Samenvatting van het proefschrift
Özenç Uludağ

"Sacral neuromodulation in patients with faecal incontinence"

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In the present thesis, the applicability, safety and feasibility of sacral neuromodulation (SNM) as a treatment for faecal incontinence is summarized. After a decade of experience with SNM in our hospital we can conclude that SNM is an effective and in the meanwhile well-established treatment for functional bowel disorders, especially in patients with faecal incontinence.[1-3] The numerous international publications on the subject not only support our findings in patients with faecal incontinence but have also paved the way for SNM in the surgical treatment of faecal incontinence.[4-6] The traditional treatment of faecal incontinence solely focusing on anal sphincter dysfunction has been abandoned and the focus has shifted towards a more complex approach.

Chapter 1 provides an overview of the literature on faecal incontinence and its treatment options. Faecal incontinence is a common but complex problem with high costs on the patient and the community. It is a psychologically devastating and socially incapacitating condition that can have profound effects on patient well being.
Adequate clinical, physiological and structural assessment through advanced imaging techniques is fundamental for assessing the cause and degree of the incontinence. Both conservative therapies (medicinal therapy, biofeedback training and colonic irrigation) and surgical interventions (sphincter repair, neosphincter formation, artificial bowel sphincter, sacral neuromodulation or formation of a stoma) are therapeutic options. However, the choice of treatment is mostly dependent on available knowledge and existing facilities.

In Chapter 2 the outcome of our first seventy five patients treated with SNM are presented. Incontinence was objectified by completion of a 3-weeks

bowel habits diary that patients also completed during ambulatory electrode stimulation at the S3 or S4 foramen. Reduction of at least 50 percent in incontinence episodes or days per week qualified patients for permanent implantation. Sixty six female and nine male patients were treated; the average age was 52 years (26-75). Sixty two patients (83%) had improved continence during trial screening. Median incontinence episodes per week decreased from 7.5 to 0.67 ($P<0.01$), median incontinence days per week from 4.0 to 0.5 ($P<0.01$). The symptomatic response remained unchanged in the fifty patients who received an implantation of a permanent electrode and pacemaker. However, after a median follow-up of 12 months this effect could only be sustained in forty eight patients. SNM proved to be a feasible treatment option for faecal incontinence in patients with structurally intact sphincters.

In Chapter 3 the effect of SNM on the rectum was evaluated by barostat measurements in patients with faecal incontinence who qualified for SNM. Fifteen consecutive patients were asked to undergo barostat measurements before and during sacral neuromodulation. An isobaric phasic distension protocol was used and patients were asked to report rectal filling sensations: first sensation (FS), earliest urge to defaecate (EUD) and irresistible, painful urge to defaecate (maximum tolerable volume (MTV)). Rectal wall tension and compliance could be calculated from these recordings. During stimulation median volume thresholds decreased significantly ($p<0.01$) for FS: 98.1 vs. 44.2 ml, EUD: 132.3 vs. 82.8 ml and MTV: 205.8 vs. 162.8 ml. Pressure thresholds tended to be lower for all filling sensations and median rectal wall tensions decreased significantly ($p<0.01$) for all filling sensations. There was no significant difference in compliance before and during stimulation. Sacral neuromodulation does affect rectal sensory perception, but it remains unclear if the success of SNM is explained solely by its effect on the rectum.

Chapter 4 describes the effect of SNM on the rectoanal angle in patients with faecal incontinence. In twelve consecutive patients who qualified for SNM a defaecography study was performed before SNM and two further studies at six months after permanent implant, one during stimulation and one with the pacemaker off. The rectoanal angle decreased during rest, squeeze and Valsalva's manoeuvre and a slight increase in rectoanal angle was seen during defaecation. However, the differences did however not reach statistical significance.

In Chapter 5 the effect of SNM on bowel frequency and (segmental) colonic transit time is described. Fourteen consecutive patients with faecal incontinence who qualified for permanent SNM underwent a colon transit study before and one month after permanent implant. The median number of bowel movements per week decreased from 14.7(6.7-41.7) to 10.0(3.7-22.7)($p=0.005$) during trial screening and to 10.0(6.0-24.3)($p=0.008$) during permanent stimulation. No significant changes were found before and during stimulation in both segmental (right colon 6(0-25) vs. 5(0-16) hours,

left colon 2(0-29) vs. 4(0-45) hours and recto sigmoid 7(28) vs. 8(0-23) hours) and total colonic transit time (17(1-65) vs. 25(0-67) hours). Although no significant change occurred in (segmental) colonic transit times a significant decrease of bowel movements was seen in patients with faecal incontinence during SNM.

Chapter 6 evaluates the long-term outcome and quality of life in patients with faecal incontinence treated with permanent SNM. Data from our first fifty patients who qualified for permanent SNM were included in this study. A three-week bowel habits diary assessed efficacy, and the Quality of life scores were obtained by the faecal incontinence quality of life questionnaire (FIQOL) and the standard short form health survey questionnaire (SF-36). With a median follow-up of 7.1 years this is the longest reported follow-up in a substantial group of patients treated by SNM hitherto. Continence improvement of 50% or more was maintained during follow-up in forty two (84%) patients. A significant decrease in median incontinent episodes and days per week was seen during trial screening and follow-up ($P < 0.002$). Quality of life improved significantly in all four categories of the FIQOL scale and in some subscales of the SF-36 QOL questionnaire. Differences in median resting and squeeze anal canal pressures did not reach clinical significance. Although initial improvement in continence with SNM could not be maintained in all patients, with an overall success rate of 80% after permanent implant, SNM proves to be a safe and effective long-term treatment in patients with faecal incontinence.

Future perspectives and research should focus on the physiological mechanism of action and the cost effectiveness of SNM in patients with faecal incontinence. A better understanding of the physiological mechanism might not only lead to a better patient selection, but may well make the test stimulation, which currently is the only predictor available, eventually obsolete. With better understanding the application of SNM could also be broadened to other groups of patients with conditions other than FI. [7] SNM has already been successfully used in the treatment of patients with 'late-onset' constipation. [8-10] Patients suffering from constipation since childhood have not been studied yet. In our institution, we started a study to treat adolescent constipation patients with SNM with very good results. These results will be published in the near future. Studies reporting the effect of SNM on peri-anal pain, clitoral/pelvic pain and erectile/sexual dysfunction have been published but need further investigation. [11-14] Furthermore a significant reduction in diarrhea-predominant irritable bowel symptoms and improvement of quality of life was seen with percutaneous sacral nerve evaluation in patients with irritable bowel syndrome. [15] These applications of SNM for various conditions solely suggest a complex mechanism of action affecting sensory and possibly autonomic function. The availability of functional brain imaging such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) are intriguing possibilities. [16,

[17] Future research using PET and fMRI should give us a better insight in both the pathophysiology of FI as well as the working mechanism of SNM.
Costs of SNM are a main concern. Although the exact costs associated with faecal incontinence are unknown the indirect or non-medical costs, such as loss of productivity, are more than half of total costs of FI.[18] Several studies have already shown SNM to be cost effective in the treatment of faecal incontinence. [19-21] Cost effectiveness studies will probably have to be performed in each country separately to convince local healthcare providers of the beneficial effect of SNM in patients with FI on both healthcare and society reducing the macro-economic burden. Further technical developments can also affect costs of SNM by reducing post-operative adverse events, such as infection, pain and lead migration. Stimulators with a longer life span or even rechargeable devices should lower costs further since the number of patients needing a replacement of the stimulator will grow in the future.

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