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Lower Urinary Tract Symptoms in Stroke Patients

A clinical study of prevalence, impact and effect of training

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Preface

This thesis has been produced during my appointment as research physiotherapist at the Department of Geriatrics and Rheumatology, Division of Physiotherapy, Copenhagen University Hospital, Glostrup, Denmark from 2002 to 2007.

I wish to express my gratitude to everyone who has contributed to the research projects and the thesis.

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September, 2007
Sigrid Tibæk

Contents

List of publications

The thesis is based on the following papers, which will be referred to by their Roman numerals:

I. Tibaek S, Jensen R, Klarskov P, Iversen HK, Gard G. The Danish Prostatic Symptom Score (DAN-PSS-1) Questionnaire is reliable in stroke patients. Neurourol Urodyn 2006;25:319-23.

II. Tibaek S, Gard G, Klarskov P, Iversen HK, Dehlendorff C, Jensen R. Prevalence of Lower Urinary Tract Symptoms (LUTS) in Stroke Patients. A cross-sectional, clinical survey. (Submitted May 2007and under revision).

III. Tibaek S, Gard G, Klarskov P, Iversen HK, Dehlendorff C, Jensen R. Are Activity Limitations related to Lower Urinary Tract Symptoms (LUTS) in Stroke Patients? (Manuscript in preparation).

IV. Tibaek S, Gard G, Jensen R. Pelvic floor muscle training is effective in women with urinary incontinence after stroke. A Randomised, Controlled and Blinded Study. Neurourol Urodyn 2005;24(4):348-57.

V. Tibaek S, Jensen R, Lindeskov G, Jensen M. Can Quality of Life be improved by Pelvic Floor Muscle Training in Women with Urinary Incontinence after Ischemic Stroke? A Randomised, Controlled and Blinded Study. Int Urogynecol J 2004;15:117-23.

VI. Tibaek S, Gard G, Jensen R. Is there a Long-Lasting Effect of Pelvic Floor Muscle Training in Women with Urinary Incontinence after ischemic Stroke? A six months follow-up study. Int Urogynecol J 2007;18:281-7.

Abbreviations and definitions

Abbreviations

DAN-PSS-1	The Danish Prostatic Symptom Score
CI	Confidence interval
CG	Control Group
ICS	International Continence Society
LUTS	Lower urinary tract symptoms
κ	The simple kappa coefficient
OR	Odds ratio
PFMT	Pelvic floor muscle training
QoL	Quality of life
SD	Standard deviation
SF-36	Short Form 36 (SF-36) Health Survey
TG	Treatment Group
UI	Urinary incontinence
$w\kappa$	The weighted kappa coefficient

Definitions

Dynamic endurance	As the point when repetitive work no longer can be sustained at a certain force level (Alaranta et al., 1994).
Prevalence	The proportion of subjects with the abnormality present during a certain time-period (Altman, 1994).
Static endurance	As the point of isometric fatigue where the muscle contraction can no longer be maintained at a certain level (Alaranta et al., 1994).
Test-retest reliability	Assessment of scores on two or more administrations of a test (Domholdt, 1993).
Validity	The extent to which a test measures what it is intended to measure (Johnston et al., 1992).

Abstract

The overall aims of this thesis were to investigate the prevalence, severity and bother of Lower Urinary Tract Symptoms (LUTS) in a clinical sample of stroke patients and to evaluate the effect of pelvic floor muscle training (PFMT) in women with urinary incontinence after ischemic stroke. The thesis consisted of 6 articles based on 4 studies and a review.

In the first study (Paper I), the Danish Prostatic Symptom Score (DAN-PSS -1) questionnaire was tested in 71 stroke patients by a prospective questionnaire-based survey and demonstrated acceptable test-retest reliability and that this system was useful in stroke patients of both genders.

Secondly the prevalence, severity and bother of LUTS were investigated in a cross-sectional, clinical survey of 482 stroke patients (Paper II). The response rate was 84 %. The period prevalence of at least one symptom of LUTS was 94 % and the most frequent symptom was nocturia (76 %). The most severe symptom was urgency and among respondents who had at least one symptom the prevalence of bother was 78 %.

The extent of self-reported activity limitations were also assessed in this clinical sample of 482 stroke patients in order to identify whether activity limitations related to prevalence, severity and impact on daily life of LUTS (Paper III). The extent of self-reported activity limitations varied from 17 % to 34 % depending on the measurements and the mobility velocity was highly significantly correlated to severity of LUTS.

In the next study the effect of 12 weeks Pelvic Floor Muscle Training (PFMT) in 26 women with urinary incontinence after ischemic stroke was evaluated in a prospective, randomized and single-blinded study design (Paper IV-V). Twenty-four subjects completed the study and a significant improvement in frequency of voiding in daytime ($p=0.018$), 24-hours pad test ($p=0.013$) and dynamic endurance of pelvic floor muscle ($p=0.028$) was demonstrated in the Treatment Group compared to the Control Group.

The long-lasting effect of PFMT was evaluated by a 6-month follow-up study and measured by quality of life parameters (Paper VI). The sample consisted of 24 women, who had completed the initial study. In the Treatment Group a trend to long-lasting effect compared to the Control Group was found.

In conclusion, the prevalence of LUTS and its bother was very high in stroke patients and the most severe symptom was urgency. PFMT had a significant effect in women with urinary incontinence after stroke and increased focus on LUTS and the possibilities of training can highly be recommended.

Summary in Danish (Sammenfatning på dansk)

De overordnede mål med afhandlingen var at undersøge prævalensen, sværhedsgraden og gener af urinvejssymptomer (LUTS) hos en klinisk gruppe apopleksi patienter samt at undersøge effekten af bækkenbundstræning til kvinder med urininkontinens (UI) efter iskæmisk apopleksi.

Afhandlingen omfatter 6 artikler (Paper I-VI) baseret på 4 studier og en oversigtsartikel.

I det første studie (Paper I) undersøgtes test-retest reliability af det Danske Prostata Symptom Score (DAN-PSS -1) spørgeskema blandt 71 apopleksi patienter ved en prospektiv, spørgeskema-baseret undersøgelse. DAN-PSS-1 spørgeskemaet blev fundet acceptabelt og anvendeligt til måling af prævalens, sværhedsgrad samt gener af LUTS hos apopleksi patienter.

I det næste studie (Paper II) undersøgtes prævalensen, sværhedsgraden og gener af LUTS blandt 482 apopleksi patienter ved en klinisk tværsnitsundersøgelse. Besvarelse procenten var 84 % (407/482). Periode prævalensen af mindst 1 LUTS symptom var 94 % og det hyppigste symptom var nykturi (76 %). Det sværeste symptom var bydende vandladningstrang (urgency) og blandt respondenter som havde mindst et LUTS symptom var prævalensen af gener 78 %.

Omfanget af selv-rapporteret aktivitets nedsættelse blev undersøgt (Paper III) blandt 482 apopleksi patienter samt om aktivitets nedsættelse var relateret til prævalens, sværhedsgrad og gener af LUTS. Undersøgelsen blev foretaget som en klinisk, tværsnitsundersøgelse og apopleksi patienterne rapporterede aktivitets nedsættelse fra 17 % til 34 % afhængig af måleredskabet. Bevægelseshastighed viste sig at være høj signifikant korreleret med sværhedsgraden af LUTS, hvorimod ingen af aktivitets nedsættelse variablerne viste nogen effekt i forhold til prævalens og gener af LUTS.

I det næste studie (Paper IV-V) undersøgtes effekten af 12 ugers bækkenbundstræning blandt 26 kvinder med urininkontinens efter iskæmisk apopleksi ved en prospektiv, randomiseret og enkelt-blindet undersøgelse. 24 kvinder gennemførte undersøgelsen og der blev påvist en signifikant forbedring i

forhold til antal vandladninger i dagtiden (p=0.018), 24-timers ble vejnings test (p=0.013) og dynamisk udholdenhed af bækkenbundsmuskulaturen (p=0.028) i trænings gruppen sammenlignet med kontrol gruppen.
Spørgeskemaerne SF-36 og Incontinence Impact Questionnairre (IIQ) påviste ingen signifikant forskel indenfor og imellem de 2 grupper.

Længerevarende effekt af bækkenbundstræning blev undersøgt (Paper VI) blandt de 24 deltagere, som tidligere havde gennemført undersøgelsen (Paper IV-V), ved en 6 måneders opfølgningsundersøgelse og målt med livskvalitets parametre.

I træningsgruppen viste SF-36 en tendens til længerevarende effekt i en af de otte domæner og IIQ viste ligeledes en tendens til reducerede gener af inkontinens i to af fire domæner sammenlignet med kontrolgruppen.

Konklusion: Prævalensen af urinvejssymptomer og dets gener var meget høj hos apopleksi patienter. Bydende vandladningstrang (urgency) var det symptom, der havde højst sværhedsgrad.

Bækkenbundstræning havde en signifikant positiv effekt hos kvinder med urininkontinens efter apopleksi og øget fokus på urinvejssymptomer og dets træningsmuligheder kan stærkt anbefales.

1 Introduction

1.1 Stroke

1.1.1 Definition

Stroke is defined by World Health Organisation (WHO) as “rapidly developing clinical signs of focal or global (in cases of deep coma or subarachnoid hemorrhage) disturbances of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin (WHO, 1989)

1.1.2 Prevalence and incidence

The prevalence of stroke in Denmark is 5.2 per 1.000 inhabitants and the incidence is 2 per 1.000 inhabitants per year, corresponding to 10.200 patients per year with a significant increase with age (Lindenstrøm et al., 1992). Similar to the level of age related figures from comparable countries (Brown et al., 1996; Thorvaldsen et al., 1995; Williams et al., 1999).

1.1.3 Deficits

Stroke survivors have various neurological deficits such as motor disability, visual field defects, cognitive problems, dysphasia and urinary incontinence (UI)

(Brittain et al., 1998; Brittain et al., 2000; Foster and Young, 1995; Hochstenbach et al., 1998; Patel et al., 2001; Pound et al., 1998). The functional status is dependent on both number and severity of the neurological deficits - however, also the interaction between the deficits plays a role for the functional outcome and quality of life (QoL).

1.2 Lower urinary tract symptoms after stroke

Previous studies have mostly focused on UI as urinary dysfunction (Barrett, 2002; Brittain et al., 1998; Jørgensen et al., 2005; Kolominski-Rabas et al., 2003; Nakayama et al., 1997) while UI often is accompanied by other lower urinary tract symptoms after stroke (Teasell et al., 2006).

1.2.1 Definitions of some Lower Urinary Tract Symptoms

Lower urinary tract symptoms (LUTS) are a broad term of subjective urinary symptoms (Abrams et al., 2002). The International Continence Society (ICS) has divided LUTS into three groups: storage, voiding and post micturition symptoms (Abrams et al., 2002).

Storage symptoms are experienced during the storage phase of the bladder; voiding symptoms are experienced during the voiding phase and post micturition symptoms are experienced immediately after micturition.

The definitions of some lover urinary tract symptoms are presented in Table 1.

Table 1. Definitions of some Lower Urinary Tract Symptoms (LUTS).

Symptom	Definition
Increase daytime frequency	Is the complaint by the patient who considers that he/she voids to often by day
Nocturia	Is the complaint that the patient has to wake up in the night to void
Urgency	Is the complaint of a sudden compelling desire to pass urine, which is difficult to defer
Urinary incontinence	Is a condition in which urine leakage is a social and hygienic problem and which had to be objective documented (Abrams et al., 1990) Is the complaint of any involuntary leakage of urine (Abrams et al., 2002)
Some types of urinary incontinence	
Stress incontinence	Is the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing
Urge incontinence	Is the complaint of involuntary leakage accompanied by or immediately preceded by urgency
Other	May be situational, e.g. report of incontinence during sexual intercourse, or giggle incontinence
Slow stream	Is reported by individuals as he/her perception of reduced urine flow, usually compared to previous performance or in comparison to others
Straining	To void describes the muscular effort used to either initiate, maintain or improve the urinary stream
Hesitancy	Is the term used when an individual describes difficulty in initiating micturition resulting in a delay in onset of voiding after the individual is ready to pass urine

Table 1. Definitions of some Lower Urinary Tract Symptoms (LUTS). continued

Symptom	Definition
Terminal dribble	Is the term used when an individual describes a prolonged final part of micturition, when the flow has slowed to a trickle / dribble
Bladder pain	Is felt suprapubically or retrepubically, usually increases with bladder filling, and may persist after voiding
Feeling of incomplete emptying	Is a self-explanatory term for a feeling experienced by the individual after passing urine

Reference: (Abrams et al., 2002).

1.2.2 Pathophysiology

The bladder performs two functions, storage and emptying.

The control of these two functions is by neural programs which perform and locate to the pons or by suprapontine influences act to switch from one state to the other.

Micturition frequency in a healthy adult with a bladder capacity of - 500 ml is likely to be about once every 3-4 hour, depending of fluid intake. Since the act of voiding lasts 2-3 minutes, this means that for > 98 % of life bladder is in its storage mode.

In the healthy and continent state the decision when to void is determined by the perceived state of bladder fullness together with an assessment of the social appropriateness to do so.

To affect both storage and voiding, connections between the pons and the sacral spinal cord must be intact as well as the peripheral innervations arising from the most caudal segments of the sacral spinal cord. From there the peripheral innervations pass through the cauda equina to the sacral plexus and via the pelvic and pudendal nerves to innervate the bladder and the sphincter. Thus, the innervations needed for physiological bladder control is extensive, requiring suprapontine inputs, intact spinal connections between the pons and the sacral cord, as well as intact peripheral nerves (Fowler, 1999).

Pathophysiology changes after stroke are complex and are not clearly established. Andrew and Nathan (1964) suggested that the antero-medial region in the frontal lobe was associated with the control of micturition (Andrew and Nathan, 1964). Also, lesion in other part of the brain lead to UI which probably is due to disruption of the pathways between the higher centres and the pontine micturition centre (Brittain et al., 1998; Brittain et al., 1999). Interference of these pathways would be expected to lead to loss of higher cerebral inhibition of detrusor reflex activity and hence an overactive bladder.

Borrie (1986) performed cystometrics in 22 acute stroke patients with moderate and severe UI that had persisted for four weeks post stroke (Borrie et al., 1986). Detrusor instability was present in 85 % of those who had been continent prior to stroke, and a further two patients showed evidence of stress UI and two were in urinary retention.

Gelber (1993) performed urodynamics studies in 19 UI patients with recent unilateral ischemic hemisphere stroke. Bladder overactivity was present in 37 % of this group, bladder atonicity in 21 %, detrusor-sphincter dyssynergia in 5 %, leaving 37 % with normal bladder function. All of the patients with normal bladder function were aphasic, demented or severe functionally impaired. All of the patients with atonic bladders had underlying diabetes or were taken ant cholinergic medication (Gelber et al., 1993).

Nazarko (2003) reported that stroke survivors who is aware of bladder fullness but cannot inhibit bladder contraction experience LUTS such as frequency, urgency and possible urge incontinence (Nazarko, 2003).

1.2.3 Epidemiology

1.2.3.1 Measurement in surveys

When assessing the prevalence, severity and bother of LUTS in stroke patients, a validated and reliable questionnaire would have been ideal. Such a questionnaire was not available when this study was initiated. This encouraged us to test-retest the reliability of The Danish Prostate Symptom Score (DAN-PSS-1) questionnaire in a sample of stroke patients (Meyhoff et al., 1993).

The DAN-PSS-1 is short (12 questions), in plain text and the original version is in Danish. The DAN-PSS-1 focuses on both the frequency and severity of symptoms and also includes questions about the bothersomeness of each symptom.

In 1999 Kay et al. used DAN-PSS-1 to describe the prevalence and overall impact of voiding problems in the general population according to gender and age (Kay et al., 1999).

1.2.3.2 Prevalence

Only one study of the prevalence, bother and quality of life effects of LUTS after stroke has been found, an Australian Government study, (Bird et al., 2001). However several prevalence studies of UI after stroke have been published.

The prevalence of UI varies from 32 % to 79 % at admission to hospital, 25 to 28 % by discharge and from 12 % to 19 %, six months after the stroke (Barrett, 2002; Brittain et al., 1998; Kolominski-Rabas et al., 2003; Nakayama et al., 1997; van Kuijk et al., 2001). Moreover, Jørgensen et al. (2005) reported that UI was present in 17 % of stroke survivors compared to 7 % in controls until 10 years poststroke in a self-reported, community-based, cross-sectional study (Jørgensen et al., 2005).

Brittain wrote: “Incontinence as a single symptom may be too exclusive and lower urinary and fecal tract symptoms could deliver a better indication of urinary symptoms in stroke survivors. For example, a stroke survivor with bladder instability, may not complain of UI but of frequency and nocturia” (Brittain et al., 1998).

1.2.3.3 Impact

Only Bird (2001) assessed the impact of LUTS three and twelve months after stroke (Bird et al., 2001), whereas several studies of the impact of UI after stroke have been published.

Barer (1989) reported that, stroke survivors with UI have significant more impact on lifestyle than non-stroke population with UI. Impact such as sleep disturbances were present in 23 % of stroke survivors compared to 9 % in non-stoke population (Barer, 1989). Moreover 24 % of stroke survivors used pads to cope with UI symptoms “most of the time” compared to 9 % of non-stroke population (Brittain et al., 2000).

In addition, UI after stroke has been shown to be strongly related to degree of institutionalisation (Ween et al., 1996). In a prospective, population-based study of 752 stroke patients Kolominski-Rabas (2003) shoved that a total of 45 % of stoke patients with UI 12 months post stroke were institutionalised compared with 5 %of patients without UI. (Kolominski-Rabas et al., 2003).

Likewise the impact of UI for stroke patients and their caregivers is significant and has been shown to have an adverse effect on stroke survival and disability rates (Patel et al., 2001). Bean (2003) noted an almost 2-fold difference in level of disability post stroke among those who were incontinent versus those who were continent (p>0.001) (Bean et al., 2003).

Another study showed that stoke patients suffering from UI at admission to hospital often had greater morbidity and mortality throughout their stay at hospital and 3 months post stroke (Garibella, 2003).

1.2.3.4 Related factors

Identification of predictors of LUTS in stroke can be valuable information with regard to future prevention or treatment of the symptoms.

Several risk factors are available related to UI after stroke such as age, severity of stroke, diabetes mellitus and comorbility of other disabling diseases in stroke patients. These risk factors may give causal information.

However, epidemiological cross-sectional studies related to potential predictors with regard to the prevalence, severity and bother of LUTS in stroke patients, has to my knowledge not been reported.

Based on clinical physiotherapeutic experiences it may be important to identify the effect of activity limitations as a related factor or predictor of LUTS.

As risk factors and predictors are closely related terms and statistically analysed by the same methods, it is important to underline the difference.

A risk factor is described as a factor or a variable that may contribute to some event (Altman, 1994).

A predictor is described as a factor or a variable, which can explain the variation of a dependent variable (Altman, 1994).

1.3 Treatment of urinary incontinence after stroke

The Agency of Health Care Policy and Research's Clinical Practice Guidelines on Urinary Incontinence in Adults update advises that "the least invasive and least dangerous procedure that is appropriate for a patient should be the choice when treating UI" (Burgio and Burgio, 1986; Fantl et al., 1996).

In contrast, to studies in non-neurological patients with UI (Berghmans et al., 1998; Berghmans et al., 2000; Burgio et al., 1998; Bø, 1990; Bø, 1998; deTayrac et al., 2004; Glazener et al., 2005; Holroyd-Leduc and Straus, 2004; Mariappan et al., 2007; Sureshkumar et al., 2003; Teunissen et al., 2004) there are few randomised trials evaluating the effect of intervention in stroke patients with UI.

Behavioural treatment such as timed voiding (Borrie et al., 1986; Fantl et al., 1991; Thomas et al., 2005) and for more immobile and not co-operative patients, pads or catheters have been used (Wade and Hewer, 1985).

In 2005, Thomas et al published a Cochrane review investigating the optimal methods for prevention and treatment of UI after stroke in adults (Thomas et al., 2005). Data were collected from January 1982 to November 2004 and only results from 7 trials (n=399) were included. Participants were from a mixture of settings, age groups and phases of stroke recovery.

Four trials (Brittain, 2001; Chiu et al., 1992; Gelber et al., 1993; Gelber and Swords, 1997; Wikander et al., 1998) tested an intervention against usual care (time voiding, acupuncture and 2 types of specialist professional intervention), Three trials tested medicine (a cross-over trial tested oestrogen vs. placebo, oxybutynin vs. timed voiding and sensory-motor bio feed back and timed voiding vs. only time voiding) (Gelber and Swords, 1997; Judge, 1969; Lewis et al., 1990).

The authors concluded that there was evidence that specialist professional input through structured assessment and management of care and specialist continence nursing may reduce UI after stroke. Data from trials of other physical, behavioural, complementary and anticholinergic drug interventions were regard as insufficient to guide continence care of adults after stroke (Thomas et al., 2005).

In 2005 Domoulin et al. conducted a systemic review investigating the benefits of behavioural therapies used to treat UI in stroke (Dumoulin et al., 2005). The study

included only four RCT (Engberg et al., 2002; McDowell et al., 1999; Tibaek et al., 2004; Wikander et al., 1998), one cohort study and recommendations from three clinical practice guidelines.

The study found limited evidence for reduction of UI in male stroke patients using bladder combination treatment including bladder retraining with urge suppression and pelvic floor muscle training.

The authors concluded that although there is increasing recognition of the benefits of using behavioural approaches as treatment for stroke patients with a high occurrence of continual UI, the evidence remains very limited for specific treatments used for stroke survivors with UI (Dumoulin et al., 2005).

1.3.1 Pelvic floor muscle training

Pelvic Floor Muscle Training (PFMT) (Abrams et al., 1990) have been used in treatment of UI in non-neurological female patients since 1948 (Kegel, 1948) and the effect rate varies from 23-94 % depending on the method, the population and type of incontinence (Borello-France et al., 2006; Bø, 1990; Hay-Smith et al., 2001; Nygaard et al., 1996; Wilson et al., 2002).

The aim of the training is to improve pelvic floor muscle (PFM) function. The treatment consists of muscle awareness training (Prigatano and Schachter, 1991), training of muscle strength and endurance and coordination. By cerebral cortical facilitation (motor learning) (Schmidt and Lee, 1999) the number of motor units may also increase.

Awareness is defined as a highly integrated brain function, encompassing the ability to perceive oneself in relatively objective terms while maintaining a sense of subjectivity (Hartman-Maeir et al., 2003).

Motor learning is defined as a relatively permanent change in the capability for responding associated with practice or experience (Kwakkel et al., 2004; Schmidt and Lee, 1999).

1.3.2 Pelvic floor muscle training in women with urinary incontinence after stroke

Based on the following facts:

- Evidence of effect of PFMT in non-neurological women with stress UI due to the strength of PFM (Bø, 1990; Bø et al., 1999; Hay-Smith et al., 2002; Wilson et al., 2002).
- Evidence of effect of PFMT in non-neurological women with urge UI due to the inhibition effect on detrusor muscle contraction by PFM contraction (Bø and Berghams, 2000).
- Evidence of effect of physical treatment in the rehabilitation of stroke patients, although no clear consensus exists concerning which techniques and methods are the best (Andersen et al., 2001).
- Standard PFMT include training of awareness, (Prigatano and Schachter, 1991)
- Standard PFMT include motor learning, (Kwakkel et al., 2004; Schmidt and Lee, 1999).

it is obvious to formulate the hypothesis that PFMT may have an effect in women with UI after ischemic stroke.

This hypothesis is a part of the background for this thesis.

2 Aims

The overall aims of this thesis were to investigate the prevalence, severity and bother of lower urinary tract symptoms (LUTS) in a clinical sample of stroke patients and to evaluate the effect of pelvic floor muscle training (PFMT) in women with urinary incontinence after ischemic stroke.

Specific aims

- To investigate the test-retest reliability of The Danish Prostatic Symptom Score (DAN-PSS-1) questionnaire in a sample of stroke patients (Paper I)
- Primarily to investigate the prevalence, severity and impact on daily life of Lower Urinary Tract Symptoms (LUTS) in a clinical sample of stroke patients and secondly to identify predictors of LUTS (Paper II)
- To assess the extent of self-reported activity limitations in a clinical sample of stroke patients and to identify whether activity limitations relate to prevalence, severity and impact on daily life of Lower Urinary Tract Symptoms (Paper III)
- To evaluate the effect of Pelvic Floor Muscle Training in women with urinary incontinence after ischemic stroke (Paper IV)
- To evaluate the effect of Pelvic Floor Muscle Training in women with urinary incontinence after ischemic stroke measured by quality of life parameters (Paper V)
- To evaluate the long-lasting effect of Pelvic Floor Muscle Training in women with urinary incontinence after stroke measured by quality of life parameters (Paper VI)

3 Material and methods

3.1 Design

This thesis based on 3 different methodological designs:

- A prospective questionnaire-based survey (Paper I)
- A cross-sectional, clinical survey (Paper II, III)
- A prospective, randomised and single-blinded design (Paper IV-VI)

3.2 Subjects

A total of 71 stroke patients were invited and 59 subjects participated in the test-retest reliability study of DAN-PSS-1 questionnaire (Table 2, Paper I).

In the following cross sectional, clinical studies 519 stroke patients were included and 482 eligible subjects participated in the prevalence (Paper II) and predictor (Paper III) studies of LUTS in stroke patients.

A total of 26 women with urinary incontinence after ischemic stoke were included and 24 subjects completed the prospective, randomised, single-blinded study (Paper IV-V) and the 6 month follow-up study (Paper VI) (Table 2).

All subjects were recruited from the clinical departments at Copenhagen University Hospital Glostrup (acute stroke unit and/or neurological department) (Paper I-III) respectively supplied from departments of geriatric, rehabilitation and general physical therapy clinics and the public rehabilitations centres in the County of Copenhagen (Paper IV-VI).

Table 2. Subjects of Stroke Patients participated in the Studies (Papers I-VI).

Paper, N°	Subjects numbers	Age years	Gender	
			women	men
Paper I	59	65 (56-75)	24 (41 %)	35 (59 %)
Paper II-III				
Respondents	407	67 (12)	181 (45 %)	226 (55 %)
Non-respondents	75	69 (12)	41 (55 %)	34 (45 %)
Paper IV-V-VI				
TG	12	59 (56-72)	12 (50 %)	
CG	12	62 (52-75)	12 (50 %)	

Mean, SD or absolute numbers (%) in Papers II-III,
Median value with interquartile range or absolute numbers (%) in Papers I, IV-VI. TG = Treatment Group, CG = Control Group.

3.3 Measurements

Initially The DAN-PSS-1 questionnaire was investigated for test-retest reliability in stroke patients. Then the DAN-PSS-1 questionnaire was used to investigate the prevalence, severity and bother of LUTS in a clinical sample of stroke patients (Brasso et al., 1994; Hansen et al., 1995; Kay et al., 1999; Meyhoff et al., 1993; Schou et al., 1993) (Paper I, II, III) (Table 3).

Four activity limitations measurements: Barthel Index (Collin et al., 1988; Mahoney and Barthel, 1965; Wade and Collin, 1988; Wade and Hewer, 1987), mobility velocity (Blanke and Hageman, 1989; Hageman and Blanke, 1986; Kollen et al., 2006), mobility distance(Holden et al., 1986; Holden et al., 1984; Wolfson et al., 1990) and mobility aids (Collen et al., 1990; Holden et al., 1986; Holden et al., 1984; Perry et al., 1995) were used to assess the extent of self-reported activity limitations in a clinical sample of stroke patients and to identify whether activity limitations could predict: prevalence, severity and impact on daily life of LUTS (Paper III) (Table 3).

The primary outcome measurements used to evaluate the effect of pelvic floor muscle training (PFMT) were: 1) diary recording the time and frequency of voiding, the number of incontinence episodes and used pads (Wyman et al., 1988); 2) 24-hr home pad test (Lose and Versi, 1992; Rasmussen et al., 1994) and as secondary outcome measurements were used; 3) vaginal palpation of pelvic floor muscle evaluating function (Thorp et al., 1991), strength (Brink et al., 1989; Laycock, 1992) static and dynamic endurance(Alaranta et al., 1994)(Paper IV) (Table III).

The short and long-lasting effect of PFMT in women with UI after ischemic stroke was also measured by two quality of life questionnaires (primary outcome): The Short Form 36 (SF-36) Questionnaire (Andersson et al., 1996; Garrat et al., 1993; Hay-Smith et al., 2001; Ware and Sherbourne, 1992) and Incontinence Impact Questionnaire (IIQ) (Shumaker et al., 1994) (Paper V-VI) (Table 3).

Table 3. Measurements used in the Study (Papers I- VI).

Measurements	Paper I	Paper II	Paper III	Paper IV	Paper V	Paper VI
Questionnaires						
DAN-PSS-1	x	x	x			
SF-36					x	x
IIQ					x	x
Other Measurements						
Diary				x		
24-hr pad test				x		
Pelvic Floor Muscle (PFM) Measurements						
PFM Function				x		
PFM Strength				x		
PFM Static endurance				x		
PFM Dynamic endurance				x		
Activity Limitations Measurements						
Barthel Index			x			
Mobility velocity			x			
Mobility distance			x			
Mobility aids			x			

3.4 Intervention

Pelvic floor muscle training (PFMT)

The aim of PFMT was to improve pelvic floor muscle (PFM): awareness, isolate contraction, strength, static and dynamic endurance, and coordination.

Treatment Group (TG)

Subjects randomized to the TG followed a systematic, controlled, intensive PFMT program during 12 weeks.

The treatment was performed in small groups of 6-8 subjects, 1 hour per week, and lead by the same specialised physiotherapist.

The PFMT program was introduced by 1 hour theory consisting of: anatomy and physiology of the bladder and the PFM; definition of incontinence types; instruction in self-palpation of PFM, and motivation and instruction in home exercises 1-2 times daily.

The group treatment consisted of: isolated PFM contraction (6 sec contraction/6 sec rest); muscle strength exercises (3 sec contraction/3 sec rest, and 6 sec contraction/6 sec rest (Nygaard et al., 1996) and endurance exercises (max 30 sec contractions/30 sec rest).

All techniques were repeated in different positions and PFM contractions were also treated before and during daily activities.
Vaginal palpation of PFM were performed 2-3 times, in order to control correct contraction and to give continually feed-back to the subjects and to evaluate the strength.

This training program is a Modified version of a standard training program for group treatment of stress incontinence (Bø, 1990).

Control Group (CG)
Subjects randomised to the CG followed the normal, standard program of general rehabilitation without any specific *treatment* of UI.

3.5 Statistics

Statistical analysis was done by means of SPSS (Statistical Package of Social Science), version 12.02 and *R*, version 2.4.1 - 2.5.1 (R Development Core Team, 2006).

An overview of the statistical methods used is presented in Table 4.

The level for statistical significance was accepted at $p < 0.05$.

Table 4. Statistical Methods used in the Studies (Papers I- VI).

Methods	Paper I	Paper II	Paper III	Paper IV	Paper V	Paper VI
Bootstrap method †		x	x			
Chi-square test (χ^2)		x				
Mann-Whitney U-test		x	x	x	x	x
Wilcoxon signed rank test				x	x	x
Student's T-test		x	x			
Simple kappa statistics (κ)	x					
Weighted kappa statistics ($w\kappa$)	x					
Generalized additive models †			x			
Fisher's exact test †			x			
Spearman's rank correlation coefficient		x	x			
Multiple logistic regression model †		x	x			
Multiple linear regression model †		x	x			

† The statistical analysis had been done by a statistical advisor.

Mean and *SD* were calculated when samples were large and an approximate gaussian distribution could be assumed. When samples were small *median* and *interquartile range* were used.

Bootstrap method (Efron, 1979) was used when the conditions for the ordinary calculation of standard deviation of means (unlimited scales, approximately normal distribution) were not fulfilled. In paper II we had to deal with variables with a limited ordinal scale (0 to 3) and a skewed distribution. Ordinary procedures produced SDs reaching beyond the limit of the scale, which make no sense. Instead *95 % confidence intervals* were calculated by means of the bootstrap method which is a data driven method for producing empirical confidence intervals.

The null-hypotheses to determine the differences between the groups (respondents and non-respondents) were tested by *unpaired Student's t-tests* for continuous data and by Chi-square (χ^2) and Mann-Whitney tests for nominal and ordinal data. Within groups *Wilcoxon signed rank test* was used.

Simple kappa statistics (κ) (Cohen, 1960) was used for testing the reliability in detecting the frequency of each symptom and its bother factor, the scores were reduced to a two-category scale (=0, >0). The kappa statistics assessed the amount of agreement beyond that expected solely by chance. As the kappa statistics is sensitive to the number of observations made and the distribution of those observations around the diagonal, a very low kappa rating can occur even though there may be 100% agreement between answers (Brennan and Hays, 1992).

Weighted kappa statistics ($w\kappa$) (Cohen, 1968) was used for testing the reliability of repeated assessment on a scale. The weighted kappa gives credit for partial agreement by assigning diminishing weight between 1 and 0 according to distance to the diagonal. Assessment of the strength of agreement is as follows: poor ($w\kappa$ < 0.20), fair (21 < $w\kappa$ < 0.40), moderate (0.41 < $w\kappa$ < 0.60), good (0.61 < $w\kappa$ < 0.80) and excellent (81 < $w\kappa$ < 100) (Landis and Koch, 1977).
Generalized additive models (Wood, 2006) were used in cases where an underlying continuous explanatory variable was to be accounted for but not of primary scientific interest. The method replaces the effect of the variable with a non-linear smooth function.

Fisher's exact test (Cochran, 1954) was used for testing in contingency tables in cases where the common chi-square tests are inaccurate.

Spearman's rank correlation coefficient was applied to estimate correlation coefficients independently of scale.

Multiple linear regressions were applied to outcomes on a continuous scale or approximately continuous scale. The outcome was modelled as a model part with the explanatory variable and a random part consisting of independent Gaussian error. The estimated effects were increases in mean value typically from a reference group.

Multiple logistic regressions were applied in cases where the outcomes were binary 0-1 variables (e.g. prevalence). Multiple logistic regressions and multiple linear regressions were both part of the modelling techniques covered by generalized linear models (Nelder and Wedderburn, 1972). The log-odds (log(odds)) were modelled by a linear predictor consisting of the explanatory variables and the relevant effects were odds-ratios. Odds were defined as the probability of a given event divided by 1 minus the probability of the event. Odds-ratios were odds in group 1 divided by odds in group 2 and were restricted to positive numbers, where a value of 1 corresponded to a neutral odds-ratio i.e. equal odds and a value above 1 to higher odds for group 1.

3.6 Ethics

The studies have been presented to The Ethical Committee of the Copenhagen County:

- The Ethical Committee for the Copenhagen County had evaluated the study (April 25th, 2003) and approved the study without comments as such questionnaire studies are not encompassed of the law of Ethic Committee (§ 6, stk 3) (KA 03047) (Paper I,II, III).
- The Ethical Committee for The Copenhagen County had approved the study (KA 98117) (Paper IV, V, and VI).

Before participation, written informed consent was given to all participants.

4 Results and discussion

4.1 Test-retest reliability of DAN-PSS -1 questionnaire (Paper I)

Frequency symptom score and corresponding bother score

The proportion of agreement for the frequency symptom score was acceptable (76 % - 97 %) and the simple kappa value ranged from poor (κ = 0.00) to excellent (κ = 0.91). For 75 % of the symptom scores the simple kappa value ranged from moderate (κ = 0.50) to excellent (κ = 0.91), and for 25 % of the symptom scores kappa value ranged from poor (κ = 0.00) to fair (κ = 0.40).

Three of the twelve questions were problematic questions, #4: Do you have to strain to start and/or maintain urination?; #9: Does it hurt or burn when you urinate?; and #12: Do you experience leakage without urge or physical activity?

Maybe these questions have been unclear or of limited relevance for this sample of stroke patients.

The proportion of agreement of the corresponding bother score was also acceptable (76 % to 95 %), likewise ranged simple kappa value ranged from good (κ = 0.61) to excellent *(*κ = 0.84).

In a previous study Brasso (1994) investigated the precision of the DAN-PSS-1 questionnaire in terms of repeated frequency of 197 randomly selected men. They found the median frequency and repeat in answers was 83.5 % (range 0-99.7 %).

Furthermore they found, that the frequency depended of the nature of the question and the severity or bother of the symptom.

The author calculated only the repeated frequency of scores on an ordinal two category scale (=0, >0), but did not calculate the simple kappa coefficient (Brasso et al., 1994).

Severity of symptom score and its corresponding bother score

The weighted kappa coefficient for the severity symptom score ranged from

moderate ($w\kappa$ = 0.43) to good ($w\kappa$ = 0.75) and the corresponding weighted kappa coefficient for bother ranged from moderate ($w\kappa$ = 0.48) to good ($w\kappa$ = 0.68).

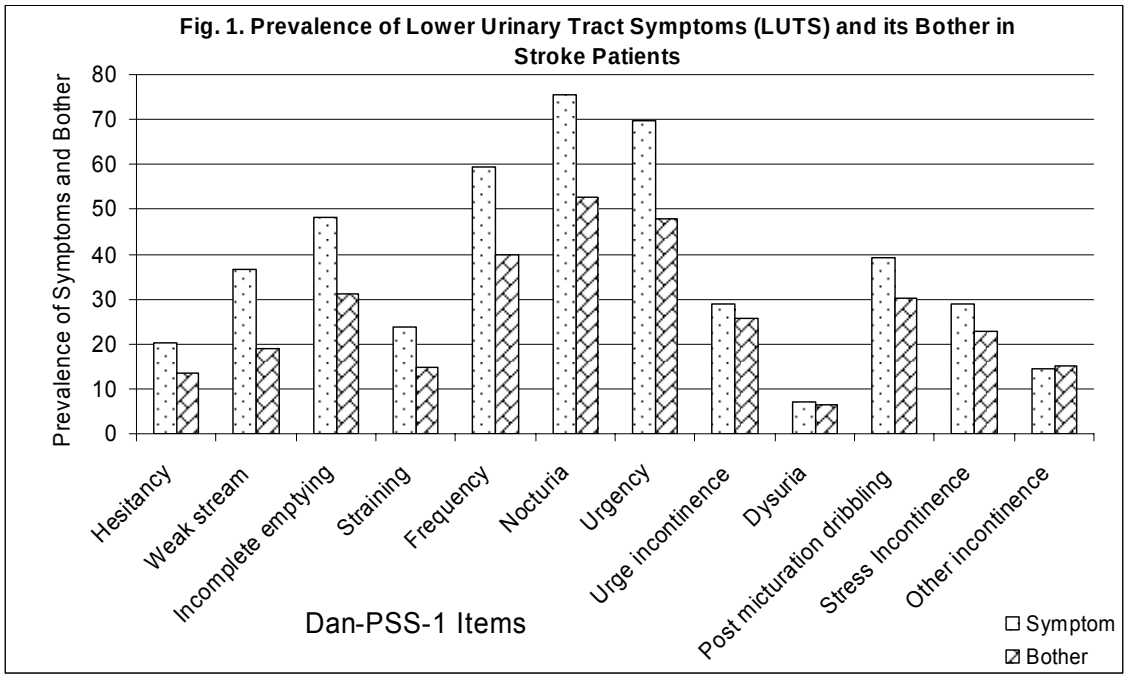
To our knowledge this is the first study using DAN-PSS-1 questionnaire in stroke patients and no other studies are thereby comparable.

4.2 Prevalence, severity and bother of LUTS (Paper II)

Prevalence

The period prevalence of at least one LUT symptom was very high (94 %), and the most frequent symptom was nocturia (76 %) followed by urgency (70 %) and daytime frequency (59 %)(Fig 1).

The mean number of symptoms was 4.6 (CI_b 4.3-4.9), and there were no gender-related differences.



In a comparable study Kay (1999) found that 84.5 % of the subjects had experienced at least one LUTS symptom and the prevalence of nocturia was experienced by 52.5 % in women and 53.5 % in men in a Danish gender- and age-stratified random sample of 500 healthy inhabitants investigated by DAN-PSS-1(Kay et al., 1999).

Although not directly comparable, the high prevalence of LUTS in an otherwise healthy population emphasizes the need for age- and gender matched control groups in future patient related surveys of stroke patients.

Britain (2000) established prevalence of urinary symptoms among community-dwelling stroke survivors and how these symptoms affected lives of these survivors compared with a non-stroke population. The study was a postal community-based survey among 14.600 people in U.K. The stroke questionnaire included questions about six defined urinary symptoms.

The prevalence of stroke was 4 % (n=423). Overall stroke survivors had a higher prevalence of urinary symptoms than the non-stroke population (64 % vs. 32 %) (Brittain et al., 2000)

As in our study nocturia was the most common symptom (49 %) although at a lower rate. But unlike our study, it was followed by urinary incontinence (33 %). The following most common symptoms were urgency (19 %) and frequency (15%) as in our study but with lower rate compare to our study (Brittain et al., 2000).

In a review from July 1966 to February 2000 of voiding dysfunction after stroke reported Marinkovic and Badlani that the predominant symptoms were urinary frequency, urgency and urge incontinence (Marinkovic and Badlani, 2001).

These studies are not comparable because of different sample and questionnaire, but are concentrated about the same types of LUTS symptoms.

Severity

The most severe symptom in the present study was urgency followed by nocturia and daytime frequency.

Unfortunately, no comparable reports of the severity of LUTS in a clinical sample of stroke patients have been found to compare with. Therefore such studies of severity are highly recommended in future research, because they can provide detailed information about a stroke patient's actual problems, need of care and abilities.

Bother

Among respondents, who had at least one symptom the prevalence of bother was

78 %. Likewise the most frequent symptom which bothered was nocturia (53 %), followed by urgency (48 %) and daytime frequency (40 %) (Figure 1).

Among those who experienced one or more symptoms, only 22 % reported that they were not bothered by their symptoms, whereas Kay (1999) reported that 36.1% of a healthy population were not bothered by their symptoms, indicating that not only the prevalence but also the bother were more pronounced in stroke patients (Kay et al., 1999).

Brittain et al., (2000) reported from the above described study that urinary symptoms had a lot of impact on the lives of the stroke survivors compared to non-stroke populations (31 % vs. 16 %) even when adjusted for age and sex differences.

4.3 Factors related to LUTS (Paper III)

Baseline characteristics

Paresis in legs, symptoms of urinary incontinence at admission and use of analgesics were significantly related to severity, whereas the prevalence and bother of LUTS could not be predicted by other patient characteristics.

Activity limitations

Among the 482 subjects a variation from 64 to 129 subjects reported activity limitations depending of the measurement. The extension and distribution of activity limitations are presented in Fig. 2.

Activity limitations measure by Barthel Index were reported by 108 (32 %) subjects, mobility velocity by 129 (34 %) subjects, mobility distance by 64 (17 %) subjects and mobility aids by 83 (20 %) subjects.

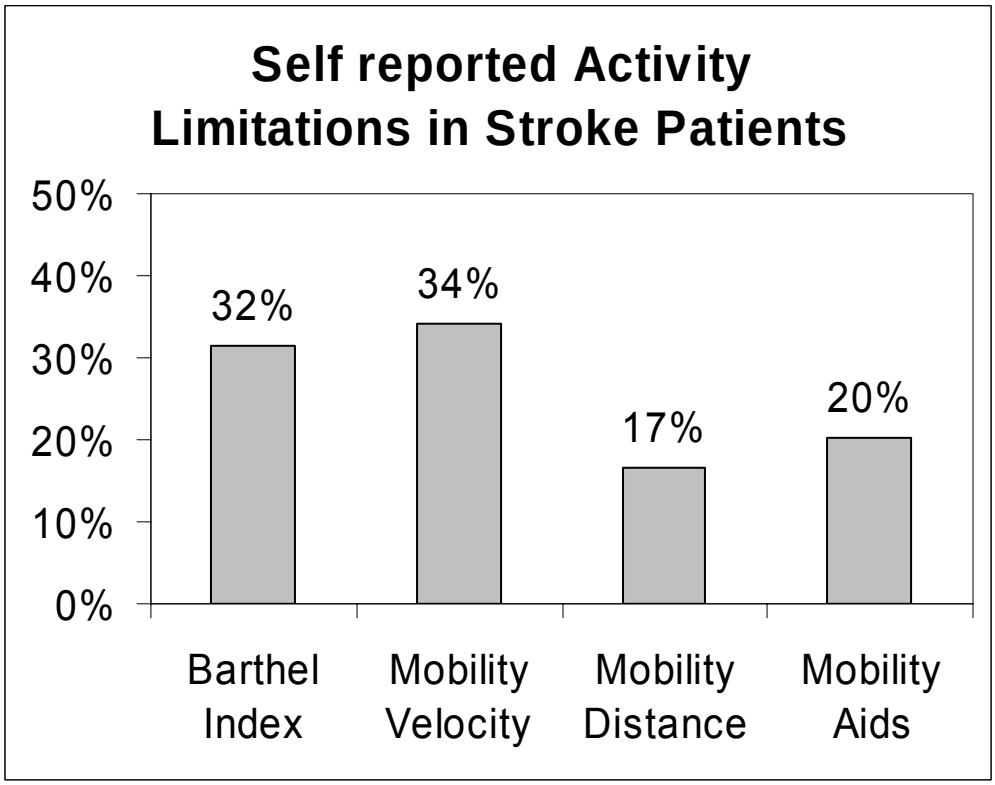


Figure 2. Self reported activity limitations in stroke patients.

The analysis showed that mobility velocity was highly significantly correlated (p=0.009; mean effect 0.370, 95 % CI 0.093 0.648,) to severity of LUTS, whereas none of activity limitations variables showed any effect to prevalence and bother of LUTS. In the symptom groups Barthel Index, mobility velocity and mobility distance were significant predictors to prevalence, severity and bother of incontinence symptom group, respectively.

4.4 Effect of PFMT in women with UI after stroke (Paper IV)

In this intervention study in total, 92 % (24/26) of the women with UI after stroke completed the study and the results showed significant effect measured by the 3 following parameters:

Voiding Diary

The frequency of voiding in daytime recorded over 3-days showed no significant

differences between groups at pre-test (Treatment Group (TG)=7, Control Group (CG)=8) but significant lower frequency in TG compared to CG at post-test (p=0.018; TG=6, CG=9).

Frequency of voiding in daytime showed significant difference between pre-test and post-test within the TG recorded over respectively 3-days (p=0.036) and 2-days (p=0.021), but not within the CG.

In healthy women the frequency of voiding in daytime per is 5-6 (Burgio et al., 1991) which is exactly the outcome we found in TG after PFMT.

Frequency of voiding, totally in TG recorded over 2-days decreased significantly (p=0.028), from 10 (8-12) to 8 (7-9) compared to the CG, which decreased from 9 (8-13) to 8 (7-12), (median, interquartile range).

There was no difference within or between groups in frequency voiding in nighttimes, number of incontinence episodes, and number of used pads.

24-hours pad test

24-hours pad test showed no significant difference between groups at pre-test, whereas at post-test a significant difference was found (p=0.013) (Table 3).

The results in TG showed reduced urine loss from 8g/24 h (medium value) to 2g/24 h, a decrease of 75 %. In CG the urine loss reduced from 12g/24h (median value) to 8 g/24h giving a decrease of 33 %.

It is surprising that we found a positive result in CG also (reduction ≥ 4g/24h). One explanation to that can be the lack of fluid intake/volume chart. Another explanation could be that the activity level of the post-test period was changed in relation to the pre-test periods.

The result of 24-hours home pad test is presented in Figure 3.

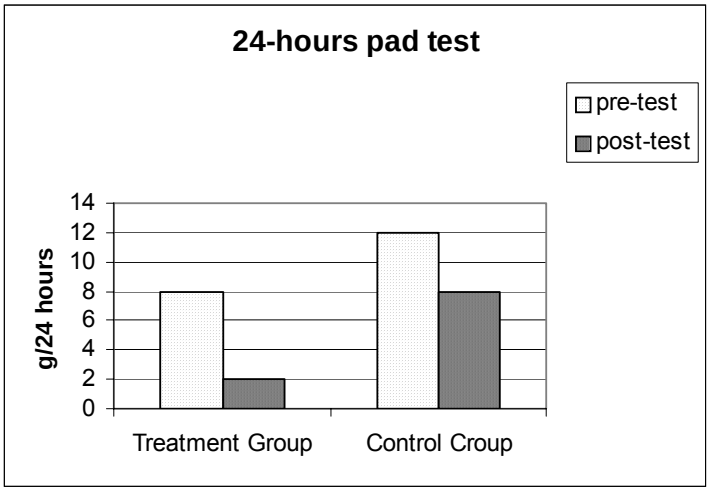


Figure 3, Results of 24 hour pad test

Vaginal palpation of PFM

Positive effects of PFMT were indicated in all four tests using vaginal palpation (Table 4).

In the TG significant improvements were demonstrated with respect to function (p=0.034), strength (.p=0.046), static endurance (p=0.028) and dynamic endurance (p=0.020) when pre-test were compared to post-test, whereas only strength in CG (p=0.034) had improved significantly.

The fact that PFM strength improved significantly in both groups although to a lesser degree in CG was indeed surprising. Why did PFM strength improve in CG? One explanation could be awareness and the learning effect at PFM during the pre-test. However, the improvement of strength in CG did not parallel the effect on urine loss at pad test or frequency of voiding in daytime and there is still a marked additional effect of the applied treatment program. Another explanation could be more theoretical. In non-neurological studies of women with stress UI and mixed UI the theoretical thesis behind PFMT effect is based on improvement of PFM strength. The question is what is the mechanism explaining the effect of PFMT in women with UI after stroke? Is it motor learning mechanism and the increased cerebral control and brain plasticity, which improves after an unspecific rehabilitation program. Or is it the other components of the PFM such as static and dynamic endurance, or in combination with PFM improvement?

We choosed to evaluate the static endurance of PFM, because the rationale behind PFMT in non-neurological women with urge UI is that PFM contraction inhibits detrusor muscle contraction (Bø and Berghams, 2000). Therefore we wanted to evaluate how long time the subjects could maintain a PFM contraction. The purpose of the present study was not to test that hypothesis, but to evaluate different components of PFM.

In the present study there were no differences between groups at pre-test, whereas at post-test a significant difference were found in dynamic endurance (p=0,028) and a tendency was found in PFM function (p=0.062). No significant changes were noted in strength (p=0.799) and in static endurance (p=0.278).

We choosed to evaluate a standard dynamic endurance test because the

number of PFM contractions according the definition of dynamics endurance, is a sign of fatigue level of the muscle.

One subject did not have PFM function at pre-test, and all subjects performed PFM function at the post test. One subject had hemi-paralysis of PFM at pre-test, whereas none had it at post-test. Four subjects could correctly perform isolated PFM contraction at pre-test (TG=1; CG=3), whereas eight subjects were able to do this at post-test (TG= 6; CG=2). The correct, isolated function in TG was 1/11 (9 %) at pre-test and improved to 6/11(55 %) at post-test.

Likewise the correct isolated PFM function in CG was 3/12 (25 %) and decreased to 2/12 (16.5 %).

Kegel (Kegel, 1956) pointed out that women with stress UI have incorrect PFM contraction. In 47 women with stress UI more than 30 % were unable to contract their PFM properly despite adequate information according to Bø et al. (Bø et al., 1988).

The results of vaginal palpation of PFM are presented in Figures 4a-d.

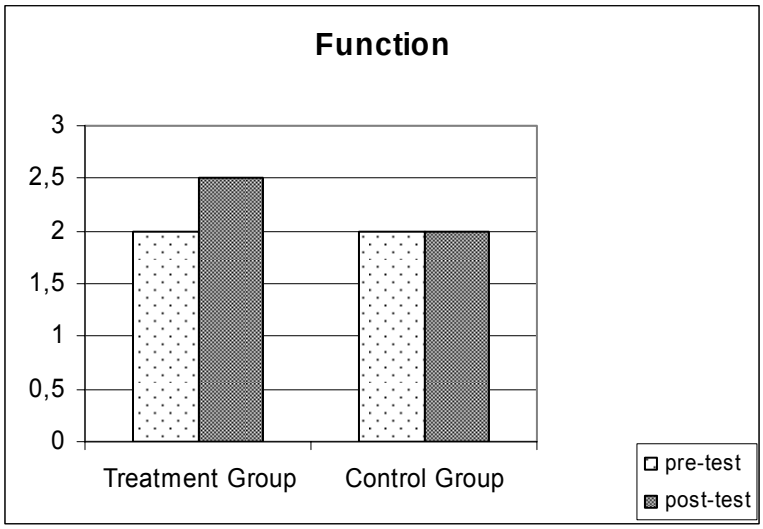


Figure 4a, Pelvic Floor Muscle function

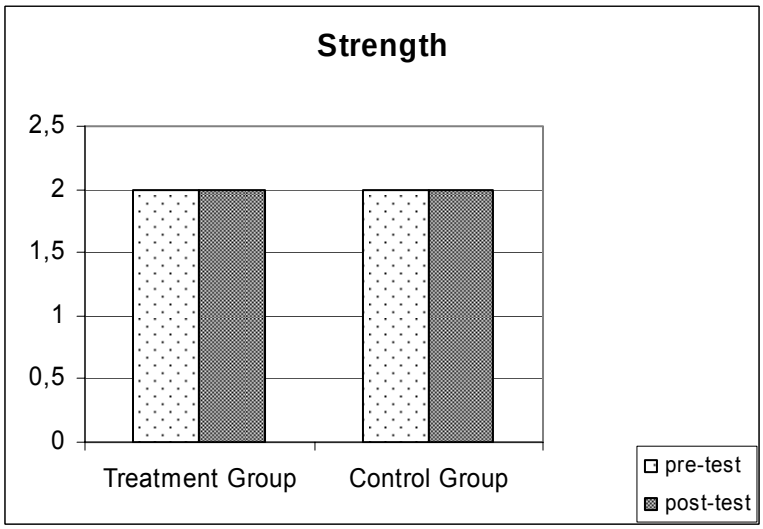


Figure 4b, Pelvic Floor Muscle strength

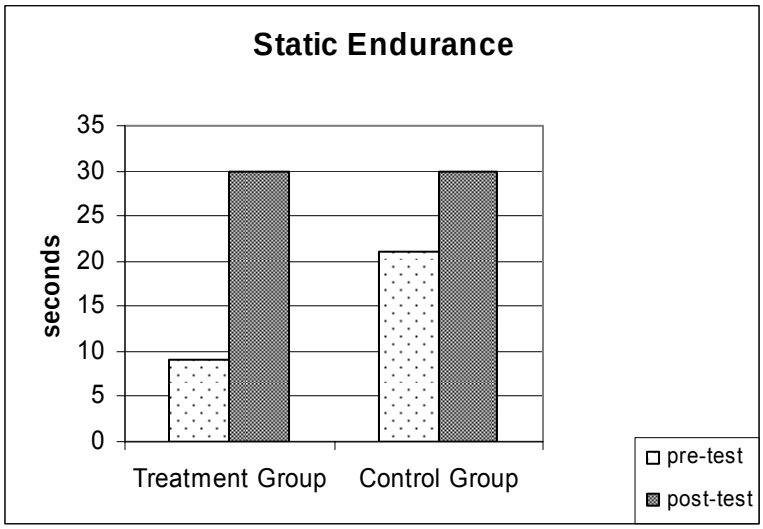


Figure 4c, Pelvic Floor Muscle static endurance

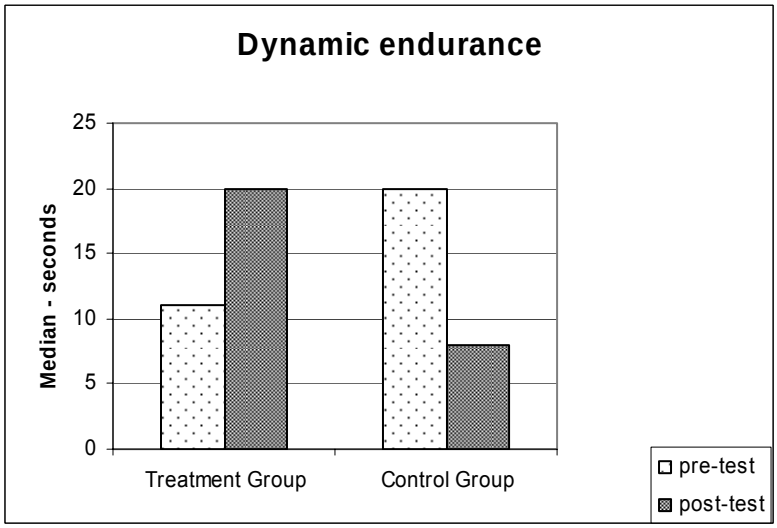


Figure 4d, Pelvic Floor Muscle dynamic endurance

4.5 Effect of PFMT measured by Quality of Life Parameters (Paper V)

The effect of 12 weeks PFMT was evaluated by the Short Form 36 (SF-36) Health Survey Questionnaire (Ware and Sherbourne, 1992) and the Incontinence Impact Questionnaire (IIQ) (Shumaker et al., 1994).

The SF-36

Seven scales in TG had changed: three scales increased (body pain, social functioning and mental health) four scales decreased (physical functioning, role limitation because of physical problems, general health perception and vitality) and one scale was unchanged (role limitation because of emotional problems). Six scales in CG had changed: three scales increased, three scales decreased and two scales were unchanged (Table 5).

There were no significant differences within or between the groups.

Sander (2000) used also SF-36 together with IIQ to assess the effect of a vaginal vice on 41 women with stress UI in their study from 2000 (Sander et al., 2000). Similar to our study they did not find the sensitivity of SF-36 sufficient to detect alterations in QoL in women with stress UI.

By means of The Nottingham Health Profile questionnaire Lagro-Jansson (Lagro-Janssen et al., 1992) noted in a controlled study that urge incontinence had a more profound impact on quality of life than stress incontinence.

Table 5. Results of Short Form (SF-36) Health Survey Questionnaire in 24 women with urinary incontinence after stroke.				
TG =Treatment group, n = 12 CG= Control group, n= 12		Pretest	Posttest	*P*
Total	TG	598 (362-713)	629 (455-692)	0,147
	CG	655 (477-692)	656 (487-729)	0,722
Physical functioning	TG	63 (43-88)	60 (48-89)	0,470
	CG	70 (43-89)	67 (50-90)	0,671
Role limitation due to Physical problems	TG	88 (6-100)	75 (50-100)	0,524
	CG	50 (6-100)	88 (13-100)	0,498
Body pain	TG	62 (44-100)	76 (44-100)	0,753
	CG	84 (63-100)	76 (52-100)	0,600
General health perceptions	TG	70 (41-91)	60 (43-87)	0,877
	CG	82 (56-92)	64 (42-90)	0,083
Vitality	TG	65 (50-74)	55 (45-78)	0,753
	CG	70 (45-89)	83 (56-85)	0,472
Social functioning	TG	88 (53-100)	100 (88-100)	0,058
	CG	100 (100-100)	100 (100-100)	0,276
Role limitation because of	TG	100 (8-100)	100 (33-100)	0,180
emotional problems	CG	100 (75-100)	100 (75-100)	1,000
Mental health	TG	68 (57-96)	82 (64-96)	0,292
	CG	84 (73-92)	86 (64-96)	0,610

The scales ranges from 0 (worst case) to 100 (best case). Median, quartile range are presented.

The IIQ

The IIQ showed the same tendency with a trend to stabilisation. One scale was unchanged (emotional health), and three scales changed slightly, but not to a significant degree (physical activity, travel and social relationship) (Table 6).

The levels of scores in the test were low: 14 is the median total value for TG before intervention and 29 after intervention on a scale ranging from 0 (best case) to 400 (worst case). 60-90 % of the answers to most of the individual questions were “no impact/no problem”. Only 3 questions of 30 (travelling more than 30 minutes, visiting places with unknown toilet facilities and impact on sleep) were answered more varied.

The changes were overall very small and statistical tests showed no significant difference between or within TG and CG.

Table 6. Results of The Incontinence Impact Questionnaire (IIQ) in 24 women with urinary incontinence after stroke.

TG =Treatment group, n = 12 CG= Control group, n=12		Pretest	Post test	*P*
Total	TG	14 (8-99)	29 (2-67)	0,374*
	CG	17 (5-80)	18 (4-116)	0,721*
Physical activity	TG	0 (0-11)	6 (0-15)	0,832*
	CG	0 (0-14)	0 (0-21)	0,414*
Travel	TG	6 (0-36)	8 (1-25)	0,445*
	CG	3 (0-26)	0 (0-29)	0,752*
Social relationships	TG	2 (0-17)	3 (0-9)	0,288*
	CG	0 (0-11)	2 (0 –13)	0,799*
Emotional health	TG	8 (4-22)	8 (1-20)	0,518*
	CG	8 (1-28)	13 (4 -21)	0,959*

The scales range from 0 (best case) to 100 (worst case). Median (quartile range) are presented.

4.6 Long-Lasting effect of PFMT (Paper VI).

The SF-36

The results at 6-month follow-up evaluating the effect of PFMT by SF-36 shoved in the TG, a weak tendency to improvement in one subscale (role limitation because of emotional problems). There were, however, no statistically significant differences within or between the TG and CG groups in any of the eight subscales of SF-36.

The IIQ

In IIQ the distribution of the results for each subscale is shown as box plots presented in Figure 5. The median value decreased in TG regarding social relationships and emotional health. In CG none of the median values decreased. Also, the 75th percentiles (shown as the top of the box in the plot) were smaller in TG regarding subscales total scores, travel, social relationships and emotional

health compared to the CG. Likewise the decrease of the 75Th percentiles in CG regarding physical activity, travel and social relationships was smaller.

In spite of these changes in the distributions, no statistical significant differences between scores at baseline and follow-up assessment were detected within or between the groups.

To our knowledge, this is the first long-lasting follow-up study, of a randomised, controlled and single-blinded trial, evaluating the effect of PFMT measured by QoL parameters in women with UI after stroke.

Recently Thomas et al (Thomas et al., 2005) included seven trials with a total of 399 participants, in a review of randomised or quasi-randomised controlled trials, evaluating the effect of interventions, designed to promote continence in people after stroke. None of the seven trials addressed the intervention in a compatible way ruling out any comparison between the trials and none had published follow-up results.

Figure 5a-e. Box plots of Incontinence Impact Questionnaire (IIQ) Scores.

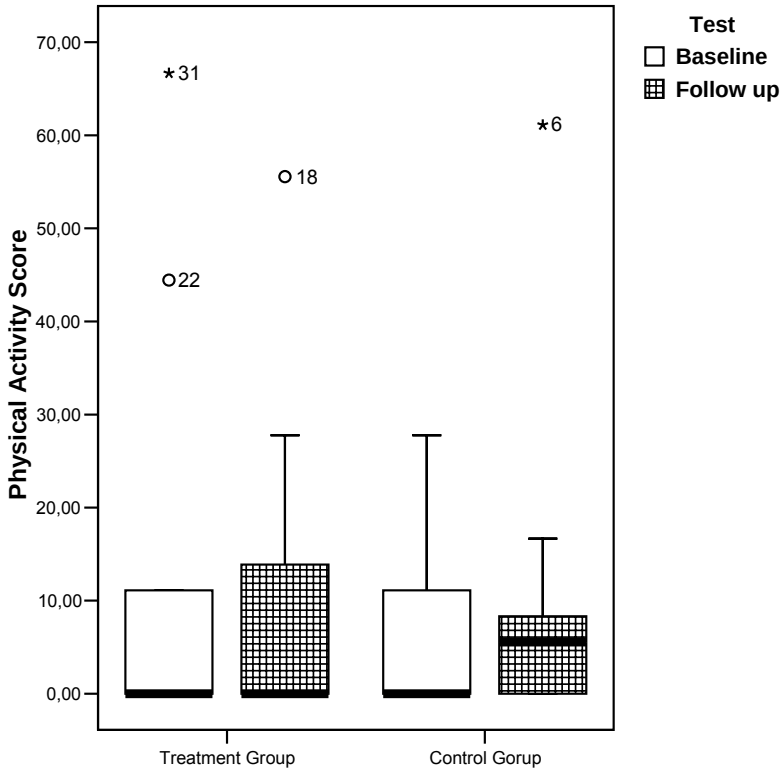


Fig. 5a, Physical Activity

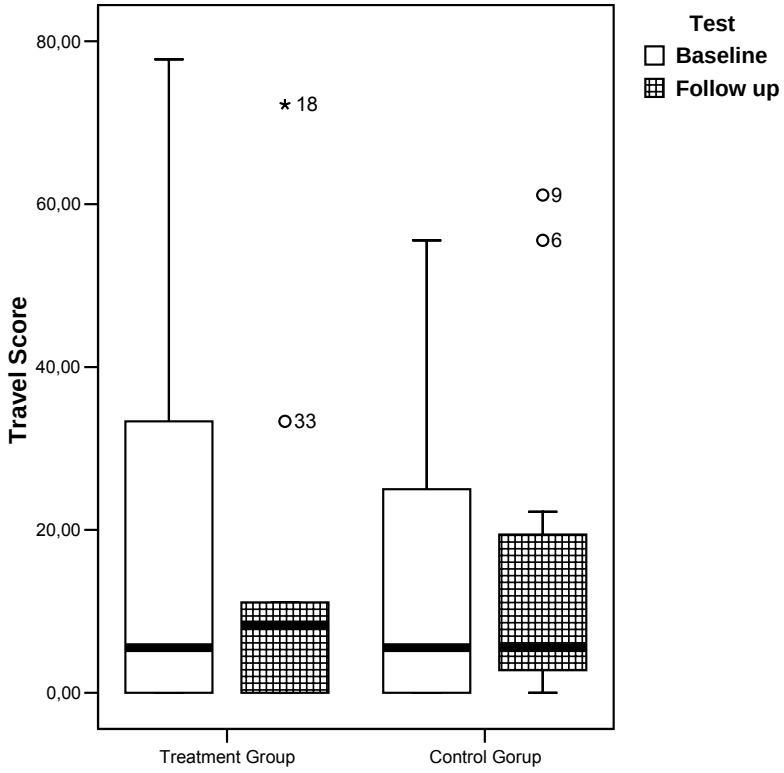


Fig. 5b, Travel Score

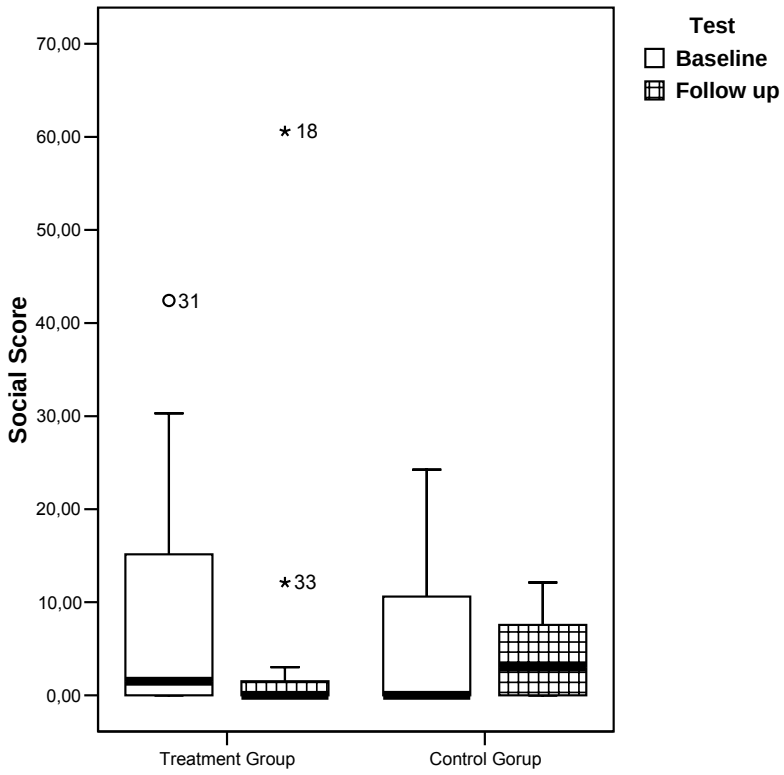


Fig. 5c, Social score

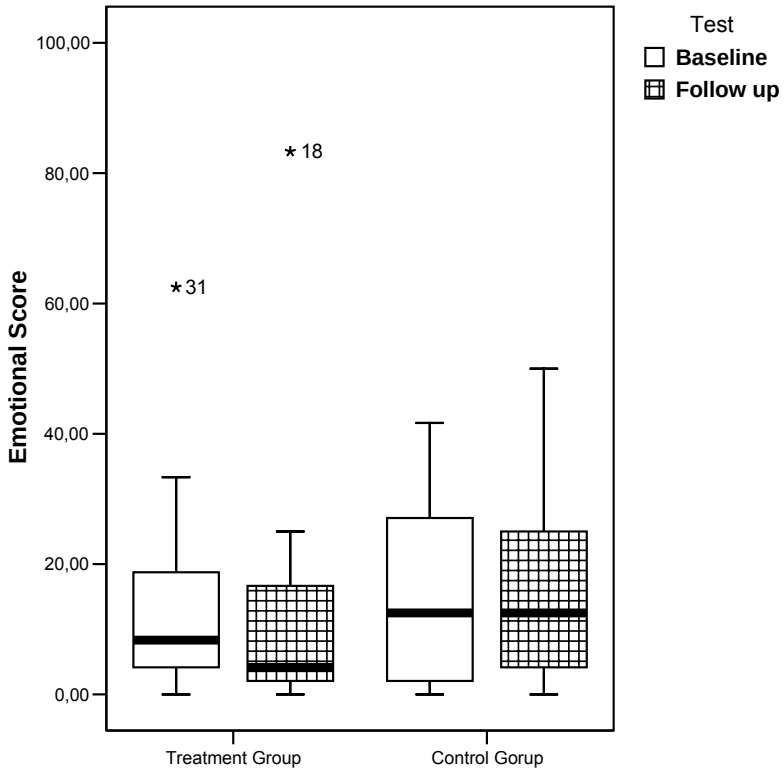


Fig. 5d, Emotional Score

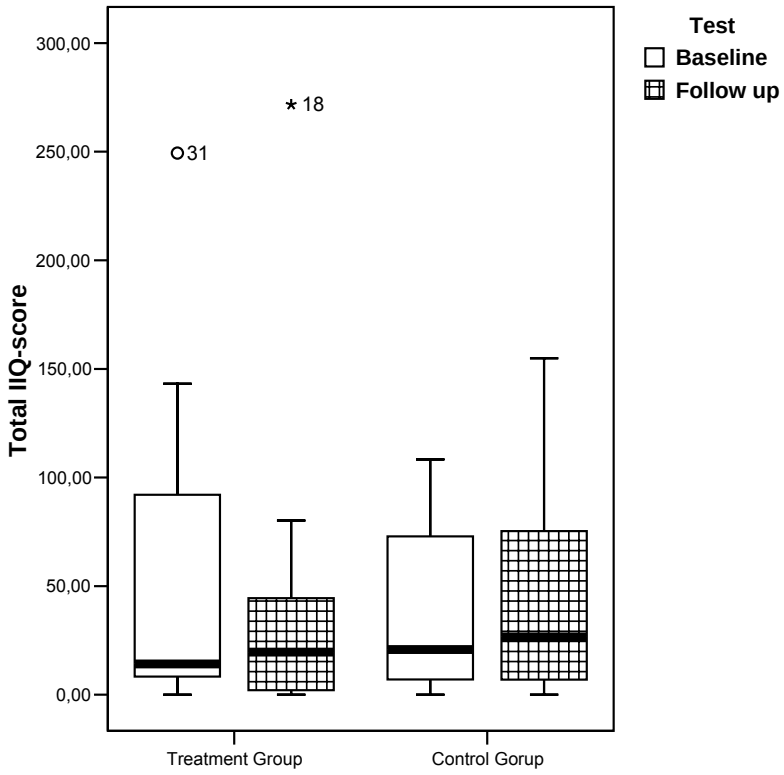


Fig. 5e, Total IIQ-score

5 Methodological considerations

A potential limitation of the study in Paper II and III was the sampling of fairly mild or moderate stroke patients that were able to respond to the questionnaire. We had excluded 45 % (451/970) mainly the most severely affected stroke patients, and if all patients were included the prevalence of LUTS would probably have been higher. The reason for the present criteria was our use of a self-administrated questionnaire to collect data.

Another limitation was the lack of an age- and gender matched healthy control group, as only indirect comparisons to prior epidemiological studies using the same methodology were possible in this study.

Strengths of the same study were the large sample size, the well characterized patients and the high response rate (84 %). Furthermore the respondents were representative of the eligible study population with regard to age and gender.

In the intervention study (Paper IV-VI) it may be argued that the study was underpowered. In our research protocol the sample size was estimated to 60 subjects, but due to the very restrictive inclusion criteria as discussed above the number of included patients was smaller. On the other hand 92 % of the subjects completed the study even the 6-mont follow-up study.

The ideal measurement had to be reliability tested and validated against objective measures. The DAN-PSS-1 had been test-retested in stroke patients, but validations remained.

Likewise problematic were the still unpublished results of reliability and validity of the four vaginal palpations test of PFM and the three specific activity limitations measurements. Especially the reliability of the four tests of PFM had to be considered.

We choosed the Modified Oxford Scale for measuring PFM strength because it was a low cost method and the simplest and in clinical practice the most used assessment tools, although there was a disadvantage of individual subjective observer.

Objective instruments measuring strength in women with UI.

One weakness of these approaches was that recording from an intra-vaginal surface EMG do not ensure absence of cross-talk coming from the electrical activity of other skeletal musculature (Fowler et al., 2002). Pressure measurements also provide an indirect indicator of muscle strength. Any contraction in the abdominal muscle may influence the pressure reading (Hahn et al., 1996; Peschers et al., 2001).

Dumoulin (2003) had developed a new, promising and reliable dynamometer for measuring PFM strength, but it has not yet been tested in any clinical trial and is only developed for women with stress UI (Dumoulin et al., 2003).

Objective measurements such as surface EMG (Gunnarsson and Mattiasson, 1994) and perinometry (Hahn et al., 1996) have been reported as useful, but at the time of initiation of the study these instruments were not validated in neurological patients.

The SF-36 questionnaire was chosen (Paper IV-VI), as this is an acknowledged method for a QoL-measurement for stroke patients (de Haan et al., 1993). The IIQ questionnaire was chosen, as this was the only available QoL-questionnaire specific towards UI in women in Danish (Sander et al., 2000). The use of the combination of SF-36 and IIQ to stroke patients with UI is new and an unproven method.

As a consequence of the above-mentioned problems, the use of SF-36 and IIQ questionnaires did not reveal any significant effects of the intervention in the treatment group.

The lack of significant results measured by SF-36 and IIQ could of course be true, but it could also mean that SF-36 and IIQ questionnaires, as the primary instruments to document the effect of the intervention are not the optimal choice. The reasons for this could be:

1. If the effect of the intervention measured by SF-36 and IIQ questionnaires gives small changes on the eight SF-36 scales and four IIQ-scales the sample must be very large to prove any significant statistical difference.
2. The IIQ questionnaire seems not to be sensitive towards patients with urge UI, which is one of the dominant types of UI for this group of patients. According to

Lagro-Janssen et al the impact of urge UI is seen as disturbance of sleep, emotional disturbances and social isolation (Lagro-Janssen et al., 1992). The IIQ has only a few items related to the special situation of women with urge UI, although the present answers to these shows some sensitivity towards urge UI.

Previous studies of urinary incontinence in stroke patients have reported the urine leakage by a subscale in Barthel Index (Kolominski-Rabas et al., 2003; Nakayama et al., 1997) or Functional Independence Measure (Wikander et al., 1998). No objective quantification has been published earlier.

The 24 hour pad test was completed by 83 % of the sample. In a larger study of 194 females with lower urinary tract symptoms (Versi et al., 1996) found similar results as 161 (83 %) subjects completed perfectly a 48 hour pad test. In this perspective we therefore suggest, that a pad test can be used as an outcome measurement in future clinical trials of stroke patients.

6 Conclusions

Paper I

- The DAN-PSS-1 questionnaire had acceptable test-retest reliability and may be suitable for measuring the prevalence and severity of LUTS and its bother factor in stroke patients

Paper II

- The results strongly indicated that LUTS are prevalent and has a major impact on daily life in a clinical sample of stroke patients

Paper III

- The results showed that 17-34 % of the stroke patients reported activity limitations assessed by specific measures
- Mobility velocity showed to be highly significantly related to severity of LUTS whereas none of the activity limitations variables were related to prevalence or bother of LUTS
- Barthel Index, mobility velocity and mobility distance were related to incontinence in symptom groups
- The study suggests that activity limitations predictors may be more focused in the treatment of LUTS in stroke patients, in particularly for stroke patients with incontinence symptoms

Paper IV

- Pelvic Floor Muscle Training had a significant effect in women with urinary incontinence after stroke measured by diaries, pad tests and vaginal palpation

Paper V

- Despite the high prevalence of stroke with urinary incontinence, it is difficult to include these patients to such studies. The samples were too small to detect any significant differences
- Development of specific instruments for Quality of Life in stroke patients with urinary incontinence can be recommended

Paper VI

- Our data indicated that PFMT may have a long-lasting effect measured by Quality of Life parameters

7 Perspectives

Methodology

International epidemiological studies of LUTS in stroke patients are few (Bird et al., 2001), and as the present study shows very high prevalence, severity and bother of LUTS, future research in this area is important and calls for large cross-sectional or longitudinal, investigations (clinical and urodynamics), leading to better prevention and treatment.

Measurements

The DAN-PSS-1 had in the present study shown high response rate in this clinical sample of stroke patients, similar was the test-retest reliability acceptable, while the validity of DAN-PSS-1 in stroke patients and its correlation to other specific QoL questionnaires as ICS male questionnaire (Donovan et al., 1996) and ICS female questionnaire (Jackson et al., 1996) remains to be investigated.

Furthermore, the DAN-PSS-1 may also be an important instrument, evaluating treatment of LUTS in stroke like it has been used in treatment of uncomplicated benign prostatic hyperplasia (Meyhoff et al., 1993).

Similar remains future methodological studies of validation and reliability in vaginal tests of PFM and specific activity limitations variables to be published.

Management of UI

In the treatment of UI after stroke had Borrie noted that a stepwise approach is best, beginning with behavioural intervention, progression to medication when needed and considering surgical intervention only as a desperate last resort (Borrie, 1998).

Our results indicate that PFMT had to be the first line in treatment of women with UI after stroke. Furthermore, PFMT had to be a standard physiotherapy offer to all women with UI after stroke according the inclusion and exclusion criteria in the present study.

Nevertheless, these results call for further studies to confirm the present results primary studies which include larger sample size.

Also research in men with UI after stroke is needed. The effect of PFMT to men with UI symptom has to be evaluated in clinical, randomised and controlled trials. Domoulin, 2005 found limited evidence for reduction of UI in male stroke in an review of treatment of UI in stroke patients (Dumoulin et al., 2005).

Recently a study from Pettersen (2007) described a new subtype of UI in stroke patients, impaired awareness of the need to void (IA-UI).

In a sample of 65 stroke patients with UI, 27 had urge UI and 38 had IA-UI. AI-UI after stroke differs from urge UI in clinical and prognostic respect and probably greater brain damage (Pettersen et al., 2007).

This knowledge may be important due to future research of PFMT in subgroups of stroke patients with UI and due to the theoretical rationale behind the effect of PFMT in stroke patients.

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