

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

14.00 Co-occurrence of psoriasis and Inflammatory Bowel Disease is associated with mild psoriasis, but severe early-onset Crohn's Disease phenotype (p.121)

H Eppinga[1,2], S. Poortinga[3], H.B. Thio[1], T.E.C. Nijsten[1], V.J.A.A. Nuij[2], C.J. van der Woude[2], R.M. Vodegel[3], G. Fuhler[2], M.P. Peppelenbosch[2], [1]Dept of Dermatology, Erasmus MC-University Medical Center Rotterdam, Rotterdam, [2]Dept of Gastroenterology and Hepatology, Erasmus MC-University Medical Center Rotterdam, Rotterdam, [3]Dept of Dermatology, Medical Centre Leeuwarden (MCL), Leeuwarden, The Netherlands

14.10 Safety of anti-TNF treatment in liver transplant recipients - a meta-analysis (p.122)

M.J.A. Westerouen van Meeteren, A. Inderson[1], A.E. van der Meulen[1], R. Altwegg R[2], B. van Hoek[1], G.P. Pageaux[2], T. Stijnen[3], D. Stein[4], P.W. Maljaars[1], [1]Leiden University Medical Centre, Dept of Gastroenterology-Hepatology, Leiden, The Netherlands, [2]University Hospital of St Eloi, Dept of Hepatology and Gastroenterology, Montpellier, France, [3]Leiden University Medical Centre, Dept of Medical statistics, Leiden, The Netherlands, [4]Froedtert Hospital & The Medical College of Wisconsin, Dept of Gastroenterology and Hepatology, Wisconsin, USA

14.20 Simple urine test to evaluate adherence to oral 5-ASA in teenagers with ulcerative colitis (p.123)

A. Dijkstra, D.J. Touw, P.F. van Rheenen, Universtair Medisch Centrum Groningen, Groningen, The Netherlands

14.30 Correlation between symptoms, endoscopic severity and treatment response in immunotherapy induced colitis (p.124)

J. van Dieren , E. Rozeman[2], S. van Wilpe[1], M. Geukes Foppen[2], C. Postma[1], C. Blank[2], J. van Thienen[2], M. van Leerdam[1], M. van den Heuvel[3], J. Haanen[2], J. van Dieren[1], [1]Dept of Gastroenterology and Hepatology, Netherlands Cancer Institute, Amsterdam, [2]Dept of Medical Oncology, Netherlands Cancer Institute, Amsterdam, [3]Dept of Thoracic Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands

14.40 A prospective, quantitative assessment of pain and quality of life before and 3 and 12 months after vascular treatment for chronic mesenteric ischemia (p.125)

L.F. Wymenga[1], L. Everlo[1], P.B. Mensink[1], M. Brusse-Keizer[2], R.H. Geelkerken[3,4], J.J. Kolkman[1,5], [1]Dept of Gastroenterology, Medical Spectrum Twente, Enschede, [2]Medical School Twente, Medical Spectrum Twente, Enschede, [3]Dept of Vascular Surgery, Medical Spectrum Twente, Enschede, [4]Faculty of Science and Technology, University of Twente, Enschede, [5]Dept of Gastroenterology, University Medical Centre Groningen, Groningen, The Netherlands

14.50 The incidence and prevalence of chronic mesenteric ischemia (p.126)

R.R. Beumer[1], J.J. Kolkman[2], M.G.J. Brusse-Keizer[3], [1]University of Groningen, Groningen [2]Gastroenterologist Medical Spectrum Twente, Enschede, [3]Clinical Epidemiologist Medical Spectrum Twente, Enschede, The Netherlands

15.00 The low FODMAP diet: one year follow up (p.127)

L.A. van der Waaij[1], M. Wassink[1], E. Kroon[2], J. Stevens[2], [1]MDL, Martini Ziekenhuis, Groningen and [2]Dietetiek, Martini Ziekenhuis, Groningen, The Netherlands

15.10 REDUCE IBS pilot project: shared decision-making provides IBS patients the power to choose the treatment that fits them best (p.128)

J.W. Kruimel[1], Y. Holierhoek[2], L. Stellingwerff Beintema[3], M. Welters[4], M. Otten[5], [1]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [2]Dept of Gastroenterology, Meander Medical Center, Amersfoort, [3]PDSB Patient Association, [4]Blauw Research Rotterdam, [5]Dept of Gastroenterology, Medical Center de Veluwe, Apeldoorn, The Netherlands

15.20 Diagnostic accuracy of the fecal Pancreas Elastase 1 Quick™ Test for exocrine pancreatic insufficiency (p.129)

S.A.M. Hoogenboom[1], S.J. Lekkerkerker[1], F.H.M. de Koning[1], O.R.C. Busch[2], M.A. Boermeester[2], P. Fockens[1], M.G. Besselink[2], J.E. van Hooft[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center Amsterdam, Amsterdam and [2]Dept of Gastrointestinal Surgery, Academic Medical Center Amsterdam, Amsterdam, The Netherlands

15.30 Einde programma

Vrije voordrachten Sectie Gastrointestinale Oncologie — Parkzaal

Voorzitters: N. van Lelyveld en V.M.C.W. Spaander

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

09.30 Lymph node yield is associated with recurrence after surgical resection of T1 colorectal cancer underlining the importance of an oncologic approach even in this early stage (p.130)

B.S. Bhoelan[1], Y. Backes[1], M.P. Schwartz[2], F.H.J. Wolfhagen[3], B.W.M. Spanier[4], T.C.J. Seerden[5], W.H. de Vos tot Nederveen Cappel[6], J.M.J. Geesing[7], K. Kessels[8], J. van Bergeijk[9], M. Kerkhof[10], J.N. Groen[11], F. ter Borg[12], N. van Lelyveld[13], G.J.A. Offerhaus[14], P.D. Siersema[1], M.M. Lacle[14], L.M.G. Moons[1] (on behalf of the Dutch T1 CRC Working Group), [1]Dept of Gastroenterology & Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology & Hepatology, Meander Medical Center, Amersfoort, [3]Dept of Gastroenterology & Hepatology, Albert Schweitzer, Dordrecht, [4]Dept of Gastroenterology & Hepatology, Rijnstate, Arnhem, [5]Dept of Gastroenterology & Hepatology, Amphia Hospital, Breda, [6]Dept of Gastroenterology & Hepatology, Isala, Zwolle, [7]Dept of Gastroenterology & Hepatology, Diakonessenhuis, Utrecht, [8]Dept of Gastroenterology & Hepatology, Flevo Hospital, Almere, [9]Dept of Gastroenterology & Hepatology, Gelderse Vallei, Ede, [10]Dept of Gastroenterology & Hepatology, Groene Hart Hospital, Gouda, [11]Dept of Gastroenterology & Hepatology, Sint Jansdal, Harderwijk, [12]Dept of Gastroenterology & Hepatology, Deventer Hospital, Deventer, [13]Dept of Gastroenterology & Hepatology, Antonius Hospital, Nieuwegein, [14]Dept of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands

09.40 Quality of life in rectal cancer patients: watch-and-wait policy versus standard treatment - a matched controlled study (p.131)

B.J.P. Hupkens[1,2], M.H. Martens[1-3], M. Maas[2,4], D.M.J. Lambregts[2,4], J. Melenhorst[1], H.J. Belgers[3], J.H. Stoot[3], R.G. Beets-Tan[4], G.L. Beets[5], S.O. Breukink[1], [1]Dept of Surgery, Maastricht University Medical Centre, Maastricht, [2]Dept of Radiology, Maastricht University Medical Centre, Maastricht, [3]Dept of Surgery, Zuyderland Medical Center, Heerlen-Sittard, [4]Dept of Radiology, Netherlands Cancer Institute, Amsterdam, [5]Dept of Surgery, Netherlands Cancer Institute, Amsterdam, The Netherlands

09.50 Clinical relevance of a grading system for anastomotic leakage following low anterior resection: results of the Dutch Surgical Colorectal Audit (DSCA) (p.132)

M.A. Frouws[*1], H.S. Snijders[1,2], S. Malm[3], C.J.H. van de Velde[1], P.A. Neijenhuis[3], H.M. Kroon[3,4], [1]Dept of Surgical Oncology, Leids University Medical Center, [2]Dutch Surgical Colorectal Audit, Leids University Medical Center, [3]Dept of Surgery, Alrijne hospital, [4]Dept of Surgery, Erasmus MC University Medical Center, Rotterdam, The Netherlands*

10.00 Follow-up with MRI of rectal cancer after transanal endoscopic microsurgery: detection of recurrence and inter-observer reproducebillity (p.133)

B.J.P. Hupkens[1-3], M. Maas[1,4], M.H. Martens[1-3], W.M.L.L.G. Deserno[5], J.W.A. Leijtens[6], P.J. Nelemans[7], D.M.J. Lambregts[2,4], G.L. Beets[3,8], R.G.H. Beets-Tan[3,4], [1]Maastricht University Medical Center, Dept of Radiology, Maastricht, [2]Maastricht University Medical Center, Dept of Surgery, Maastricht, [3]GROW School for Oncology and Developmental Biology, Maastricht, [4]The Netherlands Cancer Institute, Dept of Radiology, Amsterdam, [5]Laurentius Hospital, Dept of Radiology, Roermond, [6]Laurentius Hospital, Dept of Surgery, Roermond, [7]Maastricht University, Dept of Epidemiology, Maastricht, [8]The Netherlands Cancer Institute, Dept of Surgery, Amsterdam, The Netherlands

10.10 Whole liver CT texture analysis to predict the development of colorectal liver metastases in patient who initially present without metastases – a multi-centre study (p.134)

R.C.J. Beckers[1,2,3,4], D.M.J Lambregts[4], R.S. Schnerr[1], M. Maas[1,4], S-X Rao[5], A.G.H. Kessels[6], T. Thywissen[1], G.L. Beets[7,3], J.B. Houwers[1], C.H. Dejong[2,3,8], C. Verhoef[9], R.G.H. Beets-Tan[4,3], [1]Dept of Radiology, Maastricht University Medical Center, Maastricht, [2]Dept of Surgery, Maastricht University Medical Center, Maastricht, [3]GROW School for Oncology and Developmental Biology, Maastricht University, Maastricht, [4]Dept of Radiology, The Netherlands Cancer Institute, Amsterdam, The Netherlands, [5]Dept of Radiology, Zhongshan Hospital, Fudan University, Shanghai, China, [6]Dept of Clinical Epidemiology and Medical Technology Assessment, Maastricht University, Maastricht, [7]Dept of Surgery, The Netherlands Cancer Institute, Amsterdam, [8]NUTRIM School for Nutrition and Translational Research in Metabolism, Maastricht University, Maastricht, [9]Dept of Surgical Oncology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands

10.20 Advanced age is no contraindication for chemoradiotherapy with curative intent in oesophageal cancer (p.135)

F.E.M. Voncken[*1], R.T. van der Kaaij*[*2], K. Sikorska[3], E. van Werkhoven[3], J.M. van Dieren[4], C. Grootscholten[4], P. Snaebjornsson[5], J.W. van Sandick[2] and B.M.P. Aleman[1] *Both authors contributed equally, [1]Depts of Radiation Oncology, [2]Surgery, [3]Biometrics, [4]Gastrointestinal oncology and [5]Pathology of The Netherlands Cancer Institute - Antoni van Leeuwenhoek hospital, Amsterdam, The Netherlands*

10.30 F-18-FDG PET/CT in the evaluation of tumour response after neoadjuvant chemoradiotherapy in locally advanced oesophageal cancer (p.136)

M.J. Valkema[1], B.J. Noordman[1], B.P.L. Wijnhoven[1], J.P. Ruurda[2], G.A.P. Nieuwenhuijzen[3], M.I. van Berge Henegouwen[4], M.N. Sosef[5], J.J.B. van Lanschot[1], R. Valkema[1], [1]Erasmus MC University Medical Centre, Rotterdam, [2]University Medical Centre, Utrecht, [3]Catharina Hospital, Eindhoven, [4]Academic Medical Centre, Amsterdam, [5]Atrium MC, Heerlen, The Netherlands

10.40 The impact of histological subtype on the prognosis of oesophageal adenocarcinoma (p.137)

R.T. van der Kaaij[1], P. Snaebjornsson[2], F.E.M. Voncken[3], E.P.M. Jansen[3], K. Sikorska[4], A. Cats[5], J.W. van Sandick[1], Depts of [1]Surgical Oncology, [2]Pathology, [3]Radiation Oncology, [4]Biometrics and [5]Gastroenterology, The Netherlands Cancer Institute/Antoni van Leeuwenhoek hospital, Amsterdam, The Netherlands

10.50 FOLFIRINOX in locally advanced and metastatic pancreatic cancer: a single centre cohort study (p.138)

S.J.E. Rombouts[1,2], T.H. Mungroop[1], M.N. Heilmann[3], H.W. van Laarhoven[3], O.R. Busch[1], I.Q. Molenaar[1,2], M.G. Besselink[1], J.W. Wilmink[3], [1]Dept of Surgery, Academic Medical Center Amsterdam, [2]Dept of Surgery, University Medical Center Utrecht, [3]Dept of Medical Oncology, Academic Medical Center Amsterdam, The Netherlands

11.00 Korte Ledenvergadering Sectie Gastrointestinale Oncologie

Motiliteitssymposium **Parkzaal**

Voorzitters: A.J. Bredenoord en J. Conchillo

Symposium:
Invasive strategies for functional GI diseases

11.30 Surgical solutions for constipation
Dr. S.O. Breukink, chirurg, UMC Maastricht

11.52 Sphincterotomy for sphincter of Oddi dysfunction
Prof. dr. M.J. Bruno, MDL-arts, Erasmus MC, Rotterdam

12.14 Treatment of gastric emptying disorders after esophageal resection
Prof. dr. A.J.P.M. Smout, MDL-arts
Academisch Medisch Centrum, Amsterdam

12.36 TPN for severe enteric dysmotility and pseudo-obstruction
Dr. G.J.A. Wanten, MDL-arts, Radboudumc, Nijmegen

13.00 Lunch in expositiehal

NESPEN programma **Zaal 80**

Voorzitters: G.H. Wanten en CF. Jonkers

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

09.30 Feasibility of 1h-mrs for noninvasive assessment of liver fat content in patients using long-term home parenteral nutrition (p.139)
A. Huijbers[1], G.J.A. Wanten[1], H. M. Dekker[2], M. van der Graaf[2], [1]Intestinal Failure Unit, Dept of Gastroenterology and Hepatology and [2]Dept of Radiology, Radboudumc, Nijmegen, The Netherlands

09.40 Enteral glutamine supplementation in optimally fed critically ill patients does not affect protein metabolism (p.140)
M.A.R. Vermeulen[1,2], A. Beishuizen[3,6], P.J. Weijs[1], P.M. Bet[4], H. Schierbeek[7], H.M. Oudemans–van Straaten[3], J.B. van Goudoever[5,7] , P.A.M. van Leeuwen[2], Dept of [1]Internal Medicine, [2]Surgery, [3]Intensive Care Unit, [4]Clinical Pharmacy, [5]Pediatrics, VU University Medical Center, Amsterdam, [6]Intensive Care Unit, Medisch Spectrum Twente, Enschede, [7]Mother and Child Division, AMC, Amsterdam, The Netherlands

NESPEN programma **Zaal 80**

Voorzitters: G.H. Wanten en C.F. Jonkers

Symposium:
Behandeling van high output stomata en fistels

09.50 Medicamenteuze behandeling van een high-output fistel of stoma
Drs. F.E.E. de Vries, onderzoeker, afd. Chirurgie, AMC Amsterdam

10.10 Chirurgische behandeling van enterocutane fistels
Dr. J.A.H. Gooszen, chirurg, afd. Chirurgie, AMC Amsterdam

10.30 Verzorging van high output stoma's en fistels
Mw. W. Kuin, verpleegkundig specialist, Antoni van Leeuwenhoek

10.45 Kan voeding high output reduceren?
Mw. M.G.M. van der Werf, diëtist, AMC Amsterdam

11.00 Einde

Vrije voordrachten Sectie Gastrointestinale Endoscopie **Zaal 80**

Voorzitters: M.A.J.M Jacobs en B.L.A.M. Weusten

11.30 Colonoscopy without PSA is feasible, is well tolerated and has a high success rate in males (p.141)
F.M.L. Sandkuijl, W.T. Thijs, R.P Veenstra, L.A. van der Waaij, Afdeling MDL, Martini Ziekenhuis, Groningen, The Netherlands

11.40 Therapeutic strategy for anemia in patients with gastrointestinal bleeding: a retrospective cohort study (p.142)
M.S. van der Capellen, M. Severs, R.E. Petersen, H.H. Fidder, B. Oldenburg, Universitair Medisch Centrum Utrecht, Utrecht, The Netherlands

11.50 Early versus standard colonoscopy - a randomized controlled trial in patients with acute lower gastro-intestinal bleeding: results of the BLEED study (p.143)
I van Rongen and L.E. Perk, MC Haaglanden-Bronovo, The Hague, The Netherlands

12.00 Impact of the formation of a regional EUS interest group amongst community hospitals on the yield of EUS guided tissue acquisition in suspected pancreatic malignancy (p.144)

R. Quispel[1], L.M.W.J. van Driel[1], P. Honkoop[2], M. Hadhiti[3], M.P. Anten[4], I. Leeuwenburgh[4], G. Bezemer[5], C. Fitzpatrick[6], B.J. Veldt[1], M. Bruno[7], [1]Reinier de Graaf Gasthuis, Delft, [2]Albert Schweitzer Ziekenhuis, Dordrecht, [3]Maasstad Ziekenhuis, Rotterdam, [4]Sint Franciscus Gasthuis, Rotterdam, [5]Ikazia Ziekenhuis, Rotterdam, [6]Ijsselland Ziekenhuis, Capelle a/d IJssel, [7]ErasmusMC, Rotterdam, The Netherlands

12.10 EUS for suspected choledocholithiasis. First results of a change in strategy regarding indication and timing of ERCP (p.145)

R. Quispel[1], L.M.W.J. Driel[1], M. van der Voort[1], B.J. Veldt[1], M.J. Bruno[2], [1]Reinier de Graaf Gasthuis, Delft, [2]Erasmus MC, Rotterdam, The Netherlands

12.20 Laparoscopy-assisted transgastric endoscopic retrograde cholangiopancreatography in patients with Roux-en-Y gastric bypass (p.146)

R.M. Nijmeijer[1], P. Wahab[1], I.M. Janssen[2], F.J. Berends[2], M.J.M. Groenen[1], [1]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [2]Dept of Surgery, Rijnstate Hospital, Arnhem, The Netherlands

12.30 Diagnosis of T1 colorectal cancer in pedunculated polyps in daily clinical practice: need for a second opinion? (p.147)

Y. Backes[1], L.M.G. Moons[1], M.R. Novelli[2], J.D. van Bergeijk[3], J.N. Groen[4], T.C.J. Seerden[5], M.P. Schwartz[6], W.H. de Vos tot Nederveen Cappel[7], B.W.M. Spanier[8], J.M.J. Geesing[9], K. Kessels[10], M. Kerkhof[11], P.D. Siersema[1], G.J.A. Offerhaus[12], AN. Milne[13], M.M. Lacle[12] (on behalf of the Dutch T1 CRC Working Group), [1]Dept of Gastroenterology & Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Dept of Histopathology, University College Hospital, London, United Kingdom, [3]Dept of Gastroenterology & Hepatology, Gelderse Vallei, Ede, [4]Dept of Gastroenterology & Hepatology, Sint Jansdal, Harderwijk, [5]Dept of Gastroenterology & Hepatology, Amphia Hospital, Breda, [6]Dept of Gastroenterology & Hepatology, Meander Medical Center, Amersfoort, [7]Dept of Gastroenterology & Hepatology, Isala, Zwolle, [8]Dept of Gastroenterology & Hepatology, Rijnstate, Arnhem, [9]Dept of Gastroenterology & Hepatology, Diakonessenhuis, Utrecht, [10]Dept of Gastroenterology & Hepatology, Flevo Hospital, Almere, [11]Dept of Gastroenterology & Hepatology, Groene Hart Hospital, Gouda, [12]Dept of Pathology, University Medical Center Utrecht, Utrecht, [13]Dept of Pathology, Diakonessenhuis, Utrecht, The Netherlands

12.40 Is hybrid endoscopic submucosal dissection effective for treatment of large non- pedunculated colorectal polyps? A single center experience (p.148)

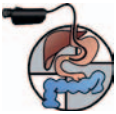
H.R. Cheng[1,2,3], R.M.M. Bogie[2,3], C. Huysentruyt[4], A.A.M. Masclee[2,5], S. Sanduleanu[2,3], J.W.A. Straathof[1,2], [1]Dept of Gastroenterology and Hepatology, Máxima Medical Center, Veldhoven, [2]Division of Gastroenterology-Hepatology, Dept of Internal Medicine, Maastricht University Medical Center, Maastricht, [3]GROW, School for Oncology and Developmental Biology, Maastricht University Medical Center, [4]Dept of Pathology, Laboratory for Pathology and Medical Microbiology (PAMM), Eindhoven, [5]NUTRIM, School of Nutrition & Translational Research in Metabolism, Maastricht University Medical Center, The Netherlands

12.50 Prevalence and characteristics of unexpected rectal cancer in benign cancer in benign appearing large non-pedunculated rectal polyps (p.149)

M.E.S. Bronzwaer[1], G.D. Musters[2], R.M. Barendse[2], L. Koens[3], E.J.R. de Graaf[4], P.J. Tanis[2], E. Dekker[1], P. Fockens[1] on behalf of the TREND study group, Dept of Gastroenterology and Hepatology[1], Surgery[2] and Pathology[3], Academic Medical Center, University of Amsterdam, Amsterdam and Dept of Surgery[4], IJsselland Ziekenhuis, Capelle aan de IJssel, The Netherlands

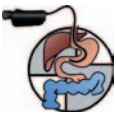
13.00 Lunchpauze in de expositiehal.

Programma V&VN MDL **Brabantzaal**



09.30	**Algemene ledenvergadering V&VN**
10.10	Welkom door Mw. T.A. Korpershoek, voorzitter
Voorzitter:	T.A. Korpershoek
10.15	Landelijk zorgpad galwegcarcinoom: diagnostiek en behandeling *Mw. A. Schoorlemmer, verpleegkundig specialist AMC, Amsterdam*
10.40	Overmatig opboeren en dyspepsie *Dr. D.B. Kessing, aios MDL, OLVG Amsterdam*
11.05	Tractus digestivus bloedingen *Dr. I.L. Holster, aios MDL, Albert Schweitzer Ziekenhuis Dordrecht*
11.30	*Koffiepauze expositiehal*
11.50	Goede voeding: de hoeksteen van behandeling bij chronische ziekten *Prof. dr. B.J.M. Witteman, Universiteit van Wageningen*
12.20	IBD bij kinderen *Dr. E.K. George, kinder-MDL-arts Noordwest Ziekenhuisgroep Alkmaar*
12.50	*Lunch expositiehal*

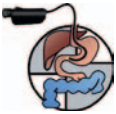
Middagprogramma Endoscopieverpleegkundigen **Brabantzaal**



Voorzitters: M. van Hout en R. van Rhee-Martha

14.00	CRM op de endoscopie-afdeling *Drs. T.E.H. Römkens, MDL-arts, Jeroen Bosch Ziekenhuis, Den Bosch* *Dhr. M. Haerkens, Wings of Care*
14.25	Rendez vous procedure ERCP *Dr. F.P. Vleggaar, MDL-arts UMC Utrecht*
14.50	Pancreascystedrainage *Dr. F.O. The, MDL-arts OLVG Amsterdam*
15.15	Videocapsule *Mw. A. Valckx, endoscopieverpleegkundige* *Elisabeth-Tweesteden ziekenhuis Tilburg*
15.35	Afsluiting met koffie en thee bij de Limburg-foyer

Middagprogramma IBD / Lever verpleegkundigen **Zaal 52**



Voorzitters: M. Bijmolen en P. Hurkmans

14.00	Casuïstiek bij levertestafwijkingen *Mw. M. Bijmolen, verpleegkundig specialist hepatologie UMC Groningen*
14.25	Levertestafwijkingen bij IBD-geneesmiddelen *Prof. dr. J.P.H. Drenth, MDL-arts, Radboudumc Nijmegen*
14.50	IBD: start-stop biologicals / combitherapie *Dr. A.G.L. Bodelier, MDL-arts Amphia*
15.15	IBD: de oudere patiënt *Mw. N. Ipenburg, verpleegkundig specialist IBD,* *Leids Universitair Medisch Centrum*
15.40	Afsluiting met koffie en thee bij de Limburg-foyer

Boehringer Ingelheim

SOMS WIL JE MEER CONTROLE HEBBEN

Pradaxa® (dabigatran etexilaat)*,[1] is een New Oral Anti-Coagulans (NOAC) dat is opgenomen in de richtlijn voor de behandeling van non-valvulair atriumfibrilleren.[2] Soms moet de antistollingsbehandeling echter worden onderbroken, bijvoorbeeld omwille ingrepen, bloedingen en/of onderzoekingen. Dan is het wenselijk om het antistollingseffect te couperen.

Praxbind® (idarucizumab)**,[3] is een gehumaniseerd monoclonaal antilichaamfragment dat zich sterk en specifiek bindt aan dabigatran.[3] Hierdoor wordt de antistollingsactiviteit van dabigatran onmiddellijk geneutraliseerd. Idarucizumab wordt in een vaste dosis intraveneus toegediend en zit in flacons die klaar zijn voor gebruik en 2 jaar houdbaar zijn.

De fase III studie RE-VERSE AD includeert Pradaxa-gebruikers die een levensbedreigende of ongecontroleerde bloeding hebben of een spoedoperatie of -procedure moeten ondergaan. Een interimanalyse van de eerste 90 patiënten laat zien dat Praxbind een onmiddellijk en aanhoudend effect heeft (bij > 90% van de patiënten tot 12 uur na toediening).[4] Deze resultaten geven aan dat Praxbind meer controle geeft in spoedeisende situaties en een algoritme voor de inzet is gepubliceerd.[5]

* Dabigatran is geregistreerd voor preventie van CVA en systemische embolie bij non-valvulair atriumfibrilleren met één of meer risicofactoren, zoals CVA of TIA in de anamnese, hartfalen (≥NYHA 2), ≥75 jaar, diabetes mellitus, hypertensie. ** Idarucizumab is geregistreerd voor volwassen Pradaxa (dabigatran etexilaat) gebruikers wanneer het anticoagulerend effect van dit middel snel moet worden geneutraliseerd voor spoedoperaties/ dringende ingrepen of bij een levensbedreigende/ongecontroleerde bloeding.

REFERENTIES:
1) SmPC dabigatran. **2)** Heidbuchel H et al. Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation. Europace 2015 doi:10.1093/europace/euv309. **3)** SmPC idarucizumab. **4)** Pollack CV et al. Idarucizumab for Dabigatran Reversal. N Engl J Med 2015;373:511-20. **5)** Eikelboom JW et al. Idarucizumab. The Antidote for Reversal of Dabigatran. Circulation. 2015;132:2412-2422.

Productinformatie elders in deze uitgave.

NL/PRA-161327

Endoscopically resectable colorectal cancer in a FIT-based screening population in the Netherlands: progress still to be made

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Detection of early colorectal cancer (CRC) increases as a result of recent CRC screening program implementation worldwide. Complete endoscopic resections of these early malignancies can potentially prevent invasive surgery. We assessed if endoscopically resectable CRCs are identified as such at colonoscopy within a fecal immunochemical tests (FIT)-based CRC screening program. In addition, we estimated final treatment of these lesions and treatment outcomes. A random sample of 13,566 persons from the Dutch general population, aged 50-74 years, were invited to participate in a FIT-based screening program, between November 2006 and October 2014. Participants were referred for colonoscopy in case of a positive FIT (cut-off ≥10µg hemoglobin per gram feces). From all detected CRCs, we included endoscopically resectable cancers, defined as a CRC confined to the submucosa, without invasion of the muscularis propria or deeper wall (T1N0M0). Endoscopic resections were considered sufficient, in case of an R0 resection and resection margin > 1mm. Dutch guidelines were followed for treatment and surveillance recommendations. Twenty patients were diagnosed with a histologically proven T1N0M0 malignant colorectal polyp (median size 16 mm (range 5-40 mm)). In total, sixteen (80%) primary endoscopic resections were performed and four (20%) primary surgical resections. Four (20%) of all T1 malignancies were correctly identified as endoscopically resectable based on its endoscopic appearance. Endoscopic R0 resection rate was 50% (2/4) in the correctly identified T1 CRCs at colonoscopy and 33% (4/12) in the non-identified T1 CRCs. Additional surgery was performed in respectively 50% and 56% of these lesions.

Conclusions: In this FIT-based CRC screening population, more than half of the endoscopically resectable CRCs were not identified as such at initial colonoscopy. Additional surgery was still required in a substantial part of these patients often due to incomplete resection margins. Our findings highlight the importance of identification and accurate removal of endoscopically resectable CRC to ensure completeness for proper pathological evaluation and staging.

Differences in quality indicators in colonoscopy performed by trainees and gastroenterologists

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Quality assurance has become an important aspect of endoscopy during the last decade, resulting in the use of a national colonoscopy quality registry in the near future. In contrast to other procedures such as ERCP, hardly any data are available on differences in quality indicators in colonoscopy between trainees and gastroenterologists. In our study we used a web-based database in which all computerized predefined reports created with a commercially available software system (Endobase) were loaded. All registered medical data in the endoscopic report are coded by the extended International Classification of Diseases 10th version called GET-C, which is accepted by the WHO. These data are automatically and anonymously transferred to a data warehouse and can be accessed using a Business Intelligence Tool. We analyzed differences in polyp-detection, cecal intubation rate, Gloucester comfort score and reported difficulty of the endoscopy for colonoscopies performed by trainees and gastroenterologists without trainee-involvement. Screening colonoscopies were excluded from the analysis. We studied the data on all colonoscopies from January 2013 until May 2016. Groups were compared using a two-sided Fisher's exact test. Data from 7741 colonoscopies were analyzed. Of these procedures, 2159 were performed by trainees, and 5582 by gastroenterologists. The cecal intubation rate was 93.5% for trainees, and 93.7% for gastroenterologists ($p=0.75$). The polyp detection rate was 46.8% for trainees, and 40.2% for gastroenterologists ($p<0.0001$). A Gloucester comfort score of 3 or 4 was recorded in 7.4% of colonoscopies performed by trainees, and 4.0% of colonoscopies performed by gastroenterologists ($p<0.0001$). The procedure was rated as difficult or very difficult in 21.6% by trainees, and 16,1% by gastroenterologists ($p<0.0001$).
In conclusion, our study demonstrated a similar cecal intubation rate and higher polyp detection rate for trainees, which are the most readily available quality indicators predictive of missed colorectal cancer. In contrast, the Gloucester comfort score as well as the reported procedure difficulty were significantly higher in colonoscopies performed by trainees. Increased attention to optimization of the trainee's colonoscopy technique in order to prevent patient discomfort might reduce the differences in patient discomfort and procedure difficulty.

Implementation of an Optical Diagnosis Strategy Saves Costs and Does Not Impair Clinical Outcomes of a FIT-based CRC Screening Programme

J.L.A Vleugels[1], M.J.E. Greuter[2], Y. Hazewinkel[1], V.M.H. Coupé[2], E. Dekker[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [2]Dept of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands

Introduction: With an optical diagnosis strategy, diminutive (1-5mm) polyps throughout the colon diagnosed with high confidence are resected and discarded and high-confidence diminutive recto-sigmoid hyperplastic polyps (HPs) are left in situ. Implementation of this strategy may result in reduced polypectomy-related complications, direct surveillance interval assignment and cost-savings. Previous modelling studies were based on primary screening colonoscopies and assumed a high percentage of high-confidence predictions. We evaluated the effectiveness and costs of an optical diagnosis strategy compared to polypectomy of all diminutive lesions followed by histopathological diagnosis. Methods: The Adenoma and Serrated pathway to Colorectal Cancer (ASCCA) model simulates a biennial faecal immunochemical testing (FIT) screening programme, with referral to colonoscopy of FIT positives, as well as a primary colonoscopy screening programme in individuals aged 55 to 75 years. Surveillance colonoscopies were included in both screening scenarios. For each scenario, we compared a histopathological diagnosis strategy to an optical diagnosis strategy. Based on recent literature, we assumed that 76% of optical diagnoses would be made with high confidence and that 88%, 91% and 88% of respectively adenomas, sessile-serrated polyps and HPs would be accurately characterized. Outcomes of each strategy included discounted life-years, costs and number of colonoscopies. Results: The model predicted that in a FIT-screening programme with a strategy of histopathological diagnosis, 17 days of life are gained in the lifetime of a 20-year old individual compared to no screening. The optical diagnosis strategy led to similar health gains. In addition, it led to cost-savings compared to the histopathological diagnosis strategy. In the optical diagnosis strategy, histopathological analysis would be performed in ~70% of diagnostic colonoscopies with polypectomy. Projected to a fully implemented FIT screening programme in the Netherlands, this would result in yearly undiscounted cost-savings of ~€2.5 million. In colonoscopy screening, comparison of both strategies led to similar conclusions, although the additional cost-savings due to the optical diagnosis strategy were higher due to a lower proportion (i.e. ~40%) of diagnostic colonoscopies with polypectomy in which pathology was required. Conclusion: Based on the ASCCA model, an optical diagnosis strategy for diminutive polyps detected within a FIT-based or colonoscopy-based screening programme does not decrease the effectiveness of the programmes. However, implementation of this strategy can lead to economic benefits, especially in colonoscopy screening.

Organized colorectal cancer screening programs and socioeconomic and ethnic inequalities in participation

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Organized colorectal cancer (CRC) screening programs have been implemented in many countries and have proven to reduce CRC related mortality. To achieve the greatest population health benefit from screening, maximum participation is crucial. Existing socio-economic inequalities in CRC outcome are expected to increase with wider implementtation of screening programs if participation is lower in lower socioeconomic groups. We performed the first review on data availability on participation by socioeconomic and ethnic inequalities for all organized CRC screening programs using guaiac Fecal Occult Blood Tests (gFOBT) or Fecal immunochemical Tests (FIT) as primary screening method. A literature review and questionnaire survey among contact persons of national or regional organized CRC screening programs were used to identify published and unpublished data on participation by socioeconomic status and ethnicity. 24 organized CRC screening programs were identified in 19 countries. General participation rates ranged from 21% to 71,3%. The majority (54%) of organized screening programs had no published data available on participation by socioeconomic status and ethnicity. 90% (29/32) of founded evidence showed a lower participation rate among lower socioeconomic groups. Most published papers provided evidence from the English national CRC screening program. Program characteristics, study methods and used indicators of socioeconomic status varied widely, thereby limiting the validity of comparison of participation rates across studies and screening programs. However, a general picture emerged, suggesting an average of 150% (up to 200%) higher participation rate in the highest socioeconomic group compared to the lowest socioeconomic group. Evidence on participation by ethnicity was scarce and not conclusive.

Conclusion. The evidence available confirms that lower socioeconomic groups are less likely to participate in organized colorectal cancer screening programs using stool tests. This in turn is likely to increase socioeconomic inequalities in CRC outcome and therefore in population health. We suggest to include participation rates by socioeconomic status and ethnicity in routine monitoring of organized CRC screening programs, and to systematically investigate the determinants of low participation, in order to develop targeted strategies to enhance equal access and informed participation in all socio-economic and ethnic groups.

External validation of a clinically based staging system for perihilar cholangiocarcinoma

T.A. Labeur, R.J.S. Coelen[1], M.P. Gaspersz[2], T.A. Labeur[3], J.L.A. van Vugt[2], S. van Dieren[1], H-J. Klümpen[3], B. Groot Koerkamp[2], T.M. van Gulik[1*] * these authors share senior authorship, [1]Dept of Surgery, Academic Medical Center, Amsterdam, [2]Dept of Surgery, Erasmus Medical Center, Rotterdam, [3]Dept of Medical Oncology, Academic Medical Center, Amsterdam, The Netherlands*

Background: Current prognostic staging systems for perihilar cholangiocarcinoma (PHC) are poorly applicable to patients with unresectable disease. A prognostic model for PHC developed at the Mayo Clinic, which uses clinical and radiological parameters, seems a promising tool for staging of patients with both unresectable and resectable disease. This staging system requires external validation before implementation in clinical practice. The aim of this study was to evaluate and validate this model in a large Dutch, multicenter cohort. Methods: All patients with PHC who were evaluated and treated in two large academic centers between 2002 and 2014 were identified and retrospectively staged according to the Mayo Clinic prognostic system. Base characteristics and staging parameters, including Eastern Cooperative Oncology Group (ECOG) performance status, CA19-9, tumor size, vascular involvement and suspected intrahepatic, peritoneal or lymph node metastases on imaging, were abstracted from the medical records. Overall survival (OS) was estimated using the Kaplan-Meier method and comparison of staging groups was done using the log-rank test and Cox-regression analysis. Performance of the staging system was assessed in terms of discrimination which was quantified by the concordance-index. Subgroup analysis of the proposed model was done for laparotomy (complete and aborted resection) and non-laparotomy treatment groups. Results: A total of 600 patients were staged according to the proposed model, allocating 24, 82, 355 and 139 patients to stages I, II, III and IV, respectively. Median OS was 11.6 months. Median OS of stages I, II, III and IV was 22.7, 19.4, 12.1 and 6.2 months, with hazard ratios (95% confidence interval [CI]) of 1.00 (reference), 1.86 (1.06-3.24), 2.50 (1.49-4.21) and 3.56 (2.08-6.08), respectively (P<0.001). In subgroups based on initial treatment type, there was only a significant prognostic stratification in the laparotomy group (P=0.014). Accuracy of OS prediction, quantified by the concordance score (95% CI), was 0.58 (0.56-0.61) for the entire cohort, 0.56 (0.52-0.60) in the laparotomy group (N=274), and 0.54 (0.51-0.58) in the non-laparotomy group (N=326).
Conclusion: In this external validation cohort, the Mayo Clinic model showed successful stratification of different staging groups for PHC, but discrimination of different prognostic groups was poor for the total cohort and subgroups based on initial treatment type. Therefore, this model may require modification prior to clinical implementation.

Online self-test identifies those at high risk for Lynch syndrome in population-based colorectal cancer screening without inducing anxiety or distress

A van Erkelens[1], B.W.M. Spanier[2], A.S. Sie[1], M. van Kouwen[3], J.B. Prins[4], N. Hoogerbrugge[1], [1]Dept of Human Genetics, Radboud University Medical Center, Nijmegen, [2]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [3]Dept of Gastroenterology and Hepatology, Radboud university medical center, Nijmegen, [4]Dept of Medical Psychology, Radboud University Medical Center, Nijmegen, The Netherlands

Individuals with Lynch syndrome have a high risk of colorectal and endometrial cancer which may potentially be prevented. Better identification of high familial colorectal cancer (FCRC) risk is essential to improve detection of those at high risk for Lynch syndrome (LS). We tested a new dynamic on family history questionnaire (self-test) with direct feedback for FCRC and LS risk in population-based CRC screening, and assessed whether it induced anxiety or distress. After pre-procedure visit for colonoscopy, individuals with a positive immunohistochemical occult fecal blood test [iFOBT] in population-based CRC screening completed the self-test and questionnaires at home (study cohort). A validation cohort of patients scheduled for diagnostic/surveillance colonoscopy was also invited to participate. The self-test is based on Dutch hereditary CRC guidelines. Anxiety (State-Trait Inventory) and distress (Hospital Anxiety-Depression Scale) were assessed at base (T0), post-test (T1), and after two weeks (T2). Primary outcome was state-anxiety. Secondary outcomes were trait-anxiety, distress, and CRC risk perception. No one had received prior genetic counseling or testing. The study cohort consists of 177 individuals who completed T0-T1, 153 (86%) also completed T2. Median age was 65 years [range 61-75]. Most respondents were male (71%). Seven out of 10 responders (71%) participated after the colonoscopy (96% at T2). A high and moderate FCRC risk was identified in 12/177 (6.7%) and 5/177 (2.8%) respondents, respectively, 4/177 (2.2%) had a first-degree relative (FDR) with endometrial cancer diagnosed before age 50. Median anxiety and distress scores were below clinical cut-off scores and remained low at T0, T1 and T2, as did CRC risk perception. Most patients (83%) would recommend the self-test to others, few (5%) would not. In the validation cohort (n=53), 14/53 (26%) had a high and 2/53 (4%) a moderate FCRC risk, 3/53 (5.7%) had a FDR with a LS-related tumor diagnosed before age 50. More than twice as many individuals at high FCRC risk were identified using the self-test compared to pre-procedure medical notes. The on self-test identified previously unknown individuals at high FCRC (6.7%) risk who should be referred for Lynch syndrome genetic testing, and did not induce anxiety or distress. We therefore recommend the addition of the self-test to population-based CRC screening.

Indications and consequences of MSI-analysis in colorectal cancer

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Background: Microsatellite instability analysis (MSI) is performed as a tool to select patients for genetic testing if Lynch syndrome (LS) is suspected by using the Bethesda criteria. The analysis is also performed to select patients that may refrain from adjuvant chemotherapy. Possible consequences of a positive test result are: (1) referral to a clinical geneticist, (2) impact on the type of surgery in case of young (<60 years) patients with a positive family history for LS associated tumors and (3) refrain from adjuvant chemotherapy. We studied the indications for MSI and consequences of a positive test result. Methods: In a retrospective single center study we analyzed all patients with colorectal cancer that were discussed in a multidisciplinary team between April 14th 2012 and January 1th 2016. Indications for MSI and consequences of MSI-high tumors were studied. Results: We included 660 patients. A total of 108 patients (16%) were tested for MSI. Indications for MSI analyses were: fulfilling the Bethesda criteria (n= 53, 49%), select patients that may refrain from adjuvant chemotherapy (n=40, 37%) and a rest group of 15 patients (mainly patients with a positive family history, not fulfilling the Bethesda criteria). A total of 12 (11%) patients had MSI high tumors. Three of them (25%) were not referred for genetic counselling accidentally. In one patient a germ MSH-6 mutation was identified, in 6 patients hypermethylation of the MLH1 promotor was found and 2 patients cancelled their appointment. In 28 patients MSI was performed on biopsies of the tumor and available preoperatively. Three of them had a MSI high tumor (indication for MSI analysis: synchronous double tumor (n=2), positive family history (n=1)). In these three patients the type of surgery has not been changed. In three of 40 patients (8%) adjuvant chemotherapy was refrained because their tumors were MSI high.
Conclusions: MSI analysis revealed a germ mutation in 1% after DNA analysis, did not influence the type of surgery and had consequences in the decision to treat with adjuvant chemotherapy in 8% of the patients. Consequences and practitioners responsibilities of MSI analysis should be part of the multidisciplinary CRC discussion as 25% of patients with MSI high tumors were not referred for genetic counseling.

A digital review platform for Barrett's esophagus: going national

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Assessment of low-grade dysplasia in Barrett' esophagus (BE) is hindered by significant observer variability. The progression risk to esophageal adenocarcinoma (EAC) increases if review by a second pathologist yields the same dysplasia grade. Therefore, most guidelines advise revision of dysplastic BE by a second expert pathologist. However, transportation between different centers often leads to breakage or loss of slides. To overcome this problem, a digital review platform for BE has been set up. The use of digital microscopy has previously been validated by the current, regional panel of 5 Barrett expert pathologists. They have achieved substantial interobserver agreement through BE histology study sets and consensus meetings. The platform is now in operation, but expansion of the number of pathologists is warranted to attain national coverage. The aim of this study was therefore, to expand the current panel with 10 Barrett expert pathologists from other Barrett expert centers across the country, while preserving homogeneity of assessment and adequate logistics. The 10 Barrett expert pathologists digitally assessed a histological study set consisting of 60 single HE-slide cases of Barrett's spectrum (NDBE; n=20, LGD; n=20, HGD; n=20). The cases were randomly and independently graded twice by all pathologists, after which a consensus meeting was held. The consensus diagnoses the current panel established earlier were considered gold standard. Agreements were calculated using a custom weighted Cohen's kappa and were corrected for the maximum possible kappa. The mean interobserver agreement of the 10 pathologists compared to the gold standard was 0.69 in 4 categories (NDBE, IND, LGD and HGD or more). The mean intraobserver agreement of the 10 pathologists was 0.77. These agreement scores are both considered substantial. The 10 Barrett expert pathologists achieved substantial digital intra- and interobserver agreement compared to the gold standard. These results suggest substantial homogeneity within the group of Barrett expert pathologists at large and support the expansion of the panel to 15 pathologists. This will enable the digital review platform to reach nationwide coverage and operate according to the upcoming national guide for BE.

The Natural Behavior of Small Colorectal Adenomas: a Systematic Literature Review

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Background: Diminutive (1-5mm) and small (6-9mm) polyps comprise almost 90% of detected lesions during colonoscopy. The current focus on high quality colonoscopy and achievement of adenoma detection rates promotes the detection of small adenomas. The risk of cancer is very low at 0.04-0.07%. However, the risk that these small adenomas progress to colorectal cancer (CRC) by time is not well understood. We performed a systematic review to explore the natural behavior of diminutive and small colorectal adenomas. Methods: We searched MED and EMBASE on 15 February 2016 for studies investigating the natural history of colorectal polyps. Studies were eligible for inclusion when they assessed patients with adenomas that were not treated with polypectomy and underwent follow-up. We independently extracted summary-level data on the study and patient characteristics and evaluated CRC, advanced adenoma (size ≥10mm, containing high-grade dysplasia (HGD) or villous features) and changes in size during follow-up as outcome parameters. Quality of the studies was assessed with the Newcastle-Ottawa Scale. Results: Of 8,775 reviewed studies from MED and EMBASE, 9 studies that prospectively evaluated the natural history of diminutive and small polyps were identified (table 1). Three studies evaluated diminutive polyps: two using colonoscopy and one barium-enema for surveillance. In those studies, between 35 and 207 diminutive adenomas were left in situ for a mean follow-up between 2 and 7.8 years. No diminutive adenoma developed into CRC; HGD was detected in 1 adenoma and 1 adenoma grew larger than 10mm. Two recently published CT-colonography studies assessed 56 and 107 small adenomas, respectively, and after a mean follow-up of 2.3 and 3.3 years, 21 (38%) and 23 (21%) of the polyps progressed to advanced adenomas. Combining both CT-studies with a total of 163 small adenomas, findings at follow-up were: one adenoma with HGD, 20 adenomas with villous features and 35 adenomas that grew larger than 10mm. In the remaining four prospective studies using endoscopy as follow-up method, in total between 30 and 408 adenomas sized 1-10mm were assessed. Mean follow-up ranged between 22 and 43 months. In these studies, at follow-up only 18 (2.6%) of adenomas contained HGD, villous features or grew beyond 10mm in size, and no CRC was found. The majority of studies was of limited quality.
Interpretation: Based on this systematic review it appears that only a very small percentage of 1-9mm adenomas progresses to advanced adenomas. It seems unlikely that the removal of these diminutive and small adenomas will contribute significantly to a reduction in CRC morbidity and mortality.

Management of Eosinophilic Esophagitis in Daily Clinical Practice

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Background: In recent years, new guidelines and recommendations have been published regarding the diagnostic criteria and therapeutic management of eosinophilic esophagitis (EoE). The aim of this study was to assess the diagnostic and therapeutic management of patients diagnosed with EoE in daily clinical practice and whether this was according to guidelines and recommendations. Methods: A population-based, retrospective cohort study was conducted using data from the national pathology registry (PALGA), medical records, and telephone interviews of patients diagnosed with EoE in two academic and two non-academic hospitals in the period 2004-2014. Data regarding demographics, clinical manifestations, endoscopic results, histologic samples and therapeutic strategies were collected. Standard statistical analyses were performed to summarize the patient characteristics. Results: In total, 119 patients were diagnosed with EoE and included in this study. The median age at onset of symptoms was 29 years (IQR, 15-42) and the median age at diagnosis was 38 years (IQR, 23-51 years), leading to a median diagnostic delay of 6.5 years (IQR, 2-14 years). The median delay in diagnosis between first contact in the hospital and diagnosis was 1.0 year (IQR, 2-14 years). The incidence of patients newly diagnosed with EoE increased steadily over a period of 11 years. Criteria for the microscopic diagnosis of EoE varied between pathologists in each hospital. Initial treatment included topical corticosteroids (30.3%), proton pump inhibitors (PPIs) (29.4%) or a combination of both (10.1%). A follow-up endoscopy was performed in 40.3% of patients. During follow-up, treatment included PPIs (76.0%), topical corticosteroids (59.6%) or a combination of both (45.4%).
Discussion: Diagnostic and therapeutic discrepancies between daily clinical practice and recommendations from current and past guidelines were observed. Remarkably, the diagnostic entity PPI-responsive EoE was only used in one center, follow-up endoscopy was performed in less than half of patients and all pathologists used different criteria for the microscopic diagnosis of EoE. Moreover, varying therapeutic strategies were utilized in the participating centers. Our results show that apart from developing guidelines, efforts should be undertaken to implement them in daily clinical practice.

Genomic and expression analysis identify WWOX as a disease modifier gene in fibrostenotic Crohn's disease

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Crohn's Disease (CD) is a chronic inflammatory disease with unpredictable disease behaviour. Multiple genetic variants are associated with susceptibility for CD, but little is known about genes influencing CD behaviour. To identify disease-modifying genes associated with the fibrostenotic phenotype in CD, we performed a within-case analysis comparing "extreme phenotypes". Using a genome-wide approach (166,251 Single Nucleotide Polymorphisms) in two independent case-control cohorts totalling 322 fibrostenotic and 619 purely inflammatory (non-penetrating/non- fistulising) CD cases, we identified and replicated WWOX as a disease-modifying gene associated with recurrent fibrostenotic CD ($P = 6.09 \times 10^{-11}$). The main mediator between intestinal inflammation and fibrosis in IBD is Transforming Growth Factor-beta (Tgf-β). Tgf-β mRNA expression in ileocecal resection material from ten patients with and without the WWOX risk allele, as well as in intestinal tissue from eight Wwox knock-out and eight Wwox wildtype mice was analysed by qPCR. CD patients carrying the risk allele showed enhanced expression of Tgf-β compared to individuals homozygous for the wildtype allele (P= 0.0079). Similarly, we observed a trend towards increased TGF-β expression in Wwox knock-out mice compared to wildtype mice. TGF-β stimulates downstream signalling pathways resulting in expression of several profibrotic gene, including matricellular PAI-1 (SERPINE1). qPCR analysis of this gene showed a trend towards increased expression in the risk-allele-carrying CD patients compared to the patients homozygous for the wildtype allele. Tgf-β also plays a critical role in M2 macrophage differentiation. We show that In vitro macrophage polarization was associated with higher levels of WWOX in M2 macrophages compared to M1 macrophages. In conclusion, we have identified WWOX as a disease-modifying gene associated with the recurrent fibrostenotic phenotype in CD and replicated this association in an independent cohort. Our expression analyses demonstrate the functional effect of the risk allele through enhanced expression of Tgf-β in risk-allele carriers and Wwox knock-out mice. This has a modulatory effect on macrophages, the key-effector cells in the inflammation-fibrosis equilibrium, and ultimately to a profibrotic expression profile. Based on the mouse studies, we conclude that the 'risk allele' most likely impairs WWOX activity. CD patients carrying the WWOX risk allele appear to have a profibrotic profile and, to avoid fibrotic complications, it might be advisable to avoid prescribing them anti-inflammatory medication that enhances Tgf-β signaling in intestinal fibroblasts.

Transanal endoscopic microsurgery versus endoscopic mucosal resection for large rectal adenomas (TREND-study)

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Non-randomised studies suggest that endoscopic mucosal resection (EMR) is equally effective in removing large rectal adenomas as transanal endoscopic microsurgery (TEM). EMR might be more cost-effective and safer. This trial compares the cost-effectiveness and cost-utility of TEM and EMR for large rectal adenomas. For this multicentre, randomised controlled non-inferiority trial, patients with rectal adenomas ≥3cm, without malignant features, at 17 Dutch and 1 Belgian hospital were included. Eligible patients were randomly assigned (1:1) to EMR or TEM, allowing endoscopic removal of residual adenoma at 3 months. Randomisation was stratified by whether patients had a primary adenoma or residual/recurrent disease after prior resection. Unexpected malignancies were excluded post randomisation. Primary outcomes were recurrence within 24 months and the number of recurrence-free days alive and out of hospital, analysed by intention to treat. The trial was designed to demonstrate non-inferiority of EMR with regards to recurrence rate with an upper limit of 10%. Secondary outcomes were complications, quality of life, anorectal function and costs. This trial is registered in the Dutch Trial Registry (NTR1422). Between Feb 3, 2009 and Sept 19, 2013, 209 patients were randomised to EMR (n=106) or TEM (n=103). In each group, 2 patients withdrew consent. There was 1 patient with prostate carcinoma instead of rectal adenoma in the EMR group, who was excluded. The remaining 204 patients (103 EMR, 101 TEM) were treated. Of those, 27 (13%) had unexpected cancer and were excluded. One additional patient withdrew consent. Of the remaining 176 (87 EMR, 89 TEM) patients, overall recurrence rates were 15% after EMR and 11% after TEM. However, EMR was statistically not non-inferior to TEM. The number of recurrence-free days alive and out of hospital was similar (EMR 609 ± 209, TEM 652 ± 188, p=0.16). Complications (mostly hemorrhage) occurred in 18% (EMR) vs. 26% (TEM) (p=0.23). Major complications occurred in 1% (EMR) vs. 8% (TEM) (p=0.064). Quality adjusted life years were equal in both groups. Although EMR patients scored more favourable on disease specific quality of life questionnaires, manometries were similar and continence improved after adenoma resection regardless of treatment. EMR was approximately €3000 cheaper and therefore more cost-effective. Conclusions: Due to initially higher recurrence rates after both treatments while being slightly in favor of TEM, non-inferiority of EMR could not be demonstrated. With the number of severe complications and the higher costs not being in favor of TEM however, judgment on which treatment to recommend should be suspended.

Durable Response in the Markers of Cholestasis through 18 Months of Open-Label Long-Term Safety Extension Study of Obeticholic Acid in Primary Biliary Cirrhosis

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Obeticholic Acid (OCA) is a selective and potent farnesoid X receptor (FXR) agonist developed for treatment of primary biliary cholangitis (PBC). The POISE trial was a randomized double-blind (DB), placebo-controlled, Phase 3 trial which demonstrated efficacy and safety of OCA over a 12 month period. 198 of 216 patients completed the DB phase with 193 patients enrolling in the open-label long-term safety extension (LTSE). The LTSE aim is to assess the durability of response to OCA. The DB phase inclusion criteria included: PBC diagnosis, ALP ≥1.67x ULN and/or total bilirubin >ULN to <2x ULN, stable UDCA dose or unable to tolerate UDCA. During the DB phase, patients were randomized to: daily Placebo (PBO), 5 to 10 mg OCA titration group (titration based on response and tolerability), or 10 mg OCA. In the LTSE, all patients were to be initially treated with 5 mg OCA with the option to increase based on response and tolerability every 3 months. The LTSE phase is currently in progress, and the analysis was performed on 136 total patients receiving ≤10 mg OCA daily for at least 18 months (PBO, n= 41; Titration OCA; n= 45; 10mg OCA, n= 50). LTSE demographics: mean age 56 y; female: 91%; white 94%. The DB base ALP (U/L) was: PBO: 310 ± 97; OCA Titration: 315 ± 122, 10 mg OCA 308 ± 98. All OCA groups had significant reductions in ALP after 12 months of DB treatment (PBO: -12 ± 80; OCA Titration: -106 ± 87, p<0.0001; 10 mg OCA: -122 ± 75, p<0.0001). This response was durable through an additional 18 months of the LTSE (PBO: -98 ±70, p<0.0001 OCA Titration: -111 ± 90, p<0.0001; 10 mg OCA: -107 ± 91, p<0.0001). DB base bilirubin (µmol/L) was: PBO: 11 ± 6; OCA Titration: 11 ± 6, 10 mg OCA: 11 ± 7. For PBO, bilirubin increased during the DB period (1.5 ± 4.3, p<0.05). OCA Titration and 10 mg groups sustained no mean increase in bilirubin in the DB (12 months) (-0.6 ± 3.5 and -1.2 ± 4.7) or LTSE (18 months) (-0.3 ± 3.9 and -1.3 ± 4.5). Patients on OCA in the DB period showed a decrease in treatment emergent pruritus incidence, from 56-68% after 12 months of DB treatment to 19-36% during ongoing LTSE treatment. Initiation of OCA treatment resulted in a decrease in HDL-C which remains stable through treatment in all groups. OCA treatment improves liver biochemistry, which is sustained throughout the course of the LTSE. Pruritus was the most common treatment emergent AE, but its incidence appeared to lessen with longer treatment.

Patients with polycystic livers more than two times the normal size are likely to develop symptoms

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Progressive growth of hepatic cysts can lead to symptomatic hepatomegaly in polycystic liver disease (PLD). Our primary aim was to determine at which threshold of liver volume PLD patients become symptomatic. As a secondary objective we investigated which symptoms are associated with higher liver volume. We used the PLD questionnaire (PLD-Q), a validated questionnaire that assesses frequency and discomfort of PLD-related symptoms, to determine the symptom burden. In a cohort of 291 PLD patients that have completed the PLD-Q and rated themselves as symptomatic or not (NCT02173080), we have defined the PLD-Q cut-off value of being symptomatic with receiver operating characteristic (ROC) analysis. The optimal PLD-Q cut-off score was 31 points with an area under the curve (AUC) of 0.832 ($p<0.001$). Next, we used base data of PLD patients from two prospective studies (DIPAK observational study and CURSOR randomized controlled trial (NCT02021110). All patients completed the PLD-Q and had liver volume imaging (CT or MRI) measured by segmentation. In order to determine the liver volume cut-off value for being symptomatic, we used the PLD-Q cut-off value from the previous step in another ROC analysis with liver volume as independent variable. Spearman correlations were calculated between symptoms and liver volume. We included 82 of the 131 patients from the prospective studies (main exclusions: no PLD n=26, no PLD-Q n=7 or no imaging n=8). Most patients were female (n=67) with a mean age of 48 years. Median liver volume was 3879 mL (IQR: 2452 – 5891). Cut-off liver volume for being symptomatic was 3472 mL (AUC 0.805, $p<0.001$) with a sensitivity of 80% and a specificity of 73%. This cut-off volume has a positive and negative predictive value of 66% and 82% respectively. Dissatisfaction with abdomen size was strongly correlated with liver volume ($r=0.63$). Fullness, early satiety, pain in rib cage, shortness of breath, limited mobility, anxiety about the future and, problems with intercourse correlated moderately ($r=0.40$-0.59). There was a weak correlation with lack of appetite, pain in side and tiredness ($r=0.20$-0.39). Nausea ($r=0.17$, $p=0.146$) and abdominal pain ($r=0.17$, $p=0.127$) were not correlated with liver volume. Conclusion: Patients with liver volumes equivalent to two times the normal size are likely to develop PLD-related symptoms. In patients with smaller livers, other causes that lead to similar symptoms should be considered. Most PLD-related symptoms are associated with larger liver volume, except for nausea and abdominal pain.

IgG4-associated cholangitis in patients resected for presumed perihilar cholangiocarcinoma

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Background: Distinguishing perihilar cholangiocarcinoma (CCA; Klatskin tumor) from benign forms of sclerosing cholangitis affecting the hilar bile ducts is challenging, since histological confirmation is difficult to obtain by brush or biopsy and accurate non-invasive diagnostic tests were lacking so far. Immunoglobulin G4-associated cholangitis (IAC), an imitator of CCA, is a newly recognized inflammatory disease that can present as sclerosing cholangitis with/without (peri-)hilar tumor formation, can be accurately diagnosed with a novel qPCR test, and is responsive to corticosteroid treatment. The aim of this study was to investigate the incidence of IAC in patients resected for presumed CCA over a period of 30 years. Material & Methods: Benign liver and bile duct resection specimens without signs of malignancy of patients resected for presumed CCA in the Academic Medical Center between 1984 and 2015 were identified from a database. Histological sections were stained for IgG4+ B cells and scored according to international consensus criteria for lymphoplasmacytic infiltration, storiform fibrosis and obliterative phlebitis. The combination of >10 IgG4+ B cells/high-power field together with two histological consensus criteria was considered highly suggestive of IAC. Results: Of the 320 patients that had undergone liver and bile duct resection for presumed CCA, 46 patients (14%) were found to have a benign stricture and/or tumor and no CCA. Histological criteria for IAC were fully met by 17 of the 46 patients (37%). The remaining patients (n=29) were diagnosed with unclassified sclerosing inflammation for which also IAC cannot be excluded.
Conclusion: Benign biliary disorders mimicking perihilar cholangiocarcinoma led to a considerable number of extended liver resections during the last three decades. Histological consensus criteria of IAC were fully met in more than a third of these patients. Novel accurate diagnostic tests for IAC might reduce misdiagnosis and unnecessary extended surgery.

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Post-transplant lymphoproliferative disease after adult liver transplantation and its prevention by pre-emptive strategy based on Epstein-Barr viral load monitoring. A single center study

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Epstein-Barr virus (EBV) primary infection or reactivation can occur after liver transplantation (LT). A serious complication that may occur after LT is post-transplant lymphoproliferative disease (PTLD). In paediatric LT recipients peripheral blood EBV-DNA Viral Load (VL) monitoring in the first year after LT, with a pre-emptive strategy in case of positivity including reduction of immunosuppression (IS), has been reported to lead to a lower incidence of PTLD. For adult LT recipients, with less primary EBV infection and a lower PTLD incidence, the value of EBV monitoring is unknown. The aim of this single centre study was to examine the impact of a strategy based on EBV-VL monitoring on the incidence of PTLD in adult LT recipients. From a single center a historic control group of consecutive first LT recipients without EBV-VL monitoring (1992-2002) was compared (Poisson regression) to consecutive first LT recipients (2003-2014) with EBV-VL monitoring. EBV-VL in plasma was quantified by RT- PCR weekly during the first month, 2-weekly in the second month, then monthly until 1 year after LT. IS was reduced in case of two positive VLs, followed by IS cessation and anti-CD20 infusion in case of no VL reduction. Demographic and clinical features, including base immunosuppression, rejection and its treatment, data from EBV serostatus and EBV-VL monitoring, and of PTLD (WHO classification 2008), its treatment and outcome were retrospectively retrieved form the electronic database and patient dossiers. EBV IgG serostatus at LT in the non-monitoring group vs monitoring group was positive in 95% vs 97% recipients (NS). In the monitoring group EBV-VL remained undetectable in 184 recipients, but became detectable in 78 recipients (6 after rejection), 48 transient (so IS was not reduced) and 30 persistent (then IS was reduced, one with cessation of IS and anti-CD20 infusion; 2 developed rejection). In the non-monitoring group 7/126 recipients developed PTLD, in the monitoring group none of 262 developed PTLD (p=0.0149 with an estimated hazard ratio of 9.7445). There was no association of PTLD with other factors, including type of immunosuppression. All PTLDs were treated with IS cessation, six anti-CD20/19, two CHOP, two radiotherapy. One died early from biliary sepsis, treatment of PTLD was successful in 6/7 cases.
Conclusion: These data for the first time demonstrate that EBV-DNA monitoring in the first year after first LT in adult recipients, with IS reduction followed by a step-up of anti-CD20 infusion in case of persistently detectable EBV-DNA, leads to a significant reduction of the incidence of PTLD -in this cohort complete prevention-.

Mitochondrial reactive oxygen species production triggers hepatic ischemia/reperfusion injury by inducing the release of high-mobility group box 1

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Hepatic ischemia/reperfusion (I/R) injury is an often unavoidable consequence of major liver surgery during which the liver is damaged by disproportional priming of the innate immune system. The release of damage-associated molecular patterns (DAMPs) activates immune cells after I/R, but the trigger for DAMP release is elusive. Based on the biochemical origin of I/R injury, it was hypothesized that DAMP release is caused by mitochondrial reactive oxygen species (ROS) production during early reperfusion. It was first investigated which DAMP is most relevant for clinical liver I/R. As such, plasma levels of the DAMPs high-mobility group box 1 (HMGB1), mitochondrial DNA, and histones were measured 1 and 6 h after surgery in 39 patients who had undergone a major liver resection with (N=26, I/R) or without (N=13, control) the use of intra-operative liver ischemia. It was next tested whether neutralizing mitochondrial ROS production could inhibit DAMP release in murine liver I/R. Male C57Bl/6J mice were therefore subjected to 30 min of partial liver ischemia or sham operation (4-10/group). Animals were sacrificed 6 or 24 h after surgery. Mice were treated intravenously with 1 mg/kg of the mitochondria-targeted antioxidant MitoQ or with sterile saline. A subgroup additionally received pro-inflammatory disulfide HMGB1 intraperitoneally at the start of reperfusion. Plasma transaminase levels and hepatocellular necrosis scores were used as primary injury readouts. Systemic HMGB1 levels were measured by ELISA. Hepatic ROS production was spectroscopically quantified in vivo using hepotargeted liposomes to deliver the oxidation-sensitive fluorogenic probe $CDCFH_2$ selectively to hepatocytes. Innate immune activity was measured using a bead-based flow cytometric cytokine array, spinning disk intravital microscopy, and whole-body imaging of neutrophil elastase activity. In patients, HMGB1 was the only DAMP that increased more substantially following liver surgery with I/R than in the control arm. HMGB1 correlated well to the used duration of ischemia and to the post-operative transaminase peak. In mice, MitoQ neutralized hepatocyte ROS production during early reperfusion and decreased HMGB1 release by ±50%. In doing so, MitoQ suppressed transaminase release, hepatocellular necrosis, neutrophil activation, and cytokine production. The protective effects of MitoQ were lost if disulfide HMGB1 was reconstituted at the start of reperfusion.

Conclusion: HMGB1 is the DAMP most relevant for clinical liver I/R injury. Detoxifying mitochondrial ROS during early reperfusion with MitoQ prevents HMGB1 release and attenuates hepatic I/R injury in mice.

Liver transplantation for cirrhosis secondary to non-alcoholic steatohepatitis is not performed at the expense of major postoperative morbidity

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Background: Non-alcoholic steatohepatitis (NASH) is an emerging indication for liver transplantation due to the obesity pandemic. NASH frequently coexists with multiple comorbidities such as type 2 diabetes mellitus (T2DM), cardiovascular disease and the metabolic syndrome(MetS). Recent studies have shown that long-term patient and graft survival of patients transplanted for NASH cirrhosis are comparable to other indications. However, limited data exists about the short-term (procedure- related) complications after transplantation. Therefore, our aim was to investigate whether these patients are at an increased risk of short-term complications following transplantation. Methods: This is a single center retrospective cohort study including all adult patients (≥18 years) who underwent liver transplantation between January 2009 and December 2015 (N=224). Exclusion criteria were liver transplantation for acute hepatic failure, non-cirrhotic liver disease or re-transplantation within 90 days. Post-operative complications within 90 days were classified according to the Clavien Dindo classification of surgical complications (Table 1). NASH was defined by either: 1) histologic evidence of NASH on biopsy or explant; 2) imaging showing hepatic steatosis; 3) a phenotypic diagnosis consisting of BMI ≥ 30 kg/m2 and presence of T2DM (by either HbA1c ≥ 47 mmol/L or glucose lowering medication use) or the presence of at least 3 out of 5 diagnostic criteria for MetS as defined by the NCEP Adult Treatment Panel (ATP III). A $p<0.05$ was considered significant. Results: Out of 152 eligible patients, 32 patients (21,1%) were transplanted for NASH cirrhosis. Patients with NASH cirrhosis were significantly older (59.2 vs. 54.8 years, $p=0.009$), more obese (BMI≥30 kg/m^2) (65.6% vs. 8.3%, $p<0.001$), had more T2DM (71.9% vs. 19.2%, $p<0.001$) and were more likely to meet criteria for MetS (82.8% vs. 35.7%, $p<0.001$). In univariate analysis, this group suffered from more grade I complications (1.5 vs. 1.03 events per patient, $p=0.016$) and more grade II urogenital infections (50.0 % vs.22.5%, $p=0.002$). Major complications as well as 90-day mortality in both groups was similar (3% vs. 3%).
Conclusion: In patients transplanted for NASH cirrhosis postoperative major morbidity and mortality rates were comparable with patients transplanted for other indications, despite increased (minor) grade I postoperative complications.

The effectiveness of non-surgical interventions in biliary duct complications after liver transplantation

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Biliary duct complications, consisting of bile duct leakage and bile duct strictures, remain the Achilles' heel of orthotopic liver transplantation (OLT), with a reported incidence of up to 40%. Treatments of first choice are endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) with a reported wide range of effectiveness of 50 till 100%. We performed a single-center retrospective cohort study to evaluate the success rate of non-surgical interventions in liver transplant recipients with biliary complications. Additionally, we looked for risk factors for failure of this mode of therapy. Study period was between January 2006 and December 2015. Graft-, recipient- and treatment characteristics were collected. Treatment was defined a success, if radiologic imaging showed resolving of bile duct complication without additional intervention in six months thereafter. A multivariate analysis was performed to identify risk factors for failure of therapy. Overall 451 transplants were included in this study. Biliary duct complications developed in 35.5 percent of liver grafts (n=160). Anastomotic bile duct stricture (AS) was the most common complication (n=100), followed by non-anastomotic bile duct strictures (NAS) (n=39) and bile duct leakage (n=14). ERCP was the primary choice of treatment in 115 cases and PTC in 34. Overall success rate was 80%. AS could be successfully treated with non-surgical interventions in 84%, bile duct leakage in 88% and NAS in 45% of the cases, respectively. No differences between ERCP and PTC were observed in relapse rate of bile duct complication, treatment related complications and duration of treatment. Prolonged warm ischemia time (WIT) in minutes (HR. 1.06, 95%CI 1.02-1.10; $p<0.01$) and diagnosis of NAS (HR. 1.92, 95%CI 1.24-2.96; $p<0.001$) were associated with failure of treatment.
Conclusion: Biliary duct complications after OLT are common. Non-surgical interventions, independently of type of procedure, are successful for management of AS and bile duct leakage. NAS and prolonged WIT are associated with less successful therapy outcome.

Bacterascites is associated with poor clinical outcome in decompensated cirrhosis

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Bacterascites is a common variant of ascitic fluid infection. Limited information is available regarding this entity and the prognostic impact. Therefore, we aimed to evaluate the prognostic significance of bacterascites. Retrospective study of all consecutive ascitic cultures obtained in 2003 to 2006 and 2013 to 2015 in patients with decompensated liver cirrhosis. Patient records were used to evaluate demographic, clinical, and laboratory data. Patients were classified in three groups: bacterascites, SBP, and non-neutrocytic sterile cultures (control). SBP was defined as a polymorphonuclear neutrophil count ≥250 cells/μL in ascites and bacterascites as bacterial presence in ascites with a polymorphonuclear neutrophil count <250 cells/μL. Patients with bacterascites developing SBP within 7 days were classified as SBP and after 7 days excluded. The clinical outcome survival was defined as no liver transplantation or death one year after ascites diagnosis. A total of 304 patients were included (62% male, mean age 56 (SD±12) years, mean MELD 19 (SD±8)). Thirty-one patients were diagnosed with bacterascites, 85 with SBP and 188 patients were considered as controls. SBP patients were younger with a mean age of 54 years (P=0.041), and control patients had a lower MELD score 18 (P=0.006). Uni- and multivariate proportional-hazard analysis identified MELD score (hazard ratio 1.066; 95% CI 1.048-1.084; P<0.001), albumin <11 g/L in ascites (hazard ratio 1.714; 95% CI 1.074-2.736; P=0.024), bacterascites (hazard ratio 1.990; 95% CI 1.226-3.232; P=0.005), and SBP (hazard ratio 1.486; 95% CI 1.040-2.122; P=0.029) as risk factors, increasing the probability of liver transplantation or death within 1 year. There was no statistically significant difference between SBP and bacterascites regarding the bacterial flora. Survival analysis indicated that the prognosis of bacterascites and SBP patients was comparable and significantly worse than in the control group (P=0.004).
Conclusions: Bacterascites is an independent prognostic factor for survival in patients with decompensated cirrhosis. Currently, the important impact of bacterascites might be underestimated. Presumably, mechanisms involved in bacterial translocation and neutrophil immune response determine the poor prognosis associated with bacterascites.

Primary Biliary Cholangitis at a Young Age - Clinical Characteristics and Prognosis

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Background: Previous studies suggest that patients diagnosed with PBC at a young age differ from those diagnosed in middle age, regarding clinical features, response to therapy and prognosis. The aim of this study was to quantify these potential differences related to age in a large, international population. Methods: The Global PBC Study Group's cohort was used. Patients <33.5 yrs of age at PBC diagnosis were classified as early onset PBC (youngest 5% of the cohort). The young group was sex- and country matched 1:2 to PBC patients of average age at diagnosis. By chart review, data were collected on symptoms, co morbidities, laboratory findings and events. Results: We included 95 early onset PBC patients and 190 matches (92% female), originating from the Netherlands, Canada and Italy. Median FU was 8.4yrs (IQR 4.7-13.6). Median age at diagnosis in the early onset group was 30.3 yrs (27.1-32.3), and 54.1 (52.2-55.8) among controls. UDCA treatment was given to 85% of young patients and 92% of controls. In the young group, 1 liver-related death and 10 liver transplantations (LTs) occurred. Among matches, 17 died (n=7 liver related) and 6 underwent LTs. Early onset PBC patients were more often symptomatic at diagnosis (76%) than their matches (45%) (p<0.001). Fatigue and pruritus were present in 62% and 52% of young patients, as opposed to 34% and 25% of matches (both p<0.001). Young patients were also more likely to have AI diseases (54%) than controls (37%) (p=0.007). Transplant-free survival of young patients with fatigue and/or pruritus was worse than that of asymptomatic young patients; after 10 years, no death's or LTs were noted in the symptomatic young patients, against 9 endpoints in the asymptomatic young group (p=0.19). Base bilirubin and ALP were comparable between groups (p=0.16, p=0.24). However, 54% of young patients responded to UDCA therapy (Paris I criteria), as opposed to 74% of matches (p=0.006). Transplant-free survival for both groups was similar (HR1.00; 95%CI0.49-2.06). Five- and 10-year transplantation-free survival was 95% and 88% of young patients, vs. 95% and 89% of matches. Survival free of liver-related death or transplantation was worse for the young group than for matches (HR1.62;0.74-3.58).

Conclusion: Patients with PBC at a young age more often show PBC-related symptoms and presence of other AI diseases at diagnosis. Young patients are also less likely to show biochemical response to UDCA. Their transplant-free survival time is similar, and worse considering liver related events. Given their young age at diagnosis; life expectancy of the early onset PBC patients is much poorer than that of middle age PBC patients.

Differences in patient characteristics and long-term outcome between Asian and European patients treated with radiofrequency ablation for hepatocellular carcinoma

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Radiofrequency ablation (RFA) is a curative treatment option for patients with unresectable hepatocellular carinoma (HCC). The Barcelona Clinic Liver Cancer (BCLC) classification system is the most widely adopted staging system for HCC worldwide and is endorsed by the European, American and Asian Pacific practice guidelines for treatment of HCC. Despite adherence to comparable treatment guidelines, there may be difference in outcome of RFA treatment between continents as a result of geographical differences in characteristics and etiology of HCC. The aim of this study was to compare patient characteristics and long-term outcome of RFA for unresectable, de novo HCC in an Asian and European patient cohort. Retrospective analysis of 279 patients treated with RFA for de novo HCC in a tertiary referral center in Singapore (n=200) and the Netherlands (n=79) was performed. A competing-risk model with recurrence and death as competing events was used to estimate the cumulative incidence of recurrence and death per center. Median follow-up time was 28 months (quartiles: 13-40 months). Mean age was higher in the Asian group (66.5 vs. 60.1 years, p<0.0001). The most common etiology was hepatitis B in the Asian group (48.0%) and alcohol-induced cirrhosis in the European cohort (54.4%). Asian patients had less advanced stages of HCC: respectively 35.5%, 55.0% and 3.0% had BCLC stage 0, A and B versus 21.5%, 58.2% and 15.2% in the European cohort (p=0.01). The cumulative incidence of disease recurrence in the Asian group at 1, 2, 3 and 5 years was 37.0%, 56.4%, 62.3% and 67.7% respectiviely, compared to 32.6%, 47.2% and 53.4% in the European cohort (p=0.474). At 1, 2, 3 and 5 years, the cumulative incidence of death in the Asian group was 2.0%, 3.9%, 4.9% and 4.9% respectively and 7.7%, 9.2%, 14.1% and 21.0% in the European cohort (p=0.155).
Conclusion: Base characteristics of patients treated with RFA for de novo HCC differ between Northern European and South-East Asian patients. Despite these differences, similar short and mid-term treatment outcomes are achieved by applying regional recommendations for RFA in HCC patietns. Long-term recurrence and death rates differ between the two cohorts as a result of differences in base patient characteristics and patient selection.

Patients' misconceptions about surveillance for hepatocellular carcinoma: Education is needed

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Current guidelines advise surveillance for hepatocellular carcinoma (HCC) in high-risk patients. However, there is widespread underuse of HCC surveillance in clinical practice. Patient knowledge and involvement in decision-making are associated with higher HCC surveillance rates. We therefore explored patients' expectations of HCC surveillance. 120 consecutive patients who visited our outpatient clinic in 2015 and underwent regular HCC surveillance (ultrasound with or without AFP at an approximately 6-month interval) were asked to fill in a 7-item questionnaire regarding their perceptions on HCC surveillance. Furthermore, expectations of 7 Dutch experts in the field of hepatology were evaluated based on a similar questionnaire. In total, 111 high-risk patients for HCC with underlying chronic liver disease filled in the questionnaire (response rate 92%). Of these patients, 91 had cirrhosis due to alcohol (n=14), hepatitis B (n=11), hepatitis C (n=32), NASH (n=11) or other risk factors (n=23), and 20 were non-cirrhotic but with increased HCC risk due to hepatitis B (n=18) or F3 fibrosis in hepatitis C (n=2)). In contrast to current knowledge, most patients think that: 1. performing regular surveillance can prevent HCC development, 2. HCC is always detected by ultrasound, and 3. surveillance is only indicated if patients have complaints. In multivariate logistic regression analyses (included variables: education level, gender, age, social-economic status, etiology of underlying liver disease, presence of cirrhosis, number of performed surveillance tests) only lower education level was an independent predictor of misconception. Second, patients largely underestimate HCC-related mortality rates. Nearly 50% of patients think that curative treatment is still possible in ≥40% of HCC cases detected without surveillance. Furthermore, many patients believed that surveillance reduces the risk of HCC deaths by ≥70%. Lower education level was no predictor for misconceptions about HCC-related mortality. Expectations of Dutch experts in the field of hepatology were markedly lower than patients' expectations. For example, most experts thought that surveillance in the current form does not lower HCC-related mortality at all. In conclusion, there is a profound discrepancy between patients' expectations of HCC surveillance and real benefits in clinical practice. In the current era of increased awareness and doctors' obligations to provide adequate information about benefits and risk, better education on HCC surveillance is needed in high-risk patients with underlying chronic liver disease.

FXR agonist obeticholic acid induces liver growth but can transiently exacerbate biliary injury in rats with obstructive cholestasis

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Obstructive cholestasis impairs liver regeneration following major hepatectomy and compromises postoperative outcomes after liver surgery. The bile salt receptor farnesoid X-receptor (FXR) is a key mediator of liver regeneration for which synthetic agonists have recently been developed. We examined the effect of FXR-agonist obeticholic acid (OCA) on liver regeneration in a rat model of bile duct ligation (BDL) and partial hepatectomy (PHx). Male Wistar rats (300-325g) were subjected to either sham surgery or BDL at t=0 followed by PHx at t=7 days. BDL rats daily received either OCA (10mg/kg/d per oral gavage) or vehicle from t=0 until sacrifice. Rats were sacrificed on days 7 (before PHx), 8, 9, 10, and 12. Outcome parameters included liver weight, histological scoring of hepatocyte proliferation (Ki-67) and liver injury (H&E), clinical chemistry, and transcriptional analysis of regeneration pathways in liver and intestinal biopsies. At t=7 (i.e., directly prior to PHx), dry liver weight was higher in the BDL-OCA group than in the control and BDL-vehicle group (6.6±0.4 g versus 4.0±0.1 g and 5.3±0.5 g respectively). Increased proliferation at t=7 was reflected by more Ki-67^{+}-hepatocytes and increased cyclinD1 mRNA expression in the BDL-OCA group. This increase in hepatocyte proliferation in the BDL-OCA group was accompanied by a >20-fold induction of mitogenic FXR target fibroblast growth factor 15 in ileal enterocytes. As a result, impaired liver regeneration in the BDL-vehicle group on day 5 post-PHx was rescued by OCA treatment. Despite these positive effects on liver (re)growth, OCA transiently increased alka phosphatase (~8-fold) and alanine aminotransferase (~3-fold) levels at t=7 in BDL rats (i.e., directly prior to PHx). This was likely caused by the ~7-fold upregulation of the prototypical FXR target and canalicular bile salt transporter bile salt export pump (BSEP) by OCA under BDL conditions. Histological assessment of hepatocellular necrosis, ductular reaction, and fibrosis was comparable between BDL-OCA and the BDL-vehicle groups. Conclusion. OCA induces liver growth in cholestatic rats prior to PHx, conceivably by inducing FXR-linked FGF19 production in enterocytes, but exacerbates biliary injury during obstructive cholestasis due to forced BA pumping into an obstructed biliary tree. OCA treatment following biliary drainage should avoid this potential problem and may further improve liver regeneration in post-cholestatic patients undergoing liver resection.

Coffee & herbal tea consumption is protective of liver stiffness in the general population: The Rotterdam Study

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Tea and coffee are the most consumed beverages worldwide and share common substances, like polyphenols and caffeine. Both substances have been proposed to exhibit beneficial effects on liver health. Several studies have shown that coffee prevents liver cirrhosis, but it is unknown if this is also true for fibrosis development in the general population. Therefore our aim is to study the effect of coffee and tea consumption on liver fibrosis, assessed by transient elastography (TE), in a large well-characterized population study. The Rotterdam study is an ongoing prospective population-based cohort study of healthy inhabitants of the suburb Ommoord since 1990. From 2009 onwards, all participants aged≥45 underwent TE and completed a validated 389-item food frequency questionnaire. Linear and logistic regression analyses were used to study the association between coffee and tea consumption and liver stiffness measurements (LSM). Clinically relevant fibrosis was defined as LSM≥8.0kPa and secondary causes of increased LSM were excluded. Coffee and tea consumption were categorized into no, low (≤2), or high (≥3) intake in cups/day. Tea was further specified into subtypes of green, black and herbal tea (categorized as no or any). Data was available for 2424 participants (age 66.5 ± 7.4; 43.8% male) of whom 125 had LSM ≥ 8.0kPa (5.2%). Overall, 93.2% and 84.7% of the individuals consumed coffee and tea, resp. Proportion of LSM ≥ 8.0kPa decreased with increasing coffee intake (7.8%, 6.9% and 4.1% for no, low and high coffee consumption resp.; P_{trend}=0.006). Logistic regression analyses confirmed this inverse relation between coffee intake and LSM ≥ 8.0kPa even after adjustment for total energy, age, sex, BMI, insulin resistance, ALT, steatosis, smoking, alcohol, milk and sugar use (OR_{low}=0.76, CI 0.37-1.54; OR_{high}=0.40 CI 0.20-0.81; P_{trend}=0.003). Overall tea consumption was not associated with LSM. Interestingly, herbal tea consumers had lower LSM in multivariate linear regression (βeta=-0.042, CI-0.069;-0.015, P=0.003) and less frequently LSM≥8kPa (5.9% vs. 3.9%, for no and any consumers resp.; P=0.035).

Conclusions: High coffee consumption appears protective of liver stiffness even in individuals with no known liver disease. Interestingly, in this first study to correlate herbal tea and liver health, herbal tea is independently associated with lower LSM. Unlike coffee, herbal tea does not contain caffeine, which leaves room for thought whether the anti-fibrotic effects can be ascribed to polyphenols. More studies confirming this association of herbal tea, coffee and LSM are needed to eventually develop preventative and therapeutic strategies for a healthy liver.

Under-reporting of complementary and alternative drug use in liver disease patients

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Complementary and alternative medicine (CAM) encompasses a huge variety of treatments including homeopathy, herbal medications and acupuncture. We hypothesize that CAM use in liver disease patients is underreported in clinical practice and this can lead to relevant pharmacological interactions. The aims of this study were to assess the prevalence and type of CAM use, and experiences with CAM use in liver disease patients. We conducted a cross-sectional survey among the members of the Dutch Liver Patients Association. All members received a questionnaire with 26 questions about demographics, liver disease, frequency and type of, and experiences with CAM use (Survey Monkey©). We received 213 completed questionnaires. Mean age of respondents was 55 years (SD 13.5), 64 (30%) respondents were male and main liver diseases were primary sclerosing cholangitis (PSC, n=51, 24%), primary biliary cholangitis (PBC, n=40, 19%), autoimmune hepatitis (AIH, n=39, 19%), PSC-PBC-AIH overlap syndrome (n=11, 5%), and viral hepatitis (n=16, 8%). A total of 96 patients (43%, 95% confidence interval 36-50%) reported CAM use; type of CAM was diverse and silymarin was most frequently reported (n=18, 8%). Up to 35% of CAM users had not divulged CAM use to their physician. The majority of patients (n=63, 76%) experienced beneficial effects of CAM and 58 patients (71%) would recommend CAM to other patients.
Conclusion: Prevalence of CAM use is high (43%) in liver disease patients and 35% of patients do not report CAM use to their physician. Physicians should actively ask for CAM use because openness about CAM use can prevent potential harmful interactions with prescribed medication.

High rate of HBsAg loss after peginterferon based combination treatment for chronic hepatitis B patients: results after 5 years of follow-up

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Several studies have shown that combining peginterferon alfa-2a (pegIFN) with a nucleotide analogue can result in higher rates of HBsAg loss than either therapy given alone. However, the long term sustainability of HBsAg loss upon such treatment regimens is not well known. In this prospective study we investigated the 5-year outcome in chronic hepatitis B (CHB) patients treated with pegIFN and adefovir combination therapy. In the initial study, 92 CHB patients were included. At baseline, patients (44 HBeAg positive, 48 HBeAg negative) had HBV DNA levels > 100,000 c/mL (17,182 IU/mL) and elevated ALT levels or histological signs of active hepatitis. Patients were treated for 48 weeks with pegIFN alfa-2a 180 mcg/week and 10 mg adefovir dipivoxil daily. For the long term follow-up study, routine check-up as well as biochemical and serological testing was performed yearly. At year 5 of follow-up 70 (32 HBeAg positive, 38 HBeAg negative) patients were still included, reasons for withdrawal were lost to follow-up (n=18), death (n=2) and inclusion in another treatment study (n=2). At year 5, 19% (6/32) of HBeAg positive patients and 16% (6/38) of HBeAg negative patients had HBsAg loss, and no sero-reversion was observed. The 5-year cumulative Kaplan-Meier estimate for HBsAg loss was 17.2% for HBeAg positive patients and 19.3% for HBeAg negative patients. In total 16 patients lost HBsAg of which 12 patients reached end-of-follow-up; 2 died and 2 were lost to follow up. 14/16 patients who lost HBsAg had positive anti-HBs antibodies (>10 IU/L) at any time point during follow-up. At the end of 5 years follow-up, 2/32 HBeAg positive patients and 5/38 HBeAg negative patients had a durable combined response (HBV DNA <2,000 IU/mL with ALT normalization and HBeAg negativity excluding retreated patients and patients with HBsAg loss). At year 5, in total 63% (20/32) of HBeAg positive and 71% (27/38) of HBeAg negative patients were retreated during follow-up. The cumulative Kaplan-Meier estimate for retreatment was 60% of patients at year 5.
Conclusion: At year 5 of follow-up, 17-19% of CHB patients treated with pegIFN based combination therapy had HBsAg loss and 88% of these had developed anti-HBs antibodies. PegIFN based combination treatment can lead to a durable functional cure in patients with chronic hepatitis B.

Addition of (pegylated) interferon to entecavir increases serological response in Hepatitis B e Antigen-positive, chronic hepatitis B patients

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Multiple treatment combinations of (pegylated) interferon (PegIFN) and nucleos(t)ide analogues have been evaluated in patients with chronic hepatitis B (CHB), but the optimal regimen to achieve serological response remains unclear. We evaluated whether PegIFN add-on to entecavir (ETV) treatment increased serological response compared to ETV monotherapy in patients with Hepatitis B e-Antigen (HBeAg) positive CHB. Secondly, we assessed whether the length of ETV pretreatment and PegIFN add-on treatment influenced response. We analyzed HBeAg-positive CHB patients from two previous investigatorinitiated, randomized trials. All patients received ETV pretreatment for at least 24 weeks. Patients were then allocated to (a) 24 to 48 weeks of ETV + PegIFN alpha-add-on, or (b) 24 to 48 weeks of continued ETV monotherapy. Combined response was defined as HBeAg loss with HBV DNA <2000 IU/mL and was assessed 24 weeks after consolidation therapy which lasted for 24 weeks as well. Logistic regression techniques with stratified analysis on previous PegIFN were applied. Out of the 251 patients, 123 started on PegIFN add-on and 128 continued NA monotherapy. Combined response was observed in 37 (31.7%) patients allocated to add-on therapy and 27 (21.6%) patients with ETV monotherapy (p=0.10). In multivariable analysis, patients with lower HBsAg and HBV DNA levels at base showed an increased response to PegIFN addition (OR (95%CI): 0.52 (0.31-0.89), p=0.02; 0.34 (0.26-0.62), p<0.005, respectively). Among IFN naive patients, add-on Peg-IFN therapy showed a significantly better combined response than ETV monotherapy (32 (35.3%) vs 20 (20.2%); p=0.02). In the overall group, the duration of ETV pretreatment showed a suggestive association with higher response in patients with PegIFN add-on (OR (95%CI): 0.98 (0.95-1.00), p=0.10). The 24 week PegIFN add-on regimen did not differ from 48 week add-on on combined response (32.1% vs 30.8%; OR (95%CI): 1.82 (0.52-6.36), p=0.35). Out of the 22 (18%) patients on PegIFN add-on therapy who discontinued treatment in case of a positive response at week 48, 13 (65%) patients had sustained response at week 96. In contrast, there were 2 (18.2%) sustained responders out of 11 ETV monotherapy patients who discontinued (p=0.02).
Conclusions: PegIFN add-on to ETV showed a suggestive association with higher serological response compared to ETV monotherapy in patients with CHB. CHB patients that are naive to PegIFN treatment are likely to benefit most from PegIFN add-on therapy. The ETV pretreatment length was indicative for better response; the duration of PegIFN add-on therapy did not influence treatment response.

Proton pump inhibitors decrease phlebotomy need in HFE-related haemochromatosis A double-blind randomized controlled trial - HE-PPI trial

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Phlebotomy is the standard of care for HFE-related haemochromatosis but its applicability can be limited due to post-phlebotomy fainting, weakness and bruising. Two retrospective studies showed that patients taking proton pump inhibitors (PPIs) needed fewer phlebotomies to maintain their target serum ferritin (SF). We conducted a prospective randomized double-blind placebo-controlled trial to confirm the finding (clinicaltrials.gov: NCT01524757). p.C282Y homozygous patients (18-75 years) were treated with PPI (Pantoprazol 40mg) or placebo for 12 months. Inclusion criteria: patients were required to be on SF 50-100 µg/L, maintenance therapy for ≥12 months with phlebotomy frequency of ≥ 3/year. Phlebotomy was performed when SF level > 100 µg/L on bimonthly checks. Primary endpoint: number of phlebotomies necessary to keep SF < 100 µg/L. 30 patients (22 males, 8 females) were enrolled (15 PPI, 15 placebo). A highly significant difference in the total amount of phlebotomies needed was observed, during one year of treatment (mean±SD) (placebo 2.60±1.55; PPI 1.27±1.03) p=0.0052). Although SF (U/L) was higher in the PPI group at the start (placebo 57.5±10, PPI 74.4±27.5; p=0.039), the placebo group reached a significantly higher SF than PPI group at the end of 12 months (125.8±37 vs 90.5±46; p=0.0145) despite double the amount of phlebotomies.
Conclusion: The use of PPI significantly reduces the need for phlebotomies in HFE-related haemochromatosis patients (p=0.0052). In view of the well-known long-term safety of PPIs, this treatment offers a valuable addition to standard therapy.

Ribavirin plasma level is an independent predictor for sustained virologic response in difficult to treat hepatitis C-infected patients treated with direct-acting antivirals + ribavirin combination

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The role of ribavirin (RBV) is controversial in the era of highly effective direct-acting antivirals (DAAs). This study assessed the potential influence of RBV steady state plasma levels on sustained virologic response (SVR) in difficult-to-treat patients, and explored RBV therapeutic ranges. Consecutive HCV patients treated with DAAs+RBV from four academic medical centers were enrolled. RBV plasma levels were measured at treatment week 8 (generally steady state) using validated HPLC assay. 131 patients were included: 44% received daclatasvir/sofosbuvir (SOF), 31% simeprevir/SOF, 20% SOF, 3% ledipasvir/SOF and 2% PEG-interferon/SOF during 12–24 weeks. 40% had genotype 1a, 25% genotype 1b, 21% genotype 3, 8% genotype 4, and 6% genotype 2. 65% were treatment-experienced, 58% had F4 fibrosis and 7% Child-Pugh scores of ≥7. 40% had 1, 43% 2 and 6% 3 difficult-to-treat characteristics (i.e. F4 fibrosis, treatmentexperienced and genotype 3). Median (range) RBV cumulative dose was 12.8 (2.3–22.4) mg/kg/day, with RBV level of 2.9 (0.4–10.0) mg/L. RBV levels correlated positively with base creatinine (R=0.30, p=.001). Patients with significant anemia (Hb<10 g/dL) during treatment tended to have higher RBV levels than those without anemia (3.3 (1.0–7.1) vs 2.5 (0.4–10.0) mg/L, p=.16). SVR_{12} was achieved in 110 (84%) patients, whereas 21 (16%) relapsed. In univariate analyses, no significant differences in age, gender, ethnicity, treatment-experience, F4 fibrosis, Child-Pugh score, base creatinine, HBV or HIV coinfection rates were found between patients with and without SVR_{12}. Patients with SVR_{12} had significantly higher frequencies of genotypes 1a (43% vs 24%) and 1b (29% vs 5%), daclatasvir/SOF (49% vs 19%) or simeprevir/SOF (34% vs 19%), 12 weeks DAA duration (83% vs 43%), and higher RBV level (2.8 (0.4–10.0) mg/L vs. 2.2 (1.6–2.6) mg/L) (all p<.05). Of all factors significantly different in univariate analyses, RBV level was the only independent predictor of SVR_{12} in multivariate analysis (Odds Ratio 2.05 (95% confidence interval 1.07–3.95), p=.032). The therapeutic range for RBV level was 2.3–3.1 mg/L (AUC: 0.68). RBV level ≥2.3 had a sensitivity of 0.69, specificity of 0.52, PPV of 0.88 and NPV of 0.24 for SVR_{12}, and RBV level ≥3.1 a sensitivity of 0.54, specificity of 0.67, PPV of 0.27, and NPV of 0.87 for significant anemia. Conclusions: In our difficult-to-treat patients treated with DAAs+RBV, RBV steady state levels were the sole independent predictor for obtaining SVR. Ribavirin may remain an important adjunct to DAA regimens in selected patients.

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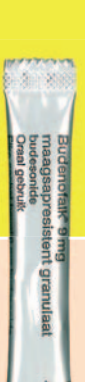

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Retrieval of chronic hepatitis B and C patients: collaboration between different healthcare professionals leads to the identification of patients lost to follow-up

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Background and Aims: Highly effective antiviral treatment regimens are now available for chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV). However, many patients diagnosed with HBV or HCV in the past have been lost to follow-up in primary care and/or hospital care. We aim to retrieve these patients and bring them back into care. Methods: We explored data files of the local Public Health Service and the local microbiological laboratory to identify all registered cases of chronic HBV and HCV in our region for the past 15 years. Identified cases were compared with patients currently known in our hospital. Patients were considered lost to follow-up if not actively known in our hospital. After patients lost to follow-up have been identified, they will be approached via their primary health care physician for evaluation at our hospital. Results: We identified 552 cases of chronic HBV. 22 (5,6%) patients were deceased. The cause of death was in 4/22 (18%) patients liver-related, 11/22 (50%) non-liver related and in 7/22 (32%) patients the cause of death was unknown. In total, 368 of 552 (66,7%) chronic HBV patients were not known in hospital care. Only 266 (72.3%) patients were eligible for retrieval. The remaining 102 patients were not eligible because of unclear legal status (33/102, 32%), imprisonment (32/102, 31%), residing in another region (9/102, 9%) or because their primary care physician was not known (28/102, 27%). 499 cases of chronic HCV were identified. 39 (7,6%) patients were deceased, 12/39 (31%) liver related death, 14/39 (36%) non-liver related death and in 13/39 (33%) the cause of death was unknown. 170 (34%) patients were considered lost to follow-up. Among them, only 107 (63%) patients were eligible for retrieval. Of the remaining 63 patients, 12/63 (19%) had an unclear legal status, 17/63 (27%) were imprisoned, 15/63 (24%) resided in another region and in 19/63 (30%) patients the primary care physician was not known. All patients eligible for retrieval are currently approached via their primary care physician and invited for evaluation at our hospital.
Conclusions: Regional retrieval of patients with chronic hepatitis B or C lost to follow-up is possible when a close collaboration is established between different healthcare professionals. We point out the need to concentrate on patients once diagnosed with HBV or HCV and bring them back into care.

Point shear wave elastography has high diagnostic accuracy for staging of liver fibrosis in patients with chronic hepatitis B and C infection

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Background and aim: Non-invasive evaluation of liver fibrosis is important in determination of prognosis and treatment strategy in patients with chronic hepatitis B (HBV) and C (HCV) virus infection. Vibration controlled transient elastography (TE) is a well-established method for assessment of liver stiffness (LS) and staging of liver fibrosis. Point shear wave elastography (pSWE) is a novel technique that measures the speed of an acoustic wave through the liver to determine LS. This method is integrated in an ultrasound device and could therefore result in more accurate assessment of liver fibrosis due to real time imaging. The aim of this study was to determine diagnostic performance of pSWE for staging of liver fibrosis in patients with chronic HBV and HCV infection. Methods: In this international multicenter study, patients with chronic HBV and/or HCV infection underwent TE and pSWE LS measurement. TE was performed with Fibroscan® (Echosens, Paris, France) and pSWE was performed with ElastPQ®, which is implemented in the EPIQ 7 ultrasound system (Philips Medical Systems, Bothel, USA). Successful TE was defined as 10 successful measurements with an interquartile range of ≤30% of the median. A minimum of 10 successful pSWE measurements was required. TE cut off points for significant fibrosis (≥F2), advanced fibrosis (≥F3) and cirrhosis (≥F4) were 7.0, 9.5 and 14.5 kiloPascal (kPa). Diagnostic accuracy of pSWE was assessed by calculating the area under the receiver operating characteristic curve (AUROC), using TE as a reference. Results: For 265 patients both a successful TE and pSWE measurement were available. The majority was female (54%), mean age was 53 years (19-79) and 67% of patients had chronic HCV infection. Median LS assessed by TE and pSWE was 10.7 kPa (2.7-75) and 7.5 kPa (0.72-44.1). There was a significant linear correlation (R: 0.86, p< 0.001) between TE and pSWE measurements and the linear regression of the Bland and Altman plot was non-significant (p=0.19), proving similar performance. The AUROC (95% confidence interval (CI)) was 0.94 (0.91-0.96) for ≥F2, 0.96 (0.94-0.98) for ≥F3 and 0.96 (0.94-0.98) for ≥F4. Sensitivity and specificity (95% CI) for pSWE were 90.1% (84.4-94.2) and 76.9% (67.6-84.6) for a cutoff point of 5.39 kPa for ≥F2, 93.6% (88.2-97) and 86.3% (79-91.8) for a cutoff point of 6.39 kPa for ≥F3, and 95.3% (89.3-98.5) and 85.5% (79.1-90.6) for a cutoff point of 8.63 kPa for ≥F4, respectively. Conclusions: pSWE performed by the novel elastPQ® method has high diagnostic accuracy for staging of liver fibrosis in patients with chronic HBV and HCV infection.

Free triiodothyronine as determinant of non-alcoholic fatty liver disease in euthyroid subjects: the LifeLines Cohort Study

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Background: Non-alcoholic fatty live disease (NAFLD) is becoming the leading cause of chronic liver disease in de Western world. The liver plays a crucial role in the metabolism of cholesterol and triglycerides and thyroid hormones interact on hepatic lipid homeostasis. Given the importance of variations in thyroid function within the euthyroid range for a considerable number of health issues, including (subclinical) atherosclerosis and biochemical markers of increased cardiovascular risk, it is relevant to examine the relationship of NAFLD with thyroid function parameters in an euthyroid population. Methods: The study was conducted in the LifeLines Cohort Study (N=167,729), a population-based cohort study examining the health and health-related behaviors of participants living in the North of The Netherlands. Only euthyroid subjects (TSH 0.5-4.0 mU/L, FT4 11-19.5 pmol/L and FT3 4.4-6.7 pmol/L) older than 18 years were included. Exclusion criteria were participants with missing data, excessive alcohol use, known hepatitis or cirrhosis, liver functions ≥ three times the upper limit, current cancer, non-white ancestry, previous or current use of thyroid medication and current use of lipid and glucose lowering medication. A priori defined liver biochemistry, thyroid function parameters and metabolic syndrome (MetS) were studied. NAFLD was defined by using the validated Fatty Liver Index (FLI); FLI ≥60 was categorized as NAFLD. A $p<0.01$ was considered significant. Results: Out of 20,289 participants, a FLI ≥60 was found in 4,274 (21.1%) individuals (62.1% men, median age 46 years). Participants with FLI ≥60 had higher ALT, AST, ALP, GGT values and higher prevalence of MetS (46.7% vs. 4.2%, $p<10^{-50}$). In age- and sex-adjusted analysis FLI ≥60 was independently predicted by a higher FT3 (OR 1.34, 95% CI 1.29-1.39, per SD increment, $p<10^{-48}$) and a lower FT4 (OR 0.73, 95% CI 0.70-0.75, $p<10^{-63}$) but not by TSH. The strongest association was found for the FT3/FT4 ratio (OR 1.41, 95% CI 1.39-1.49, $p<10^{-92}$). These associations remained similar after additional adjustment for the presence of MetS (OR 17.9, 95%CI 16.2-19.8, $p<10^{-400}$). In subjects with enlarged waist circumference TSH and FT4 were lower but FT3 was higher, resulting in a higher FT3/FT4 ratio ($p<10^{-46}$).
Conclusion: In this large cross-sectional study of 20,289 participants, we discovered that euthyroid people with suspected NAFLD are characterized by a higher FT3/FT4 ratio, probably secondary to central obesity.

Is nighttime really not the right time for a laparoscopic cholecystectomy?

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A laparoscopic cholecystectomy is a commonly performed operation and is generally considered safe. However, the impact of an out-of-hours procedure on outcome is controversial. We sought to determine the association between an out-of-hours laparoscopic cholecystectomy and post-operative complications within 90days. In 2014, 450 consecutive intended laparoscopic cholecystectomies were performed at our hospital. Therapeutic, operative and outcome data were prospectively collected and subsequently analyzed. We defined out-of-hours as during weekends, national holidays and daily between 5PM-8AM. Of the 450 procedures performed, most were on females(n=286;63.6%), with an overall median age of 54[range:20-84yrs]. The majority were elective procedures(n=395;87.8%) and for symptomatic gallstones(n=310;68.9%). While all were performed with a laparoscopic intent, 16(3.6%) were converted to an open procedure. In total, 39(8.7%) procedures were out-of-hours, all non-elective and in most cases for acute cholecystitis(n=27; 6.0%). Seven(17.9%) out-of-hours laparoscopic cholecystectomies were converted to open(vs n=9 (2.2%);p<0.001). Overall, there were 39 complications in 36 patients(8.0%), these included: surgical-site-infection(n=19;4.2%), bile leak/biloma(n=7;1.6%), retained stones(n=6;1.3%) and death(n=1;0.2%).
Most(n=24;5.3%) complications were classified as minor(Clavien<3). There seemed to be a trend towards an increased incidence of complications among patients who underwent an elective procedure (vs an emergency procedure: (28(7.1%) vs 8(14.5%);p=0.056); moreover, complication rate was significantly higher among out-of-hours cases(n=7(17.9%) vs n=29(7.1%);p=0.017). While, gender, indication for surgery and bile spill were not related to complications(all p>0.05); univariate analyses revealed out-of-hours procedure(OR=2.88;p=0.02) and conversion(OR=4.20;p=0.02) to be associated with an increased risk of complications. Moreover, non-elective laparoscopic cholecystectomy bordered on being a significant factor(OR=2.22;p=0.06). However, on multivariate analysis, these associations with complications were not confirmed(all p>0.05). In conclusion, performance of an out-of-hours laparoscopic cholecystectomy was not found to be an independent risk factor for developing postoperative morbidity and time of day should therefore only be viewed as a relative contraindication. However, the risks of performance of an out-of-hours procedure should be weighed against its benefits and therefore select high-risk patients (i.e. possible complex cases) should be prioritized to undergo a laparoscopic cholecystectomy during the next day, instead of during nighttime.

Conditional Survival After Surgical Resection of Gallbladder Carcinoma: A Multi-Institutional Analysis

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Introduction: While survival after malignancies is traditionally reported as actuarial survival, conditional survival (CS) may be more clinically relevant. CS gives an estimate of overall survival at a certain time point by accounting for "accrued" survival time as time progress. We sought to provide empiric and practical CS data for patients having undergone curative-intent surgery for gallbladder carcinoma (GBC). Methods: 312 patients who underwent resection for GBC between 2000 and 2014 were identified from 10 major hepato-biliary centers. Cox proportional hazard models were used to evaluate factors associated with overall survival. CS estimates were calculated as the probability of surviving an additional 3 years at year "x" after surgery using the formula $CS_3=S_{(x+3)}/S_x$. Results: Median patient age was 66 (IQR, 56-73) and most patients were female (66.7%). At the time of surgery, the majority of patients underwent radical cholecystectomy (77.2%). While actuarial survival decreased over time from 51.1% at 2 years to 31.6% at 5 years following surgery, 3-year CS increased over time among those patient who survived. The CS_3 at 2 years (i.e. the probability of surviving to postoperative year 5 after having already survived to postoperative year 2) was 61.8% compared with the 5-year actuarial OS of 31.6%. In addition, the chance of surviving an additional 3 years if the patient was alive at 3-, 4- and 5-years was 70.5%, 74.1% and 78.2% respectively. Factors associated with reduced actuarial OS were included margin status (HR 3.61; 95%CI:2.47-5.26), tumor size (HR 1.02; 95%CI:1.01-1.02), high tumor grade (HR 2.98; 95%CI:1.47-6.04), residual disease found at reresection (HR 2.78;95%CI:1.49-3.49;p<0.001), and lymph node metastasis (HR 1.95; 95%CI:1.39-2.75)(all p<0.001). The calculated CS_3 exceeded the actuarial survival for all of these high-risk subgroups. For example, patients with residual disease at re-resection had an actuarial survival 23.1% at 5 years versus a CS_3 of 56.3% in patients alive at 2 years (Δ=33.2%). Discussion: The probability of surviving increases as time elapsed after surgery, reflecting the dynamic nature of survival after resection for GBC. Patients with the worst initial prognosis, demonstrated the greatest increase in CS over time. CS may provide surviving patients with a more accurate prognosis, as well as help guide provider recommendations for post-operative treatment and surveillance.

A Comparison of Prognostic Schemes for Perihilar Cholangiocarcinoma

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Introduction: Although widely used, the 7th edition American Joint Committee on Cancer (AJCC) staging system for perihilar cholangiocarcinoma (PHC) may be limited. Disease-specific nomograms have been proposed as a better means to predict long-term survival for individual patients. We sought to externally validate the AJCC staging system, as well as externally validate and improve upon a previously proposed nomogram for PHC from Memorial Sloan Kettering Cancer Center (MSKCC). Individualized risk prediction models, such as this nomogram, may have a role in selecting and guiding postoperative treatment in the future. Methods: 407 patients who underwent surgery for PHC between 1988 and 2014 were identified using an international, multi-center database. Standard clinicopathologic, perioperative and outcome data were collected. The predictive power of the AJCC staging system and nomogram were assessed using Harrell's concordance index (C-index) and calibration plots. Results: Median patient age was 66 (IQR, 58-73) and most patients were male (n=250; 61.6%). At the time of surgery, the majority of patients underwent a hemi-hepatectomy or a larger liver operation (74.9%). On final pathology, surgical margin status was R0 (n=179; 51.4%), R0 after re-resection (n=41; 11.8%) or R1 (n=128; 36.8%). N-status was N0 with more than 4 lymph nodes (n=84; 23.5%), N0 with fewer than 4 lymph nodes (n=135; 37.8%) or N1 (n=138; 38.7%). Tumor grade was well- (n=63; 17.4%), moderate- (n=220; 60.6%) or poorly- (n=75; 20.7%) differentiated. Overall, the majority of patients had AJCC stage I (n=34; 11.0%), stage II (n=119; 38.4%), or stage III (n=129; 41.6%) disease. Median survival was 24.4 months; 3- and 5-year survival was 37.2% and 20.8%, respectively. While the AJCC 7th edition staging system performed poorly (C-index: 0.570), and the previously proposed MSKCC nomogram performed only a little better (C-index: 0.587). Our improved nomogram, based on age, lymphovascular invasion, perineural invasion and lymph node metastases, performed noticeably better (C-index: 0.682) The calibration plot of our proposed PHC nomogram demonstrated good calibration in the validation cohort. Conclusion: The current 7th edition AJCC staging system for PHC has a poor ability to predict long-term survival for individual patients. The MSKCC nomogram performed only marginally better. Our multi-center PHC nomogram provided a more accurate prediction of survival and therefore may be a more useful tool for clinical decision-making and prognostic stratification.

Stereotactic body radiation therapy for colorectal liver metastases: is it equal to hepatic resection? A matched case-control study

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Colorectal hepatic metastasis (CRLM) can be treated with curative intent with hepatic resection (HR). However, only 20% of patients with CRLM are resectable. Stereotactic body radiation therapy to the liver (SBRT) is a relatively new and non-invasive technique to control livermetastases in patients unfit for hepatic resection with reported 2-year local control rates as high as 90%. We conducted a matched case-control study to compare SBRT with HR with respect to morbidity, mortality and local recurrence rate. All consecutive SBRT cases from our institution till December 2014 were prospectively included in this study. From our prospective database we selected controls who underwent surgery for solitary colorectal liver metastases. These controls were matched for sex, age and size of metastasis. Eighteen SBRT cases were matched with 41 patients with a total of 45 metastasectomies. Base characteristics of cases and controls were similar. In the SBRT-group there were no complications and no radiation-induced toxicity above grade 2 was reported. Sixteen of 45 controls had a complication during their admission in the hospital (p=0.003). In both SBRT cases and HR controls there was no mortality. The median follow-up for the HR controls and for SBRT group was, respectively, 38 and 27 months (p=0.04). During this period no local recurrence was seen after surgery. Two patients who underwent SBRT had a local recurrence (p=0.078). This is the first study to compare SBRT and HR for colorectal liver metastases in a case-control study. We found similar recurrence rates in SBRT cases and HR controls. Furthermore, there were more complications in the HR control group. Both groups had similar base- characteristics, but SBRT cases were selected as they or the hepatobiliairy team preferred an alternative for surgery.The SBRT cases may represent a less favourable group. Nevertheless, the recurrence rate is comparable and complication rate is lower. SBRT is a serious alternative for HR especially in cases unfit for surgery and/or with high surgical risk.

RFA in locally advanced pancreatic cancer: CT-Findings 1 week after RFA and at follow-up

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In Europe, pancreatic cancer is the fourth leading cause of cancer related death. Forty percent of patients are diagnosed with locally advanced pancreatic cancer (LAPC), which has a poor prognosis despite new combination chemotherapies, such as FOLFIRINOX. In recent years, radiofrequency ablation (RFA), a local ablative therapy, is being explored as a new treatment option. In order to evaluate the effect of RFA on the pancreatic tumor, CT-imaging is used during follow-up. Literature on radiological changes after RFA in LAPC is limited. This article aims to provide a systematic evaluation of the CT findings in LAPC, directly after RFA and during follow-up (FU), by describing the characteristics and changes of the tumor, ablation zone and their relation to surrounding vessels. Eighteen patients with LAPC received RFA therapy during a phase II safety study. All CT-studies of these patients performed prior to RFA and during follow-up were reassessed by two dedicated radiologists, using standardized radiological scoring lists. A total of 69 CT-scans prior to and after RFA were reassessed. The tumor was located in the pancreatic head in 72% of the cases, with a mean size of 4.4 cm and with superior mesenteric vein (SMV) involvement in 94%. One week after RFA, the ablation zone was clearly visible in all patients, as a (partially) well-defined (83%), heterogeneous area (94%). In 2 patients (11%), the ablation zone covered the entire tumor. At 3 months follow-up, 67% of the ablation zones were completely obliterated and in 33% still present, but decreased in size. The SMV (44%) and portal vein (28%) were partially included in the ablation zone, leading to thrombosis (n=1) and/or occlusion (n=2) of only the SMV in 21%. The occlusions persisted during FU without any clinical consequences and the thrombosis disappeared. In 15%, the arteries were partially involved in the ablation zone, which let only to temporarily lumen reduction in 25%. Regarding the tumor, a decrease in size and in the extent of vascular involvement was seen one week post RFA. Subsequent FU showed tumor progression in diameter and a gradual increase in the vascular involvement of the tumor.
Conclusion The effect of RFA is evident on CT-imaging directly after the procedure, but the ablation zone is usually obliterated at 3 months FU. While the tumor bulk is often decreased one week after RFA, tumor progression is evident during follow-up. The ablation zone regularly includes vascular structures. In case of arterial involvement this was without adverse effects. In a minority of cases with venous involvement, asymptomatic venous occlusion or thrombosis occurred.

Long-term quality of life after pancreatic surgery: do complications affect QoL?

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Pancreatic cancer is the fourth leading cause of cancer death and has a very poor prognosis with an overall 5-year survival of 4%. Because of the limited survival, quality of life (QoL) after pancreatic surgery is important. Postoperative complications are common and several studies show that severe postoperative complications tend to negatively affect quality of life. The aim of this study is to compare QoL 6 months after surgery for patients with and without complications. Quality of life was measured by the RAND-36 questionnaire, the European Organization for Research and Treatment of Cancer (EORTC) core questionnaire (QLQ-C30) and the pancreatic cancer-specific EORTC-QLQ-PAN-26. QoL was measured before surgery and 1, 3, 6 months postoperatively, and every 6 months afterwards until death. Prospectively scored complications were delayed gastric emptying, post-operative pancreatic fistula, bile leakage and post-pancreatectomy hemorrhage. Complications were divided in grade A (mild), grade B (moderate) and grade C (severe) according to definitions set by the International Study Group of Pancreatic Surgery (ISGPS). Ninety-three patients were included between March 2012 and March 2016 with a malignant disease (n=70) and a premalignant disease of the pancreas (n=23). Moderate and/or severe complications arose in 64 patients. At 1 month postoperatively, social functioning (RAND36), physical functioning (QLQ-C30), cognitive functioning (QLQ-C30) and being limited in social activity (QLQ-C30) were worse in patients with grade B and/or C complications. At 3 months, physical functioning (RAND36) and role restriction (QLQ-C30) were worse in patients with moderate and/or severe complications. At 6 and 12 months and every 6 months afterwards, there were no statistically significant differences between both groups.
Conclusion: Severe complications lead to a temporary decrease in QoL. These differences disappear 6 month after operation and do not affect QoL on the long term. These results can be used to inform patients with postoperative complications.

Worldwide survey on current use, value and safe implementation of minimally invasive pancreatic resection

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The introduction of minimally invasive pancreatic resection (MIPR) into surgical practice has been slow. Randomized trials in this field are lacking. Existing cohort studies comparing MIPR with the open approach are virtually always retrospective and influenced by selection bias. Furthermore, the worldwide utilization of MIPR and attitudes towards MIPR remain unknown. We developed a worldwide survey consisting of 61 questions in order to gain knowledge on opinions and use of MIPR. The anonymous on (Google Docs, Google, Mountain View, CA) survey was sent to all surgeon members of the 6 largest hepato-pancreato-biliary associations. The survey on both laparoscopic and robot-assisted pancreatic resections included demographic information, experience with MIPR, patient selection, learning curve, healthcare costs, quality of life, and education in MIPR. In total, 435 surgeons from 50 countries completed the survey. Median surgical experience was 12 years (interquartile range (IQR) 6-20) and responders performed a median of 22 pancreatic resections (IQR 0-450) as primary surgeon annually. Minimally invasive distal pancreastectomy (MIDP) was performed by 345 (79%) surgeons with a median total personal experience of 20 MIDPs (IQR 10-50). Of surgeons performing MIDP, 338 (98%) considered the overall value of MIDP superior or equivalent to the open approach. Minimally invasive Whipple (MIW) was performed by 124 surgeons (29%) with a median total personal experience of 12 MIWs (IQR 4-40). Involvement of other organs was considered the most important contra-indication for MIDP (n = 141 (32%)) and arterial involvement for MIW (n = 222 (51%)). Of surgeons performing MIW, 96 (77%) considered the overall value of MIW superior or equivalent to the open approach. The most important mentioned reason for not performing MIPR was a lack of specific training and 275 (63%) and 350 (81%) surgeons felt they would benefit from training in MIDP or MIW, respectively. Specific MIPR training had been completed by 161 (37%) surgeons, but even in this group 101 (63%) and 135 (84%) thought they would benefit from additional training in respectively MIDP or MIW. Proctoring on-site was considered the most important training element by 140 surgeons (32%) and 392 (90%) would consider participation in an international registry. Conclusions: This worldwide survey on MIPR showed that the current median annual number of MIPRs performed per surgeon is low. Whereas most surgeons considered MIDP superior or equivalent to open distal pancreatectomy, this was less clear for MIW. Specific training in MIPR, especially proctoring on-site, and an international registry seem required.

Impact of a nationwide training program in minimally invasive distal pancreatectomy (LAELAPS)

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Expert centers report superior outcomes of minimally invasive distal pancreatectomy (MIDP) compared with open distal pancreatectomy. In the Netherlands (2005-2013) 10% of distal pancreatectomies was MIDP (38% conversion) and MIDP training was welcomed by 85% of surgeons.[1] The feasibility and impact of a nationwide MIDP training program was unknown. Aim of this study was to assess the impact of a nationwide training program in MIDP. From Jan-2014 to Jul-2015, 32 pancreatic surgeons from 17 centers of the Dutch Pancreatic Cancer Group participated in a nationwide MIDP training program, including video training, detailed technique description and on-site proctoring by two (inter)national proctors (LAELAPS). Participating surgeons had experience with laparoscopic gastrointestinal surgery and worked in a high-volume pancreatic center performing ≥20 pancreatoduodenectomies annually. Retrospectively collected MIDP outcomes before training (Jan-2005 to Dec-2013) were compared with prospectively collected MIDP outcomes after training (Jan-2014 to Nov-2015). Sensitivity analysis was performed by excluding centers that performed > 10 MIDPs after training. In total, 180 patients were included, of whom 71 patients underwent MIDP in 9 years before training vs. 130 patients in 22 months after training (7-fold increase; P < 0.001). Groups were comparable for base characteristics, operative time and blood loss. The conversion rate (38% (n = 27) vs. 8% (n = 11) patients; P < 0.001) and operative blood loss were lower in the period after training. After training, relatively more pancreatic adenocarcinomas were resected (7 (10%) vs. 28 (22%); P = 0.03), with comparable R0 resection rates (4/7 (57%) vs. 19/28 (68%); P = 0.51). ISGPF grade B/C pancreatic fistulas (20 (28%) vs. 41 (32%) patients; P = 0.62) and Clavien-Dindo ≥3 complications (15 (21%) vs. 19 (15%) patients; P = 0.24) for both groups. Length of stay was shorter after training (9 (7-12) vs. 7 (5-8) days; P < 0.001) and 30-day mortality was 3% vs. 0% (P = 0.07). Sensitivity analysis showed similar conversion rate, complication rate and length of stay. Conclusion: A nationwide training program in MIDP was feasible and was followed by an increase in the MIDP use, including in cancer patients, and decreased conversion rates. Future studies will have to determine whether these training programs are also applicable in other settings. Reference: [1]De Rooij et al. J Am Coll Surg. 2015.

Usefulness and reliability of upper gastro intestinal contrast studies in assessment of pouch size in patients with weight loss failure after Roux-en-Y gastric bypass

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Weight loss failure or weight regain occurs in up to 25% of patients with a Roux-en-Y gastric bypass(RYGB). Postoperative anatomical changes, such as pouch or stoma dilatation, might contribute to this failure due to increased volume intake. The aim of this study is to assess the usefulness and reliability of upper gastro intestinal(UGI) contrast studies to detect pouch dilatation in patients with weight loss failure following RYGB. Retrospective case-control study of 101 patients presenting with weight loss failure between 2010 and 2015 (failure group) and a control group of 101 patients with adequate weight loss. Two trained researchers, blinded for the initial radiology report, independently reassessed all source images. Cut off point for pouch dilatation was set on pouch dimension transcending twice the adjacent vertebral height. Pivotal assessment by an expert radiologist was used in case of disagreement. Amount of weight loss and possible additional treatment was extracted from the electronic patient records. Systematic reassessment of the UGI contrast studies showed 23/101(23%) pouch dilatation in the failure group, compared to 11/101(11%) in the control group(p.0.024). Only a fair interobserver agreement was found(kappa 0.25). Revisional surgery was performed on 43/101 patients in failure group, including nonadjustable banding of the pouch(n=11), adjustable banding(n=29), laparoscopic pouch resizing(n=6) and conversion to distal bypass(n=3). There was no difference in return to adequate weight loss (>50% excess weight loss) between these patients and those managed conservatively(30%vs28%). Patients with weight loss failure and detection of pouch dilatation on UGI were more likely to reach adequate weight loss following conservative treatment compared to surgical treatment(27%vs8%). Systematic reassessment of UGI contrast studies showed pouch dilatation in 23% of patients with weight loss failure after RYGB. However, the low interobserver agreement and the observed discrepancy in weight loss during follow-up greatly questions the reliability of this diagnostic modality.

Perineal wound complications after abdominoperineal resection for rectal cancer

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Perineal wound complications are a significant clinical problem after abdominoperineal resection (APR) for rectal cancer. The extralevator APR and neoadjuvant radiotherapy are increasingly used at the expense of more perineal wound complications and the development of a perineal hernia. This retrospective study determined the prevalence of perineal wound complications for patients after APR for rectal cancer in our center.
Between 2011 and 2015 all patients undergoing APR in our hospital were retrospectively recorded in a registry, from which the data were analyzed. Patient and surgical characteristics, preoperative therapy and all postoperatively complications were reported. The primary end points were perineal wound problems as primary wound infection, presacral abscess and perineal hernia rate. Secondary end points were overall general complications. All 95 patients treated for rectal cancer with an abdominoperineal resection between 2011 and 2015 in our institution were included. Median age was 67 years (34-90). There was an unequal distribution in sex with 59 men (62%) and 36 women (38%). 81 patients (77%) received neoadjuvant radiotherapy of which 47 patients also underwent chemotherapy. The follow-up was 5-65 months. The percentage of overall perineal wound complications after APR was 34 percent. Perineal wound infections occurred in 7% and presacral abscess in 9% of all patients. Sixteen patients developed a perineal hernia. In half of these patients the hernia was symptomatic and a perineal correction was performed. The pelvic floor was closed with a mesh in 35 patients. There was no difference in developing perineal wound infections or a perineal hernia between primary wound closure and closure using a mesh ($p = 0.56$). Radiation therapy did not increased the risk of perineal wound complication (35 vs. 29 percent, $p = 0.77$). We found a complication rate of 34% perineal wound complications (including 16% perineal hernias) after abdominoperineal resection for rectal cancer in our hospital. These findings are consistent with the literature.

Limited endoscopic assisted wedge resection for excision of colon polyps

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Background: Combined endoscopic laparoscopic surgical (CELS) removal is used for polyps in the colon that are not suitable for endoscopic removal due to size, location or scarring. However, the placement of a linear stapler can be challenging. Up to now, a wedge resection is mostly documented in the cecum or ascending colon. We would like to report on our experience with limited endoscopy assisted wedge resections (LEAWR) in the entire colon. Methods: A retrospective single-center study of 8 patients between March 2015 and April 2016 was performed. Medical data were collected (i.e., indication for referral for surgery, location and size of the polyp, duration of surgical procedure, length of hospital stay and peri- and postoperative complications). Operative time was defined as total time of general anesthesia. The laparoscopic surgical technique consisted of placing a suture under endoscopic view through the base of the polyp into the lumen. Subsequently, traction was given on the suture to enable stapling of a wedge of the colon. Results Eight patients, with a mean age of 74.5 years (range 68-82), were treated. Main indications for laparoscopic resection were the size and difficult location of the polyp. There were no complications. Mean operative time was 132 minutes. Five patients were discharged the day after surgery, the other 3 patients were admitted a total of 2 days. Conclusion: Our study found that LEAWR is a feasible and easy technique for the removal of colon polyps and residual adenomatous tissue in scars not accessible for endoscopic removal. Due to traction given on the suture through the base of the polyp, the linear stapler is easily used for wedge resections of polyps even for those that are not in favorable positions.

The effect of preoperative optimization of nutritional status in patients with significant bowel obstruction

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Bowel obstruction is a frequent complication of both malignant and benign bowel diseases. Obstruction is often preceded by symptoms like abdominal pain, nausea and anorexia, resulting in weight loss and malnutrition. Traditionally, bowel obstruction is treated with acute resection or deviating stoma. However, acute surgery is associated with high complication numbers and high mortality rates (up to 19%). Studies have shown that good preoperative nutritional status leads to better postoperative outcome due to less perioperative complications. We hypothesized that more patients could benefit from laparoscopic surgery and primary anastomosis when acute surgery can be avoided and better nutritional status can be achieved. The purpose of this study was to introduce a new preoperative feeding protocol for patients with signs of bowel obstruction and to examine its effect on surgery and postoperative outcome. In February 2013 a new preoperative feeding protocol for patients with signs and symptoms of bowel obstruction was introduced. Patients presenting with an acute abdomen based on acute obstruction were excluded. All patients received one of the following diets depending on the degree of symptoms and weight loss: residue low diet with protein enriched drinks, complete diet of protein enriched drinks, enteral nutrition (EN) through a nasoenteral tube, or total parenteral nutrition (TPN). Patients were evaluated for 1. weight gain and 2. relieve of obstructive symptoms. All patients were prospectively included in a database and perioperative parameters were recorded. A total of 44 patients were included. Patients were treated with: a residue low diet (n=7), a complete diet of protein enriched drinks (n=15), a combination of both (n=1), EN (n=13) or TPN (n=8). 3 out of 44 patients received emergency surgery as obstructive symptoms worsened. Laparoscopic elective surgery was performed in 32 patients, conversion to open surgery was necessary in 2. Primary anastomosis was performed in 32/38 patients, 6 patients received abdominoperineal rectal resection. Minor postoperative complications (Clavien Dindo 1-2) occurred in 15 patients (34.1%), major post-operative complications occurred in 4 patients (8.9%) No anastomotic leakages occurred.

Conclusion: Our study shows that patients with obstructive bowel disease can be safely treated with this study protocol and moreover, it results in good surgical outcome with majority of patients receiving elective laparoscopic resection with primary anastomosis, little postoperative complications and no stoma. Therefore, we suggest to implement using this protocol for all patients with signs and symptoms of bowel obstruction.

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FERRING
PHARMACEUTICALS

Double-Blind Randomized Clinical Trial of Laparoscopic Toupet versus 180° Anterior Fundoplication for Gastroesophageal Reflux Disease

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Background: Recent meta-analyses have demonstrated that partial fundoplications provide similar reflux control with less postfundoplication symptoms compared to Nissen fundoplication for gastroesophageal reflux disease (GERD). It remains unclear which partial fundoplication is surgical therapy of choice. The aim of the present study was to compare the subjective and objective outcome of 270° posterior laparoscopic Toupet (LFT) with 180° anterior fundoplication (180° LAF). Methods: A double-blind randomized clinical trial was conducted between August 2012 and May 2015 in two teaching hospitals specialized in antireflux surgery. Patients were randomized to undergo primary LTF or 180° LAF. Subjective outcome was analyzed at one, three, six, and 12 months following surgery using validated questionnaires. Objective reflux control was assessed using endoscopy, manometry and 24-hr esophageal pH-monitoring before and three months after surgery. Results: A total of 94 patients were randomized to LTF (n=47) or 180° LAF (n=47). Data on subjective outcome was available in 90% of the patients at 12 months, demonstrating no significant differences in control of reflux or postfundoplication symptoms between the two groups, except for an increased prevalence of increased flatulence and chest pain after LTF at one and six months respectively (71% vs. 49%, p=0.034; 23% vs. 7%, p=0.039). Furthermore, there were no significant differences in satisfaction and willingness to undergo surgery again. Postoperative endoscopy and 24-hr pH-monitoring demonstrated no significant differences in esophagitis, hiatal hernia, mean esophageal acid exposure time or recurrent pathological esophageal acid exposure between the two groups. Conclusions: The results of this trial provide evidence for equal short-term outcomes of LTF and 180° LAF as surgical procedures for GERD, with similar subjective and objective reflux control, postfundoplication symptoms and patient satisfaction. The long-term results of this RCT need to be awaited to evaluate whether differences develop with extension of follow-up beyond 12 months.

Outcome of laparoscopic hiatal hernia repair: why use mesh?

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Introduction: Hiatal hernia is an important cause of pyrosis, dysphagia and regurgitation. Standard surgical treatment includes laparoscopic correction by cruraplasty with or without reinforcement with mesh, and fundoplication. Currently, the use of mesh remains controversial, with fear of mesh-related complications such as oesophageal erosion. This study compares the outcome of a large cohort of patients after correction of a large hiatal hernia with and without usage of mesh. Methods: All consecutive patients who underwent primary laparoscopic correction of a hiatal hernia (types II, III and IV) in two tertiary hospitals, with at least six months follow-up, were included and retrospectively analysed. Surgical procedures were performed by three gastrointestinal surgeons specialised in antireflux surgery. Cruraplasty was performed in all patients using non-absorbable sutures, together with an additional partial fundoplication. The additional use of mesh was based upon the size of the crural defect and the surgeons preference. Symptomatic outcome was assessed six and 12 months following surgery, and on a yearly basis thereafter. A barium swallow X-ray was performed three months following surgery, or in case of recurrent symptoms. Results: Between 2009 and 2016, a total of 165 consecutive patients underwent laparoscopic hiatal hernia repair and were included. Type II hiatal hernia was present in 10,6%, type III in 40,7%, and type IV in 48,8%. 59 patients (32,9%) received a mesh to enforce the cruraplasty. Operation time was 96 minutes in the group without mesh, 103 minutes in the group with mesh (P=0.192). Overall, radiologic recurrence was present in 36 patients (28,3%). 24 (26,1%) in the group with primary correction and 12 (34,3%) in the group with usage of a mesh (P=0.384). Symptomatic recurrence (radiologic recurrence combined with symptoms) was present in 18 patients (13,2%) in the complete group. There was no difference between the group with mesh (n=6, 15,8%) and without mesh (n=12, 12,2%; P=0.581). In total, 14 patients (8,5%) underwent a reoperation for symptomatic recurrence and was equal in both groups (P=0.148). We did not see any mesh-related complications in this cohort. Mean satisfaction after surgery was 8,3 and was equal in both groups (P=0.728).
Conclusion: Symptomatic recurrence rate after laparoscopic hiatal hernia repair is 13%. Hiatal repair with or without additional reinforcement using mesh results in a comparable recurrence rate. Eight percent of the included patients underwent redo surgery. Patients report a high satisfaction score after laparoscopic hiatal hernia repair, irrespective of the use of mesh.

Diaphragmatic hernia following esophagectomy for cancer

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Background: The development of diaphragmatic hernia (DH) after esophagectomy is becoming more relevant due to improvements in survival. This retrospective study aimed to evaluate and compare the occurrence and clinical course of DH following open and minimally invasive (MI) esophagectomy. Methods: The prospectively recorded characteristics of patients treated with esophagectomy for cancer at two tertiary referral centers in the UK and the Netherlands between 2000 and 2014 were reviewed. All computed tomography (CT) reports were reviewed to identify DH. Results: Of 657 patients, 473 (72%) had a CT-scan and were selected for evaluation. MI esophagectomy was performed in 310 (58%) and open esophagectomy in 163 (37%) patients. DH was diagnosed in 44 patients (9%) after 19 (0-101) months. The occurrence of DH was comparable in the MI and open group (10% vs. 7%, p=0.199), but was higher in the MI group after transthoracic esophagectomy (11% vs. 5%, p=0.039). A total of 14 patients presented as a surgical emergency at the moment of diagnosis. Of the remaining 30 patients, 16 were symptomatic and 14 were asymptomatic. Elective surgery was performed in 9 symptomatic patients, all others were treated conservatively. Emergency surgery resulted in a prolonged intensive care unit stay compared to elective surgery (3 vs. 0 days, p=0.001). In-hospital mortality was solely seen after emergency surgery (19%). Conclusion: DH is a significant long-term complication after esophagectomy, occurring in a substantial part of the patients. The incidence of DH is higher after a MI approach. Emergency surgery is associated with dismal outcomes.

Costs of complications after esophagectomy for cancer

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Background: More knowledge regarding the clinical and economic impact of specific postoperative complications after esophagectomy would allow health care resources to be allocated more efficiently. The most important complications with regard to severity and costs can then be addressed for quality improvement efforts. Therefore, the purpose of this study was to estimate the economic burden of several specific postoperative complications after esophagectomy, in order to optimally allocate resources for quality improvement initiatives in the future. Methods: Retrospective analysis of clinical and financial outcomes after esophageal cancer surgery in a tertiary referral center in the Netherlands. Detailed clinical data was extracted from consecutive patients registered in the Dutch upper GI Cancer Audit between 2011 and 2014 (n=201). Costs were measured up to 90-days after hospital discharge and based on Time-Driven Activity-Based Costing. The additional costs of complications were estimated using multiple linear regression models. Results: The average costs for one patient after esophagectomy, corrected for comorbidity, was €22.493 (95% CI: 20.496-24.661). Patient characteristics associated with additional costs in multivariable analysis included age >70 (+€4437, 95%CI: 1.036-8360, p=0.009) and pulmonary comorbidity (+€5790, 95%CI: 1.463-10.863, p=0.005). The estimated costs of an esophagectomy without complications was €20.951 (±6.260). Mean costs after mild and severe complications were €26.427(±16.706) and €40.306 (±21.281) (p<0.001), respecttively. Severe complications occurred in 29% of the patients and were accountable for 40% of the total postoperative costs. Complications associated with a significant increase in costs after multivariable analysis were anastomotic leakage (+€5.425, 95% CI: 1.935-9.440, p=0.002), postoperative bleeding (+€31.337 95%CI: 14.377-56.362, p<0.001), cardiac complications (+€7.077 95%CI: 2.570-12.435, p=0.001) and chyle leakage (+€7.248, 95%CI: 3.053-12.166, p<0.001).
Conclusions: The results of this study show that complications after esophageal surgery are associated with a substantial increase in costs. Although not all postoperative complications can be prevented, implementation of preventive measures to reduce complications could result in a considerable cost reduction.

Short-term quality of life after neoadjuvant chemoradiation followed by surgery compared to surgery alone

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The CROSS-trial showed a significant increased long-term survival for neoadjuvant chemo radiotherapy (nCRT) plus surgery compared to surgery alone in esophageal cancer patients. Therefore, nCRT plus surgery is considered standard treatment in many countries. However, the effect of the CROSS-regimen on quality of life (QoL) is unknown. The primary aim of this study was to compare short-term-QoL (≤1 year after surgery) after nCRT plus surgery with surgery alone. Furthermore, the effect of nCRT on QoL prior to surgery and the impact of surgery on short-term-QoL were examined.Details of this multicenter, randomized trial have been reported previously. Cancer-specific-QoL and tumor-specific-QoL were measured using the EORTC-QLQ-C30 and QLQ-OES24 questionnaires. Questionnaires were sent pretreatment and at 3, 6, 9 and 12 months after surgery. The nCRT-group also completed questionnaires two weeks following nCRT (prior to surgery).Primary endpoints were physical functioning (QLQ-C30) and eating (QLQ-OES24). Secondary endpoints were global health status, fatigue (both QLQ-C30) and emotional functioning (QLQ-OES24). We used repeated measurement analysis to evaluate within and between group differences. A total of 363 patients participated. No differences in endpoints were found between the two randomized groups at base and at 3, 6, 9 and 12 months postoperatively. Two weeks after completion of nCRT (prior to surgery), the nCRT-group showed a decrease in all above-mentioned endpoints ($p<0.001$). After surgery, physical functioning declined in both treatment-arms compared to base ($p<0.001$), improved during follow-up, but did not return to base within 12 months after surgery ($p<0.001$). Eating-symptoms worsened after surgery ($p<0.001$), but exceeded base levels after 9 months post-surgery ($p=0.017$). Global quality of life and emotional functioning declined after surgery in both groups ($p<0.001$) and returned to base during follow-up, whereas both groups reported more fatigue after surgery ($p<0.001$), which improved during follow-up, but did not return to base levels within 12 months ($p<0.001$).
Conclusions: Although QoL declines immediately after nCRT, no impact of nCRT plus surgery is apparent on postoperative short-term-QoL compared to patients who undergo surgery alone. Compared with baseline, QoL-scores declines after surgery but are restored within 1-year in both groups, except for physical functioning and fatigue. These data under the relatively mild toxicity of the CROSS-regimen.

Long-term quality of life after neoadjuvant chemoradiation followed by surgery compared to surgery alone

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Neoadjuvant chemoradiotherapy (nCRT) followed by surgery as presented in the CROSS-trial significantly increases long-term survival compared to surgery alone in esophageal cancer patients. nCRT plus surgery is nowadays considered standard treatment in many countries. However, the effect of the CROSS-regimen on quality of life (QoL) is unknown. The aim of this study was to examine and compare long-term-QoL (≥5 year after surgery) following nCRT plus surgery and surgery alone within the CROSS-trial.
Cancer-specific QoL and tumor-specific QoL were measured using the EORTC-QLQ-C30 and QLQ-OES24 questionnaires. Questionnaires were sent to all patients who participated in the randomized CROSS-trial and were still alive at the start of this study (July 2015). To allow for examination of effects over time, pretreatment and 12-months-postoperative questionnaires were used from our recently performed short-term-QoL-study (≤1 year after surgery). Primary endpoints were physical functioning (QLQ-C30) and eating-problems (QLQ-OES24). Secondary endpoints were global health status (QLQ-C30) and emotional functioning(QLQ-OES24). We used repeated measurement analysis to evaluate within and between group differences. A total of 366 patients participated in the CROSS-trial, of whom 125 were still alive at the start of this study (70 nCRT plus surgery, 55 surgery alone). Median follow-up was 100 months (range 77-132). No differences in primary and secondary endpoints were observed between the two groups at baseline, 12 months and ≥5 years postoperatively. Physical functioning declined in both treatment-arms one year after surgery compared to pretreatment levels ($p<0.001$), and remained at that level during long-term follow-up. Eating-problems improved within a year after surgery compared to baseline ($p=0.005$), and further improved in both groups during long-term follow-up compared to 12 months postoperatively ($p=0.01$). Global health status was comparable to baseline levels 12 months after surgery in both arms, and did not change during follow-up. Emotional problems returned to baseline levels within a year from surgery compared to baseline and further improved during long-term follow-up ($p=0.014$, compared to 12 months postoperatively).
Conclusions: Long-term QoL is comparable after nCRT plus surgery and surgery alone. Eating and emotional problems further improved compared to one-year-postoperative-levels in both groups. These data underline the relatively mild toxicity of the CROSS-regimen.

Effects of different levels of vagotomy and nicotinic receptor agonists on the development of LPS induced lung injury in rats

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Background: Pulmonary complications frequently occur following esophagectomy. As part of this procedure, the autonomic vagus nerve branches to the lungs are transected. In the last decade, the autonomic nervous system has been demonstrated to be involved in regulation of proinflammatory cytokines released by LPS-stimulated macrophages. Potentially this mechanism may contribute to the increased incidence of pneumonia following esophagectomy. The aim of the current study was to determine the local anti-inflammatory effect of the vagus nerve on pulmonary injury in rats. Methods: Rats were anesthetized with intraperitoneal urethane (10%, 1000mg/kg) and randomized into 4 groups each consisting of 12 animals according to the intervention: sham group, bilateral cervical vagotomy (CVGX) group, abdominal subdiaphragmatic vagotomy group(AVGX) and CVGX plus GTS-21 (a α7 nicotinic acetylcho receptor agonis, 4 mg/kg intraperitoneal) group. Following surgery all rats received LPS (50 ug/kg) intratracheally. Five and a half hours after administration of LPS a pulmonary function test was conducted, 30 minutes afterwards rats were euthanized by an overdose of intraperitoneal barbiturates. Subsequently TNF-alpha, interleukine 6 (IL-6), leukocyte numbers and differentiation were determined in blood and bronchoalveolar fluid (BALF). Results: Bilateral cervical vagotomy resulted in a significant increase in pulmonary resistance (P= 0.007) and macrophages in BALF (p= 0.002) in comparison to the AVGX- and sham group. The increase in pulmonary resistance was nullified after administration of GTS-21, whereas macrophages in BALF did not change. There was a significant increase in total number of lymphocytes in the BALF (P=0.036), total cell numbers in serum (p=0,044), and total number of mononuclear cells in blood (p= 0,036) when comparing the sham group to the CVGX group. In contrast, cervical vagotomy had no significant influence on TNF-alpha and IL-6 levels in BALF and blood.
Conclusion: This study shows that vagotomy above the level of the pulmonary branches deteriorates pulmonary function and increases macrophages. Vagotomy during esophagectomy may contribute to the increased incidence of pulmonary complications.

The early introduction of minimally invasive gastrectomy in the Netherlands: short-term oncological outcomes comparable to open gastrectomy

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Background: Minimally invasive techniques for gastric cancer surgery have been recently introduced in the Netherlands. The aim of this population-based cohort study was to compare the short-term oncological outcomes of minimally invasive gastrectomy (MIG) to open gastrectomy (OG). Methods: The Netherlands Cancer Registry identified all patients with gastric adenocarcinoma that underwent gastrectomy with curative intent between 2010 and 2014. Multivariable analysis was performed to determine the effect of MIG and OG on the lymph node yield, R0 resection rate, and 1-year overall survival. The pooled learning curve of MIG was analysed by ranking the first 25 procedures per center. Results: Out of a total of 1961 included patients, 281 (14%) underwent MIG and 1680 (86%) patients underwent OG. From 2010 to 2014, the median lymph node yield increased from 12 to 19 ($p<0.001$), the R0 resection rate remained stable between 87% and 91% ($p=0.103$), and the percentage of MIG increased from 3% to 39% ($p<0.001$). In multivariable analysis MIG and OG had a comparable median lymph node yield (18 vs. 15, $p=0.591$), R0 resection rate (OR 0.8, 95% CI [0.5–1.3], $p=0.443$) and 1-year overall survival (HR 1.0, 95% CI [0.8 – 1.4], $p=0.801$). A pooled learning curve of MIG was demonstrated in a decreasing conversion rate after 10 procedures (from 13% to 2%) ($p=0.001$).
Conclusion: During the introduction of MIG in the Netherlands, short-term oncological outcomes were comparable to OG. A pooled learning curve of 10 procedures was demonstrated for the conversion rate of MIG.

Laparoscopic and open surgery for gastric cancer from a business intelligence viewpoint

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Laparoscopic surgery for gastric cancer has been worldwide been gaining popularity. Is has been shown to be a safe technique for early gastric cancer. Cost aspects of this new technique have not been evaluated so far. The aim of this study was to analyze time efficiency in operative time and costs for hospitalization form business intelligence viewpoint for both laparoscopic and open gastrectomy for cancer. All data from patients who underwent gastrectomy for cancer January 2010 and January 2015 were included in this study. Primary outcome was costs of operating room usage and total cost of admission (including re-admission and complication management) Secondary outcomes were efficiency in operating room processes, complications, length of stay, ICU stay and complications (including costs of these parameters). Al these data were prospectively collected in the hospitals fully digitized patient information system. A total of 228 patients were included in this study. The laparoscopic gastrectomy was performed in 71 patients (mean age 67 years) and open gastrectomy in 157 patients (mean age 70 years). Mean length of hospital stay was significantly shorter for laparoscopic procedure: mean 7.04 (±4.09) days for laparoscopic procedure vs. 14.30 (±12.54) days for open procedure ($p<0.001$). There were significantly fewer complications in patients who underwent laparoscopic gastrectomy (21.1% vs. 36.9% in open gastrectomy, $p=0.021$). Total costs of hospitalization (i.e. total costs of surgery, ward stay/ICU and medical imaging) were significantly higher for open procedure €7857 (± €6097) vs. €6366 (±€2123) for laparoscopic procedure ($p=0.007$). Time of surgery was significantly longer for laparoscopic surgery 247 ±85min vs. 183 ±68min, $p<0.001$. Difference in mean preparation time (i.e., time from arrival in theatre to incision) was 27 ±7min and 36 ±59min for open and laparoscopic gastrectomy respectively ($p=0.181$). Also, difference in emergence from anesthesia was 30 ±102min for open surgery and 13 ±42min for laparoscopic surgery ($p=0.043$).

Conclusion: The analysis from business intelligence shows that laparoscopic gastric surgery is more efficient in terms of operative time and hospital stay compared to open surgery. In this study the laparoscopic approach appears to be safer without expanding hospital costs.

Quality control of surgicopathological compliance in the CRITICS gastric cancer trial

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The British MAGIC (Cunningham et al; NEJM; 2005) and the American Intergroup 0116-study (Macdonald et al; NEJM; 2011) influenced current clinical practice for resectable gastric cancer greatly by showing an improved survival with perioperative chemotherapy and postoperative chemo radiotherapy respectively. However, these studies were criticized by a low rate of completing treatment (42%, Cunningham et al; NEJM; 2005)and suboptimal surgery (54% had a D0 lymph node dissection, Macdonald et al; NEJM; 2011). Therefore, the multicenter CRITICS trial (ChemoRadiotherapy after Induction chemotherapy In Cancer of the Stomach) was designed to compare both strategies with strict quality assurance. A quantitative estimate of residual nodal disease after gastric cancer surgery, the "Maruyama Index of Unresected Disease" (MI), is the most decisive quality indicator as proven in the Intergroup 0116 and D1-D2 trial with a cutoff of MI <5 for a favourable outcome (Hundahl et al; ASO; 2002; Hundahl et al; J Gastric Cancer; 2007). An overview of surgicopathological quality control in the CRITICS trial is given in this analysis. The CRITICS trial is a large international, prospectively randomized, phase III trial in which 788 patients with resectable gastric cancer were included between 2007-2015. All patients were intended to receive three courses of chemotherapy followed by surgery including a D1+ lymphadenectomy (removal of stations 1-9 and 11, in distal tumors without station 2 and 4s) according to the protocol (surgical compliance) and with a minimum of 15 lymph nodes (surgicopathological compliance). The allocation of the three additional courses of chemotherapy (arm A), or chemoradiotherapy (arm B) postoperatively occurred after primary diagnosis. The Maruyama Index was determined. For the current analyses all 646 patients who underwent a gastric resection with curative intent were eligible. The surgicopathological compliance rate (at least removal of 15 lymph nodes) was 71.1% (n=459) and increased over the years from 57.1% (2007) to 89.5% (2015). The median of the MI was 2 (n=333). Further results will be presented. Surgicopathological compliance improved over the years as a result of quality assurance and centralization of gastric cancer surgery. Surgical quality assurance remains a crucial factor in randomized clinical trials.

MLDS Voordracht

Endoscopic or surgical step-up approach for necrotizing pancreatitis, a multi-center randomized controlled trial

S. van Brunschot on behalf of the Dutch Pancreatitis Study Group

Infected necrotizing pancreatitis is a potentially lethal disease that almost always requires an invasive intervention. In recent years, the surgical step-up approach has become standard of care replacing primary open necrosectomy. A promising minimally invasive alternative is the endoscopic step-up approach. We conducted a multicenter randomized trial (TENSION trial) comparing a endoscopic and surgical step-up approach in patients with infected necrotizing pancreatitis. Patients with infected necrotizing pancreatitis were randomly assigned to the endoscopic or surgical step-up approach. The endoscopic step-up approach consisted of endoscopic transluminal drainage followed, if necessary, by endoscopic necrosectomy. The surgical step-up approach consisted of percutaneous catheter drainage followed, if necessary, by video-assisted retroperitoneal debridement (VARD). The primary endpoint was a composite of major complications (i.e. new onset organ failure, bleeding, perforation of a visceral organ, enterocutaneous fistula and incisional hernia) or death during 6 months of follow-up. Secondary endpoints included, among other, pancreatic fistula, length of hospital stay and costs. A total of 98 patients were enrolled in 19 Dutch hospitals. The primary endpoint occurred in 10 of 51 patients (20%) in the endoscopic group and in 13 of 49 patients (28%) in the surgical group (risk ratio 0.75; 95% CI 0.37 to 1.52, P=0.35). There were no significant differences in the individual components of the primary endpoint (e.g. death 18% versus 13%; P=0.50). In the endoscopic group, 21 patients (41%) as compared with 23 patients (49%) in de surgical group did not need necrosectomy after drainage as first step of treatment (risk ratio 0.84; 95% CI 0.54 to 1.31, P=0.43). There was a lower incidence of pancreatic fistula (5% versus 32%; P=0.001) and length of hospital stay was shorter (median 36 days versus 69 days; P=0.03) in the endoscopic group. Furthermore, the difference in total mean costs was €13655 (19%, BCa 95% CI -10836 – 35782) in favour of the endoscopic group.

Conclusion: the TENSION trial did not show superiority of the endoscopic step-up approach, as compared with a surgical step-up approach, in reducing major complications or death in patients with infected necrotizing pancreatitis. However, the rate of pancreatic fistula, length of hospital stay and costs were significantly reduced in the endoscopic group.

MLDS Voordracht

Next generation whole exome sequencing to discover genetic aberrations associated with poor outcome in untreated lymph node negative colon cancer

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Colorectal cancer is the second most common malignancy in the Western World with over 15,000 new cases in the Netherlands. The standard treatment for lymph node negative colon cancer is radical surgical resection. However, up to 20% of the patients with lymph node negative colon cancer will develop metastatic disease. Although several clinicopathological features have been associated with recurrence of disease in this group of patients, identifying patients at risk for recurrence is still an unmet need. The main aim of the project was to identify mutations associated with recurrent disease in untreated lymph node negative colorectal cancer. A set of 44 patients (22 with and 22 without recurrence of disease) was selected from the MATCH study, an ongoing prospective cohort study from 2007 onwards including adult patients undergoing curative surgical resection for colorectal cancer in the region of Rotterdam. Fresh frozen tumor containing at least 40% tumor cells, and matched normal samples were used to isolate tumor and normal DNA respectively. Whole exome sequencing was performed with a minimal coverage 120X (40-70% tumor cells) or 90X (>70% tumor cells) for tumor samples and 60X for normal samples. For all tumor samples MSI status was determined. The two groups were comparable for base characteristics. A median of 50 amino-acid changing somatic mutations were found in the tumor samples with one (MSI) sample exceeding 2,000 mutations. In total 33 mutations were found to be recurrent in at least five patients such as APC (34%), TP53 (23%), SMAD4 (9%) and BRAF (2%). Of these mutated genes, TTN was significantly less (13,6% vs 45,5%) and ISLR2 significantly more often (22,7% vs 0%) mutated in patients who developed metastatic disease compared to patients who did not (p=0.046). However, these recurrent mutations are not known to be cancer-related mutations, possibly limiting their clinical significance. In conclusion, no apparently somatic derived mutations in driver genes were found that will enable us to identify patients likely to develop recurrent disease in untreated lymph node negative colorectal cancer. However, these initial results have worked as a catalyst for subsequent studies focusing on epigenetic changes as well as mRNA and protein expression within a larger cohort of 180 untreated lymph node negative colon cancer patients.

Long term management and outcome of patients with hepatocellular adenoma presenting with massive bleeding

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Background: Hepatocellular adenoma (HCA) is a rare benign liver tumor that occurs mostly in women in their reproductive phase. Hemorrhage and rupture of the tumor is a relatively common and potentially life-threatening complication. The aim of this study was to evaluate the outcome of acute management in patients with massive hemorrhage due to ruptured HCA and its sequelae, including the risk of rebleeding and need for elective tumor resection. Method: In a retrospective cohort study we included all subsequent patients with massive hemorrhage due to ruptured HCA who were admitted in the hospital between 1999 and 2016. Medical records were reviewed for demographic features, clinical presentation, tumor features, initial and subsequent management including surgery or intervention techniques, short- and long term complications and follow-up.
Results: Included were 22 female patients. In the acute phase 12 patients were treated conservatively, 8 underwent embolization, 1 embolization as well as resection and 1 drainage of the hematoma. Four patients suffered short term complications, 1 conservatively treated patient a hypovolemic shock, 1 patient acute liver failure after embolization with spontaneous recovery and 2 abscess formation after embolization and resection respectively, necessitating additional percutaneous drainage. Median follow-up of the whole cohort was 39 months (IQR 20,3 - 80,8). 4 patients underwent elective treatment (1 resection, 1 embolization, 2 RFA) because of HCA >5cm and/or an active pregnancy wish. In 19 patients with a follow-up of at least six months regression of the median tumor size was documented from 75,5 to 24mm, of the remaining 3 patients 2 did not have residual HCA tissue after resection; 1 had a follow-up time of <6 months. One case of rebleeding was documented three months after the initial bleeding in a patient who continued oral contraceptives. No long term complications were documented.
Conclusion: Patients with massive hemorrhage due to ruptured HCA may be treated conservatively in the acute situation; in case of hemodynamic stability embolization is indicated. As the risk of rebleeding is very low and most HCA regress spontaneously secondary treatment may only be considered in patients with persistent HCA >5cm after subsequent follow-up and/or in patients with an active pregnancy wish.

ADHD and functional defecation disorders problems in childhood

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Functional defecation disorders (FDD), including functional constipation (FC) and functional non-retentive fecal incontinence (FNRFI), are common problems of childhood. Both conditions are associated with behavior problems. ADHD is the most common behavioral disorder of childhood, with a reported prevalence of 5% in school-aged children. The aim of this study is to prospectively assess the prevalence of ADHD in children presenting with FDD and the prevalence of FDD in children with ADHD. A prospective study was performed in children (aged 6-16 years) referred for FDD (according to the Rome III criteria) or ADHD (according the DSM-IV) to specialized outpatient clinics. Group 1: children with FC or FNRFI. Parents completed the Child Behavior Checklist (CBCL) and the "Vragenlijst voor Gedragsproblemen bij Kinderen" (VvGK). A CBCL score of >69 and VvGK score of ≥16 is a strong indicator for the presence of ADHD. Patients with positive screening questionnaires were referred for further behavioral evaluation to determine if they met DSM-IV criteria for ADHD. Group 2: children with a known DSM-diagnosis of ADHD. Parents completed a standardized questionnaire regarding the defecation pattern of their child. A diagnosis of FDD was made if a child fulfilled the Rome III criteria. In total, 272 consecutive patients were included in group 1. Of these, 249 (91.5%) were diagnosed with FC and 23 (8.5%) with FNRFI. Twenty-four children (8.8%) had previously been diagnosed with ADHD. A total of 30 children (11%) had scores above the cut-off scores for one or both screening questionnaires. Of these 30 children, 21 had a previously known behavior disorder (ADHD, n=10; PDD-NOS, n=5; both ADHD and PDD-NOS, n=1; other, n=5), 3 patients refused further participation and 6 were referred to the specialized ADHD outpatient clinic for further diagnostic evaluation. In 1/6 patients, a new diagnosis of ADHD was made (preliminary data). In total, prevalence of ADHD in children with FDD was 9.2% (25/272 children), indicated by the children with previous diagnose of ADHD and the number of children with a new diagnosis of ADHD (preliminary data). In the group 2, a total of 176 children were included. Forty-one children (23.3%) met criteria for FDD: 38 children (21.6%) met criteria for FC and 3 children (1.7%) for FNRFI.
Conclusions: 9.2% of children presenting with FDD has concomitant ADHD symptoms. A substantial amount of children with ADHD has FDD symptoms (23.3%). Clinicians should be aware of the coexistence of FDD and ADHD.

The difference in endoscopic diagnostic yield in patients with either iron-deficiency anemia or anemia with normal ferritin

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Objective: current Dutch General Practioner-guidelines recommend gastroduodenoscopies (GDS) and colonoscopies in patients with iron deficiency anemia (IDA). In daily practice not all patients, referred because of IDA, appear to have anemia with an overt iron deficiency. Design: a retrospective single-center survey was performed in which we compared how often endoscopies revealed a source for anemia in patients with real IDA and anemia's otherwise. Logistic regression analyses were performed to find the best predicting models for GDS and colonoscopy. Results: a total of 917 patients with anemia were included. In patients without known GE medical history and without other complaints (N=373), the diagnostic yield of gastroduodenoscopies was 3 times higher if they had real IDA. In that population people with a high ferritin had a 16-fold smaller chance to have a bleeding source found in GDS than patients with ferritin below 30 ug/l. In the overall population (N=917), IDA could not discriminate for patients who would benefit from endoscopy. A statistical tree model shows that in women < 56 years without macroscopic bleeding only 3,9% of colonoscopies reveal an explanation for anemia.
Conclusion: non-IDA patients without GE history or localizing complaints are 3 times less likely to have a bleeding source found on GDS compared to IDA patients. In all other cases the yield of GDS and colonoscopy is the same in IDA and non-IDA patients. We recommend to consider non-IDA as an indication for GDS and colonoscopy, as is IDA. Diagnostic tree models were made to decide which patients would benefit most from endoscopy.

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Valvular heart disease, localization and number of angiodysplasias are predictors for symptomatic angiodysplasia bleeding

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Angiodysplasias are the most common vascular anomalies of the gastrointestinal tract and an important cause of gastrointestinal bleeding in the elderly. Angiodysplasias can be found incidentally on endoscopy or present as symptomatic disease with (overt) gastrointestinal bleeding. Known risk factors for the presence of angiodysplasias are aortic stenosis, end-stage renal disease and Von Willebrand disease. Which factors predict symptomatic disease with anaemia, melaena or rectal blood loss in the presence of angiodysplasias is unknown. The aim of this study is to determine which patient and disease characteristics are predictors for symptomatic angiodysplasias. We established a cohort with patients who have the term 'angiodysplasia' in an endoscopy or video capsule report between 2010-2015. Exclusion criteria were gastric antral vascular ectasia and patients with positive faecal occult blood test as only indication for a colonoscopy. Abstracted data from patients included patient and disease characteristics, methods of diagnosis and treatment strategy. Symptomatic angiodysplasia was defined as anaemia, rectal blood loss or melaena as indication for endoscopy. Asymptomatic angiodysplasia as an indication for endoscopy not related to gastrointestinal bleeding, i.e. an incidental finding. Multivariate logistic regression was performed for variables that were significantly associated with symptomatic disease in a univariate model. A total of 281 patients were included (62% male, mean age 65 years) with a mean BMI of 26.5. Median follow-up was 26 months (range 0-245). Hypertension (41%), diabetes mellitus (23%) and COPD (23%) were the most common comorbidities. In the majority of patients (80%) colonoscopy was the method of diagnosis. Symptomatic disease was the indication for endoscopy in 64% (anaemia 40%; melaena / rectal blood loss 24%) and 36% asymptomatic. Angiodysplasias were most often located to the colon (57%). Twenty-one patient and disease characteristics were significantly ($P < 0.03$) associated with symptomatic disease, including age (1.06 per year, 95% CI 1.03-1.08), chronic kidney disease (OR 11.3, 95% CI 2.7-48.2), hypertension (OR 2.2, 95% 1.3-3.7) and COPD (OR 2.0, 95% CI 1.1-3.8). In the multivariate model, jejunum localized angiodysplasias (OR 10.6, 95% CI 1.01-112.6), valvular heart disease (OR 7.0, 95% CI 1.2-39.6) and number of angiodysplasias (OR 1.5 per angiodysplasia, 95% CI 1.1-2.0) were independently associated with symptomatic angiodysplasias.

In conclusion, angiodysplasias in the jejunum, presence of valvular heart disease and the number of angiodysplasias are predictors for symptomatic angiodysplasia bleeding.

Epidemiology of abdominal pain-related functional gastrointestinal disorders and the influence of biopsychosocial factors among adolescents in Curacao

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Background: Abdominal pain-related functional gastrointestinal disorders (AP-FGIDs) are common among children and adolescents, but prevalence numbers and etiological data from the Caribbean are lacking. Therefore the aim of our study was to determine the prevalence of AP-FGIDs in adolescents in Curacao and to assess the influence of biopsychosocial factors on the prevalence of AP-FGIDs. Methods: We studied the prevalence of AP-FGIDs in 946 adolescents living on the isle Curacao, aged 11-18 years, who completed the Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III version (QPGS-III). AP-FGIDs were diagnosed according to the Rome III criteria. Results: Out of 946 questionnaires, 782 were included for further analysis. The mean age was 14.8 ± 1.8 years with 62% being female. AP-FGIDs were present in 119 adolescents with a prevalence of 15.2%. In total, 77 patients met Rome III criteria for irritable bowel syndrome (9.7%), 19 for abdominal migraine (2.4%), 19 for functional abdominal pain (syndrome) (2.4%) and 9 for functional dyspepsia (1.1%). AP-FGIDs were more common in females (OR 2.33; CI 1.48 – 3.37, $p<0.001$). After multiple logistic regression and correction for sex, nausea, loss of appetite and photophobia remained significantly associated with the presence of an AP-FGID. An alcohol drinking parent, domestic violence, emotional abuse and stress as defined by the adolescents were also associated with AP-FGIDs ($p<0.05$). Conclusions: AP-FGIDs are common in adolescents at the Caribbean isle Curacao. Somatic symptoms and stressful related events are associated with the prevalence of AP-FGIDs.

Objectively diagnosing rumination syndrome in children using ambulatory 24 hour esophageal pH-impedance and manometry

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Rumination syndrome is a functional gastrointestinal disorder characterized by persistent or recurrent regurgitation of recently ingested food into the mouth. The diagnosis in children is currently exclusively based on clinical features, but differentiation with other diagnoses is difficult. The aim of this study was to determine diagnostic criteria based on gastroesophageal pressure and flow characteristics using combined ambulatory gastroesophageal pH-impedance(pH-MII) and manometry testing. Clinical data and combined ambulatory 24 hour pH-MII and manometry recordings of children with a clinical suspicion of rumination syndrome were reviewed. All recordings were analyzed for gastroesophageal reflux events extending into the proximal esophagus. Peak gastric and intraesophageal pressures closely related to these events were recorded and checked for a pattern compatible with rumination. Rumination events were grouped into i) primary rumination, ii) secondary rumination and iii) supragastric belch-associated rumination. Twenty-five consecutive patients (11 male, median age 13.3 years (IQR 5.9-15.75)) with a clinical suspicion of rumination syndrome were referred for 24 hour pH-MII and manometry. Prior other diagnostics were performed in 88% of patients and 80% had used empirical medication. Recordings of 7/25 patients were excluded from analysis as these were incomplete due to patient's intolerance and/or technical failure. A pattern compatible with rumination was identified in 16/18 remaining patients, with 50% of events occurring <30 minutes postprandially. Fifteen out of 16 patients showed at least one gastric pressure peak >30mmHg, whilst only 50% of all recorded events was characterized by pressure peaks >30mmHg and an additional 20% by peaks >25mmHg. All patients showed at least one gastric pressure peak >25mmHg. Four patients had evidence of pathologic reflux disease, all of them showed a pattern compatible with secondary rumination.
In conclusion, application of combined pH-MII and manometry monitoring can be used to diagnose rumination syndrome in children, but also to distinguish rumination syndrome from secondary rumination as a result of pathologic reflux disease. Establishing the right diagnosis may prevent children from extensive diagnostic testing and lead to earlier appropriate treatment. Rumination patterns in children are similar when compared to adults, albeit with lower gastric pressure increase. We propose a diagnostic cutoff for gastric pressure increase to >25mmHg associated with a retrograde bolus flow into the proximal esophagus.

Excessive crying during infancy predisposes to behavioral problems in early childhood

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Objectives: Excessive crying during infancy may predispose to the development of behavioral problems in early childhood. However, results from studies to date have not been unequivocal. Therefore the aim of our study was to assess whether excessive crying predisposes to the development of behavioral problems in the early years of life by using the Child Behavior Checklist (CBCL). Methods: The study group consisted of 240 former excessively crying infants, as defined by Wessel's criteria, who were 0-3 months old when they participated in an RCT, conducted between February 2001-March 2003. In 2006, at the age of 3-5 years, their caregivers filled out the CBCL. The caregivers of 393 randomly selected children from the municipal registers of a Dutch province (aged 3-5 years at assessment, referred to as the normative sample), filled out the CBCL between December 2003-April 2005. Scores were obtained on the Internalizing, Externalizing and Total Problems scale of the CBCL and compared between the former excessively crying infants and the normative sample using Mann Whitney U-tests and Independent T-tests. The proportion of children scoring in the clinical range of the CBCL scales was compared between the two groups using Chi-square. Logistic regression was used to evaluate the effects of possible covariates. Results: The study group had a significantly higher median age (5.0 yrs(IQR 4.6-5.4) vs. 4.3 yrs(IQR 3.7-5.2),p<0.001,respectively), maternal educational level was significantly higher (p=0.015) and parents were significantly more Dutch (p=0.005) compared to the normative sample. Former excessively crying infants scored significantly higher on the Internalizing scale of the CBCL than children of the norm group (8.0(IQR 4.0-14.0) vs 7.0(IQR 3.0-11.0), p=0.015). The percentage of children scoring in the clinical range of the Internalizing and Total Problems scale was significantly higher in the group of former excessive criers compared to the normative sample (29%vs.16%,p<0.001; 20%vs.11%,p=0.001,respectively). Former excessively crying infants had an increased risk of scoring in the clinical range of the Internalizing (OR=2.14;CI 1.40-3.27), Externalizing (OR=2.03;CI 1.20-3.41) and the Total Problems Scale (OR=2.43;CI 1.47-4.03) compared to the children of the normative sample, independent of age at time of assessment, gender, maternal educational level and ethnicity of both parents. Conclusion: Excessive crying in early infancy is associated with behavioral problems as perceived by the parents at preschool age. Therefore parents of former excessively crying infants may be helped by offering support in the early years of their child's development.

The economic impact of the introduction of biosimilars in inflammatory bowel disease

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Goal: Inflammatory bowel disease (IBD) entails a high economic burden to society. We aimed to estimate the current and future impact of the introduction of biosimilars for infliximab on IBD-related healthcare costs. Methods: We designed a stochastic economic model to simulate the introduction of biosimilars in IBD, using a five year time horizon, based on the Dutch situation. Prevalence data on ulcerative colitis (UC) and Crohn's disease (CD) and IBD-related healthcare costs data were used as input. Assumptions were made on price reductions of anti-TNF therapy, increase of anti-TNF prescription rate; and development of hospitalization costs. The base case scenario included a gradual decrease in prices of biosimilars up to 60%, a gradual decrease in prices of original anti-TNF compounds up to 50%, and an annual increase of anti-TNF prescription rate of 1%, and this was compared with no introduction of biosimilars. Sensitivity analyses were performed. Results: For the base case, cost savings over the total of five years were on average €9,850 per CD patient and €2,250 per UC patient, yielding in €493 million total cost savings (a reduction of 28%) for the Netherlands. Results were predominantly determined by price reduction of anti-TNF therapy, threshold price reduction at which physicians switch patients towards biosimilars and the extent to which switching will take place.
Conclusions: The introduction of biosimilars for infliximab can be expected to have a major impact on the cost profile of IBD. The economic impact will depend on local pricing, procurement policies and the physician's willingness to switch patients to biosimilars.

Pharmacokinetics of golimumab in patients with moderate to severe ulcerative colitis

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Background: Golimumab is an established treatment for patients with moderate to severe ulcerative colitis (UC). However, after an initial response a substantial proportion of patients loses response over time. This may be due to the development of antibodies to golimumab (ATG) or insufficient target engagement. Moreover, therapeutic antibodies are lost via degradation by metalloproteinases and enteric protein shedding. In this trial the pharmacokinetics (PK) of golimumab in UC patients is investigated in order to further understand the dose-response relationship of golimumab. Methods In this ongoing prospective observational trial, patients with moderate to severe UC received induction treatment with subcutaneous golimumab (200 mg (day 1) and 100 mg (day 14)) followed by maintenance treatment with 50 or 100 mg every 4 weeks, in patients with a bodyweight of less or more than 80 kg, respectively. Serum golimumab concentrations, CRP, albumin and ATG levels and SCCAI were measured at day 0, 4, 7, 14, 18, 28, 42 and 56. Endoscopy was performed at base and after induction treatment at week 8 using the endoscopic Mayo score. PK analysis was performed using nonlinear mixed effects modelling (NONMEM). Results Preliminary data from 12 patients during induction treatment were available. Median age at start was 44 (interquartile range [IQR], 34-57 years) and median base parameters were: CRP 1.65 mg/L [1.03-13.7], albumin 44 g/L [42-45], SCCAI 8.5 [7-10.5] and endoscopic Mayo score 2.0 [2.0-2.0]. Concentration versus time profiles were best described by a 2-compartment PK model with first-order absorption and elimination. Mean values (plus between subject variability) for clearance, central and peripheral volume of distribution, inter-compartment clearance and absorption rate constant for a patient with CRP of 1.7 mg/L were 0.80 L/day (11%), 3.93 L (31%), 4.86 L, 0.77 L/day and 0.157 L/day, respectively. A non-significant correlation was seen between CRP and clearance, which increased with 2.3% per mg/L CRP rise (p-value = 0.13). Median outcome patient parameters were: CRP 2.0 mg/L [0.78 – 4.8], albumin 42.5 g/L [41-44], SCCAI 5 [1.3-10.8] and endoscopic Mayo score 1.5 [1.0 -2.3]. None of the patients developed ATG, based on a drug sensitive assay.
Conclusion: A non-significant correlation was seen between CRP and clearance. This may indicate that clearance is dependent on the severity of inflammation. Upon inclusion of more patients the developed population PK model will be extended to determine the factors influencing PK. Furthermore, faecal concentrations and the relationship between exposure and clinical/endoscopic outcome will be determined.

Disappearance of anti-drug antibodies to infliximab and adalimumab after addition of an immunomodulator in patients with inflammatory bowel disease

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Background: Since therapeutic options for patients with inflammatory bowel disease (IBD) who lose response to anti-TNF therapy are limited, optimal use of these agents is crucial. Loss of response is often caused by anti-drug antibody (ADA) formation and subsequent neutralization of the effect of the drug. Addition of an immunomodulator (IM) to anti-TNF therapy has been suggested to reduce ADA formation, increase serum drug concentrations and to regain clinical response. Methods We investigated whether addition of an IM to anti-TNF monotherapy can lead to decreased ADA levels and regained clinical response in patients who suffered loss of response due to immunogenicity. Therefore, we retrospectively collected data of infliximab (IFX) and adalimumab (ADL) serum concentration measurements together with ADA levels from 602 patients at our IBD centre (September 2005-September 2015). ADA levels were determined with a drug sensitive assay by Sanquin Laboratory. We identified all ADA positive patients with secondary loss of response to IFX or ADL who received an IM in an attempt to eliminate ADA and to regain clinical response. Detailed documentation of disease activity was collected. Results In 98 out of 376 patients ADA directed against IFX and in 61 out of 226 patients ADA against ADL were detectable. Seventeen out of 159 ADA positive patients (144 Crohn's disease and 15 ulcerative colitis), had received an IM in addition to continued anti-TNF treatment , because of secondary loss of clinical response. Seven patients received MTX, ten patients a thiopurine (4 azathioprine, 4 mercaptopurine and 2 6-TG). In 7 out of 8 patients treated with IFX, addition of an IM resulted in increased serum drug levels with a median of 2.84 µg/ml; (IQR: 1.19-4.98) accompanied by a decrease in ADA to undetectable levels after a median time of 11 months (IQR 6-28). In patients treated with ADL, increased serum drug concentrations were reached in 6 out of 9 patients after addition of an IM. The median increase of ADL serum levels was 3.10 µg/ml (IQR:1.45-4.45). The median time for ADA levels to be undetectable was 11 months (IQR 2-37). Clinical response was established in 6 out of 9 patients receiving a TP and in all patients receiving MTX.
Conclusion: In IBD patients with secondary loss of response due to ADA formation against IFX or ADL, addition of an IM led to a decrease of ADA levels and an increase in serum drug concentrations in the majority of the patients. Patients who regained response due to this strategy could continue the current anti-TNF treatment and switching to another agent was not necessary. This strategy warrants further investigation in prospective trials.

Infliximab trough levels in inflammatory bowel disease patients: results of a prospective observational study from a Dutch peripheral hospital

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There is evidence suggesting that optimal infliximab trough levels (TLs) correlate with clinical response, clinical remission and mucosal healing in inflammatory bowel disease (IBD) patients. It has been shown that less than 50% of patients treated with infliximab had optimal infliximab TLs. We aimed to investigate infliximab TLs in a cohort of IBD patients under maintenance infliximab treatment. Parameters for clinical and biological remission were also measured. A single center, prospective, observational study was carried out. All IBD patients on maintenance infliximab treatment were included between April 2014 and August 2015. Patients needed to be in stable clinical response. Data were collected on partial Mayo score (PMS), Harvey Bradshaw index (HBI), IBDQ score, infliximab TLs, antibody to infliximab (ATI), CRP and fecal calprotectin. A total of 66 IBD patients were included. Infliximab TLs were successfully measured in 63 patients (43 had Crohn disease and 20 ulcerative colitis (UC)). 24 patients (38%) had a normal range of infliximab TLs between 3µg/ml and 7µg/ml; 25 patients (40%) had high infliximab TLs (>7µg/ml) and 14 patients (22%) had low infliximab TLs (<3µg/ml). Only four patients were ATI positive and all of these patients had low infliximab TLs (<3µg/ml). IBDQ scores were not significantly different (p = 0.192) between the three groups (186 ± 23 in the optimal, 165 ± 36 in the low and 172 ± 35 in the high TLs group). All three groups had normal CRP concentration (6.8mg/l ± 15.1 in the optimal, 6.7mg/l ± 7.1 in the low and 1.2mg/l ± 1.9 in the high infliximab TLs group). Fecal calprotectin was lower in patients with high infliximab TLs (median 40mg/kg (0-4230)) compared to those with low (median 330mg/kg (40-1780)) or optimal infliximab TLs (median 130mg/kg (0-1620)). This difference was not statistically significant (p=0.107). Of the CU patients, 100% (8/8) with high infliximab TLs, 87.5% (7/8) with optimal and 75% (3/4) with low infliximab TLs were in remission (defined by PMS<3). Of the Crohn patients, 65% (11/17) with high infliximab TLs, 75% (12/16) with optimal and 70% (7/10) with low infliximab TLs were in remission (defined by HBI<5). These differences were not statistically significant (p=0.451 and p=0.512 respectively). This study confirms that less than half of the patients on maintenance infliximab treatment has optimal infliximab TLs. However, there are no significant differrences in clinical and biological parameters for clinical remission between patients with low, high or optimal infliximab TLs in this IBD cohort.

Anti-tumor necrosis factor alpha therapy is associated with modulation of extracellular matrix in Crohn's disease

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Introduction: Intestinal fibrosis in Crohn's disease (CD) is stimulated by chronic inflamemation, and characterized by an increased presence of myofibroblasts and collagen deposition in all layers of the intestinal wall. Infliximab (IFX) is a highly effective anti-inflammatory treatment in CD, which promotes rapid wound healing. As wound healing is associated with alterations in the extracellular matrix (ECM), we aimed to investigate whether IFX modulates the ECM. Methods Between 2005 and 2012, patients with ileocecal CD failing thiopurine treatment were randomized to ileocolonic resection (=IFX naïve) or medical therapy with IFX in the LIRIC trial. Patients not responding to at least 3 doses of IFX also underwent subsequent resection (=IFX exposed). H&E stained resection specimens were scored for severity of inflammation with the Geboes score (range 0-13). Immunohistochemistry was used to stain for collagen 1 and 3 and fibronectin. All layers of the intestinal wall were assessed. Staining intensity was measured as positive stained area divided by the total surface area as indicated by H&E staining. mRNA was isolated from FFPE tissue in order to investigate gene expression. Results We examined 20 specimens from patients operated after IFX treatment (median IFX duration 38 weeks), and 20 specimens from IFX-naive patients. Median CRP levels were comparable among both groups (17 vs 6 mg/L). Both IFX-naïve and IFX-exposed groups had considerable intestinal inflammation, the severity of which was comparable in both groups (10 vs 11 points). In the IFX-exposed group, significantly more collagen I deposition was found in the submucosa (respectively 67% vs 58%, p=0.03); in the other intestinal layers a similar trend was observed. The collagen III deposition was more pronounced in the IFX-exposed patients in the submucosa and muscularis propria (60% vs 48%, p=0.01; and 43% vs 32%, p=0.01). Most importantly, IFX-exposed patients had significant more expression of fibronectin in the lamina propria, muscularis mucosa and submucosa (22% vs 10%, p=0.001; 19% vs 7%, p=0.001; and 29% vs 13%, p=0.03 On mRNA level, the myofibroblast marker alpha smooth muscle actin, procollagen peptidase (responsible for formation of collagen fibrils) and spliced variant of fibronectin, extra domain A (known to be involved in activation of myofibroblasts), showed significantly enhanced expression in CD patients exposed to IFX. Conclusion: Infliximab treatment is associated with modulation of the extra cellular matrix in Crohn's disease patients, predominantly in the deeper layers of the intestine.

Tertiary lymphoid organ formation in gut mucosa of newly diagnosed, untreated Inflammatory Bowel Disease patients

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Introduction: While naive and central memory T lymphocytes (T_N and T_{CM}) are thought to migrate exclusively to secondary lymphoid organs (SLOs), we have recently shown that these subsets are infiltrating the inflamed gut mucosa in newly diagnosed, untreated, Inflammatory Bowel Disease (IBD) patients. T_N and T_{CM} lymphocytes express L-selectin, which is the ligand for peripheral lymph node adressin (PNAd). The homing of TN and TCM lymphocyte subsets to the gut might be explained by the ectopic formation of tertiary lymphoid organs (TLOs), which contain PNAd$^+$ high endothelial venules (HEVs). Aims & Methods: We have determined the presence of PNAd-expressing HEVs and TLOs in relation to the presence of T_N and T_{CM} lymphocytes in the inflamed intestinal mucosa of 39 newly diagnosed, untreated, IBD patients and eight healthy controls that were prospectively included. Intestinal biopsy samples were analysed for blood vessels (CD31) and PNAd expression (MECA-79) by immunohistochemistry to assess the presence of lymphoid follicles and the density of PNAd$^+$ vessels. Lymphocytes subsets in the tissue samples were identified by flowcytometric immunophenotyping, including T_N (CD45RA$^+$CD27$^+$), T_{CM} (CD45RA$^-$CD27$^+$) and effector memory T cells (CD45RA$^-$CD27$^-$). We discriminated patients with high and low HEV density using a cut-off point set at the median density of extrafollicular MECA-79$^+$ vessels/mm^2 in the inflamed colon of UC patients. Results: We have found a statistically significant higher number of extra-follicular PNAd$^+$ vessels in the inflamed colon of patients with ulcerative colitis (median density of 3.05 PNAd$^+$ vessels/mm^2; interquartile range (IQR) 0-6.39) and ileum of patients with Crohn's disease (1.40 PNAd$^+$ vessels/mm^2; IQR 0-4.34) compared to healthy control colon and ileum (both 0 PNAD$^+$ vessels/mm^2; p=0.033). A high density of PNAd$^+$ HEV-like vessels (HEV^{high}) was associated with increased numbers of T_N and T_{CM} in the inflamed gut mucosa (median 87%; IQR 82-93% of total T cell population), compared to the inflamed mucosa of patients from the HEV$_{low}$ group (58%; IQR 38-81%; p=0.003). Furthermore, the number of colonic follicles was higher in HEV^{high} patients (median 0.54/mm^2; IQR 0.28-0.84) compared to HEV^{low} patients (median 0.25/mm^2; IQR 0.08-0.45; p=0.031) and controls (0.31/mm^2; IQR 0.23-0.45; p=0.043).
Conclusion: For the first time, we show in a subgroup of newly diagnosed IBD patients that presence of PNAd$^+$ extra-follicular HEV-like vessels and TLOs were strongly associated with T_N and T_{CM} cell mucosal infiltration. Different T cell migration phenotypes based on TLO formation in the early phase of IBD might allow risk-stratification of patients and enable more effective, individualized treatment.

Pooled resequencing of 122 ulcerative colitis genes in a large Dutch cohort suggests population-specific associations of rare variants in MUC2

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Genome-wide association studies have revealed several common genetic risk variants for ulcerative colitis (UC). However, little is known about the contribution of rare, large effect genetic variants to UC susceptibility. In this study, we performed a deep targeted re-sequencing of 122 genes in Dutch UC patients in order to investigate the contribution of rare variants to the genetic susceptibility to UC. The selection of genes consists of 111 established human UC susceptibility genes and 11 genes that lead to spontaneous colitis when knocked-out in mice. In addition, we sequenced the promoter regions of 45 genes where known variants exert cis-eQTL-effects. Targeted pooled re-sequencing was performed on DNA of 790 Dutch UC cases. The Genome of the Netherlands project provided sequence data of 500 healthy controls. After quality control and prioritization based on allele frequency and pathogenicity probability, follow-up genotyping of 171 rare variants was performed on 1021 Dutch UC cases and 1166 Dutch controls. Single-variant association and gene-based analyses identified an association of rare variants in the MUC2 gene with UC. The MUC2 gene encodes a member of the mucin protein family and is the major mucin secreted in the large intestine. The associated variants in the Dutch population could not be replicated in a German replication cohort (1026 UC cases, 3532 controls). In conclusion, this study has identified a putative role for MUC2 on UC susceptibility in the Dutch population and suggests a population-specific contribution of rare variants to UC.

Complications and disease recurrence after primary ileocecal resection in pediatric Crohn's disease: a multicenter cohort analysis

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Up to 25% of pediatric-onset Crohn's disease (CD) patients undergo surgical resection before adulthood. Limited data are available on the complications and long-term outcome of surgery in children with CD. Therefore, the aim of this multi-center study was to investigate (I) complication and disease recurrence rates, (II) identify predictors for these adverse outcomes and (III) assess catch-up growth after primary ileocecal resection for pediatric CD. Methods: This is a retrospective cohort analysis of all children (<18 years) who underwent primary ileocecal resection for CD between 1990 and 2015 at one of seven tertiary hospitals in the Netherlands. Severe postoperative complications were defined as a Clavien-Dindo classification grade ≥III (requiring surgical, endoscopic or radiological intervention)[1]. Clinical recurrence was defined as any symptomatic or endoscopic asymptomatic recurrence (Rutgeerts score of ≥ i2) requiring the start of medical treatment or a treatment intensification[2].Surgical recurrence was defined as disease recurrence requiring new resection or strictureplasty for active inflammation or (anastomotic) strictures. Multivariate logistic and Cox regression analyses of risk factors were performed for severe complications and disease recurrence, respectively. Results: In total, 122 children were included (52% male; median age 15.5 years [IQR 14.0–16.0]). Severe postoperative complications were observed in 10% of patients. Positive predictors for severe complications were ileocolonic disease (OR: 4.6 [95%CI: 1.2–18.2], p=0.029), emergency surgery (OR: 5.7 [95%CI 1.2–26.9], p=0.027) and microscopically positive resection margin (OR: 18.4, p=0.003). Clinical and surgical recurrence rates after 1, 5 and 10 years were 19%, 49%, 71% and 2%, 12%, 22%, respectively. Negative predictors for clinical recurrence were male gender (HR: 0.5 [95%CI: 0.3 – 0.9], p=0.023) and immediate post-operative therapy (HR: 0.3 [95%CI: 0.1–0.6], p=0.001). Disease beyond the ileocecal region (HR: 0.3 [95%CI: 0.1–0.8], p = 0.002), immediate post-operative therapy (HR: 0.45 [95%CI: 0.1–0.9], p=0.036) and microscopically positive resection margin (HR: 9.5 [95%CI: 1.2–74.1], p=0.031) were predictors for surgical recurrence. Height improved in the year following surgery in patients younger than 16 years (mean Δ Z height score 0.29 [95%CI 0.13–0.47], p = 0.005). Conclusion: Ileocecal resection is an effective and durable treatment for pediatric CD. Nonetheless, patients should be carefully monitored because of frequent postoperative complications.

Colorectal cancer risk in a nationwide inflammatory bowel disease cohort with low grade dysplasia

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Introduction: Patients with long-standing colonic inflammatory bowel disease (IBD) bear an increased colorectal cancer (CRC) risk. Endoscopic surveillance allows early detection and removal of precancerous lesions such as low-grade dysplasia (LGD), and may subsequently prevent CRC. However, the long-term outcome after LGD and the subsequent risk to develop CRC remains uncertain. To this end, we established a nationwide cohort of IBD patients with a history of LGD to 1) determine the cumulative CRC incidence, and 2) identify risk factors for developing CRC. Methods: Using the Dutch National Pathology Registry (PALGA) we identified all IBD patients diagnosed with LGD between 1991 and 2005 in the Netherlands. Subsequently, follow-up data were extracted until 2016. We determined the cumulative CRC incidence with Kaplan Meier curves censuring patients at the end of colorectal surveillance or colectomy. A case control study, comparing IBD patients with LGD who developed CRC (cases) versus patients who did not develop CRC (controls), was performed to identify risk factors for developing CRC. Results: We identified 1177 IBD patients with colonic LGD with a median follow-up time of 9.8 years per patient after LGD diagnosis (total follow-up time: 11741 patient years). 825 (70.1%) patients had ulcerative colitis, 216 (18.4%) Crohn's disease and 136 (11.6%) indeterminate colitis. 109 out of 1177 (9.3%) patients underwent colectomy. CRC developed in 86 out of 1177 patients resulting in a cumulative incidence of 2.9%, 5.8%, 11.1%, and 18.7% after respectively 5, 10, 15 and 20 years. Patients with an IBD duration of more than 5 years before LGD development had a significantly higher cumulative CRC incidence (14.7% after 15 years) compared to those with a shorter IBD duration (9.4% after 15 years; log rank p=0.001). Furthermore, patients with recurrent LGD had a higher CRC risk compared to patients with single LGD (10.5% after 15 years versus 4.5% after 15 years; log rank p=0.026). Multivariable Cox regression identified both a longer IBD duration (hazard ratio 2.5, 95% confidence interval 1.5-4.3) and recurrent LGD (hazard ratio 1.9, 95% confidence interval 1.1-3.4) as independent factors associated with increased CRC risk.

Conclusion: We showed a cumulative CRC risk of 18.7% after 20 years in a large nationwide cohort of IBD patients with a history of LGD. Both a longer IBD duration and recurrent LGD were identified as independent risk factors for CRC development following LGD. These findings may aid in risk stratification following a diagnosis of LGD in IBD patients.

Co-occurrence of psoriasis and Inflammatory Bowel Disease is associated with mild psoriasis, but severe early-onset Crohn's Disease phenotype

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Inflammatory Bowel Disease (IBD), psoriatic arthritis (PsA) and psoriasis are related immune-mediated diseases, with considerable overlap. However, it is as yet unclear whether co-occurrence of these diseases affects disease course and characteristics of the individual complaints. The aim of this study was to identify the prevalence of IBD and PsA in a psoriasis cohort and to examine whether patients with concurrent psoriasis and IBD carry a distinct phenotype. Clinical characteristics of 1669 psoriasis patients visiting a general hospital in the Netherlands between 2009-2014, were retrospectively retrieved from electronic patient files. Clinical characteristics of patients with concomitant psoriasis and IBD (n=40) were compared with psoriasis-only (n=1643) and IBD-only (n=385) cohorts. Among 1669 hospital based psoriasis patients, the prevalence of PsA was 12.2% (n=203, 95%CI 10.5-13.7) and of IBD 1.6% (n=26, 95%CI 1.0-2.2), including 12 Crohn's Disease (CD) and 14 Ulcerative Colitis (UC). Psoriasis-PsA patients were more likely to have IBD than psoriasis-only (3.0 vs 1.4%). Psoriasis-CD patients were younger at CD diagnosis (20.0 vs 32.0 yrs, p=0.001), and psoriasis diagnosis (28.0 vs 43.5 yrs, p=0.004) than psoriasis-only patients. Psoriasis-IBD patients had a mild psoriasis phenotype similar to psoriasis-only patients, but the CD phenotype (not UC) was more severe than in CD-only patients.

Conclusions The prevalence of IBD in a psoriasis cohort in the Netherlands was approximately four times higher than in the general population, with the highest risk for psoriasis-PsA patients. Psoriasis-CD patients have a mild (early-onset) psoriasis phenotype but an earlier-onset and severe CD phenotype.

Safety of anti-TNF treatment in liver transplant recipients- a meta-analysis

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Primary Sclerosing Cholangitis (PSC) patients with refractory ulcerative colitis (UC) after liver transplantation (LT) pose a dilemma for treating physicians, as little is known about the risk of serious infection when combining anti-TNF therapy with immunosuppression for prevention of rejection. Our aim was to investigate infection risk in this patient group by systematic review and meta-analysis of the available data. A literature search was conducted for full papers and conference proceedings through September 2015 regarding post-transplant patients and anti-TNF therapy. Two reviewers independently extracted study and control-patient data (age, duration of follow up, number of all infections, number of serious infections, time since transplant). As additional control population, patients from the LUMC LT cohort were used. Poisson regression was used to compare serious infections (according to ICH-definition) per patient year follow up between the anti-TNF and control group, correcting for mean time since transplant. Initially, 397 papers and 168 meeting abstracts were identified, of which 10 were included. These 10 studies contained 58 patients on anti-TNF therapy contributing 117.99 person-years (py) of follow up and 23 post-LT control patients not on anti-TNF therapy contributing 289.77 py. From the LUMC LT cohort, 41 PSC-patients with UC but without anti-TNF therapy were included as control population, contributing 278.3 py. Serious infection rates differed from 0 to 0.38 in the anti-TNF therapy group, and 0.04 to 0.24 in the control group. No patients died during infliximab treatment. No significant difference in serious infection rate (rate ratio 1.202, p=0.785, 95%CI 0.32-4.5) was found between patients treated with anti-TNF (0.12/py CI 0.035-0.40) and control patients (0.14/py CI 0.086-0.24).When correcting for mean time since transplant, it remained non-significant (rate ratio 0.84, 95%CI 0.41-1.7, p=0.63; infection rate 0.09 in controls (95%CI 0.06-0.14) and 0.11 in anti-TNF treated patients (0.059-0.2). Mean time since LT was associated with the serious infection rate (rate ratio 0.87, p<0.001, 95%CI 0.82-0.92). As a sensitivity analysis, all case reports (n=4) were excluded. This did not affect the results (rate ratio 0.794, p=0.58, 95%CI 0.35-1.81; infection rate anti-TNF treated: 0.12, control group: 0.093).

Conclusion: No significant increase in the serious infection rate was observed in LT-recipients after exposure to anti-TNF therapy. However, the wide confidence intervals of these results show that more data is needed to provide a definitive conclusion on the safety of anti-TNF therapy in these patients.

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Simple urine test to evaluate adherence to oral 5-ASA in teenagers with ulcerative colitis

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Introduction: 5-aminosalicylic acid (5-ASA) is an important maintenance drug for patients with ulcerative colitis. A proportion of the ingested dose is excreted in the urine. Measuring 5-ASA and its metabolites in urine requires mass spectrometry, which is not widely available for this purpose. Urinary salicylate can be measured by colorimetry and is a reliable surrogate marker of 5-ASA ingestion. We evaluated whether patients with poor adherence have lower urinary salicylate levels compared to high-adherers.
Methods: Teenagers who were prescribed more than 40 mg/kg/day of 5-ASA were invited to collect urine samples with various time lapses since their last presumed 5-ASA ingestion. We measured urinary salicylates and corrected for creatinine excretion. In the absence of a perfect reference standard for adherence we used a composite method by combining a patient-reported adherence scale (MMAS-8) with the results of 6-thioguanine (6-TG) levels in erythrocytes.
Results: Eight teenagers, who were identified as “poor-adherers”, collected 45 random urine samples. In thirty samples (67%; 95% confidence interval (CI) 52-79%) salicylate was undetectable. Seventeen “good adherers” collected 69 urine samples, of which 3 (4%; 95%CI 1-13%) had undetectable salicylate levels ($p<0.000$). Adherent teenagers who use 5-ASA once daily may have undetectable salicylate levels shortly before the next dosage, but their first morning urine always contains salicylate.
Conclusion: Detectable salicylates in the first morning urine rules out short-term non-adherence.

Correlation between symptoms, endoscopic severity and treatment response in immunotherapy induced colitis

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Checkpoint inhibitors are successfully used in anti-cancer treatment. However, they may induce severe immune related adverse events such as colitis. In current treatment algorithms for colitis patients are treated symptomatically or with steroids based on the severity of their symptoms. Infliximab is started in patients with steroid refractory diarrhea. The role of endoscopy is not clear. The aim of this study was to analyze the correlation between symptoms and endoscopic features and to find endoscopic predictors for steroid refractory diarrhea. Melanoma and lung cancer patients treated with checkpoint inhibitors who underwent endoscopy were identified retrospectively. Data on symptoms and treatment were collected. Endoscopies were scored using endoscopy reports and images. Because of the diverse endoscopic appearance of immunotherapy induced colitis, both Mayo and Tytgat score were used. Number and size of ulcers were also scored. Correlations between symptoms and endoscopic features were calculated using the Spearman correlation. Eighty-seven patients (76 melanoma, 11 lung cancer) with 91 episodes of diarrhea were included (mean age 58 years, range 30-88, 45% male). Fifty-six percent of episodes were due to anti-CTLA-4, 21% to anti-PD1 and 23 % to a combination of both. Eleven percent of episodes were grade 1, 42% grade 2 and 46% grade 3 diarrhea. Sixty-eight times a colonoscopy was performed and 23 times a sigmoidoscopy. Systemic steroids were started in 86 episodes. In 57% steroid therapy was started before endoscopy was performed (mean 8,5 days; range 1-56 days). Median Mayo and Tytgat scores were 1 and 6 respectively. In 30 endoscopies ulcers were seen. Correlation between grade of diarrhea and Mayo score, Tytgat score, number or size of ulcers was poor: r=0.08 (p=0.48), r=0.13 (p=0.21), r=-0.012 (p=0.91), r=0.067 (p=0.535), respectively. No strong correlation was found between bloody stools or abdominal pain and endoscopic scores. Eighty percent of patients with ulcers and 42% of patients without ulcers were treated with infliximab ($p<0.01$) because of persistent diarrhea. Mean time between start of prednisone and start of infliximab was 11 days (range 0-45).
In conclusion, the correlation between grade of diarrhea and scores for endoscopic severity of inflammation is poor. Patients with ulcers were more frequently treated with infliximab. Endoscopy seems necessary to evaluate the severity of immunotherapy induced colitis as it may change the treatment approach.

A prospective, quantitative assessment of pain and quality of life before and 3 and 12 months after vascular treatment for chronic mesenteric ischemia

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Objective: There are no prospective data on pain or health related quality of life (HRQOL) in patients treated for chronic mesenteric ischemia (CMI). This prospective study was designed to determine the change of pain intensity and HRQOL in CMI patients treated for atherosclerosis or celiac artery compression. Methods: Patients with CMI treated with percutaneous mesenteric artery stenting or retroperitoneal endoscopic release of the arcuate ligament in celiac artery compression syndrome between August and December 2013 were enrolled. For pain we used the visual analogue scale for pain intensity (VAS-PI, graded 0-100 mm). We assessed overall pain, postprandial pain and pain after exercise in the preceding week. We also assessed the number of pain free days, and use of analgetics for abdominal pain. For HRQOL we used the 36-item Short Form Health Survey (SF-36). All parameters were obtained before (baseline; BL) and at three (FU3) and twelve months (FU12) after the intervention. Results: Thirty patients were included, 80% female, mean age 57 (range 20-90) years. Diagnoses were single vessel (n=8) and multi-vessel intraluminal atherosclerotic stenoses or occlusions (n=15), and celiac artery compression (n=7). The VAS-overall pain improved from median 60 (IQR 48-72) at BL to 2 (IQR 0-4) at FU3 and 10 (IQR 0-40) at FU12, $p<0.0001$. At these time-points the postprandial VAS improved from 74 (IQR 67-84) to 2 (IQR 0-40) and 10 (IQR 0-48), $p<0.0001$. The VAS-pain after exercise improved from 65 (IQR 50-80), to 4 (0-20) and 10 (IQR 0-35), $p<0.0001$. Analgetic use for abdominal pain decreased from 74% to 17% and 19% of patients ($p< 0.009$), the number of pain free days per week increased from median 0.9 (IQR 0-2) to 6 (IQR 1-7) at FU3 and 7 (IQR 0-7) at FU12, $p<0.0001$. In all cases the difference between BL and FU3 and F12 was highly significant, but no significant difference between FU3 and FU12 was seen. Of the three diagnosis groups the differences showed similar significant improvements from BL to FU3 and FU12 for single- and multivessel atherosclerosis, but not for CACS patients. The HRQOL measured with SF-36 improved for five of eight dimensions (role physical, bodily pain, vitality, social functioning and mental health) and the both (physical and mental) component summary scores.

Conclusions: This prospective study showed marked pain reduction after 3 and 12 months, associated with improved quality of life. The magnitude of change underscores the potential benefit CMI patients may experience from restore of the mesenteric artery inflow.

The incidence and prevalence of chronic mesenteric ischemia

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Background: Chronic mesenteric ischemia (CMI) is a relatively rare disease and there are no previous studies that report the exact incidence and prevalence. This study aims to analyze the incidence and prevalence in a well-defined area. For over the last twenty years this region has great attention to this disease and patients are referred here from over all the Netherlands. Therefore we expect the incidence to be found here will approximate reality. Also we describe the differences in clinical presentation and doctors-delay between patients inside and outside the catchment area ofâ€‹â€‹ Medisch Spectrum Twente (MST). Methods: All patients diagnosed with CMI between 1997 and 2015 in MST were included. In these years the work up and diagnostic criteria remained the same. Patient records were collected prospectively. Contingent missing patients and data was collected retrospectively from medical files. Results: Because of the small number of patients, the annual incidence was averaged over four (first period six) consecutive years. The cumulative incidence of CMI between 1997- 2002, 2003-2006, 2007-2010 and 2011-2014 was 0.9, 2.0, 2.7 and 5.6/100,000 persons/year respectively. Even in the last period the incidence seemed to increase. The point prevalence on 31 December 2014 amounted to 32.0/100,000 persons. Clinical presentation between patients inside and outside the catchment area of MST differed at three levels. First acute on chronic mesenteric ischemia was found significantly more in patients outside the catchment area (3.1 vs. 8.4%, p-value = 0.04). Second these patients had a long duration of symptoms at time of diagnosis (in months 7.0 median (2.0-18.0 range) vs. 10.0 median (5.0-24.0 range), p-value = 0.003) and thirdly, more weight loss over the past twelve months (6.3 average ± 6.3 versus 8.8 average ± 7.9 kilogram, p-value <0.001). A difference in survival was not found. Conclusions: The incidence of CMI measured in this study appears to increase from 0.9 to 5.6/100,000 persons/years over the past two decades. Even the last years the incidence kept increasing. This seemed to be the effect of improvement in attention and diagnostics, rather than the reflection of a true increase in incidence. On 31 December 2014 the point prevalence of CMI was 32.0/100,000 persons. Patients outside the catchment area of MST were more likely of having imminent acute mesenteric ischemia, longer doctors-delay and more weight loss.

The low FODMAP diet: one year follow up

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The low FODMAP diet may be effective in IBS in the short term. Long term data, however, are scarce. In the present study we held telephonic interviews with adult IBS patients without significant co-morbidity who experienced a clinical relevant reduction of symptoms after starting the low FODMAP diet and had at least one year follow up. All 189 patients referred for the low FODMAP diet to the dietary clinic of our hospital during Sept 2013 – Dec 2014 were included. Patients were referred by both medical specialists and GP's. Of the 189 referred patients 18 patients decided not to start with the diet. 33 of the remaining 171 patients were excluded: 4 were < 18 years old, 21 did not have IBS but had another GE diagnosis, and 8 had an eating disorder and/or severe weight loss. 138 patients fulfilled the ROME III criteria for IBS. 90 /138 (65%) patients, experienced a relevant clinical effect during the elimination phase of the diet defined as decrease of at least 2 points in their VAS (0-10), opposed to 12 of 29 (41%) non-IBS patients. These 90 IBS patients (19 males, mean age 44 yr): were sent a letter and offered a telephonic interview at one year follow up. 79 (88%) patients agreed to participate. The study was approved by the local medical ethical comity. After one year 67 of 79 patients (85%; itt 67/90 = 74%) still adhered to the diet, however, none of them strictly. Patients reported that they had learned which foods to avoid and some patients did not consider avoidance of foods as adhering to a diet anymore. Due to the diet 85% (57/67) experienced control of their IBS symptoms with a VAS of 7.3 +/- 1.8. If IBS symptoms increased 38/67 said to follow the diet more precisely and 30/67 tried to reduce stress factors. 91% considered the diet effective (mean 7.9 +/- 2,0). FODMAPS still causing symptoms (mostly 2 fodmaps/patient) were: Fructanes 51/67, Lactose 42/67, Galactanes 29/67, Polyoles 27/67, and Fructose 21/67. At one year follow up 67% experienced no or little trouble adhering to the diet (mean 2.2, on a scale 1-5), however, some patients considered the diet difficult. Eating with other people was experienced most difficult by 45%, 19% considered the diet expensive. Reasons for not adhering to the diet anymore (12 patients) were: too much effort (n=5), no IBS symptoms anymore (n=2), diet not effective (n=5). At one year follow up the mean IBSSS of still users was 173 +/- 107, 54% (36/67) had an IBSSS < 175, 13 % (9/67) still had an IBSSS > 300.
Conclusion: at one year follow up 85% (itt 74%) still uses the low fodmap diet, although not strictly. Patients experience an increased control of their symptoms due to the diet.

REDUCE IBS pilot project: shared decision-making provides IBS patients the power to choose the treatment that fits them best

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Although IBS symptoms can deteriorate patients' lives, the general acceptance of the disorder is often limited and the support from doctors is frequently hampered by lack of time and frustration by shortcomings in communication tools and knowledge of emerging treatment options. A pilot project named REDUCE IBS was designed to study the effect of a novel management strategy for IBS patients in 13 gastroenterology clinics. At first visit specialist nurses screened referred patients for ROME III criteria. After excluding alarm symptoms and diagnostic confirmation by a gastroenterologist, patients were offered 10 electronic handouts with possible therapies: general information, elimination diet, FODMAP-restricted diet, probiotics, hypnotherapy, antibiotics, peppermint oil, spasmolytics and amitripty or citalopram. Patients were asked to study the rationale of information and to choose the 3 most appreciated options. After 2 weeks, patients were seen by the gastroenterologist and nurse together. The nature of IBS was explained and the nurse discussed the chosen therapies. Patients were then referred back to the GP who treated them with the 3 chosen treatment modalities for 2 months each. Questionnaires about symptoms and appraisal were requested at intake and after each therapy episode (range 0-10, given as mean scores). Of 217 patients included, 198 (76% female, mean age 30 yrs) were evaluable. Completed questionnaires were collected from 116 patients (59%). An IBS-sensitizing event was present in 73%. Food increased symptoms in 79%. The preferred therapy choices were peppermint oil (51%), probiotics (49%), low-FODMAP diet (46%), hypnotherapy (36%) and elimination diet (27%). Patients appreciated the given information on therapy options (score 7.7), the care by specialist nurses (7.6) and the possibility of shared decision-making (7.6). Time spent by gastroenterologists was reduced from a calculated average patient contact time of 45 minutes in 2 consultations per IBS-patient to a standardized consultation time in the pilot of 10 minutes. The percentage of colonoscopies performed in IBS patients was reduced from 25% (historic controls) to 15% in the pilot.
Conclusion: This pilot study indicates that extensive and comprehensive information about IBS and potential therapies, individual approach by nurses, 10 therapy options and shared decision-making are greatly appreciated by IBS patients, giving them self-control. Nutrition and nutritional interventions were important topics for patients. Doctor-time and percentage of colonoscopies were substantially reduced. The REDUCE IBS (PDS) protocol will be available at the NVMDL website.

Diagnostic accuracy of the fecal Pancreas Elastase 1 Quick™ Test for exocrine pancreatic insufficiency

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Exocrine pancreatic insufficiency (EPI) is a common complication of chronic pancreatitis or pancreatic surgery. The fecal pancreatic elastase-1 (PE-1) ELISA test is most commonly used to diagnose EPI. Recently, a more rapid and cheaper test became available; the PE-1 Quick™ Test (ScheBo Biotech AG, Giessen, Germany). Our aim was to examine the diagnostic accuracy of the Quick™ Test for detecting EPI in comparison with the PE-1 ELISA test. All consecutive patients with an indication to test for EPI on specialized pancreatic gastroenterology and surgery outpatient clinics were included in the study. The PE-1 ELISA test and Quick™ test were performed from the same stool sample. Quick™ test results are dichotomous based on the presence or absence of a on the test cassette. PE-1 ELISA test results are continuous; PE-1 concentrations <200 µg/g feces were considered as insufficient. Two physicians independently scored the results of the Quick™ test, i.e. the visibility of a on the test cassette. Only those Quick™ test results where the observers agreed on the outcome were used to evaluate the diagnostic accuracy of the Quick™ test compared with the PE-1 ELISA test. Diagnostic accuracy was evaluated based on the agreement between the tests, which was calculated using Cohen's kappa (kappa). The accuracy was also evaluated separately for patients with more severe decreased PE-1 concentrations (<100 µg/g and <15 µg/g). Interobserver agreement between the two physicians on scoring the Quick™ test results was also calculated using kappa. In total, 66 patients were included with a mean age of 62.2 years (SD 12.6). In 44/66 (67%) test results, the two physicians agreed on outcome and these cases were included in the comparison with the PE-1 ELISA test. Calculated kappa on the agreement between the PE-1 ELISA test and the Quick™ test was 0.28, implying only fair agreement. Agreement (kappa) between the two tests in the patient group with PE-1 concentrations <100 µg/g (n=35) was moderate (0.49) and substantial (0.71) in the group of ≤15 µg/g (n=28). Interobserver agreement between the two physicians on the results of the Quick™ test was moderate (0.47). Conclusions. The Quick™ test is not accurate for diagnosing EPI compared to the PE-1 ELISA test. Besides, the Quick™ test results have moderate interobserver agreement.

Lymph node yield is associated with recurrence after surgical resection of T1 colorectal cancer underlining the importance of an oncologic approach even in this early stage

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In patients with stage II colorectal cancer (CRC) the number of surgically retrieved lymph nodes (LNs) is associated with prognosis. Most guidelines recommend a minimum of 10 to 12 LNs. Whether this minimum should be used for T1 CRCs has yet to be determined. To date, a cut-off of 4 LNs has been suggested in literature as well as a limited resection to minimize the risk of complications of surgery in T1 CRCs. We aimed to validate the cut-off of 10 surgically retrieved LNs in T1 CRC on risk for recurrent cancer and explored whether this number is feasible in clinical practice. Data from patients treated with surgical resection of pT1 CRC between 2000 and 2012 were retrospectively collected from 13 hospitals. Multiple imputation was used to adjust for missing data. Multivariate Cox regression analysis was performed to analyse the association between retrieved LNs and recurrence. A cut-off value of 10 retrieved LNs was validated with Kaplan-Meier five-year recurrence free survival curves. In total, 856 pT1 CRCs were included with a median follow-up time of 57.3 months (IQR 30.5-89.1). Forty patients (4.7%) developed recurrent cancer corresponding to 8.9 events (95%CI 6.5-12.1) per 1000 person years of follow-up. Number of LNs retrieved was independently inversely associated with recurrence (HR 0.89; 95%CI 0.81-0.97; p=0.005). Recurrence free survival was significantly better when a minimum of 10 LNs was retrieved (94.8% versus 98.6%, p=0.03). This survival benefit was also observed in a sub-analysis with T1 CRCs without lymph node metastases (N=787; 95.3% versus 98.8%, P=0.05). LN yield icreased over the years from a median of 4 (IQR 2-8) before 2010 (N=576) to 11 (IQR 7-13) from 2010 onwards (N=280, p<0.001). Substantial variance in LN yield was found between hospitals, both before 2010 (p<0.001) as from 2010-2012 (p=0.005). If a minimum of 10 LNs retrieved was considered an adequate resection, this threshold value was achieved in 19.3% of patients treated before 2010 versus 60.4% of patients treated from 2010 onwards (p<0.001).

Conclusion: The number of retrieved LNs at surgery was an independent risk factor for recurrence of pT1 CRC, underlining the importance of an oncologic approach even in this early stage. A median of 10 retrieved LNs was found to be feasible in a routine clinical setting. However, this was only achieved in 60% of resections in recent years and differed significantly between hospitals, suggesting that there is still room for improvement.

Quality of life in rectal cancer patients: watch-and-wait policy versus standard treatment - a matched controlled study

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In 15-20% of the patients with rectal cancer, chemoradiation (CRT) leads to a clinical complete response (cCR). Instead of surgery, these patients follow a stringent post-treatment schedule, called the watch-and-wait protocol (W&W). The aim of this study is to compare the quality of life (QoL) of W&W-patients to the quality of life of a matched-controlled group of patients who underwent CRT & surgery (TME). QoL of W&W-group was compared to the TME-group. Treatments of all patients were finished more than 2 years ago. Patients were patched on age, sex, T-stadium and tumour hegiht. QoL was objectivized with the EORTC-QLQ-C30 and -CR38, SF-36, International Index of Erectile Function (IIEF), Female Sexual Function Index (FSFI), Internatinal Prostate Symptom Score (IPSS), Vaizey-score and LARS-score. 41 patients were included in each group. The W&W-group showed significant less defecation problems according to the Vaizey-score (p=0.021) and LARS-score (p=0.044). The SF-36 showed a better physical function (p=0.016) and physical role (p=0.006) in favour of the W&W-group. The EORTC-QLQ-CR30 and -CR38 showed better body image (p=0.047), sexual function (p=0.040), general health (p=0.051), physical function (p=0.041), role function (p=0.015), and cognitive function (p=0.015) in favour of the W&W-group. Besides, the W&W group had less defecation problems (p=0.012) and financial problems (p=0.001) according to the EORTC-questionnaires. Men in the W&W-group showed less intermittency problems (p=0.002), better QoL (p=0.003), and a better total score (p=0.022) on the IPSS-scale.
Conclusions: On different domains of the questionnaires, W&W-patients showed better quality of life compared to the TME-group. The most important difference is the less defecation problems in the W&W-group according to the LARS- and Vaizey-score.

Clinical relevance of a grading system for anastomotic leakage following low anterior resection: results of the Dutch Surgical Colorectal Audit (DSCA)

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Anastomotic leakage (AL) is a severe complication following a low anterior resection (LAR) for rectal cancer, however, AL comes in different gradients requiring different interventions. Since measuring quality of care and registration initiatives are becoming increasingly important, the need for uniform definitions and grading systems is growing. The aim of this study was to assess the validity and applicability of the grading system for AL as proposed by the International Study Group of Rectal Cancer (ISREC): AL grade B 'necessitating radiological drainage' and AL grade C ' requiring reoperation', using data from the DSCA. All patients who underwent a LAR in the Netherlands with a primary anastomosis between 2009 and 2013 were included. Clinical outcomes (e.g. hospital stay, AL) were recorded and the differences in clinical outcome between AL grade B and C was assessed using an independent sample t-test for continuous variables and using a Chi-square test for categorical variables. Univariate and multivariate logistic regression models were used to identify risk factors for both grades AL. A total of 4287 patients underwent a LAR with a primary anastomosis. In 418 patients (10%) AL was reported; 159 (4%) AL grade B and 259 (6%) with AL grade C. Patients with AL grade C experienced a significantly longer mean hospital stay, a longer mean intensive care unit (ICU) stay and a higher percentage of ICU visits. Absolute 30-day mortality rates were higher in patients with AL grade C (5.8%) versus patients with AL grade B (2.5%), although not statistically significant (p=0.12). Multivariate analysis showed that patients with a diverting stoma (n=2866) had a decreased risk of developing AL grade C compared to AL grade B (OR 0.17, 95% C.I. 0.10-0.29). Male patients and patients without neo-adjuvant treatment had a higher risk of AL grade C versus AL grade B. In our cohort, AL following a LAR was a frequently observed complication. Patients with AL grade C have significantly worse clinical outcomes than patients with AL grade B. Patients selected for a diverting stoma have a lower risk of developing AL grade C compared to patients with AL grade B. These results show that the consequences of AL (drainage or reoperation) may be limited in case a diverting stoma is constructed. However, a diverting stoma is not without risks and can lead to additional (long-term) complications, such as persistent leakage, parastomal hernias and reoperations to remove the stoma. This study shows that the grading system of the ISREC is clinically relevant and applicable. It is advisable to consider AL grade B and C as separate entities in the future.

Follow-up with MRI of rectal cancer after transanal endoscopic microsurgery: detection of recurrence and inter-observer reproducebillity

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Transanal endoscopic microsurgery (TEM) is generally used for the treatment of early rectal cancer, e.g. resection of adenomas and T1sm1 tumours. Recently, TEM has been proposed as an alternative for TME in small residual tumours after neoadjuvant treatment, in with the increasing interest for organ preserving treatment after neoadjuvant treatment.
The aim of this study was to evaluate the diagnostic performance and reproducibility of MRI for the follow-up after TEM (with and without neoadjuvant treatment). Patients with TEM for small rectal tumours without (neo)adjuvant treatment (group 1) and patients with a small residual tumour after neoadjuvant therapy (group 2) were included. Patients underwent local follow-up with ERUS, MRI and endoscopy (group 1) or MRI, and endoscopy (group 2). All MRIs were evaluated by two independent readers, who evaluated morphology and signal intensity of the rectal wall and the mesorectal tissue and compared with histophathology in case of a local recurrence. Presence of a local and/or nodal recurrence was evaluated by means of a 5-point confidence level. Diagnostic performance is evaluated with ROC curves and diagnostic parameters were assessed and compared between readers. Interobserver agreement was assessed with kappa statistics. 52 patients were included in group 1 and 28 patients in group 2 (total N=81). 293 MRIs were performed, of which 203 with DWI. 18 patients developed a recurrence. Overall AUCs for local recurrence detection were 0.71 (sensitivity 62%, specificity 96%) (R1) and 0.80 (sensitivity 62%, specificity 95%) (R2) for T2W-MRI. For DWI AUCs were 0.70 (sensitivity 46%, specificity 94%) (R1) and 0.89 (sensitivity 96%, specificity 95%) (R2). In some cases DWI showed an earlier recurrence than T2W-MRI. For nodal recurrence AUC was 0.72 (sensitivity: 43%, specificity 96%) (R1) and 0.80 (sensitivity: 43%, specificity 95%) (R2) for T2W-MRI. An increase in AUC was seen during follow-up for both T2W- and DWI-MRI in detecting local and nodal recurrence. IOA was good for standard MRI, and moderate for DWI. The number of equivocal scores decreased over time. Isointensity of the rectal wall was a predictive factor for local recurrence.
Conclusions: Follow-up with MRI (including DWI) is a valuable tool to for follow-up after TEM for rectal cancer. Postoperative changes at first follow-up after TEM are confusing, but during follow-up diagnostic performance and interobserver agreement increase to a level high enough for clinical decision making. DWI can be of help in identifying recurrences earlier than on T2W-MRI.

Whole liver CT texture analysis to predict the development of colorectal liver metastases in patient who initially present without metastases – a multicentre study

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Up to 15% of colorectal cancer (CRC) patients have no metastases at primary diagnosis but develop metachronous liver metastases within 5 years. If we can predict the patients at risk, additional chemotherapy or more intense follow-up may be chosen. In addition to known clinical factors (increased CEA, lymph node metastases) imaging could play a role in predicting patients at risk. CT texture is a mathematical post-processing method to assess tissue heterogeneity using routinely acquired clinical CT-examinations. Previous research showed that whole-liver CT-texture analysis may help identify CRC patients at risk for developing liver metastases, albeit in a very small patient cohort. Aim of this multicentre study was to confirm in a larger cohort the value of CT-texture to predict the development of metachronous metastases. The clinical contrast-enhanced CTs of 165 CRC patients were retrospectively analysed. Patients were divided into 3 groups: [A] patients without metastases (>24 months after diagnosis, n=57), [B] patients with synchronous liver metastases (n=54) and [C] patients with liver metastases ≤24 months after diagnosis (n=54). The following texture parameters were calculated for the whole liver: mean grey-level intensity (M), entropy (E; measure of heterogeneity) and uniformity (U; a measure of homogeneity), each with different filter values (small/medium/coarse to highlight structures of varying sizes). The clinical parameters sex, age, CEA, tumour and nodal stage were also assessed. Univariable logistic regression was performed (group A vs. B) to identify potentially predictive texture/clinical parameters. These were then tested in multivariable analyses (group A vs. C) to test their value to predict metachronous metastases with subgroup analyses for early (≤6 months), intermediate (7-12 months) and late (13-24 months) metastases. Receiver operator characteristics (ROC) curve analysis was performed to test diagnostic performance. Uniformity with a small filter ($U_{0.5}$), N-stage and CEA were selected as the best potential predictors and assessed in multivariable analysis. $U_{0.5}$ remained a significant predictor (P=0.05), with an AUC of 0.74 to predict metastases ≤6 months. Combining $U_{0.5}$ with CEA + N-stage resulted in an AUC of 0.78, with a trend towards improved results compared to only N-stage + CEA (P=0.08). None of the texture or clinical parameters could predict metastases within 7-24 months. Whole-liver CT-texture analysis has potential to help predict patients at risk of developing liver metastases ≤6 months after initial diagnosis. It is, however, not robust enough to identify patients at risk of developing metastases at later stage.

Advanced age is no contraindication for chemoradiotherapy with curative intent in oesophageal cancer

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Purpose To compare long-term outcomes of chemoradiotherapy between older (≥70 years) and younger oesophageal cancer patients treated with curative intent. Methods Oesophageal cancer patients treated between 1998 and 2013 in our institute with neoadjuvant (nCRT) or definitive (dCRT) chemoradiotherapy were retrospectively analysed. nCRT consisted of 36-50Gy with concurrent 5-fluorouracil/cisplatin or 41.4Gy with concurrent carboplatin/paclitaxel. dCRT consisted of 50Gy with concurrent fluorouracil/-cisplatin or 50.4Gy with concurrent carboplatin/paclitaxel. Overall survival (OS), disease-free survival (DFS) and locoregional control (LRC) were compared between older (³70 years) and younger patients (< 70 years). Cox models were used to obtain adjusted hazard ratios (HR) and 95% confidence intervals (CI). Results Seventy-six of a total 253 patients (median age 64 years, interquartile range 58-72) were ³70 years (median age 75, interquartile range 73-78). Median follow-up was 4.9 years. Most patients had stage II-IIIA disease (83%). Planned treatment was nCRT with surgery for 169 patients (41 patients ³70 years) and dCRT for 84 patients (31 patients ³70 years). Although surgery was the intent, 32% of the older nCRT patients were not operated versus 16% of the younger nCRT patients (p=0.01). In 33 patients (13 patients ³70) planned surgery was not performed, because of disease progression(n=18), toxicity of nCRT(n=7) or patients choice(n=8). OS at 3-years was 42% with no difference between the older and younger age groups. At baseline, the two age groups (older vs. younger) differed significantly regarding smoking (33% vs. 59%; p<0.001), alcohol abuse (47%; vs. 63%; p=0.01), Charlson comorbidity index (median 1 vs 0; p<0.001) and weight loss prior to CRT (median 3 vs. 4 kg; p=0.03). Also, there was a significant difference in the distribution of final treatment given (nCRT + surgery, dCRT or nCRT without surgery; p=0.006). In the multivariable analysis no statistical difference was found in OS nor in DFS between the two age groups (old vs. young); OS (HR 0.88, 95% CI 0.61–1.28, p=0.51), DFS (HR 0.87, 95% CI 0.60–1.25, p=0.45).
Conclusion Long-term outcomes of elderly oesophageal cancer patients (³70 years) selected for treatment with neoadjuvant chemoradiotherapy followed by surgery or definitive chemoradiotherapy were comparable to the outcomes of younger patients. Advanced age alone should not be a contraindication for chemoradiotherapy-based treatment in oesophageal cancer patients with locally advanced disease.

F-18-FDG PET/CT in the evaluation of tumour response after neoadjuvant chemoradiotherapy in locally advanced oesophageal cancer

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Neoadjuvant chemoradiotherapy (nCRT) with "CROSS" (NEJM 2012) is effective in reducing tumour load preoperatively. Many patients (92%) had radical resections after nCRT, with pathologically complete response (tumour regression grade = TRG1) in 29%. In future, we aim at postponing surgery using adequate clinical response evaluations (CRE) until residual locoregional disease without distant metastases has been identified. A multicentre feasibility study is underway (preSANO trial, NL41732.078.13) including endoscopy, biopsies, ultrasound and FDG-PET/CT with surgery 12 weeks after nCRT. The current preliminary analysis focuses on FDG-PET/CT to predict residual vital tumour (minimal: ≤10% vital cells = TRG1+2, substantial: >10% = TRG3+4) after nCRT. FDG-PET/CT at base and CRE was performed according to EANM guidelines 1.0 (2.3MBq/kg F-18-FDG; scanning 60±5min.). Visual assessment: presence of residual tumour and/or metastases. SUV and SUV/lean body mass (SUL) measurements at tumour, lymph nodes, oesophagus, liver and bloodpool were recorded and compared with the resection specimen. Of 75 patients analysed, 7 withdrew before CRE. Ten patients had no surgery (1 died, 1 metastases before CRE, 5 FDG-positive metastases, 3 surgery postponed). Eight patients had surgery without FDG-PET/CT at CRE. In the remaining 50 operated patients FDG-PET/CT at CRE was positive in 36 (72%). In 3/36 patients tumours appeared irresectable, 33/36 patients had radical resections. In 18/33 TRG3 or TRG4 residual tumour was found. SUL-max in these tumours was 3.67±0.97 and SUL-max-ratio tumour/oesophagus (SULR) 1.83±0.41. In 8/33 patients TRG2 residual tumour was present; SUL-max 4.35±2.52 and SULR 2.24±1.41. In 1/33 patients TRG score was missing. In total, FDG-PET/CT was true positive in 29/36 patients (81%). 6/36 patients had no vital tumour (TRG1; 17% false positive); SUL-max 2.84±0.97, SULR 1.60±0.69. In 14/50 operated patients FDG-PET/CT at CRE was negative. No vital tumour (TRG1) was found in 6/14 patients (43% true negative); SUL-max 1.94±0.29, SULR 1.14±0.16. Conversely, 1 patient had minimal (TRG2) and 7/14 patients had substantial residual tumour (TRG3 or TRG4); SUL-max 2.49±0.71, SULR 1.43±0.09. Two patients (1 irradical resection) had non-FDG avid base scans, 6 (1 irradical resection) had good FDG-response compared to baseline. Conclusions: Positive FDG-PET/CT after nCRT predicts substantial residual tumour in 81% of patients. However, visual and quantitative FDG-PET/CT alone is not sufficiently accurate for detection or exclusion of substantial vital tumour; results of FDG-PET/CT performance combined with endoscopy, biopsies, ultrasound have to be awaited.

The impact of histological subtype on the prognosis of oesophageal adenocarcinoma

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The prognosis of gastric adenocarcinoma differs per histological subtype (according to Laurén: intestinal, diffuse or mixed type). Patients with an intestinal type tumour have a more favourable prognosis than patients with a diffuse type tumour. In oesophageal adenocarcinomas the same histological subtypes exist, but there are no data available on the association between these subtypes and survival. This study analysed the association between histological subtype (according to Laurén) and survival after potentially curative treatment for oesophageal adenocarcinoma. Data were collected from all oesophageal adenocarcinoma patients who were treated with curative intent in our institute between 1998 and 2014. Treatment consisted of neoadjuvant chemoradiotherapy (36-50Gy) followed by an oesophagectomy or definitive chemoradiotherapy (50-50.4Gy). Radiotherapy was combined with 5-fluorouracil/cisplatin or carboplatin/ paclitaxel. Clinical data were collected from patient files. An expert pathologist reassessed all endoscopic biopsies and surgical resection specimens to determine the histological subtype (diffuse/ intestinal/ mixed), and, other histological variables including tumour regression grade (according to Mandard). The impact of histological subtype on survival was calculated with a Cox model. In surgically treated patients, postoperative tumour characteristics were compared between the histological subgroups. Tumour characteristics and type of treatment (neoadjuvant chemoradiotherapy and surgery or definitive chemoradiotherapy) were equally distributed between patients with an intestinal (n=120), a diffuse (n=28) or a mixed type (n=11) oesophageal adenocarcinoma. Overall survival (median: 29 months), was significantly different between patients with an intestinal (34 months), a diffuse (18 months) or a mixed type (25 months) tumour (log rank, p=0.026). In multivariable analysis, the diffuse type was independently associated with a shorter survival (diffuse vs. intestinal: HR 1.990, p=0.009). A pathologically complete or subtotal response, was seen more often in intestinal type than in diffuse type adenocarcinomas (59% vs. 24%; p=0.016). Conclusions: Patients with a diffuse type adenocarcinoma of the oesophagus had a significantly worse prognosis than those with an intestinal type tumour. Intestinal type tumours responded considerably better to neoadjuvant chemoradiotherapy than diffuse type tumours. These differences call for a more differentiated approach in the potentially curative treatment of oesophageal adenocarcinomas.

FOLFIRINOX in locally advanced and metastatic pancreatic cancer: a single centre cohort study

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FOLFIRINOX is emerging as new standard of care for fit patients with locally advanced pancreatic cancer (LAPC) and metastatic pancreatic cancer (MPC). However, several physicians are reluctant to use FOLFIRINOX due to high toxicity rates reported in earlier studies. We reviewed our experience with FOLFIRINOX in LAPC and MPC, focusing on dose adjustments, toxicity and efficacy. We reviewed all patients with LAPC or MPC treated with FOLFIRINOX in our institution between April 2011 and December 2015. Unresectability (stage III and IV) was determined by the institution's multidisciplinary team for pancreatic cancer. Fifty patients (18 LAPC and 32 MPC) were enrolled, with a median age of 55 years (IQR 49-66) and WHO performance status of 0/1. FOLFIRINOX was given as first- treatment in 82% of patients. Dose modifications were applied in 90% of patients. The median number of completed cycles was 8 (IQR 5-9). Grade 3-4 toxicity occurred in 52% and grade 5 toxicity in 2%. The response rate was 25% (12% in LAPC, 32% in MPC). Median overall survival and progression-free survival were 14.8 and 10.3 months in LAPC, and 9.0 and 5.9 months in MPC, respectively. Overall 1- and 2-year survival was 65% and 10% in LAPC and 40% and 5% in MPC. Within the LAPC group, 6 patients (33%) underwent local ablative therapy and 1 patient (6%) a resection, leading to a median survival of 21.8 months.
Conclusion FOLFIRINOX treatment with nearly routine dose modification, was associated with acceptable toxicity rates, relatively high response rates and an encouraging overall survival.

Feasibility of 1h-mrs for noninvasive assessment of liver fat content in patients using long-term home parenteral nutrition

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Aim Home Parenteral Nutrition (HPN) is the mainstay of treatment for patients with long-term intestinal failure. One of the complications in this patient group is intestinal failure associated liver disease (IFALD), a complication ranging from disturbed liver enzymes to end stage liver disease. Steatosis is a dominant feature of IFALD in adults. Proton MRS (1H-MRS) is a non-invasive method to assess liver fat content, which enables monitoring of the disease over time. To this end, liver fat content was determined in patients using long-term HPN with 1H-MRS, taking into account the possibility of altered magnetic resonance signal relaxation behavior as a result of the PN treatment. Methods Liver fat content was measured in 15 HPN patients (5 males, age 49 ± 14 yrs, median BMI 21.5 ±3) who had been on HPN (6 ± 1.6 times per week) for 3.6 yrs (6 mo-33 yrs) due to intestinal failure caused by a benign underlying disease. 1H-MR spectra and images of the liver were obtained using a 3T whole body MRI-system. 1H-MRS was obtained with multiple echo times to account for altered signal relaxation behavior of water that might result from accumulation of paramagnetic PN constituents. Patients with low (< 5%) vs high (≥ 5%) liver fat content were compared using Mann-Whitney U test. Results Liver 1H-MR spectra of good quality were obtained in 14 out of 15 patients. 1H-MRS analysis revealed an increased liver fat content in 5 out of 15 patients (mean 10.8 ± 2.8%), 10 patients had a normal liver fat content (1.3 ± 1.1%). All patients showed shortened T2-relaxation behavior of water to some extent , suggesting accumulation of paramagnetic constituents in the liver. Patients with high liver fat content had higher ALAT values than patients with low liver fat content (median 60 U/L ± 56.6 vs. 27.5 U/L ± 15.2) and frequency of HPN use per week was lower (4 ± 1.6 times a week vs 7 ± 1.1 times a week) in the high liver fat group. In one patient with a serum ferritin of 3632 µg/L after recent infusion with a ferric compound, MR spectra were not representative with broadened resonances. MR imaging revealed novel findings in 10 patients (gall bladderstones (6), enlarged adrenal gland (2), (hepato)splenomegaly (1) and bile duct stones with normal liver function tests (1).
Conclusion 1H-MRS enables a reliable non-invasive quantitative assessment of liver fat content for patients receiving long-term HPN. Altered MR signaling in the form of increased T2 relaxation behavior, possibly due to hepatic accumulation of PN constituents, has to be taken into account. Hepatic lipid fat content seems difficult to obtain with 1H-MRS after recent ferric compound infusion.

Enteral glutamine supplementation in optimally fed critically ill patients does not affect protein metabolism

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During critical illness muscle and protein wasting occurs, but the effect of optimal enteral nutrition in critically ill patients on protein synthesis remains unclear. Critically ill patients have significantly decreased muscle glutamine levels sometimes accompanied by reduced plasma glutamine concentrations. Hence in order to counteract catabolism glutamine has been supplied in the past decades. The objective was to investigate the effect of targeted enteral nutrition with or without enteral glutamine, on protein synthesis. This was an open label randomized clinical trial including 2 groups of 10 critically ill patients, assigned to receive full enteral nutrition (CON), or isocaloric isonitrogenous enteral nutrition including 0.5 g/kg L-alanyl-L-glutamine per day (ALA-GLN). Tracer methodology was used to determine rate of appearance and turnover of phenylalanine and tyrosine. Both groups received intravenous and enteral tracers in a cross-over design on separate days to calculate splanchnic extraction. Most kinetic aspects for tyrosine and phenylalanine in intravenously measured experiments were significantly different from the enteral experiments. Protein breakdown was not different for both groups. Phenylalanine hydroxylation was significantly higher in the ALA-GLN group (CON 0.75 µmol/kg/h; ALA-GLN 1.72 µmol/kg/h, p=0.028). Protein synthesis was not different between groups (CON 14.0 (IQR12.4-23.6) µmol/kg/h; ALA-GLN 19.5 (SEM±2.7) µmol/kg/h, p=0.354). Protein balances were nearly zero and were more negative in the ALA-GLN group (CON -0.75 (SEM±0.36) µmol/kg/h; ALA-GLN -1.72 (SEM±0.17) µmol/kg/h, p=0.028). Splanchnic extraction of tyrosine and phenylalanine was not different between groups. Conclusions: This study proves that in critically ill stable non-septic patients with optimal nutrition and a target protein intake of 1.2-1.7 g/kg/day, protein balances approach zero. Enteral glutamine supplementation has no positive effect on protein synthesis in this population.

Colonoscopy without PSA is feasible, is well tolerated and has a high success rate in males

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Unsedated colonoscopy has advantages for both patients and health care settings. In the present study a prospective cohort of unselected patients was offered to start the procedure without procedural sedation or analgesia (PSA) by 3 experienced endoscopists using water immersion. Medication could be requested at any point during the procedure. The study was approved by the local medical ethical committee. 249 patients were eligible, the endoscopists decided not to ask 21 patients (10 males) to participate. 223 patients (133 male (59 % of 223), mean age 62 yr; female: 58 yr) were asked and 123 (55%) chose to start without PSA. Significantly more males (n=92 (69%), mean age 60 yr) than females (n=31 (34%), mean age 58 yr) choose to start without PSA (p<0,001). The procedure was successful without PSA in significantly more males (n=85, 92%) than females (n=23, 58%) (p<0,001)). Itt: 59% (85/143) of the males and 22% of the females had a successful colonoscopy without PSA (p<0,001). The intention to treat success rates differed between the 3 endoscopists, for males: 38–79% (p<0,001). In 3 patients the cecum was not reached. The mean cecum intubation time was 2-3 minutes longer (males: p<0,001) in patients without PSA (male: 7.0 min±4,3; female: 8,7 min±4,7) as compared to patients that started with PSA (male: 4.2 min±2,2, female: 7.1 min±4,3). In the 16 patients that received PSA during the procedure it took 11.5 min±6.1 (p<0,01) to reach the cecum. The mean cecum intubation time in patients without PSA differed between the 3 endoscopists: 4,9–8,8 minutes (p<0,001). Pain scores (VAS 0-10) were available in 104 (81 males) of the 123 patients who started and finished colonoscopy without PSA. The mean pain score in males (2.5±2.2) was lower (p<0,05) compared to females (3.7±1.9). 77% males and 61% females had a pain score < 5. Pain scores in the group that started with PSA (92 pain scores available) were lower compared to without PSA: males (N=38) 0.8±1.3 (p<0,001) and females (N=54) 2.4±2.6 (p<0,05). The 16 patients that received PSA during the procedure had a mean pain score of 5,0 (p<0,001). The VAS scores of patients without PSA dit not differ between the 3 endoscopists. Despite VAS >4 in 23-39%, nearly all patients (100/104 responders: 96%) who successfully underwent the colonoscopy without PSA, were willing to undergo a future colonoscopy without PSA. In the PSA-group only 10 patients (11%) were willing to undergo a future colonoscopy without PSA.

Conclusion: starting colonoscopy without PSA is feasible, is well tolerated and has a high success rate in males, but at the expense of 2-3 minutes extra procedure time.

Therapeutic strategy for anemia in patients with gastrointestinal bleeding: a retrospective cohort study

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The optimal strategy of treating anemia secondary to gastrointestinal (GI) bleeding is presently not clear. We aimed to study the changes in therapeutic strategy over the past years and aimed to identify the most effective therapeutic strategy for anemia in adults with GI bleeding. We performed a retrospective cohort study, including adult patients who were hospitalized because of GI bleeding in a single center between 2010 and 2014. Data were extracted from medical records. Treatment of associated anemia (iron treatment or blood transfusion) and hemoglobin (Hb) levels were collected at baseline. Hb levels of patients were collected for up to 12 months or until death. Different therapeutic strategies for anemia at base were plotted against corresponding Hb levels at base and follow-up using cross tabulations and chi-square tests, and independent sample t-tests where appropriate. In total, 303 hospital admissions for GI bleeding in 294 patients were recorded, of whom 217 patients (73.8%) were anemic. Of these, 74.2% received treatment for their anemia (oral iron treatment (6.9%), intravenous iron treatment (2.8%), blood transfusion (48.8%) or combination of oral iron treatment and blood transfusion (10.1%) or intravenous iron treatment and blood transfusion (5.5%)). Mean follow-up was 2.8 months and 71 (23.4%) patients died. Between 2010 and 2014 the percentage of patients who received blood transfusions decreased significantly from 61.1% to 45.9% ($p=0.02$), whereas treatment with iron increased from 21.1% to 38.5% ($p=0.06$). Blood transfusion in anemic patients was associated with higher increases of Hb levels as compared with patients who did not receive transfusion (mean ΔHb after one month 1.47 mmol/L versus 0.26 mmol/L, $p<0.01$). Patients receiving blood transfusions had an even higher increase of Hb levels when blood transfusions were combined with iron therapy (mean ΔHb after one month 1.86 versus 1.26, $p=0.10$). For patients who did not receive blood transfusion, iron therapy was associated with higher increases of Hb levels during long-term follow-up as compared with patients who did not receive iron (mean ΔHb after 12 months 1.34 versus 0.99, not significant).
Conclusions: Our data suggests that fewer blood transfusions are administered over the years, balanced by an increase of iron supplements (both oral and intravenous) in patients admitted for treatment of a GI bleeding. The combination of blood transfusion with iron therapy seems to induce the highest increase in Hb levels.

Early versus standard colonoscopy - a randomized controlled trial in patients with acute lower gastro-intestinal bleeding: results of the BLEED study

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The incidence of acute lower gastro-intestinal bleeding (LGIB) is estimated at 21 adults per 100.000 person years and is increasing with the ageing of the population. Diagnostic management of LGIB has been extensively debated in recent literature, especially whether colonoscopy within 24 hours of presentation is feasible and safe. The aim of our study was to examine differences in length of hospital stay in patients with LIGB receiving either early colonoscopy (within 24 hours of presentation) or standard colonoscopy (within 1-3 days).
We performed a single centre, non-blinded randomized controlled trial, including patients presenting at the emergency Dept with acute hematochezia and excluding patients with an upper bleeding source. Primary outcome was the length of hospital stay. Secondary outcomes included yield of colonoscopy, complications and subsequent diagnostic or therapeutic interventions related to bleeding and 30-day mortality. The follow up period was one month. In total, 132 patients were randomized: 63 for early colonoscopy and 69 for standard colonoscopy. Three patients were excluded from analysis due to a protocol violation - the standard colonoscopy was performed after hospital discharge. Base characteristics of both groups were comparable. The length of hospital stay was significantly lower in patients that underwent an early colonoscopy, compared to the standard colonoscopy group (median 2 days [range 1-13] vs median 4 days [range 1-31]; p=0.02). Also, an active bleeding at colonoscopy was more frequently diagnosed in the early group: 9 patients (14%) versus 2 patients (3%) in the standard group (p = 0.02). Complications were comparable in both groups: 9 patients (14%) in the early colonoscopy group versus 4 patients (6%) in the standard group (p = 0.12), of which 8 (13%) versus 2 (3%) patients with rebleeding and 0 (0%) versus 1 (2%) perforation respectively. Re-admission was significantly more frequent in the early colonoscopy group: 7 patients (11%) required re-admission, versus 1 patient (2%) in the standard group (p=0.02). Of the 8 patients in the early colonoscopy that experienced a rebleeding, 4 underwent a second colonoscopy during re-admission; in the standard group, this applied to both patients with rebleeding. Thirty-day mortality in both groups was zero.
Conclusions: in patients with LIGB, colonoscopy within 24 hours of admission reduces the length of hospital stay compared to colonoscopy within 1 to 3 days of admission. Also, it appears that early colonoscopy is safe, although the re-admission rate is higher.

Impact of the formation of a regional EUS interest group amongst community hospitals on the yield of EUS guided tissue acquisition in suspected pancreatic malignancy

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Background The use of EUS guided tissue acquisition (TA) in diagnosing pancreatic malignancy has increased throughout the past two decades. Data on the diagnostic accuracy of this technique have almost exclusively been generated in tertiary referral centers. To our knowledge no data are available on role and quality of EUS guided TA in diagnosing pancreatic malignancy in community hospitals i.e. in general gastroenterology practice neither regarding ways to potentially improve its diagnostic yield.
Aim To determine quality of EUS-guided TA in diagnosing pancreatic malignancy in community hospitals, in particular after the formation of a regional EUS group interactively discussing cases, techniques and outcomes on a regular basis. Patients and methods First, we retrospectively analysed the yield of 143 EUS guided TA procedures for suspected pancreatic malignancies from 7 different hospitals in the southwestern part of the Netherlands before the regional EUS interest group was established. Next, after initiating the regional EUS interest group and after having had several meetings discussing cases and the specifics of various EUS-FNA/FNB techniques, we prospectively recorded data on EUS guided TA procedures from January to October 2015 in 5 of these hospitals. Patient characteristics, size and localization of the pancreatic mass, EUS-characteristics of the mass, size and type of needles, use of suction techniques, number of needle passes, and types of cytology medium for cellblock were recorded. Outcome measures were the results of histo-, and cytopathological analysis, which were compared to a gold standard of 6 months follow-up and histopathology from resected tissue and/or metastatic tissue. The results of the first 75 prospective cases were compared to the retrospective data using chi-square and Mann-Whitney U tests when appropriate. Results Both the increase in procedures diagnostic for malignancy and decrease in procedures yielding insufficient material for diagnosis were significant ($p<0.05$). Sensitivity, specificity, PPV , NPV and diagnostic accuracy in the retrospective cohort were: 65%, 100%,100%, 44%, and 72% respectively. In the prospective cohort sensitivity, specificity, PPV, NPV and diagnostic accuracy were: 86%,100%,100%,50%, and 88%.Significant differences between retrospective and prospective series were: the number of needle passes, the use of suction techniques and needle size. In the prospective series less 19G needles were used, and both more needle passes and more suction were applied. Both groups were comparable with regards to age, gender and final histopathological diagnosis.

EUS for suspected choledocholithiasis. First results of a change in strategy regarding indication and timing of ERCP

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EUS has an excellent diagnostic accuracy for diagnosing CBD stones. In a recent retrospective study, the proportion of positive findings at ERCP in patients with EUS-confirmed bile duct stones was relatively low (58%). This appeared to be related to both the time interval between EUS and ERCP, allowing for spontaneous stone and sludge passage, and the decision to regard biliary sludge as an indication for ERCP. In this study, we aim to re-evaluate the time interval and the proportion of positive findings on ERCP. We also adopted a more conservative attitude towards patients with mild symptoms and a non-dilated CBD with sludge at EUS. Between January 2015 and March 2016, 40 out of 100 (40%) consecutive patients undergoing EUS for suspected bile duct lithiasis had positive findings. Patients with CBD stones on EUS all underwent an ERCP + sphincterotomy. In patients with sludge and a non-dilated CBD on EUS with mild symptoms, ERCP vs watchful waiting was discussed with the patient. Patients opting for the conservative strategy were followed at the outpatient clinic. Data were compared to our retrospective series. Thirty-four out of 40 (85%) patients with positive EUS findings had one or more CBD stones. Six of those only had sludge. Only one of these patients underwent ERCP and sphincterotomy. In the remaining 5 patients a watchful waiting strategy was adopted. None of these patients developed cholangitis, pancreatitis or any indication for ERCP for biliary symptoms at six months follow-up. In patients in whom an ERCP was performed, 26 of 35 (74.3%) had positive findings. This was substantially higher compared to our retrospective series. The interval between EUS and ERCP was 2 days (interquartile range 1-8) and shorter compared to our retrospective series (4 days, p=0.05). Sludge was detected and removed in 3 out of 35 cases (8.5%). One or more stones were found in 23 of 35 cases (66%). The one patient with CBD sludge at EUS had an unremarkable ERCP. Patient characteristics including age, gender and cholecystectomy history were comparable in both the retrospective and prospective cohorts.

Conclusions. Shortening the interval between EUS and ERCP results in a higher proportion of positive findings at ERCP as expected. Although evidence is limited, a more conservative approach, i.e. not immediately performing an ERCP in patients with mild non-specific symptoms with sludge in a non-dilated CBD, appears justifiable without an apparent increase in the incidence of biliary complications.

Laparoscopy-assisted transgastric endoscopic retrograde cholangiopancreatography in patients with Roux-en-Y gastric bypass

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Endoscopic retrograde cholangiopancreatography (ERCP) is indicated for the treatment of biliopancreatic disease, such as choledocholithiasis, cholangitis and biliary pancreatitis. After bariatric surgery, about 40% of patients develop cholelithiasis. Gastroenterologists are often confronted with patients who previously underwent bariatric surgery, changing the gastrointestinal anatomy. After Roux-en-Y gastric bypass (RYGB) it can be challenging to reach the major duodenal papilla due to this changed anatomy. Our hospital is a referral center for bariatric surgery and ERCPs in patients with RYGB are performed regularly. Several years ago, we started performing ERCPs using single balloon enteroscopy (SBE); currently we perform laparoscopy-assisted ERCPs. The procedure starts with a laparoscopy, during which the surgeon provides access to the excluded stomach. An extra 15 mm trocart is introduced to facilitate introduction of the duodenoscope into the abdominal cavity and subsequently in the stomach remnant through a small incision. After this, the major duodenal papilla is reached with the duodenoscope. The aim of the current project was to analyze retrospectively the procedures that were performed over the last years to assess the feasibility of this method. We collected patients with a previous medical history of RYGB that underwent ERCP either by SBE or by laparoscopy-assisted ERCP. Cholecystectomy was performed in the same session if indicated. In total, 41 procedures were performed in 30 patients between July 2009 and June 2016. Indications for ERCP were biliary pancreatitis, cholangitis, choledocholithiasis and biliary leakage after cholecystectomy. Nine ERCPs by SBE were performed in 7 patients, 32 laparoscopy-assisted ERCPs were performed in 27 patients. Four patients underwent both methods of ERCP over time. ERCP by SBE failed in 5 out of 9 procedures: in 3 procedures the major duodenal papilla was not reached, in 2 procedures the papilla could not be cannulated. Laparoscopy-assisted ERCP was not successful in 2 patients: in 1 patient stone extraction was unsuccessful, in 1 patient the papilla could not be cannulated. Cholecystectomy was performed in 11 patients in the same session. The mean length of laparoscopy-assisted ERCP was 78 minutes, or 95 minutes when combined with cholecystectomy. Although the length of SBE procedures was not recorded, in our experience laparoscopy-assisted ERCP takes less time than ERCP by SBE.

We conclude therefore that laparoscopy- assisted ERCP is a feasible method to use in biliopancreatic disease after bariatric surgery, which allows cholecystectomy to be performed during the same session if indicated.

Diagnosis of T1 colorectal cancer in pedunculated polyps in daily clinical practice: need for a second opinion?

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Diagnosing T1 colorectal cancer (CRC) in pedunculated polyps on hematoxylin-eosin (H&E) stained slides is challenging due to overlapping features with so-called pseudoinvasion and intramucosal carcinoma (the latter most often classified as high grade dysplasia). United Kingdom guidelines are currently one of the few which recommend diagnostic confirmation of the diagnosis T1 CRC by a second pathologist. The aim of this study was to provide insights into the accuracy of histological diagnosis of pedunculated T1 CRCs in daily clinical practice. A sample of 128 cases diagnosed as pedunculated T1 CRC between 2000 and 2014 from ten Dutch hospitals was selected for histological review. Firstly, two expert Dutch gastrointestinal pathologists reviewed all H&E slides. In 20 cases the diagnosis T1 CRC was not confirmed (15.6%, 95%CI 9.5 – 22.0). In 14 of these cases the patients had undergone surgical resection. The percentage of discordant diagnoses remained the same in recent years (14.8% between 2000-2010 vs. 17.5% between 2011-2014, p=0.69). The discordant cases were subsequently discussed in a consensus meeting with a third Dutch pathologist and a consensus diagnosis was agreed. The revised diagnoses included pseudo-invasion in 10 cases (7.8%; 95%CI 3.8 – 12.7), dysplasia or intramucosal carcinoma in 4 cases (3.1%; 95%CI 0.8 – 6.3) and equivocal in 6 cases (4.7%; 95%CI 1.6 – 8.7%). To further validate the Dutch consensus diagnosis, the discordant cases were reviewed by an independent expert pathologist from the United Kingdom. A total of 39 cases were reviewed blindly including the 20 cases with a revised diagnosis and 19 control cases where the Dutch expert panel agreed with the original reporting pathologist diagnosis. In 19 of the 20 cases with a revised diagnosis the British pathologist independently agreed that T1 CRC could not be confirmed. Additionally, amongst the 19 control cases the British pathologist was unable to confirm T1 CRC in a further four cases. Conclusion: Both generalist and expert pathologists experience diagnostic difficulty distinguishing pseudo-invasion and intramucosal carcinoma from T1 CRC. In order to prevent overtreatment, review of the histology of pedunculated T1 CRCs by a second pathologist should be considered with discussion of these cases at a multidisciplinary team meeting.

Is Hybrid Endoscopic Submucosal Dissection Effective for Treatment of Large Non-Pedunculated Colorectal Polyps? A Single Center Experience

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Introduction: There is wide variation in endoscopic treatment strategies of large non-pedunculated colorectal polyps (LNPCP) among gastroenterology practices. Both endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) techniques are applied. The hybrid ESD (hESD) is an alternative resection technique, but its effectiveness in the treatment of LNPCPs is still unclear. Because the learning-curve of ESD is steep and lengthy, hESD might be an intermediate step to acquire technical skills. The aim of this study was to evaluate the complete resection rate and local recurrence rate of hESD and EMR in our daily practice. Methods: We prospectively included all consecutive patients who underwent endoscopic resection of LNPCPs at a community hospital from January 2008 to October 2015. Follow-up data were collected. We defined LNPCPs as large (≥20mm) sessile, flat, and depressed colorectal neoplasms or combinations (Paris classification). Complete resection rate was defined as complete resection after 1, 2 or ≥3 sessions. Early local recurrence was defined as presence of residual adenoma at first follow-up examination after resection. All procedures were performed by one experienced therapeutic endoscopist. Results: Fifty-six patients (mean age 69.8 yrs, 48.2% male) and 35 patients (mean age 74.9 yrs, 74.3% male) with 58 LNPCPs and with 42 LNPCPs were included in the hESD group and EMR group, respectively. Mean polyp size for hESD vs EMR was 29.7 mm [20-60] vs 25.1 mm [20-53]. LNPCPs in the hESD group were more distally located (79.3% vs 50%), contained more flat morphology (79.3% vs 52.4%) and high grade dysplasia (43.1% vs 28.5%) or early cancer (12.1% vs 4.8%) than the EMR group. Complete resection rate after 1, 2 or ≥3 sessions was 74.1%, 87.9% and 89.7% for hESD and 76.2%, 78.6% and 85.7% for EMR. Early recurrence rate after hESD and EMR was 25.9% (95% CI 15.3%-39%) vs 23.8% (95% CI 12.1-39.5%) after a median follow-up duration of 5 (0.7-14.9) months and 5.2 (1.2-24.4) months. En-bloc resection rate was similar in the hESD group (43.1%) and EMR group (45.2%). Referral rate to surgery was similar in both groups. Four (6.6%) and 2 (4.8%) post procedural complications requiring hospital admission occurred after hESD vs EMR, without the need for surgery. Conclusion: To our knowledge, this is the first study to report outcomes of hESD of LNPCPs in the Netherlands. In this single center experience, both hESD and EMR appeared to be safe and equally effective in resecting LNPCPs, albeit some cases require multiple sessions. Larger multicenter randomized studies are needed to investigate whether hESD can help to speed up the learning-curve of ESD.

Prevalence and characteristics of unexpected rectal cancer in benign cancer in benign appearing large non-pedunculated rectal polyps

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Objective: Transanal endoscopic microsurgery (TEM) and endoscopic mucosal resection (EMR) are the most common resection techniques for large non-pedunculated rectal polyps. Despite thorough preoperative investigation, unexpected rectal cancer is occasionally encountered at pathological examination of the resected specimen. Little is known about the prevalence and characteristics of unexpected cancer in those lesions that appear benign. This study describes the prevalence of unexpected rectal cancers, lesion and procedural characteristics and its subsequent treatment and recurrence rates.
Methods: Patients in this post-hoc analysis were selected from a multicentre RCT (TREND study) investigating the recurrence of neoplasia after treatment of rectal polyps with either EMR or TEM between 2009-2013. Patients with a non-pedunculated rectal polyp of ≥ 3 cm located between 1-15 cm from the anal verge without endoscopic suspicion of invasive growth, were eligible. If histopathology of the resected specimen revealed invasive growth, patients were included in this analysis. Data concerning patient, lesion and procedural characteristics as well as additional therapy and surveillance were collected. Results: Unexpected rectal cancer was found in 13% of the patients in the TREND study (27/204); 15 treated with EMR and 12 with TEM. The majority consisted of a T1 cancer (n=22, 81.5%) but also 3 T2 (11.1%) and 2 T3 cancers (7.4%) were detected. The mean lesion size was 47 ± 11.6 mm, 18 (78.3%) cancers were moderately-well differentiated and no lymphatic or vascular invasion was detected. Resection procedures of malignant lesions were more often assessed as being irradical compared to benign lesions (25.0% vs 8.5%, p = 0.02). The success of submucosal lifting during EMR was also lower (60.0% vs 93.1%, p < 0.001). Patients initially treated with EMR received completion surgery in 80.0%, which consisted in 50% of TME (66.7% LAR, 33.3% APR) and in 50% of TEM. Five patients (41.7%) initially treated with TEM received completion surgery, which was according to the TME principle (20% LAR, 80% APR) in all patients. After a mean follow up of 4.4 ± 1.2 years, all patients were alive and one malignant recurrence was detected. Distant metastases were found in 3 patients (11%), whom all underwent surveillance after treating a T1Sm3 carcinoma with TEM.
Conclusion: Despite careful lesion assessment, unexpected cancers were encountered in 13% of patients treated for large non-pedunculated rectal polyps. This might impact the strategy how to treat these polyps in the future, since incomplete procedural resection and non-lifting sign during EMR occurred more often in the cancers.

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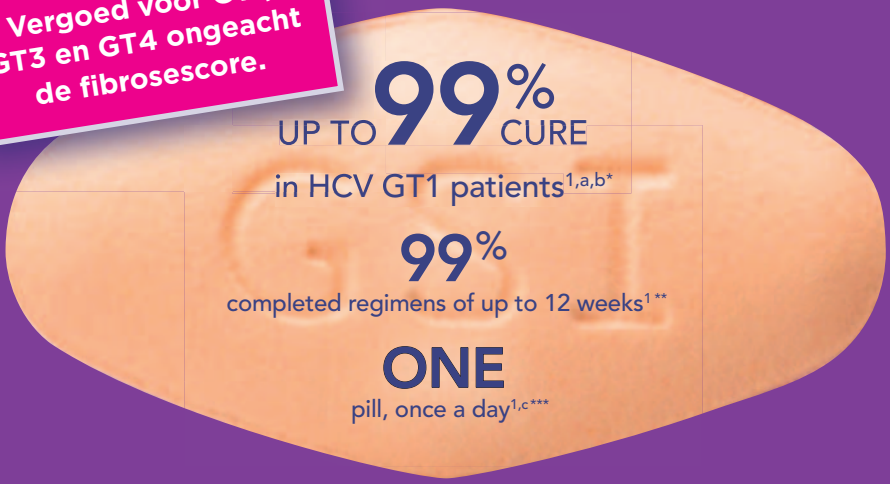

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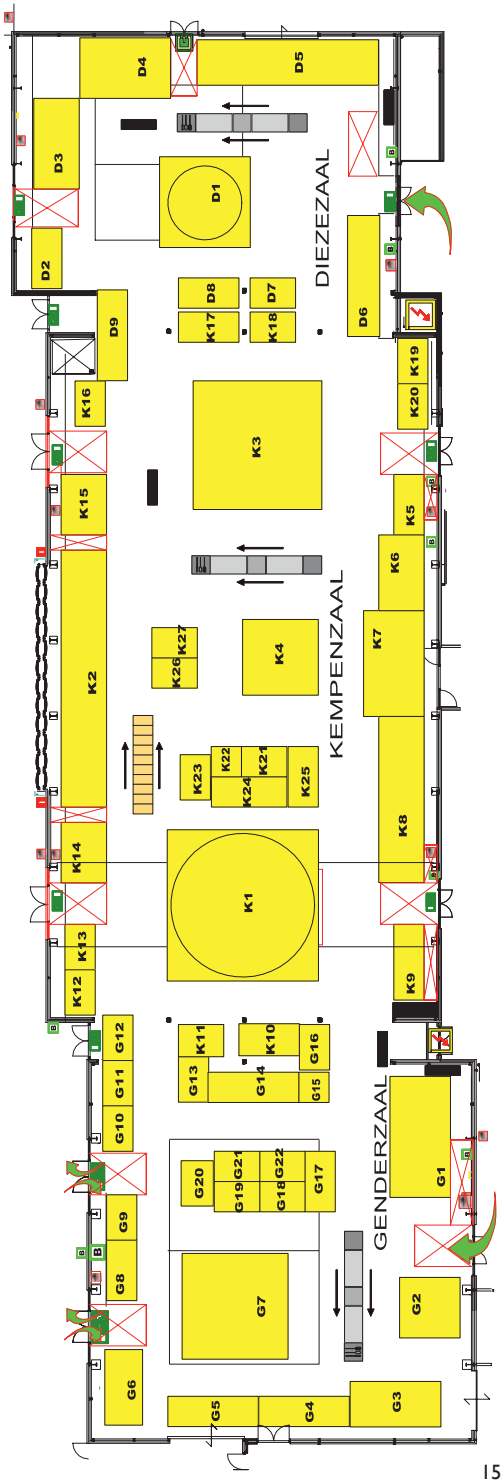
[a] 99% cure rates were observed in the ION-1 study in previously untreated HCV GT1 patients treated with HARVONI for 12 weeks. Across the ION studies, SVR rates between 94–99% were observed in HCV GT1 patients treated with HARVONI for 8–24 weeks.[1]
[b] EASL define cure as SVR12.
[c] HARVONI offers a single-tablet, RBV-free regimen for the majority of HCV GT1 patients, excluding those with decompensated cirrhosis, or who are pre- or post-liver transplant.[1]

Referenties en productinformatie elders in deze uitgave.

HAR/NL/15-09/PM/1789

Lijst van standhouders, najaarscongres NVGE, 6 en 7 oktober 2016 te Veldhoven

G = Genderzaal, D = Diezezaal, K = Kempenhal	*Standnummer*
AbbVie	K1
Alexion Pharmaceuticals	K25
Allergan BV	G4
Aquilant Nederland	K18
B.Braun Medical BV	K26
Bayer BV, HealthCare Costumer Care	G3
Biogen	K15
Biolitec Biomedical technology GmbH	G16
Boston Scientific Nederland BV	D1
Bristol-Myers Squibb BV	D8
Cablon Medical BV	D2
Campro Scientific GMBH	G19
Cobra Medical BV	D6
Cook Nederland BV	G2
Crohn en Colitis Ulcerosea Vereniging Nederland	K24
Dr. Falk Pharma Benelux BV	G1
EndoChoice GmbH	G21
Endoss BV	G22
Endotechniek	K5
Ferring BV	K8
FMH Medical BV	D5
Fresenius Kabi Nederland BV	K16
GE Healthcare BV	K12
Gettinge BV	G18
Gilead Sciences Nederland BV	K4
Hitachi Medical systems BV	K6
Hospira , a Pfizer company	G17
Ingeborg Kuys Healthcare Communications	K21
Intercept Pharma Nederland BV	G9
Janssen - Cilag BV	D4
LABORIE-MMS	K27
Lamepro BV	D7
M.E.C.	G20
Medify	G15
Meditec BV	K11
Medivators BV	K9
Medtronic Trading NL BV	G8
Mermaid Medical	K13
MSD	K3
Mundipharma Pharmaceuticals BV	G6
Norgine	D3
Olympus Nederland BV	K2
Pentax Nederland BV	K7
Prion Medical BV	G13
Quest Medical Imaging	G12
RVC BV	K17
Sananet Care BV	G11
Selinion Medical	K20
Sinomedik BV	K14
Stichting Opsporing Erfelijke Tumoren	K22
Stöpler Instumenten & Apparaten BV	G14
Takeda Nederland BV	G7
Teva Nederland	G10
Tramedico BV	D9
V&VN MDL	K23
Vifor Pharma Nederland BV	K10
Will Pharma Nederland/ PDS Vereniging	G5
Zambon Nederland BV	K19



Genderzaal

G 1	Dr. Falk Pharma Benelux BV
G2	Cook Nederland BV
G3	Bayer BV, HealthCare Costumer Care
G4	Allergan BV
G5	Will Pharma Nederland/ PDS Vereniging
G6	Mundipharma Pharmaceuticals BV
G7	Takeda Nederland BV
G8	Medtronic Trading NL BV
G9	Intercept Pharma Nederland BV
G 10	Teva Nederland
G 11	Sananet Care BV
G 12	Quest Medical Imaging
G 13	Prion Medical BV
G 14	Stöpler Instumenten & Apparaten BV
G 15	Medify
G 16	Biolitec Biomedical technology GmbH
G 17	Hospira, a Pfizer company
G 18	Gettinge BV
G 19	Compro Scientific GMBH
G20	M.E.C.
G21	EndoChoice GmbH
G22	Endoss BV

Kempenzaal

K 1	AbbVie
K 2	Olympus Nederland BV
K 3	MSD
K 4	Gilead Sciences Nederland BV
K 5	Endotechniek
K 6	Hitachi Medical systems BV
K 7	Pentax Nederland BV
K 8	Ferring BV
K 9	Medivators BV
K 10	Vifor Pharma Nederland BV
K 11	Meditec BV
K 12	GE Healthcare BV
K 13	Mermaid Medical
K 14	Sinomedik BV
K 15	Biogen
K 16	Fresenius Kabi Nederland BV
K 17	RVC BV
K 18	Aquilant Nederland
K 19	Zambon Nederland BV
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K 22	Stichting Opsporing Erfelijke Tumoren
K 23	V&VN MDL
K 24	Crohn en Colitis Ulcerosea Vereniging Nederland
K 25	Alexion Pharmaceuticals
K 26	B.Braun Medical BV
K 27	LABORIE-MMS

Diezezaal

D 1	Boston Scientific Nederland BV
D 2	Cablon Medical BV
D 3	Norgine
D 4	Janssen - Cilag BV
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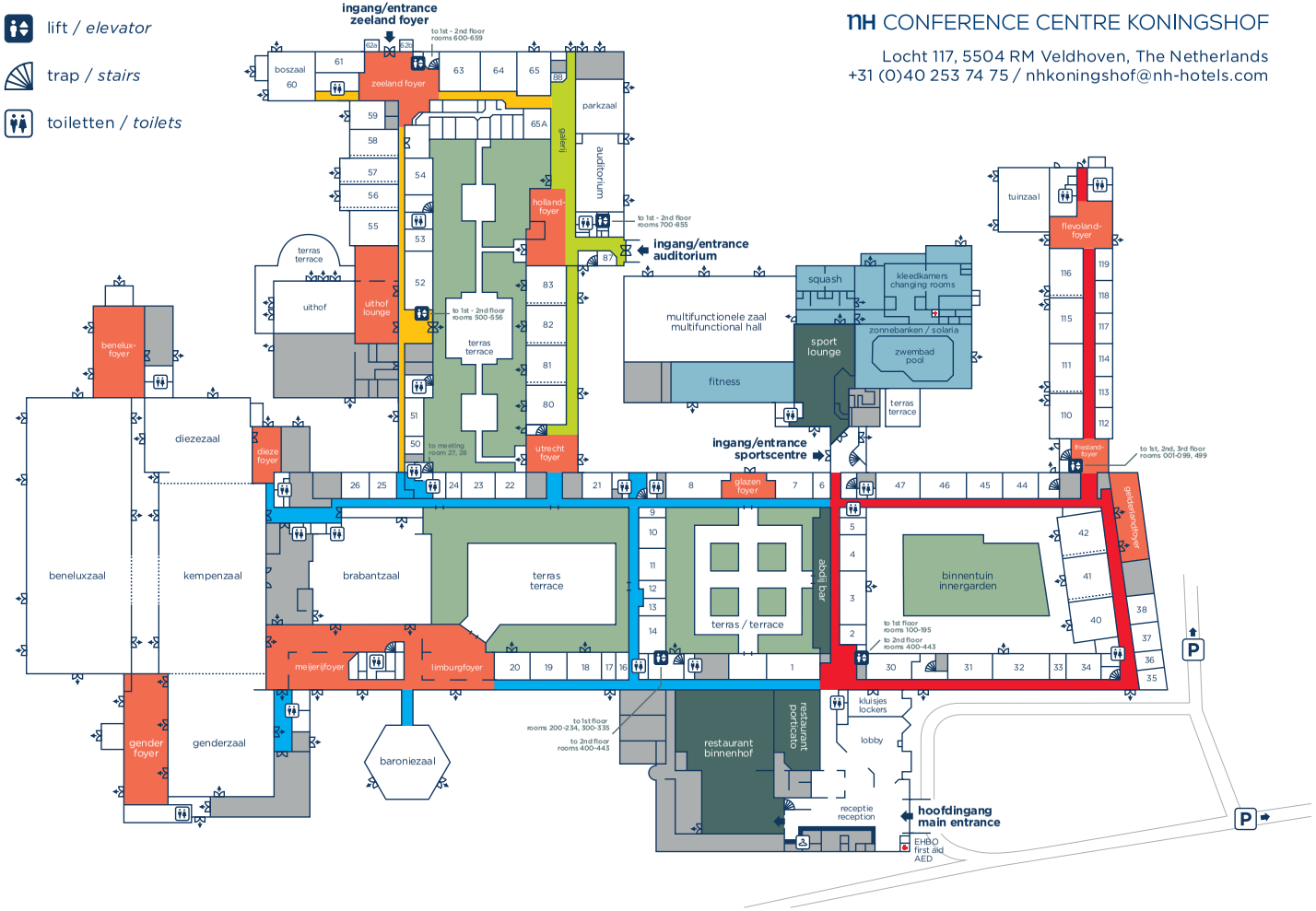

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Samenstelling: 75 mg, 110 mg of 150 mg dabigatran etexilaat (als mesilaat) per capsule. Farmacotherapeutische categorie: directe trombineremmers. **Farmaceutische vorm:** harde capsules. **Therapeutische indicaties: 1.** Preventie van cerebrovasculair accident (CVA) en systemische embolie bij volwassen patiënten met non-valvulair atriumfibrilleren met één of meer risico factoren zoals: CVA of TIA in de anamnese, symptomatische hartfalen (≥ NYHA 2), ≥75 jaar, diabetes mellitus, hypertensie. **2.** Behandeling van diep veneuze trombose (DVT) en longembolie (PE) en preventie van recidiverende DVT en PE bij volwassenen.**3.** Primaire preventie van veneuze trombo-embolische (VTE) aandoeningen bij volwassen patiënten die electief een totale heupvervangende operatie (THO) of een totale knievervangende operatie (TKO) hebben ondergaan. **Dosering en wijze van toediening:** Capsules niet openen, innemen met een glas water, met of zonder voedsel. Preventie van CVA of systemische embolie, behandeling van DVT/PE, preventie van recidiverende DVT/PE: 300 mg per dag, ingenomen als één capsule van 150 mg tweemaal daags. Patiënten van 80 jaar en ouder: 220 mg ingenomen als één capsule van 110 mg tweemaal daags. Preventie VTE na electieve TKO: éénmaal daags 220 mg, ingenomen als 2 capsules van 110 mg. Behandeling binnen 1 – 4 uur na de operatie starten, daarna 10 dagen voortzetten met 2 capsules éénmaal daags. Preventie VTE na electieve THO: éénmaal daags 220 mg, ingenomen als 2 capsules van 110 mg. Behandeling binnen 1-4 uur na de operatie starten met 1 capsule, daarna 28-35 dagen voortzetten met 2 capsules éénmaal daags. Na TKO of THO is bij patiënten met een matig verminderde nierfunctie (creatinineklaring 30 – 50 ml/min) en ouderen (> 75 jaar) de aanbevolen dosis 150 mg per dag, ingenomen als 2 capsules van 75 mg. Zolang geen hemostase is vastgesteld moet het begin van de behandeling bij TKO en THO worden uitgesteld. Begint de behandeling niet op de dag van de operatie, dan moet worden gestart met éénmaal daags 2 capsules. **Contra-indicaties:** Overgevoeligheid voor het werkzame bestanddeel of voor één van de hulpstoffen, ernstig verminderde nierfunctie (creatinineklaring < 30 ml/min), actieve, klinisch significante bloedingen, laesie of aandoening die als een significante risicofactor voor majeure bloedingen wordt beschouwd, gelijktijdige behandeling met andere anticoagulantia, verminderde werking van de lever of leveraandoeningen die naar verwachting invloed hebben op de overleving, gelijktijdige behandeling met systemische ketoconazol, ciclosporine, itraconazol, en dronedarone, kunsthartklep waarvoor antistollingsbehandeling vereist is. **Bijzondere waarschuwingen en voorzorgen voor gebruik:** Voor de start van de behandeling met dabigatran dient de nierfunctie bepaald te worden door berekening van de creatinineklaring (m.b.v. de Cockcroft-Gaultmethode). Tijdens de behandeling dient de nierfunctie bepaald te worden in klinische situaties waarbij verwacht wordt dat de nierfunctie zal afnemen of verslechteren en tenminste eens per jaar bij patiënten ≥75 jaar of met nierinsufficiëntie. Bij patiënten met een verhoogde kans op bloedingen dient een dosis van 220 mg dabigatran, ingenomen als één capsule van 110 mg tweemaal per dag, overwogen te worden voor de preventie van CVA of systemische embolie en bij de behandeling van DVT/PE en preventie van recidiverende DVT/PE. Een stollingstest (dTT, ECT of aPTT) kan worden gebruikt om patiënten met verhoogde dabigatran concentraties te identificeren. Een INR-test is onbetrouwbaar bij patiënten die dabigatran gebruiken. Patiënten die dabigatran gebruiken, hebben, wanneer zij een operatie of invasieve procedure ondergaan, een verhoogd risico op bloedingen. Er is een specifiek antidotum (Praxbind, idarucizumab) beschikbaar. Bij patiënten met verhoogde leverenzymen > 2 maal ULN, wordt dabigatran niet aanbevolen. Er is geen ervaring bij kinderen en adolescenten. Anesthesie via een postoperatieve inwendige epidurale katheter wordt niet aanbevolen. Na het verwijderen van de katheter moet ten minste twee uur gewacht worden met de eerste toediening van dabigatran. Niet gebruiken tijdens zwangerschap of borstvoeding. **Interacties met andere geneesmiddelen:** Er is geen of weinig ervaring met de volgende behandelingen die de kans op bloedingen, in combinatie met het gebruik van dabigatran, kunnen verhogen: anticoagulantia zoals UFH, LMWH en heparinederivaten, trombolytische middelen, vitamine K-antagonisten, rivaroxaban of andere orale anticoagulantia en plaatjesaggregratieremmers zoals GPIIb/IIIa-receptorantagonisten, ticlopidine, prasugrel, ticagrelor, dextran en sulfinpyrazon. Zowel het gebruik van acetylsalicylzuur, clopidogrel, SSRI's, SNRI's, als chronisch gebruik van NSAID's verhoogden in de RE-LY-studie het risico op bloedingen bij zowel dabigatran als warfarine. Dabigatran wordt niet gemetaboliseerd door het cytochroom-P450-systeem en heeft geen effect *in vitro* op menselijke cytochroom-P450-enzymen. De pro-drug dabigatran etexilaat is een substraat voor de effluxtransporter Pglycoproteïne. Proteaseremmers beïnvloeden Pglycoproteïne en gelijktijdige behandeling met dabigatran en deze middelen wordt daarom niet aanbevolen. Gelijktijdige toediening van P-glycoproteïne-inductoren (zoals rifampicine, sint-janskruid (Hypericum Perforatum), carbamazepine of fenytoïne) dient vermeden te worden. Preventie van CVA en systemische embolie, behandeling van DVT/PE, preventie van recidiverende DVT/PE: Voorzichtigheid is geboden bij gelijktijdig gebruik van dabigatran en lichte tot matig sterke Pglycoproteïneremmers (bv. amiodaron, kinidine, verapamil en ticagrelor), in het bijzonder bij patiënten met een licht tot matig verminderde nierfunctie. Bij patiënten die tegelijk dabigatran en verapamil krijgen, dient de dosis dabigatran te worden verlaagd naar 220 mg ingenomen als één capsule van 110 mg tweemaal per dag. Gelijktijdige behandeling met tacrolimus wordt niet aanbevolen. Gelijktijdige behandeling met protonpompremmers (PPI) leek de werkzaamheid van dabigatran niet te verminderen. De toediening van ranitidine samen met dabigatran had geen klinisch relevant effect op de mate waarin dabigatran werd geabsorbeerd. Preventie van VTE: Bij patiënten die gelijktijdig dabigatran en amiodaron, kinidine of verapamil gebruiken dient de dosering verlaagd te worden tot 150 mg dabigatran eenmaal daags. Bij patiënten met matige nierinsufficiëntie die gelijktijdig dabigatran en verapamil gebruiken dient een dosis van 75 mg dabigatran overwogen te worden. Bij patiënten die gelijktijdig dabigatran en claritromycine gebruiken dient nauwgezet klinisch toezicht te worden gehouden, in het bijzonder wat betreft het optreden van bloedingen, speciaal bij patiënten met milde tot matige nierinsufficiëntie. **Bijwerkingen:** De meest gemelde bijwerkingen zijn bloedingen. Ernstige bloedingen kunnen, ongeacht waar ze in het lichaam optreden, leiden tot invaliditeit, levensbedreigend zijn of zelfs een dodelijke afloop tot gevolg hebben. Indien ernstige bloedingen optreden moet de behandeling worden gestopt en de bron van de bloeding worden onderzocht. Er is geen antidotum voor dabigatran. Andere vaak voorkomende klachten zijn buikpijn, diarree, dyspepsie, misselijkheid en abnormale leverfunctie / leverfunctietest (minder dan 10%). Preventie van CVA en systemische embolie: Bloedingen kwamen in totaal bij ongeveer 16,6% van de patiënten voor; ernstige bloedingen werden zelden gerapporteerd in het klinisch onderzoek (minder dan 3,5%). Dabigatran werd in de RELY studie gerelateerd aan een hogere incidentie van majeure gastro-intestinale bloedingen. De toediening van een protonpompremmer kan overwogen worden om een gastro-intestinale bloeding te voorkomen. Behandeling van DVT/PE, preventie van recidiverende DVT/PE: Bloedingen kwamen in totaal bij ongeveer 19,4% van de patiënten voor; ernstige bloedingen werden zelden gerapporteerd in het klinisch onderzoek (minder dan 1,0%). Preventie van VTE: Bloedingen kwamen in totaal bij ongeveer 14% van de patiënten voor; ernstige bloedingen (inclusief wondbloedingen) werden zelden gerapporteerd (minder dan 2%). **Verpakking:** Pradaxa 75 mg, 110 en 150 mg worden geleverd in aluminium blisterverpakkingen van 60 stuks. **Afleverstatus:** U.R. **Registratie:** EU/1/08/442/003, EU/1/08/442/007, EU/1/08/442/011. Registratiedatum 18 mrt 2008 (VTE preventie na THO/TKO), 04 aug 2011 (CVA), 03 juni 2014 (acute DVT/LE, preventie recidiverende DVT/LE). **Vergoeding en prijzen:** Pradaxa wordt volledig vergoed binnen het GVS, mits geïnitieerd door een specialist. Voor prijzen, zie KNMP taxe. Voor volledige productinformatie is de 1B tekst op aanvraag beschikbaar**.** Boehringer Ingelheim bv., Comeniusstraat 6, 1817 MS Alkmaar. Tel. 0800-2255889. **Datum herziening van de tekst:** 28 januari 2016.

VERKORTE PRODUCTINFORMATIE PRAXBIND®

▼ Dit geneesmiddel is onderworpen aan aanvullende monitoring. Daardoor kan snel nieuwe veiligheidsinformatie worden vastgesteld. Beroepsbeoefenaren in de gezondheidszorg worden verzocht alle vermoedelijke bijwerkingen te melden. **Samenstelling:** Elke injectieflacon bevat 2,5 g idarucizumab, 2 g sorbitol en 25 mg natrium in 50 ml. Farmacotherapeutische categorie: specifiek antidotum voor dabigatran. **Farmaceutische vorm:** Oplossing voor injectie/infusie. **Therapeutische indicaties:** Volwassen Pradaxa (dabigatran etexilaat) gebruikers wanneer het anticoagulerend effect van dit middel snel moet worden geneutraliseerd voor spoedoperaties/ dringende ingrepen of bij een levensbedreigende/ongecontroleerde bloeding. **Dosering en wijze van toediening:** Uitsluitend voor gebruik in het ziekenhuis. De aanbevolen dosis is 5 g (2 x 2,5 g/50 ml), intraveneus toegediend als twee achtereenvolgende infusies van elk 5 tot 10 minuten of als bolusinjectie. **Contra-indicaties:** Geen. **Bijzondere waarschuwingen en voorzorgen voor gebruik:** Idarucizumab heft alleen het anticoagulerend effect van dabigatran, niet van andere anticoagulantia. Idarucizumab kan worden gebruikt in combinatie met standaard ondersteunende maatregelen, die vanuit medisch oogpunt in aanmerking dienen te komen. Het risico van het gebruik van Praxbind bij patiënten met een bekende overgevoeligheid (bijv. anafylactoïde reactie) voor idarucizumab of voor een van de hulpstoffen (bijv bij erfelijke fructose intolerantie) moet zorgvuldig worden afgewogen tegen het mogelijke voordeel. Indien een anafylactische reactie of een andere ernstige allergische reactie optreedt, dient de toediening van Praxbind onmiddellijk te worden gestaakt en een passende behandeling te worden gestart. Door neutralisatie van de dabigatrantherapie worden patiënten blootgesteld aan het verhoogde trombotisch risico van hun onderliggende aandoening en moet worden overwogen om de anticoagulatiebehandeling te hervatten zodra dat medisch verantwoord is. Praxbind veroorzaakt een voorbijgaande proteïnurie die niet wijst op nierschade, waarmee bij urineonderzoek rekening dient te worden gehouden. Praxbind bevat 2,2 mmol (of 50 mg) natrium per dosis waarmee bij patiënten met een natriumbeperkt dieet rekening te worden gehouden. **Interacties met andere geneesmiddelen:** Klinisch relevante interacties met andere geneesmiddelen worden onwaarschijnlijk geacht. In preklinische onderzoeken zijn er geen interacties aangetoond met infusievloeistoffen voor volume expansie, concentraten van stollingsfactor (bijv. (geactiveerde) protrombinecomplex concentraten, recombinant factor VIIa) en andere anticoagulantia (bijv. andere trombineremmers dan dabigatran, factor Xa remmers, inclusief laagmoleculairgewichtheparine, vitamine K antagonisten, heparine). **Bijwerkingen:** De veiligheid van Praxbind is onderzocht bij 224 gezonde deelnemers en in een lopend fase III onderzoek bij 123 patiënten. Er zijn daarbij geen bijwerkingen vastgesteld.
Verpakking: Oplossing van 50 ml in glazen injectieflacon (type I glas), met butylrubber stop, aluminium kap en etiket met geïntegreerde ophanglus. **Afleverstatus:** U.R. **Registratie:** EU/1/15/1056/001. **Vergoeding en prijzen:** Voor prijzen, zie KNMP taxe. Voor volledige productinformatie is de 1B tekst op aanvraag beschikbaar**.** Boehringer Ingelheim bv., Comeniusstraat 6, 1817 MS Alkmaar. Tel. 0800-2255889. **Datum herziening van de tekst:** 20 november 2015.

Boehringer Ingelheim

Verkorte SPC-tekst **Budenofalk® 9 mg maagsapresistent granulaat.**
Kwalitatieve en kwantitatieve samenstelling: Sachets met budesonide 9 mg maagsapresistent granulaat. **Therapeutische indicaties:** Inductie van remissie bij milde tot matige ziekte van Crohn waarbij het ileum en/of colon ascendens is aangedaan. Inductie van remissie bij actieve collagene colitis. **Dosering:** Aanbevolen dosis bedraagt eenmaal daags 9 mg (1 sachet van 9 mg), in de ochtend ongeveer een half uur voor het ontbijt, duur van de behandeling dient beperkt te worden tot 8 weken. Ouderen: doseren als onder 'volwassenen', de ervaring bij ouderen met Budenofalk® is echter beperkt. Kinderen (18 jaar of jonger): Budenofalk® moet niet genomen worden door kinderen en adolescenten vanwege onvoldoende ervaring in deze leeftijdsgroep. Patiënten met verminderde nierfunctie: er zijn geen specifieke doseringsaanbevelingen voor patiënten met nierinsufficiëntie. Patiënten met verminderde leverfunctie: er kan geen specifieke doseringsaanbeveling worden gemaakt omdat informatie over deze patiëntenpopulatie ontbreekt. **Wijze van toediening:** De inhoud van de sachet moet ingenomen worden voor het ontbijt. Het granulaat moet op de tong gelegd worden en in zijn geheel doorgeslikt worden met veel vloeistof (bv. een glas water). Het granulaat moet niet gekauwd of gebroken worden ter voorkoming van de afbraak van de maagsapresistente coating van het granulaat. Vroegtijdige desintegratie zal de vrijgifte van het geneesmiddel op een onvoorspelbare manier beïnvloeden. Stoppen van de behandeling: De behandeling dient niet abrupt gestaakt te worden in verband met mogelijk optreden van bijnierschorsinsufficiëntie. Aan het einde van de behandeling moeten Budenofalk® in verlengde intervallen gegeven worden, bv. om de dag gedurende 2 weken. Daarna kan de behandeling gestaakt worden. **Bijwerkingen:** Voedings- en stofwisselingstoornissen: Cushing syndroom (bv. met vollemaansgezicht, obesitas van de romp, afgenomen glucosetolerantie, diabetes mellitus, hypertensie, natriumretentie met oedeem, toegenomen kaliumexcretie, inactiviteit of atrofie van de adrenale cortex, rode striae, steroïden acne, verstoring van de secretie van geslachtshormonen (met als gevolg bv. amenorroe, hirsutisme, impotentie) (vaak ≥1/100 - <1/10). Groeiachterstand bij kinderen (zeer zelden <1/10.000). Oogaandoeningen: glaucoom, cataract (zeer zelden <1/10.000). Maagdarmstelselaandoeningen: maagklachten, gastroduodenale ulcera, pancreatitis, obstipatie (zeer zelden <1/10.000). Immuunsysteemaandoeningen: toegenomen risico op infectie (vaak ≥1/100 - <1/10). Skeletspierstelsel-, bindweefselaandoeningen: spier- en gewrichtspijn, spierzwakte en stuitpretkkingen, osteoporose (vaak ≥1/100 - <1/10). Aseptische botnecrose (femur en kop van de humerus) (zeer zelden <1/10.000). Zenuwstelselaandoeningen: hoofdpijn (vaak ≥1/100 - <1/10). Pseudotumor cerebri inclusief papillair oedeem bij jongvolwassenen (zeer zelden <1/10.000). Psychische stoornissen: depressie, prikkelbaarheid, euforie (vaak ≥1/100 - <1/10). Meervoudige psychiatrische effecten zoals een gedragsstoornis (zeer zelden <1/10.000). Huid- en onderhuidaandoeningen: allergisch exantheem, petechiën, ecchymose, vertraagde wondgenezing, contact dermatitis (vaak ≥1/100 - <1/10). Bloedvataandoeningen: toegenomen risico op trombose, vasculitis (ontwenningsverschijnsel na langetermijnbehandeling) (zeer zelden <1/10.000). Algemene aandoeningen en toedieningsplaatsstoornissen: vermoeidheid, malaise (zeer zelden <1/10.000). Incidenteel kunnen bijwerkingen optreden die karakteristiek zijn voor systemisch werkzame glucocorticosteroïden. Deze bijwerkingen zijn afhankelijk van dosering, behandelingsduur, gelijktijdige of eerdere behandeling met andere glucocorticosteroïden en individuele gevoeligheid. In klinische studies is aangetoond dat de frequentie van glucocorticosteroïd gerelateerde bijwerkingen bij gebruik van oraal Budenofalk lager is dan bij orale behandeling met equivalente doseringen prednisolon. Een exacerbatie of recidive van extra-intestinale manifestaties (met name gericht op de huid en gewrichten) kan optreden wanneer de patiënt wordt overgezet van systemisch werkzame glucocorticosteroïden naar het lokaal werkzame budesonide. **Contra-indicaties:** Overgevoeligheid voor budesonide of voor één van de hulpstoffen. Levercirrose. **Waarschuwingen:** Behandeling met Budenofalk® resulteert in lagere systemische corticosteroïden spiegels dan behandeling met conventionele orale corticosteroïden. Overschakeling van andere corticosteroïden therapie kan leiden tot symptomen die gerelateerd zijn aan de verandering van de systemische corticosteroïden spiegels. Voorzichtigheid is geboden bij patiënten met tuberculose, hypertensie, diabetes mellitus, osteoporose, ulcus ventriculi, glaucoom, cataract, een familie-anamnese van diabetes mellitus of glaucoom, of elke andere aandoening waarbij glucocorticosteroïden ongewenste effecten kunnen hebben. Gelijktijdige behandeling met ketoconazol of andere CYP3A4 remmers dient te worden vermeden. Budenofalk® maagsapresistent granulaat bevat lactose, sucrose en sorbitol. Patiënten met zeldzame erfelijke aandoeningen als galactose- of fructoseintolerantie, glucose-galactose malabsorptie, sucrase-isomaltase insufficiëntie, Lapp lactasedeficiëntie of congenitale lactase deficiënte dienen dit geneesmiddel niet te gebruiken. **Verpakking:** Doos met 30 sachets. **Afleverstatus en vergoeding:** U.R. en volledig vergoed. RVG 106117. **Registratiehouder:** Dr. Falk Pharma GmbH, Leinenweberstrasse 5, D-79108 Freiburg, Duitsland. **Voor informatie:** Dr. Falk Pharma Benelux B.V., Breda, 076-5244200, of raadpleeg de volledige SPC. **Versie verkorte SPC-tekst:** 20160515.

Referenties:
1. SPC Budenofalk® granulaat RVG 106117. 2. SPC Budenofalk® capsules RVG 22557. 3. Dignass et al. J Crohn's Colitis 2014; 8: 970-80.

Focus op perfectie

Dr. Falk

76-2016-NL

Verkorte productinformatie *Daklinza*®

▼ Dit geneesmiddel is onderworpen aan aanvullende monitoring. Samenstelling: Daklinza filmomhulde tabletten bevatten daclatasvir dihydrochloride overeenkomend met 30 mg of 60 mg daclatasvir. **Farmacotherapeutische categorie**: direct werkend antiviraal middel, ATC-code: J05AX14. **Indicaties**: Daklinza is in combinatie met andere geneesmiddelen geïndiceerd voor de behandeling van chronische hepatitis C-virus (HCV) infectie bij volwassenen. Zie verder SPC voor compleet overzicht van de verschillende combinatietherapieën met Daklinza en behandelduur (rubriek 4.2, 4.4 en 5.1). **Dosering**: De aanbevolen dosis Daklinza is 60 mg eenmaal daags, oraal ingenomen, met of zonder maaltijd. Daklinza moet worden toegediend in combinatie met andere geneesmiddelen. *Speciale populaties:* Er is geen dosisaanpassing voor Daklinza nodig bij ouderen (patiënten ≥ 65 jaar), patiënten met nierfunctiestoornis en patiënten met lichte (Child-Pugh A, score 5-6), matige (Child-Pugh B, score 7-9) of ernstige (Child-Pugh C, score ≥ 10) leverfunctiestoornis. *Pediatrische patiënten:* De veiligheid en werkzaamheid van Daklinza bij kinderen en jongeren in de leeftijd tot 18 jaar zijn nog niet vastgesteld. Er zijn geen gegevens beschikbaar. **Contra-indicaties**: Overgevoeligheid voor de werkzame stof of voor (één van) de hulpstoffen. Gelijktijdig gebruik van geneesmiddelen die cytochroom P450 3A4 (CYP3A4) en P-glycoproteinetransporter (p-gp) sterk induceren en daarom kunnen leiden tot een lagere blootstelling aan en verlies van werkzaamheid van Daklinza. Deze groep van geneesmiddelen omvat, maar is niet beperkt tot, fenytoïne, carbamazepine, oxcarbazepine, fenobarbital, rifampicine, rifabutine, rifapentine, systemisch dexamethason en het kruidenmiddel Sint-Janskruid *(Hypericum perforatum)*. **Waarschuwingen en voorzorgsmaatregelen**: Daklinza mag niet als monotherapie worden toegediend. Daklinza moet worden toegediend in combinatie met andere geneesmiddelen voor de behandeling van chronische HCV-infectie. De veiligheid en werkzaamheid van Daklinza is niet vastgesteld voor de behandeling van patiënten met gelijktijdige infectie met hiv of HBV. De werkzaamheid van Daklinza als onderdeel van een herbehandelregime bij patiënten met eerdere blootstelling aan een NS5A-remmer is niet vastgesteld. Ernstige bradycardie en hartblok: Er zijn gevallen van ernstige bradycardie en hartblok waargenomen bij gelijktijdig gebruik van Daklinza in combinatie met sofosbuvir en amiodaron, met of zonder andere geneesmiddelen die de hartslag vertragen. Het mechanisme hiervan is niet vastgesteld. Omdat de gevallen potentieel levensbedreigend zijn, mag amiodaron bij patiënten, die Daklinza en sofosbuvir gebruiken, uitsluitend worden gebruikt wanneer andere antiaritmische behandelingen niet worden verdragen of gecontra-indiceerd zijn en wordt nauwlettende controle aanbevolen. Vanwege de lange halfwaardetijd van amiodaron dient ook geschikte monitoring plaats te vinden bij patiënten die in de afgelopen maanden zijn gestopt met amiodaron en die gaan beginnen met Daklinza in combinatie met sofosbuvir. Genotype-specifieke activiteit: De gegevens van het ALLY-3 (AI444218) onderzoek ondersteunen een behandelduur van 12 weken van Daklinza + sofosbuvir voor behandelnaïeve en al eerder behandelde patiënten met genotype 3-infectie zonder cirrose. De gegevens van *Compassionate Use* programma's, inclusief patiënten met genotype 3-infectie en cirrose, ondersteunen het gebruik van Daklinza + sofosbuvir gedurende 24 weken bij deze patiënten. De relevantie van het toevoegen van ribavirine aan deze behandelcombinatie is onduidelijk. De klinische gegevens die het gebruik van Daklinza en sofosbuvir ondersteunen bij patiënten die zijn geïnfecteerd met HCV genotype 4 en 6 zijn beperkt. Er zijn geen klinische gegevens bij patiënten met genotype 5. Patiënten met Child-Pugh C leverziekte: De veiligheid en werkzaamheid van Daklinza voor de behandeling van HCV-infectie bij patiënten met Child-Pugh C leverziekte is vastgesteld in het ALLY-1 (AI444215, Daklinza + sofosbuvir + ribavirine gedurende 12 weken) klinische onderzoek; de SVR-percentages waren echter lager dan in patiënten met Child-Pugh A en B. Daarom wordt een conservatief behandelregime van Daklinza + sofosbuvir +/- ribavirine gedurende 24 weken voorgesteld voor patiënten met Child-Pugh C. Ribavirine kan worden toegevoegd op basis van een klinische beoordeling van een individuele patiënt. Zwangerschap en anticonceptievereisten: Daklinza dient niet te worden gebruikt tijdens de zwangerschap en bij vrouwen die zwanger kunnen worden en geen anticonceptie gebruiken. Het gebruik van zeer effectieve anticonceptie dient gecontinueerd te worden gedurende 5 weken na voltooien van de Daklinza behandeling. Interacties met geneesmiddelen: Gelijktijdig gebruik van Daklinza kan de concentratie van andere geneesmiddelen beïnvloeden en andere geneesmiddelen kunnen de concentratie van daclatasvir beïnvloeden. Zie rubriek 4.3 voor een overzicht van geneesmiddelen die gecontra-indiceerd zijn voor gebruik met Daklinza wegens mogelijk verlies van therapeutisch effect. Zie rubriek 4.5 voor bekende en andere mogelijk significante geneesmiddelinteracties. Pediatrische patiënten: Daklinza wordt niet aanbevolen voor gebruik bij kinderen en jongeren tot 18 jaar omdat de veiligheid en werkzaamheid niet zijn vastgesteld bij deze patiënten. Belangrijke informatie over bepaalde bestanddelen van Daklinza: Daklinza bevat lactose. Patiënten met zeldzame erfelijke aandoeningen als galactose-intoleratie, Lapp lactasedeficiëntie of glucose-galactose malabsorptie dienen dit geneesmiddel niet te gebruiken. **Bijwerkingen**: *Daklinza in combinatie met sofosbuvir ± ribavirine:* De meest gemelde bijwerkingen waren vermoeidheid, hoofdpijn en misselijkheid. Bijwerkingen van graad 3 werden bij minder dan 1% van de patiënten gemeld en er waren geen patiënten met een graad 4 bijwerking. Vier patiënten zijn met het Daklinza behandelregime gestopt wegens bijwerkingen, waarvan maar één als gerelateerd aan de onderzoeksbehandeling werd beschouwd. Bij de behandelcombinatie *Daklinza + sofosbuvir* werden de volgende bijwerkingen zeer vaak gemeld: hoofdpijn en vermoeidheid. Vaak werden gemeld: insomnia, duizeligheid, migraine, nausea, diarree, buikpijn, artralgie en myalgie. Bij de behandelcombinatie *Daklinza + sofosbuvir + ribavirine* werden de volgende bijwerkingen zeer vaak gemeld: anemie, hoofdpijn, nausea en vermoeidheid. Vaak werden gemeld: verminderde eetlust, insomnia, prikkelbaarheid, duizeligheid, migraine, opvlieger, dyspneu, inspanningskortademigheid, hoesten, neusverstopping, diarree, braken, buikpijn, gastro-oesofageale refluxziekte, constipatie, droge mond, flatulentie, rash, alopecia, pruritus, droge huid, artralgie en myalgie. Het veiligheidsprofiel van daclatasvir in combinatie met peginterferon alfa en ribavirine was vergelijkbaar met wat wordt gezien bij peginterferon alfa en ribavirine alleen, ook bij patiënten met cirrose. **Afleverstatus:** UR **Vergoeding en prijzen:** voor prijzen zie Z-index. Voor volledige productinformatie, zie Samenvatting van de Productkenmerken. Bristol-Myers Squibb B.V., Utrecht, SPC Januari 2016.

Referenties

1. EASL guidelines: Journal of Hepatology 2015 vol. 63, 199–236, EASL Clinical Practice Guidelines: Management of hepatitis C virus infection European Association for the Study of the Liver.
2. HCV richtsnoer www.hcvrichtsnoer.nl update november 2015.
3. Daklinza® Summary of Product Characteristics.

Bristol-Myers Squibb

Daklinza® (daclatasvir)

1392NL16PR00021

Naam van het geneesmiddel: Pentasa®. Kwalitatieve en kwantitatieve samenstelling: Pentasa tablet met verlengde afgifte bevat 500 mg of 1 g mesalazine, granulaat met verlengde afgifte bevat 1, 2 of 4 g mesalazine, suspensie voor rectaal gebruik bevat 1 g mesalazine per 100 ml, zetpil bevat 1 g mesalazine. **Therapeutische indicaties:** Oraal: ter behandeling van lichte tot matige vormen van colitis ulcerosa en de ziekte van Crohn, zowel in de acute fase als ter voorkoming van recidieven hiervan. Suspensie voor rectaal gebruik: proctitis, proctosigmoiditis en linkszijdige colitis. Zetpil: proctitis. **Contra-indicaties:** Overgevoeligheid voor mesalazine of overige bestanddelen van het product, of voor salicylzuurderivaten. Ernstige lever- en/of nierfunctiestoornissen. **Bijzondere waarschuwingen en voorzorgen bij gebruik:** Voorzichtig bij patiënten met bekende overgevoeligheid voor sulfasalazine en met een verminderde leverfunctie. Bij verminderde nierfunctie niet aanbevolen. De nierfunctie regelmatig controleren met name in het begin van de behandeling. Bij cardiale overgevoeligheidsreacties en ernstige bloedbeeldafwijkingen de behandeling staken. **Bijwerkingen:** Na rectale toediening kunnen lokale reacties, zoals pruritus, rectaal ongemak en aandrang optreden. Verder komt vaak voor: hoofdpijn, diarree, buikpijn, misselijkheid, braken, huiduitslag inclusief urticaria. Zelden tot zeer zelden: myo- en pericarditis, pancreatitis, bloedbeeldafwijkingen allergische longreacties, hepatotoxiciteit, lupus erythematosus-achtige reacties, abnormale nierfunctie. **Registratiehouder:** Ferring B.V., Postbus 184, 2130 AD , Hoofddorp. **Registratienummers:** Tabletten onder RVG 14797 (500 mg) en RVG 105712 (1 g); Granulaat onder RVG 18706 (1 g), RVG 31379 (2 g) en RVG 114015 (4 g), Suspensie voor rectaal gebruik onder RVG 11782, zetpil onder RVG 15064. **Afleverstatus:** UR. **Datum tekst:** mei 2014.

PENTASA® MESALAZINE
Zet de toon, met passie

FERRING PHARMACEUTICALS

VERKORTE PRODUCTINFORMATIE THIOSIX®

▼ Dit geneesmiddel is onderworpen aan aanvullende monitoring. Daardoor kan Teva snel nieuwe veiligheidsinformatie vaststellen. Beroepsbeoefenaren in de gezondheidszorg worden verzocht alle vermoedelijke bijwerkingen te melden via dso.nl@tevanederland.com. **Handelsnaam:** Thiosix, tabletten **Kwalitatieve & kwantitatieve samenstelling:** Thiosix 10 mg bevat 10 mg tioguanine per tablet.
Thiosix 20 mg bevat 20 mg tioguanine per tablet. **Indicaties:** onderhoudsbehandeling van inflammatoire darmziekten (ziekte van Crohn of ulceratieve colitis), bij volwassen patiënten die onvoldoende reageren op of intolerant zijn voor standaard tiopurine behandeling (azathioprine, mercaptopurine). **Contra-indicaties:** Overgevoeligheid voor een van de stoffen. Vrouwen die borstvoeding geven. **Belangrijkste waarschuwingen/voorzorgen:** Tioguanine is een actief cytotoxisch middel en mag alleen onder supervisie van een arts met ervaring gebruikt worden. Er is een verhoogd risico op levertoxiciteit met vasculaire endotheel beschadiging. Behandeling met tioguanine dient gestaakt te worden bij bewezen levertoxiciteit, omdat bij tijdig staken de levertoxiciteit meestal omkeerbaar is. Routinematige controles, zoals omschreven in de volledige SPC, worden ten sterkte aanbevolen. Patiënten met erfelijke deficiëntie van het enzym tiopurinemethyltransferase (TPMT) kunnen ongewoon gevoelig zijn voor het myelosuppressieve effect van tioguanine en snel neigen tot beenmergsuppressie na de start van de behandeling. Patiënten dienen tijdens de tioguanine therapie onder zorgvuldige controle te staan met bloedcel tellingen. Vaccinatie met levende vaccins wordt ontraden. Gebruik van tioguanine bij patiënten die het enzym hypoxanthineguaninefosforibosyltransferase missen, zoals in het geval van Lesch-Nyhan syndroom, wordt ontraden. **Belangrijkste bijwerkingen:** De hierna beschreven bijwerkingen en bijbehorende frequenties zijn geobserveerd in leukemie patiënten die behandeld werden met hogere doseringen. Gewoonlijk wordt tioguanine bij deze patiënten in combinatie met andere cytotoxische middelen toegepast. Hierdoor is het niet altijd mogelijk om bijwerkingen aan één specifiek geneesmiddel toe te schrijven. Dezelfde bijwerkingen, mogelijk met andere frequenties, zijn geobserveerd in patiënten met inflammatoire darmziekten die behandeld werden met 20-80 mg tioguanine per dag. Beenmergsuppressie komt zeer vaak voor. Stomatitis, gastro-intestinale intolerantie en levertoxiciteit met vasculaire endotheelbeschadiging komen vaak voor. De volgende ernstige bijwerkingen komen zelden voor: intestinale necrose en perforatie en centrilobulaire hepatisch necrose is beschreven bij patiënten met combinatietherapie, orale contraceptiva, hoge dosering van tioguanine en alcohol. **Afleverstatus:** UR. **Registratiehouder:** Teva Nederland BV, Swensweg 5, 2031 GA Haarlem, Nederland. **Datum laatste herziening SPC:** 10 april 2015. Raadpleeg voor volledige productinformatie de geregistreerde samenvatting van productkenmerken www.cbg-meb.nl of neem contact op met Teva Nederland BV. Tel. 0800 0228 400. NL/TSX/16/0002.

Nederland

Improving health, making people feel better

Thiosix® TIOGUANINE

VERKORTE PRODUCTINFORMATIE HARVONI®▼

▼ Dit geneesmiddel is onderworpen aan aanvullende monitoring.

SAMENSTELLING: 90 mg ledipasvir en 400 mg sofosbuvir. **FARMACEUTISCHE VORM:** filmomhulde tablet **INDICATIES:** Harvoni is geïndiceerd voor de behandeling van chronische hepatitis C (CHC) bij volwassenen. Voor specifieke activiteit tegen de verschillende genotypes van het hepatitis C-virus (HCV), zie SmPC. **DOSERING:** De therapie met Harvoni moet worden gestart en gecontroleerd door een arts die ervaren is in de behandeling van patiënten met CHC. De aanbevolen dosering van Harvoni is één tablet eenmaal daags met of zonder voedsel. **CONTRA-INDICATIES:** Overgevoeligheid voor de werkzame stoffen of voor één van de hulpstoffen. Gelijktijdige toediening met rosuvastatine of met krachtige P-gp inductoren. **BIJZONDERE WAARSCHUWINGEN EN VOORZORGEN BIJ GEBRUIK:** Harvoni mag niet gelijktijdig worden toegediend met andere geneesmiddelen die sofosbuvir bevatten. ***Specifieke activiteit tegen verschillende genotypes:*** zie SmPC. De klinische gegevens die het gebruik van Harvoni bij patiënten geïnfecteerd met HCV-genotype 2, 3 en 6 ondersteunen zijn beperkt ***Ernstige bradycardie en hartblok:*** Er zijn gevallen van ernstige bradycardie en hartblok waargenomen bij gelijktijdig gebruik van Harvoni met amiodaron, met of zonder andere geneesmiddelen die de hartslag vertragen. Omdat de gevallen potentieel levensbedreigend zijn, mag amiodaron bij patiënten die Harvoni gebruiken, uitsluitend worden gebruikt wanneer andere antiaritmische behandelingen niet worden verdragen of gecontra-indiceerd zijn. Patiënten die in de afgelopen maanden zijn gestopt met amiodaron en beginnen met Harvoni dienen aan geschikte monitoring te worden onderworpen. Zie voor meer informatie de SmPC ***Behandeling van patiënten met eerdere blootstelling aan direct werkende antivirale middelen tegen HCV:*** Bij patiënten bij wie de behandeling met ledipasvir/sofosbuvir faalt, wordt in de meeste gevallen selectie van NS5A-resistentie-mutaties gezien die de gevoeligheid voor ledipasvir aanzienlijk verminderen. Er zijn op dit moment geen gegevens die de effectiviteit ondersteunen van herbehandeling van patiënten bij wie de behandeling met ledipasvir/sofosbuvir faalde met een daaropvolgend regime dat een NS5A-remmer bevat. Patiënten kunnen daarom afhankelijk zijn van andere geneesmiddelen- klassen voor klaring van HCV-infectie ***Nierfunctiestoornis***: De veiligheid van Harvoni is niet onderzocht bij patiënten met een ernstige nierfunctiestoornis (eGFR < 30 ml/min/1,73 m2) of ESRD die hemodialyse vereist. Raadpleeg de SmPC van ribavirine voor patiënten met een creatinineklaring (CrCl) < 50 ml/min ***Gedecompenseerde cirrose/ levertransplantatie:*** zie SmPC ***Gebruik met matige P-gp inductoren:*** matige inductoren van P-glycoproteïne (P-gp) in de darm (bijv. oxcarbazepine), kunnen leiden tot een daling van de plasmaconcentraties van ledipasvir en sofosbuvir, wat resulteert in een verminderd therapeutisch effect van Harvoni. Gelijktijdige toediening van dergelijke geneesmiddelen wordt niet aanbevolen. ***Gebruik met bepaalde antiretrovirale regimes tegen HIV:*** Het is gebleken dat Harvoni de blootstelling aan tenofovir verhoogt, met name bij gebruik in combinatie met een HIV-regime dat tenofovirdisoproxilfumaraat en een farmacokinetische booster (ritonavir of cobicistat) bevat. De veiligheid van tenofovirdisoproxilfumaraat in het kader van een behandeling met Harvoni en een farmacokinetische booster is niet vastgesteld. Er moet rekening worden gehouden met de mogelijke risico's en voordelen van gelijktijdige toediening van Harvoni met de tablet met de vaste-dosiscombinatie die elvitegravir/cobicistat/emtricitabine/tenofovirdisoproxilfumaraat bevat of tenofovirdisoproxilfumaraat in combinatie met een gebooste HIV-proteaseremmer (bijv. atazanavir of darunavir), vooral bij patiënten met verhoogd risico op een nierfunctie-stoornis. Patiënten die Harvoni gelijktijdig met elvitegravir/cobicistat/ emtricitabine/tenofovirdisoproxilfumaraat of met tenofovirdisoproxil fumaraat en een gebooste HIV-proteaseremmer krijgen, moeten worden gecontroleerd op tenofovir-gerelateerde bijwerkingen. Raadpleeg de SmPC van tenofovirdisoproxilfumaraat, emtricitabine/tenofovirdisoproxilfumaraat of elvitegravir/cobicistat/emtricitabine/tenofovirdisoproxilfumaraat voor aanbevelingen over niercontrole ***Gebruik met HMG-CoA-reductaseremmers:*** Gelijktijdige toediening van Harvoni met HMG-CoA-reductaseremmers (statines) kan leiden tot een significante stijging van de concentratie van het statine, wat het risico op myopathie en rabdomyolyse verhoogt ***Hulpstoffen***: Harvoni bevat de azokleurstof zonnegeel FCF aluminiumpigment (E110), die allergische reacties kan veroorzaken. Het bevat ook lactose **INTERACTIES:** Voor een compleet overzicht en informatie over geneesmiddeleninteracties van Harvoni met potentieel gelijktijdig gebruikte geneesmiddelen, zie SmPC **VRUCHTBAARHEID, ZWANGERSCHAP EN BORSTVOEDING**: Het heeft de voorkeur het gebruik van Harvoni te vermijden tijdens de zwangerschap en tijdens de periode dat borstvoeding wordt gegeven. Bij gebruik van Harvoni in combinatie met ribavirine moet uiterste voorzichtigheid worden betracht om een zwangerschap te vermijden bij vrouwelijke patiënten en bij vrouwelijke partners van mannelijke patiënten. Significante teratogene en/of embryocide effecten zijn aangetoond bij alle diersoorten die aan ribavirine werden blootgesteld. Vrouwen die zwanger kunnen worden of hun mannelijke partners moeten een effectieve vorm van anticonceptie toepassen tijdens de behandeling en gedurende een periode na beëindiging van de behandeling, zoals wordt aanbevolen in de SmPC van ribavirine **BEÏNVLOEDING VAN DE RIJVAARDIGHEID EN VAN HET VERMOGEN OM MACHINES TE BEDIENEN:** Harvoni (alleen toegediend of in combinatie met ribavirine) heeft geen of een verwaarloosbare invloed op de rijvaardigheid en op het vermogen om machines te bedienen. Patiënten moet echter worden verteld dat vermoeidheid vaker voorkwam bij patiënten behandeld met ledipasvir/sofosbuvir in vergelijking met placebo **BIJWERKINGEN:** Zeer vaak: vermoeidheid,hoofdpijn. Vaak: huiduitslag ***Harvoni en ribavirine***: zie SmPC van Harvoni en ribavirine **FARMACOTHERAPEUTISCHE GROEP:** Direct werkend antiviraal middel, ATC-code: J05AX65 **AFLEVERSTATUS:** U.R. **PRIJS**: Zie Z-index **VERGOEDING:** Op verstrekking van dit geneesmiddel bestaat aanspraak krachtens en onder de voorwaarden van de Nederlandse Zorgverzekeringswet en begeleidende uitvoeringswetgeving. **VERGUNNING:** EU/1/14/958/001-002 **REGISTRATIEHOUDER:** Gilead Sciences International Ltd., Verenigd Koninkrijk **LOKALE VERTEGENWOORDIGER:** Gilead Sciences Netherlands B.V., Claude Debussylaan 22, 1082 MD Amsterdam **DATUM:** deze tekst is het laatst herzien in juli 2016. HAR/NL/16-04/PM/1439a. Voor de volledige productinformatie zie de geregisteerde Samenvatting van de Productkenmerken.

HAR/NL/16-04/PM/1439

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