Najaarsvergadering

NEDERLANDSE VERENIGING VOOR GASTRO-ENTEROLOGIE

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

6 en 7 oktober 2011

CONGRESCENTRUM

NH KONINGSHOF

VELDHOVEN

NEDERLANDSE VERENIGING VOOR GASTRO-ENTEROLOGIE

NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

NEDERLANDSE VERENIGING VOOR GASTRO-INTESTINALE CHIRURGIE

NEDERLANDSE VERENIGING VAN MAAG-DARM-LEVERARTSEN

Programma najaarsvergadering 6 en 7 oktober 2011

NH Conference Centre Koningshof te Veldhoven

NEDERLANDSE VERENIGING VOOR GASTROENTEROLOGIE

Sectie Gastrointestinale Endoscopie
Netherlands Society for Parenteral and Enteral Nutrition
Sectie Neurogastroenterologie en Motiliteit
Sectie Experimentele Gastroenterologie
Sectie Kinder-MDL
Sectie Endoscopie Verpleegkundigen en Assistenten
Vereniging Maag Darm Lever Verpleegkundigen

NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

NEDERLANDSE VERENIGING VOOR GASTROINTESTINALE CHIRURGIE

NEDERLANDSE VERENIGING VAN MAAG-DARM-LEVERARTSEN

INHOUDSOPGAVE

Tijdstippen diverse ledenvergaderingen tijdens najaarsvergadering:

Nederlandse Vereniging voor Gastroenterologie	6 oktober, 11.30 uur - Brabantzaal
Nederlandse Vereniging voor Hepatologie	6 oktober, 15.30 uur - Baroniezaal

INHOUDSOPGAVE

Tijdstippen diverse ledenvergaderingen tijdens najaarsvergadering:

V&VN-MDL	7 oktober, 11.45 uur - Diezezaal
Ned. Vereniging van Maag-Darm-Leverartsen	7 oktober, 12.00 uur - Genderzaal
IBD Werkgroep	7 oktober, 15.00 uur - Brabantzaal

Een aandachtspunt voor de sprekers: u dient zich strikt te houden aan de beschikbare spreektijd! U vindt dit aangegeven bij de betreffende sessie. In **zaal 25** kunt u uw PowerPoint presentatie tot een half uur voor uw voordracht inleveren.

VOORWOORD

Hierbij treft u het programma aan van de najaarsvergadering op 6 en 7 oktober 2011 in NH Conference Centre Koningshof te Veldhoven. Dit keer voor de eerste maal zonder abstracts. Op proef is het abstractboek digitaal beschikbaar op de NVGE-website.

Ook dit keer worden deze dagen vooraf gegaan door het cursorisch onderwijs in maag-darm-leverziekten, waarvan u het programma aantreft op bladzijde 4.

Het programma zal donderdag 6 oktober **om 10.00 uur** van start gaan met een drietal parallelle sessies met vrije voordrachten van de Nederlandse Vereniging voor Gastro-enterologie, de Nederlandse Vereniging voor Hepatologie en de Nederlandse Vereniging voor Gastrointestinale Chirurgie. Na de lunch in de expositiehal, vindt onder andere een symposium van de Sectie Neurogastroenterologie en Motiliteit plaats, getiteld *'Functional Dyspepsia, Gastroparesis and Intestinal Pseudo-Obstruction Syndromes'* en eveneens in de middag een symposium van de NVH: *'Direct Acting Antivirals in the treatment of Hepatitis C: The Future is about to Start'* Aansluitend kunt u in dezelfde zaal een lezing bijwonen van prof. dr. P.L.M. Jansen, getiteld*: 'Hepatology beyond the liver'.* De Nederlandse Vereniging voor Gastrointestinale Chirurgie organiseert naast de vrije voordrachten een minisymposium over de stand van zaken bij de behandeling van diverticulitis.

Aan het einde van de middag zal in de Brabantzaal de 'Tytgat Lecture' worden gegeven, ditmaal door prof. dr. Th. Seufferlein met een voordracht getiteld: '*The Future Roles of the Gastroenterologist in Digestive Oncology – a European Perspective'.* Om 17.00 volgt aansluitend de President Select en tot slot om 18.00 uur de uitreiking van de Janssen Gastrointestinale Research Award 2011. De eerste prijswinnaar zal na de uitreiking een erevoordracht houden. Met deze lezing wordt het programma van de donderdag afgesloten. In de avond is er verder geen wetenschappelijk programma gepland. Het diner vindt plaats in de Genderzaal, daarna, vanaf omstreeks 22.30 uur, is er muziek in de Baroniezaal en de gebruikelijke congresborrel in de Limburgfoyer.

Op vrijdag staan er twee symposia op het programma: in de ochtend een symposium van de Sectie Gastrointestinale Endoscopie *'Bent u goed genoeg'* en in de middag een symposium van de Werkgroep IBD, getiteld: *'Actuele ontwikkelingen rondom de behandeling met TNF alfa blokkers'.* Daarnaast kunt in de verschillende zalen vrije voordrachten volgen. In de Diezezaal tenslotte, wordt op vrijdag door de V&VN - MDL een eigen programma met lezingen verzorgd.

Dr. R.J.F. Felt-Bersma, secretaris
Nederlandse Vereniging voor Gastroenterologie

Belangrijke mededeling
over de aanwezigheid van farmaceutische industrieën

Aan alle deelnemers aan de najaarsvergadering

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.
In de Geneesmiddelenwet die per 1 juli 2007 in werking is getreden is een hoofdstuk Geneesmiddelenreclame (hoofdstuk 9) opgenomen waarin de regels hieromtrent zijn vastgelegd. Daarnaast gelden per 1 juli 2007 de 'Beleidsregels nadere invulling begrip gunstbetoon'. De wet 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 kunnen zijn.
De aanwezigheid van artsen, niet-artsen en farmaceutische industrieën tijdens de najaarsvergadering kan de NVGE ongewild in aanraking brengen met de inspectie voor de gezondheidszorg, sectie reclametoezicht, en daarmee in diskrediet worden gebracht.
Dat willen wij te allen tijde voorkomen.

Wij delen u dan ook het volgende mede:
Reclame-uitingen en merkproductinformatie van farmaceutische industrieën in het voorliggende programmaboekje zijn alleen gericht op personen die bevoegd zijn om de betreffende geneesmiddelen voor te schrijven.
Al het aanwezige reclamemateriaal, reclame-uitingen en merkproductinformatie van farmaceutische industrieën die aanwezig zijn op het najaarscongres, zijn alleen bedoeld en alleen gericht 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) meent u allen, en met name de niet BIG geregistreerde personen, voldoende te hebben ingelicht en kunnen niet verantwoordelijk worden gehouden indien u geen acht slaat op deze mededeling.

Het bestuur van de NVGE

Cursorisch onderwijs in maag-darm-leverziekten, 5 oktober 2011 **Auditorium**

Cursuscommissie: Prof. dr. P.D. Siersema (voorzitter) (MDL-arts, UMCU)
Dr. E. van der Harst (chirurg, Maasstad Ziekenhuis)
Dr. D.J. de Jong (MDL-arts, UMCN)
Prof. dr. J.H. Kleibeuker (MDL-arts, UMCG)
Dr. R. Timmer (MDL-arts, Antonius Nieuwegein)
M. Bargeman (aios MDL, UMCG)
J. Bosman (aios MDL, UMCU)

Onderwerp: **Neurogastroenterologie, motiliteit en functiestoornissen**

Voorzitter: J.H. Kleibeuker +AIOS

15.00 – 15.15 Evaluatie toets

15.15 – 15.45 GORZ: Functie-onderzoek en behandeling
Dr. A.J. Bredenoord, MDL-arts i.o.,
Academisch Medisch Centrum Amsterdam

15.45 – 16.15 Motoriekstoornissen van de slokdarm
Prof. dr. G.E.E. Boeckxstaens, MDL-arts,
Katholieke Universiteit Leuven, België

16.15 – 16.45 Maagontledigingsstoornissen
Prof. dr. G.E.E. Boeckxstaens, MDL-arts,
Katholieke Universiteit Leuven, België

16.45 – 17.15 Pauze

Voorzitter: E. van der Harst + AIOS

17.15 – 17.45 Chronische intestinale pseudo-obstructie
Prof. dr. A.J.P.M. Smout, MDL-arts,
Academisch Medisch Centrum Amsterdam

17.45 – 18.15 Prikkelbaredarmsyndroom
Prof. dr. A.A.M. Masclee, MDL-arts,
Maastricht Universitair Medisch Centrum

18.15 – 18.45 Chronische obstipatie
Prof. J.F.W.M. Bartelsman, MDL-arts,
Academisch Medisch Centrum Amsterdam

18.45 – 20.00 Dinerbuffet

Voorzitter: P.D. Siersema + AIOS

20.00 – 20.30 Bekkenbodemproblematiek
Mw. dr. R.J.F. Felt-Bersma, MDL-arts
VU medisch centrum, Amsterdam

20.30 – 21.00 Chirurgische behandeling van incontinentie
Prof. dr. C.G.M.I. Baeten, chirurg,
Maastricht Universitair Medisch Centrum

Voorzitter: P.D. Siersema + AIOS

21.00 – 22.00 Paneldiscussie met C.G.M.I. Baeten, J.F.W.M. Bartelsman, R.J.F. Felt-Bersma en A.J.P.M. Smout aan de hand van casuïstiek.

1. Moeilijke reflux-patiënt (VUmc)
2. Moeilijke obstipant (Ziekenhuis Rijnstate)
3. syndroom van Ogilvie (Erasmus MC)

22.00 – 22.15 Afsluitende kennistoets

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

Programma donderdag 6 oktober 2011

Donderdag	Brabantzaal	Baroniezaal	Auditorium
10.00 - 11.30	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie pagina 11-13	Vrije voordrachten Nederlandse Vereniging voor Hepatologie pagina 13-15	Vrije voordrachten Ned. Vereniging voor Gastrointestinale Chirurgie pagina 15-17
11.30 - 12.00	Ledenvergadering NVGE	Geen programma i.v.m. Ledenvergadering NVGE	Geen programma i.v.m. Ledenvergadering NVGE
12.00 - 13.00	Lunch in expositiehal	Lunch in expositiehal	Lunch in expositiehal
13.00 - 15.30	Symposium Sectie Neurogastroenterologie en Motiliteit: *'Functional Dyspepsia, Gastroparesis and Intestinale Pseudo-Obstruction Syndromes'* gevolgd door vrije voordrachten pagina 18-19	Vrije voordrachten NVH, gevolgd door Symposium: *''Direct Acting Antivirals in the treatment of Hepatitis C: The Future is about to Start'* pagina 22-24	Vrije voordrachten Ned. Vereniging voor Gastrointestinale Chirurgie pagina 26-29
15.30 - 16.00	Theepauze	Theepauze	Symposium NVGIC: *'Behandeling van diverticulitis, stand van zaken'* pagina 30
16.00 - 16.30	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie pagina 19-20	Lezing prof. dr. P.L.M. Jansen: *'Hepatology beyond the liver'* pagina 25	
16.30 - 17.00	Tytgat lecture: prof. dr. Th. Seufferlein: '*The Future Roles of the Gastroenterologist in Digestive Oncology – a European Perspective'* pagina 20	Vrije voordrachten Nederlandse Vereniging voor Hepatologie pagina 25-26	Geen programma in deze zaal
17.00 - 18.00	President Select pagina 21-22	Geen programma in deze zaal	Geen programma in deze zaal
18.00 - 18.30	Uitreiking Janssen Gastro-intestinale Researchprijs gevolgd door voordracht eerste prijs winnaar	Geen programma in deze zaal	Geen programma in deze zaal
18.30 - 19.30	Borrel in expositiehal		
19.30 - 22.00	Diner Genderzaal		
22.00 - 01.00	Borrel / Muziek in foyer		

In het programma vindt u achter de titel het paginanummer van het betreffende abstract

Programma vrijdag 7 oktober 2011

Vrijdag	Brabantzaal	Baroniezaal	Diezezaal
08.30 - 09.00	Vrije voordrachten Sectie Gastrointestinale Endoscopie pagina 31	Vrije voordrachten Nederlandse Vereniging voor Hepatologie pagina 33-34	
09.00 - 10.30	Symposium Sectie Gastrointestinale Endoscopie: *'Bent u goed genoeg?* pagina 31	Vrije voordrachten Nederlandse Vereniging voor Hepatologie pagina 34-37	Programma Verpleegkundigen en Verzorgenden Nederland MDL pagina 42
10.30 - 11.00	Koffiepauze	Koffiepauze	
11.00 - 12.00	Vrije voordrachten Sectie Gastrointestinale Endoscopie pagina 32-33	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie pagina 37-38	
12.00 - 13.30	Ledenvergadering Nederlandse Vereniging van Maag-Darm-Leverartsen in de Genderzaal	Lunch in expositiehal	Lunch in expositiehal
13.30 - 15.00	Symposium Werkgroep IBD: *'Actuele ontwikkelingen rondom de behandeling met TNF alfa blokkers'* pagina 39	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie pagina 40-41	Vervolg Programma Verpleegkundigen en Verzorgenden Nederland MDL pagina 43
15.00 - 15.30	Afsluiting met hapje en drankje expositiehal	Afsluiting met hapje en drankje expositiehal	Afsluiting met hapje en drankje expositiehal

In het programma vindt u achter de titel het paginanummer van het betreffende abstract

Nederlandse Vereniging Gastroenterologie **Brabantzaal**

Voorzitter: J.J. Keller en J.Ph. Kuijvenhoven

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

10.00 Computed tomography angiography compared to digital subtraction Angiography for finding and grading mesenteric artery stenoses in patients suspected of having chronic mesenteric ischemia: a retrospective comparative study (p. 45)
M.P. de Wringer[1], L.M.G. Moons[1], J.N.L. Schouten[1], A. Moelker[2], E.J. Kuipers[1], M. Ouhlous[2], [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands, [2]Dept. of Radiology, Erasmus MC, Rotterdam, The Netherlands

10.10 Comparison of MR enteroclysis with video capsule endoscopy in the investigation of small-intestinal disease (p. 46)
S.J.B. van Weyenberg[1], K. Bouman[1], M.A.J.M. Jacobs[1], B.P. Halloran[1, 2], D.L. van der Peet[3], C.J.J. Mulder[1], C. van Kuijk[4], J.H.T.M. van Waesberghe[4], [1]Dept of Gastroenterology and Hepatology, VU University Medical Centre, Amsterdam, The Netherlands, [2]Dept of Gastro-enterology and Hepatology, University of Alberta Hospital, Edmonton, Alberta, Canada, [3]Dept of Surgery, VU University Medical Centre, [4]Dept of Radiology, VU University Medical Centre, The Netherlands

10.20 A prospective study of the impact of endoscopic and surgical treatment of early Barrett's neoplasia on quality of life and fear of cancer recurrence. (SWO 04-11 MLDS-voordracht) (p. 47)
W.D. Rosmolen, P.T. van Nieuwkerk[2], M. van Berge Henegouwen[3], M.A.G. Sprangers[2], J.J.G.H.M. Bergman[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, [2]Dept of Medical Psychology, Academic Medical Centre, Amsterdam, [3]Dept of Surgery, Academic Medical Centre, Amsterdam, The Netherlands

10.30 Concomitant Coeliac Disease in adult Type 1 Diabetes patients: Glycemic control and the Risk of Micro vascular Complications (p. 48)
S.F. Bakker[1], C.J.J. Mulder[1], B.M. von Blomberg[2], S. Simsek[3], [1]Dept of Gastroenterology and Hepatology, VU University Medical Center Amsterdam, The Netherlands, [2]Dept of Immunology, VU Medical Center, [3]Dept of Internal Medicine, Medical Center Alkmaar, The Netherlands

10.40 The effect of delay in the diagnosis of neuroendocrine tumors RET (p. 49)

S. van Roosmalen[1], T. Korse[2], M. Tesselaar[3], H. Boot[1], B.G. Taal[1], [1]Dept of Gastroenterology, [2]Clinical Chemistry, [3]Medical Oncology; Nederlands Kanker Instituut/ Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, The Netherlands

10.50 Centralization of pancreaticoduodenectomy in The Netherlands (p. 50)

R.F. de Wilde[1], M.G. Besselink[1], I. van der Tweel[2], I.H. de Hingh[3], C.H. van Eijck[4], C.H.C. Dejong[5], R.J. Porte[6], I.H. Borel Rinkes[1], D.J. Gouma[7], O.R. Busch[7], I.Q. Molenaar[1]; for the Dutch Pancreatic Cancer Group, [1]Dept of Surgery, University Medical Center Utrecht, [2]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, [3]Dept of Surgery, Catharina Hospital Eindhoven, [4]Dept of Surgery, Erasmus Medical Center Rotterdam, [5]Dept of Surgery, Maastricht University Medical Center, Maastricht, [6]Dept of Surgery, University Medical Center Groningen, The Netherlands [7]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

11.00 The risk of non-colorectal malignancies in serrated polyposis syndrome patients and their first-degree relatives (p. 51)

Y. Hazewinkel[1], J.B. Reitsma[2], J.J. Koornstra[3] , F.M. Nagengast[4], M.E. van Leerdam[5] , T.A.M van Os[6], H.F. Vasen[7], E. Dekker[1], [1]Depts of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands, [2]Dept of Clinical Epidemiology & Biostatistics, Academic Medical Center, Amsterdam, The Netherlands, [3]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [4]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands, [5]Dept of Gastroenterology and Hepatology. Erasmus University Medical Centre, Rotterdam, The Netherlands, [6]Dept of Clinical Genetics, Academic Medical Center, Amsterdam, The Netherlands, [7]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands

11.10 Feasibility, safety and efficacy of a prospective annual colonoscopic surveillance program in serrated polyposis syndrome patients (p. 52)

Y. Hazewinkel[1], K.M.A.J.Tytgat[1], S. van Eeden[2], P. Fockens[1], E. Dekker[1], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Pathology, Academic Medical Center, Amsterdam, The Netherlands

11.20 Impact of late anorectal complaints on quality of life after prostate radiotherapy (p. 53)
R. Krol[1], W.P.M. Hopman[1], R.J. Smeenk[2], E.N.J. Th. Van Lin[2] , Depts of [1]Gastro-enterology and Hepatology and [2]Radiation Oncology, Radboud University Nijmegen Medical Centre, The Netherlands

11.30 Einde abstractsessie

11.30 **Ledenvergadering NVGE**

12.00 Lunchbuffet in expositiehal

Nederlandse Vereniging voor Hepatologie — Baroniezaal

Voorzitters: M. Coenraad en C.M.J. van Nieuwkerk

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

10.00 Biliary involvement in untreated autoimmune hepatitis is an underestimated feature (p. 55)
M.F. Lozano[1], A.S.H. Gouw[1], A.P. van den Berg[2], E.B. Haagsma[2], R.C. Verdonk[2], from the Dept of Pathology and Laboratory Medicine[1] and the Dept of Gastro-enterology and Hepatology[2] of the University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

10.10 Higher physical activity level is associated with decreased prevalence and severity of non-alcoholic fatty liver disease in elderly (p. 56)
E..M. Koehler[1], J.N.L..Schouten[1], B.E.. Hansen[1,2], F.J.A. van Rooij[3], A. Hofman[3], B.H. Stricker[3], H.L.A. Janssen[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Public Health, [3]Dept. of Epidemiology, Erasmus MC, Rotterdam, The Netherlands.

10.20 Hepatocellular carcinoma in The Netherlands: changes in incidence, treatment, and survival during the last two decades (p. 57)
C.D.M. Witjes[1] , H.E. Karim-Kos[2] , O. Visser[3] , S.A.W. van den Akker[2] , E. de Vries[2], J.N.M. IJzermans[1], R..A. de Man[4], J.W.W. Coebergh[2,5], C. Verhoef[6], Dept of Hepatobiliary and Transplantation Surgery[1], Public Health[2], Hepato-Gastroenterology[4], Surgical Oncology[6], Erasmus MC, University Medical Centre Rotterdam, Dept of Registration and Research,

Amsterdam[3], Eindhoven Cancer Registry, Eindhoven[5], Comprehensive Cancer Centre Netherlands, The Netherlands

10.30 Ribavirin concentrations at week 8 predict treatment response in naive genotype 1 or 4 HCV patients (p. 58)
L.G. van Vlerken[1], C.T.M.M. de Kanter[2,3], G.J. Boland[1,4], A.M. van Loon[4], H. van Soest[1], P.D. Siersema[1], G. Koek[5], J.P.H. Drenth[6], K.J. van Erpecum[1], DM Burger[2,3], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, [2]Dept of Pharmacy, Radboud University Nijmegen Medical Center, [3]Nijmegen Institute for Infection, Inflammation and Immunology (N4i), Radboud University Nijmegen Medical Center, [4]Dept of Virology, University Medical Center Utrecht, [5]Dept of Gastro-enterology and Hepatology, Maastricht University Medical Center, [6]Dept of Gastro-enterology and Hepatology, Radboud University Nijmegen Medical Center, The Netherlands

10.40 Treatment of persistent hepatocellular secretory failure with rifampicin (p. 59) *R. van Dijk[1], B. van den Elzen[1], T. van Gulik[2] , D. Gouma[2], J. S. Lameris[3], V. Enemuo[4,] P.L.M. Jansen[1], U.H.W Beuers[1], Depts of [1]Gastro-enterology & Hepatology, [2]Surgery, and [3]Radiology, Academic Medical Centre, Univer-sity of Amsterdam, Amsterdam, The Netherlands, Dept of [4]Pediatric Gastroenterology, Louisiana State University Health Sciences Centre, New Orleans, USA*

10.50 A simplified NAFLD-score to distinguish simple steatosis from steatohepa-titis (p. 60)
B.J. Veldt[1], A. van Leeuwen[2], J.T. Brouwer[1], Reinier de Graaf Hospital Delft, The Netherlands, Depts of [1]Gastroenterology & Hepatology and Internal Medicine and [2]Pathology, The Netherlands

11.00 Mycophenolate mofetil: role in autoimmune hepatitis and overlap syn-dromes (p.61)
A.M.C. Baven-Pronk[1], M.J. Coenraad[1], H.R. van Buuren[2], R.A. de Man[2], K.J. van Erpecum[3], M.M.H. Lamers[4], J.P.H. Drenth[4], A.P. van den Berg[5], U.H. Beuers[6], J. den Ouden[7], G.H. Koek[8], C.M.J. van Nieuwkerk[9], G. Bouma[9], J.T. Brouwer[10], B. van Hoek[1] for the Dutch Autoimmune Hepatitis Group, Depts. of Gastroenterology and Hepatology of Leiden University Medical Center, Leiden, [1]Erasmus Medical Center, Rotterdam, [2]University Medical Center Utrecht, Utrecht, [3]Radboud University Medical Center, Nijmegen, [4]University Medical Center Groningen, Groningen, [5]Academic Medical Center, Amsterdam, [6]Haga Hospital, The Hague, [7]Maastricht

University Medical Center, Maastricht ,[8]Free University Medical Center, Amsterdam, [9]Reinier de Graaf Gasthuis, Delft, [10]The Netherlands

11.10 Sequential liver chemistry profiling and abdominal ultrasound assessments predict biliary strictures after liver transplantation (p. 62)
K. Sebib Korkmaz[1], W.R. ten Hove[1], J. Dubbeld[2], R. Wolterbeek[3], A. van Erkel[4], B.J.F. de Rooij[1], M.J. Coenraad[1], J. Ringers[2], H.W. Verspaget[1], B. van Hoek[1], Depts of Gastroenterology and Hepatology[1], Transplantation Surgery[2], Medical Statistics[3] and Interventional Radiology[4], Leiden University Medical Center, Leiden, The Netherlands

11.20 The Long-Term Outcome of the Kasai Operation in Patients with Biliary Atresia: A systematic review (p. 63)
E.J. Bijl, K.D. Bharwani, R.A. de Man, Dept of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands

11.30 Leden van de NVGE kunnen zich voor de ALV begeven naar de Brabantzaal

12.00 Lunchbuffet in expositiehal

Nederlandse Vereniging voor Gastrointestinale Chirurgie — Auditorium

Voorzitters: M.G.H. Besselink en R.M. van Dam

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

10.00 Recurrence and fistula formation after incision and drainage of primary perianal abscesses (p. 64)
M. Meerdink[1], A. Prent[2], A. Kusters[3], A.B. Francken[1], A.D. van Dalsen[1], [1]Isala Klinieken Zwolle, [2]Deventer Ziekenhuis, [3]Diaconessenhuis Leiden, The Netherlands

10.10 Ligation of the intersphincteric fistula tract as an adjunct to transanal advancement flap repair: useful or not? (p. 65)
R.S. van Onkelen[1,2], M.P. Gosselink[1], E. Mitalas[1,] W.R. Schouten[1], [1]Dept of Surgery, Erasmus MC, University Medical Center, Rotterdam, The

Netherlands, [2]Dept of Immunology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

10.20 Colonoscopy after conservatively treated diverticulitis only indicated in patients with symptoms associated with an increased risk for colon cancer (p. 66)

P.J.C. Schout[1], E.J. Spillenaar Bilgen[1], M.J.M. Groenen[2], Rijnstate ziekenhuis Arnhem, afdeling Heelkunde[1], afdeling Maag-, Darm- en Leverziekten[2], The Netherlands

10.30 How to distinguish between a rectum and sigmoid carcinoma in advance to treatment: a prospective study comparing endoscopy and MRI measurements (p. 67)

L. van Nunspeet[1], H.W. Wiersma[2], M. Ledeboer[3], R.A.J.M. van Dijk[2], K. Koster[2], R.J.I. Bosker[1], E.H. Eddes[1], M. Eeftinck Schattenkerk[1], [1]Dept of Surgery, Deventer Hospital, [2]Dept of Radiology, Deventer Hospital, [3]Dept of Gastroenterology, Deventer Hospital, The Netherlands

10.40 Transanal single port surgery is feasible and safe (p. 68)

R.M. Barendse[1], P.G. Doornebosch[2], W.A. Bemelman[3], P. Fockens[1], E. Dekker[1], E.J.R. de Graaf[2], [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [2]Dept. of Surgery, Academic Medical Center, Amsterdam, [3]Dept. of Surgery, IJsselland Hospital, Capelle aan den IJssel, The Netherlands

10.50 Better fecundity preservation after laparoscopic restorative proctocolectomy: a cross-sectional study (p. 69)

S.A.L. Bartels[1], A. D'Hoore[2], M.A. Cuesta[3], A.J. Bensdorp[4], C. Lucas[5], W.A. Bemelman[1], [1]De-partment of Surgery, Academic Medical Center, Amsterdam, The Netherlands, [2]Dept of Abdominal Surgery, University Hospital Leuven, Leuven, Belgium, [3]Dept of Surgery, VU University Medical Center, Amsterdam, The Netherlands, [4]Dept of Obstetrics and Gynaecology, Academic Medical Center, Amsterdam, The Netherlands, [5]Dept of Clinical Epidemiology, Biostatics and Bioinformatics, Academic Medical Center, Amsterdam, The Netherlands

11.00 Increased risk of anastomotic leakage with Non-Steroidal Anti-Inflammatory Drugs in colorectal surgery (p. 70)

K. Gorissen[1], M. Sosef[1], D. Benning[2], K. Hulsewe[2], M. Luyer[3], [1]Atrium Medisch Centrum Heerlen, [2]Orbis Medisch Centrum Sittard, [3]Catharina Ziekenhuis Eindhoven, The Netherlands.

Donderdag 6 oktober 2011

11.10 Quality of life of older rectal cancer patients is not impaired by a permanent stoma (p.71)

R.G. Orsini[1], M.S.Y. Thong[2, 3], L.V. van de Poll-Franse[2,3], G.D. Slooter[4], I.H.J.T. de Hingh[1], H.J.T. Rutten[1], [1]Dept of Surgery, Catharina Hospital Eindhoven, Eindhoven, [2]CoRPS - Center of Research on Psychology in Somatic Diseases, Dept of Medical Psychology, Tilburg University, [3]Comprehensive Cancer Centre South (CCCS), Eindhoven Cancer Registry, Eindhoven, [4]Dept of Surgery, Máxima Medical Centre Veldhoven, Veldhoven, The Netherlands

11.20 Four years after implementation of a Enhanced Recovery After Surgery (ERAS) in a Dutch Hospital (p. 72)

H. Cakir[1], M.F.M. van Stijn[1], A.M.F. Lopes Cardozo[1], B.L.A.M. Langenhorst[1], W.H. Schreurs, P. Fockens[2], W.A. Bemelman[3], M.J.M. Serlie[4], A.P.J. Houdijk[1], [1]Dept of Surgery, Medical Centre Alkmaar, The Netherlands, [2]Dept of Gastroenterology, Academic Medical Centre Amsterdam, The Netherlands, [3]Dept of Surgery, Academic Medical Centre Amsterdam, The Netherlands, [4]Dept of Endocrinology and Metabolism, Academic Medical Centre Amsterdam, The Netherlands

11.30 Einde abstractsessie

11.30 **Ledenvergadering NVGE in de Brabantzaal**

12.00 Lunchbuffet in expositiehal

Symposium Sectie Neurogastroenterologie en Motiliteit **Brabantzaal**

'Functional Dyspepsia, Gastroparesis and Intestinal Pseudo-Obstruction Syndromes'

Voorzitters: A.J.P.M. Smout en M.A. Benninga

13.00 Introduction: Where are the boundaries?
Prof. dr. A. J.P.M. Smout (Amsterdam)

13.10 Pathophysiology of Functional Dyspepsia
Dr. S. Kuiken (Amsterdam)

13.30 Management of Functional Dyspepsia
Prof. dr. J. Tack (Leuven)

13.50 Panel discussion on management of FD
Prof. J.F.W.M. Bartelsman (Amsterdam)

14.15 Gastroparesis
Prof. dr. A.A.M. Masclee (Maastricht)

14.35 Intestinal pseudo-obstruction syndromes
R. De Giorgio (Bologna, Italy)

15.00 End of symposium

Sectie Neurogastroenterologie en Motiliteit **Brabantzaal**

Voorzitters*:* A.J.P.M. Smout en M.A. Benninga

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

15.00 The serotonin precursor 5-hydrotryptophan induces rectal hyperalgesia in patients with irritable bowel syndrome (p. 73)
D. Keszthelyi[1,2], F. Troost[1,2], D. Jonkers[1,2], J. Dekker[1], A. Masclee[1,2] ,[1]Top Institute Food and Nutrition, Wageningen, The Netherlands, [2] Division of

Gastroenterology-Hepatology, Depart-ment of Internal Medicine, Maastricht University Medical Centre+, Maastricht, The Netherlands

15.10 Supragastric belches are associated with severe belching complaints in patients with gastro-oesophageal reflux disease (p. 75)
B.F. Kessing, A.J. Bredenoord, M. Velosa, A.J.P.M. Smout, Dept of Gastroenterology and Hepatology, Academic Medical Center Amsterdam, Amsterdam, The Netherlands

15.20 PPI therapy is as effective in well-defined NERD patients as in patients with reflux oesophagitis; a meta-analysis (p. 76)
P.W. Weijenborg[1], F. Cremonini[2], A.J.P.M. Smout[1], A.J. Bredenoord[1], [1]Dept. of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands, [2]Division of Gastro-enterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

15.30 Koffie / thee in expositiehal

Nederlandse Vereniging voor Gastroenterologie **Brabantzaal**

Voorzitters: A.A.M. Masclee en C.J.J. Mulder

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

16.00 Association of antidepressant use and gastrointestinal symptoms in the general adult population explained by channelling bias (p. 77)
B. Schurink[1], M.M. Tielemans[1,2], B.R.R.Z. Aaldering[1], T. Eikendal[3], J. Jaspers Focks[4], R.J.F. Laheij[2], J.B.M.J. Jansen[5], L.G.M. van Rossum[6] , M.G.H. van Oijen[2], [1]Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, [2]Gastroenterology and Hepatology, University Medical Centre Utrecht, Utrecht, [3]Emergency Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, [4]Cardiology, Radboud University Nijmegen Medical Centre, Nijmegen,[5]Gastroenterology and Hepatology, Elkerliek hospital, Helmond, [6]Epidemiology, Biostatistics and Health Technology Assessment, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

16.10 Use of VSL#3® , a Probiotic Combination, Is Associated With a Lower Frequency and Severity of Abdominal Pain and Improved Quality of Life in Irritable Bowel Syndrome (IBS): Data from the VIP ("VSL#3® In PDS") Study, a Multi-Centre, Prospective, Observational Study (p. 78)
W.A. de Boer[1], M.H. Otten[2] , W.K.H. Man, A Hing[3], [1]Dept of Gastroenterology, Bernhoven Hospital, Oss, The Netherlands, [2]Dept of Gastroenterology, Meander Medical Centre, Amersfoort, The Netherlands, [3]Ferring BV, Hoofddorp, The Netherlands

16.20 A randomised, placebo controlled, double blind study to assess the efficacy of a probiotic dairy product containing Lactobacillus casei Shirota on symptoms in Irritable Bowel Syndrome (p. 79)
A.Y. Thijssen[1], D.M.A.E. Jonkers[1], V. Vankerckhoven[2], H. Goossens[2], B. Winkens[3], C.H.M. Clemens[4], A.A.M. Masclee[1], [1]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, Maastricht University Medical Center, [2]Vaccine & Infectious Disease Institute (Vaxinfectio), University of Antwerp, [3]Dept of Medical Statistics, Maastricht University Medical Center, [4]Dept of Internal Medicine, Diaconessen Hospital Leiden[1-4] The Netherlands

16.30 Einde abstractsessie

Tytgat Lecture **Brabantzaal**

16.30 **'Digestive oncology; how to organize based on German experience'**
Prof. dr. Th. Seufferlein, Direktor Klinik für Innere Medizin I Universitätsklinikum der Martin-Luther-Universität Halle-Wittenberg

Na deze lezing wordt het programma vervolgd met de President Select

President Select — Brabantzaal

Voorzitter: C.J.J. Mulder

Voordrachten in het Nederlands, spreektijd 10 minuten, discussietijd 5 minuten

17.00 Long-term effectiveness and tolerability of allopurinol and thiopurine combination therapy in inflammatory bowel disease patients (p. 80)
M.L. Seinen[1], F. Hoentjen[2], N.K.H. de Boer[1], D.T. Rubin[2], G. Bouma[1], L. Harrell[2], C.J.J. Mulder[1], A.A. van Bodegraven[1], S.B. Hanauer[2], [1]VU University Medical Center, Amsterdam, The Netherlands, [2]Inflammatory Bowel Disease Center, University of Chicago, Chicago, United States

17.15 Immune function of patients on olive oil-based home parenteral nutrition without an immune modulating underlying disease (p. 81)
E.D. Olthof[1], H.M. Roelofs[1], M. Versleijen[1], R.H. te Morsche[1], E.R. Simonetti[2], P.W.M. Hermans[2], G.J. Wanten[1], [1]Dept of Gastroenterology and Hepatology, Radboud Uni-versity Nijmegen Medical Centre, Nijmegen, The Netherlands, [2]Laboratory of Pediatric Infec-tious Diseases, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

17.30 Total liver volume measurement by CT corrected for body surface area is an objective parameter of the extent of polycystic liver disease (p. 82)
F. Temmerman[1], R. Vanslembrouck[2], W. Coudyzer[2], B. Bammens[3], W. Laleman[1], C. Verslype[1], D. Cassiman[1], W. van Steenbergen[1], J. van Pelt[1], J. Pirenne[4], F. Nevens[1], [1]Depart-ment of Hepatology, University Hospitals Leuven, Belgium, [2]Dept of Radiology, University Hospitals Leuven, Belgium, [3]Dept of Nephrology, University Hospitals Leuven, Belgium, [4]Dept of Abdominal Transplant Surgery, University Hospitals Leuven, Belgium

17.45 Can MRI replace CT in patients with suspected acute appendicitis? A multicenter diagnostic accuracy study (p. 83)
M.M.N. Leeuwenburgh[1,2], B.M. Wiarda[3], A.P.J.Houdijk[4], B.C. Vrouenraets[5], S. Jensch[6], M.J. Wiezer[7], H.W. van Es[8] , W.H. Bouma[9], J.W.C. Gratama[10], H.B.A.C. Stockmann[11], A. Spilt[12], L.P.J. Cobben[13], P.M.M. Bossuyt[14], J. Stoker[2], M.A. Boermeester[1] on behalf of the OPTIMAP study group, [1]Dept of Surgery, Academic Medical Centre, University of Amsterdam, [2]Dept of Radiology, Academic Medical Centre,

University of Amsterdam, [3]Dept of Radiology, Alkmaar Medical Centre, Alkmaar, [4]Dept of Surgery, Alkmaar Medical Centre, Alkmaar, [5]Dept of Surgery, Sint Lucas Andreas Hospital, Amsterdam, [6]Dept of Radiology, Sint Lucas Andreas Hospital, Amsterdam, [7]Dept of Surgery, Sint Antonius Hospital, Nieuwegein, [8]Dept of Radiology, Sint Antonius Hospital, Nieuwegein, [9]Dept of Surgery, Gelre Hospitals, Apeldoorn, [10]Dept of Radiology, Gelre Hospitals, Apeldoorn, [11]Dept of Surgery, Kennemer Gasthuis, [12]Dept of Radiology, Kennemer Gasthuis, [13]Dept of Radiology, Medisch Centrum Haaglanden, Leidschendam, [14]Dept of Clinical Epidemiology, Academic Medical Centre, University of Amsterdam, The Netherlands

Prijsuitreiking — Brabantzaal

18.00 Uitreiking van de **Janssen Gastrointestinale Researchprijs** door de voorzitter van de jury, gevolgd door een erevoordracht door de prijswinnaar

18.30 Congresborrel in expositiehal

19.30 Diner in de Genderzaal

Nederlandse Vereniging voor Hepatologie — Baroniezaal

Voorzitters: J.P.H. Drenth en R.J. de Knegt

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

13.00 Virological response to entecavir is associated with a lower probability of disease progression: Results from 377 chronic hepatitis B patients (p. 84)
R. Zoutendijk[1], J.G.P. Reijnders[1], F. Zoulim[2], A. Brown[3], D. Mutimer[4], K. Deterding[5], W.P. Hofmann[6], J. Petersen[7], M. Fasano[8], M. Buti[9], T. Berg[10], M.J. Sonneveld[1], B.E. Hansen[1], H. Wedemeyer[5], H.L.A. Janssen[1] for the VIRGIL Surveillance Study Group, [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Dept of Hepatology, Hospices Civils de

Lyon, Lyon, France, [3]Dept of Hepatology and Gastroenterology, Imperial College London, London, United Kingdom, [4]NIHR Biomedical Research Unit and Centre for Liver Research, Queen Elizabeth Hospital, Birmingham, United Kingdom, [5]Dept of Gastroenterology, Hepatology, and Endocrinology, Medical School Hannover, Hannover, Germany, [6]Medizinische Klinik 1, Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt am Main, Germany, [7]Ifi Institute, Asklepios Klinik St. Georg, Hamburg, Germany, [8]Clinic of Infectious Diseases, University of Bari, Bari, Italy, [9]Dept of Hepatology, Hospital Vall de Hebron, Barcelona, Spain, [10]Dept of Hepatology, University Clinic Leipzig, Leipzig, Germany

13.10 Preventive versus "on-demand" nutritional support to maintain nutritional state and quality of life during antiviral therapy for hepatitis C: a randomized controlled trial (p. 85)

E.J. Huisman[1-2], B. van Hoek[2], H. van Soest[3], C.M. van Nieuwkerk[4], J.E. Arends[5], P.D. Siersema[1], K.J. van Erpecum[1], Depts of Gastroenterology and Hepatology, University Medical Center Utrecht[1], University Medical Center Leiden[2], Free University Medical Center Amsterdam[4] and Medical Center Haaglanden The Hague[3], The Netherlands. Dept of Internal Medicine and Infectious Diseases, University Medical Center Utrecht, The Netherlands[5]

13.20 Diagnosis and clinical consequences of hepatitis E virus infection in orthotopic heart transplant recipients (p. 86)

R.A. de Man[1], S.Pas[2], A.H.M.M. Balk[3], A.D.M.E. Osterhaus[2], A.A. Baltissen-van der Eijck[2], Depts of Gastroenterology[1], Virology[2] and Cardiology[3] Erasmus MC, Rotterdam, The Netherlands

13.30 Sustained virological response improves overall survival in chronic heaptitis C patients with advanced fibrosis (p. 87)

A.J.P. van der Meer[1], B.J. Veldt[1], J.J. Feld[2], H. Wedemeyer[3], J.-F. Dufour[4], F. Lammert[5], A. Duarte-Rojo[2], E.J. Heathcote[2], M.P. Manns[3], L. Kuske[4], S. Zeuzem[6], W.P. Hofmann[6], R.J. de Knegt[1], B.E. Hansen[1], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Liver centre, Toronto Western hospital, University Health Network, Toronto, Ontario, Canada, [3]Dept of Gastroenterology, Hepatology, and Endocrinology, Medical School Hannover, Hannover, Germany, [4]Institute of Clinical Pharmacology, University of Bern, Bern, Switserland, [5]Klinik für Innere Medizin II, Universitätsklinikum des Saarlandes, Homburg/Saar, Germany,

[6]Medizinische Klinik 1, Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt am Main, Germany

13.40 A prognostic model to select patients for prophylactic SSRI therapy during antiviral treatment for chronic hepatitis C infection (p. 88)
D.M. Hotho[1], G. Bezemer[1], B.E. Hansen[1, 3], A.R. van Gool[2], R.J. de Knegt[1], B.J. Veldt[1], H.L.A. Janssen[1], Depts of [1]Gastroenterology and Hepatology and [2]Psychiatry, [3]Public Health, Erasmus MC University Medical Center, Rotterdam, The Netherlands

13.50 Once daily dose regimen of ribavirin is pharmacokinetically comparable to twice daily dose regimen (p. 89)
J.M. Balk[1], G.R.M.M. Haenen[1], R. Peters[2], A. Bast[1], G.H. Koek[3], [1]Dept of Toxicology, University Maastricht, Maastricht, [2]DSM Resolve, Sittard, [3]Dept of Internal Medicine, division of gastroenterology/hepatology Maastricht University Medical Center, The Netherlands

14.00 Einde abstractsessie

Symposium Nederlandse Vereniging voor Hepatologie **Baroniezaal**

Voorzitters: J.P.H. Drenth en R.J. de Knegt

"Direct-Acting Antivirals in the treatment of Hepatitis C: The Future is about to Start"

14.00 How will we use protease inhibitors in 2012. Review of pivotal trials on telaprevir and boceprevir in naieves and previous nonresponders.
Prof. dr. C. Hézode, Parijs

14.30 Potential role of HCV-protease inhibitors in special populations: cirrhosis, renal insufficiency, HIV-HCV coinfection, post-livertransplantation.
Prof. dr. T. Goeser, Keulen

15.00 Side-effects, treatment failure and resistance in HCV with proteaseinhibitors: should we fear, or can we neglect?
Prof. dr. J.M. Pawlotsky, Parijs

Donderdag 6 oktober 2011

15.30 Theepauze en Ledenvergadering NVH

Nederlandse Vereniging voor Hepatologie **Baroniezaal**

16.00 **'Hepatology beyond the liver'**
Prof. dr. P.L.M. Jansen, maag-darm-leverarts,
Academisch Medisch Centrum Amsterdam

Nederlandse Vereniging voor Hepatologie **Baroniezaal**

Voorzitters: L.C. Baak en K.J. van Erpecum

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

16.30 Effectiveness of Neoadjuvant Chemoradiation Followed by Liver Transplantation for Hilar Cholangiocarcinoma: The United States National Experience (p. 90)
S. Darwish Murad[1, 2], W.R. Kim[1], D.M. Harnois[3], D.D. Douglas[4], J. Burton[5], L.M. Kulik[6], J.F. Botha[7], J.D. Mezrich[8], W.C. Chapman[9], J.J. Schwartz[10] , J.C. Hong[11] , J.C. Emond[12] , H. Jeon[13], G.J. Gores[1], C.B. Rosen[14], J.K. Heimbach[14], [1]Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; [2]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands; [3]Division of Gastroenterology and Hepatology, Mayo Clinic Florida, Jacksonville, FL; [4]Division of Gastroenterology and Hepatology, Mayo Clinic Arizona, Phoenix, AZ; [5]Division of Gastroenterology and Hepatology, University of Colorado, Denver, CO; [6]Dept of Hepatology, Northwestern University, Chicago, IL; [7]Division of Transplantation, University of Nebraska Medical Center, Omaha, NE; [8]Division of Transplantation, University of Wisconsin School of Medicine and Public Health, Madison, WI; [9]Section of Transplantation, Washington University School of Medicine, St Louis, MO; [10]Dept of Surgery, University of Utah, Salt Lake City, UT; [11]Dept of Surgery, University of California, Los Angeles, CA; [12]Dept of Surgery, Columbia University Medical Center, New York, NY; [13]Division of Transplant, University of Illinois at Chicago, Chicago, IL; [14]Division of Transplantation Surgery, Mayo Clinic, Rochester, MN

16.40 Circulating hepatocyte-derived microRNAs are highly sensitive biomarkers associated with the necro-inflammation level in chronic hepatitis C patients (p. 91)

A.J.P. van der Meer[1], W.R.R. Farid[2], M.J. Sonneveld[1], P. de Ruiter[2], A.J. van Vuuren[1], J. Verheij[3], A. Boonstra[1], B.E. Hansen[1,4], R.J. de Knegt[1], L.J.W. van der Laan[2], Harry L.A. Janssen[1], Depts of [1]Gastroenterology & Hepatology, [2]Surgery, [3]Pathology and [4]Biostatistics, Erasmus MC-University Medical Center, Rotterdam, The Netherlands

16.50 Role of the Lectin Complement Pathway in the Outcome of Orthotopic Liver Transplantation. A unique target to improve the outcome of liver transplantation (SWO 07-18, MLDS-voordracht) (p. 92)

B-J.F. de Rooij[1], B. van Hoek[1], M.J. Coenraad[1], R.J. Porte[2], H.W. Verspaget[1], Dept. [1]Gastro-enterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. Dept. [2]Hepatobiliary Surgery and Liver Transplantation, University Medical Center Groningen, Groningen, The Netherlands

17.00 Einde abstractsessie

Voor de President Select en de uitreiking van de Janssen Gastrointestinale Research prijs 2011 kunt u zich begeven naar de Brabantzaal.

Nederlandse Vereniging voor Gastrointestinale Chirurgie — Auditorium

Voorzitters: M.I. van Berge Henegouwen en J. Heisterkamp

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

13.00 Patient preferences in screening for recurrent disease after potentially curative esophagectomy (p. 93)

R.L.G.M. Blom[1], P.T. Nieuwkerk[2], M. van Heijl[1], P. Bindels[1], J.H.G. Klinkenbijl[1], M.A.G. Sprangers[2], M.I. van Berge Henegouwen[1], [1]Dept of Surgery, Academic Medical Center, Amsterdam, [2]Dept of Medical Psychology, Academic Medical Center, Amsterdam, The Netherlands

13.10 Survival after recurrent esophageal carcinoma has not improved over the past 18 years (p. 95)
R.L.G.M. Blom, K. van Oudenaarde, S.M. Lagarde, J.H.G. Klinkenbijl, O.R.C. Busch, M.I. van Berge Henegouwen, Dept of Surgery, Academic Medical Center, The Netherlands

13.20 Enterocutaneous fistula model in a rat: long-term continuous biliary drainage resulting in liver damage and an altered FXR pathway, lipid and cholesterol metabolism (p. 96)
K.V.K. Koelfat[1,2], R.G.J. Visschers[1,2], C.M. Hodin[1,2], R. Shiri-Sverdlov[3,2], W.A. Buurman[1.2], K. Lenaerts[1,2], S.W.M. Olde Damink[1,2,4], [1]Dept of Surgery, Maastricht University Medical Centre+, Maastricht University, Maastricht, The Netherlands, [2]Nutrition and Toxicology Research Institute Maastricht, Maastricht University, The Netherlands, [3]Dept of Molecular Genetics, Maastricht University Medical Center+, The Netherlands, [4]Dept of HPB Surgery and Liver Transplantation, Royal Free Hospital, University College London, London, UK

13.30 Liver mobilisation during liver resection induces profound hepatic inflammation: a mouse model (p. 97)
J.J.W. Schreurs[1], D.K. Dhar[2] , L. Mpabanzi[1,2,4] , T. Hendrikx[3,4] , M. Malagó[2], C.H.C. Dejong[1,4], R. Shiri-Sverdlov[3,4], S.W.M. Olde Damink[1,2,4], [1]Dept of Surgery, Maastricht University Medical Centre, Maastricht, The Netherlands, [2]Dept of HPB Surgery and Liver Transplantation, Royal Free Hospital, University College London, London, UK, [3]Dept of Molecular Genetics, Maastricht University Medical Center+, The Netherlands, [4]Nutrition and Toxicology Research Institute Maastricht, Maastricht University, The Netherlands

13.40 Malnutrition at and during admission for a first attack of acute pancreatitis (p. 98) *E. Brons[1], E. Roovers[2], B. Spanier[1], [1]Gastroenterology and Hepatology, [2]Epidemiology Rijnstate hospital Arnhem, The Netherlands*

13.50 Treatment results of necrotizing pancreatitis in a prospective multicenter cohort of 639 patients (p. 99)
H.C. van Santvoort[1], O.J. Bakker[1], T.L. `Bollen[2], M.G. Besselink[1], U. Ahmed Ali[1], A.M. Schrijver[1], M.A. Boermeester[3], H. van Goor[4], C.H. Dejong[5], C.H. van Eijck[6] , Bert van Ramshorst[7], A.F. Schaapherder[8], E. van der Harst[9], H.S. Hofker[10], V.B. Nieuwenhuijs[10], M.A. Brink[11], P.M. Kruyt[12], E.R. Manusama[13], G.P. van der Schellin[14], T. Karsten[15], E.J. Hesselink[16], C.J. van Laarhoven[17], C. Rosman[18], K. Bosscha[19], R.J. de

Wit[20], A.P. Houdijk[21], M.A. Cuesta[22], P.J. Wahab[23], H.G. Gooszen[1], for the Dutch Pancreatitis Study Group, [1]Dept. of Surgery, University Medical Center Utrecht, Utrecht, [2]Dept of Radiology St. Antonius Hospital, Nieuwegein, [3]Dept. of Surgery, Academic Medical Center, Amsterdam, [4]Dept. of Surgery, Radboud University Nijmegen Medical Center, Nijmegen, [5]Dept. of Surgery and NUTRIM, Maastricht University Medical Center, Maastricht, [6]Dept. of Surgery, St. Antonius Hospital, Nieuwegein, [7]Dept. of Surgery, Erasmus Medical Center, Rotterdam, [8]Dept. of Surgery, Leiden University Medical Center, Leiden, [9]Dept. of Surgery, Maasstad Hospital, Rotterdam, [10]Dept. of Surgery, University Medical Center Groningen, Groningen, [11]Dept. of Gastroenterology, Meander Medical Center, Amersfoort, [12]Dept. of Surgery, Gelderse Vallei Hospital, Ede, [13]Dept. of Surgery, Leeuwarden Medical Center, [14]Dept. of Surgery, Amphia Medical Center, Breda, [15]Dept. of Surgery, Reinier de Graaf Hospital, Delft, [16]Dept. of Surgery, Gelre Hospital, Apeldoorn, [17]Dept. of Surgery, St. Elisabeth Hospital, Tilburg (currently: Dept. of Surgery, Radboud University Nijmegen Medical Centre, Nijmegen), [18]Dept. of Surgery, Canisius Wilhelmina Hospital, Nijmegen, [19]Dept. of Surgery, Jeroen Bosch Hospital, Den Bosch, [20]Dept. of Surgery, Medisch Spectrum Twente, Enschede, [21]Dept. of Surgery, Medical Center Alkmaar, Alkmaar, [22]Dept. of Surgery, Vrije Universiteit Medical Center, Amsterdam, [23]Dept. of Gastroenterology, Rijnstate Hospital, Arnhem, The Netherlands

14.00 Timing of Surgery in Chronic Pancreatitis as a Determinant of Success Assessed by aNomogram (p. 100)

Ahmed Ali[1,6], V. B. Nieuwenhuijs[2], C.H. van Eijck[3], H.G. Gooszen[4], R. van Dam[5], O. R. Busch[6], M.G. Dijkgraaf[7], F.A. Mauritz[1], S. Jens[1], J. Mast[3], H. van Goor[8], M.A. Boermeester[6] and the Dutch Pancreatitis Study Group, [1]Dept of Surgery, University Medical Center Utrecht, Utrecht, [2]Dept of Surgery, University Medical Center Groningen, Groningen, [3]Deptof Surgery, Erasmus Medical Center Rotterdam, Rotterdam, [4]Deptof Operations/ Evidence Based Surgery, Radboud University Nijmegen Medical Center, Nijmegen, [5]Dept of Surgery, Maastricht University Medical Center, Maastricht, [6]Dept of Surgery, [7]Clinical Research Unit, Academic Medical Center Amsterdam, Amsterdam, [8]Dept of Surgery, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

14.10 Signs of preoperative gastric outlet obstruction are associated with delayed gastric emptying after pancreatoduodenectomy (p. 101)

J.J. Atema, W.J. Eshuis, O.R.C. Busch, T.M. van Gulik, D.J. Gouma, Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

14.20 The HEPATICA study: A randomized, multicenter, two arm, phase III study in patients post radical resection of liver metastases of colorectal cancer to investigate bevacizumab in combination with capecitabine plus oxaliplatin (CAPOX) vs CAPOX alone as adjuvant treatment (p. 102)

S.B. Schouten[1], N. Snoeren[1], A.M. Bergman[2], A. Cats[2], O. Dalesio[2], T.J.M. Ruers[2], H.M. Verheul[3], M.P. van den Tol[3], R.A.Tollenaar[4], E.J. Hesselink[5], J.M. Smit[5], J.R. van der Sijp[6], T.M. van Gulik[7], O.R.C. Busch[7], A. Rijken[8], K.P. de Jong[9], R.J. Porte[9], C. de Jong[10], M.H.A. Bemelmans[10], I.H. Borel Rinkes[1], E.E. Voest[1], R. van Hillegersberg[1]; on behalf of HEPATICA working group, [1]UniversitairMedisch Centrum Utrecht, [2]Nederlands Kanker Instituut - Antoni van Leeuwenhoek Ziekenhuis, [3]VU Medisch Centrum, [4]Leids Universitair Medisch Centrum, [5]Gelre Ziekenhuizen, [6]Medisch Centrum Haaglanden, [7]Academisch Medisch Centrum Amsterdam, [8]AmphiaZiekenhuis Breda, [9]Universitair Medisch Centrum Groningen, [10]Maastricht Universitair Medisch Centrum, The Netherlands

14.30 Extended indication criteria of liver resection for colorectal cancer liver metastases. A single centre comparison of outcome (p. 103)

T.M. Lodewick, R.M. van Dam, M.C. de Jong, M.A.J. van den Broek, M.H.A. Bemelmans, S.W.M. Olde Damink, C.H.C Dejong, Dept of Surgery, Maastricht University Medical Centre, Maastricht, The Netherlands

14.40 Liver-First Approach for Synchronous Colorectal Liver Metastasis: a Five-Year Single-Center Experience (p. 104)

M.C. de Jong[1,2], R.M. van Dam[1], M. Maas[1,3], M.H.A. Bemelmans[1], S.W.M. Olde Damink[1], G.L Beets[1], C.H.C. Dejong[1,2],[1]Dept of Surgery, Maastricht University Medical Centre+, Maastricht, [2]NUTRIM ~ School for Nutrition, Toxicology and Metabolism, Maastricht University, Maastricht, [3]Dept of Radiology, Maastricht University Medical Centre+, Maastricht, The Netherlands

14.50 Endobarrier® Gastrointestinal liner rapidly improves diabetes parameters paralleled by increased postprandial GLP-1 and PYY levels in obese type 2 diabetic patients (p. 105)

C. de Jonge[1], F.J. Verdam[1], S.S. Rensen[1], R.P. Vincent[2], S.R. Bloom[2], M.A. Ghatei[2], W.A. Buurman[1], C.W. le Roux[2], N.D. Bouvy[1], J.W.M. Greve[3], [1]Maastricht University Medical Centre, Maastricht, The Netherlands, [2]Hammersmith Hospital, Imperial College London, London, UK, [3]Atrium Medical Centre Parkstad, Heerlen, The Netherlands

15.00 Einde abstractsessie, theepauze

Minisymposium NVGIC **Auditorium**

'Behandeling van diverticulitis, stand van zaken'

Voorzitters: R. Bleichrodt en R. van Hillegersberg

15.30 Klinische en beeldvormende diagnostiek van diverticulitis
Dr. J. Kiewiet, AIOS Heelkunde, AMC, Amsterdam

15.45 Niet-antibiotische conservatieve behandeling van diverticulitis
Dr. R.J.F. Felt-Bersma, MDL-arts, VU medisch centrum Amsterdam

16.00 Antibiotische behandeling van diverticulitis: facts and fiction
Dr. H.B.A.C. Stockmann, chirurg, Kennemer Gasthuis, Haarlem

16.15 Percutane behandeling van gecompliceerde diverticulitis
Prof. dr. R. Bleichrodt, chirurg, UMC St. Radboud Nijmegen

16.30 Chirurgische behandeling van diverticulitis
Prof. dr. W.A. Bemelman, chirurg, Academisch Medisch Centrum Amsterdam

16.45 Einde symposium

Voor de plenaire sessie (President Select) en de aansluitende uitreiking van de Janssen Gastrointestinale Researchprijs 2011 kunt u zich om 17.00 uur begeven naar de Brabantzaal.

Sectie Gastrointestinale Endoscopie — Brabantzaal

Voorzitters: J.J.G.H.M Bergman en J.W. Poley

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

08.30 Comfort scores in colonoscopy performance (p. 106)
V.E. Ekkelenkamp[1,2], I. Shaw[1], R. Valori[1], P. Dunckley[1], [1]Gloucestershire Hospitals NHS Foundation Trust, Gloucestershire Royal Hospital, Gloucester, UK, [2]Erasmus MC University Medical Center, Rotterdam, The Netherlands

08.40 Quality of colonoscopy and surveillance protocols after curative surgery for colorectal cancer (p. 107)
L.C. Steinbusch, J. Smit, J.R. Vermeijden, M.A. Brink, Meander Medisch Centrum, locatie Amersfoort Lichtenberg, The Netherlands

08.50 Endoscopic management of large colorectal polyps: safety and effectiveness aspects in a real-life cohort (p. 108)
G. Veldhuijzen, E.J.A. Rondagh, M. Bouwens, R.J.J. de Ridder, W. Hameeteman, A.A.M. Masclee, S. Sanduleanu, Division of Gastroenterology and Hepatology, Dept of Internal Medicine Maastricht University Medical Centre, The Netherlands

Symposium 'Bent u goed genoeg?' — Brabantzaal

Voorzitters: J.J.G.H.M. Bergman en J.W. Poley

09.00 De helft van u moet stoppen met ERCP's
Dr. E.A.J. Rauws, maag-darm-leverarts, AMC, Amsterdam

09.30 EUS: bij u of in een verwijscentrum?
Prof. dr. M.J. Bruno, maag-darm-leverarts, Erasmus MC, Rotterdam

10.00 Doet u de coloscopie bij mijn partner?
Dr. F.M. Nagengast, maag-darm-leverarts, UMC St. Radboud, Nijmegen

10.30 Koffie / thee in expositiehal

Sectie Gastrointestinale Endoscopie — Brabantzaal

Voorzitters: W. Hameeteman en B.L.A.M. Weusten

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

11.00 Endoscopic Submucosal Dissection (ESD) with the Water-jet HybridKnife (p. 109) *J. Haringsma, S. Ganesh, M. Hadhiti, Dept of Gastroenterology and Hepatology, Maasstad Hospital, Rotterdam, The Netherlands*

11.10 Cryospray ablation using pressurized carbon dioxide gas for the treatment of Barrett's esophagus with early neoplasia (p. 110)
R.E. Verbeek, F.P. Vleggaar, J.W.P.M. van Baal, P.D. Siersema, Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands

11.20 Radiofrequency ablation combined with endoscopic resection, for eradication of Barrett's oesophagus containing early neoplasia in 130 patients: results of a European multicenter study (EURO-II) (p. 111)
R.E. Pouw[1], R. Bisschops[2], O. Pech[3], K. Ragunath[4], B.L. Weusten[5], B. Schumacher[6], B. Rembacken[7], A. Meining[8], H. Messmann[9], E.J. Schoon[10], L. Gossner[11], J. Mannath[4], C.A. Seldenrijk[12], M. Visser[13], T. Lerut[14], J.M. Deviere[15], F.J. ten Kate[13], C. Ell[3], H. Neuhaus[6], J.J. Bergman[1], [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, Netherlands, [2]Dept. of Gastroenterology and Endoscopy, University Hospitals Leuven, Leuven, Belgium, [3]Internal Medicine II, Dr. Horst-Schmidt-Kliniken, Wiesbaden, Germany, [4]Division of Gastroenterology, Wolfson Digestive Diseases Centre, Nottingham, United Kingdom, [5]Dept. of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, Netherlands, [6]Dept. of Gastroenterology, Evangelisches Krankenhaus Düsseldorf, Düsseldorf, Germany, [7]Dept. of Gastroenterology, The General Infirmary at Leeds, Leeds, United Kingdom, [8]Second Medical Dept, Technical University of Munich, Munich, Germany, [9]Third Medical Clinic, Klinikum Augsburg, Augsburg, Germany, [10]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, Netherlands, [11]Dept. of Medicine I, Klinikum Karlsruhe, Karlsruhe, Germany, [12]Dept. of Pathology, St. Antonius Hospital, Nieuwegein, Netherlands, [13]Dept. of Pathology, Academic Medical Center, Amsterdam, Netherlands, [14]Dept. of Thoracic Surgery, University Hospitals Leuven, Leuven, Belgium, [15]Dept. of Gastroenterology and Hepatopancreatology, Erasme University Hospital, Brussels, Belgium

11.30 Concurrent biodegradable esophageal stent placement with single-dose brachytherapy for palliation of dysphagia is associated with high complication rates: results from a pilot study (p. 112)
M.M.C. Hirdes[1], J.E. van Hooft[3], H.K. Wijrdeman[2], M.C.C.M. Hulshof[4], P. Fockens[3], O. Reerink[2], F.P. Vleggaar[1], P.D. Siersema[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Radiotherapy, University Medical Center Utrecht, [3]Dept. of Gastroenterology and Hepatology, [4]Dept. of Radiotherapy, Academic Medical Center Amsterdam, The Netherlands

11.40 Weekend admission is associated with an adverse outcome, irrespective of time of admission and patient-related factors in patients with suspected upper gastrointestinal bleeding (p. 113)
N.L. de Groot[1], J.H. Bosman[1], P.D. Siersema[1], M.G.H. van Oijen[1], A.J. Bredenoord[1], [1]Dept. Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht.

11.50 Learning curve, intra-and interobserver agreement and accuracy of endoscope-based confocal laser endomicroscopy for the differentiation of colorectal lesions (p. 114)
T. Kuiper[1], C.Y. Ponsioen[1], R. Kiesslich[2], P. Fockens[1], E. Dekker[1], [1]Depts of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands, [2]I. Medical Clinic, Johannes Gutenberg University of Mainz, Mainz, Germany

12.00 Algemene ledenvergadering Nederlandse Vereniging van Maag-Darm-Leverartsen in de Genderzaal

Nederlandse Vereniging voor Hepatologie — Baroniezaal

Voorzitters: A. v.d. Berg en G.H. Koek

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

08.30 Stavudine and didanosine treatment are risk factors of HIV-associated idiopathic non-cirrhotic portal hypertension (p. 115)
H.H.M. Rossing[1], J.N.L. Schouten[1], T. Koëter[1], M.E. van der Ende[2], B.E. Hansen[1,3], H.L.A. Janssen[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Internal Medicine, [3]Dept. of Public Health, Erasmus MC University Hospital, Rotterdam, The Netherlands

08.40 The association of activated complement factor 3 with liver fat and liver enzymes (p.116)

N. Wlazlo[1,2,3], M.M.J. van Greevenbroek[2,3], I. Ferreira[2,3,4,5], C.J.H. van der Kallen[2,3], C.G. Schalkwijk[2,3], B. Bravenboer[1], C.D.A. Stehouwer[2,3], [1]Dept of Internal Medicine, Catharina Hospital, Eindhoven, [2]CARIM School for Cardiovascular Diseases, Maastricht University, Maastricht, [3]Dept of Internal Medicine/Laboratory for Metabolism and Vascular Medicine, Maastricht University Medical Centre, Maastricht, [4]Dept of Clinical Epidemiology and Medical Technology Assessment (KEMTA), Maastricht University Medical Centre, Maastricht, [5]CAPHRI School for Public Health and Primary Care, Maastricht University Medical Centre, Maastricht, The Netherlands

08.50 Need and timing of kidney transplantation in relation to liver transplantation in polycystic liver disease (p. 117)

F. Temmerman[1], T. Darius[2], J. Pirenne[2], D. Monbaliu[2], R. Aerts[2], B. Bammens[3], W. Laleman[1], D. Cassiman[1], C. Verslype[1], W. van Steenbergen[1], D. Kuypers[3], F. Nevens[1], [1]De-partment of Hepatology, University Hospitals Leuven, Belgium, [2]Dept of Abdominal Transplant Surgery, University Hospitals Leuven, Belgium, [3]Dept of Nephrology, University Hospitals Leuven, Belgium

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

09.00 Improved platelet count and smaller spleen size long after sustained virological response in chronic hepatitis C patients with advanced fibrosis (p. 118)

A.J.P. van der Meer[1], B.J. Veldt[1], J.J. Feld[2], H. Wedemeyer[3], J.-F. Dufour[4], F. Lammert[5], A. Duarte-Rojo[2], E.J. Heathcote[2], M.P. Manns[3], L. Kuske[4], S. Zeuzem[6], W.P. Hofmann[6], R.J. de Knegt[1], B.E. Hansen[1,7], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Liver centre, Toronto Western hospital, University Health Network, Toronto, Ontario, Canada, [3]Dept of Gastroenterology, Hepatology, and Endocrinology, Medical School Hannover, Hannover, Germany, [4]Institute of Clinical Pharmacology, University of Bern, Bern, Switserland, [5]Klinik für Innere Medizin II, Universitätsklinikum des Saarlandes, Homburg/ Saar, Germany, [6]Medizinische Klinik 1, Klinikum der Johann Wolfgang Goethe- Universität, Frankfurt am Main, Germany, [7]Dept of Biostatistics, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands

09.10 Presence of precore and core promoter mutants limits the probability of achieving a sustained virological response to peginterferon in HBeAg-positive chronic hepatitis B3 (p. 119)

M.J. Sonneveld[1], V.W.-S. Wong[2], S. Zeuzem[3], E.J. Heathcote[4], H.-Y. Chan[2], S.D. Pas[5], G.L.H. Wong[2], B.E. Hansen[1,6], H.L.Y. Chan[2], H.L.A Janssen[1], Depts of [1]Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands; [2]Gastroenterology and Hepatology, Prince of Wales Hospital, Hong Kong SAR, China; [3]Medical Clinic 1, Johann Wolfgang Goethe University Medical Center, Frankfurt, Germany; [4]Division of Gastroenterology, University of Toronto, Toronto, Canada, [5]Virology, Erasmus MC University Medical Center Rotterdam, The Netherlands and [6]Public Health, Erasmus MC University Medical Center Rotterdam, The Netherlands

09.20 Costs and complications associated with treatment of chronic hepatitis C infection: results of a large cohort study (p. 120)

L.G. van Vlerken[1], K.J. van Erpecum[1], P.D. Siersema[1], M.G.H. van Oijen[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands

09.30 HBsAg levels at six months post-treatment predict sustained response through long-term follow-up in HBeAg-positive patients treated with peg-interferon alfa-2b (p. 121)

M.J. Sonneveld[1], V. Rijckborst[1], R. Zoutendijk[1], G. Gerken[2], F. Tabak[3], T. Mach[4], C.A.B. Boucher[5], B.E. Hansen[1,6], H.L.A. Janssen[1], Depts of [1]Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, The Netherlands; [2]Gastroenterology and Hepatology, University Essen, Essen, Germany; [3]Dept of infectious diseases, Istanbul University Cerrahpasa Medical School, Istanbul, Turkey; [4]Gastroenterology and Hepatology, Collegium Medicum UJ, Krakow, Poland; [5]Virology, Erasmus MC University Medical Center, Rotterdam, The Netherlands and [6]Public Health, Erasmus MC University Medical Center, Rotterdam, The Netherlands

09.40 Peginterferon treatment reduces intrahepatic HBsAg and HBcAg expression in patients with HBeAg-negative chronic hepatitis B: Relation to serum HBsAg decline and long-term response (p.123)

V. Rijckborst[1], P.E. Zondervan[2], Y. Cakaloglu[3], M. Raptopoulou-Gigi[4], F. Tabak[5], M. Akdogan[6], K. Simon[7], P. Ferenci[8], E. Verhey[1], B.E. Hansen[1,9], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Dept

of Pathology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [3]Dept of Gastroenterohepatology, Istanbul University Medical School, Istanbul, Turkey, [4]Second Medical Dept, Aristototle University of Thessaloniki, Thessaloniki, Greece, [5]Dept of Infectious Diseases, Istanbul University Cerrahpasa Medical School, Istanbul, Turkey, [6]Dept of Gastroenterology, Turkiye Yuksek Ihtisas Hospital, Ankara, Turkey, [7]Dept and Clinic of Infectious Diseases, Hepatology and Acquired Immune Deficiences, Medical University Wroclaw, Wroclaw, Poland, [8]Dept of Internal Medicine 3, Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria, [9]Dept of Biostatistics, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

09.50 Common bile duct dilatation, an erroneous and misleading sign in the diagnostic approach of methadone users at the hepatology outpatient clinic (p. 124)

D.M. Hotho[1], J.N.L. Schouten[1], P. Taimr[1], B.E. Hansen[1,2], H.L.A. Janssen[1], R.J. de Knegt[1], Depts of [1]Gastroenterology and Hepatology, [2]Public Health, Erasmus MC University Medical Center, Rotterdam, The Netherlands

10.00 A new HBsAg/anti-HBs immune complex assay for prediction of treatment outcome in chronic hepatitis B patients (p.125)

A. de Niet[1], U. Klause[2], B. Takkenberg[1], H. Zaaijer[4], T.C.[3], R. Petric[3], H. Reesink[1], [1]Academic Medical Center, Dept of Gastroenterology and Hepatology, Amsterdam, The Netherlands, [2]Roche Diagnostics, Penzberg, Germany, [3]Hoffmann La-Roche, Nutley, New Jersey, USA, [4]Academic Medical Center, Dept of Virology, Amsterdam, The Netherlands

10.10 Matrixmetalloproteinase 2 genotype is associated with nonanastomotic biliary strictures after orthotopic liver transplantation (p. 126)

W. R. ten Hove[1], K. Sebib Korkmaz[1], S. op den Dries[2], B-J.F. de Rooij[1], B. van Hoek[1], R.J. Porte[2], J.J. van der Reijden[1], M.J. Coenraad[1], J. Dubbeld[3], D.W. Hommes[1], H.W. Verspaget[1], [1]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands, [2]Dept of Hepatobiliary Surgery and Liver Transplantation, University Medical Center Groningen, Groningen, The Netherlands, [3]Dept of Surgery, Leiden University Medical Center, Leiden, The Netherlands

10.20 Elevated ALT is only Predictive for a sustained virological response to peginterferon in HBeAg-positive chronic hepatitis B patients with wildtype virus (p.127)
B.E. Hansen[1,2], M.J. Sonneveld[1], V.W.-S. Wong[3], H.-Y. Chan[3], H.L.Y. Chan[3], H.L.A Janssen[1], Depts of [1]Gastroenterology and Hepatology, [2]Public Health, Erasmus MC University Medical Center, Rotterdam, The Netherlands, [3]Gastroenterology and Hepatology, Prince of Wales Hospital, Hong Kong SAR, China

10.30 Koffie / thee in expositiehal

Nederlandse Vereniging voor Gastroenterologie **Baroniezaal**

Voorzitters: A. van Bodegraven en D.J. de Jong

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

11.00 Gastroprotective strategies in chronic NSAID users: A cost-effectiveness Analysis comparing a single tablet formulation with individual component strategies (p. 128)
N.L. de Groot[1], P.D. Siersema[1], N.J. de Wit[2], B.M.R. Spiegel[3], M.G.H. van Oijen[1,3], [1]Dept.Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands, [3]University of California Los Angeles/Veterans Affairs Center for Outcomes Research and Education (CORE), Los Angeles, CA, USA

11.10 Bacterial infection risk in cirrhotic patients: role of proton pump inhibitors and intestinal permeability (p. 129)
L.G. van Vlerken[1], E.J. Huisman[1], B. van Hoek[2], W. Renooij[3], F.W.M. de Rooij[4], P.D. Siersema[1], K.J. van Erpecum[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, [2]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, [3]Dept of Surgery, University Medical Center Utrecht, [4]Dept of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands

11.20 Increased risk of advanced neoplasia in IBD patients with atypical adenomas: a case control study (p. 130)

E. Mooiweer[1], F.D.M. van Schaik[1], M. van der Have[1], T.D.G. Belderbos[1], F.J.W. ten Kate[2], G.A. Offerhaus[2], M.E.I. Schipper[2], G. Dijkstra[3], M. Pierik[4], P.C.F. Stokkers[5], D.J. de Jong[6], D.W. Hommes[7], A.A. van Bodegraven[8], P.D. Siersema[1], M.G.H. van Oijen[1], B. Oldenburg[1] on behalf of the Dutch Initiative on Crohn and Colitis (ICC), [1]University Medical Center Utrecht, Dept of Gastroenterology and Hepatology, [2]University Medical Center Utrecht, Dept of Pathology, [3]University Medical Center Groningen, Dept of Gastroenterology and Hepatology, [4]Academic Medical Center Maastricht, Dept of Gastroenterology and Hepatology, [5]Academic Medical Center Amsterdam, Dept of Gastroenterology and Hepatology, [6]Radboud University Nijmegen Medical Center, Dept of Gastroenterology and Hepatology [7] Leiden University Medical Center, Dept of Gastroenterology and Hepatology [8] VU University Medical Center Amsterdam, Dept of Gastroenterology and Hepatology, The Netherlands

11.30 The protease genes CYLD and USP40 are associated with Crohn's disease: results from a European Consortium (p. 131)

H.W. Verspaget[3], I. Cleynen[1], D. Lottaz[10], M. Artieda[2], M. Szczypiorska[2], P.L. Lakatos[4], F. Seibold[5], T. Ahmad[6], R.K. Weersma[7], S. Müller[5], A. Tordai[8], D.W. Hommes[3], K. Parnell[6], C. Wijmenga[7], K. van Steen[9], P. Rutgeerts[1], S. Vermeire[1], [1]KU Leuven – Gastroenterology, [2]Progenika Biopharma, S.A., [3]LUMC – Gastroenterology and Hepatology, [4]Semmelweiss University – Medicine, [5]Spitalnetz – Gastroenterology, [6]Peninsula Medical School, [7]UMC Groningen- Gastroenterology and Hepatology, [8]Hungarian National Blood Transfusion Service - Molecular Diagnostics, [9]Montefiore Institute - Electrical engineering and computer science, [10]Inselspital – Rheumatology

11.40 Long-term treatment results of rectovaginal fistulas in Crohn`s Disease, a descriptive study (p. 132)

U.S. Wiersema, P. Dewint, E.J. Kuipers, C.J. van der Woude, Erasmus Medisch Centrum, Dept of Gastroenterology and Hepatology, The Netherlands

11.50 High rates of non-adherence for anti-TNF treatment in Crohn's disease: results of a systematic review (p. 133)

M.M.J. Singendonk, H.H. Fidder, P.D. Siersema, B. Oldenburg, M.G.H. van Oijen, Dept of Gastroenterology, University Medical Center, Utrecht, The Netherlands

Vrijdag 7 oktober 2011

12.00 Lunch in expositiehal
Algemene ledenvergadering NVMDL in Genderzaal

Symposium IBD-werkgroep **Brabantzaal**

Actuele ontwikkelingen rondom de behandeling met TNF alfa blokkers

Voorzitters: B. Oldenburg en D.J. de Jong

13.30 Anti-TNF bij IBD; Update van de IBD richtlijnen
Dr. A.E. van der Meulen, MDL-arts LUMC

14.00 De klinische implicaties van antistoffen tegen TNF Antistoffen
Drs. Ch. Krieckaert, arts-onderzoeker reumatologie Reade

14.30 Vergoedingsproblematiek rondom dure geneesmiddelen
Mr. N. Kien, advocaat in de gezondheidszorg, o.m. werkzaak voor stichting EGV

14.55 Afsluiting

15.00 Huishoudelijke vergadering IBD werkgroep

15.45 Sluiting

Nederlandse Vereniging voor Gastroenterologie **Baroniezaal**

Voorzitters: A. Cats en P.D. Siersema

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

13.30 A novel prognostic FISH biomarker assay for Barrett's esophagus (BE): Results from a long term prospective 5-year follow up study (FIBAR I) (p. 134)
A.F. Pacha[1,2], A.M. Rygiel[1,2], W.M. Rosmolen[1], B. Elzer[1], H. Verhulst[1], M. Visser[1], F.J.W. ten Kate[3], M. Dijkgraaf[4], J.J. Bergman[1,11], K.K. Krishnadath[1,2,1], [1]Dept of Gastro-enterology and Hepatology, [2]Center for Experimental Molecular Medicine, [3]Dept of Pathology, [4]Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, Amsterdam, The Netherlands

13.40 The GerdQ instrument identifies a large proportion of high impact GERD in website visitors; and reveals high prevalence of partial responsiveness in PPI users (p. 135)
M.M. Tielemans[1,2], J.B.M.J. Jansen[3], M.G.H. van Oijen[2], [1]Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [2]University Medical Centre Utrecht, Utrecht, The Netherlands, [3]Elkerliek Hospital, Helmond, The Netherlands

13.50 All low dose aspirin users benefit from gastroprotection: results of a cost-utility analysis of competing strategies (p. 136)
H.G.M. van Haalen[1], N.L. de Groot[1], J. Jaspers Focks[2], P.D. Siersema[1], M.G.H. van Oijen[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Dept of Cardiology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

14.00 Acute esophageal food bolus impaction. A prospective study (p. 137)
H. van der Sluis[1], E.J. van der Wouden[1], F.C.P. Moll[2], M.G. Havenith[2], M.A.C. Meijssen[1], J. Vecht[1], Dept of Gastroenterology and Hepatology[1], Dept of Pathology[2], Isala clinics, Zwolle, The Netherlands

14.10 Psychological, physical and nutritional impact of prophylactic gastrectomy in CDH1 mutation carries and comparison with curative gastrectomy for gastric cancer (p. 138)
I. Kluijt[1], E. Bleiker[1], M.G.E.M. Ausems[2], A. Hartig[1], M. de Boer[1], R. van Hillegersberg[2], E. van Riel[2], R.H. Sijmons[3], L. Spruijt[4], M. Oldenrode-Berends[3], N. Hoogerbrugge[4], J.T. Plukker[3], A. Cats[1], [1]The Netherlands Cancer Institute Amsterdam, [2]University Medical Centre Utrecht, [3]University Medical Center Groningen, [4]Radboud University Medical Centre Nijmegen, The Netherlands

14.20 Evaluation of gastrectomy in patients with delayed gastric emptying after antireflux surgery or large hiatal hernia repair (p. 139)
A. Gerritsen[1], E.J.B. Furnée[1], H.G. Gooszen[2], E.J. Hazebroek[1,3], [1]University Medical Centre Utrecht, Utrecht, The Netherlands, [2]University Medical Centre St Radboud, Nijmegen, The Netherlands, [3]St. Antonius Hospital, Nieuwegein, The Netherlands

14.30 Fluoroscopy prior to gastrostomy tube placement predicts success of percutaneous endoscopic procedure in high-risk children (p. 140)
J.M. Pruijsen, A. de Bruin, G. Sekema, P.F. van Rheenen, Beatrix Children's Hospital, University Medical Center Groningen, The Netherlands

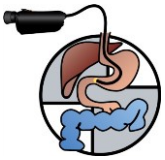
14.40 Sarcopenic obesity affects adverse outcome after cardiac surgery (p. 141)
M. Visser[1, 2] /L.M.W. van Venrooij[1, 3], L. Vulperhorst[4], R. de Vos[5], W. Wisselink[2], P.A.M. van Leeuwen[2], B.A.J.M. de Mol[1], [1]Cardiothoracic Surgery, Academic Medical Center University of Amsterdam, [2]Surgery, VU University Medical Center, [3]Dietetics, Academic Medical Center University of Amsterdam, [4]Institute of Health Sciences, Faculty Earth and Life Sciences, VU University, [5]Clinical Epidemiology and Biostatistics, Academic Medical Center University of Amsterdam, Amsterdam, The Netherlands

14.50 Increased gastroduodenal permeability in human obesity (p. 142)
F.J. Verdam[1], C. de Jonge[1], H. van Eijk[1], K. van Wijck[1], N. Bouvy[1], J.W. Greve[2], W.A. Buurman[1], S.S. Rensen[1], [1]Dept of General Surgery, NUTRIM, Maastricht University Medical Centre, Maastricht The Netherlands, [2]Dept of General Surgery, Atrium Medical Centre, Heerlen, The Netherlands

15.00 Drankje en hapje in expositiehal, afsluiting congres

Vrijdag 7 oktober 2011

Verpleegkundigen en Verzorgenden Nederland MDL **Diezezaal**



10.15 Opening door de voorzitter

10.20 Dunne darm tumoren
Dr. M.A.J.M. Jacobs, MDL-arts
VUmc, Amsterdam

10.40 Vaardigheidstraining voor plaatsen neus-maagsonde
Mevr. A. de Ruiter en mevr. A. Westendorp,
verpleegkundig specialist voedingsteam,
Medisch Centrum Leeuwarden

11.10 Behandeling ziekte van Crohn
Dr. M.G.V.M. Russel, MDL-arts,
Medisch Spectrum Twente Enschede

11.30 Behandeling van hepatitis C met Telaprevir en Boceprevir
(triple therapie met peginterferon en ribavirine)
Dr. R.J. de Knegt, MDL-arts,
Erasmus MC Rotterdam

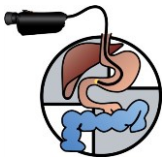
11.50 Algemene Ledenvergadering

12.15 Lunchbuffet in de Kempenhal

Tijdens de middagpauze is er de gelegenheid te oefenen voor het plaatsen van een neus-maagsonde in *de stent van de V&VN in de expositiehal*

Verpleegkundigen en Verzorgenden Nederland MDL **Diezezaal**

v&vn
Beroepsvereniging van zorgprofessionals
Maag Darm Lever



13.50 Research in de MDL
Mevr. Y. van Oossanen, research verpleegkundige,
Meander Medisch Centrum, Amersfoort

14.10 Klinische aspecten van auto-immune leverziekten: AIH, PBC en overlapsyndromen
Mw. Dr. K.F. Kok, MDL-arts,
Canisius Wilhelmina ziekenhuis Nijmegen

14.40 Project veilige endoscopie en BIG registratie
Mevr. M. Knops, endoscopieverpleegkundige,
Atrium Medisch Centrum, Heerlen

15.00 Afsluiting voorzitter

ABSTRACTS

Computed tomography angiography compared to digital subtraction angiography for finding and grading mesenteric artery stenoses in patients suspected of havingchronic mesenteric ischemia: a retrospective comparative study

M.P. de Wringer[1], L.M.G. Moons[1], J.N.L. Schouten[1], A. Moelker[2], E.J. Kuipers[1], M. Ouhlous[2], [1]Dept.of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands, [2]Dept. of Radiology, Erasmus MC, Rotterdam, The Netherlands

Computed tomography angiography (CTA) is often used in the diagnostic work-up of patients suspected of having chronic mesenteric ischemia (CMI). It is presumed that CTA has a good sensitivity and specificity for detecting mesenteric artery stenoses. However, to our knowledge, CTA has never been properly compared to the gold standard, digital subtraction angiography (DSA). Since the indication for treatment depends on the presence of a stenosis detected by CTA, the diagnostic value of CTA was studied. In this retrospective study, all patients analyzed for CMI with a CTA in the period of 2006- 2011 and a DSA within 6 months after CTA were included from a hospital database. Stenoses of both the celiac artery (CA) and the superior mesenteric artery (SMA) were graded as: <50%, 50-70% and >70%. Stenoses on CTA were graded by the radiologist, and agreed upon in a consensus meeting with radiologists, vascular surgeons and gastroenterologists. Stenoses on DSA were assessed by the interventional radiologist. Stenosis etiology was determined by the radiologist. CTA was thought to best show atherosclerotic lesions, and DSA to show respiratory dependent stenoses: CA compression syndrome (CACS).In total, 165 patients (mean age: 64, std. dev.: 15 yrs; 72% female) were included. Data was available on CA stenosis of 109 pts, and of 88 pts for the SMA. Etiology of the stenosis was atherosclerosis in 82%, CACS in 11%, and of other origin in 7%. CTA categorized 75 out of 109 CA stenoses correctly (agreement 69%; kappa 0,445; p=0,067). Underestimation occurred in 19/109 (17%) cases, and overestimation in 15/109 (14%) cases. Using a threshold of ≥50% for a significant CA stenosis, agreement was 82% (kappa 0,499; p= 0,096) with a sens. of 92%, spec. 53%, positive predictive value (PPV) 84%, and NPV of 73%. Using a threshold of >70%, agreement was 80% (kappa 0,581; p=0,078) with a sens. of 78%, spec. 84%, PPV 90% and NPV of 67%.For SMA stenoses, CTA categorized 64 out of 88 SMA stenoses correctly (agreement 73%; kappa 0,547; p=0,071) Underestimation occurred in 10/88 (11%) cases, overestimation occurred in 14/88 (16%) cases. Using a ≥50% threshold for a significant SMA stenosis, agreement was 83% (kappa 0,657; p = 0,079) with a sens. of 93%, spec. 72%, PPV 78% and NPV of 91%. Using the 70% threshold, agreement was 81% (kappa 0,610; p=0.085) with a sens. of 76%, spec. 85%, PPV 82%, and NPV of 80%.

Conclusion: CTA is a fairly accurate technique to identify mesenteric artery stenosis, with a better test performance for correctly grading SMA than CA stenoses.

Comparison of MR enteroclysis with video capsule endoscopy in the investigation of small-intestinal disease

S.J.B. van Weyenberg[1], K. Bouman[1], M.A.J. M. Jacobs[1], B.P. Halloran[1, 2], D.L. van der Peet[3], C.J.J. Mulder[1], C. van Kuijk[4] , J.H.T.M. van Waesberghe[4], [1] Department of Gastroenterology and Hepatology, VU University Medical Centre, Amsterdam, The Netherlands, [2] Department of Gastroenterology and Hepatology, University of Alberta Hospital, Edmonton, Alberta, Canada, [3]Department of Surgery, VU University Medical Centre, [4]Department of Radiology, VU University Medical Centre

Abstract Introduction: Advances in both radiological as endoscopic techniques have resulted in improved non-invasive diagnostic options for patients with suspected small-intestinal diseases. Despite recent studies highlighting the diagnostic accuracy of MR enteroclysis, there are no studies comparing MR enteroclysis and VCE. We aimed to evaluate the diagnostic accuracy of MR enteroclysis and to compare this with VCE.Aims: We performed retrospective analysis of 77 patients who underwent both studies. As a standard of reference for the presence of abnormalities, we used (histopathology) findings of DBE or surgery, or the results of clinical follow-up lasting > 2 years.Results: Final diagnosis included malignant neoplasms (n=13), benign neoplasms (n=10), refractory celiac disease (n=4), Crohn's disease (n=2) and miscellaneous conditions (n=10). The specificity of MR enteroclysis was higher than that of VCE (0.97 vs. 0.84, p=0.047), whereas the sensitivity was similar (0.79 vs. 0.74, p=0.591). In 2/32 (6.3%) patients with both negative VCE and negative MR enteroclysis, a positive diagnosis was established. A positive diagnosis was established in 5/11 (45.5%) patients in whom VCE was positive and MR enteroclysis was negative (likelihood ratio 8.1; p=0.004), in 9/11 (81.8%) patients in whom MR enteroclysis was positive and VCE was negative (likelihood ratio 23.5; p<0.0001), and in all 23 patients in whom both VCE and MR enteroclysis showed abnormalities (likelihood ratio 60.8; p<0.0001).
Conclusion: VCE and MR enteroclysis seem complementary modalities. They can both be used to confirm negative or positive single-study findings. Additionally, both can be used to further investigate patients with a high clinical suspicion of having small-intestinal disorders, despite negative single-study findings.

A prospective study of the impact of endoscopic and surgical treatment of early Barrett's neoplasia on quality of life and fear of cancer recurrence. (SWO 04-11 MLDS-voordracht)

W.D. Rosmolen , P.T. van Nieuwkerk[2], M. van Berge Henegouwen[3], M.A.G. Sprangers[2], J.J.G.H.M. Bergman[1], [1]Department of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, [2]Department of Medical Psychology, Academic Medical Centre, Amsterdam, [3]Department of Surgery, Academic Medical Centre, Amsterdam

Endoscopic treatment (ETx) of early neoplasia in Barrett's esophagus (BE) is an accepted alternative to surgical treatment (STx). The effect of ETx on quality of life (QOL) and fear of cancer recurrence (FOCR) has not been investigated prospectively. To prospectively evaluate QOL and FOCR in ETx pts and compare the findings to 3 reference groups. Between 2006 and 2009, 114 pts were included in 4 groups based on tumour size and stage. ETx pts: 35 pts undergoing endoscopic therapy treatment with EMR and/or RFA for early neoplasia (HGIN – T1smN0M0). Surveillance pts: 37 Pts with a non-dysplastic BE undergoing endoscopic surveillance. STxE pts: 21 pts undergoing surgical therapy for early BE neoplasia (HGIN – T2N0M0)STxA pts: 21 pts undergoing surgical therapy for advanced BE neoplasia (T1N1M0 – T3N1M0). QOL and FOCR were measured at baseline, 2 and 6 mo after treatment (Tx). QOL was measured by using the SF-36 which measures general QOL; the EORTC-QLQ-C30 (a cancer-specific questionnaire) and the EORTC-QLQ-OES18 (an esophageal-cancer specific questionnaire). FOCR was measured by the Worry of Cancer Scale (WOCS) and the Fear of Recurrence Scale (FORS). ETx pts had significantly better scores on the functional scales of the SF-36 and EORTC-QLQ-C30; for example physical functioning and role functioning. The differences between ETx and STx patients decreased at 6 mo after Tx. ETx pts had significantly less esophageal cancer specific symptoms such as dysphagia, eating problems and appetite loss two mo after Tx. Again, the differences between ETx and STx pts decreased over time. Fear of cancer recurrence was comparable between ETx pts and STx pts. There were no significant differences on the WOCS and the FORS. ETx and STX pts improved between 2 mo and 6 mo follow-up.
Conclusion: This is the first comparative prospective study of QOL and FOCR after endoscopic and surgical therapy for early BE neoplasia. Patients who are treated endoscopically have a better functional QOL and less esophageal cancer related symptoms than patients who are treated surgically, yet these differences diminish over time. Endoscopically treated pts worry as much about cancer recurrence as surgically treated pts.

Concomitant Coeliac Disease in adult Type 1 Diabetes patients: Glycemic control and the Risk of Micro vascular Complications

S.F. Bakker[1], C.J.J. Mulder[1], B.M. von Blomberg[2], S. Simsek[3], [1]Department of Gastro-enterology and Hepatology, VU University Medical Center Amsterdam, The Netherlands, [2]Department of Immunology, VU Medical Center, [3]Department of Internal Medicine, Medical Center Alkmaar, The Netherlands

The estimated prevalence of Coeliac Disease (CD) in patients with Type 1 Diabetes Mellitus (T1DM) is 4.5%. Screening for CD in adult patients with T1DM is still under debate as the effects of adult onset of CD in adult T1DM patients is scarcely studied. Objective of the present study is to investigate 1) the course of glycemic control before CD diagnosis and after initiation of a gluten free diet in T1DM patients 2) the micro vascular profile in T1DM patients with and without CD. Adult patients are recruited by means of a call in the magazine of the Dutch Celiac Disease society. We retrospectively collected Hba1c levels one year prior to CD diagnosis, at CD diagnosis, after 1 and 2 years of a gluten free diet and the most recent HbA1c levels. Nephropathy is defined as the presence of microalbuminuria in a portion of urine, neuropathy based on clinical assessment and retinopathy when a minimum of background changes were seen in the retina. The control group consists of patients diagnosed with T1DM and is matched on age, gender, BMI and T1DM duration. All patients were sero negative for auto antibodies against Endomysium or Tissue Transglutaminase. Twenty-three adult patients (median age 44 years IQR 37-53) were eligible with a median duration of T1DM and CD of 29 years (IQR 12-65) and 3 years (IQR 1.0-5.2), respectively. The matched control group consists of 36 patients. The HbA1c levels before and after the diagnosis of CD remained stable. Median HbA1c levels in T1DM patients with CD were: one year before CD diagnosis (7.6 %), at CD diagnosis (7.7 %), after one (7.4 %) and two years (7.6 %). However, cross sectional comparison of the study group with the control group revealed a significantly lower HbA1c in the T1DM +CD group (7.3 % ± 0.6 versus 8.5 %± 1.7 P=0.003). The presence of neuro- (8.7 % versus 27.8 % P= 0.11), nephro- (21.7 % versus 19.4 % P= 0.54) and retinopathy (34.8 % versus 61.0 % P = 0.08) was not significantly different between the two groups.
Conclusion: Glycemic control in adults with T1DM and CD after initiation of a gluten free diet is better compared to patients without CD. The current observational study suggests that screening for CD in adults with T1DM might be mandatory.

The effect of delay in the diagnosis of neuroendocrine tumors (NET)

S. van Roosmalen[1], T. Korse[2], M. Tesselaar[3], H. Boot[1], B.G. Taal[1], [1]Department of Gastroenterology, [2]Clinical Chemistry, [3]Medical Oncology; Nederlands Kanker Instituut/ Antoni van Leeuwenhoek Ziekenhuis, Amsterdam

Background: The diagnosis of neuroendocrine tumours can be difficult as they may arise in any organ and produce various peptides. The variation in the site of the primary tumor and hormone producing metastases causes a large variety of presenting symptoms and often an incorrect initial diagnosis. In the literature there is only one US study in 115 NET patients in 2004 revealing a delay of 66 months, but a correlation with stage of disease was not found. We wondered whether this is also true in Dutch patients and whether is has an effect on clinical outcome. Aim: to evaluate the effect of the delay in diagnosis on stage of disease, grade of malignancy and survival. Methods: new NET patients presenting in our hospital in 2003-2006 were included. Patients still alive received a questionnaire. For the deceased patients data were obtained from the medical record, based on information provided by the patient at referral. Results: of 160 patients alive 41 returned the questionnaire; data of all 44 deceased patients were retrieved from the medical record. Thus, 85 patients (38m and 47 f, median age 60 yr) were included in the study. Presenting symptoms were: abdominal pain (60%), weight loss (38%), flushes (27%), malaise (12%), fatigue (14%), dyspnea (11%) and diarrhea (6%). In 59% metastases were present at the time of diagnosis. In 51% the initial diagnosis was incorrect: in half no diagnosis was made and the others 21 various diagnoses were mentioned, usually irritable bowel syndrome, diverticulosis, or no diagnosis at all. Mean patient delay (first symptom-visit of general practitioner) was 5 months; for the general practitioner a mean delay of 16 months (0-425) and for the specialist it was 15 months (23-426). A statistical significant correlation was found between Chromogranin A and the doctor's delay (correlation coefficient 0,296). The longer the doctor's delay, the higher the CgA-value. No clear correlation was present with the stage of disease. The primary tumor originated in the ileoceal region in 28, pancreas in 9, appendix 2, rectum 2, stomach 2 lung 8 and remained unknown in 19 patients. Survival dropped from 150 to 55 months with a patients delay of more than 1 year; similar as in the GP delay, but unexpectedly, in the specialist delay the opposite was found: 49 vs 117 months. Conclusions: a long patient and doctor's delays are common among NET patients and appear to play a role in the prognosis; a long patient and GP delay are associated with a worse survival, in contrast to the specialist delay: a short delay has a worse prognosis. Whether this might be explained by more tumor mass will be evaluated in a follow-up study.

Centralization of pancreaticoduodenectomy in The Netherlands

R.F. de Wilde[1], M.G. Besselink[1], I. van der Tweel[2], I.H. de Hingh[3], C.H. van Eijck[4], C.H. Dejong[5], R.J. Porte[6], I.H. Borel Rinkes[1], D.J. Gouma[7], O.R. Busch[7], I.Q. Molenaar[1]; for the Dutch Pancreatic Cancer Group, [1]Department of Surgery, University Medical Center Utrecht, [2]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, [3]Department of Surgery, Catharina Hospital Eindhoven, [4]Department of Surgery, Erasmus Medical Center Rotterdam, [5]Department of Surgery, Maastricht University Medical Center, Maastricht, [6]Department of Surgery, University Medical Center Groningen, The Netherlands [7]Department of Surgery, Academic Medical Center, Amsterdam, The Netherlands

Hospitals performing higher volumes of PD have lower mortality rates. In The Netherlands, the first initiative to centralize PD was taken in 1997. Evaluation of this process in 1999 and 2005 showed no change in referral patterns or decrease in mortality. We evaluated the centralization of pancreaticoduodenectomy (PD) and mortality after PD in The Netherlands in the period 2004-2009. Nationwide data on ICD-9 code 5-526 (pancreaticoduodenectomy, including Whipple), patient age, sex and in-hospital mortality were retrieved from the Dutch independent registry KiwaPrismant. Based on established cut-off points of annually performed PDs, hospitals were categorized as very-low- (< 5), low- (5-10), medium- (11-19), or high- (≥ 20) volume. In total, 2,155 PDs were included. The number of hospitals performing PD decreased from 48/94 in 2004 to 30/94 in 2009 (P = 0.011). In these respective years, the percentage of patients undergoing PD in a medium- or high-volume center increased from 52.9% to 91.2% (P = 0.0005). Nationwide mortality after PD decreased from 9.8% in 2004 to 5.1% in 2009 (P = 0.044). The mortality during the 6-year period for hospitals categorized by annual PD volume (< 5, 5-10, 11-19 or ≥ 20) was respectively 14.7%, 9.8%, 6.3% and 3.3% (P = 0.0005). The difference in mortality between medium- and high-volume centers was statistically significant (P = 0.004).
Conclusions: Centralization of PD in The Netherlands is succeeding and nationwide mortality after PD has decreased. Further centralization of PD is required in an attempt to further decrease mortality.

The risk of non-colorectal malignancies in serrated polyposis syndrome patients and their first-degree relatives

Y. Hazewinkel[1], J.B. Reitsma[2], J.J. Koornstra[3] , F.M. Nagengast[4], M.E. van Leerdam[5] , T.A.M van Os[6], H.F. Vasen[7], E. Dekker[1], [1]Departments of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands, [2]Department of Clinical Epidemiology & Biostatistics, Academic Medical Center, Amsterdam, The Netherlands, [3]Department of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, the Netherlands, [4]Department of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, The Netherlands, [5]Department of Gastroenterology and Hepatology. Erasmus University Medical Centre, Rotterdam, The Netherlands, [6]Department of Clinical Genetics, Academic Medical Center, Amsterdam, The Netherlands, [7]Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands

Introduction: Serrated polyposis syndrome (SPS) is characterized by the presence of multiple hyperplastic polyps (HPs) and sessile serrated adenomas (SSAs) spread throughout the colon and is associated with an increased colorectal cancer (CRC) risk. Although the underlying genetic causes of SPS are unknown, first degree relatives (FDRs) of SPS patients have an increased risk for both SPS and CRC suggesting an inheritable component. In other polyposis syndromes an increased risk for extracolonic tumors has been described, therefore the aim of this study was to assess the risk of malignancies other than CRC in both SPS patients and their FDRs. Methods: The medical history of all SPS patients in 5 medical centres was retrospectively collected. Regarding the incidence of non-colorectal malignancies in FDRs, self-reported family history was derived from SPS patients by examining data from the department of Clinical Genetics. The incidence rates of non-colorectal malignancies in both SPS patients and their FDRs were compared with the general population through a person-year analysis, adjusted for age and sex. Population-based incidence data were derived from the Eindhoven Cancer Registry during the period 1989-2008. Results: In this study, 105 SPS patients (57% male) and 341 FDRs from 53 pedigrees (50% male) were included, resulting in 6.423 and 18.935 person years of follow up, respectively. During this follow up, 9 SPS patients (9%) developed a non-colorectal malignancy, which was not higher that the expected number of 13 (RR 0.69 95%-CI 0.36-1.33; p=0.27). In 44 FDRS (13%) a non-colorectal malignancy was detected, compared to 48 expected malignancies (RR 0.92 95%-CI 0.69-1.24; p=0.60).
Conclusion: Our results show that the overall incidence of non-colorectal malignancies is not increased in SPS patients and their FDRs in comparison with the general population.

Feasibility, safety and efficacy of a prospective annual colonoscopic surveillance program in serrated polyposis syndrome patients

Y. Hazewinkel[1], K.M.A.J.Tytgat[1], S. van Eeden[2], P. Fockens[1], E. Dekker[1], [1]Department of Gastroenterology and Hepatology, [2]Department of Pathology, Academic Medical Center, Amsterdam, the Netherlands

Introduction: Serrated polyposis syndrome (SPS) is characterized by the presence of multiple hyperplastic polyps (HPs) and sessile serrated adenomas (SSAs) throughout the colon and is associated with an increased colorectal cancer (CRC) risk. No uniform treatment protocol exists regarding polyp-removal and surveillance intervals. This is the first prospective study assessing the feasibility, safety and efficacy of a systemised endoscopic surveillance protocol in SPS patients. Methods: SPS patients satisfying the WHO-criteria underwent an initial colonoscopy with the intention to remove all polyps, except polyps <3 mm with a non-adenomateus appearance. If this was not achieved during one procedure, an additional colonoscopy was planned within 6 months. After clearance, all patients received annual surveillance colonoscopies. Results: In this ongoing study, 41 SPS patients underwent an initial colonoscopy. After the initial colonoscopy 12 patients were referred to colonic surgery. Reasons were CRC (6), an extremely high polyp burden (5) and a stenosed sigmoid (1). The remaining 29 patients were treated endoscopically. At initial endoscopy, 267 polyps were removed: 32 conventional adenomas (ADs), 51 SSAs and 184 HPs. A total of 5 advanced adenomas were detected in 5 patients (17%). In one patient a mild complication (post polypectomy syndrome) occurred. During subsequent surveillance, with a mean follow-up period of 1.9 years (SD ± 0.5) and a mean interval of 1.1 year (SD ± 0.1) between colonoscopies, no CRCs occurred. A total of 240 polyps were removed: 32 ADs, 48 SSAs, 158 HPs and 2 mixed polyps. In 2 patients (7%), one advanced adenoma was detected. The median number of polyps decreased significantly from 8 at initial colonoscopy to 3 during the second surveillance colonoscopy (p= 0.002). One patient was converted to surgery due to a high polyp burden. No complications occurred during surveillance. At multivariate logistic regression, an increasing number of SSAs and/or ADs at initial colonoscopy was significantly associated with detection of ≥ 5 SSAs and/or ADs during surveillance (OR 1.69 per SSA or AD, 95% CI 1.09-2.62).
Conclusion: If colonic clearing is achievable, annual surveillance colonoscopy with removal of polyps ≥3 mm is a feasible, safe and efficient treatment protocol in SPS patients. Considering the number of removed polyps during surveillance, strict colonoscopic surveillance seems justified, especially in patients with SSAs and ADs at initial colonoscopy, as they seem at risk to develop multiple SSAs or ADs during surveillance.

Impact of late anorectal complaints on quality of life after prostate radiotherapy

R. Krol[1], W.P.M. Hopman[1], R.J. Smeenk[2], E.N.J. Th. Van Lin[2] ,Departments of [1]Gastro-enterology and Hepatology and [2]Radiation Oncology, Radboud University Nijmegen Medical Centre.

Late anorectal toxicity comprises different symptoms and is a frequent adverse event of prostate radiotherapy. To optimize treatment modalities it is important to know which symptoms have the largest impact on health related quality of life (QoL). Especially urgency and fecal incontinence are expected to have a profound impact. Our goal was to determine the relative impact of anorectal symptoms on QoL in patients irradiated for prostate cancer.Eighty-five men (mean age 72 yrs; range 53-84 yrs) completed a validated questionnaire at least one year after radiotherapy (mean time 28 months; range 10-82 months) for localized prostate cancer. QoL was measured by the Fecal Incontinence Quality of Life scale (FIQL) and the Expanded Prostate Cancer Index Composite Bowel domain (EPICB). Frequency of the following complaints was rated: bowel movements, rectal urgency, uncontrolled leakage of stool, loose or liquid stool, bloody stool, painful defecation and lower abdominal cramps.Sixty-two men (73%) reported one or more complaints. Loose stool was mostly reported (48%). Painful bowel movements and fecal incontinence were the least reported complaints (14% and 18%). Mean spearman rank correlation coefficient of FIQL domains and EPICB bother scores with individual symptoms ranged 0.23-0.53 for FIQL domains and 0.36-0.73 for EPICB bother scores. The correlation coefficients indicated a strong relationship of fecal incontinence and urgency and a moderate relationship of rectal blood loss and frequent defecation with Qol outcomes. Multiple regression analysis revealed that fecal incontinence and urgency were independent predictors and had the largest impact on most QoL outcomes. Standardized regression coefficients (β) were 0.39 and 0.38 for urgency with the lifestyle and coping domain ($p<0.001$) and β's for incontinence ranged between 0.29 and 0.52 ($p<0.001$ for all FIQL domains). Frequent defecation was also an independent predictor for lifestyle and coping, but had lower β's (0.18; $p<0.05$) and abdominal cramps for the depression self perception domain ($\beta = 0.42$; $p < 0.001$). All symptoms of anorectal toxicity were independently associated with the EPICB bother score except painful defecation.Conclusions: Fecal incontinence and rectal urgency have the largest impact on QoL in anorectal radiation toxicity. Other symptoms such as frequent defecation and lower abdominal cramps also contribute, but less profoundly. This underscores the importance of preserving adequate continence mechanism in radiotherapy planning.

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Biliary involvement in untreated autoimmune hepatitis is an underestimated feature

M.F. Lozano[1], A.S.H. Gouw[1], A.P. van den Berg[2], E.B. Haagsma[2], R.C.Verdonk[2], From the Department of Pathology and Laboratory Medicine[1] and the Department of Gastro-enterology and Hepatology[2] of the University Medical Center Groningen, University of Gro-ningen, Groningen, the Netherlands

Background/aim: In all applicable diagnostic criteria of autoimmune hepatitis (AIH), biliary changes are not considered as features of AIH. However, the prevalence of biliary features in untreated AIH is not precisely documented. The present study aims to investigate the prevalence and relevance of biochemical and histological biliary changes (BC) in untreated AIH patients who were selected according to the simplified criteria (SC). Methods: We analyzed the biochemical, serological and histological data in 36 cases of newly diagnosed AIH. Biochemical biliary features were defined according to Paris criteria as alka phosphatase (APH) > 2 x upper limit of normal (ULN) or gammaglutamyl transferase (GGT) of > 5 x ULN. In all 36 patients pretreatment liver biopsies were available and in 13 cases a follow-up biopsy was present. Histological assessment was performed according to the SC and the Metavir-system to grade fibrosis. An additional scoring was conducted for BC. Histological BC was defined as PBC-like, PSC-like or mixed. A PBC-like pattern included a dense periductal inflame-mation and bile duct epithelial damage. Bile duct epithelial atrophy and/or concentric fibrosis were designated as PSC-like. When both types were present the biliary changes were scored as mixed. Presence or absence of ductular reaction (DR) was also scored. Results: The vast majority of patients (31/36, 86%) fulfilled the criteria of definite AIH based on a score of > 7 of the SC. A score of 6, equivalent to probable AIH was present in 5 patients (14%). In none of the cases the diagnosis was revised during treatment. A biochemical biliary pattern as defined for this study was observed in 10 cases (29%). In 30/36 pretreatment biopsies (83%) histological BC were present, consisting of 20 PBC-like (56%), 5 PSC-like (14 %) and 5 mixed features (14%). DR was present in 26 (72%) cases. Fibrosis was absent in 5% of the cases whereas grade F1 was found in 28%, F2 in 39% F3 in 14% and F4 in 14 % of the cases. There was no correlation between the biochemical and the histological BC. Furthermore there was no relation between BC and age, severity of inflammation or presence of fibrosis. In the 13 follow-up biopsies (all contained BC in the initial biopsies) BC subsided in 7 patients (58%) but a DR was still present in 10 patients (77%).
Conclusion: Histological biliary changes are common (86%) in untreated AIH. A biochemical cholestatic signature was less prominent (29%). This finding and the fact that the histological biliary damage subsided after AIH treatment suggests that these histologic features are part of the spectrum of AIH and not necessarily part of an overlap-syndrome.

Higher physical activity level is associated with decreased prevalence and severity of non-alcoholic fatty liver disease in elderly

E..M. Koehler[1], J.N.L..Schouten[1], B.E.. Hansen[1,2], F.J.A. van Rooij[3], A. Hofman[3], B.H. Stricker[3], H.L.A. Janssen[1], [1]Dept.. of Gastroenterology and Hepatology, [2]Dept.. of Public Health, [3]Dept. of Epidemiology, Erasmus MC, Rotterdam, The Netherlands

Background and aim: Although there is a theoretical basis supporting physical activity (PA) as a lifestyle change in subjects with non alcoholic fatty liver disease (NAFLD), epidemiological evidence of an independent association of PA and NAFLD is limited. The aim of this study was to determine the association of PA and intensity of PA with NAFLD in a large elderly population. Methods: Abdominal ultrasound was performed in all participants (72-96 years) of the first cohort of the Rotterdam Study. Diagnosis and grading of fatty liver was determined according to the protocol by Hamaguchi et al. Severity of fatty liver was classified as 'no fatty liver'(0-1), 'mild fatty liver'(2-3), or 'moderate to severe fatty liver'(4-6). PA was assessed by a validated questionnaire, containing questions about walking, housekeeping activities, diverse sports and hobbies. Durations of all activities were converted to hours/week (h/wk) and multiplied by activity expenditure costs (expressed in the ratio of work metabolic rate to resting metabolic rate: MET). Vigorous activities include all activities with a MET-value ≥4 (e.g. cycling, swimming, gardening, fitness), moderate activities include all activities with a MET-value between 2 and 4 (e.g. walking, light housekeeping activities, bowling, volleyball). Participants with secondary causes of NAFLD were excluded from the analyses. Results: Data on PA and ultrasound features were available for 1415 participants. A total of 188 participants were excluded (incomplete PA-questionnaire: 54; pharmacological agents: 47; positive anti-HCV: 10, positive HBsAg: 1; past or current excessive alcohol consumption: 81). Of 1227 included subjects, 36.6% had NAFLD (65.9% female; mean age 78.8 ± 4.1). Total time spent on PA in men was 14.2 h/wk versus 17.1 h/wk in women ($p<0.001$). Higher total PA level (MET-h/wk) was significantly associated with lower prevalence and severity of NAFLD ($p=0.009$ and $p=0.008$ respectively) in logistic and ordinal regression analysis after adjustment for age, BMI, and gender. MET-h/wk spent on vigorous activities were also inversely correlated with NAFLD ($p=0.03$), whereas a trend for significance was demonstrated for MET-h/wk spent on moderate activities ($p=0.08$). Predicted probability of NAFLD decreased 14% for every 3 MET-h/day (equal to 30 minutes of cycling) spent on vigorous PA.

Conclusion: Total physical activity level was independently associated with a decreased prevalence of NAFLD in elderly subjects. Moreover, total expenditure on activities with vigorous intensity showed stronger association with lower probability of NAFLD than activities with moderate intensity.

Hepatocellular carcinoma in the Netherlands: changes in incidence, treatment, and survival during the last two decades

C.D.M. Witjes[1] , H.E. Karim-Kos[2] , O. Visser[3] , S.A.W. van den Akker[2] , E. de Vries[2] , J.N.M. IJzermans[1], R..A. de Man[4], J.W.W. Coebergh[2,5], C. Verhoef[6], Department of Hepatobiliary and Transplantation Surgery[1], Public Health[2], Hepato-Gastroenterology[4] , Surgical Oncology[6], Erasmus MC, University Medical Centre Rotterdam, Department of Registration and Research, Amsterdam[3], Eindhoven Cancer Registry, Eindhoven[5], Comprehensive Cancer Centre Netherlands, The Netherlands

Aim: To examine recent trends in incidence and outcome among patients with hepato-cellular carcinoma (HCC) in an unselected population in the Western world. Methods: Data from the nationwide Netherlands Cancer Registry were used to estimate trends in incidence for all 6,040 patients diagnosed with primary liver cancer between 1989 and 2008. Trends in incidence, treatment and relative survival according to gender, age and stage of disease were studied in 3,451 patients with HCC. Rates were age-standardised to the European Standard population (European Standardised Rates (ESR)). Results: Age-standardised incidence rates for primary liver cancer increased overall significantly, although the ESR for HCC barely changed between 1989 and 2008. Only among males aged 75 and over was an increasing trend in HCC incidence observed. Surgery for HCC increased from 14% in 1989 to 28% in 2008 and chemotherapy and/or irradiation increased from 5% to 14% in the same period. Fewer patients received non-cancer-related HCC therapy, i.e. best supportive care, which decreased from 82% in 1989 to 67% in 2008. One-year HCC relative survival rate increased significantly from 21% in 1989-1992 to 37% in 2003-2008 ($p= 0.03$). Corresponding increase in 5-year relative survival was 6% to 14% ($p< 0.001$). Five-year relative survival of HCC patients who underwent surgery also increased significantly from 35% to 53% ($p=0.01$).
Conclusions: Unexpectedly the incidence of HCC remained stable. The number of HCC patients receiving curative or palliative treatment increased, the overall relative survival for HCC patients increased. The relative survival of patients treated with curative intent improved.

Ribavirin concentrations at week 8 predict treatment response in naive genotype 1 or 4 HCV patients

L.G. van Vlerken[1], C.T.M.M. de Kanter[2,3], G.J. Boland[1,4], A.M. van Loon[4], H. van Soest[1], P.D. Siersema[1], G. Koek[5], J.P.H. Drenth[6], K.J. van Erpecum[1], DM Burger[2,3], [1]Department of Gastroenterology and Hepatology, University Medical Center Utrecht, [2]Department of Pharmacy, Radboud University Nijmegen Medical Center, [3]Nijmegen Institute for Infection, Inflammation and Immunology (N4i), Radboud University Nijmegen Medical Center, [4]Department of Virology, University Medical Center Utrecht, [5]Department of Gastroenterology and Hepatology, Maastricht University Medical Center, [6]Department of Gastro-enterology and Hepatology, Radboud University Nijmegen Medical Center.

There is increasing evidence that higher steady-state ribavirin (RBV) concentrations are associated with response to peg-interferon (PEG-IFN) and RBV treatment in chronic hepatitis C (CHC) patients. However, the optimal timing of RBV concentration measurement remains unknown and data on PEG-IFN concentrations are lacking. Therefore, we aimed to assess the association between serum RBV or PEG-IFN concentrations at various time points and viral response to PEG-IFN / RBV therapy in treatment-naive CHC patients. We analyzed data of 61 genotype 1 or 4 patients who were treated with PEG-IFNα-2b (1.5 µg/kg/week after high-dose induction with interferon-α-2b for 12 days) and RBV (1000 or 1200 mg/day depending on weight) for up to 52 weeks. RBV and PEG-IFN concentrations were determined in serum samples obtained after approximately 1, 2, 4, 8 and 12 weeks of treatment. The majority of patients (79%) had base viral load >800.000 IU/mL and 27% exhibited severe fibrosis or cirrhosis at liver biopsy. RBV levels increased steadily during the first weeks of treatment until steady-state was reached after 8 weeks. Median (IQR) RBV concentrations were 1.4 mg/L (1.0-1.8), 1.9 mg/L (1.4-2.4), 2.4 mg/L (1.7-3.0), 3.1 mg/L (2.2-3.8) and 3.0 mg/L (2.3-4.1) at week 1, 2, 4, 8 and 12 respectively. In contrast, median PEG-IFN levels did not differ after 4, 8 and 12 weeks of treatment with 1712 pg/mL (602-2295), 1053 pg/mL (522-2038) and 1159 pg/mL (628-2036) respectively. RVR, EVR, week 24 response and SVR were achieved in 41%, 75%, 71% and 58% of patients (per-protocol analysis). Week 8 serum RBV concentrations were significantly higher in patients who reached EVR (3.3 vs. 2.1 mg/L, p=0.003), week 24 response (3.2 vs. 2.6 mg/L, p=0.04) and SVR (3.4 vs. 2.6 mg/L, p=0.049) compared to those who did not. Week 12 serum RBV concentrations were significantly higher in EVR vs. non-EVR patients only (3.0 vs. 2.2 mg/L, p=0.03). No association between earlier RBV concentrations and viral response was found. After adjustment for base viral load and RVR achievement, week 8 serum RBV levels predicted EVR (adjusted OR 3.8, 95%CI 1.3-11.3) and SVR (adjusted OR 2.3, 95%CI 1.1-4.9). The optimal cut-off for the prediction of both EVR and SVR was 2.2 mg/L (sensitivity 87-90%, specificity 39-42%, PPV 64-87%, NPV 64-71%). In contrast to RBV concentrations, no association between PEG-IFN concentrations and treatment response was found, even after accounting for time between serum sampling and last PEG-IFN injection.
Conclusions: RBV concentrations are associated with treatment response in treatment-naive CHC patients. Week 8 RBV concentration is an independent predictor of EVR and SVR.

Treatment of persistent hepatocellular secretory failure with rifampicin

R. van Dijk[1], B. van den Elzen[1], T. van Gulik[2] , D. Gouma[2], J. S. Lameris[3], V. Enemuo[4], P.L.M. Jansen[1], U.H.W Beuers[1], Departments of [1]Gastroenterology & Hepatology, [2]Surgery, and [3]Radiology, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands Department of [4]Pediatric Gastroenterology, Louisiana State University Health Sciences Centre, New Orleans, USA

Background and aims: Hepatocellular secretory failure with deep jaundice and severe pruritus may persist weeks to months after the offending drugs, toxins, or biliary obstruction have been removed. This type of cholestasis is best called persistent hepatocellular secretory failure (PHSF). Vanishing bile duct syndrome or functional failure of the canalicular bile acid or bilirubin transporting ABC transporters (BSEP, MRP2) to resume their activity, may be causes of PHSF. Currently there is no established treatment of PHSF. When serum bilirubin levels exceed 170-255 µmol/L (10-15 mg/dL), the anti-cholestatic agent ursodeoxycholic acid is ineffective. The pregnane X receptor (PXR; NR1I2) plays a key role in regulating the expression of biotransformation enzymes and canalicular ABC transporters. Here, we report the effect of the PXR agonist rifampicin on PHSF in patients with serum bilirubin >255 mmol/L. Patients and Methods: Seven patients (age 18-81 years, 4 female, 3 male) with PHSF over 30 +/- 15 days induced by benign (3) or malignant (1) biliary obstruction, drugs (2) or toxins (1) were included in this study. Other causes of liver disease had been ruled out by standard biochemical tests, imaging, histology and/or endoscopic techniques. Patients were treated with the PXR agonist rifampicin 300 mg daily for one week to six months. Results: Serum bilirubin levels ranged from 264 µmol/L to 577 µmol/L before start of rifampicin treatment. Within weeks after starting therapy serum bilirubin levels declined in all patients to levels below 33 µmol/L. All patients reported relief of pruritus. Conclusions: Therapeutic activation of PXR by short-term treatment with rifampicin should be considered as a therapeutic option in critically ill patients with PHSF after elimination of biliary obstruction and other cholestasis-inducing factors. Controlled studies are needed to further validate our observations.

A simplified NAFLD-score to distinguish simple steatosis from steatohepatitis

B.J. Veldt[1], A. van Leeuwen[2], J.T. Brouwer[1], Reinier de Graaf Hospital Delft, the Netherlands, Departments of [1]Gastroenterology & Hepatology and Internal Medicine and [2]Pathology

Introduction: Obesity is a major health problem and obese people are at risk of developing non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH). Clinical models such as the NAFLD-fibrosis score and BARD-score have been developed to distinguish patients with advanced fibrosis due to NASH from patients with less advanced disease. However, patients with lower degrees of fibrosis may still be at risk of ongoing inflammation and disease progression. Aim: To investigate whether existing NASH-scores can be used or adjusted to distinguish between simple steatosis and steatohepatitis. Methods: All outpatients with elevated liver enzymes and a diagnosis of NAFLD or NASH between 2006 and 2007 were included. Liver biopsies were scored according to the revised Brunt classification by a single pathologist, who was blinded for the clinical data. Approval was obtained from the ethics committee and the study was performed according to the declaration of Helsinki. Results: 105 patients were diagnosed with probable NAFLD based on history, physical examination and laboratory testing and 60 of these patients (57%) underwent liver biopsy:24 patients had simple steatosis without inflammation, ballooning or fibrosis, 25 patients had inflammation without fibrosis and 11 patients had fibrosis stage 1 or 2. The NAFLD fibrosis score and the BARD score were not statistically significantly different between patients with simple steatosis compared to patients with inflammation and to patients with fibrosis (Kruskall Wallis p=0.85 and p=0.06 respectively).In logistic regression analysis body mass index (BMI) and aspartate aminotransferase (AST) were independently associated with inflammation and/or fibrosis. A prediction model for NASH was built using the following formula, derived from the regression analysis:-2.296 + (0.007*AST) + (0.053*BMI). In the area under the receiver operating curve, a cutoff of -0.45 was selected to identify the presence of NASH. Using this cuttoff, the sensitivity for detection of NASH was 77% and the specificity was 74% (AUC 0.80; 95% CI 0.69-0.92, p<0.001). The presence of NASH could be established with a positive predictive value of 81% and the absence of NASH with a negative predictive value of 69%.

Conclusion: BMI and transaminases, which are also included in the NAFLD fibrosis score and the BARD score, were good predictors of the presence of inflammation. Therefore, after validation in other populations, a simplified scoring system using only base AST and BMI might be useful to distinguish patients with simple steatosis from those with NASH. This may help to decide which patients are eligible for closer follow-up.

Mycophenolate mofetil: role in autoimmune hepatitis and overlap syndromes

A.M.C. Baven-Pronk[1], M.J. Coenraad[1], H.R. van Buuren[2], R.A. de Man[2], K.J. van Erpecum[3], M.M.H. Lamers[4], J.P.H. Drenth[4], A.P. van den Berg[5], U.H. Beuers[6] , J. den Ouden[7], G.H. Koek[8], C.M.J. van Nieuwkerk[9], G. Bouma[9], J.T. Brouwer[10], B. van Hoek[1] for the Dutch Autoimmune Hepatitis Group , Depts. of Gastroenterology and Hepatology of Leiden University Medical Center, Leiden, [1]Erasmus Medical Center, Rotterdam, [2]University Medical Center Utrecht, Utrecht, [3]Radboud University Medical Center, Nijmegen, [4]University Medical Center Groningen, Groningen, [5]Academic Medical Center, Amsterdam, [6]Haga Hospital, The Hague, [7]Maastricht University Medical Center, Maastricht ,[8]Free University Medical Center, Amsterdam, [9]Reinier de Graaf Gasthuis, Delft, [10]The Netherlands

Treatment failure occurs in 20% of autoimmune hepatitis patients on prednisolone and azathioprine (AZA). There is no established second treatment. The aim of the present study was to assess the efficacy of mycophenolate mofetil as second treatment after AZA-intolerance or AZA-nonresponse in autoimmune hepatitis and overlap syndromes.Consecutive patients from the Dutch Autoimmune Hepatitis Group cohort, consisting of 661 patients, with autoimmune hepatitis or overlap syndromes, AZA-intolerance or AZA-nonresponse and past or present use of mycophenolate mofetil were included. Primary endpoint of mycophenolate mofetil treatment was biochemical remission. Secondary endpoints were biochemical response (without remission), treatment failure and prevention of disease progression. Forty-five patients treated with mycophenolate mofetil were included. In autoimmune hepatitis remission or response was achieved in 13% and 27% in the AZA-nonresponse group compared to 67% and 0% in the AZA-intolerance group (P = 0.008). In overlap-syndromes remission or response was reached in 57% and 14% in the AZA-nonresponse group and 63% and 25% of the AZA-intolerance group (N.S.); 33% had side-effects and 13% discontinued mycophenolate mofetil. Overall 38% had treatment failure; this was 60% in the autoimmune hepatitis AZA-nonresponse group. Decompensated liver cirrhosis, liver transplantations and death were only seen in the autoimmune hepatitis AZA- nonresponse group (P < 0.001).
Conclusion: Mycophenolate mofetil induced response or remission in a majority of patients with autoimmune hepatitis and azathioprine-intolerance and with overlap syndromes, irrespective of intolerance or nonresponse for azathioprine. In autoimmune hepatitis with azathioprine nonresponse, mycophenolate mofetil is less often effective.

Sequential liver chemistry profiling and abdominal ultrasound assessments predict biliary strictures after liver transplantation

K. Sebib Korkmaz[1], W.R. ten Hove[1], J. Dubbeld[2], R. Wolterbeek[3], A. van Erkel[4], B.J.F. de Rooij[1], M.J. Coenraad[1], J. Ringers[2], H.W. Verspaget[1], B. van Hoek[1], Departments of Gastroenterology and Hepatology[1], Transplantation Surgery[2], Medical Statistics[3] and Inter-ventional Radiology[4], Leiden University Medical Center, Leiden,The Netherlands

Early detection of biliary strictures (BS) after orthotopic liver transplantation (OLT) is important in order to prevent morbidity and mortality. Transplantation centers differ in how they routinely assess liver biochemistry and abdominal ultrasound (US) for early detection of rejection, recurrence of primary disease (e.g., PSC or hepatitis) and bile duct pathology, such as stricture formation. Previous studies indicated that early signs of stricture formation may be seen on US and by assessing liver biochemistry. Our aim was to evaluate the predictive value of routine serum liver chemistry profile and US in a time-dependent regression model as non-invasive diagnostic tools to screen for the development of BS during the first year after OLT. We performed a retrospective study on 141 OLTs performed between 1992 and 2007 with complete data sets and at least 1 year follow-up. During this period we routinely assessed serum levels of alka phosphatase (ALP), alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), gamma glutamyl transpeptidase (gGT) and bilirubin at 3, 6, 9 and 12 months, as well as US at 3, 6 and 12 months after OLT. Strictures requiring endoscopic, percutaneous or surgical intervention were counted as BS. Time-dependent Cox regression analysis was performed to identify predictive factors for the development of BS.Eighteen grafts developed non-anastomotic strictures (12.8%) and 18 grafts (12.8%) developed anastomotic strictures requiring intervention. Time-dependent regression analysis showed a significant relationship between the increase in routinely assessed serum level of gGT and the development of BS, both in the univariate and in the multivariate analysis (hazard ratios 1.35 and 1.25 per 100 IU/L increase, $p < 0.001$ and $p = 0.04$, respectively). Furthermore, a significant relationship existed between detection of dilated bile ducts on US and the successive development of BS, in both the univariate (hazard ratio = 4.48, $p < 0.001$) and multivariate analysis (hazard ratio = 3.54, $p < 0.01$). Elevation of bilirubin or the other studied liver enzymes were not independently predictive for the development of BS. Our time-dependent regression analysis showed that detection of dilated bile ducts on US or elevated gGT are independent predictive factors for the development of BS requiring intervention in the first year after OLT. Routine assessment by serum gGT and US at 3-month intervals during the first year post-OLT is useful to screen for BS post-OLT. Elevated gGT or dilated bile ducts on US in the first year post-OLT should prompt cholangiography and may allow timely intervention before complications like cholangitis develop.

The Long-Term Outcome of the Kasai Operation in Patients with Biliary Atresia: A systematic review

E.J. Bijl, K.D. Bharwani, R.A. de Man, Department of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands

Biliary Atresia (BA) is a progressive inflammatory destructive process of the bile ducts occurring in about 1 of every 20.000 live births. If left untreated, biliary atresia can lead to liver failure. The only effective treatments for BA at the moment are the Kasai operation and liver transplantation. Kasai portoenterostomy increases the survival for children with BA and postpones sub-sequential liver transplantation. Because long-term survival is rare, there is not much known about the long-term efficacy of the Kasai operation. The aim of this review was to study the outcome of patients with BA who survived more than 20 years on their native liver. We performed a systematic search on PUBMED using MeSH-Terms for articles describing the long-term outcomes of patients with Biliary Atresia. We searched for patients who lived as least 20 years with their native liver and we registered the number of complications. The end-points identified in these articles were: death, cholangitis, portal hypertension and gastro-intestinal bleeding. From 48 articles we included 13 articles for analysis. In total 156 patients were above the age of 20 years. Of these 156 patients, 86% (134/156) were still alive with their native liver. 64% (85/134) were suffering from liver-related complications. All of them already had experienced episodes of cholangitis. 76% (65/85) of the patients with cholangitis developed portal hypertension and of this group of patients 51% (33/65) experienced gastro-intestinal bleeding. In one patient a hepatocellular carcinoma developed.
Conclusions: It is possible for patients with Biliary Atresia to survive for more than 20 years on their native liver after being operated with Kasai during early infancy. However of the long-term survivors alive with their own liver 64% end up suffering from progressive liver related complications. Until the age of 18 these patients are generally managed by the paediatrician or paediatric surgeon after the age of 18 most of these patients are managed by the gastroenterologist. Especially for this gastroenterologist it is important to realise that in long-term survivors after Kasai operation developing recurrent cholangitis and portal hypertension liver transplantation should be considered early to avoid death to liver related mortality.

Recurrence and fistula formation after incision and drainage of primary perianal abscesses

M. Meerdink[1], A. Prent[2], A. Kusters[3], A.B. Francken[1], A.D. van Dalsen[1], [1]Isala Klinieken Zwolle, [2]DeventerZiekenhuis, [3]Diaconessenhuis Leiden

The clinical course after simple incision and drainage of acute primary perianal abscess (PAA) is variable. Recurrence and development of perianal fistula (PAF) are not well documented. Patients who presented with a PAA were prospectively included, treated according a standardized study protocol and received 12 months follow-up. Recurrences and PAF were registered. Predicting factors for recurrence and PAF development were identified in a multivariate logistic regression analysis. Hundred-and-forty-three patients were included of whom 135 (96.4%) patients (102 men, 33 women) received complete follow-up. Twenty-four patients (17.8%) required surgical reintervention for a recurrence of whom 10 patients developed a PAF subsequently. Another 16 patients developed a PAF, without prior reintervention. Duration of complaints prior to seeking medical attention of more than 5 days was an independent predicting factor for PAF formation (RR 3.35 [1.31-8.59] p=0.012) as well as failing wound closure over 6 weeks (RR 52.06 [13.23-204.9], p<0.001). PAF rate after primary PAA drainage was 19.3% (n=26). Patient delay before - and delayed wound closure after drainage were found to be predictive factors for PAF formation. Patients with recurrence or delayed wound closure seem to be at risk for PAF formation and underlying cause such as Crohn's disease. Typically these patients would need close observation, whereas all other patient might be discharged from medical care soon after primary treatment. Our standardised treatment protocol might have contributed to the relatively low count of PAF formation.

Ligation of the intersphincteric fistula tract as an adjunct to transanal advancement flap repair: useful or not?

R.S. van Onkelen[1,2], M.P. Gosselink[1], E. Mitalas[1,] W.R. Schouten[1], [1]Department of Surgery, Erasmus MC, University Medical Center, Rotterdam, The Netherlands, [2]Department of Immunology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

Transanal advancement flap repair (TAFR) is successful in two of every three patients with a high transsphincteric fistula. It has been suggested that ongoing disease in the remaining fistula tract contributes to failure. Ligation of the intersphincteric fistula tract (LIFT-procedure) might be a useful tool to eradicate this ongoing disease. Aim of the present study was to evaluate the outcome of the LIFT-procedure as an adjunct to flap repair. A consecutive series of 41 patients (male/female: 32/9, median age: 42 (range 20-69) years) with a high transsphincteric fistula of cryptoglandular origin, underwent a LIFT-procedure in addition to their flap repair. Median duration of follow-up was 15 months. Wound infection at the intersphincteric groove was observed in 29% of the cases. Primary healing was observed in only 21 patients (51%). In the 20 patients without primary healing, persistence of the original transsphincteric fistula was observed in 12 subjects. In eight patients the transsphincteric fistula was found to be transformed into a simple low intersphincteric fistula. All eight fistulas were treated successfully by subsequent fistulectomy, resulting in an overall healing rate of 71%.
Conclusion: The LIFT-procedure is prone to infection and does not enhance the outcome of TAFR.

Colonoscopy after conservatively treated diverticulitis only indicated in patients with symptoms associated with an increased risk for colon cancer

P.J.C. Schout[1], E.J. Spillenaar Bilgen[1], M.J.M. Groenen[2], Rijnstate ziekenhuis Arnhem, afdeling Heelkunde[1] , afdeling Maag-, Darm- en Leverziekten[2]

Diverticulitis is an increasingly common disorder of the large bowel in western countries, and conservative treatment has gained a more prominent place over the last decades. Symptoms and labarotory findings of patients presenting with (perforated) colon cancer may be deceivingly similar to those in patients with diverticulitis, resulting into a delay in the diagnosis of colon cancer. This effect is enhanced by the common etiology and epidemiologic characteristics between both diseases. With routine colonoscopy or radiologic imaging after a conservatively treated episode of diverticulitis these malignancies could be found. In our hospital, the routine conduction of either colonoscopy or, as a second choice, radiologic imaging (barium enema colon X-ray or CT-colography) has been standard practice over the last decade. We retrospectively collected all colonoscopy and radiologic imaging results that were conducted of all 516 patients who were diagnosed as having diverticulitis and treated conservatively in this period.Of those 516 patients, 378 had undergone colonoscopy, 45 radiologic imaging and 93 did not undergo any additional investigation. 8 cases of malignant neoplasia were found in those patients (2.1%), and an additional number of 40 adenomatous polyps (9.5%). Almost all (6 out of 8) patients with a malignant tumour reported one or more of the following symptoms: rectal blood loss, significant weight loss or persisting abdominal pain after being treated for diverticulitis.
Conclusions: By routinely performing either colonoscopy or radiologic imaging in patients who are treated conservatively for apparent diverticulitis, a malignant tumour is found in the colon in 2.1% of those patients. Almost all of those patients reported rectal blood loss, significant weight loss and/or persisting abdominal pain after being treated for diverticulitis. The use of colonoscopy or radiologic imaging after a conservatively treated episode of diverticulitis for detecting colon cancer therefore could be limited to this specific group. In this study, a malignant tumour would have been missed in only 2 out of 423 patients (= 0.5%).

How to distinguish between a rectum and sigmoid carcinoma in advance to treatment: a prospective study comparing endoscopy and MRI measurements

L. van Nunspeet[1], H.W. Wiersma[2], M. Ledeboer[3], R.A.J.M. van Dijk[2], K. Koster[2], R.J.I. Bosker[1], E.H. Eddes[1], M. Eeftinck Schattenkerk[1], [1]Department of Surgery, Deventer Hospital, [2]Department of Radiology, Deventer Hospital, [3]Department of Gastroenterology, Deventer Hospital

The indication for preoperative radiation therapy for rectum carcinoma makes the distinction with sigmoid carcinoma of great importance. This distinction is anatomically made by the peritoneal fold. Endoscopically however, this fold is not always visible and an arbitrary 15cm of the linea dentata is used to distinguish between the rectum and sigmoid. Also, when the carcinoma is situated under the radiographic between promontorium and symphysis (PS-line), it is considered to be a rectum carcinoma. This prospective study determines the value of the PS- and the use of different MRI measurements to distinguish between rectum and sigmoid. Patients in whom a distal colon malignancy was identified up tot 30cm of the linea dentata were included in this study. The distinction between rectum and sigmoid was endoscopically made at 15cm of the linea dentata. Patients underwent a regular MRI. Apart from this they also underwent a regular work-up and treatment as determined in the multidisciplinary meeting. The MRI images were blinded and judged by two experienced radiologists. They scored whether the peritoneal fold was visible and judged the position of the carcinoma with respect to the PS-line. Peroperative identification of the carcinoma in relation to the peritoneal fold was considered the golden standard. Between September 2009 and July 2010 23 patients were included. The gastroenterologists identified 17 rectum carcinoma and 4 sigmoid carcinoma. Two carcinoma were seen lying at the transition of rectum and sigmoid. MRI images showed that all carcinoma were positioned under the PS-line. The peritoneal fold was visible in 10 patients. The mean distance of the peritoneal fold to the linea dentata was 13,5cm. The radiologists judged 11 carcinoma lying in the rectum and 9 in the sigmoid. In 3 cases no firm distinction could be given. During surgery the carcinoma appeared to be positioned in the rectum in 13 patients. In 10 patients a sigmoid carcinoma was found.
Conclusion: The PS- is not a reliable measurement for the distinction between rectum and sigmoid carcinoma. The distance between the peritoneal fold and the linea dentata measured on MRI images seems to correspond with the endoscopic 15cm criterion. This seems a reliable measurement. Further investigation with is desirable.

Transanal single port surgery is feasible and safe

R.M. Barendse[1], P.G. Doornebosch[2], W.A. Bemelman[3], P. Fockens[1], E. Dekker[1], E.J.R. de Graaf[2], [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [2]Dept. of Surgery, Academic Medical Center, Amsterdam, [3]Dept. of Surgery, IJsselland Hospital, Capelle aan den IJssel

Transanal Endoscopic Microsurgery (TEM) is the current standard surgical method for the resection of various rectal lesions. It is a complex technique requiring expensive instrumentation. Single access surgery is easy, relatively cheap and is already broadly applied in laparoendoscopy. Studies evaluating transanal use of single access ports are scarcely available. We aimed to evaluate transanal single port surgery for the resection of rectal lesions using the Single Site Laparoscopic Access System (SSL). Consecutive patients with a rectal lesion otherwise eligible for TEM were operated using the SSL and standard laparoscopic instrumentation. Patient and lesion characteristics, procedure and hospitalisation length as well as per- and postoperative complications were recorded. Fifteen patients were planned for single port transanal surgery. In 2 patients (13.3%), intrarectal expansion of the retractor seemed not possible, and conversion to conventional TEM was necessary. The remaining 13 patients were successfully operated. Rectal lesions (mean maximum diameter 36 mm, standard deviation ± 25 mm, mean distance from the dentate 6cm (± 4.5)) included 7 adenomas, one T1 adeno-carcinoma, three T2 adenocarcinomas and one carcinoid. In one case, only fibrosis (after prior polypectomy) was detected at histopathology. Although only 4 lesions were situated on the dorsal rectal wall, all patients were operated in lithotomy position. A stable pneumorectum without port dislocation was achieved in all patients. Resections were en bloc, full thickness and had complete margins. Resection specimens measured 65 (± 35) x 52 (± 24) mm. All but one rectal defects were sutured. One peroperative pneumoscrotum occurred. Mean operating time was 57 (± 39) minutes. One patient presented with postoperative hemorrhage, treated conservatively (postoperative morbidity rate 7.7%). Two patients underwent synchronous total mesorectal excision and left hemicolectomy for more proximal carcinomas, respectively. Mean hospitalisation lasted 2.5 days (± 2.7) overall and 1.5 days (± 0.8) for patients undergoing transanal single port surgery only.
Conclusions: Transanal single port surgery via the SSL is feasible and safe for the resection of rectal lesions. Minor technical adjustments of the retractor may be necessary for optimal transanal insertion. Perioperative features were comparable with published data on TEM. This technique may be associated with lower costs. If its safety and effectiveness prove comparable, transanal single port surgery via the SSL may become a promising alternative to TEM.

Better fecundity preservation after laparoscopic restorative proctocolectomy: a cross-sectional study

S.A.L. Bartels[1], A. D'Hoore[2], M.A. Cuesta[3], A.J. Bensdorp[4], C. Lucas[5], W.A. Bemelman[1], [1]De-partment of Surgery, Academic Medical Center, Amsterdam, the Netherlands, [2]Department of Abdominal Surgery, University Hospital Leuven, Leuven, Belgium, [3]Department of Surgery, VU University Medical Center, Amsterdam, the Netherlands, [4]Department of Obstetrics and Gynaecology, Academic Medical Center, Amsterdam, the Netherlands, [5]Department of Clinical Epidemiology, Biostatics and Bioinformatics, Academic Medical Center, Amsterdam, the Netherlands

Restorative proctocolectomy with ileal pouch anal anastomosis (IPAA) is associated with tubal factor infertility in female patients. Although studies have shown that there is less adhesion formation after laparoscopic colectomy, it is unknown what the clinical consequences of this observation are. The aim of this study is to determine if pregnancy rate after laparoscopic IPAA was higher than after open IPAA. This cross-sectional study was carried out in three university hospitals in the Netherlands and Belgium. All female patients currently over 18 years that underwent IPAA under age 41 and between 1993 and 2009 were eligible. A questionnaire addressing patients medical and fertility history was sent. The primary endpoint was time to first natural pregnancy after IPAA. Of all eligible patients 160 (89%) returned the questionnaire. Following IPAA, 50 (31%) patients attempted to conceive. Of these, 23 (46%) underwent open and 27 (54%) underwent laparoscopic IPAA. Patient characteristics were similar in both groups. Indication for surgery was ulcerative colitis (UC) in 37 patients, familial adenomatous polyposis (FAP) in 12 patients, and colonic ischemia in one patient. A Kaplan-Meier survival function was plotted for time to first natural pregnancy and showed a higher pregnancy rate after laparoscopic IPAA (log-rank p=0.023). Subsequent survival analysis for UC patients showed a similar outcome; a higher pregnancy rate for the laparoscopic group (log-rank p=0.033). There was no difference in time to first pregnancy in 12 FAP patients.
Conclusion: patients having had laparoscopic IPAA had significant higher pregnancy rates than after open IPAA. The approach in IPAA must therefore be laparoscopically in women with a desire for children.

Increased risk of anastomotic leakage with Non-Steroidal Anti-Inflammatory Drugs in colorectal surgery

K. Gorissen[1], M. Sosef[1], D. Benning[2], K. Hulsewe[2], M. Luyer[3], [1]Atrium Medisch Centrum Heerlen, [2]Orbis Medisch Centrum Sittard, [3]Catharina Ziekenhuis Eindhoven

Anastomotic leakage is one of the most severe complications in colorectal surgery leading to a profound increase in mortality, morbidity and cancer recurrence. Several factors increase the risk for anastomotic leakage such as steroid use, malnutrition, malignancy and peri-operative adverse events. Recently it has been suggested that Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) may be added. NSAIDs are increasingly being used in fast-track surgery programs for pain control thereby reducing use of opioids and enhancing recovery. The aim of our study was to examine the role of NSAID-use in the occurrence of anastomotic leakage. All patients that underwent colorectal surgery with primairy anastomosis between 2008 and 2010 were prospectively registered in a database. Of 778 patients demographic and perioperative data were recorded including the use of selective and non-selective NSAIDs. According to NSAID use four groups could be identified: group 1; no NSAIDs (n=445), group 2 ; non-selective NSAIDs (n=205), group 3; selective COX2-inhibitors (n=84), group 4; combined or consecutive use of both selective and non-selective NSAIDs (n=44). All four groups were homogenous regarding most patient and peri-operative characteristics. In univariate analysis five risk factors for anastomotic leakage could be identified i.e.: operative time, blood loss, diverting stoma, post-operative systolic blood pressure and the use of NSAIDs. In multivariate analysis NSAIDs were significantly associated with an increased anastomosal leakage rate of 16.1% compared to 9.2% in patients who used no NSAIDs (p=0.022). Use of selective COX2-inhibitors alone seemed to be of no influence (9.5%, p 0.717) while the incidence of anastomotic leakage in patients who received both selective and non-selective NSAIDs was strongly increased (18.2%, p 0.151).
Conclusion: Our data show a significant increase in anastomotic leakage (OR 2.16) in patients using NSAIDs, even after correction for other known risk factors in multivariate analysis. In order to decrease anastomotic leakage after colorectal surgery, NSAIDs should be avoided in the postoperative phase.

Quality of life of older rectal cancer patients is not impaired by a permanent stoma

R.G. Orsini[1], M.S.Y. Thong[2, 3], L.V. van de Poll-Franse[2,3], G.D. Slooter[4], I.H.J.T. de Hingh[1], H.J.T. Rutten[1], [1]Department of Surgery, Catharina Hospital Eindhoven, Eindhoven, The Netherlands, [2]CoRPS - Center of Research on Psychology in Somatic Diseases, Department of Medical Psychology, Tilburg University, The Netherlands [3]Comprehensive Cancer Centre South (CCCS), Eindhoven Cancer Registry, Eindhoven, The Netherlands [4]Department of Surgery, Máxima Medical Centre Veldhoven, Veldhoven, The Netherlands

The association between age at treatment and health-related quality of life (HRQL) of older rectal cancer patients is poorly understood. The aim of this study was to investigate whether HRQL of older rectal cancer (≥70 years) patients treated for a tumor in the lower two-third of the rectum differs from younger patients (<70 years). Furthermore the influence of a permanent stoma was taken into account.Patients with rectal cancer from 4 hospitals diagnosed in 1998-2007 were identified from the Eindhoven Cancer Registry. All patients were treated with either abdominoperineal or low anterior resections. Survivors completed the Short-Form-36 (SF-36) health survey and the EORTC Quality of Life Questionnaire-Colorectal 38 (QLQ-CR38). HRQL scores were compared after dividing the patients in four groups, stratified by stoma status and age at time of operation (<70 and ≥70). The SF-36 and the QLQ-CR38 sexuality subscale scores of the survivors were compared with a normal age- and sex-matched Dutch population. In this study 143 patients were included. Median follow-up was 3.4 years. Older patients had significantly worse physical function (p=0.0003) compared to younger patients on the SF-36 subscales. On the QLQ-CR38 domains, older patients (p=0.005) and patients without a stoma (p=0.009) had slighty worse sexual functioning compared to younger patients and patients with a stoma, respectively. There was a significant age effect (p=0.01) for male sexual dysfunction, where older males had more sexual dysfunction compared to younger males. Older patients with a stoma had worse physical function (p<0.01), but slightly better mental health (p<0.05) compared to the Dutch normative population. Older patients without a stoma had better emotional role function (p<0.01) compared to the normative population. However younger patients had worse sexual functioning and enjoyment compared to the normative population (both p<0.0001).
Conclusions: This study shows that older patients with a stoma have comparable HRQL to older patients without a stoma or the normative population. Our findings indicate that a permanent stoma for elderly patients with a low situated rectal carcinoma could be feasible. Patients who are sexually active after treatment could benefit from receiving psychosocial and clinical support in the management of potential sexual dysfunction following treatment.

Four years after implementation of a Enhanced Recovery After Surgery (ERAS) in a Dutch Hospital

H. Cakir[1], M.F.M. van Stijn[1], A.M.F. Lopes Cardozo[1], B.L.A.M. Langenhorst[1], W.H. Schreurs, P. Fockens[2], W.A. Bemelman[3], M.J.M. Serlie[4], A.P.J. Houdijk[1], [1]Department of Surgery, Medical Centre Alkmaar, The Netherlands, [2]Department of Gastroenterology, Academic Medical Centre Amsterdam, The Netherlands, [3]Department of Surgery, Academic Medical Centre Amsterdam, The Netherlands, [4]Department of Endocrinology and Meta-bolism, Academic Medical Centre Amsterdam, The Netherlands

Enhanced recovery after surgery (ERAS) or fast track programs are developed to improve the perioperative condition of the patient resulting in a reduction in length of hospital stay (LOS) after colorectal surgery. Several randomized controlled trials have shown that the ERAS program leads to a reduction in LOS and complication rates in patients undergoing major colorectal surgery. Here we report on the results of the first four years after introducing the ERAS-program in patients undergoing colonic resections in our department. In 2006 the ERAS program was introduced in the Medical Center Alkmaar. For this study, all consecutive patients who were above 18 years and were scheduled for elective colonic resection for malignancy were entered into the ERAS program. Prospectively data were entered into the ERAS database from January 2006 till December 2009 and retrospectively analyzed. Data from the year 2005 were used as a control. The LOS in 2006 and 2007 was significantly shorter compared to 2005 (resp. $p \leq 0.04$ and $p \leq 0.03$). For the years 2008 and 2009, this reduction in LOS was no longer achieved (resp. $p \leq 0.11$ and $p \leq 0.55$). We studied whether this relapse in longer LOS in 2008 and 2009 could be attributed to changes in base characteristics and/or not achieving ERAS goals. The following items were found to be significantly associated with the disappearance of the reduction in LOS in 2008 and 2009 compared to 2006 and 2007. Fewer patients received the preoperative carbohydrate-loaded drink and anti-emetics and were mobilized within 24 hours after surgery, less administration of laxative at the first postoperative day and lower numbers of thoracic epidural catheters that were removed within 3 days. 2009 had a significant higher number of patients with cardiac co-morbidity.During the first 2 years of the ERAS- introduction, no difference in LOS was found between laparoscopic surgery and open surgery (2006: 0.629 and 2007: 0.092). However, for the years that showed less compliance to the protocol a significant difference in LOS was found in favor of laparoscopic surgery (2008: <0.001 and 2009: 0.004).

Conclusion: In the first two years of the ERAS program a significant reduction in LOS was achieved with no difference in LOS between laparoscopic and open resections. After two years the increase in LOS could be attributed to violations of 5 items the ERAS program with a return of significantly lower LOS in the laparoscopic operated group. These results further support the success of the ERAS program and that adherence to the protocol is vital to achieve this.

The serotonin precursor 5-hydrotryptophan induces rectal hyperalgesia in patients with irritable bowel syndrome

D. Keszthelyi[1,2], F. Troost[1,2], D. Jonkers[1,2], J. Dekker[1], A. Masclee[1,2] ,[1]Top Institute Food and Nutrition, Wageningen, The Netherlands, [2] Division of Gastroenterology-Hepatology, Depart-ment of Internal Medicine, Maastricht University Medical Centre+, Maastricht, The Netherlands

Introduction: Hypersensitivity to mechanical distension of the gut (rectum) is considered a hallmark of irritable bowel syndrome (IBS). Alterations in serotonergic metabolism have been associated with the pathogenesis of IBS. Serotonin (5-HT) has an important role in the regulation of human gastrointestinal function, especially for intestinal sensing and signaling. The direct precursor of 5-HT, 5-hydroxytryptophan (5-HTP), is a potential substance to influence intestinal serotonin availability and may therefore influence intes-tinal sensory responses. Aim: To assess the effect of oral supplementation of a bolus of 100 mg 5-HTP in comparison to placebo on visceroperception to mechanical distension in IBS patients. Methods: 15 patients with IBS (5 male; age 52±4 yrs; BMI 28±01 kg/m^2) participated in this randomized double-blind placebo controlled study. Visceroperception was measured by rectal barostat using a semi-random staircase distension procedure (17 pressure steps in the range of 0-50 mmHg above minimal distention pressure) on two separate occasions, one hour after oral intake of a bolus of 100 mg 5-HTP or placebo, with an interval between experiments of at least one 1 week. The intensity of pain perception was measured using a visual analogue scale (VAS, 0-100 mm). Results: During distension, the intensity of pain perception in the middle (17-32 mmHg) and high pressure range (35-50 mmHg) was significantly higher after 5-HTP vs placebo (VAS scores 20.7±3 vs 12.8±2 mm, $p<0.001$; and 35.0±4 vs 28.9±3, $p<0.001$, respectively). Pressure thresholds (defined as the distension pressure where VAS scores>10 mm) for pain perception were not altered following 5-HTP vs placebo (19±5 vs 21±5 mmHg; $p=0.1$).

Conclusion: Oral administration of a bolus of 100 mg 5-HTP increases intensity of visceroperception and induces rectal hyperalgesia. These observations in viscerosensory responses emphasize the role of serotonin and the involvement of the gut-brain axis in the mediation of visceroperception.

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Binnen de gastroenterologie uit zich dit in geneesmiddelen die, zeker bij de behandeling van chronische aandoeningen, niet alleen effectief zijn maar vooral ook bijdragen aan het verbeteren van de kwaliteit van leven, zodat de patiënt zo normaal mogelijk kan leven.

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Supragastric belches are associated with severe belching complaints in patients with gastro-oesophageal reflux disease

B.F. Kessing, A.J. Bredenoord, M. Velosa, A.J.P.M. Smout, Department of Gastro-enterology and Hepatology, Academic Medical Center Amsterdam, Amsterdam, The Netherlands

Background: Patients with gastro-oesophageal disease (GORD) frequently report severe and excessive belching but it is not known what determines the severity of these complaints. Intraluminal impedance monitoring can differentiate between gastric and supragastric belches. We aimed to determine which type of belches is associated with an increased symptom severity. Methods: We prospectively included 50 patients who were referred to our center for an ambulatory 24-h pH-impedance measurement as part of the work-up for reflux symptoms. Overall severity of belching was reported by the patients using a three-point scale. Furthermore, patients reported each perceived belch during the ambulatory measurement. Results: The frequency of belches identified by impedance monitoring was significantly higher in patients with severe complaints (n=25) compared to patients with moderate complaints (n=13) and compared to those with none to mild complaints (n=12) (60±5 vs 39±8 vs 33±4, both $p<0.05$). No significant difference in median frequency of gastric belches (35 (19-39) vs 12 (7-39) vs 27 (20-39)) or gastric belches with a liquid reflux component (15 (10-23) vs 6 (2-18) vs 15 (7-23)) was found. However, the median number of supragastric belches was significantly higher in patients with severe belching complaints (25 (4-47)) compared to patients with none to mild complaints (2 (1-6), $p<0.05$) but not significantly different from patients with moderate complaints (4 (1-25)). Moreover, the median number of supragastric belches which coincided with a reflux episode was significantly higher in patients with severe complaints than in those with moderate and none to mild complaints (14 (3-20) vs 1 (0-8) vs 1 (0-2), $p<0.05$). Per-patient analysis showed that supragastric belches were more often perceived as a belch than gastric belches (37±5 vs 28±4 %, $p<0.05$). Supragastric belches coinciding with a liquid reflux event were significantly more often perceived than isolated supragastric belches (38±7 vs 23±4 %, $p<0.05$). Likewise, gastric belches containing a liquid component were perceived more often than gastric belches containing only gas (32±4 vs 22±4 %, $p<0.05$).
Conclusion: These data suggest that the belching pattern determines the burden of belching complaints in GORD patients. Supragastric belches are associated with more severe belching complaints and are perceived more often than gastric belches.

PPI therapy is as effective in well-defined NERD patients as in patients with reflux oesophagitis; a meta-analysis

P.W. Weijenborg[1], F. Cremonini[2], A.J.P.M. Smout[1], A.J. Bredenoord[1], [1]Dept. of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands, [2]Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

Introduction: Proton pump inhibitor (PPI) therapy is the most effective treatment for symptom relief in gastroesophageal reflux disease. It has been suggested that patients with non-erosive reflux disease (NERD) respond less to PPI than patients with erosive reflux disease (ERD), however inconsistencies in NERD definition across clinical trials may cause an underestimation of the effect of PPI in patients with NERD. Aims of this meta-analysis were: 1) to estimate the response to PPI in true NERD patients compared to ERD, 2) to estimate whether response to PPI would vary according to different diagnostic criteria for NERD. Methods: Meta-analysis of randomized controlled clinical trials that included patients with heartburn, treated with PPI for at least 4 weeks. Patients classified as NERD in the clinical trials were subdivided into three groups: 1) empirically treated patients, 2) patients that were defined as NERD after negative endoscopic assessment, or 3) patients defined as NERD after both a negative endoscopy and a positive pH-test. The first two groups also include patients with functional heartburn according to the Rome III criteria and only the latter group can be regarded as true NERD. Medline, Embase and Cochrane databases were searched. Studies that reported complete or partial relief of heartburn after 4 and/or 8 weeks of PPI therapy were combined using random-effects models. Results: 59 clinical trials enrolling 26641 patients were included. The pooled estimate of complete relief of heartburn after 4 weeks of PPI therapy in patients with ERD was 0.72 (95%CI 0.69-0.74)(32 studies), versus 0.50 (0.43-0.57)(8 studies) in empirically treated patients, 0.49 (0.44-0.55)(12 studies) in patients defined as NERD by a negative endoscopy, and 0.73 (0.69-0.77)(2 studies) in patients defined as NERD by both a negative endoscopy and a positive pH-test. The pooled estimate of partial relief of heartburn after 4 weeks of PPI was 0.75 (0.71-0.78)(6 studies) in patients with ERD, versus 0.71 (0.59-0.81)(8 studies) in empirically treated patients, 0.65 (0.61-0.69)(10 studies) in NERD defined by endoscopy, and 0.85 (0.55-0.96)(1 study) in pH-test positive NERD.
Conclusion: In well-defined NERD patients, characterized by a negative endoscopy and a positive pH-test, the PPI failure rate is only between 15 and 27%, depending on the definition used, which is similar to patients with ERD. The lack of response (i.e. higher rate of PPI failure) in studies with NERD patients defined by endoscopy alone and by empirically treated patients is likely the result of contamination of the study population with patients with functional heartburn.

Association of antidepressant use and gastrointestinal symptoms in the general adult population explained by channelling bias

B. Schurink[1], M.M. Tielemans[1,2], B.R.R.Z. Aaldering[1], T. Eikendal[3], J. Jaspers Focks[4], R.J.F. Laheij[2], J.B.M.J. Jansen[5], L.G.M. van Rossum[6] , M.G.H. van Oijen[2], [1]Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, [2]Gastroenterology and Hepatology, University Medical Centre Utrecht, Utrecht, [3]Emergency Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, [4]Cardiology, Radboud University Nijmegen Medical Centre, Nijmegen, [5]Gastroenterology and Hepatology, Elkerliek hospital, Helmond, [6]Epidemiology, Biostatistics and Health Technology Assessment, Radboud University Nijmegen Medical Centre, Nijmegen

Antidepressants are among the most commonly used medications in the general population, and gastrointestinal symptoms are reported frequently as an adverse event. On the other hand, antidepressants have been associated with positive effects on gastrointestinal motility, gastric relaxation and nociception in patients with functional gastrointestinal disorders. We aimed to assess the association between antidepressant use and gastrointestinal symptoms in the general population. A total of 51,869 questionnaires, with questions regarding gastrointestinal symptoms, medication use and co-morbidity were sent to a representative sample of the general adult population. Prevalence of gastrointestinal symptoms was compared between persons that did or did not report antidepressant use. Multivariable regression analysis was used to assess the association between antidepressant use and gastrointestinal symptoms. In total 18,307 questionnaires (35%) were returned, of which a random sample of 6,795 were used in these preliminary analyses. Of all participants, 257 (4%) used antidepressants: 61% selective serotonin reuptake inhibitors (SSRIs), 18% tricyclic antidepressants (TCAs), 13% serotonin norepinephrine reuptake inhibitors (SNRI), and 9% other antidepressants (tetracylic antidepressants, other serotonin inhibitors and non-specified). Prevalence of gastrointestinal symptoms was 42% in antidepressant users compared to 27% in non-users (unadjusted OR 1.99, 95%CI 1.54–2.56; p<0.01). Most frequently reported symptoms in antidepressant users with gastrointestinal complaints were: nausea (49%), epigastric pain during daytime (54%), constipation (42%) and vomiting (19%). However the association between antidepressant use and gastrointestinal symptoms was not statistically significant after adjusting for demographics, co-morbidity (e.g. self-reported depression) and other drugs (adjusted OR 0.83, 95%CI 0.59–1.18).
Conclusion: antidepressant use is associated with a significantly higher prevalence of gastrointestinal symptoms compared to non-users. After adjustment for various confounders, including the presence of depression, this association was no longer statistically significant indicating channeling bias.

Use of VSL#3® , a Probiotic Combination, Is Associated With a Lower Frequency and Severity of Abdominal Pain and Improved Quality of Life in Irritable Bowel Syndrome (IBS): Data from the VIP ("VSL#3® In PDS") Study, a Multi-Centre, Prospective, Observational Study

W.A. de Boer[1], M.H. Otten[2] , W.K.H. Man A Hing[3], [1]Dept of Gastroenterology, Bernhoven Hospital, Oss, the Netherlands, [2]Dept of Gastroenterology, Meander Medical Centre, Amersfoort, the Netherlands, [3]Ferring BV, Hoofddorp, the Netherlands

Introduction: The microbiota of IBS patients differs in composition from healthy controls. Therefore interest in the effect of probiotics in IBS is advocated and warranted. VSL#3® is a probiotic combination containing 8 different strains of bacteria. The aim of this study was to assess the course of IBS symptoms and to evaluate quality of life after intake of VSL#3® for 5 weeks. Methods: This was a multi-centre, prospective, open-label observational study. Patients fulfilling the ROME III diagnostic criteria for IBS and for whom VSL#3® was prescribed as standard of care for the relief of their IBS symptoms were recruited. The daily dose was 1 sachet of VSL#3® containing 450 billion bacteria. Questionnaires to assess the frequencies and severities of IBS symptoms as well as the quality of life (IBS-QOL questionnaire) were completed at Visit 1 and Visit 2 (end of study). Results: A total of 97 patients were recruited (mean age 41.3 years; 67.0% female). Changes were observed in stool frequency, the frequency and severity of abdominal pain, severity of bloating, and quality of life. In women with >3 bowel movements per day the frequency decreased significantly (p=0.004). Fewer patients had abdominal pain 5 to 7 days per week at end of study (34.9% vs. 72.4%). Moreover, a higher number of patients experienced abdominal pain only one day per week or none at end of study (38.4% vs. 8.0%). The VAS-scores for the severity of abdominal pain during the week prior to study end decreased (p<0.001) with a higher mean decrease in men (-30%) than in women (-19%). The VAS-scores for the severity of abdominal distension and/or bloating during the week prior to study end decreased (p<0.001) almost equally in men and women (-23% vs. -21%). The overall IBS-QOL scores (p<0.001) and all quality of life subscales scores were significantly better at end of study.
Conclusions: The use of VSL#3® in IBS patients was associated with significant changes in the stool frequency in women, abdominal distension and/or abdominal pain, and bloating. Furthermore, the quality of life improved significantly. Given the design of the current study these results should be interpreted with caution. However, the reported results are encouraging and VSL#3® appears to be a promising new treatment for IBS patients.

A randomised, placebo controlled, double blind study to assess the efficacy of a probiotic dairy product containing Lactobacillus casei Shirota on symptoms in Irritable Bowel Syndrome

A.Y. Thijssen[1], D.M.A.E. Jonkers[1], V. Vankerckhoven[2], H. Goossens[2], B. Winkens[3], C.H.M. Clemens[4], A.A.M. Masclee[1], [1]Department of Internal Medicine, Division of Gastroenterology and Hepatology, Maastricht University Medical Center, [2]Vaccine & Infectious Disease Institute (Vaxinfectio), University of Antwerp, [3]Department of Medical Statistics, Maastricht University Medical Center, [4]Department of Internal Medicine, Diaconessen Hospital Leiden[1-4] The Netherlands

Introduction: Alterations in the gut microbiota (composition) have been described in IBS patients and are proposed as one of various pathophysiological mechanism in IBS, which can potentially be influenced by probiotic treatment. Several studies with probiotics in IBS have pointed to beneficial results with improvement of IBS symptoms. Aim of the present study was to assess in a randomised placebo controlled double blind trial the effect of a probiotic product containing Lactobacillus casei Shirota on symptoms in patients with IBS. Materials and methods: IBS patients between 18 and 65 years of age, fulfilling the Rome II criteria, were included. Probiotic and placebo product were provided by Yakult Europe, Almere, NL. Patients had to take 2 bottles daily for 8 weeks, containing at least 6.5 x 10^9 CFU living Lactobacillus casei Shirota (LcS) per bottle. All subjects completed a daily symptom diary (ranging from no to very severe symptoms) during 3 periods of 2 weeks: before intervention (week -2/0), at the end of intervention (week 6/8) and during follow-up (week 14/16). Mean symptom scores (MSS) were based on discomfort, pain, constipation, diarrhoea and bloating. Results: 39 patients (26F; 41 ± 15 yrs) in the probiotic group and 41 patients (29F; 42 ± 14 yrs) in the placebo group were included. The compliance was > 95% in both groups (LcS in stool, bottles used) . Demographic data did not differ between groups. An improvement in symptoms of ³30% was predefined as clinically relevant. After follow-up, an improvement ³ 30% was reached for all symptoms, apart from bloating, in the probiotic group, but for none of the symptoms in the placebo group. The improvement was significantly higher in the probiotic group compared to the placebo group for discomfort (34 ± 7%; 12 ± 9%), flatulence (33 ± 7%; 7 ± 10%) and total symptom score (33 ± 7%; 10 ± 9%) (all $p \leq 0.05$), and showed a non significant improvement for pain (33 ± 12%; -17 ± 25%, $p = 0.10$) and MSS (34 ± 7%; 13 ± 8%, $p = 0.06$). Logistic regression showed a possible interaction with gender for the treatment given. In males (13 probiotics / 12 placebo), probiotic treatment resulted in a significantly higher improvement in each symptom score compared to placebo treatment (all $p < 0.05$). In females (26 probiotics / 29 placebo) treatment did not influence any symptoms (all $p > 0.10$).
Conclusion: Intervention with Lactobacillus casei Shirota resulted in a significantly higher percentage of patients with improvement of symptoms in the probiotic compared to the placebo group. This significant benefit was observed in males but not in females.

Long-term effectiveness and tolerability of allopurinol and thiopurine combination therapy in inflammatory bowel disease patients

M.L. Seinen[1], F. Hoentjen[2], N.K.H. de Boer[1], D.T. Rubin[2], G. Bouma[1], L. Harrell[2], C.J.J. Mulder[1], A.A. van Bodegraven[1], S.B. Hanauer[2], [1]VU University Medical Center, Amsterdam, The Netherlands, [2]Inflammatory Bowel Disease Center, University of Chicago, Chicago, United States

Thiopurines are the mainstay of conventional maintenance therapies after steroid-induction for the treatment of IBD. Unfortunately, up to 60 percent of patients are intolerant or discontinue therapy. Small studies have shown a clinically relevant change of thiopurine metabolism by combining allopurinol with low dose thiopurine for patients with preferential metabolism towards 6-methylmercaptopurine (6-MMP) although duration of follow-up was limited. The aim of this study was to assess maintenance effectiveness and tolerability of allopurinol-thiopurine therapy in a larger multi-center cohort of IBD patients. Adult IBD patients failing monotherapy with thiopurines and subsequently treated with combination therapy of allopurinol and low dose thiopurine were selected from two tertiary referral IBD centers. Therapeutic effectiveness was assessed by calculating the cumulative number of patients still using combination therapy at 6, 12, 24 and 60 months whilst being in clinical remission, based on standard criteria. Eighty-five patients (55 % female) were included with a mean duration of follow-up of 20 months. Enrolled patients had Crohn's disease (n=54), ulcerative colitis (n=28), and miscellaneous (n=3). Patients started combination therapy due to prior thiopurine refractoriness (54%), hepatotoxicity (47%), non-hepatic adverse reactions (8%), or others (5%). The mean 6-TGN concentration increased from 161 (SD 89) at base to 309 (SD 137) pmol/8x10^8 RBC ($p<0.001$). In contrast mean 6-MMP concentrations decreased from 12.721 (SD 11173) to 803 (SD 1545) pmol/8x10^8 RBC ($p<0.001$). Leucopenia occurred in 11 patients. Before combination treatment existing liver-test abnormalities normalized in 78%. Seventeen (20%) patients had to discontinue combination therapy, usually within 2 months (median 2; IQR 0.5-16 months), due to adverse reactions (n=6), lack of efficacy (n=7) or others (n=3). The percentage of patients still using combination therapy at 6, 12, 24 and 60 months was 88%, 84%, 76% and 73%, respectively. Combination therapy with allopurinol and low-dose thiopurines is an effective and well-tolerated treatment. This therapy is an alternative long-term maintenance strategy for IBD patients failing conventional thiopurine therapy with a preferential 6-MP metabolism to 6-MMP.

Immune function of patients on olive oil-based home parenteral nutrition without an immune modulating underlying disease

E.D. Olthof[1], H.M. Roelofs[1], M. Versleijen[1], R.H. te Morsche[1], E.R. Simonetti[2], P.W.M. Hermans[2], G.J. Wanten[1], [1]Department of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [2]Laboratory of Pediatric Infec-tious Diseases, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

It remains unclear whether the increased risk for infectious complications seen in patients on Home Parenteral Nutrition (HPN), apart from the presence of a venous access device, also results from impaired host defenses. Especially lipids in HPN formulations can influence immune functions by incorporation of their fatty acids into the phospholipids of leukocyte cell membranes, thus altering the responses of these cells. This study therefore compared immune functions of HPN without an immune modulating underlying disease on olive-oil based PN and controls. Venous blood samples from 20 patients (Clinoleic®, ≥6 months; >3 times/ week), and 21 age and sex matched healthy controls were analyzed. Neutrophil function was assessed by evaluating the capacity of neutrophils to kill Streptococcus pneumoniae, and by measuring leukocyte expression of markers for adhesion (CD11b), -activation (CD62L) and -degranulation (CD66b) as well as stimulus induced oxygen radical production by neutrophils. Non-parametric statistical analysis was performed using the Mann-Whitney U test. Neutrophils from HPN patients displayed a similar capacity to kill Streptococcus pneumoniae compared to controls (mean ± SEM: 49 ± 5% and 45 ± 5% killing respectively, p=0.513). Also, levels of CD66b (p=0.725) in granulocytes and of CD11b and CD62L in granulocytes (p=0.106 and p=0.121 respectively) and monocytes (p=0.958 and p=0.211 respectively) were not different in patients and controls. Spontaneous, phorbol ester- and zymosan- induced oxygen radical production was also not different in whole blood (p=0.068, p=0.835 and p=0.167 respectively) or isolated neutrophils (p=0.696, p=0.784 and p=0.835 respec-tively) of patients and controls.
Conclusion: We found no evidence for the presence of compromised immune functions in patients with long-term intestinal failure without an immune modulating underlying disease on olive-oil based home parenteral nutrition to explain the increased susceptibility to infections seen in these patients.

Total liver volume measurement by CT corrected for body surface area is an objective parameter of the extent of polycystic liver disease

F. Temmerman[1], R. Vanslembrouck[2], W. Coudyzer[2], B. Bammens[3], W. Laleman[1], C. Verslype[1], D. Cassiman[1], W. van Steenbergen[1], J. van Pelt[1], J. Pirenne[4], F. Nevens[1], [1]Depart-ment of Hepatology, University Hospitals Leuven, Belgium, [2]Department of Radiology, University Hospitals Leuven, Belgium, [3]Department of Nephrology, University Hospitals Leuven, Belgium, [4]Department of Abdominal Transplant Surgery, University Hospitals Leuven, Belgium

Background: The most common complication of polycystic liver disease (PCLD) is extensive hepatomegaly, which may lead to invalidating abdominal symptoms and malnutrition. Liver transplantation (LT) is the only curative option in those patients. Currently, a decreased mid-upper arm circumference (MUAC) in the non-dominant arm, - a parameter of severe malnutrition-, can be used to give those patients priority on the LT waiting list (Eurotransplant). However, this measurement is subjective. Moreover, this parameter has never been validated in this condition. Aim: To investigate a more objective parameter to assess the extent of the disease. Materials and methods: 84 patients with PCLD (Gigot type II and III) were screened; 47 were selected because of volume-related symptoms. The extent of the hepatomegaly (actual liver volume : ALV) was calculated by CT-scan volumetry software, validated in our previous placebo-controlled trial with lanreotide (interobserver variability by Pearson correlation: $r = 0.994$, $p < 0.01$). The estimated standard liver volume (ESLV) was obtained based on the body surface area (BSA) of the patient and Urata's equation, in order to calculate ALV/ESLV. Results: There were 42 women (89%) and 5 men (11%) with a mean age of 52 ± 9 years: 37 (79%) suffered from ADPKD and 10 (21%) ADPLD. The mean ESLV was 1254 ± 127 ml; the mean ALV 5542 ± 2390ml; and the mean ALV/ESLV 4.4 ± 1.8. Between the ADPKD and ADPLD group, there was no significant difference in ALV and ALV/ESLV (t-test, P value resp.: 0.6 and 0.9). These data were compared with MUAC (mean 25.2 ± 3.0 cm). Pearson's correlation showed that an increased ALV was correlated with a decreased MUAC (Correlation Coefficient: -0.351; $P < 0.05$). The correlation coefficient increased when ALV/ESLV was used (- 0.473). Finally, the study group was divided in patients who were considered for LT (n = 20) and those who did not (n = 27). This decision was based on clinical judgement. Patients in group LT had a significant lower MUAC vs group no LT (resp. 24.1 ± 2.7cm and 25.9 ± 3.1cm; p = 0,04). No significant difference was observed in ALV between the two groups (Mann-Whitney Rank Sum test resp.: 5438ml and 4891ml; p=0.07). However, ALV/ESLV was higher in the group LT vs group no LT (Mann-Whitney Rank Sum test resp.: 4.8 and 4.2; P= 0.025). ALV/ESLV offered additional prognostic information to MUAC for the need of LT (difference in AUC: 0.130; p = 0.01).

Conclusion: The size of hepatomegaly in PCLD can accurately and in an objective way be measured by CT volumetry and reflects the severity of the liver disease. It is correlated with the mid-upper arm circumference and offers additional information on the extent of the liver disease.

Can MRI replace CT in patients with suspected acute appendicitis? A multicenter diagnostic accuracy study

M.M.N. Leeuwenburgh[1,2], B.M. Wiarda[3], A.P.J. Houdijk[4], B.C. Vrouenraets[5], S. Jensch[6], M.J. Wiezer[7], H.W. van Es[8] , W.H. Bouma[9], J.W.C. Gratama[10], H.B.A.C. Stockmann[11], A. Spilt[12], L.P.J. Cobben[13], P.M.M. Bossuyt[14], J. Stoker[2], M.A. Boermeester[1] on behalf of the OPTIMAP study group, [1]Department of Surgery, Academic Medical Centre, University of Amsterdam, [2]Department of Radiology, Academic Medical Centre, University of Amsterdam, [3]Department of Radiology, Alkmaar Medical Centre, Alkmaar, [4]Department of Surgery, Alkmaar Medical Centre, Alkmaar, [5]Department of Surgery, Sint Lucas Andreas Hospital, Amsterdam, [6]Department of Radiology, Sint Lucas Andreas Hospital, Amsterdam, [7]Department of Surgery, Sint Antonius Hospital, Nieuwegein, [8]Department of Radiology, Sint Antonius Hospital, Nieuwegein, [9]Department of Surgery, Gelre Hospitals, Apeldoorn, [10]Department of Radiology, Gelre Hospitals, Apeldoorn, [11]Department of Surgery, Kennemer Gasthuis, [12]Department of Radiology, Kennemer Gasthuis, [13]Department of Radiology, Medisch Centrum Haaglanden, Leidschendam, [14]Department of Clinical Epidemiology, Academic Medical Centre, University of Amsterdam, the Netherlands

In patients with suspected appendicitis, imaging is needed to substantiate the clinical diagnosis. The accuracy of US is suboptimal and the use of ionizing radiation in CT has the risk of inducing malignancy. MRI is an alternative imaging option. The aim of this study was to compare imaging strategies in adult patients with suspected appendicitis. Data were collected in a multicenter study in which patients with clinically suspected appendicitis were prospectively included at the emergency department of six hospitals. Consenting patients underwent a standard protocol, with initial US, followed by CT in case of negative or inconclusive US results. Additionally, all patients underwent MRI (HASTE, HASTE SPAIR, DWI), with the MRI reader blinded for the results of the other imaging methods. A final diagnosis was assigned by an expert panel based on histopathology and clinical follow up after 3 months. We evaluated the sensitivity and specificity of three imaging strategies: (1) US in all patients followed by CT after a negative or inconclusive US; (2) US followed by MRI after a negative or inconclusive US; (3) MRI only. Statistical differences in accuracy between strategies were evaluated with the McNemar test. In total, 230 patients were included; 223 patients underwent MRI according to the study protocol; their mean age was 38 years, 41% were male. The expert panel assigned acute appendicitis as final diagnosis in 118 patients (51%). Conditional imaging strategies with CT or MR after a negative or inconclusive US resulted in comparable sensitivity of 0.97 (95%CI 0.93 to 0.99) and 0.99 (95%CI 0.95 to 1.00, p=0.50) at a specificity of 0.91 (95%CI 0.84 to 0.95) and 0.88 (95%CI 0.81 to 0.93, p=0.45) respectively. The MRI only strategy had a similar high sensitivity (0.97, 95% CI 0.92 to 0.99) and specificity (0.93, 95%CI 0.87 to 0.97).
Conclusion: MRI is an appropriate replacement for CT in detecting acute appendicitis in adult patients in the emergency department. Strategies with conditional CT or MRI after a negative or inconclusive US have comparable accuracy. An MRI only strategy could be an alternative approach.

Virological response to entecavir is associated with a lower probability of disease progression: Results from 377 chronic hepatitis B patients

R. Zoutendijk[1], J.G.P. Reijnders[1], F. Zoulim[2], A. Brown[3], D. Mutimer[4], K. Deterding[5], W.P. Hofmann[6], J. Petersen[7], M. Fasano[8], M. Buti[9], T. Berg[10], M.J. Sonneveld[1], B.E. Hansen[1], H. Wedemeyer[5], H.L.A. Janssen[1] for the VIRGIL Surveillance Study Group, [1]Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Department of Hepatology, Hospices Civils de Lyon, Lyon, France, [3]Department of Hepatology and Gastroenterology, Imperial College London, London, United Kingdom, [4]NIHR Biomedical Research Unit and Centre for Liver Research, Queen Elizabeth Hospital, Birmingham, United Kingdom, [5]Department of Gastroenterology, Hepatology, and Endocrinology, Medical School Hannover, Hannover, Germany, [6]Medizinische Klinik 1, Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt am Main, Germany, [7]Ifi Institute, Asklepios Klinik St. Georg, Hamburg, Germany, [8]Clinic of Infectious Diseases, University of Bari, Bari, Italy, [9]Department of Hepatology, Hospital Vall de Hebron, Barcelona, Spain, [10]Department of Hepatology, University Clinic Leipzig, Leipzig, Germany

The ultimate goal of hepatitis B virus treatment is to reduce disease progression to (decompensated) cirrhosis, hepatocellular carcinoma (HCC) and premature death. Entecavir (ETV) inhibits hepatitis B virus (HBV) replication, but whether ETV induced viral suppression is associated with an improved clinical outcome is not well known. The aim of this study was to investigate the effect of ETV therapy on event-free survival in chronic HBV patients. In this investigator-initiated project we studied all HBV monoinfected patients treated with ETV monotherapy from 10 large European referral centers within the Virgil Network. Virological response (VR) was defined as serum HBV DNA <80 IU/mL. Clinical endpoints considered were hepatic decompensation, occurrence of HCC and death. Probability of event-free survival was estimated by Kaplan Meier and Cox analysis. A total of 377 patients (mean age 43±14 years; 75% male; 41% HBeAg+; HBV DNA 5.7±2.1 log IU/ml, 30% nucleos(t)ide analogue (NA) and 22% (peg)interferon experienced) treated with ETV monotherapy were included. A total of 133 patients had advanced liver disease (by ultrasound or histology) of whom 30 (23%) patients had advanced fibrosis (F3), 93 (70%) patients had compensated cirrhosis and 10 (8%) patients had decompensated cirrhosis at baseline. Cumulative probability of achieving VR was comparable between these groups (p=0.49). Six patients developed decompensation, four were diagnosed with HCC and eight patients died during a median follow up of 19 [IQR 11-32] months. Median time to event was 36 (IQR 22-85) weeks. Patients with an event were older (p=0.08) and had a higher MELD score at base (p=0.02). Occurrence of events was not influenced by sex (p=0.37), HBeAg status (p=0.32), previous NA-therapy (p=0.16), base ALT (p=0.95), HBV DNA (p=0.46) and follow up duration (p=0.31). Cumulative probability of an event was higher in cirrhotic patients, also when excluding decompensated patients (both p<0.001). Importantly, patients with a VR during ETV therapy had a higher probability of disease-free survival in a Cox model (HR 0.20, 95% CI 0.06-0.67, p=0.009) with VR as time dependent covariate after adjusting for age, both in the overall cohort and among patients with advanced liver disease (HR 0.18, 95% CI 0.05-0.73, p=0.02). When excluding events during the first three months of ETV therapy this association remained significant. This study shows that suppression of HBV by ETV improves the probability of an event free survival in CHB. Importantly, the improved clinical outcome is still apparent in patients with advanced liver disease.

Preventive versus "on-demand" nutritional support to maintain nutritional state and quality of life during antiviral therapy for hepatitis C: a randomized controlled trial

E.J. Huisman[1-2], B. van Hoek[2], H. van Soest[3], C.M. van Nieuwkerk[4], J.E. Arends[5], P.D. Siersema[1], K.J. van Erpecum[1], Departments of Gastroenterology and Hepatology, University Medical Center Utrecht[1], University Medical Center Leiden[2], Free University Medical Center Amsterdam[4] and Medical Center Haaglanden The Hague[3], The Netherlands. Department of Internal Medicine and Infectious Diseases, University Medical Center Utrecht, The Netherlands[5]

Although antiviral treatment for hepatitis C (HCV) is highly effective, side effects often occur, including weight loss, digestive symptoms and impaired quality of life. We assessed beneficial effects of nutritional intervention during antiviral therapy. 53 HCV patients were randomized to "on demand" support (n=26: nutritional intervention if weight loss >5%) or preventive support (n=27: regular dietary advice: 5 energy- and protein-rich meals/day plus bedtime Nutridrink protein®). Nutritional state (including validated Jamar Hand Grip Strength), quality of life (SF-36 survey) and digestive symptoms (visual analog score) were evaluated at baseline, after 24 and 48 weeks peginterferon α-2b plus ribavirin. Genotype 1-4 occurred in 57% and F3-4 fibrosis in 45%, without differences between groups. In treatment-naïve patients (87% of total), sustained virologic response did not differ between "on demand" and preventive groups (64 and 62%, intention to treat). In both groups, 22 patients were treated during at least 24 weeks. Weight decreased markedly in the "on demand" group (decrease at 24 weeks: 5.4 kg [95% CI 4.0-6.8 kg] or 6.9% [95% CI 5.2-8.6%], but not in the preventive group (decrease 0.3 kg [95% CI -1.0-1.5 kg] or 0.3% [95% CI -1.3-1.8%]: P<0.001 for difference between groups). Jamar Hand Grip Strength deteriorated in the "on demand" group (from 40.3±15.5 kg to 32.0±13.1 kg, p<0.001) but not in the preventive group (from 40.7±10.4 kg to 39.7±8.9 kg resp. P=NS: P<0.001 for difference between groups at T=24). Intake of energy and proteins and fat decreased markedly in the "on demand" group but increased in the preventive group. At baseline, quality of life did not differ. Quality of life Physical Component Summary decreased significantly in both groups (from [mean±SD] 69±23 to 42±19 in "on demand" and from 75±19 to 59±20 in preventive group), but decrease was significantly less in the preventive group (P=0.003 for comparison between groups at T=24). Mental Component Summary decreased significantly from 70±20 to 44±19 in "on demand" and from 71±20 to 60±18 in preventive group (P=0.006 for comparison between groups at T=24). Although digestive symptoms deteriorated, impairment was significantly less in the preventive group. In 15 patients (7 "on demand" and 8 preventive) treated during 48 weeks, beneficial effect of preventive nutritional suppletion persisted throughout treatment course.

Conclusion: Pre-emptive nutritional advice plus supplementation prevents weight loss and catabolic state during antiviral therapy for HCV, with improved digestive symptoms and quality of life.

Diagnosis and clinical consequences of hepatitis E virus infection in orthotopic heart transplant recipients

R.A. de Man[1], S.Pas[2], A.H.M.M. Balk[3], A.D.M.E. Osterhaus[2], A.A. Baltissen-van der Eijck[2], Departments of Gastroenterology[1] , Virology[2] and Cardiology[3] Erasmus MC, Rotterdam, the Netherlands

Recently autochthonous hepatitis E infection has been recognized in the Netherlands. We studied the prevalence and clinical consequences of HEV-infection in heart transplant (HTX) recipients. Included were all living patients transplanted in our HTX program of which a serum or plasma sample was available in the serobank. Screening was performed by real time polymerase chain reaction (PCR), based on amplification of ORF3 genomic region, in all pcr(+) IgG,IgM serology (MP Diagnostics) was performed. A case was defined as a patient with a positive PCR result, chronic HEV infection as HEV RNA positive > 6 months. All cases were evaluated extensively including additional history and physical, additional lab tests for liver dysfunction, repeated HEV-virology both of plasma and stools, HEV-PCR in blood and stools of spouse (if present), HEV-genotyping by sequence analysis, ultrasonography and liver histology. In all cases the time frame of infection was determined by retrospective testing of routinely stored samples. In total 263 HTX patients were studied, immunosuppresion was prednisolone and Tacrolimus based, in some cases combined with Mycophenolate mofetil or Everolimus. Overall seven cases were detected of which six were defined as chronic HEV infection; estimated point prevalence was 3% (7/263). No positive cases were detected in spouses. Cases were predominantly older males (6/7), with a median age of 52 years (range 39-63), HEV infection occurred median 8 years (range 1-20) after HTX whereas infections clustered in recent years: 2009 (n=1), 2010 (n=5), 2011 (1). Genotyping showed all infections to be genotype 3, phylogenetic analysis showed no direct relation between the isolated viruses. IgM antibodies at presentation were only positive in 2/7 (29%) of cases. Median follow-up after case detection was 9 months (range 3-24 months).In 6/7 cases chronic HEV infection developed with persistent HEV PCR positivity in blood and stools. Activity of the liver disease at last follow up showed a wide range of enzyme activity: median AST 112 IU/l (range 39-457), median ALT 158 IU/l (range 21-353), and median gamma-gt 256 IU/l (range 196-336). Liver biopsies showed inflammatory activity compatible with chronic viral hepatitis, F1-F2 fibrosis, and grade 1-2 steatosis.

Conclusion: autochthonous sporadic acute HEV infection with genotype 3 in heart transplant recipients occurred in 3% of the population studied. An unexplained clustering of cases occurred in 2009-2011. The consequences of this infection vary from mild transient viraemia to severe potentially progressive hepatitis with a marked steatosis in the liver biopsy. As the majority of cases would not be detected by IgM-HEV serology, we advice PCR as preferred method to diagnose HEV infection in immune compromised patients.

Sustained virological response improves overall survival in chronic hepatitis C patients with advanced fibrosis

A.J.P. van der Meer[1], B.J. Veldt[1], J.J. Feld[2], H. Wedemeyer[3], J.-F. Dufour[4], F. Lammert[5], A. Duarte-Rojo[2], E.J. Heathcote[2], M.P. Manns[3], L. Kuske[4], S. Zeuzem[6], W.P. Hofmann[6], R.J. de Knegt[1], B.E. Hansen[1], H.L.A. Janssen[1], [1]Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Liver centre, Toronto Western hospital, University Health Network, Toronto, Ontario, Canada, [3]Department of Gastroenterology, Hepatology, and Endocrinology, Medical School Hannover, Hannover, Germany, [4]Institute of Clinical Pharmacology, University of Bern, Bern, Switserland, [5]Klinik für Innere Medizin II, Universitätsklinikum des Saarlandes, Homburg/Saar, Germany, [6]Medizinische Klinik 1, Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt am Main, Germany

Clinical outcomes of chronic hepatitis C virus (HCV) infection include liver failure, hepatocellular carcinoma (HCC) and liver-related death. We aimed to assess the impact of sustained virological response (SVR) on overall survival, the most definite clinical endpoint. We assessed survival and occurrence of cirrhosis-related complications in our previously described international multicenter cohort of HCV patients from 5 large tertiary care hospitals in Europe and Canada. All consecutive patients with biopsy-proven advanced fibrosis or cirrhosis (Ishak 4-6) were included from their first interferon-based treatment between 1990 and 2003.Follow-up was completed up to 2010, if needed also by recontacting the patient or general physician. Five hundred twenty nine patients were followed up to 20.2 years (median follow-up 7.7 years, IQR 5.6-10.9).Median age was 47 years (IQR 42-55) and 339 (68%) had genotype 1. 140 patients (27%) had Ishak fibrosis score 4, 102 (19%) had Ishak 5 and 287 (54%) had Ishak 6 at start of follow-up. In total 191 (36.1%) patients achieved SVR. The 10-year occurrence of liver failure was 2.4% (95%CI 0.0-5.2) in SVR vs. 31.7% (95%CI 25.9-37.5) in non-responders (NR), of HCC 5.3% (95%CI 0.9-9.7) in SVR vs. 23.1% (95%CI 17.7-28.5) in NR and of liver-related death 2.1% (95%CI 0.0-4.5) in SVR vs. 27.5% (95%CI 21.7-33.3) in NR. Moreover, there was a substantial difference in 10-year overall mortality between SVR (9.8%; 95%CI 3.0-16.6) and NR (23.0%; 95%CI 17.6-28.4).Time-dependent multivariate Cox regression analysis, adjusted for age, gender, treatment center, fibrosis score, diabetes mellitus, heavy alcohol use and treatment period, showed that SVR was significantly associated with improved overall survival (HR 3.2 NR vs. SVR; 95%CI 1.6-6.1, $p<0.001$).
Conclusion: Our study clearly demonstrates that SVR is associated with prolonged overall survival in chronic HCV patients with advanced fibrosis.

A prognostic model to select patients for prophylactic SSRI therapy during antiviral treatment for chronic hepatitis C infection

D.M. Hotho[1], G. Bezemer[1], B.E. Hansen[1, 3], A.R. van Gool[2], R.J. de Knegt[1], B.J. Veldt[1], H.L.A. Janssen[1], Departments of [1]Gastroenterology and Hepatology and [2]Psychiatry, [3]Public Health, Erasmus MC University Medical Center, Rotterdam, The Netherlands

Introduction: In chronic hepatitis C (HCV) patients, psychiatric side effects of antiviral therapy (AVT) are the most important cause of early treatment discontinuation. Since interferon (IFN) may induce depression in patients who never suffered psychiatric illness before, it is hard to predict which patients will be affected. Aim: To identify HCV patients most likely to benefit from prophylactic treatment with selective serotonin reuptake inhibitors (SSRI) during AVT. Methods: 1. Retrospective study on incidence and risk factors for depression among 321 consecutive HCV patients treated with AVT between 2000–2009 in our center. 2. Analysis of risk factors for depression and effect of escitalopram (Esc) on depressive symptoms among 78 HCV patients included in a prospective randomized controlled trial of Esc versus placebo. Psychiatric symptoms were monitored with the Symptom Check List-90 (SCL-90). Results: 1. Incidence of depression was 30% among the 321 patients treated with AVT. Previous intravenous drug use (IVDU) was the only variable associated with IFN-induced depression (OR 2.15, 95% confidence interval (CI) (1.14-4.07, p=0.02). 2. In the prospective study, depression occurred in 14 patients in the placebo-group and 5 in the Esc-group (Pearson χ^2, p=0.01). The combination of a history of depression and previous IVDU was strongly associated with IFN-induced depression (OR 12.60; 95% CI 2.47–64.34, p<0.01). Moreover, SSRI treatment was associated with a significant reduction in depressive symptoms (estimated mean depression score 35 versus 22 on the SCL-90 by week 4, for placebo versus SSRI respectively (Pearson χ^2 p=0.02), see figure.
Conclusion: HCV patients with a history of IVDU and depression are most vulnerable for IFN-induced depression. Prophylactic SSRI treatment reduces the incidence and severity of depressive symptoms in these patients.

Once daily dose regimen of ribavirin is pharmacokinetically comparable to twice daily dose regimen

J.M. Balk[1], G.R.M.M. Haenen[1], R. Peters[2], A. Bast[1], G.H. Koek[3], [1]Department of Toxicology, University Maastricht, Maastricht, [2]DSM Resolve, Sittard, [3]Department of Internal Medicine, division of gastroenterology/hepatology Maastricht University Medical Center

Introduction: Ribavirin twice a day, in combination with peginterferon, is effective in the treatment of HCV infections. Reducing the dose regimen to once a day is expected to improve compliance. Therefore the aim of the study was to compare the pharmacokinetics of ribavirin once daily dose regimen to the standard, twice daily regimen, in patients with type 1 HCV infection with weight above 75kg. Methods: The study was approved by the medical ethical committee of the University Hospital Maastricht and written informed consent was given by the patients. Ten chronic HCV positive patients were enrolled in the study and treated with 180 µg peginterferon weekly and 1200mg ribavirin daily for 24 weeks. In a cross-over design, the patients received ribavirin dosed either as 1200mg single dose daily or as 600mg twice daily for the first 12 weeks. From week 13, the patients switched to the other dose regimen. In week 11 and 23, a time profile of ribavirin plasma concentration was determined during one dosing interval (12 or 24 hours). Additionally, the haematological profile was determined according to standard procedures and side effects were registered according to good clinical practice. The ribavirin concentrations in plasma were determined using LC-MS/MS. The maximum concentration (Cmax) of ribavirin in plasma was determined and the area under the time-concentration curve (AUC), adjusted for the difference in dose, was calculated. Results: Eight out of ten patients completed the study, two stopped for reasons not related to the study. Five of them started with 600mg twice daily and three started with the once daily dose regimen. Haematological analysis did not show any signs of an increased toxicity for the 1200mg once daily dose regimen compared to the 600mg twice daily. Neither the Cmax of Ribavirin (range 7.0 – 14.6µM) nor the AUC (range 4.2 – 9.6 µM.min) were significantly different between both treatments (P-value 0.54 and 0.46 respectively). No differences in side effects were observed. Discussion: This study indicates that a once daily dose regimen of ribavirin in the treatment of HCV is pharmacokinetically comparable to twice daily dose regimen. This is in with the reported half life of ribavirin (±270h) which exceeds largely the dosing interval. The standard dose regimen could be changed to once daily to improve compliance. However, a larger study has to be performed to evaluate the sustained virological response at once daily dose regimen of ribavirin.
Conclusion: A single dose regimen is pharmacokinetically comparable to a two times daily dosing and does not show an increased incidence or severity in side effects.

Effectiveness of Neoadjuvant Chemoradiation Followed by Liver Transplantation for Hilar Cholangiocarcinoma: The United States National Experience

S. Darwish Murad[1, 2], W.R. Kim[1], D.M. Harnois[3], D.D. Douglas[4], J. Burton[5], L.M. Kulik[6], J.F. Botha[7], J.D. Mezrich[8], W.C. Chapman[9], J.J. Schwartz[10] , J.C. Hong[11] , J.C. Emond[12] , H. Jeon[13], G.J. Gores[1], C.B. Rosen[14], J.K. Heimbach[14], [1]Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; [2]Department of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, the Netherlands; [3]Division of Gastroenterology and Hepatology, Mayo Clinic Florida, Jacksonville, FL; [4]Division of Gastroenterology and Hepatology, Mayo Clinic Arizona, Phoenix, AZ; [5]Division of Gastroenterology and Hepatology, University of Colorado, Denver, CO; [6]Department of Hepatology, Northwestern University, Chicago, IL; [7]Division of Transplantation, University of Nebraska Medical Center, Omaha, NE; [8]Division of Transplantation, University of Wisconsin School of Medicine and Public Health, Madison, WI; [9]Section of Transplantation, Washington University School of Medicine, St Louis, MO; [10]Department of Surgery, University of Utah, Salt Lake City, UT; [11]Department of Surgery, University of California, Los Angeles, CA; [12]Department of Surgery, Columbia University Medical Center, New York, NY; [13]Division of Transplant, University of Illinois at Chicago, Chicago, IL; [14]Division of Transplantation Surgery, Mayo Clinic, Rochester, MN,

Excellent outcomes of liver transplantation (LTx) for hilar cholangiocarcinoma (CCA) using a protocolized approach with neoadjuvant therapy and strict selection criteria have been reported by several single centers. However, the generalizability of these results has never been established in a multicenter study. Our aim was to investigate the effectiveness of this treatment modality across all US large-volume transplant centers, each with varied neoadjuvant protocols. To this end, all large-volume transplant centers with a UNOS-approved protocol for neoadjuvant therapy that transplanted at least 3 patients with hilar CCA from 1993 – 2010 were invited to participate in this multicenter study. Twelve centers fulfilled these criteria and contributed a total of 287 eligible patients. Center-specific protocols and medical charts were reviewed onsite by 1 investigator. Survival was analyzed by the Kaplan Meier method and compared by the log-rank test. All 287 patients completed local neoadjuvant treatment consisting of combinations of external radiation (99%), brachytherapy (74%), chemotherapy boost (98%) and/or maintenance (66%). The median age was 59 years (range 17-70), 72% were male and 63% had underlying primary sclerosing cholangitis. In total, 71 (25%) dropped out before LTx for tumor progression (N=63), death (N=5) or treatment intolerance (N=2). The incidence of dropout on the waiting list was 12% per 3 months. Overall intent-to-treat survival was 68% (95% CI 62-92) and 54% (95% CI 47-61) at 2 and 5 years, respectively, with no significant difference between the center with the largest number of patients (N=193) and all others (P=.21). A total of 214 patients (75%) underwent LTx. Recurrence-free survival at 2 and 5 years was 79% (95% CI 73-85) and 66% (95% CI 58-74), respectively, with again no difference between the largest center and others (P=.31). Patients treated outside of OPTN/UNOS selection criteria (i.e. mass >3 cm (N=33), history of cancer (excluding skin) in the preceding 5 years (N=11), direct tumor biopsy (N=22) and metastatic disease (N=4)) had significantly worse 5-year recurrence-free survival as compared to those within criteria (40% vs. 72%; P<.001).

Conclusion: This multicenter study confirms that neoadjuvant therapy followed by LTx for patients with CCA has excellent outcomes, despite variations in protocols. The risk of waiting list dropout in this study is at par with the OPTN/UNOS MELD exception scheme recently established for CCA in the US, which presumes a 10% dropout every 3 months. Adherence to rigorous selection criteria is of utmost importance for the continuing success of this treatment modality.

Circulating hepatocyte-derived microRNAs are highly sensitive biomarkers associated with the necro-inflammation level in chronic hepatitis C patients

A.J.P. van der Meer[1], W.R.R. Farid[2], M.J. Sonneveld[1], P. de Ruiter[2], A.J. van Vuuren[1], J. Verheij[3], A. Boonstra[1], B.E. Hansen[1,4], R.J. de Knegt[1], L.J.W. van der Laan[2], Harry L.A. Janssen[1], Departments of [1]Gastroenterology & Hepatology, [2]Surgery, [3]Pathology and [4]Biostatistics, Erasmus MC-University Medical Center, Rotterdam, The Netherlands

The tissue-specific expression profile of microRNAs (miRNAs) - small non-coding RNAs - potentiates a role as circulating biomarkers for various diseases, as they are stable and detectable in serum. MiR-122 and miR-192 are hepatocyte-derived miRNAs which rapidly increase in the circulation upon drug-induced acute liver injury in rodents. We investigated the association between circulating levels of MiR-122 and miR-192 with hepatic inflammation, as indicated by histology and serum alanine transaminase (ALT) levels in chronic hepatitis C (CHC) patients. MiRNA levels were quantified by RT-PCR in stored serum samples of 102 CHC patients (38 with normal ALT and 64 with elevated ALT). Twenty-four subjects with normal levels of ALT were included as healthy controls (HC). The Ishak necroinflammation score was blindly assessed in 52 liver biopsies taken from CHC patients at the time of serum sampling. Median concentration of miR-122 and miR-192 was 23.4- and 8.3-times higher in CHC patients, when compared to HC ($p<0.001$). Both miR-122 and miR-192 serum levels correlated with each other ($r=0.803$, $p<0.001$) and with ALT ($r=0.674$ and $r=0.622$, respectively, $p<0.001$). MiR-191, which is not expressed in the liver but in blood cells, did not show any correlation with the ALT level ($R = 0.097$). Among CHC patients with normal ALT, the concentration of miR-122 was 11.6 and that of miR-192 4.1 times higher as compared to HC ($p<0.001$). Adjusting for age, gender and elevated versus normal ALT subgroup, linear regression analysis within the CHC patients showed that the presence of cirrhosis was significantly associated with a lower miR-122 level ($p=0.037$). MiR-122 ($r=0.30$, $p=0.031$) but not miR-192 expression significantly correlated with the overall Ishak necroinflammation score. Both miRNA levels as well as ALT activity were associated with the presence of CHC. When including all 3 markers in a multivariate logistic regression model only miR-122 remained a significant predictor of the presence of CHC ($p=0.026$). ROC analysis within the normal ALT subgroup showed that miR-122 was better capable to discriminate patients from HC than the ALT level (resp. AUC =0.969 and AUC = 0.779, $p=0.007$).

Conclusion: Circulating hepatocyte-derived miRNAs are associated with the level of liver injury as assessed by histopathological inflammation and serum ALT activity. Our study further suggests that miR-122 may represent a sensitive marker to identify patients with minor levels of hepatocellular injury, who are currently at risk not to be identified by routine blood testing.

Role of the Lectin Complement Pathway in the Outcome of Orthotopic Liver Transplantation. A unique target to improve the outcome of liver transplantation (SWO 07-18, MLDS-voordracht)

B-J.F. de Rooij[1], B. van Hoek[1], M.J. Coenraad[1], R.J. Porte[2], H.W. Verspaget[1], Dept. [1]Gastro-enterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands. Dept. [2]Hepatobiliary Surgery and Liver Transplantation, University Medical Center Groningen, Groningen, The Netherlands

Infections are a major cause of morbidity and mortality after orthotopic liver transplantation (OLT). During immune suppressive treatment, the OLT patients critically depend on their innate immunity for the protection against microorganisms. A key component of innate immunity is the lectin complement pathway, which uses Mannose-Binding Lectin (MBL) and Ficolins as pathogen-associated molecular pattern recognition proteins. These molecules form complexes with MBL-Associated Serine Proteases (MASPs), which activate the complement pathway upon target recognition. MBL, Ficolins and MASPs show significant genetic variation in the human population. In an initial study we found that the donor liver MBL genotype determines the post-transplantation MBL serum level and has a major impact on the protection against clinically significant bacterial infections after transplantation (LH Bouwman, et al. Gastroenterology. 2005;129:408-14).Additional studies, performed with the MLDS project support, revealed that particularly high MBL-producing recipients have an increased infection and mortality risk after transplantation of an MBL-deficient liver (1). Similar observations have now been made regarding (re)infections with CMV after OLT (2). Furthermore, assessment of MBL, Ficolins and MASP levels in OLT patients revealed seroconversion of these factors after transplantation, illustrating the donor liver gene-impact on the lectin complement pathway. This project provided further insight into the contribution of MBL-Ficolin-MASP genotypes and proteins, and the balance between hepatic (donor) and extrahepatic (recipient) production of these factors, to the clinical outcome of OLT. The results give rationale to prospective infection prevention treatment studies of OLT patients, based on their donor-recipient MBL-Ficolin-MASP genotypes. Ultimate goal is to improve OLT graft and patient survival. 1. B-JF de Rooij, et al.. Lectin complement pathway gene profile of donor and recipient determine the risk of bacterial infections after orthotopic liver transplantation. Hepatology. 2010;52:1100-10.2. B-JF de Rooij, et al. Mannose-binding lectin and Ficolin-2 gene polymorphisms predispose to cytomegalovirus (re)infection after orthotopic liver transplantation. J Hepatol (2011), doi:10.1016-j.jhep.2011.01.039.

Patient preferences in screening for recurrentdisease after potentially curative esophagectomy

R.L.G.M. Blom[1], P.T. Nieuwkerk[2], M. van Heijl[1], P. Bindels[1], J.H.G. Klinkenbijl[1], M.A.G. Sprangers[2], M.I. van Berge Henegouwen[1], [1]Department of Surgery, Academic Medical Center, Amsterdam, [2]Department of Medical Psychology, Academic Medical Center, Amsterdam, the Netherlands

Background: Routine imaging as part of follow-up after potentially curative esophagectomy is currently not widely accepted. If detected recurrent disease could be adequately treated, it remains unclear whether patients would want to take part in a screening program. The aim of this study was to determine the extent to which patients that underwent esophagectomy prefer follow-up with or without routine imaging.
Methods: A consecutive series of patients that underwent esophagectomy for carcinoma in the past year and who did not have evidence of recurrent disease were included in this study. An interview administered questionnaire was used to assess fear of recurrence and elicit patient preferences for the frequency and duration of the proposed follow-up strategies and hypothetical changes of survival chances (1% to 10%). Results: Of the 54 eligible patients, 45 patients (83%)participated in this study. The majority of patients preferred follow-up withroutine imaging (67%) even if such screening would not provide a survival benefit and this proportion increased up to 93% if the proposed chances of survival improved. Younger patients and patients with a lower histopathological tumor stage were more likely to desire follow-up with routine imaging.
Conclusion: The majority of patients that underwent potentially curative esophagectomy preferred routine imaging as part of the follow up strategy over outpatient clinic visits only, even if such screening would not provide a survival benefit. Further research is needed to determine the most accurate screening modality and most efficient follow-up interval.

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Survival after recurrent esophageal carcinoma has not improved over the past 18 years

R.L.G.M. Blom, K. van Oudenaarde, S.M. Lagarde, J.H.G. Klinkenbijl, O.R.C. Busch, M.I. van Berge Henegouwen, Department of Surgery, Academic Medical Center

Introduction Surgical resection in patients with esophageal carcinoma is the most important part of a potentially curative treatment. A substantial number of patients will develop recurrent disease after esophagectomy. In the literature, survival after recurrent esophageal cancer is generally around 6-8 months. Factors affecting survival after diagnosis of recurrence remain largely unknown. The aim of this study was to evaluate prognostic factors for survival after recurrent disease after potentially curatively treated esophageal carcinoma. Methods All esophageal cancer patients that underwent esophagectomy between 1993 and 2010 were included in this analysis. Prognostic factors for the development of recurrent disease were determined. Subsequently, patients without recurrent disease and patients that died postoperatively were excluded. The correlation between several clinicopathological factors and survival after diagnosis of recurrence was evaluated. These factors included histopathological tumor type, neo-adjuvant treatment and the site of metastases. Furthermore, patients were divided into 3 groups based on the year of surgery to determine whether survival after recurrence had improved over the past years. Results Between 1993 and 2010 a total of 1106 esophageal cancer patients underwent surgical resection. 294 patients were neoadjuvantly treated of whom 39% developed recurrent disease compared to 47% of patients that underwent surgery alone (p=0.018). Prognostic factors for the development of recurrent disease included stage II or III disease compared to stage I (HR=0.123 and 0.613 respectively, p<0.001), N1 disease (HR=1.887, p=<0.001), no preoperative therapy compared to chemoradiotherapy (HR=3.208, p<0.001) and a microscopically irradical resection (HR=2.194, p<0.001). The total number of patients with recurrent disease was 486 (44%). Median overall survival in these patients was 15 months; median survival after diagnosis of recurrence was 2.7 months. Of the evaluated factors, only the site of metastases was significantly associated with duration of survival after recurrence (locoregional recurrence versus systemic: HR=1.320, p=0.006). When patients were divided into 3 groups of 6 years, depending on the year of surgery there was no significant difference in duration of survival after diagnosis of recurrent esophageal carcinoma (p=0.728).

Conclusion Patients with systemic metastases have a worse prognosis than patients with locoregional recurrence. Survival in patients with recurrent disease after esophagectomy has not improved over the past 18 years. In the present series it is lower than in series in which patients underwent follow up including diagnostic imaging. This may be a reason to include diagnostic imaging in follow up after potentially curative esophagectomy.

Enterocutaneous fistula model in a rat: long-term continuous biliary drainage resulting in liver damage and an altered FXR pathway, lipid and cholesterol metabolism

K.V.K. Koelfat[1,2], R.G.J. Visschers[1,2], C.M. Hodin[1,2], R. Shiri-Sverdlov[3,2], W.A. Buurman[1.2], K. Lenaerts[1,2], S.W.M. Olde Damink[1,2,4], [1]Department of Surgery, Maastricht University Medical Centre+, Maastricht University, Maastricht, the Netherlands, [2]Nutrition and Toxicology Research Institute Maastricht, Maastricht University, the Netherlands, [3]Department of Molecular Genetics, Maastricht University Medical Center+, the Netherlands, [4]Department of HPB Surgery and Liver Transplantation, Royal Free Hospital, University College London, London, UK

We hypothesized that the development of intestinal failure associated liver disease (IFALD) caused by an enterocutaneous fistula in which the enterohepatic circulation is interrupted without obstructive cholestasis leads to reduced farnosoid X receptor (FXR) signaling, ultimately leading to liver damage. Previous studies have primarily been performed in models of bile duct obstruction. Therefore we aimed to develop an enterocutaneous fistula model in the rat with long-term continuous biliary drainage and determined its effect on hepatic function and lipid metabolism. In rats (n=7-9), the bile duct was cannulated and externalized to accomplish biliary drainage. Sham controls underwent laparotomy without cannulation. Rats were sacrificed after 3 and 7 days, and liver samples were collected for histological assessment (necrosis, inflammation, bile duct proliferation, fibrosis and steatosis). QPCR was performed for genes involved in the FXR pathway (FXR, SHP, BSEP and CYP7A1), lipid and cholesterol metabolism. Serum levels of AST, ALT, AP, GGT and bilirubin (total and direct) were also assessed. Continuous biliary drainage resulted in increased hepatic inflammation and necrosis at day 3 and day 7 ($P<0.05$) and was accompanied by bile duct proliferation (absent in controls). Fibrosis was only seen at day 7 ($P<0.05$). A trend towards decreased lipid droplets was apparent in the experimental group. Hepatic expression of FXR was markedly decreased in the experimental group at day 3 (1.11 ± 0.19;$P<0.05$) compared to sham (1.76 ± 0.18), but not at day 7. SHP expression was downregulated at day 7 (0.29 ± 0.15;$P<0.05$) compared to sham (1.38 ± 0.53). CYP7A1 was upregulated in the drainage group at day 3 (1.59 ± 0.45 vs. 0.32 ± 0.11;$P<0.05$) suggesting stimulation of bile acid biosynthesis. BSEP expression was decreased at day 3 (0.84 ± 0.09 vs. 1.34 ± 0.24;$P<0.05$), suggesting impaired canulicular bile acid transport. Genes involved in fatty acid metabolism were downregulated in biliary diverted rats. Fatty acid synthase (0.65 ± 0.24) and acetyl-CoA carboxlyase (0.82 ± 0.21) were decreased at day 7 ($P<0.05$). HMG-CoA reductase expression was upregulated at day 3 (0.69 ± 0.12;$P<0.05$) compared to sham controls (0.35 ± 0.06), suggesting stimulated cholesterol synthesis. AST, ALT, AP, GGT and bilirubin (total and direct) were significantly increased at day 7 ($P<0.05$). Biliary diversion in rats induced hepatic inflammation, necrosis, fibrosis and bile duct proliferation. Biliary diversion had evident hepatic effects with respect to FXR signaling and lipid metabolism. This model is suitable to assess long-term effects of continuous bile drainage to test therapeutic interventions aimed to reduce IFALD.

Liver mobilisation during liver resection induces profound hepatic inflammation: a mouse model

J.J.W. Schreurs[1], D.K. Dhar[2] , L. Mpabanzi[1,2,4] , T. Hendrikx[3,4] , M. Malagó[2] , C.H.C. Dejong[1,4], R. Shiri-Sverdlov[3,4], S.W.M. Olde Damink[1,2,4], [1]Department of Surgery, Maastricht University Medical Centre, Maastricht, the Netherlands, [2]Department of HPB Surgery and Liver Transplantation, Royal Free Hospital, University College London, London, UK, [3]Department of Molecular Genetics, Maastricht University Medical Center+, The Netherlands, [4]Nutrition and Toxicology Research Institute Maastricht, Maastricht University, the Netherlands

Liver surgery requires mobilisation of the liver from its surrounding ligaments to free major blood vessels, and results in a significant amount of squeezing of the organ. We recently showed that liver mobilisation is the predominant cause of hepatocyte damage during liver surgery and jeopardizes post-operative liver function. Thus, there is a critical need to investigate the mechanisms by which damage occurs during mobilisation. However, there is a lack of validated animal models to study the effects of liver mobilIsation. Our aim was to establish a mouse model to study the mechanisms of mobilisation-induced liver damage. C57BL/6 mice (n=8) underwent surgery during which the liver was manipulated to mimic what occurs in humans during major abdominal surgeries including standard liver resection, and organ recovery for transplantation. Under inhalation anaesthesia the abdomen was opened by mid incision. Next, gentle manipulation was carried out by the same surgeon touching, dissecting ligaments, retracting, and moving the liver lobes in situ for 15 minutes uniformly and intermittently with cotton-wool applicators. The same manipulation routine was used in all mice. Blood and liver samples were obtained 2 hours after mobilisation. Controls for liver mobilisation were subjected to laparotomy only. The number of neutrophils was determined by immunohistochemistry for Nimp, the number of macrophages were determined by Mac-1 staining, and the number of T-cells were determined by CD3 staining. Moreover, gene expression of interleukin (IL) 1β and 6, tumor necrosis factor alpha (TNFα), serum amyloid A (SAA1), and monocyte chemotactic protein 1 (MCP1) were analyzed by real-time RT-PCR. The amount of inflammatory cells was increased after mobilisation (Mac1, p=0.0008), (Nimp, p=0.0002), (CD3, p=0,0008), compared to control mice. Similar to the increase in inflammatory cells, mRNA levels of some, but not all inflammatory cytokines was higher in the mobilisation group than in control group (TNF p=0.0004), (IL-6 p=0.05), (MCP1 p=0.007), (IL1b p=0.14), and (SAA1 p=0.22).
Conclusion: The current model provides an excellent opportunity to study the effects of liver mobilisation in vivo. Furthermore, this study showed that inflammation is one of the important mechanisms of mobilisation-induced liver damage. These data produce insight into the mechanisms of surgery related liver damage and post-resection liver failure, and facilitate designing interventions aiming at decreasing liver inflammation during the period of mobilisation. This will be beneficial to improve the safety of liver surgery and to diminish graft damage during organ retrieval.

Malnutrition at and during admission for a first attack of acute pancreatitis

E. Brons[1], E. Roovers[2], B. Spanier[1], [1]Gastroenterology and Hepatology, [2]Epidemiology Rijnstate hospital Arnhem, the Netherlands

Studies about the prevalence of malnutrition in patients with acute pancreatitis (AP) at or during hospital admission are scarce. One retrospective study showed that approximately 30% of AP patients suffered from some extend of malnutrition at the first admission. Moreover, the prevalence of malnutrition is higher (34.6%) at the Dutch gastroenterology departments of public hospitals. Data concerning the influence of malnutrition on the outcome of AP are lacking. Malnutrition could result in an extended recovery time, an increased length hospital stay, a higher incidence of morbidity and mortality. The aim of the study was to identify the prevalence of malnutrition in AP patients with a first attack and to monitor the nutritional status of these patients during admission. This observational, prospective cohort, one centre study, was conducted from 1 October 2009 until 1 May 2011. The validated subjective global assessment of nutritional status (SGA) tool has been used to evaluate the nutritional status. The assessment was done within 24 hours (maximum 48 hours) after admission and at the day of discharge. Malnutrition was defined when a SGA score was ≤ 5. Dec of nutritional status was defined when a SGA score was lower at discharge than at admission. The goal of our treatment guide was to feed the patients within 48 to 72 hours after admission, up to an adequate nutritional intake (orally or enteral). 79 out of 108 patients have been included in this study, 87.3% suffered from a mild AP, and 12.7% from a severe AP. Totally, 8.9% (n = 7) were malnourished (SGA ≤ 5) at admission. Concerning etiology, the severity of AP and length of hospital stay, no significant differences between the malnourished and the well nourished patient groups were found. At discharge, 12.7% of patients showed a dec in nutritional status (SGA score from 7 to 6). However, neither of them was defined as malnourished at admission and at discharge (SGA ≤ 5).
Conclusion: The prevalence of malnutrition in AP is lower than expected. Although, 12.7% of the patients declined in nutritional status during hospital stay. A nutritional screening and intervention plan is essential to prevent malnutrition and the dec of nutritional status during hospital stay for this patient group.

Treatment results of necrotizing pancreatitis in a prospective multicenter cohort of 639 patients

H.C. van Santvoort[1], O.J. Bakker[1], T.L. Bollen[2], M.G. Besselink[1], U. Ahmed Ali[1], A.M. Schrijver[1], M.A. Boermeester[3], H. van Goor[4], C.H. Dejong[5], C.H. van Eijck[6] , Bert van Ramshorst[7], A.F. Schaapherder[8], E. van der Harst[9], H.S. Hofker[10], V.B. Nieuwenhuijs[10], M.A. Brink[11], P.M. Kruyt[12], E.R. Manusama[13], G.P. van der Schellin[14], T. Karsten[15], E.J. Hesselink[16], C.J. van Laarhoven[17], C. Rosman[18], K. Bosscha[19], R.J. de Wit[20], A.P. Houdijk[21], M.A. Cuesta[22], P.J. Wahab[23], H.G. Gooszen[1], for the Dutch Pancreatitis Study Group, [1]Dept.of Surgery, University Medical Center Utrecht, Utrecht, [2]Dept of Radiology St. Antonius Hospital, Nieuwegein, [3]Dept. of Surgery, Academic Medical Center, Amsterdam, [4]Dept. of Surgery, Radboud University Nijmegen Medical Center, Nijmegen, [5]Dept. of Surgery and NUTRIM, Maastricht University Medical Center, Maastricht, [6]Dept. of Surgery, St. Antonius Hospital, Nieuwegein, [7]Dept. of Surgery, Erasmus Medical Center, Rotterdam, [8]Dept. of Surgery, Leiden University Medical Center, Leiden, [9]Dept. of Surgery, Maasstad Hospital, Rotterdam, [10]Dept. of Surgery, University Medical Center Groningen, Groningen, [11]Dept. of Gastroenterology, Meander Medical Center, Amersfoort, [12]Dept. of Surgery, Gelderse Vallei Hospital, Ede, [13]Dept. of Surgery, Leeuwarden Medical Center, [14]Dept. of Surgery, Amphia Medical Center, Breda, [15]Dept. of Surgery, Reinier de Graaf Hospital, Delft, [16]Dept. of Surgery, Gelre Hospital, Apeldoorn, [17]Dept. of Surgery, St. Elisabeth Hospital, Tilburg (currently: Dept. of Surgery, Radboud University Nijmegen Medical Centre, Nijmegen),[18]Dept. of Surgery, Canisius Wilhelmina Hospital, Nijmegen, [19]Dept. of Surgery, Jeroen Bosch Hospital, Den Bosch, [20]Dept. of Surgery, Medisch Spectrum Twente, Enschede, [21]Dept. of Surgery, Medical Center Alkmaar, Alkmaar, [22]Dept. of Surgery, Vrije Universiteit Medical Center, Amsterdam, [23]Dept. of Gastroenterology, Rijnstate Hospital, Arnhem, the Netherlands.

Background & Aims: In recent years, treatment of necrotizing pancreatitis has changed towards more conservative and less invasive strategies but prospective data are lacking. We describe treatment results in a prospective multicenter cohort covering the entire clinical spectrum of necrotizing patients. Methods: From 2004 to 2008, 639 consecutive patients with necrotizing pancreatitis from 21 Dutch hospitals were prospectively included in this observational cohort study. Data on disease severity, interventions (i.e., radiological, endoscopical, surgical) and outcome were recorded. Results: Overall mortality was 15% (n=93). Organ failure occurred in 240/639 patients (38%), with 35% mortality. Treatment was conservative in 397/639 patients (62%) with 7% mortality. An intervention was performed in 242/639 patients (38%), with 27% mortality: this included early emergency laparotomy in 32/639 patients (5%), with 78% mortality. The longer the time between admission and intervention, the lower the risk of mortality: 0-14 days; 56%, 14-29 days; 26% and >29 days; 15%, P<0.001. 208/639 patients (33%) underwent intervention for infected necrosis, with 19% mortality. Catheter drainage was most often performed (63%) as first intervention, without additional necrosectomy in 35% of patients. Primary catheter drainage had fewer complications than primary necrosectomy (42% vs. 64%, P=0.003). Patients with pancreatic parenchymal necrosis (n=324), as compared to patients with peripancreatic necrosis alone (n=315), had a higher risk of organ failure (50% vs. 24%, P<0.001) and mortality (20% vs. 9%, P<0.001).

Conclusion: Two-thirds of patients with necrotizing pancreatitis can be treated without an intervention and have relatively low mortality. In patients with infected necrosis, delayed intervention and catheter drainage as first treatment improve outcome.

Timing of Surgery in Chronic Pancreatitis as a Determinant of Success Assessed by a Nomogram

U. Ahmed Ali [1,6], V. B. Nieuwenhuijs [2], C. H. van Eijck [3], H. G. Gooszen [4], R. van Dam [5], O. R. Busch [6], M. G. Dijkgraaf [7], F. A. Mauritz [1], S. Jens [1], J. Mast [3], H. van Goor [8], M. A. Boermeester[6] and the Dutch Pancreatitis Study Group[1]Department of Surgery, University Medical Center Utrecht, Utrecht, [2]Department of Surgery, University Medical Center Groningen, Groningen, [3]Department of Surgery, Erasmus Medical Center Rotterdam , Rotterdam, [4]Department of Operations / Evidence Based Surgery, Radboud University Nijmegen Medical Center, Nijmegen, [5]Department of Surgery, Maastricht University Medical Center, Maastricht, [6]Department of Surgery, [7]Clinical Research Unit, Academic Medical Center Amsterdam, Amsterdam, [8]Department of Surgery, Radboud University Nijmegen Medical Center , Nijmegen, Netherlands.

Optimal timing of surgery for chronic pancreatitis (CP) has not been well-studied, despite several reports indicating that this could be an important factor in the success of surgery.
This multi-center cohort study evaluated the influence of timing of surgery on long-term outcome in CP. Consecutive patients who underwent surgical pancreatic drainage or resection in 5 hospitals were included. Data regarding patient characteristics and past medical history were collected from medical records. Additionally, patients prospectively filled out questionnaires and visited the outpatient clinic. Primary outcomes were pain relief (VAS ≤ 4), pancreatic function and quality of life. The timing of surgery was determined in relation to three clinical events, i.e. onset of pain symptoms, use of opioids and number of endoscopic interventions prior to surgery. The effect on outcome of these and other potential risk factors was evaluated in multivariate regression analysis. Based on these results, a nomogram indicating the probability of post-operative pain relief was constructed. A total of 266 patients with long-term follow-up were included. The median duration of follow-up was 62 months (IQR 31 to 112). Long-term pain relief (VAS ≤ 4) was achieved in 149 (58%) patients. Early surgery in relation to all three clinical events was found to be independently associated with improved outcome. Surgery within 3 years of onset of symptoms was independently associated with better pain relief (OR 1.9, 95% CI 1.1 to 3.3, p 0.02) and less endocrine pancreatic insufficiency (OR 0.57, 95% CI 0.33 to 0.98, p 0.04). Patients without preoperative opioid use (OR 2.3, 95% CI 1.34 to 4.0, p 0.003) and those with 5 or less endoscopic treatments prior to surgery (OR 2.4, 95% CI 1.0 to 5.5, p 0.04) also had higher chance of pain relief. The nomogram showed that patients scoring favorably on all three factors of timing of surgery had a 77% probability of achieving postoperative pain relief compared to 24% for patients scoring unfavorably on all three factors.
Conclusion: Timing of surgical intervention in CP has an important effect on the long-term outcome of surgery. Present findings strongly suggest that surgery should be considered at an early phase of CP, preferable before use of opioids and without lengthy delays due to repetitive endoscopic interventions.

Signs of preoperative gastric outlet obstruction are associated with delayed gastric emptying after pancreatoduodenectomy

J.J. Atema, W.J. Eshuis, O.R.C. Busch, T.M. van Gulik, D.J. Gouma, Department of Surgery, Academic Medical Center, Amsterdam, The Netherlands

Delayed gastric emptying (DGE) is one of the most common complications after pancreatoduodenectomy (PD) and often requires enteral or parenteral nutritional support. Preoperative identification of patients at risk of developing DGE could facilitate selective placement of a feeding tube at time of operation. The aim of the present study was to investigate whether symptoms of preoperative gastric outlet obstruction (GOO) are associated with DGE after PD. We investigated a series of 322 consecutive pancreato-duodenectomies from our prospective database. The severity of DGE was determined according to the International Study Group of Pancreatic Surgery (ISGPS) classification. The following signs of preoperative GOO were evaluated: nausea, vomiting, loss of appetite, dysphagia, postprandial complaints, necessity of preoperative tube feeding and weight loss. The overall incidence of clinically relevant DGE (grade B/C) was 29%. Preoperative nausea, vomiting and postprandial complaints were all related to a higher incidence of postoperative DGE (43% vs 26%, P=0.013; 61% vs 26%, P<0.001; 63% vs 28%, P=0.036). Weight loss was not associated with DGE. Patients having two or more symptoms of GOO other than weight loss, were at a two times greater risk of developing clinically relevant DGE (55% vs 26%, P<0.001). In multivariable logistic regression analysis including age, gender and American Society of Anesthesiologists Classification, the presence of two or more GOO-symptoms other than weight loss remained a significant predictor of DGE (OR 4.1, 95%CI 2.0-8.2).
Conclusions: The preoperative presence of two or more symptoms of GOO other than weight loss, is a significant predictor of DGE after PD. By applying this novel risk factor, we can identify patients at risk of developing DGE, in whom we can consider placement of a feeding tube at time of operation.

The HEPATICA study: A randomized, multicenter, two arm, phase III study in patients post radical resection of liver metastases of colorectal cancer to investigate bevacizumab in combination with capecitabine plus oxaliplatin (CAPOX) vs CAPOX alone as adjuvant treatment

S.B. Schouten[1], N. Snoeren[1], A.M. Bergman[2], A. Cats[2], O. Dalesio[2], T.J.M. Ruers[2], H.M. Verheul[3], M.P. van den Tol[3], R.A.Tollenaar[4], E.J. Hesselink[5], J.M. Smit[5], J.R. van der Sijp[6], T.M. van Gulik[7], O.R.C. Busch[7], A. Rijken[8], K.P. de Jong[9], R.J. Porte[9], C. de Jong[10], M.H.A. Bemelmans[10], I.H. Borel Rinkes[1], E.E. Voest[1], R. van Hillegersberg[1]; on behalf of HEPATICA working group, [1]Universitair Medisch Centrum Utrecht, [2]Nederlands Kanker Instituut - Antoni van Leeuwenhoek Ziekenhuis, [3]VU Medisch Centrum, [4]Leids Universitair Medisch Centrum, [5]GelreZiekenhuizen, [6]Medisch Centrum Haaglanden, [7]AcademischMedisch Centrum Amsterdam, [8]AmphiaZiekenhuis Breda, [9]Universitair Medisch Centrum Groningen, [10]Maastricht Universitair Medisch Centrum

Most patients will develop local or distant recurrences after surgery for colorectal liver metastases (CRLM). Adjuvant chemotherapy with 5FU-based chemotherapy has shown to improve the prognosis of these patients. In the metastatic setting, bevacizumab prolongs PFS and improves the response rate of chemotherapy. This study aims to achieve an improved disease free survival (DFS) for patients after resection of colorectal liver metastases by adding the angiogenesis inhibitor bevacizumab to an adjuvant regimen of capecitabine and oxaliplatin. The Hepatica trial is a 2- arm, multicenter, randomized, comparative efficacy and safety study. Initially, patients were randomized after radical resection/RFA to receive CAPOX with bevacizumab (Arm A) or CAPOX alone (Arm B). The study was designed to detect a 33% reduction in the hazard ratio of relapse, (HR=0.67) at a predicted median DFS of 17 months. The total number of events that was necessary to provide 80% power to detect such a decrease was 191 requiring 300 patients to be randomized. Due to changing clinical practice, the study was amended in October 2009 to allow the inclusion of patients that received 3 cycles of neo-adjuvant chemotherapy. The Hepatica study was approved in 30 centres, of which two Swedish centres. Between January 2007 and October 2010 (the time of study closure) a total of 79 patients were randomized toxicity was evaluated for 74 patients. No significant differences in toxicity between the 2 arms were found. No suspected unexpected serious adverse reaction (SUSAR) was reported. At the time of analysis (January 2011) 16 events were encountered in arm A and 8 events in arm B. The HEPATICA study shows a non-significant improvement in 2-year DFS (52% versus 70%) by adding bevacizumab to CAPOX chemotherapy after resection of colorectal liver metastases (p=0.074). The results of this study may suggest that patients with already established metastases differ from patients receiving adjuvant treatment with bevacizumab after resection of the primary tumor.

Extended indication criteria of liver resection for colorectal cancer liver metastases. A single centre comparison of outcome

T.M. Lodewick, R.M. van Dam, M.C. de Jong, M.A.J. van den Broek, M.H.A. Bemelmans, S.W.M. Olde Damink, C.H.C Dejong, Department of Surgery, Maastricht University Medical Centre, Maastricht, The Netherlands

Background: Currently liver resection criteria for colorectal cancer liver metastases (CRCLM) are only limited by the functional reserve of liver tissue that remains after resection. Strategies to improve resectabiliy, like induction chemotherapy to reduce hepatic tumor load, staged resections and preoperative portal vein embolisation to increase future remnant liver volume and resection combined with tumour ablation, are becoming standard in liver units worldwide. Due to these strategies more patients become eligible for liver resection of CRCLM and morbidity and survival after resection may rise. Aim of this study was to compare morbidity and survival of patients who have undergone liver resection for CRCLM with classic or extended indication criterria in our centre between January 2000 and December 2010. Methods/Design: Patients with classical (Group I, n=137) and extended indication criteria (Group II, n=98) after 2000 were identified in a prospectively collected database of all patients undergoing liver surgery for CRCLM at our hospital. Data on co-morbidity, resection margin, short and long-term morbidity, disease free and overall survival were compared. Disease free and five-year survival rates were calculated and compared according to the Kaplan-Meier Method. Results: There were no differences in co-morbidity, ASA classification and age in both groups. Patients with classic indication criteria for liver surgery had less frequent complications (29.2% vs 44.8%), a lower in hospital mortality rate (2.9% vs 6.7%) and more R0 resections (85.4% vs 77.1%). The median disease free survival and overall survival were 22 months (CI 15-29) and 85 months (CI 48-121) respectively in the classic indication group vs 10 months (CI 9-12) and 35 months (CI 24-46) in the extended indication group (P<0,05). The 5 years overall survival rate was 60% in the classic vs 21% in the extended indication group (P<0,05).
Conclusion: Modern criteria for liver resection of CRCLM are associated with higher hospital mortality and complication rates, earlier recurrence and a lower overall survival. Median overall survival for patients with extended indication criteria is 35 months. The survival benefit compared to classical criteria or palliative chemotherapy, justifies the relatively high incidence of perioperative mortality and complications.

Liver-First Approach for Synchronous Colorectal Liver Metastasis: a Five-Year Single-Center Experience

M.C. de Jong[1,2], R.M. van Dam[1], M. Maas[1,3], M.H.A. Bemelmans[1], S.W.M. Olde Damink[1], G.L Beets[1], C.H.C. Dejong[1,2],[1]Department of Surgery, Maastricht University Medical Centre+ ,Maastricht, [2]NUTRIM ~ School for Nutrition, Toxicology and Metabolism, Maastricht University, Maastricht, [3]Department of Radiology, Maastricht University Medical Centre+ , Maastricht, the Netherlands

For patients who present with synchronous colorectal carcinoma and colorectal liver metastasis (CRLM), a reversed treatment sequence in which the CRLM are resected prior to the primary carcinoma has been proposed (liver-first approach). The aim of the current study was to assess the feasibility and outcomes of the liver-first approach for the treatment of synchronous CRLM. Between 2005-2010, 90 patients who underwent surgery for synchronous CRLM were queried from an institutional database. Of these, 22 patients (24.4%) were planned to undergo the liver-first approach. Feasibility and outcomes were prospectively evaluated. All of the 22 patients planned to undergo the liver-first strategy received some form of pre-operative treatment (i.e. short-course radiotherapy only (n=1); short-course radiotherapy and systemic chemotherapy (n=7); long-course radiotherapy+chemosensitizer only (n=4); long-course radio-therapy +chemosensitizer and systemic chemotherapy (n=9); pre-operative chemotherapy only (n=1)). In total, the approach was completed in 18 patients (81.8%). The main reason for treatment-failure was disease progression (n=4). In two patients (9.1%), a complete response of the primary tumor occurred and these patients are presently included in the follow-up protocol for complete responders to chemo-radiation. Compared with patients who completed treatment, patients who deviated from the protocol did not differ in location of primary tumor nor in size, number and distribution of CRLM (all p>0.05). Post-operative morbidity and mortality were 27.3% and 0% following liver resection and 44.4% and 5.6% after colorectal surgery, respectively. On an intention-to-treat basis, overall median survival (3-year-survival) was 35.5 months (41.1%). However, 37.5% of the patients who completed the liver-first approach had developed recurrent disease at time of last follow-up (intra- and extrahepatic: n=4; extrahepatic only: n=2).
Conclusion: The liver-first approach is feasible in approximately four-fifth of patients and can be performed with a peri-operative mortality and morbidity comparable to the traditional treatment paradigm. Patients treated with this novel strategy derive a considerable overall survival benefit, although disease-recurrence rates remain relatively high, necessitating a multidisciplinary approach.

Endobarrier® Gastrointestinal liner rapidly improves diabetes parameters paralleled by increased postprandial GLP-1 and PYY levels in obese type 2 diabetic patients

C de Jonge, C. de Jonge[1], F.J. Verdam[1], S.S. Rensen[1], R.P. Vincent[2], S.R. Bloom[2], M.A. Ghatei[2], W.A. Buurman[1], C.W. le Roux[2], N.D. Bouvy[1], J.W.M. Greve[3] [1]Maastricht University Medical Centre, Maastricht, the Netherlands, [2]Hammersmith Hospital, Imperial College London, London, UK, [3]Atrium Medical Centre Parkstad, Heerlen, the Netherlands

Excluding the proximal intestine by bariatric techniques rapidly improves Type 2 Diabetes (T2DM). Herein the gut peptides Glucagon-like Peptide-1 (GLP-1) and Peptide YY (PYY) are thought to play an important role. The effects of the EndoBarrier® Gastrointestinal Liner (EBL), a new minimally invasive duodenaljejunal bypass sleeve, on diabetes, GLP-1, and PYY were investigated. Seventeen obese T2DM patients received EBL and a low calorie diet for 24 weeks. Patients were studied prior to and one week after implantation, and prior to and one week after explantation. Blood was sampled before and at 10,20,30,60,90 and 120 minutes after a liquid 500kcal test meal. HbA_{1c}, glucose, insulin, GLP-1, and PYY concentrations were measured. At explantation, patients showed 29.8±3.5% loss of excess weight. HbA_{1c} improved from 8.4±0.2% to 7.0±0.2% ($p<0.01$). Anti-diabetic medication was lowered in most patients (16/17). Interestingly, already at one week after implantation, fasting and AUC glucose concentrations had improved (11.4±0.5 vs. 8.9±0.4mmol/L and 1,999±88 vs. 1,535±53, both $p<0.01$). In parallel, AUC GLP-1 and AUC PYY concentrations increased (4,440±242 vs. 6,448±527 and 2,584±144 vs. 4,112±441, both $p<0.01$). At 24 weeks, glucose parameters remained decreased and GLP-1 and PYY concentrations remained elevated.
Conclusion: EBL treatment results in significant weight reduction and rapid, long lasting diabetic improvement. The early changes in gut peptides and the rapid diabetic improvement are in with the so-called hindgut hypothesis, which attributes diabetic improvement to increased secretion of gut peptides in response to the presence of undigested nutrients in the distal small intestine.

Comfort scores in colonoscopy performance

V.E. Ekkelenkamp[1,2], I. Shaw[1], R. Valori[1], P. Dunckley[1], [1]Gloucestershire Hospitals NHS Foundation Trust, Gloucestershire Royal Hospital, Gloucester, UK, [2]Erasmus MC University Medical Center, Rotterdam, the Netherlands

Introduction: The principle indicator for assessing competence in colonoscopy is caecal intubation rate (CIR). Comfort is a key auditable outcome for colonoscopy but there are no standards for patient comfort during colonoscopy and no reports of comfort scores in relation to other quality indicators. The aim of this study is to analyse the role of different factors in determining an individual's performance in colonoscopy and to explore the significance of patient comfort scores in colonoscopist performance. Methods: All colonoscopies performed in 4 endoscopy centres in the UK are recorded in customised reporting systems (SQLscope and Unisoft), which log all key performance indicators. Data was extracted between 2008 and 2010. The following variables were measured: CIR, nurse-reported comfort levels (NRCL) on a 5-point scale (1=no discomfort, 2=minimal discomfort, 3=mild discomfort, 4=moderate discomfort, 5=severe discomfort), polyp detection rate (PDR) (hyperplastic and adenomatous), patient's experience (PE) of the procedure (better than expected, as expected, worse than expected) and use of sedation. Significant discomfort was defined as a NRCL of 4 or 5 or a PE of worse than expected. Results: A total of 12499 colonoscopies were recorded with NRCL and PE. NRCL of 4 or 5 was measured in 1122 cases (9.0%). The average number of procedures performed per endoscopist per year was 196 (range 21-493). There was a significant negative correlation between CIR and NRCL of 4-5 ($R= -0.54$; $p=0.007$). A positive correlation was found between PDR and CIR ($R=0.57$; $p<0.005$). The amount of midazolam given during the procedure was negatively correlated with CIR ($R= -0.54$; $p=0.007$). Finally, fewer than one in 20 patients rated their experience worse than expected and a worse than expected PE of colonoscopy showed a negative correlation with CIR ($R= -0.58$; $p<0.005$).

Conclusion: This study shows that endoscopists with a high CIR perform colonoscopies with less patient discomfort than those with lower CIRs, use less midazolam and see and remove more polyps. Thus achieving a high CIR and high PDR does not need to be associated with more pain and more sedation. Comfort scores should be included in the assessment of overall performance in colonoscopy to provide a fuller picture of performance.

Quality of colonoscopy and surveillance protocols after curative surgery for colorectal cancer

L.C. Steinbusch, J. Smit, J.R. Vermeijden, M.A. Brink,Meander Medisch Centrum, locatie Amersfoort Lichtenberg

In colorectal carcinoma (CRC) early staging is the hallmark for curative treatment. In surveillance programs several factors, including adequate bowel preparation, cecal intubation and withdrawal time are mandatory for a high adenoma detection rate. Especially, patients who had undergone curative surgery for colorectal cancer are at risk of local recurrence and newly developing adenomas and carcinomas. Therefore, the National Working Group on Gastrointestinal Cancers recommends a surveillance colonoscopy within three years postoperatively. The objectives of this study were to analyze the percentage of post-operative surveillance colonoscopies. Furhermore we analyzed all patients with proven CRC, who underwent a “normal” colonoscopy for any reason in the past. Retrospectively 237 patients who were diagnosed with CRC in 2006 in a Dutch teaching hospital were identified. We investigated whether in patients with curative surgery colonoscopy was performed within three years after surgery. Secondly, all patients with CRC diagnosed in 2010 were analyzed whether colonoscopy was performed previous ten years. Tumor-, patient- and colonoscopy characteristics were taken into account. Four out of 166 patients (2,4%) developed an interval carcinoma after curative surgery in 2006. In two patients Lynch syndrome was diagnosed. Although surveillance colonoscopy was indicated in 166 patients, in 37 patients (22,3%) no endoscopy was performed within three years. Eight of 218 patients (3,7%) with colon cancer in 2010 had a normal endoscopy the previous ten years (6 –100 months). In the majority of patients (7 cases) the tumor was located in the right-sided colon, in two of these patients a sigmoidoscopy was performed and in two cases there was inadequate bowel preparation.
Conclusion: in almost a quarter of patients with curative surgery for CRC surveillance was not performed according to the Dutch guidelines. In almost all CRC patients having a colonoscopy before diagnosis the tumor was located in the right colon suggesting that the cecum was not intubated or not adequately cleaned. The study advocates strict adherence to surveillance protocols and stresses the importance of registration of endoscopy quality indicators.

Endoscopic management of large colorectal polyps: safety and effectiveness aspects in a real-life cohort

G. Veldhuijzen, E.J.A. Rondagh, M. Bouwens, R.J.J. de Ridder, W. Hameeteman, A.A.M. Masclee, S. Sanduleanu ,Division of Gastroenterology and Hepatology, Department of Internal Medicine Maastricht University Medical Centre, The Netherlands

Introduction: Although endoscopic resection of large colorectal polyps may be challenging and associated with complications, this procedure, when safe and effective, is the preferred therapeutic option over surgery. Aim: We aimed to assess the safety and effectiveness of endoscopic resection of large colorectal polyps and referral to surgery at our academic hospital. Methods: We reviewed a prospectively updated database of all colonoscopies performed at our centre from February 2008 through February 2010. All 19 endoscopists were previously trained on endoscopic resection of large colorectal neoplasms. We included all consecutive patients presenting with ≥1 large colorectal polyp (≥1 cm). Polyp size, location, endoscopic appearance (Paris classification), presence of advanced histology (high-grade dysplasia, HGD; or early cancer), treatment modality (snare cautery, EMR, surgery) and complications (bleeding, perforations) were recorded. Endoscopic follow-up (FU) was performed according to international guidelines. During FU, residual/recurrent tissue at the initial polypectomy site was reported. Results: In this cohort, we included a total of 4754 patients with 5407 polyps. Overall, we found 310 patients with 406 large polyps (1 out of 8-9 colonoscopies), of which 336 were adenomas, 50 serrated polyps and 20 early cancers. Of the polyps, 48.3% were pedunculated, 28.1% sessile and 23.6% flat. In total, 359 (88.4%) of the large polyps were treated endoscopically, while 47 (11.6%) were referred to surgery (61.7% immediately and 38.3% after an attempted polypectomy). Multiple logistic regression analysis, adjusting for age and gender, showed that proximal location (OR 2.40, 95% CI 1.04– 5.33), size ≥2 cm (OR 4.90, 95% CI 2.36–10.2), flat/sessile morphology (OR 4.76, 95% CI 1.93–11.72) and advanced histology (OR 6.84, 95% CI 3.15–14.83) were independent predictors for referral to surgery. Complications occurred in 5 (1.2%) of the large polypectomies; all of them were post-procedure bleedings, no perforations occurred. To assess the effectiveness of polypectomy, a total of 184 (55.1%) polypectomy regions were re-examined (median FU 3.3 months, interquartile range 1.7–7.6). Of these polyps, 166 (90.2%) were completely removed by endoscopic resection, of which 143 (86.1%) after the first attempt and 23 (13.9%) after ≥1 attempt. In 6 cases the residual/recurrent tissue contained HGD and in 1 case early cancer.
Conclusion: In this real-life cohort study, 88.4% of the large colorectal polyps were completely removed by endoscopic resection, with a low complication rate. Our data strongly favor primary endoscopic treatment of large colorectal polyps as a safe and effective approach.

Endoscopic Submucosal Dissection (ESD) with the Water-jet HybridKnife

J. Haringsma, S. Ganesh, M. Hadhiti, Department of Gastroenterology and Hepatology, Maasstad Hospital, Rotterdam, the Netherlands

Background: Endoscopic submucosal dissection (ESD) is a novel technique that enables endoscopic en-bloc resection of superficial neoplastic lesions in the GI tract. ESD is more expensive, technically more demanding and caries a higher complication rate than EMR. A new instrument, the HybridKnife, using waterjet technology is designed to overcome some of these obstacles. Methods: Consecutive patients referred for ESD of an early GI neoplasia were included and followed. We investigated radical resection rate, 30-day complication rate and tumor recurrence at follow-up. ESD was performed as a single instrument procedure using the Hybrid knife T-type or I-type (Erbe Gmbh, Tübingen). After marking the lesion with a 5 mm margin using soft coagulation, needleless injection was performed with a mix of normal saline, epinephrin, and methylene blue. Submucosal dissection and hemostasis were performed with the same instrument. Resected specimen were carefully oriented, fixed, measured and classified histologically according to the revised Vienna classification. Results: A total of 18 patients (mean age: 69 yr, range 40–89) were included. Lesions were located in the esophagus (2), stomach (12), and colorectum (4). Median size of the specimen was 25 mm (range 12-43). Duration of the procedure was 62 min (25-114). The series included 2 granular cell tumors, 7 mucosal gastric cancers, 5 submucosal gastric cancers and 4 high-grade colorectal adenomas. Of the gastric cancers 3/12 were poorly differentiated. Radical resection was therefore achieved in 13/18 (72%) patients. Of the five patients with irradical resection one subsequently underwent surgical resection All others were considered unfit for surgery. No perforations occurred. Major complications occurred in 3 patients (16%) including gastric outlet obstruction (1), mediastinal emphysema (1), and post-procedural hemorrhage (1).
Conclusion: Waterjet hybrid ESD is feasible and simplifies the procedure. Exchange of accessories is rarely needed. Since submucosal injection can be easily repeated this increased swiftness, and may increase the efficacy and safety of ESD. injection can be easily repeated this increased swiftness, and may increase the efficacy and safety of ESD.

Cryospray ablation using pressurized carbon dioxide gas for the treatment of Barrett's esophagus with early neoplasia

R.E. Verbeek, F.P. Vleggaar, J.W.P.M. van Baal, P.D. Siersema, Dept. of Gastro-enterology and Hepatology, University Medical Center Utrecht, The Netherlands

Endoscopic cryospray ablation is a novel modality for the treatment of Barrett's esophagus (BE) with early neoplasia. Data with regard to the use of pressurized carbon dioxide (CO_2) for cryospray ablation are scarce. The aim of this study was to determine safety and efficacy of cryospray ablation using CO_2 (Polar wand, GI supply) in the treatment of BE with early neoplasia.In this single-center pilot study, 10 patients with BE and early neoplasia were included. Visible neoplastic lesions were treated with endoscopic mucosal resection (EMR). The residual BE mucosa was then treated using cryospray ablation. Cryospray treatments were performed every 4 weeks until the complete BE segment was eliminated, with at most 8 treatment sessions. If no response was observed after 3 sessions, cryospray ablation was stopped. Treatments consisted of 6 applications with the CO_2 catheter of 20 seconds per 2-3 cm hemi circumferential BE mucosa, with active suctioning of the stomach between applications. Response was defined as complete when total endoscopic and histologic eradication of BE was observed, as intermediate with endoscopic and/ or histologic improvement and as non-response with no endoscopic and histologic improvement. Biopsies of BE and neo-squamous epithelium were obtained in 4-quadrants every 1-2 cm pre- and 1, 3 and 6 months post-treatment using a disposable large capacity forceps. In total, 7 patients with intramucosal carcinoma (IMC) and 3 with high-grade dysplasia (HGD) were included. Nine patients underwent prior EMR. Pre-cryoablation diagnoses were intestinal metaplasia (IM; n=4), low-grade dysplasia (LGD; n=5) and HGD (n=1), with a median BE length of 5.0 cm (IQR 1.8-7.3). A median of 3.0 (IQR 1.8-4.8) cryospray treatment sessions were performed. In none of the patients a complete response was achieved, in 3 (30%) an intermediate response and in 6 (60%) no response, with post-cryoablation diagnoses of IMC (n=1), HGD (n=1), LGD (n=3), IM (n=2) and gastric metaplasia (n=2). The median post-cryoablation BE length was 2.5 cm (IQR 0.9-6.3) after a median follow-up of 7 months (IQR 2.8-10.5). No buried BE glands were detected. In 1 patient, a gastric perforation occurred after the first treatment as a result of gastric distention caused by CO_2 gas. This patient was withheld from further cryospray treatments. Apart from esophageal laceration in another patient, cryospray ablation was tolerated well.
Conclusion: After a short learning curve, cryospray ablation using CO_2 gas is a well tolerated treatment modality. However, in our experience, the efficacy of CO_2 cryospray ablation is disappointing for the treatment of BE associated neoplasia.

Radiofrequency ablation combined with endoscopic resection, for eradication of Barrett's oesophagus containing early neoplasia in 130 patients: results of a European multicenter study (EURO-II)

R.E. Pouw[1], R. Bisschops[2], O. Pech[3], K. Ragunath[4], B.L. Weusten[5], B. Schumacher[6], B. Rembacken[7], A. Meining[8], H. Messmann[9], E.J. Schoon[10], L. Gossner[11], J. Mannath[4], C.A. Seldenrijk[12], M. Visser[13], T. Lerut[14], J.M. Deviere[15], F.J. ten Kate[13], C. Ell[3], H. Neuhaus[6], J.J. Bergman[1], [1]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, Netherlands, [2]Dept. of Gastroenterology and Endoscopy, University Hospitals Leuven, Leuven, Belgium, [3]Internal Medicine II, Dr. Horst-Schmidt-Kliniken, Wiesbaden, Germany, [4]Division of Gastroenterology, Wolfson Digestive Diseases Centre, Nottingham, United Kingdom, [5]Dept. of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, Netherlands, [6]Dept. of Gastroenterology, Evangelisches Krankenhaus Düsseldorf, Düsseldorf, Germany, [7]Dept. of Gastroenterology, The General Infirmary at Leeds, Leeds, United Kingdom, [8]Second Medical Department, Technical University of Munich, Munich, Germany, [9]Third Medical Clinic, Klinikum Augsburg, Augsburg, Germany, [10]Dept. of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, Netherlands, [11]Dept. of Medicine I, Klinikum Karlsruhe, Karlsruhe, Germany, [12]Dept. of Pathology, St. Antonius Hospital, Nieuwegein, Netherlands, [13]Dept. of Pathology, Academic Medical Center, Amsterdam, Netherlands, [14]Dept. of Thoracic Surgery, University Hospitals Leuven, Leuven, Belgium, [15] Dept. of Gastroenterology and Hepatopancreatology, Erasme University Hospital, Brussels, Belgium

Barrett's oesophagus (BO) containing high-grade dysplasia (HGD) or early cancer (EC), can be treated by radiofrequency ablation (RFA) with prior endoscopic resection (ER) in case of focal lesions, as demonstrated by a number of relatively small-sized, single-center studies. Aim of this prospective study was to evaluate efficacy of RFA, with or without prior ER, for BO with early neoplasia, in 12 European centers with expertise in management of BO neoplasia. Patients with BO ≤12cm with HGD/EC were included. ER was performed in case of focal lesions limited to <2cm length and <50% circumference. RFA was performed at 0-3-6-9-12 months, with max. 2 circumferential and 3 focal RFA treatments. Escape-ER as part of treatment protocol, was allowed for residual BO after RFA treatment, or for suspicious lesions found during the treatment period. To ensure uniformity and protocol compliance, investigators were trained at the coordinating site and the first 4 RFA cases were supervised on-site by the principal investigator. A coordinating study team attended all treatments and first follow-up at each site. Central pathology review of ER-specimens and study biopsies was performed at the coordinating site. Primary outcomes were eradication of intestinal metaplasia (IM) and neoplasia. 130 patients (107 men, mean 65yrs, median BO length C3M6) underwent en-bloc (n=62), piecemeal ER (n=55, median 3 (IQR 2-4) pieces) or no ER (n=13). Worst ER histology: EC (n=75), HGD (n=32), LGD (n=7), no dysplasia (n=3). Worst histology pre-RFA: HGD (n=37), LGD (n=44), no-dysplasia (n=49, all had HGD/EC in ER). By May 2011, 11 patients were still under treatment, 5 patients dropped-out due to unrelated causes. Per intention-to-treat analyses (i.e. counting unrelated drop-outs as failures) complete eradication of IM and neoplasia was reached in 108/119 (91%) and 114/119 (96%) patients, respectively. In a per-protocol analysis complete eradication of IM and neoplasia was reached in 108/114 (95%) and 114/114 (100%) patients, respectively. Escape-ER for suspicious lesions found during treatment was performed in 3 patients (EC, n=1; HGD, n=2), and for residual BO after RFA in 4 patients (LGD, n=1; IM, n=3). Adverse events during RFA occurred in 10% of patients, all superficial mucosal lacerations at an ER-scar or proximal reflux-stenosis, all graded as "mild". Conclusion: This is the largest prospective multicenter study on RFA combined with ER for treatment of BO containing HGD/EC. These outcomes suggest that this treatment approach is very effective and safe, when performed by trained, expert endoscopists in carefully selected patients.

Concurrent biodegradable esophageal stent placement with single-dose brachytherapy for palliation of dysphagia is associated with high complication rates: results from a pilot study

M.M.C. Hirdes[1], J.E. van Hooft[3], H.K. Wijrdeman[2], M.C.C.M. Hulshof[4], P. Fockens[3], O. Reerink[2], F.P. Vleggaar[1], P.D. Siersema[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Radiotherapy, University Medical Center Utrecht, [3]Dept. of Gastroenterology and Hepatology, [4]Dept. of Radiotherapy, Academic Medical Center Amsterdam, The Netherlands

Single-dose brachytherapy as well as self-expanding stent placement are effective palliative treatments for malignant dysphagia. Brachytherapy provides better long term (>3 months) relief of dysphagia compared to stent placement, but fails to provide immediate improvement, which is one of the main benefits of stent placement. We hypothesized that concurrent treatment with brachytherapy and biodegradable (BD) stent (Ella-CS, Hradec-Kralove, Czech Republic) placement could provide both immediate and long term relief of dysphagia. The aim of our study was to evaluate technical feasibility and safety of concurrent, single dose brachytherapy and BD stent placement in patients with inoperable esophageal cancer. From Dec 2009 - April 2011, we aimed to include 20 consecutive patients with dysphagia for at least solid food due to inoperable esophageal cancer with an expected survival of > 3 months. Patients were treated with 12 Gy intraluminal brachytherapy on day 1 and BD stent placement on day 2. Patients were monthly followed-up for dysphagia and serious adverse events (SAE; defined as each unexpected event for which endoscopy or admission was indicated). Primary endpoint was a stent-related SAE, with a pre-defined threshold of <25% for safety and >40% to be harmful. All SAE's were evaluated by an expert panel for a potential relation with stent placement. In total, 19 patients (13 males, median age 66 (range 39-87) years) were included. Six (32%) patients also received palliative chemotherapy. Technical success of both procedures was 100%. After 19 inclusions, the study was ended prematurely because the safety threshold was exceeded. In total, 24 SAEs occurred in 17 (89%) patients. Eight (42%) of these SAEs were determined by the expert panel to be stent-related (severe retrosternal pain n=5, bleeding n=1, recurrent dysphagia n=2). Of the other 16 SAEs (determined to be not stent-related), 12 included admission for varying combinations of the following symptoms: persisting retrosternal pain, nausea and vomiting. Only 2 patients with nausea and vomiting also received chemotherapy. Despite adequate luminal patency in 17 (89%) patients, oral intake was severely impaired in 11 (58%) patients due to the severe retrosternal pain, nausea and vomiting. Median total weight loss per patient was 9 kg (-17 to +7) and median weight loss per patient per month was 3.5 kg. Median survival was 82 (25-300) days.
Conclusion: Due to an unacceptably high SAE rate, particularly severe pain, but also nausea and vomiting, concurrent treatment with brachytherapy and BD stent placement cannot be recommended for the palliative treatment of dysphagia from esophageal cancer.

Weekend admission is associated with an adverse outcome, irrespective of time of admission and patient-related factors in patients with suspected upper gastro-intestinal bleeding

N.L. de Groot[1], J.H. Bosman[1], P.D. Siersema[1], M.G.H. van Oijen[1], A.J. Bredenoord[1], [1]Dept. Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, the Netherlands

Patients that present with upper gastrointestinal bleeding (UGIB) during the weekend have a worse outcome, with an increased risk on recurrent events and mortality. Whether this is solely related to weekend vs. weekday, or that time of admission and/or patient-related factors may play a role as well, is unclear. We therefore prospectively investigated 1) the association between the day and time of admission and adverse outcome after UGIB and 2) patient-related factors predicting adverse outcome. We are currently performing a multicenter prospective cohort study to examine the outcome of patients who were admitted to the hospital with suspected UGIB. Time and day of admission were recorded, and a follow-up of 30 days was used for the composite endpoint “adverse outcome”, which included 30-day mortality and 30-day rebleeding rates. We compared adverse outcomes between different times of admission and studied the association with patient-related factors. A total of 425 patients were prospectively included, of which 122 (29%) patients were admitted during the weekend. Patients admitted during the weekend showed a significantly higher risk of an adverse outcome (25% vs. 15%; p=0.01). Moreover, radiological or surgical interventions were more often performed for weekend admissions than for weekday admissions (5% vs. 0.7%; p<0.01 and 5.7% vs. 2.0%; p=0.04, respectively). On both weekend- and weekdays 239 (56%), 107 (25%) and 74(17%) patients were admitted during the day (8AM – 6PM), evening (6PM-11PM) and night (11PM-8AM), respectively. When comparing day, evening and night, we found no differences in adverse outcomes (17%, 16%, 21%; p=0.71, respect-tively). Patients with suspected UGIB admitted during the weekend tended to present more often with lower systolic blood pressure, hematemesis and rectal blood loss and were more likely to have a confirmed UGIB compared to patients admitted during the week, although this difference was not statistically significant. Time to endoscopy was not different between weekend and weekday admissions (13.6 hours vs. 14.3 hours; p=0.69). Notably, in patients admitted during the day, time to endoscopy was significantly longer compared to evening and night admissions (p<0.01).
Conclusion: Weekend admission is associated with adverse outcome in patients with suspected UGIB. This is likely to be due to more severe bleedings during weekend days as neither time of admission, nor time to endoscopy affected outcome of patients admitted with a suspected UGIB.

Learning curve, intra-and interobserver agreement and accuracy of endoscope-based confocal laser endomicroscopy for the differentiation of colorectal lesions

T. Kuiper[1], C.Y. Ponsioen[1], R. Kiesslich[2], P. Fockens[1], E. Dekker[1], [1]Departments of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, the Netherlands, [2]I. Medical Clinic, Johannes Gutenberg University of Mainz, Mainz, Germany

Background: The endoscope-based confocal laser endomicroscopy (eCLE) system allows in vivo imaging of colorectal epithelium. Accurate interpretation of confocal images could potentially lead to omission of histopathology. Little is known about the learning curve for accurate interpretation of confocal images acquired with eCLE. The current study aimed to determine the learning curve of eCLE and assess its diagnostic accuracy. Furthermore, the intra- and interobserver agreement of eCLE confocal images for the differentiation of colorectal lesions was assessed. Methods: Three endoscopists without previous training in confocal image interpretation participated as observers. They received an introduction on the Mainz criteria as well as a training set of 10 eCLE confocal images prior to evaluating a set of 90 images. Observers were blinded for the endoscopic image and assessed all 90 eCLE confocal images post-hoc using the Mainz classification. After each set of 30 images, accuracy of each observer was assessed and each image that was inaccurately scored was discussed. The same procedure was repeated 6 months later using the same set of images which were shown in a different order. Results: Histopathology of the confocal images demonstrated normal tissue (n=37), hyperplastic polyps (n=5), inflammation (n=15), adenomas (n=16), colorectal cancers (n=7) and colitis-associated dysplasia (n=10). During the first assessment, accuracy was 85.6%, 94.4% and 92.2% for each observer. Accuracy of all three observers remained high during the first assessment, with no significant changes between the first set of 30 images and the second or between the first set and the last 30 images (p=0.08 and p=0.180, respectively). During the second assessment 6 months later, accuracy for each observer was 88.9%, 90.0% and 88.9%. Kappa-values of the intraobserver agreement were 0.68, 0.84 and 0.77 for each observer. The kappa-value for interobserver agreement was 0.73 during the first assessment and 0.72 during the second assessment.
Conclusions: Our results suggest accurate post-hoc interpretation of eCLE confocal images can be learned quickly. Using a short introduction and training set of images, high diagnostic accuracy was achieved by all 3 observers during the initial stage of the assessment, which remained high thereafter. Furthermore, intra- and interobserver agreement was substantial for all 3 observers. Future studies should focus on the real-time assessment of eCLE confocal images.

Stavudine and didanosine treatment are risk factors of HIV-associated idiopathic non-cirrhotic portal hypertension

H.H.M. Rossing[1], J.N.L. Schouten[1], T. Koëter[1], M.E. van der Ende[2], B.E. Hansen[1,3], H.L.A. Janssen[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Internal Medicine, [3]Dept. of Public Health, Erasmus MC University Hospital, Rotterdam, The Netherlands

Idiopathic non-cirrhotic portal hypertension (INCPH) has been reported in patients with chronic HIV infection. However, its prevalence and outcome remain to be elucidated. Furthermore, since most studies suffer from selection bias and small study size, contrasting results have been reported concerning its risk factors. The aim of our study was to evaluate the reported prevalence, risk factors and outcome of HIV associated INCPH. All Dutch physicians treating HIV patients (in 22 secondary and tertiary hospitals) were contacted and requested to notify INCPH cases observed in their population. INCPH was defined as the presence of portal hypertension in the absence of cirrhosis, portal vein thrombosis, hepatic vein obstruction and chronic liver disease. A case-control study was performed to identify its risk factors. The cases were group-matched to controls for years of HIV follow-up in a 1:6 ratio. Controls were selected from a database of HIV patients with negative screening for signs of portal hypertension by abdominal ultrasound. Univariate and multivariate conditional logistic regression analyses were performed. Best model fit was achieved by comparing the log likelihood and Akaike's Information Criterion. Within the Dutch HIV population (n=18,085) sixteen INCPH patients were identified. These data suggest a reported prevalence of INCPH in HIV patients of 1/1130 (about 1‰). Control patients and INCPH patients were similar in duration of follow-up (10.9 vs. 11.5 years, p = 0.44) and age at HIV diagnosis (48.1 vs. 50.7 years, p = 0.30). At the time of INCPH diagnosis, cases had a lower CD4 count (255 vs. 511/mm^3, p <0.001), a lower platelet count (130 vs. 228 giga/L, ρ <0.001), a higher AST level (64 vs. 29 IU/L, p <0.001) and ALT level (65 vs. 28 IU/L, p <0.001). In multivariate analysis, adjusted for years of HIV follow-up, didanosine [OR 2.15 (1.37-3.39), p <0.001] and stavudine [OR 3.57 (1.36-9.42), p = 0.01] were independently associated with an increased risk of developing INCPH. Similar results were obtained after one by one adjustment for AST, ALT, CD4 and platelet count. During a mean follow-up of 69 months, 3 patients died (malignancy (2), infection (1)). No liver related mortality occurred. HIV associated INCPH appears to be a rare disease. Didanosine and stavudine treatment are the most important risk factors of this disorder. Mortality is related to HIV associated disorders. This study suggests that screening for the development of INCPH may be recommended in HIV-patients treated with didanosine or stavudine in combination with elevated aminotransferase levels or thrombocytopenia.

The association of activated complement factor 3 with liver fat and liver enzymes

N. Wlazlo[1,2,3], M.M.J. van Greevenbroek[2,3], I. Ferreira[2,3,4,5], C.J.H. van der Kallen[2,3], C.G. Schalkwijk[2,3], B. Bravenboer[1], C.D.A. Stehouwer[2,3], [1]Department of Internal Medicine, Catharina Hospital, Eindhove,; [2]CARIM School for Cardiovascular Diseases, Maastricht University, Maastricht, [3]Department of Internal Medicine/Laboratory for Metabolism and Vascular Medicine, Maastricht University Medical Centre, Maastrich, [4]Department of Clinical Epidemiology and Medical Technology Assessment (KEMTA), Maastricht University Medical Centre, Maastricht, [5]CAPHRI School for Public Health and Primary Care, Maastricht University Medical Centre, Maastricht

Background & Aims: The complement system may be involved in the pathogenesis of alcoholic and non-alcoholic liver disease, though studies in humans are scarce. For this reason, we investigated whether circulating levels of activated complement factor 3 (C3a), which is generated upon activation of the central complement component C3, were associated with hepatic steatosis and hepatocellular damage in none-to-moderate and heavy alcohol consumers. Methods: Plasma C3a, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma glutamyltransferase (GGT) were determined in 524 individuals (61% men, mean age 59±7.0 yrs) with an increased risk of diabetes mellitus and/or cardiovascular diseases. Liver fat content was estimated using a predictive equation that was validated on magnetic resonance spectrometry. Markers of hepatocellular damage (AST, ALT, GGT) were standardized and compiled into an average liver enzyme score. Cross-sectional associations between C3a and liver fat or liver enzymes were investigated with multiple linear regression analyses, stratified by none-to-moderate and heavy alcohol consumers, who were defined on consumption of >30 g/day for men and >20 g/day for women. Results: Median C3a levels were 59.8 ng/ml (IQR 50.1-72.9) in none-to-moderate alcohol consumers and 56.9 ng/ml (IQR 49.4-71.5) in heavy alcohol consumers. C3a (per unit increase in $\log_e$ transformed C3a) was associated with liver fat percentage both in the none-to-moderate (β=0.221; 95%CI 0.034-0.407) and the heavy alcohol consumers (β=0.632; 95%CI 0.259-1.004). Adjustment for waist circumference largely attenuated these associations to 0.071 (95%CI -0.085 to 0.228) and 0.336 (95%CI -0.050 to 0.674). The interpretation of this attenuation is very complex, but either overadjustment or confounding could have played a role. Moreover, C3a was independently associated with the liver enzyme score in subjects with heavy alcohol consumption (β=0.918; 95%CI 0.443-1.393). This association remained significant after adjusting for waist circumference (β=0.775; 95%CI 0.283-1.267). Within the none-to-moderate drinkers, C3a showed a similar trend with the liver enzyme score (β=0.891; 95%CI -0.344 to 2.127) in a subgroup of severe obese subjects (BMI > 35 kg/m^2; n=32). Similar results were also observed for all liver enzymes individually.

Conclusion: The associations of C3a with liver enzymes in heavy alcohol consumers and severely obese subjects suggest that complement activation may be primarily related to hepatocellular injury in the metabolically challenged liver. These findings justify further exploration of the role of the complement system in metabolic liver diseases in humans.

Need and timing of kidney transplantation in relation to liver transplantation in polycystic liver disease

F. Temmerman[1], T. Darius[2], J. Pirenne[2], D. Monbaliu[2], R. Aerts[2], B. Bammens[3], W. Laleman[1], D. Cassiman[1], C. Verslype[1], W. van Steenbergen[1], D. Kuypers[3], F. Nevens[1], [1]Department of Hepatology, University Hospitals Leuven, Belgium, [2]Department of Abdominal Transplant Surgery, University Hospitals Leuven, Belgium, [3]Department of Nephrology, University Hospitals Leuven, Belgium

Background: The most common complication of polycystic liver diseases (PCLD) is extensive hepatomegaly which may lead to invalidating abdominal symptoms. In case of ADPKD (autosomal dominant polycystic kidney disease), renal failure develops in 50% of the affected patients. Liver (LT) and/or kidney transplantation (KT) are the only curative therapeutic options for some of these patients. Aim: To study the need and the timing of KT in relation to LT in patients with PCLD. Methods: The outcome of patients who underwent a LT for PCLD between 1995 and 2011 in our center was studied. Results: Study population, 48 patients: 44 ADPKD (92%) and 4 ADPLD (8%) (autosomal dominant polycystic liver disease). In the ADPKD subgroup there were 36 women (82%) and 8 men (18%); in the ADPLD group all patients were women. In the ADPKD sub-group, 31 patients (70.5%) developed renal failure and underwent a KT at some time in their disease process: 18 patients (58%) received immediately a combined LT+KT (the indication for combined KT in case of LT was a clearance of < 30ml/min). 7 patients (23%) first received a KT and received then a combined LT+KT or a LT ; 6 patients (19%) first received a LT and subsequently a KT . None of the ADPLD patients required a KT. The 5 years liver graft and patients survival of LT was 91.6%. The 5 year graft and patient survival of combined LT+KT was 80%.
Conclusion: Post-transplant survival rates in PCLD are excellent. 70.5% of ADPKD patients, who received a LT, need a KT at some point during their disease process. After a KT, a LT was needed in 16% on average after 15 years; and this occurred especially in men and mostly because of liver volume related problems and recurrent liver cysts infections. After a LT, in 14% of the patients, especially women, a KT was needed on average after 8 years. Finally, combined LT+KT was necessary in 41% of the ADPKD patients.

Improved platelet count and smaller spleen size long after sustained virological response in chronic hepatitis C patients with advanced fibrosis

A.J.P. van der Meer[1], B.J. Veldt[1], J.J. Feld[2], H. Wedemeyer[3], J.-F. Dufour[4], F. Lammert[5], A. Duarte-Rojo[2], E.J. Heathcote[2], M.P. Manns[3], L. Kuske[4], S. Zeuzem[6], W.P. Hofmann[6], R.J. de Knegt[1], B.E. Hansen[1,7], H.L.A. Janssen[1], [1]Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands, [2]Liver centre, Toronto Western hospital, University Health Network, Toronto, Ontario, Canada, [3]Department of Gastroenterology, Hepatology, and Endocrinology, Medical School Hannover, Hannover, Germany, [4]Institute of Clinical Pharmacology, University of Bern, Bern, Switserland, [5]Klinik für Innere Medizin II, Universitätsklinikum des Saarlandes, Homburg/ Saar, Germany, [6]Medizinische Klinik 1, Klinikum der Johann Wolfgang Goethe- Universität, Frankfurt am Main, Germany, [7]Department of Biostatistics, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands

Platelet count and spleen size are surrogate markers for portal pressure in cirrhotic patients. The long term effect of sustained virological response (SVR) in chronic hepatitis C (CHC) patients with advanced fibrosis on these two markers is not well known. We aimed to investigate the effect of achieving SVR in CHC patients with advanced fibrosis on platelet count, spleen size and fibroscan measurements. Pre-treatment as well as the last available platelet counts were collected in our international multicenter cohort of consecutively treated CHC patients from 5 large tertiary care hospitals in Europe and Canada. Patients were included from their first interferon-based treatment, following biopsy-proven advanced fibrosis (Ishak 4-6). For this study patients with at least one year follow-up and paired base and follow-up platelet count are included. Annual change in platelet count was calculated as the difference from base to end of follow-up divided by the years of follow-up. Spleen size and fibroscan measurements during follow-up were also analyzed. In 416 of the 529 patients from the total study, a paired base and follow-up platelet count was available. In 154/416 (37%) patients an SVR was observed. At base the distribution of the Ishak fibrosis score was not significant different between non-responders (NR) (Ishak 4, 5 and 6 : 23.7%, 20.6% and 55.7%) and patients with an SVR (Ishak 4, 5 and 6 : 29.2%, 15.6% and 55.2%), p=0.29. Median base platelet count was 149 (IQR 105-196) in NR and 158 (IQR 122-204) in SVR patients (p=0.093). The last available platelet count was measured after a median of 6.5 (IQR 4.6-9.1) years after the start of follow-up. The median annual platelet change was -3.2 (IQR -9.4- 1.4) in NR versus an increase of 7.9 (IQR 1.2-16.3) in SVR patients (p<0.001). The spleen size was assessed in a large subgroup of 340 patients at the end of follow-up. The median spleen size was 13.6 (IQR 11.8-16.0) cm in NR and 10.8 (IQR 9.5-11.9) cm in SVR patients, p<0.001. In a random subgroup of 75 NR and 65 SVR patients a fibroscan measurement at last follow-up was available. In NR the median fibroscan result was 17 (IQR 10-29) kPa versus 7 (IQR 5-11) kPa in SVR patients, p<0.001.

Conclusion: The results of our study show an improvement of platelet count and a smaller spleen size after achieving SVR in CHC patients with advanced fibrosis. This suggests a reduction in portal pressure probably attributable to a decrease in the level of liver fibrosis.

Presence of precore and core promoter mutants limits the probability of achieving a sustained virological response to peginterferon in HBeAg-positive chronic hepatitis B

M.J. Sonneveld[1], V.W.-S. Wong[2], S. Zeuzem[3], E.J. Heathcote[4], H.-Y. Chan[2] , S.D. Pas[5], G.L.H. Wong[2], B.E. Hansen[1,6], H.L.Y. Chan[2], H.L.A Janssen[1], Departments of [1]Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, the Netherlands; [2]Gastro-enterology and Hepatology, Prince of Wales Hospital, Hong Kong SAR, China; [3]Medical Clinic 1, Johann Wolfgang Goethe University Medical Center, Frankfurt, Germany; [4]Division of Gastroenterology, University of Toronto, Toronto, Canada, [5]Virology, Erasmus MC University Medical Center Rotterdam, The Netherlands and [6]Public Health, Erasmus MC University Medical Center Rotterdam, The Netherlands

Background: Peginterferon (PEG-IFN) may result in HBeAg seroconversion in HBeAg-positive patients, but HBVDNA undetectability and clearance of HBsAg is rarely achieved. Persistent replication after HBeAg clearance may be accounted for by presence of precore (PC) and basal core promoter (BCP) mutants. Methods: 263 HBeAg-positive patients treated with PEG-IFN±lamivudine for 52 weeks were classified at base as wildtype (WT) or non-WT (detectable mutants at PC or BCP by line-probe assay). Response was assessed at 6 months post-treatment and through long-term follow-up (LTFU, mean 3.1 years). Results: Patients harboured HBV genotypes A(28%), B(12%), C(24%), D(33%) or other(3%). PC and/or BCP mutants were detected in 70%, in varying frequencies across genotypes A-D. Patients with only WT had higher HBVDNA levels (8.49 versus 7.98 log IU/mL, p<0.001) and higher HBsAg levels (4.56 versus 4.12 log IU/mL, p<0.001), also after adjustment for HBV genotype. WT patients were more likely to achieve a combined response (HBeAg loss with HBVDNA <2,000 IU/mL), HBVDNA undetectability and HBsAg clearance at week 78 and at LTFU (figure), also after adjustment for HBV genotype, age and base HBVDNA and ALT (combined response: OR 2.55, 95%CI: 1.09 – 5.99, p=0.031; HBV DNA undetectability: OR 4.18, 95%CI: 1.32-13.23, p=0.012; HBsAg clearance: OR 5.48, 95% CI: 1.16 – 26.01, p=0.021). Among WT patients who achieved HBeAg clearance at week 78, 76% had undetectable HBVDNA and 56% achieved HBsAg clearance at LTFU (versus 21% and 10% in non-WT, p<0.001).
Conclusion: Absence of PC or BCP mutants at base is a strong predictor of response to PEG-IFN in HBeAg-positive chronic hepatitis B. Patients with non-A genotypes with detectable PC and/or BCP mutants have a low probability of response and are suboptimal candidates for PEG-IFN.

Costs and complications associated with treatment of chronic hepatitis C infection: results of a large cohort study

L.G. van Vlerken[1], K.J. van Erpecum[1], P.D. Siersema[1], M.G.H. van Oijen[1], [1]Department of Gastroenterology and Hepatology, University Medical Center Utrecht

Although current treatment of chronic hepatitis C (CHC), with peg-interferon and ribavirin, reached sustained viral response (SVR) rates of 50-80%, associated costs are considerable. With newer antiviral interventions, which can be used as add-on therapies, efficacy will probably increase. We aimed to assess costs associated with current treatment and progression of CHC infection, and use of adjuvant erythropoietin or G-CSF in a large cohort in the Netherlands, to serve as a threshold for future interventions. Data were collected from a computerized database of a health insurance company covering 1.2 million Dutch subjects. Patients with a diagnosis (DTC code) of viral hepatitis B or C and at least one combined prescription of peg-interferon and ribavirin between 1-1-2005 and 31-12-2010 were classified as treated CHC patients. All hepatitis C-related claims (prescription information and DTCs) over the entire study period were used to calculate costs during and after antiviral treatment. Patients who initiated treatment before 31-12-2008 were divided into three groups and outcomes were compared between these groups. Of the 530 identified treated CHC patients, 74% were male, mean age was 47 years, 12% were HIV-positive and 25% were in a methadone maintenance program. The number of antiviral treatments remained relatively stable over the last 6 years, with a dec in the most recent years. Fourteen patients (3%) were treated with erythropoietin during treatment (average €6,593 per patient) of which most were treated in the period 2008-2010. G-CSF was only prescribed in two patients (average €5,434 per patient). Both pharmacy costs and costs for active monitoring during treatment increased with treatment duration and averaged €7,316 and €207 per patient, respectively, for patients treated for 24 weeks and €17,276 and €338 per patient, respectively, for a treatment duration of 48 weeks. After 1,174 patient-years of follow-up, 19 patients (1.6 per 100 PYFU) developed compensated cirrhosis (n=7) or hepatic complications: decompensated cirrhosis (n=8), hepatocellular carcinoma (n=5) and liver transplantation (n=5). Complication-rate and costs during follow-up were higher in the 130 patients who prematurely discontinued treatment (2.3 per 100 PYFU, €713 per PYFU) compared to the 173 non-SVR patients (1.2 per 100 PYFU, €601 per PYFU) and 93 SVR patients (1.6 per 100 PYFU, €195 per PYFU).
Conclusion: CHC is associated with high costs in the Netherlands, mainly due to high costs of peg-interferon and ribavirin and progressive disease. Costs after treatment were considerably lower in patients with SVR compared to drop-outs and non-SVR patients.

HBsAg levels at six months post-treatment predict sustained response through long-term follow-up in HBeAg-positive patients treated with peginterferon alfa-2b

MJ Sonneveld ,M.J. Sonneveld[1], V. Rijckborst[1], R. Zoutendijk[1], G. Gerken[2], F. Tabak[3], T. Mach[4], C.A.B. Boucher[5], B.E. Hansen[1,6], H.L.A. Janssen[1], *Departments of [1]Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, the Netherlands; [2]Gastroenterology and Hepatology, University Essen, Essen, Germany; [3]Department of infectious diseases, Istanbul University Cerrahpasa Medical School, Istanbul, Turkey; [4]Gastroenterology and Hepatology, Collegium Medicum UJ, Krakow, Poland; [5]Virology, Erasmus MC University Medical Center, Rotterdam, the Netherlands and [6]Public Health, Erasmus MC University Medical Center, Rotterdam, The Netherlands*

Background: One year of treatment with peginterferon (PEG-IFN) may induce an immune response in a substantial proportion of HBeAg-positive chronic hepatitis B patients. Response to treatment is assessed at six months after treatment discontinuation, but relapse has also been observed beyond 6 months post-treatment. We investigated whether assessment of serum HBsAg levels may help predict long-term sustained response. Methods: Serum HBsAg was measured in samples taken at baseline, on-treatment and 6 months post-treatment (week 78) in 148 HBeAg-positive patients treated with PEG-IFN±lamivudine for 52 weeks with available data on long-term off-treatment follow-up (LTFU, mean duration 3.0 years). Combined response was defined as HBeAg loss with HBV DNA <10,000 copies/mL and was assessed at week 78 and at LTFU. Results: Patients were predominantly male (80%), of Caucasian ethnicity (71%), and harboured HBV genotypes A (29%), B (8%), C (18%), D (41%) or other (4%). A total of 26 (18%) patients achieved a combined response at week 78. Only 4 (15%) patients with a combined response at week 78 relapsed during LTFU. Patients with a relapse had higher HBsAg levels at week 78 than did patients who sustained the response (P<0.001). Importantly, none of the 18 patients with a combined response at week 78 with HBsAg levels <1,000 IU/mL experienced a relapse (PPV 100%, table), compared to 4 (50%) with HBsAg ≥1,000 IU/mL. Furthermore, 14 / 18 (78%) combined responders with HBsAg <1,000 IU/mL at week 78 were HBsAg negative at LTFU. Only 1 of 40 patients in the overall cohort without a dec of HBsAg at week 78 achieved a response at LTFU (NPV 98%, table), and none cleared HBsAg (NPV 100%).
Conclusion: HBsAg levels at 6 months post-treatment predict response through LTFU in HBeAg-positive patients treated with PEG-IFN. Patients with HBeAg loss and HBV DNA <10,000 copies/mL with concomitant HBsAg levels <1,000 IU/mL are unlikely to relapse and have a very high chance of HBsAg loss during 3 years of additional post-treatment follow-up. Patients who fail to achieve a dec in serum HBsAg levels by week 78 have little chance of achieving disease remission and retreatment with other agents should be considered.

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Peginterferon treatment reduces intrahepatic HBsAg and HBcAg expression in patients with HBeAg-negative chronic hepatitis B: Relation to serum HBsAg decline and long-term response

V. Rijckborst[1], P.E. Zondervan[2], Y. Cakaloglu[3], M. Raptopoulou-Gigi[4], F. Tabak[5], M. Akdogan[6], K. Simon[7], P. Ferenci[8], E. Verhey[1], B.E. Hansen[1,9], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Dept of Pathology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [3]Dept of Gastroenterohepatology, Istanbul University Medical School, Istanbul, Turkey, [4]Second Medical Department, Aristototle University of Thessaloniki, Thessaloniki, Greece, [5]Dept of Infectious Diseases, Istanbul University Cerrahpasa Medical School, Istanbul, Turkey, [6]Dept of Gastroenterology, Turkiye Yuksek Ihtisas Hospital, Ankara, Turkey, [7]Dept and Clinic of Infectious Diseases, Hepatology and Acquired Immune Deficiences, Medical University Wroclaw, Wroclaw, Poland, [8]Dept of Internal Medicine 3, Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria, [9]Dept of Biostatistics, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

We aimed to investigate whether peginterferon (PEG-IFN) therapy for hepatitis B e antigen (HBeAg-)negative chronic hepatitis B (CHB) reduces the intrahepatic expression of hepatitis B surface antigen (HBsAg) and core antigen (HBcAg) and how this correlates with treatment response and serum HBsAg decline. Sixty-seven HBeAg-negative patients, with liver biopsies taken at base of 48 weeks of PEG-IFN alfa-2a treatment (±ribavirin) and after 24 weeks of follow-up (week 72), were studied. The degree of intrahepatic HBsAg and HBcAg expression was ranked on a scale of 0 to 5 (0%, 1-10%, 11-25%, 26-50%, 51-75% and 76-100%). HBsAg in serum was quantified using the Abbott ARCHITECT assay. Most patients harbored hepatitis B virus (HBV) genotype D (81%), mean base serum HBsAg and HBV DNA were 3.9 and 6.0 log IU/ml, respectively. At week 72, 15 (22%) patients had a combined response (HBV DNA <2,000 IU/mL and normal alanine aminotransferase). Base intrahepatic HBcAg was negative in most (84%) patients, while HBsAg was expressed, in different degrees, in the vast majority (99%) of patients. The degree of HBsAg expression at base did not correlate with serum HBsAg or HBV DNA. At week 72 a significant dec in intrahepatic HBcAg ($p=0.035$) and HBsAg ($p<0.001$) compared to base was observed. Intrahepatic HBcAg and HBsAg staining was absent in 63 (94%) and 10 (15%) patients, respectively. In contrast to baseline, the degree of intrahepatic HBsAg staining at week 72 was correlated with serum HBsAg ($\rho=0.31$, $p=0.01$) and HBV DNA ($\rho=0.34$, $p=0.007$). Among the 10 patients without intrahepatic HBsAg expression at week 72, 6 (60%) achieved a combined response versus 9 (16%) of those who still expressed HBsAg ($p=0.006$). These patients also had a more profound serum HBsAg dec (1.7 vs 0.4 log IU/mL, $p=0.005$). Long-term follow-up (LTFU) data (mean duration 2.1 years) were available for 50 patients. Of 8 patients without intrahepatic HBsAg expression at week 72, 5 (63%) had a combined response at LTFU versus 3 (7%) of those with HBsAg expression ($p=0.001$). HBsAg was negative in 3 patients at LTFU of whom 2 had negative intrahepatic HBsAg at week 72.
Conclusion: PEG-IFN therapy for HBeAg-negative CHB results in a significant dec in intrahepatic HBsAg and HBcAg expression. HBsAg clearance from the liver on immune-histochemical staining is associated with a strong degree of serum HBsAg dec and good long-term outcome.

Common bile duct dilatation, an erroneous and misleading sign in the diagnostic approach of methadone users at the hepatology outpatient clinic

D.M. Hotho[1], J.N.L. Schouten[1], P. Taimr[1], B.E. Hansen[1, 2], H.L.A. Janssen[1], R. J. de Knegt[1], Departments of [1]Gastroenterology and Hepatology, [2]Public Health, Erasmus MC University Medical Center, Rotterdam, the Netherlands

Introduction: Methadone is widely used as maintenance therapy for drug users. Because chronic hepatitis C (HCV) infection is highly prevalent in these individuals, many need to undergo liver imaging. Narcotics have shown to increase sphincter of Oddi pressure and thereby induce bile duct dilatation. Common bile duct dilatation (CBDD) is a clinically significant finding that warrants exclusion of malignancy. However, the prevalence and clinical importance of CBDD in methadone users is unclear. Methods: From July 2010 until May 2011, we prospectively studied the diameter of the common bile duct (CBD) in all patients that underwent abdominal ultrasonography. CBDD was defined as a diameter >= 6.0 mm. When the CBD could not be measured, it was considered not dilated. Exclusion criteria were history of liver transplantation, cholecystectomy, diseases of the biliary tract, focal lesions or interventions that could have disturbed anatomy of liver, pancreas or biliary tract. Base characteristics were compared with Pearson chi-square and the independent samples t-test. With logistic regression analysis, associations of base characteristics with CBDD were studied. Results: 1183 patients underwent abdominal ultrasound, 628 were excluded. Of the remaining 552 patients 47 (9%) used methadone. Most frequent indications for imaging: hepatocellular carcinoma surveillance for cirrhosis (21%), hepatitis B (19%), HCV (19%). In 44/47 and 238/505 patients with and without methadone use, CBD diameter could be measured with a mean of 7.0 mm (95%C.I. 6.2-7.9) and 3.5 mm (95%C.I. 3.3-3.7) ($p<0.01$), respectively. Overall 36 of the 552 (7%) had CBDD. Among these patients 77% used methadone, versus 4% methadone use in those without CBDD at time of imaging ($p<0.01$). CBDD was present in 27/47 patients (57%) with and in 9/505 (1.8%) without methadone use. Currently additional imaging (endoscopic ultrasonography, magnetic resonance imaging, computed tomography) is being performed, until now, in the first 10 no explanation was found. In univariate analysis use of methadone ($p<0.01$, OR: 81.68 (32.98-202.28)), anti-depressants ($p<0.01$, OR: 4.52 (1.57-13.01)), benzodiazepines ($p<0.01$, OR: 8.41 (3.72-19.04)) and antipsychotics ($p<0.01$, OR: 9.75 (3.60-26.44)) were associated with CBDD. Multivariate analysis identified methadone use as the only covariate significantly associated with CBDD ($p<0.01$, OR: 91.74 (34.61-243.13)).
Conclusion: Asymptomatic CBDD is highly prevalent among methadone users. Because methadone users constitute an increasing part of the HCV patient population, this should be taken into account when interpreting abdominal imaging to prevent invasive investigation.

A new HBsAg/anti-HBs immune complex assay for prediction of treatment outcome in chronic hepatitis B patients

A. de Niet[1], U. Klause[2], B. Takkenberg[1], H. Zaaijer[4], T.C.[3], R. Petric[3], H. Reesink[1], [1]Academic Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, The Netherlands, [2]Roche Diagnostics, Penzberg, Germany, [3]Hoffmann La-Roche, Nutley, New Jersey, United States, [4]Academic Medical Center, department of Virology, Amsterdam, The Netherlands

Background and aim: Quantitation of HBsAg has become a predictor of response in the treatment of chronic hepatitis B (CHB) patients. The clinical relevance of HBsAg/anti-HBs immune complexes however has not been studied yet. A technique to determine HBsAg/anti-HBs immune complex formation has been developed as an early indication of host immune response. It is of interest to know the relationship between HBsAg, anti-HBs, complex levels and treatment outcome. Therefore serum samples of a selection of CHB patients treated with peg-interferon and adefovir for 48 weeks with 24-weeks of follow up were analyzed with this new assay. Methods: Samples of HBeAg positive (n=15) and negative (n=11) patients were analyzed for HBsAg, anti-HBs, and complex levels at 4 time points. (BL, wk12, 2-6 wks before and after HBsAg clearance). Patients that did not clear HBsAg served as matched controls. To determine complex levels an array-based assay was used (IMPACT - Immunological Multi-Parameter Chip Technology, Roche Diagnostics). HBsAg and anti-HBs levels were quantified using the same novel technology. Both assays were standardized using WHO-standard material as reference. Results: Four of 15 HBeAg positive and 5 of 11 HBeAg negative patients cleared HBsAg. Complex levels at BL and wk 12 did not differ between patients who cleared HBsAg and those who did not. A positive correlation was found between HBsAg and complex levels in HBeAg positive patients who achieved HBeAg seroconversion ($R=0.69$, $p<0.05$) or who lost HBsAg ($R=0.55$, $p=<0.05$) and in HBeAg negative patients who lost HBsAg ($R=0.64$, $P<0.05$). No correlation was found in patients with HBsAg or HBeAg persistence. No correlation was observed between complex levels and anti-HBs levels. In one HBeAg positive patient with HBsAg clearance, complex levels increased as HBsAg declined. In the other HBeAg positive and negative patients that cleared HBsAg, complex levels followed the same pattern of dec as HBsAg, with HBsAg negativity preceding undetectable HBsAg complex levels.
Conclusion: We analyzed for the first time the dynamics of HBsAg/anti-HBs immune complexes and the relation to treatment outcome in CHB patients. Complexes were present in all patients at baseline. Although, complex formation varied between patients, in general complex patterns followed the dec in HBsAg in patients with HBsAg clearance after therapy. Complexes became negative in all patients just weeks after HBsAg clearance, while free anti-HBs antibodies were not yet detectable. Further research is necessary to better understand the context of antigen-antibody complexes in CHB to determine its value for prediction of treatment outcome.

Matrixmetalloproteinase 2 genotype is associated with nonanastomotic biliary strictures after orthotopic liver transplantation

W. R. ten Hove[1], K. Sebib Korkmaz[1], S. op den Dries[2], B-J.F. de Rooij[1], B. van Hoek[1], R. J. Porte[2], J.J. van der Reijden[1], M.J. Coenraad[1], J. Dubbeld[3], D.W. Hommes[1], H.W. Verspaget[1], [1]Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, the Netherlands, [2]Department of Hepatobiliary Surgery and Liver Transplantation, University Medical Center Groningen, Groningen, the Netherlands, [3]Department of Surgery, Leiden University Medical Center, Leiden, the Netherlands

Nonanastomotic biliary strictures (NAS) are a serious complication after orthotopic liver transplantation (OLT). Matrix metalloproteinases (MMPs) are involved in connective tissue remodelling in chronic liver disease and complications after OLT. Our aim was to evaluate the relationship between MMP-2 and MMP-9 gene polymorphisms and NAS. MMP-2 (- 1306 C/T) and MMP-9 (- 1562 C/T) gene promoter polymorphisms were analysed in 314 recipient–donor combinations. Serum levels of these MMPs were determined in subgroups of patients as well. NAS were identified with various radiological imaging studies performed within 4 years after OLT and defined as any stricture, dilation or irregularity of the intra- or extrahepatic bile ducts of the liver graft followed by an intervention, after exclusion of hepatic artery thrombosis and anastomotic strictures. The average incidence of NAS was 15%. The major clinical risk factor for the development of NAS was PSC in the recipient. The presence of the MMP-2 CT genotype in donor and/or recipient was associated with a significantly higher incidence of NAS, up to 29% when both donor and recipient had the MMP-2 CT genotype (P = 0.003). In the multivariate analyses, pre-OLT PSC (hazard ratio 2.1, P = 0.02) and MMP-2 CT genotype (hazard ratio 3.5, P = 0.003) were found to be independent risk factors for the development of NAS after OLT. No obvious association was found between NAS and the MMP-9 genotype and serum levels of the MMPs.
Conclusion: MMP-2 CT genotype of donor and recipient is an independentrisk factor, in addition to PSC, for the development of NAS after OLT.

Elevated ALT is only Predictive for a sustained virological response to peginterferon in HBeAg-positive chronic hepatitis B patients with wildtype virus

B.E. Hansen[1,2], M.J. Sonneveld[1], V.W.-S. Wong[3], H.-Y. Chan[3], H.L.Y. Chan[3], H.L.A Janssen[1], Departments of [1]Gastroenterology and Hepatology, [2]Public Health, Erasmus MC University Medical Center, Rotterdam, the Netherlands, [3]Gastroenterology and Hepatology, Prince of Wales Hospital, Hong Kong SAR, China

Elevated levels of ALT may signify an active immune response against HBeAg positive chronic hepatitis B (CHB), and confer an increased probability of response to peg-interferon (PEG-IFN). Possibly, the presence of pre-core (PC) and core promoter (BCP) mutants may influence this association through a reduced susceptibility to an immune reaction against the virus.263 HBeAg-positive CHB patients were treated with PEG-IFN ± lamivudine for 52 weeks. Combined response (HBeAg loss with HBV DNA <2,000 IU/mL) was assessed at 6 months post-treatment. Patients were classified at base as wildtype (WT) or non-WT (detectable mutant at PC (at G1896) or BCP (at A1762 and G1764) by Inno-Lipa line-probe assay. All HBV genotypes were represented: A (28%), B (12%), C (24%) and D (33%). PC and/or BCP mutants were detected across all HBV genotypes, but were significantly ($p<0.001$) more present in genotype B (75%), C (88%) and D (90%) when compared to A (31%). ALT levels were similar across WT versus non-WT (3.7xULN versus 4.1xULN, $p=0.30$). Combined response to PEG-IFN was associated with presence of WT, genotype A, low HBVDNA and older age, whereas the effect of ALT proved to be significantly different depending on WT or non-WT ($p = 0.01$). Among WT patients ALT was a strong predictor (OR = 1.27, 95%CI: 1.02-1.57, $p=0.03$), while in the group of patients with non-WT the effect of ALT disappeared (OR = 0.96, 95%CI: 0.81-1.10, $p=0.62$).
Conclusion: The role of ALT as a predictor to response to PEG-IFN depends on WT/non-WT HBV. High ALT levels is a strong predictor of response to PEG-IFN in HBeAg-positive CHB patients with only WT virus, whereas ALT levels do not predict response to PEG-IFN in patients with detectable PC and/or BCP mutants.

Gastroprotective strategies in chronic NSAID users: A cost-effectiveness analysis comparing a single tablet formulation with individual component strategies

N.L. de Groot[1], P.D. Siersema[1], N.J. de Wit[2], B.M.R. Spiegel[3], M.G.H. van Oijen[1,3], [1]Dept. Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, the Netherlands, [2]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, the Netherlands, [3]University of California Los Angeles/Veterans Affairs Center for Outcomes Research and Education (CORE), Los Angeles, CA, United States of America

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used in the treatment of patients with chronic arthritis. However, NSAID-use is associated with a wide spectrum of gastrointestinal side effects, including dyspepsia, peptic ulcers and peptic ulcer bleeding. Co-therapy with proton pump inhibitors (PPI) is recommended for gastroprotection. However adherence to guidelines for prescribing PPI co-therapy and patient compliance to PPI is low. We evaluated the cost-effectiveness of various therapeutic strategies in the prevention of gastrointestinal complications taking compliance to PPI into account. A cost-utility analysis was performed comparing 1) NSAID monotherapy, 2) NSAID and PPI co-therapy and 3) single tablet NSAID plus PPI formulation, by using a Markov model. The model was run for a hypothetical 60 year old patient with chronic arthritis requiring long term NSAID-therapy. Estimates on clinical outcomes, utilities and costs were derived from medical literature. Our primary outcome was incremental cost per quality adjusted life year (QALY) gained (ICER). Sensitivity analyses were performed to assess the effect of relative risk of GI complications, PPI compliance rates, and costs of PPIs and single tablet formulation. In our base case patient, NSAID and PPI co-therapy therapy was dominant (more effective and less costly) over NSAID monotherapy. The incremental cost-effectiveness ratio (ICER) of the single tablet formulation was €85,568 per QALY compared to NSAID and PPI co-prescribed. In the sensitivity analysis, the single tablet formulation for the base case patient became “viable” (i.e. ICER < €20,000 per QALY gained) when the cost of PPI increased from €0.03 to €0.59 per tablet or when the costs of the single tablet formulation fell from €0.78 to €0.39 per tablet. PPI compliance did not influence the cost-effectiveness of the single tablet formulation in this base case patient. In high risk patients (patients with a 3x higher risk of GI-complications) the single tablet formulation was cost-effective (ICER €19,963). However, if PPI compliance increased beyond a threshold of 68%, NSAID and PPI co-prescription became more cost-effective.

Conclusion: NSAID and PPI co-therapy therapy is the preferred treatment strategy in chronic arthritis patients at average risk for gastrointestinal complications. A single tablet formulation is only cost-effective in high-risk patients with a low compliance to PPI therapy.

Bacterial infection risk in cirrhotic patients: role of proton pump inhibitors and intestinal permeability

L.G. van Vlerken[1], E.J. Huisman[1], B. van Hoek[2], W. Renooij[3], F.W.M. de Rooij[4], P.D. Siersema[1], K.J. van Erpecum[1], [1]Department of Gastroenterology and Hepatology, University Medical Center Utrecht, [2]Department of Gastroenterology and Hepatology, Leiden University Medical Center, [3]Department of Surgery, University Medical Center Utrecht, [4]Department of Internal Medicine, Erasmus Medical Center, Rotterdam, the Netherlands

Cirrhotic patients are at a considerable risk for bacterial infections, possibly by increased intestinal permeability and bacterial overgrowth. Proton pump inhibitors (PPIs) may increase infection risk. We aimed to explore the association between PPI use and risk of bacterial infections in cirrhotic patients and potential underlying mechanisms in complementary patient and animal models. In the rat model, bacterial overgrowth was determined in jejunal tissue after 6-weeks PPI treatment, gastrectomy plus esophagojejunostomy or control (each group 10 rats). In 84 consecutive cirrhotic outpatients, risk of bacterial infections was prospectively assessed and related to PPI use. In 12 cirrhotic patients and 9 healthy controls, intestinal permeability was determined by administration of polyethylene glycols of various molecular sizes. In jejunal tissue of rats treated with PPI or gastrectomy, bacterial overgrowth was more frequently detected compared to control rats: with particularly Clostridium perfringens and Bacteroides species being cultured in 100% and 33%, respectively of the gastrectomy group and both in 44% of the PPI group but not in the control group. Base Child-Pugh class of the cirrhotic patients was A, B or C in 58%, 35% and 7% respectively. Underlying causes of cirrhosis were viral hepatitis in 31%, alcohol in 25%, cholestatic liver disease in 18% and other in 26% of cases. Twenty-four patients (29%) had a bacterial infection during a median follow-up of 28 months: including spontaneous bacterial peritonitis (n=9), pneumonia (n=3), urinary tract infection (n=3), bacterial gastrointestinal infection (n=2), erysipelas (n=2) and other bacterial infections (n=5). Fifty-two patients (62%) used PPIs during the study period and in 82% of those no documented indication could be found. Although PPI users tended to develop infection more often than patients without PPI therapy (log-rank test 0.11), PPI use was not an independent predictor of bacterial infection (HR 1.2, 95%CI 0.5–3.0, p=0.72), after correction for Child-Pugh class (HR 3.6, 95%CI 1.5–8.7, p=0.004) and age (HR 1.05, 95%CI 1.01–1.09, p=0.02). In cirrhotic patients, 24-hour urinary recoveries of polyethylene glycols with the largest molecular sizes (1500 and 3350) were significantly higher compared to healthy controls.

Conclusion: Although in our animal model PPIs induced intestinal overgrowth, stage of liver disease rather than PPI use is the predominant factor determining infection risk in cirrhotic patients. Increased intestinal permeability may be a factor contributing to infection risk.

Increased risk of advanced neoplasia in IBD patients with atypical adenomas: a case control study

E. Mooiweer[1], F.D.M. van Schaik[1], M. van der Have[1], T.D.G. Belderbos[1], F.J.W. ten Kate[2], G.A. Offerhaus[2], M.E.I. Schipper[2], G. Dijkstra[3], M. Pierik[4], P.C.F. Stokkers[5], D.J. de Jong[6], D.W. Hommes[7], A.A. van Bodegraven[8], P.D. Siersema[1], M.G.H. van Oijen[1], B. Oldenburg[1] on behalf of the Dutch Initiative on Crohn and Colitis (ICC), [1]University Medical Center Utrecht, Department of Gastroenterology and Hepatology, [2]University Medical Center Utrecht, Department of Pathology, [3]University Medical Center Groningen, Department of Gastroenterology and Hepatology, [4]Academic Medical Center Maastricht, Department of Gastroenterology and Hepatology, [5]Academic Medical Center Amsterdam, Department of Gastroenterology and Hepatology, [6]Radboud University Nijmegen Medical Center, Department of Gastroenterology and Hepatology [7] Leiden University Medical Center, Department of Gastroenterology and Hepatology [8] VU University Medical Center Amster-dam, Department of Gastroenterology and Hepatology

Patients with inflammatory bowel disease (IBD) are at an increased risk of developing colorectal cancer (CRC). Previous studies suggested that colonic adenomas in colitis patients do not lead to a further increased risk of CRC during follow-up. The aim of the current study was to confirm these findings and compare the frequency of development of advanced neoplasia in IBD patients with adenomas to non-IBD patients with adenomas and IBD patients without adenomas. The nationwide pathology database (PALGA) was used to identify IBD patients with a histological diagnosis of adenoma (IBD-A), age-matched IBD patients without adenoma (IBD-noA) and patients with adenoma without IBD (noIBD-A) in 7 university hospitals in the Netherlands between 1995 and 2005. Medical charts, endoscopy, pathology and surgery reports were reviewed for adenoma characteristics and development of advanced neoplasia (high grade dysplasia or CRC) during follow-up. The endoscopic description of the adenomas reported in the endoscopy report were characterized as typical (solitary sessile or pedunculated) or atypical polyps (the latter comprising all other endoscopic descriptions including post-inflammatory polyps). Survival analysis was used to assess the frequency of development of advanced neoplasia in the 3 patient groups. A total of 110 IBD-A patients (73 UC), 123 IBD-noA patients (53 UC) and 180 noIBD-A patients were identified, with an overall mean duration of follow-up of 88 (SD ±41) months. Polypectomy was performed in 146 (81%) noIBD-A patients compared to 68 (61%) IBD-A patients ($p<0.01$). The cumulative incidence of advanced neoplasia was 18% for IBD-A, 5% for noIBD-A and 5% for IBD-noA ($p<0.01$, log-rank test). Base adenomas were endoscopically described as atypical polyps in 28 (25%) of IBD-A patients compared to 5 (3%) in noIBD-A patients ($p<0.01$). Within the IBD-A group, patients with an atypical polyp at base had a higher cumulative incidence of advanced neoplasia during follow-up (29% versus 12%, $p=0.03$). IBD patients with a histological diagnosis of adenoma have a significantly higher risk of developing advanced neoplasia during follow-up than adenoma patients without IBD and age-matched IBD patients without adenoma. This is associated with a higher prevalence of atypical polyps in IBD patients, apparently explaining the higher risk for advanced dysplasia in these patients.

The protease genes CYLD and USP40 are associated with Crohn's disease: results from a European Consortium

H.W. Verspaget[3], I. Cleynen[1], D. Lottaz[10], M. Artieda[2], M. Szczypiorska[2], P.L. Lakatos[4], F. Seibold[5], T. Ahmad[6], R.K. Weersma[7], S. Müller[5], A. Tordai[8], D.W. Hommes[3], K. Parnell[6], C. Wijmenga[7], K. van Steen[9], P. Rutgeerts[1], S. Vermeire[1], [1]KU Leuven – Gastroenterology, [2]Progenika Biopharma, S.A., [3]LUMC - Gastroenterology and Hepatology, [4]Semmelweiss University – Medicine, [5]Spitalnetz – Gastroenterology, [6]Peninsula Medical School, [7]UMC Groningen - Gastroenterology and Hepatology, [8]Hungarian National Blood Transfusion Service - Molecular Diagnostics, [9]Montefiore Institute - Electrical engineering and computer science, [10]Inselspital – Rheumatology

Proteases and protease inhibitors affect mucosal barrier integrity and therefore may be important players in the pathophysiology of Inflammatory Bowel Disease (IBD). We aimed to elucidate whether and which proteases/protease inhibitors are involved in IBD pathogenesis. Firstly, all relevant genetic studies in Crohn's disease (CD) and ulcerative colitis (UC), were prioritized to a comprehensive list of known associated proteases/ protease inhibitor genes. Secondly, the top-ranked genes for CD and UC were followed up in a genetic association study. A total of 185 haplotype tagging SNPs in 23 genes were genotyped in an exploratory cohort of 650 CD (CD1), 721 UC (UC1), and 542 healthy controls (HC1). Replication of SNPs with p-uncorrected<0.1 was performed in 4 independent cohorts: CD2-5 (n=634, 377, 432, and 227), UC2-5 (n=528, 290, 432, and 141), HC2-3 (n=900 and 354). Cases and controls were compared according to the additive model of inheritance using SNPassoc in R2.9.1. False Discovery Rate (FDR) correction was applied to correct for multiple testing.All SNPs showing significant associations (pFDR<0.05 are shown in Table 1. Strongest evidence was found in CD for CYLD (a cytoplasmic deubiquitinating enzyme), located 9kb downstream of CARD15, with 2 risk increasing and 2 protective SNPs. To test whether the signal seen in CYLD is driven by the well-established CARD15 association, logistic regression was performed. CARD15 data was available in 1135 CD and 674 HC. The final model included both CARD15 and CYLD, pointing to independent signals coming from both genes (pCYLDrs12324931<0.001, OR=2.1[1.6-2.8]; pCARD15rs2066845<0.001, OR=2.9 [1.8-4.8]; pCARD15rs2066847<0.001, OR=3.7[2.5-5.5]). Patients without CARD15 variants showed a significant association with rs12324931 (p=0.005, OR=2.9[1.3-6.6]). Another interesting outcome is the strong signals seen in CD for USP40 (a ubiquitin-specific peptidase), which is located near ATG16L1. Logistic regression analysis in CD1 (versus HC1), showed that rs10929178 and rs12472244 (USP40), and rs2241880 (ATG16L1) are independently associated with risk for CD (p=0.009, OR[0.6-0.9]; p=0.05, OR[0.8-1.0]; and p=0.009, OR[0.6-0.9] respectively).
Conclusion: We provide strong evidence for association of CYLD on 16q12.1 in CD patients, which is independent from CARD15. CYLD is a key negative regulator of NF-κB and has been shown to be significantly down-regulated in the intestine of IBD patients. Moreover, we identified several other genetic variants in protease/protease inhibitor genes which are implicated in either CD (USP40) or UC pathogenesis (DAG1, MST1, PSMB8), or both (APEH, USP3).

Long-term treatment results of rectovaginal fistulas in Crohn`s Disease, a descriptive study

U.S. Wiersema, P. Dewint, E.J. Kuipers, C.J. van der Woude, Erasmus Medisch Centrum, Dept. of Gastroenterology, The Netherlands.

The development of enterovaginal fistulas is a distressing complication of Crohn's Disease (CD), which may be difficult to treat. Limited series exist on treatment and outcome of these patients. Only the ACCENT II trial reported successful response to infliximab in patients with rectovaginal fistulas. Current treatment strategies include both pharmaceutical and surgical approaches. Our goal was to evaluate diagnostic approach and long-term pharmaceutical and surgical treatment results of enterovaginal fistulas in CD in a tertiary referral centre. Patients with CD and enterovaginal fistulas between 1983 and 2011 were included. Patient charts were reviewed for demographics, phenotype of CD according to the Montreal Classification, diagnosis, type and treatment of enterovaginal fistulas and clinical response. Twenty-eight patients were evaluated. The mean age was 49 years (range 27-77) and mean follow-up duration was 11 years (range 1-23). Location of enterovaginal fistulas was rectovaginal (89%) or enterovaginal (11%). The diagnosis enterovaginal fistula was made by either endoscopic ultrasound (29%), MRI (21%), exploration under anaesthesia (21%), endoscopy (11%) or fistulography (7%). Seventeen (61%) of the patients received TNF-alfa inhibitors, 10 (36%) received 6-mercaptopurine, 6 (22%) received methotrexate, 3 (11%) received cyclosporine, 3 (11%) received antibiotics and one patient (3%) received thalidomide. Nineteen (68%) of the patients received surgical treatment, 8 (28%) underwent a rectum amputation, 8 (28%) underwent a (sub)total colectomy with ileostomy and 3 (11%) underwent transsphincteric reconstruction. Complete remission of rectovaginal fistulas, defined as permanent absence of vaginal gas or feces and absence of abscess was accomplished in 5 patients (17%).
Conclusion: In our series, the long-term response to both medical treatment and surgical treatment of CD-associated enterovaginal fistulas was disappointing. A large percentage of females still had draining fistulas.No standardised diagnostic or therapeutic pathway is available yet for enterovaginal fistulas in CD, therefore we feel that further studies are urgently needed tot evaluate and optimise multidisciplinary diagnostic and treatment strategies of enterovaginal fistulas in CD.

High rates of non-adherence for anti-TNF treatment in Crohn's disease: results of a systematic review

M.M.J. Singendonk, H.H. Fidder, P.D. Siersema, B. Oldenburg, M.G.H. van Oijen, Gastroenterology, University Medical Center, Utrecht, the Netherlands

Anti-TNF treatment has been proved effective in the treatment of luminal and fistulizing Crohn's disease. Adequate adherence is pivotal for a successful outcome of treatment, since non-adherence to drug regimens contributes to inadequate response and failure of treatment. Moreover, it has been shown that non-adherence is associated with higher healthcare costs. However, data on non-adherence in Crohn's disease is scant and published studies show a great variation in non-adherence rates. The aim of our study was to investigate non-adherence rates in anti-TNF treatment in Crohn's disease by systematic review of published medical literature. We conducted a structured search of Pubmed to identify relevant English-language publications involving anti-TNF treatment in adult patients with Crohn's disease that provided data about non-adherence rates over the last 10 years. As definitions vary among studies, we used the definitions used by the authors in order to calculate the sample size-weighted pooled proportions of patients non-adherent to therapy and we compared non-adherence rates between adalimumab and infliximab. Out of 75 identified titles, we selected three studies involving a total of 953 patients that met our predefined in- and exclusion criteria. Two studies (total number of patients n=845) reported non-adherence in Crohn's disease patients on infliximab, and one on adalimumab (n=108). The calculated overall sample size-weighted pooled proportion for non-adherence was 30% (95% CI 27%-33%). The non-adherence rate for adalimumab (45%) was statistically significantly higher compared to infliximab (28%), with a relative risk of 1.61 (95% CI 1.27-2.03).
Conclusion: One-third of Crohn's disease patients treated with anti-TNF treatment were non-adherent. Although the different routes and schedules of administration between infliximab and adalimumab may impede a direct comparison, we found higher non-adherence rates with adalimumab therapy.

A novel prognostic FISH biomarker assay for Barrett's esophagus (BE): Results from a long term prospective 5-year follow up study (FIBAR I)

A.F. Pacha[1,2], A.M. Rygiel[1,2], W.M. Rosmolen[1], B. Elzer[1], H. Verhulst[1], M. Visser[1], F.J.W. ten Kate[3], M. Dijkgraaf[4], J.J. Bergman[1,11], K.K. Krishnadath[1,2,11], [1]Department of Gastro-enterology and Hepatology, [2]Center for Experimental Molecular Medicine, [3]Department of Pathology, [4]Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, Amsterdam, The Netherlands

Surveillance programs based on biopsy and histopathological staging of dysplasia for identifying BE patients at risk are inefficient. We applied a novel assay assessing biomarkers on brush cytology by using DNA flouresence in situ hybridisation (FISH) for the tumor suppresors p16 (9p21), p53 (17p13.1) and for aneuploidy (aneusomy for Cep17 & Cep 7). The aim of this study was to determine the prognostic value of this novel assay in a 5 year prospective FU study of a BE surveillance cohort. From 2002 until dec 2005, all BE patients with No dysplasia/indefinite for dysplasia (ND/IND), or LGD and no previous treatment for BE were included. At index endoscopy (t=0) biopsies were taken following ACG guidelines and brush cytology performed. Patients than underwent prospective surveillance. Histology and FISH on the cytology samples were performed in a blinded manner. Diagnosis of LGD or HGD was confirmed by a panel of expert pathologists. The DNA FISH assay tested positive when any of the markers were abnormal. The endpoints were histological progression of ND/IND into LGD/HGD/EAC, or LGD into HGD/EAC, or a FU of60 months. In this study, 135 patients reached an endpoint or an average of 58 months of FU, 24 either died or were lost to FU and were excluded. Of the 135, 112 were males (83%). Mean age at entry was 61(SD±12). Mean Barrett length was 3.6cm (SD±2.5). ND/IND was seen in 127 (95%), while 8 (5%) had LGD at t=0. 11 progressed from ND/IND to LGD or HGD, while 2 progressed from LGD to HGD. The FISH assay tested positive in 42/135 (32%). Of the marker positive group 11/42 (28%) progressed, versus 2/93 (2%) of the marker negatives. Kaplan Meier curves showed that progression intervals were significantly shorter in the marker positive group versus the negative group (p=0.02). A Cox regression model showed that a positive test correlated with an OR of 5.5 (p=0.002) to progress.
Conclusion: In this prospective long term FU study we proved that a novel FISH biomarker assay on cytology specimens of BE patients correlated with a 5.5 increased risk for progression. Validation of these markers is currently being performed in long term FU study of an unselected cohort of BE patients. This assay may serve as a useful tool to improve risk stratification of BE patients and increase the efficacy of surveillance.

The GerdQ instrument identifies a large proportion of high impact GERD in website visitors; and reveals high prevalence of partial responsiveness in PPI users

M.M. Tielemans[1,2], J.B.M.J. Jansen[3], M.G.H. van Oijen[2], [1]Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [2]University Medical Centre Utrecht, Utrecht, The Netherlands, [3]Elkerliek Hospital, Helmond, The Netherlands

Many persons with GERD symptoms do not visit a general practitioner but search the internet for information and treatment. PPI users with persistent GERD symptoms, also infrequently visit their general practitioner and real-life data regarding PPI efficacy are scarce. The GerdQ is a self-assessment questionnaire that can be used for the diagnosis and follow-up of gastroesophageal reflux disease (GERD), and measures both symptoms and impact of symptoms on person's daily life. The aim of this study was to study: 1) the prevalence of GERD, 2) the prevalence of partial responsiveness in PPI users, and 3) the association with health-related quality of life. Visitors (18-79 years of age) of a website with GERD information and education between December 2008 and March 2011, were invited to fill in the GerdQ instrument. The GerdQ contains six questions, with a score ranging from 0 to 3 for every question. Respondents who scored ≥8 were asked to complete the Quality of Life in Reflux and Dyspepsia (QOLRAD) questionnaire. GERD with high impact was present if respondents without PPI use scored ≥3 on GerdQ items regarding sleep disturbance and/ or over-the-counter (OTC) medication use. In PPI users, partial responsiveness was defined as reporting more than one day per week either 1) heartburn; 2) regurgitation; 3) sleep disturbance; or 4) over-the-counter (OTC) medication use, all during the preceding week. QOLRAD scores were compared in non-PPI using respondents with high vs. low impact and with adequate relief vs. partial responsiveness in PPI users. A total of 70,307 visitors completed the GerdQ, of whom 56,179 (80%) did not use PPIs. A total of 33,704 (60%) scored ≥8, of which 51% and 49% reported high and low impact, respectively. In PPI users 12,012 (85%) reported partial responsiveness. Mean QOLRAD score was 4.15 (SD=1.14) for non-PPI users with GERD with high impact, and 4.77 (SD=0.90) for GERD with low impact ($p< 0.01$). Mean QOLRAD score in PPI users was 3.62 (SD=1.26) for partial responders and 4.85 (SD=1.22) for adequate responders ($p<0.01$). The statistically significant difference was consistently present over all domains: physical/ social functioning, sleep disturbance, emotional distress, vitality, food/ drink problems.
Conclusion: The GerdQ instrument was completed by over 70,000 website visitors, of which 60% of non-PPI users reported a score associated with presence of GERD. The majority of PPI users reported partial responsiveness and this was associated with a decreased health-related quality of life.

All low dose aspirin users benefit from gastroprotection: results of a cost-utility analysis of competing strategies

H.G.M. van Haalen[1], N.L. de Groot[1], J. Jaspers Focks[2], P.D. Siersema[1], M.G.H. van Oijen[1], [1]Department of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, the Netherlands, [2]Department of Cardiology, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands

Gastroprotection by proton pump inhibitors (PPIs) is recommended for patients with upper gastrointestinal (UGI) risk factors using low-dose aspirin for cardiovascular prevention. Yet patient compliance to PPIs is low, which increases patients' susceptibility for UGI complications, thereby increasing non-compliance to low-dose aspirin. In view of decreasing PPI costs due to generic availability and the introduction of aspirin+PPI single tablet formulations, we determined the cost-utility of gastroprotective strategies in low-dose aspirin users considering both aspirin and PPI compliance. A Markov model was constructed to compare low-dose aspirin monotherapy to standard PPI cotherapy and aspirin+PPI single tablet formulation. The risk of acute coronary syndrome (ACS), UGI bleeding and dyspepsia was modeled as a function of compliance and the relative risk of the medication. Input parameters were based on published medical literature. Costs and Quality Adjusted Life Years (QALYs) were evaluated for primary (10-year ACS risk of 10%) and secondary prevention of ACS for a 60-year old male with a variable base risk of UGI bleeding. Predefined sensitivity analyses were performed on 1) costs of single tablet formulation, 2) costs of PPI and 3) compliance to PPI. We determined a cost-effectiveness threshold of €20,000 per QALY gained following national guidelines. For a patient with average GI risk, standard PPI cotherapy was cost-effective in both primary and secondary prevention of ACS, with incremental cost-effectiveness ratios (ICERs) of €2240 and €587 per QALY, respectively. In secondary prevention, the ICER of the single tablet formulation was €29,736 per QALY compared to standard PPI co-therapy, while a 3-fold higher base risk of UGI complications resulted in an ICER of €19,877 per QALY. Sensitivity analyses for the average-risk patient showed that the single tablet formulation is cost-effective in secondary prevention of ACS in case 1) the single tablet formulation costs less than €0.43; 2) PPI costs more than €0.14 per dose; or 3) average PPI compliance is below 41%. In primary prevention, these thresholds were €0.33, €0.24 and 17%, respectively.

Conclusion: PPI cotherapy is cost-effective in all patients taking low dose aspirin for primary and secondary prevention of ACS. In secondary prevention, a single tablet formulation is the most favorable dosage form in patients with elevated risk for UGI bleeding or moderate PPI compliance.

Acute esophageal food bolus impaction. A prospective study

H. van der Sluis[1], E.J. van der Wouden[1], F.C.P. Moll[2], M.G. Havenith[2], M.A.C. Meijssen[1], J. Vecht[1].,Dept of Gastroenterology and Hepatology[1], Dept of Pathology[2], Isala clinics, Zwolle

Acute esophageal food bolus impaction (AEFBI) has an estimated incidence of 13 episodes per 100.000. This makes AEFBI one of the most common endoscopic emergencies in gastroenterology. To date, AEFBI has been studied mainly retrospectively. In addition, there has been a growing interest in food bolus obstruction caused by eosinophilic esophagitis. The aim of this study was to determine the etiology of AEFBI in a prospective manner. New consecutive patients (≥18yrs) who needed endoscopic intervention because of AEFBI were evaluated. Patients were excluded when analysis of food bolus impaction already took place in the past or when evaluation was not possible due to co-morbidity. Included patients underwent a second esophagogastroduodenoscopy in order to inspect the esophagus. During endoscopy a minimum of five biopsies were randomly taken from the esophageal squamous epithelium and examined by two independent pathologists. AEFBI was considered to be caused by eosinophilic esophagitis if the number of eosinophils was equal to or higher than 20 per high-power field. When AEFBI was insufficiently explained by endoscopy, additional analysis by esophageal manometry and a barium esophagogram was performed. From October 2009 until June 2011 58 patients needed endoscopic intervention because of AEFBI. All patients were successfully treated. 11 patients were excluded from evaluation (4 patients because they were previously analyzed for esophageal food impaction, 5 patients because of co-morbidity and 2 patients did not show up for the evaluation). 18 of the 47 remaining patients were female, 29 patients were male, mean age was 66 years (range 18-93). A final diagnosis was made in 45 patients (96%). In 29 patients (62%) AEFBI was caused by gastroesophageal reflux disease with or without a peptic stenosis. A motility disorder was found in 5 patients (11%), candida esophagitis in 5 patients (11%), radiation-induced stenosis in 3 patients (6%) and denture-related problems in 1 patient (2%). In two patients (4%) AEFBI was caused by an eosinophilic esophagitis. None of the patients had an esophageal malignancy.
Conclusion: Acute esophageal food bolus impaction indicates underlying esophageal pathology in most patients, which can be found by additional workup. In this prospective study most esophageal food bolus obstructions were caused by gastroesophageal reflux disease with or without a peptic stenosis. Eosinophilic esophagitis remains a rare cause of AEFBI.

Psychological, physical and nutritional impact of prophylactic gastrectomy in CDH1 mutation carries and comparison with curative gastrectomy for gastric cancer

I. Kluijt[1], E. Bleiker[1], M.G.E.M. Ausems[2], A. Hartig[1], M. de Boer[1], R. van Hillegersberg[2], E. van Riel[2], R.H. Sijmons[3], L. Spruijt[4], M. Oldenrode-Berends[3], N. Hoogerbrugge[4], J.T. Plukker[3], A. Cats[1], [1]The Netherlands Cancer Institute Amsterdam, [2]University Medical Centre Utrecht, [3]University Medical Center Groningen, [4]Radboud University Medical Centre Nijmegen

Carriers of a CDH1 gene mutation have a risk of up to 80% to develop gastric cancer (GC). Prophylactic total gastrectomy is offered to mutation carriers to prevent invasive GC development. In this usually young and asymptomatic population, however, the psychosocial, physical and nutritional consequences are largely unknown. Therefore, the aim of this study was to investigate the impact of preventive gastrectomy in CDH1 mutation carriers. Questionnaires were sent to individuals with a CDH1 gene mutation, who had undergone a prophylactic gastrectomy. Disease-free sporadic GC patients, who had undergone a total gastrectomy 2-5 years earlier also received these questionnaires and served as a comparison group. The questionnaire assessed psychosocial (quality of life [QLQ C30, STO22], anxiety and depression [HADS], social impairment), physical (fatigue [CIS]) and nutritional variables. Of the 21 CDH1 carriers who underwent a prophylactic gastrectomy, 20 (95%) participated (45% males). Of 23 addressed GC patients, 20 (87%) participated (70% males). Mean age was 41 years (range 20-68 years) and 59 years (range 37-74), respectively. Mean time since gastrectomy was 34 months (SD= 18 months, range 5-63 months) and 47 months (SD= 22 months; range 15-80 months), respectively. The levels of quality of life, anxiety, depression, and fatigue as reported by the two groups (preventive vs. curative resection) did not differ significantly. All together, 48% reported complaints about fatigue (28% had severe fatigue), and 18-48% of the patients reported (severe) impairment in daily activities (work, hobbies, personal relationships). Mean ±SD weight loss of 15% ± 6% was found. Food and drink products that patients were unable to consume were: dairy products (73%), fried products (25%), and soft drinks (13%).Conclusions. Following total gastrectomy, patients experience fatigue, impairment of everyday life, and weight loss. Patients with a preventive gastrectomy (carriers) did not differ from cancer patients treated by a curative gastrectomy. However, complaints varied widely among participants.

Evaluation of gastrectomy in patients with delayedgastric emptying after antireflux surgery or large hiatal hernia repair

A. Gerritsen[1], E.J.B. Furnée[1], H.G. Gooszen[2], E.J. Hazebroek[1,3], [1]University Medical Centre Utrecht, Utrecht, The Netherlands, [2]University Medical Centre St Radboud, Nijmegen, The Netherlands, [3]St. Antonius Hospital, Nieuwegein, The Netherlands

Revisional antireflux surgery and large hiatal hernia repair requires extensive dissection around the gastro-oesophageal junction, which may lead to vagal nerve damage and interference with the physiological function of the stomach. As a result, troublesome symptoms due to delayed gastric emptying may occur, eventually requiring gastrectomy in a subset of patients. The aim of this study was to evaluate the role and symptomatic outcome of gastrectomy for symptoms of severely delayed gastric emptying after redo antireflux surgery or large hiatal hernia repair.Eleven patients who underwent gastrectomy for delayed gastric emptying after one or more failed antireflux procedures or repair of a large hiatal hernia between 1990 and 2010 were identified. Pre- and operative data, including the results of gastricemptying studies, were retrospectively collected. Standardized questionnaires to evaluate symptomatic outcome after gastric-tomy were sent to all patients. Eleven patients were included. The primary intervention was Nissen fundoplication in nine patients, Toupet fundoplication in one and cruraplasty in another, for refractory gastro-oesophageal refluxdisease in five and a symptomatic large hiatal hernia in six patients. Before gastrectomy, seven patients underwent one or more redo procedures after the primary intervention for recurrent gastro-oesophageal reflux disease or troublesome dysphagia. Ten patients had severely delayed gastric emptying dual isotope studies. Gastrectomy was partial in four patients, subtotal in six and total in one. Mean (±SD) duration of operation was 144 ± 37 minutes. The mean hospital stay was 12 ± 5 days. One patient had a minor complication during the postoperative period. After a mean duration of 102 ± 59 months, nine patients were available for symptomatic follow-up, as one patient died during the follow-up period which was not related to gastrectomy and one patient refused collaboration. Eight patients experienced daily symptoms related to dumping at follow-up. Mean general quality of life was increased from 3.8 ± 2.2 before gastrectomy to 5.4 ± 1.8 at follow-up. Eight patients reported gastrectomy as worthwhile and if given the choice, five patients would undergo the same procedure again, three were in doubt and one would disagree.
Conclusion: Gastrectomy after previous antireflux surgery or large hiatal hernia repair is safe with the potential to add to quality of life. Although upper gastrointestinal symptoms tend to persist, gastrectomy can be considered a reasonable, last resort surgical option for disabling upper gastrointestinal symptoms after antireflux surgery or large hiatal hernia repair.

Fluoroscopy prior to gastrostomy tube placement predicts success of percutaneous endoscopic procedure in high-risk children

J.M. Pruijsen, A. de Bruin, G. Sekema, P.F. van Rheenen,Beatrix Children's Hospital, University Medical Center Groningen, the Netherlands

Percutaneous endoscopic gastrostomy (PEG) tube placement has been shown to be a safe and effective procedure for children with feeding problems who need long-term tube feeding. In our hospital PEG insertions are performed in the endoscopy unit under general anaesthesia. In case of unexpected failure of endoscopic insertion, the child needs to be rescheduled for a surgical procedure in the operating room. We evaluated the efficiency of using fluoroscopy in the preparatory phase to predict the success of the percutaneous endoscopic procedure and avoid rescheduling. We performed a single center cohort study in a tertiary care hospital in the Netherlands. Eligible patients were identified from our gastrostomy care registry and had their tubes inserted between January 2000 and December 2010. They were included in the analysis when fluoroscopy was performed in the preparatory phase prior to tube insertion. Fluoroscopy was considered normal when the stomach projected distal to the costal margin. Primary endpoint was the success rate of PEG insertion. Multivariate logistic regression analysis was used to identify factors associated with PEG insertion failure. We included 304 children (age range 0.3 to 18.1 years) and PEG tube insertion was successful in 288 (95%). Probability of success after normal fluoroscopy was 97% (95% confidence interval 95 to 99%), and after abnormal fluoroscopy 64% (53 to 84%). In a multivariate logistic regression model the major risk factors for PEG insertion failure were abnormal fluoroscopy (Odds ratio 23.1 [95% confidence interval 6.5 to 82.0]), previous abdominal surgery (OR 6.0 [1.5 to 23.1]), and neurological impairment (OR 4.4 [1.3 to 15.82]). The probability of successful PEG tube insertion in high-risk children with an abnormal fluoroscopy was 29% (0 to 65%).
Conclusion: The strategy of performing fluoroscopy in children with previous abdominal surgery or neurological impairments enables the endoscopist to identify those that should primarily undergo surgical gastrostomy placement.

Sarcopenic obesity affects adverse outcome after cardiac surgery

M. Visser[1, 2] /L.M.W. van Venrooij[1, 3], L. Vulperhorst[4], R. de Vos[5], W. Wisselink[2], P.A.M. van Leeuwen[2], B.A.J.M. de Mol[1], [1]Cardiothoracic Surgery, Academic Medical Center University of Amsterdam, [2]Surgery, VU University Medical Center, [3]Dietetics, Academic Medical Center University of Amsterdam, [4]Institute of Health Sciences, Faculty Earth and Life Sciences, VU University, [5]Clinical Epidemiology and Biostatistics, Academic Medical Center University of Amsterdam, Amsterdam, Netherlands

Both undernutrition - low fat free mass (FFM) - and obesity - high fat mass (FM) - have been associated with adverse outcome in cardiac surgical patients. However, if there is an additional effect of these risk factors present at the same time, i.e. sarcopenic obesity (SO), is unknown. Therefore, the aim of our study was to assess the association between SO and adverse outcome after cardiac surgery. In this prospective cohort of patients undergoing elective open-heart surgery, preoperative FFM and FM measured using bioelectrical impedance spectroscopy were established on hospital admission and linked to postoperative adverse outcomes. A total of 325 patients were included. SO, present in 2.2%, was associated with postoperative infections (28.2% vs. 5.3%, adj.OR: 7.9; 95%CI: 1.2-54.1; p = 0.04). Also a low FFM index (FFMI; kg/m^2) was associated with postoperative infections (18.5% vs. 4.7%, adj.OR: 6.6; 95%CI: 1.7-25.2; p = 0.01). A high FM index (FMI; kg/m^2) was not associated with any parameter of adverse outcome.
Conclusion: SO is associated with an increased occurrence of adverse outcome after cardiac surgery. Our results suggest an additional risk of a low FFMI and high FMI present at the same time. We advocate determining body composition in cardiac surgical patients to classify and treat undernourished patients, in particular those who are also obese.

Increased gastroduodenal permeability in human obesity

F.J. Verdam[1], C. de Jonge[1], H. van Eijk[1], K. van Wijck[1], N. Bouvy[1], J.W. Greve[2], W.A. Buurman[1], S.S. Rensen[1], [1]Department of General Surgery, NUTRIM, Maastricht University Medical Centre, Maastricht the Netherlands, [2]Department of General Surgery, Atrium Medical Centre, Heerlen, the Netherlands

Increased intestinal permeability in obese mouse models is related to glucose intolerance, body weight gain, and systemic inflammation. This led us to investigate the relation between intestinal permeability, co-morbidities, and systemic and intestinal inflammation in obese and lean subjects. Fasting blood samples and fecal samples were collected of 28 subjects (BMI 18.6-60.3kg/m^2). Intestinal permeability was assessed after an ibuprofen challenge by means of an oral multi sugar test containing sucrose, lactulose, erythritol, sucralose, and L-rhamnose. Gastro-duodenal permeability (sucrose), and permeability of the small (lactulose/rhamnose) and large intestine (sucralose/erythritol) was examined. Plasma markers for systemic inflammation (CRP), for insulin resistance (glucose, insulin, HbA_{1c}) and for enterocyte turnover as reflected by intestinal fatty acid binding protein (IFABP) were determined. Fecal calprotectin was used as parameter of intestinal inflammation. Data are presented as mean±SEM. Gastroduodenal permeability, as reflected by urinary sucrose concentrations after one hour, was twice as high in obese subjects compared to lean subjects (4.1±0.7µmol vs. 1.9±0.3µmol, $p<0.05$). At this early time point, urinary rhamnose excretion was also increased in obese versus lean subjects (73±11µmol vs. 39±8.1µmol, $p<0.05$). In contrast, after five hours, rhamnose excretion was similar in both groups (276±52µmol vs. 327±61µmol, $p=0.68$). These data led to an increased lactulose/rhamnose ratio in lean versus obese subjects after one hour (0.06±0.01 vs. 0.02±0.01; $p<0.05$), whereas this ratio was similar after five hours (0.06±0.02 vs. 0.05±0.01; $p=0.9$). At both time points, permeability of the small intestine was positively correlated with enterocyte turnover as reflected by plasma levels of intestinal fatty acid binding protein (for both, $R_s=0.5$, $p<0.05$). Permeability of the large intestine, as reflected by the sucralose/erythritol ratio after five hours, showed similar results for both groups (0.03±0.01 vs. 0.04±0.01; $p=0.65$). Fecal calprotectin was detected more frequently in obese versus lean subjects (n=9 vs 2, $p<0.05$), and ranged from 80-570ng/ml.

Conclusion: These data indicate an increased gastroduodenal permeability in obese subjects. Moreover, our data show that obese individuals have an enhanced permeability for rhamnose in their proximal small intestine, as reflected by an increased urinary excretion after one hour, whereas total urinary excretion was similar compared to lean individuals. There was no statistically significant difference in large intestinal permeability between the groups.

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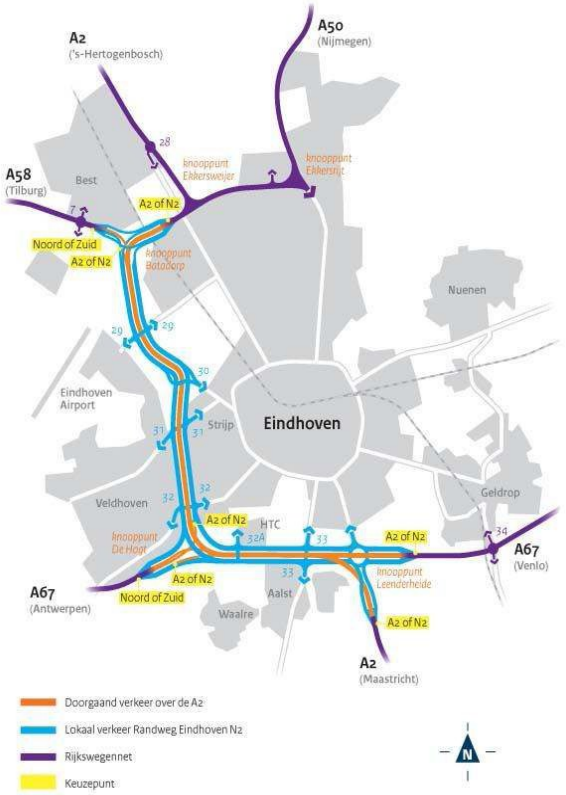

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