Tension-free Vaginal Tape at a Medium Sized Hospital in Sweden

Short- and Long-term Results in Different Patient Groups

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Dissertation presented at Uppsala University to be publicly examined in Rosénalen, Akademiska sjukhuset, Ing 96, Kvinnokliniken, Uppsala, Tuesday, June 8, 2010 at 13:00 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in Swedish.

Abstract

In the years 1995 to 2001, 970 women with urinary incontinence underwent surgery with tension-free vaginal tape (TVT) at the Department of Obstetrics and Gynecology, Falun Hospital. In 2002 the charts of all these women were reviewed and a questionnaire was sent in 2004. 760 women (78.4%) answered the questions. The mean time since surgery was 5.7 years. The mean age at surgery was 58.7 years. Of all patients, 580 had pure stress urinary incontinence (SUI) and 112 had mixed urinary incontinence (MUI) prior to surgery. Of the women with SUI, 85% were subjectively and persistently cured. Of the women with MUI, 60% were subjectively cured up to 3 years after the TVT operation. However this figure declined to 30% among women operated on 6-8 years previously. The increasing incontinence was due to urgency symptoms and urge urinary incontinence (UUI). The IIQ-7 and UDI-6 questionnaires were used for measuring quality of life. The women showed dramatic improvement after TVT surgery irrespective of time since surgery. Women with chronic diseases also had relative improvement in QOL scores. Sixty-seven of the women with pure SUI preoperatively (14.5%) reported persistent de novo urgency symptoms postoperatively and 51 of the women also had UUI. Old age, history of cesarean section, increasing parity and BMI were risk factors for developing de novo urgency after TVT procedure. Among women ≥ 75 years 55.7% reported cure after TVT, compared to 79.7% of women < 60 years. The overall cure rate in the very overweight women (BMI ≥ 35) was 52.1%, compared to 81.2% in women of normal weight (BMI < 25).

Conclusions. The subjective results after TVT surgery for SUI are very good even after 8 years. Short-term effect of TVT on MUI is acceptable, but declines after 3 years. Improvements in measures of quality of life after TVT surgery are dramatic and persistent in both the SUI and MUI groups. Women who developed de novo urgency symptoms after TVT surgery reported poorer quality of life. The TVT procedure is simple and safe, but the results in the oldest or most overweight women are not as good as in the younger or normal weight women.

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Dedicated to all those who knowingly or unconsciously have in any way helped me during this work.
List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


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### Abbreviations

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<tr>
<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>ICS</td>
<td>International Continence Society</td>
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<td>IIQ-7</td>
<td>Incontinence impact questionnaire</td>
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<td>ISD</td>
<td>Intrinsic sphincter deficiency</td>
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<td>LUTS</td>
<td>Lower urinary tract symptoms</td>
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<td>MUCP</td>
<td>Maximum urethral closure pressure</td>
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<td>MUI</td>
<td>Mixed urinary incontinence</td>
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<tr>
<td>OAB</td>
<td>Overactive bladder</td>
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<tr>
<td>PFR</td>
<td>Peak urinary flow rate</td>
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<tr>
<td>POP</td>
<td>Pelvic organ prolapse</td>
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<tr>
<td>QOL</td>
<td>Quality of life</td>
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<tr>
<td>SUI</td>
<td>Stress urinary incontinence</td>
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<tr>
<td>TVT</td>
<td>Tension-free vaginal tape</td>
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<tr>
<td>UDI-6</td>
<td>Urogenital distress inventory</td>
</tr>
<tr>
<td>UI</td>
<td>Urinary incontinence</td>
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<td>UUI</td>
<td>Urge urinary incontinence</td>
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Introduction

Definition and prevalence
The International Continence Society (ICS) is an international, multidisciplinary organization that publishes its opinions and recommendations concerning various aspects of incontinence. ICS defines urinary incontinence (UI) as the complaint of any involuntary leakage of urine (1). There is a wide variation in the reported prevalence of UI. This is readily explained by the use of different definitions of UI, variations in the populations studied and the use of different diagnostic instruments. Urinary incontinence occurs more frequently in older women. There are reports on a UI prevalence of 12 % among 50 year old women, rising to 25 % in women aged 80 (2,3).

According to the ICS definition, stress urinary incontinence (SUI) is the complaint of urinary leakage on effort, or on sneezing or coughing. Urge urinary incontinence (UUI) is defined as the complaint of urinary leakage accompanied or immediately preceded by urgency. Mixed urinary incontinence (MUI) is the complaint of leakage associated with urgency and also with exertion, effort, sneezing, or coughing. Approximately 55 % of cases of incontinence in women are SUI, 10 % UUI and 35 % MUI. Stress urinary incontinence (SUI) occurs more frequently in younger women, UUI and MUI are more prevalent in older women (4).

Pathophysiology
Stress urinary incontinence
Urinary leakage occurs when the intraabdominal pressure exceeds the urethral pressure. There are several important factors preventing urinary leakage. The pelvic floor with its complexity of muscles and ligaments supports the urethra, thus preventing leakage when the intraabdominal pressure increases. Adequate neuromuscular function is needed to control the detrusor muscle of the bladder, the smooth muscle of the urethra and the urethral sphincter muscle, as well as the muscles of the pelvic floor. Damage of the connective tissue of the pelvic floor can also cause incontinence. Vascular plexuses in the urethral wall and the urethral epithelium are other
important factors that prevent incontinence. Pregnancy and delivery can damage these structures and are known to predispose women to SUI (5,6). Changes in muscles, nerves, connective tissue and hormonal function occur with aging, leading to a higher prevalence of UI in elderly(7).

In the middle of the 20th century the intraabdominal pressure equalization theory was proposed. This theory concerning underlying mechanisms of stress urinary incontinence, was dominant for a long period. According to this theory, a passive pressure transmission from the abdomen to the proximal urethra counteracting pressure on the bladder is crucial to maintain continence in situations with rising abdominal pressure. As a result of this theory, the surgical procedures introduced at that time aimed to elevate the proximal urethra and bladder neck to improve and secure the transmission of the abdominal pressure.

In 1990, Professor Ulmsten at the Department of Obstetrics and Gynecology, University Hospital of Uppsala, presented the “integral theory” of incontinence (8). This theory is currently the dominating pathophysiologic theory underlying SUI, together with the hammock hypothesis. According to the integral theory, continence is maintained by the integral function of the pubourethral ligament, which attach the urethra to the pubic bone, the suburethral vaginal hammock and the levator ani muscles (m.pubococygeus/m.puborectalis and m.iliococcygeous). In women without SUI, the pubococcygeal muscle is able to contract pulling the suburethral hammock forward against the pubourethral ligament, thus closing off the urethra and maintaining continence. However, the pubococcygeal muscle can only contract over a limited extent; thus, if there is significant laxity of vaginal support, if there are defects in any of these structures, the vaginal hammock may not be pulled sufficiently forward against the pubourethral ligament to maintain urethral closure. Not only SUI but also urge symptoms can occur for the same reason. According to the integral theory, defective support of the vagina can lead to stimulation of stretch receptors in the proximal urethra and bladder neck, causing frequency, urgency, and nocturia with or without incontinence Today the golden standard for surgical treatment of stress urinary incontinence is the tension-free vaginal tape procedure (TVT). During this surgical procedure a synthetic sling is put under midurethra. The TVT procedure has been shown to stabilize the urethra anatomically and thus to significantly increase the pressure transmission ratio on the proximal and distal urethra without influencing maximum urethral closure pressure (MUCP) at rest (9,10).

Finally there is a third theory concerning underlying mechanisms of stress urinary incontinence. The hammock hypothesis does not contradict the integral theory but emphasizes the support of the urethra by the anterior vaginal wall, compressing the urethra when the abdominal pressure rises. The support depends on an intact anterior vaginal wall and vaginal part of endopelvic fascia, connecting to the tendinous arch.
In some women there is damage to structures of the actual urethra leading to intrinsic sphincter deficiency (ISD). These structures include urethral muscles, connective tissue, vascular plexuses in the urethral wall and the urethral epithelium. The condition is more common in older women. This dysfunction of the urethra is a variant of stress urinary incontinence and can be difficult to cure.

Urge urinary incontinence

The function of the urinary bladder is regulated by the central nervous system. The mechanisms of storing urine and micturition are complex, involving several different areas of the central nervous system. Neurological disease in different parts of the central nervous system can result in lower urinary tract symptoms (LUTS). The condition of LUTS includes storage symptoms such as daytime frequency, nocturia, urgency and various types of urinary incontinence. LUTS also includes voiding symptoms and postmicturition symptoms. Abnormalities in the bladder and in the pelvis are also related to UUI (11). However, in many women with UUI, there is no obvious cause of their symptoms.

Risk factors of urinary incontinence

Pregnancy in itself seems to be a risk factor for UI. There is also a greater risk of UI after vaginal deliveries than after cesarean sections (12-14). Other well known risk factors are age and overweight (15,16). Chronic diseases such as constipation, chronic obstructive pulmonary disease, diabetes, neurological disease, previous hysterectomy, or prolapse surgery (17,18) are also suggested as risk factors for urinary incontinence.

Diagnostic approach

When evaluating urinary incontinence, it is important to take into consideration underlying mechanisms, risk factors and medication that might contribute to the symptoms. It is also important to determine the impact of the patients symptoms on her quality of life and be aware of her own therapeutic goals.

There are different diagnostic tools to provide the clinical diagnosis of the various types of urinary incontinence The mainstays of the evaluation are a careful history and physical examination, together with a two day voiding diary. An objective verification of the urinary incontinence is optional. In patients with urinary incontinence advanced testing such as urodynamics and cystoscopy should be carried out in selected cases (19).
During history taking, women are asked about the frequency and amount of leakage in daily life and their pad use. The women are also questioned about pregnancy and childbirth. Questions should include the medical history, surgical interventions, and current medication. It is important in women with SUI to ask about their actual and desired physical activity level.

The gynecological examination rules out abdominal masses, pelvic organ prolapse, and genital atrophy. The pelvic floor muscles are palpated and some clinicians determine to what extent the anterior vaginal wall moves during straining. A cough test may verify urinary incontinence.

A two-day voiding diary should be included in the basic evaluation. The patient notes the time of each void and the volume voided. In some diaries the women also records fluid intake and activity leading to the leakage. Sometimes the woman can also note the approximate amount of leakage. The voiding diary is not only used for diagnosing urinary incontinence but also for assessing treatment effectiveness.

When examining the woman a positive cough test, when the leakage is visualized at the moment of cough, is helpful to confirm the diagnosis of SUI. There are several different types of standardized quantification tests for objectifying the leakage. The magnitude of the patients UI can be checked by weighing the perineal pad. The pad test is not only used for diagnosing urinary incontinence but also for assessing treatment effectiveness (20).

A urine examination should be performed in the basic evaluation to exclude bacterial infection, hematuria or glucosuria.

The postvoiding residual volume can be measured by catheter or ultrasound. This test excludes urinary retention.

Urodynamic testing refers to a combination of tests that involve simultaneous measurements of various physiological parameters of bladder and urethral function during bladder filling and emptying. Urodynamic testing can be a valuable complement to the rest of the evaluation. Cystometry provides information about the neurological control of the bladder, the detrusor muscle function and the compliance of the bladder wall (21). The urethral pressure profile gives data on the urethral pressure and the urethral length, which can be of interest in treating patients with intrinsic sphincter deficiency (ISD) (22).

Cystoscopy should be performed in a woman with a short history of urinary incontinence, bladder pain and hematuria, to rule out bladder tumor or inflammation.

Conservative treatment of urinary incontinence

Lifestyle interventions such as fluid restriction and weight loss is known to decrease urinary incontinence (23,24). An optimal medication for diabetes, chronic constipation, chronic obstructive pulmonary disease and heart failure
is of importance. Some women only suffer from SUI in certain situations, for example during physical training, and in these women a device can be an acceptable treatment.

Supervised pelvic floor muscle training is an effective form of treatment for SUI and should be offered as first line conservative therapy. However, the training must be correct and regular and the training only has effect as long as the woman is exercising (25).

Bladder training and anticholinergic/antimuscarinic medication play an essential role in the treatment of UUI and MUI. The bladder training involves a gradual increase in voiding intervals with voiding by the clock rather than when the urge to void occurs. Anticholinergic drugs block receptors in the bladder wall thus affecting the central nervous system ability to contract the bladder. The development of selective anticholinergic drugs with main activity on the smooth muscle of the urinary bladder may reduce the side effects. A low dose of vaginally administered estrogen is beneficial in postmenopausal women with UUI, but there is no evidence for any effect in women with SUI (26,27).

Duloxetine, a selective serotonin and noradrenaline reuptake inhibitor, is thought to increase the tonus in the urethral sphincter. It has been shown to reduce the number of incontinence episodes but its clinical use is limited by side effects and low compliance (28).

Electrical stimulation can be used to activate the pelvic floor muscles in women with SUI and MUI. This stimulation in women with UUI aims to activate inhibitory reflexes on the bladder. The electrical stimulation is given by a transducer in the vagina. The best results are in women with UUI, but unfortunately the effects decline in the long-term (29,30).

Surgical treatment of stress urinary incontinence

One object of incontinence surgery is to increase outlet obstruction. This can be done by means of the traditional open vesico-urethral suspension (e.g Marschall-Marchetti-Krantz, Lapides) or Burch colposuspension. These surgical techniques aim to replace the bladder neck in its correct anatomical position, restoring the transmission of abdominal pressure to the bladder neck, an important mechanism which is believed to contribute to continence. The laparoscopic colposuspension has the advantage of being a minimally invasive procedure with an outcome similar to that of traditional open Burch colposuspension (31-36). Since the late 1950s there have been many attempts to emulate the good results achieved by open surgery, but with minimally invasive techniques. Needle suspensions (Pereya, Stamey, Raz, Gittes) have been used in attempts to reposition the bladder neck in the same way as with colposuspension. However they do not have the long-term outcome of colposuspension (37).
Today incontinence surgery focus on the object of increasing the support of the urethra. Since the beginning of the 20th century there has been a large variation in sling materials and the position of the sling, method of placement and degree of tension. It was on the basis of the integral theory that the TVT procedure was introduced. The TVT procedure is preferably carried out under local anaesthesia and in a day care setting. Through a small incision in the vaginal wall under the mid urethra, a polypropylene sling is placed without tension. Cystoscopy is performed to check for bladder perforation when putting the sling up on both sides of the urethra and to the posterior surface of the symphysis. When placed mid-urethrally the pubovaginal sling produces a platform against which the urethra is compressed during abdominal straining (38). The tension free vaginal tape (TVT), has become the golden standard procedure for SUI because of its simplicity, safety and good results (39-41). Development of de novo urgency symptoms with or without UI is the most common long-term complication after TVT surgery. In a recent Danish national survey undertaken by Ammendrup et al (42), 32% of TVT treated women reported complete cure, 36% much improvement, 17% were subjectively improved and 15% were unchanged or worse.

In order to avoid the blind passage through the retropubic space, two alternative ways of putting the sling through the obturator membrane have been developed. The tension-free vaginal tape obturator route (TVT-O) and the trans obturator TVT route (TOT) are equally effective as TVT procedures in the treatment of stress urinary incontinence according to studies with a three-year follow-up time (43,44).

Trans- or periurethral injection of different bulking agents into the wall of the urethra can be an option in selected women with SUI, especially those with intrinsic sphincter deficiency. The procedure is simple but less effective than sling surgery (45,46).

Summary

According to the World Health Organisation (WHO), “health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity” (47). Thus the definition of health is indeed subjective. Changes in patient-related quality of life are of great importance when evaluating the result of TVT in patients with SUI or MUI.

Elderly people form a growing section of western society and their health can be good even when they are diagnosed with chronic diseases. Urinary incontinence is a frequent problem among elderly women (48) and there are studies suggesting good results of TVT in older women with stress urinary incontinence (49).
Obesity is a growing health problem in the western society. The prevalence of UI is higher among obese women. A simple, minimally invasive operation under local anesthesia such as TVT is preferable in this patient group and there are studies presenting good results (50).

The TVT procedure is a safe method with few acute complications provided that appropriate training is provided. However one troublesome late complication after TVT and other incontinence surgery is de novo urgency with or without urinary incontinence. The prevalence of this varies in different studies between 3 and 30% (51,52). These patients are not satisfied with their operation. The mechanism underlying de novo urgency after incontinence surgery is still unknown.
Aims of the study

Together with Professor Ulmsten at the Department of Obstetrics and Gynecology at the University Hospital of Uppsala, the Department of Obstetrics and Gynecology at Falun Hospital performed TVT surgery as early as the beginning of the 1990s, when the procedure was still new. In 1995 we started to use the polypropylene tape which is the tape in current use. This thesis is based on the results from all women who underwent TVT surgery for SUI or MUI in the region of Dalarna and during the years of 1995 to 2001. The overall aims of this research were to review the results of the TVT procedure consistently in all these different women, thus reflecting clinical reality.

Paper I
The aim of this study was to examine the long-term subjective results after TVT surgery in women with MUI compared to SUI.

Paper II
The aim of study 2 was to evaluate the long-term effects of a TVT procedure on quality of life in women with SUI or MUI. The subjective results in women with certain chronic diseases were also studied.

Paper III
Through long-term follow up, the aim of study 3 was to identify potential risk factors for developing de novo urge symptoms with or without incontinence after TVT surgery.

Paper IV
This study was undertaken to review the long-term subjective results of the TVT procedure in very obese women (BMI ≥35) compared to women of normal weight (BMI<25), and in the oldest women (≥75 years) compared to women younger than 75 years.
Methods

Study design
The study had a retrospective observational design. The study population consisted of a hospital cohort of all women who underwent TVT surgery in the region of Dalarna, between October 1995 and December 2001. Women seeking health care for UI were diagnosed at different hospitals and outpatient clinics of the region, but at that time all TVT procedures were performed at the Department of Obstetrics and Gynecology at the Falun Hospital. Specific groups of patients were compared with others within the study population concerning the result of TVT surgery.

At that time, no results of TVT procedures in such a large study population had been presented. In a benign condition such as UI, subjective cure is obviously of great importance, and hence we focused on subjective results. Today we know that urinary incontinence has a great negative impact on quality of life. Thus change in quality of life assessments after TVT surgery have become of increasing interest since the study began. The Incontinence Impact Questionnaire and the Urogenital Distress Inventory, especially their short forms IIQ-7 and UDI-6, have gained wide popularity. In the same year as the first study patients underwent surgery with TVT, the IIQ-7 and UDI-6 were presented, but they were not then in use. The women of the study population were informed about the study and when they had given their consent all records were reviewed in 2002.

TVT surgery was performed on 970 women during the study period of October 1995 to December 2001. Data concerning BMI, medical history, estrogen therapy, previous surgery because of UI or pelvic organ prolapse (POP) and preoperative diagnostics and type of UI (e.g SUI or MUI) were reviewed. Any peroperative or postoperative complications were also recorded. The doctoral student reviewed all patient records and checked the given preoperative diagnose of their UI according to earlier definitions. Seventeen women had unclassifyable UI and thus were excluded from the study.

One doctor had been trained in the TVT operation technique at the Department of Obstetrics and Gynecology of the University Hospital in Uppsala. The same doctor gave instructions and trained all 10 surgeons performing TVT in the study patients. Three of these surgeons carried out the majority of the operations. There were no significant differences in
operation results between the surgeons. The same type of tape (polypropylene) was used at all operations.

All women had been diagnosed preoperatively on the basis of their history, gynaecological examination, voiding chart, urine examination, and a cough test. A cough test is performed when the bladder is filled to 3 dl and the patient is asked to cough vigorously. In the event of urinary leakage the urethra can be stabilized by lifting digitally on one side, paraurethrally to check if the leakage stops (Bonney’s test). If a woman had a history of SUI or MUI but no urinary leakage could be verified by a cough test, a pad test was performed, in which the women weighed the pad before using it and again when changing the pad. For a woman to be accepted for TVT surgery, the urinary leakage was not to be less than 10 grams per day. Urine analysis was used for screening and urine culture was made when there was a sign of urinary tract infection. Cystoscopy and cystometry were performed in 473 (49%) of the women when appropriate, generally when there was a history of mixed urinary incontinence. A complete urodynamic evaluation with measurement of maximal urethral closure pressure and urethral length was performed in 156 patients (16%), generally in older women. Together with the history, an objective verification of urinary leakage was necessary for a diagnosis of SUI. A history of both SUI and UUI and an objective verification of urinary leakage were necessary for a diagnosis of MUI.

TVT surgery was performed as described in the Introduction. The patients were operated on under local anesthesia. When required, small doses of sedatives were given intravenously. A small incision was made at the mid-urethral level and after minimal paraurethral dissection the polypropylene tape was introduced retropubically on both sides of the urethra. The bladder was filled with 300 ml of saline and a cystoscopy was performed to confirm that the bladder was intact. The tape was then adjusted to check continence while the patient coughed. The TVT procedure was ambulatory in 221 (23%) women, and the remaining patients generally stayed in hospital for 1-2 nights. The patient was discharged when there were no signs of complications and when she was able to void twice with <100 ml of residual urine. The mean age at surgery was 58.7 years (SD 12.3 years; range 29-89).

The women who underwent TVT surgery between 1999 and 2001 received a mailed questionnaire after 3 months. The questionnaire was answered by 477 (85.5%) of the women. The subjective result was given as four alternatives: 1. “worsened”, 2. “unchanged”, 3. “improved”, 4. “completely cured”. There were questions about urgency before and after surgery and also concerning difficulties in emptying the bladder.

In early 2004, a further questionnaire with a prepaid addressed envelope was mailed to the women. The average follow-up was 5.7 years. Five alternative answers could be given regarding the result of the TVT procedure: 1. “worsened”, 2. “unchanged”, 3. “improved”, 4. “almost cured”, 5. “completely cured”. The last two alternatives were analyzed together for
comparison with the three month follow-up data. In addition there were questions about de novo urgency with or without urinary incontinence, frequency and nocturnal incontinence, difficulties in emptying the bladder, and urinary infections after the TVT surgery. We asked about any changes in sexual life and if there were any, whether they were for better or worse, and if the women had any dyspareunia. The questionnaire was also designed to obtain demographic data and information on the reproductive history, as well as the history of chronic diseases such as diabetes, neurological disorders, bronchitis, and chronic constipation and questions were also asked about smoking habits and recurrent urinary infections. Nonresponders received a reminder 1 month after the initial request.

The questionnaire was answered by 760 women (78.4%). Forty-nine (5%) of the women had died at long-term follow-up, 8 women (0.8%) were too ill to answer. Seventeen women had UI that could not readily be classified and were thus excluded. Fifty-one women with SUI developed de novo urgency with UI and were studied separately. Nonrespondents differed from respondents by having a higher mean age (67.3 versus 62.2 years, p<0.001) and a higher BMI (27.7 versus 26.9, p=0.01). There were no significant differences in parity, estrogen treatment, incontinence classification, or peroperative or postoperative complications between the two groups. Since there were fewer TVT procedures in 1995-1997, these women were analyzed together in one group.

The studies were approved by the Research Ethical Committee, Uppsala University.
This study comprised 580 women (83.8%) diagnosed with SUI and 112 (16.2%) with MUI. Seventeen women with UI that could not be classified were excluded. Fifty-one women with de novo urge incontinence were also excluded from study 1. In total 692 women had SUI or MUI prior to the TVT procedure. The women were grouped into cohorts by number of years since TVT surgery. The cohorts of women with SUI were as follows: 2 years n=93, 3 years n=116, 4 years n=113, 5 years n=102 and 6-8 years n=156. The cohorts of women with MUI were: 2 years n=29, 3 years n=32, 4 years n=21, 5 years n=17 and 6-8 years n=13. Five alternative results after TVT surgery were given in the long-term follow-up Questionnaire, as described above.
The study comprised 768 women diagnosed with SUI or MUI prior to TVT surgery. Eight of these women were too ill to fill in the questionnaire by themselves. A telephone interview was conducted with the patient, relatives or other caregivers. These patients were excluded from the other studies described in this thesis. To undertake a long-term follow-up of quality of life after the TVT procedure, we used two validated instruments designed for UI. The Incontinence Impact Questionnaire (IIQ) relating to the degree to which UI affects different activities, mainly of a social nature, and the Urogenital Distress Inventory (UDI), relating to the extent to which symptoms of lower urinary dysfunction (LUTS) affects the woman (53). Later short forms of IIQ and UDI namely IIQ-7 and UDI-6 were presented and evaluation showed just as good validity and reliability as in the longer versions (54) (Appendix). We used the short form questionnaires IIQ-7 and UDI-6 in the present study. The questionnaires have four different response levels, describing the degree to which the woman is bothered about her symptoms: 0=not at all, 1=slightly, 2=moderately, 3=greatly. The average score (0-3) is multiplied by a factor of 33.33 to give a best score of 0 and a worst score of 100. In addition to IIQ-7 and UDI-6 questions were asked about chronic diseases such as diabetes, chronic constipation, bronchitis, and recurrent urinary infections. There were also questions about the patients sexual life. The women were asked to recall the situation before the TVT surgery and to describe the present situation.
All charts of 970 women undergoing TVT surgery because of SUI or MUI were analyzed. Cystoscopy and cystometry were performed in 473 women (49.7%), generally when there was a history of MUI. At long-term follow-up a questionnaire was mailed to the women. The questionnaire included general results of the operation, concomitant diseases, sexual health and the quality of life instruments IIQ-7 and UDI-6 as previously described. The patients were asked about urgency before and after the TVT procedure, and also about medication for urgency and frequency, UI and difficulties in emptying the bladder, and recurrent urinary infections. Women with preoperative MUI or transient postoperative urgency symptoms were excluded. De novo urgency with or without UI should be persistent and the follow-up was at least 2 years. The women were grouped by duration since TVT surgery, and those who had TVT surgery during 1995-1997 were analyzed together. Four hundred and sixty-three (60.9%) women had a preoperative diagnosis of SUI according to a review of their records and their questionnaires.
One hundred and thirteen of the women undergoing TVT surgery because of UI were ≥75 years of age. At long-term follow-up 36 of these women were dead giving 77 women eligible for analysis, and of these women 61 answered the questionnaire. Sixty-one of the women who had TVT surgery had a BMI of ≥35. At long-term follow-up one of these women was dead leaving 60 women to be enrolled in the study, of these women 48 answered the questionnaire. The diagnostic criteria for SUI and MUI were as previously described. Cystoscopy and cystometry were performed in 473 women (48.8%) mainly in women with MUI, including 38 (62.3%) of the women aged ≥75 years and 23 (47.9%) of the women with BMI ≥35. A complete urodynamic evaluation with measurement of maximum urethral closure pressure and urethral length was carried out in 156 (16.4%) of the women, including 17 (27.9%) of the oldest women and 10 (20.8%) of the very obese women.

The questionnaires for short-and long-term follow-up as previously described were analyzed in different groups of women. Regarding age, the women were divided into groups of <40 years (n=63), 40-49 (n=219), 50-59 (n=289), 60-74 (n=273), and 75-96 years (n=113). The subjective outcome after TVT surgery was compared between women aged ≥75 years and <75 years. BMI was grouped into <20 (n=6), 20-24 (n=285), 25-29 (n=433), 30-34 (n=155), and ≥35 (n=61). Mean BMI in the latter group was 38. The
subjective outcome after the TVT procedure was compared between women with BMI ≥35 and those with BMI<25.

Statistics
Continuous variables were compared with t-tests giving p-values. Nominal variables were compared with the chi 2 test. Odds ratios and 95% Confidence Intervals (CI) were estimated by logistic regression, which was also used in multivariable analyses to adjust for confounding factors.
Results

Paper I

There was a large age difference between the women with MUI and those with SUI (mean age 67 years versus 61.2 years, p<0.001) thus adjustment was made for age in subsequent comparisons. The women with MUI also had a slightly higher BMI than the women with SUI (30.0 versus 26.7, p=0.007). Cesarean delivery was more common among the women with MUI (n:=7, 7.1%) than among the women with SUI (n=14, 2.6%) and the review of the patients records showed that the difference was significant (OR 2.49, 95% CI 1.09-5.34). A review of the patients charts also revealed that more women with MUI used locally applied estrogen compared with women with SUI (OR 1.65, 95% CI 1.01-2.73) (Table 1).

Table 1. Demographic characteristic of women with stress urinary incontinence and those with mixed urinary incontinence.

<table>
<thead>
<tr>
<th></th>
<th>Mixed (%)</th>
<th>Stress (%)</th>
<th>Odds ratio/</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=112</td>
<td>N=580</td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td>Mean age, years</td>
<td>67.0</td>
<td>61.2</td>
<td>0.0001(^1)</td>
<td></td>
</tr>
<tr>
<td>Only compulsory school</td>
<td>67 (60.9)</td>
<td>274 (49.2)</td>
<td>1.10</td>
<td>0.70-1.75</td>
</tr>
<tr>
<td>Body mass index</td>
<td>30.0</td>
<td>26.7</td>
<td>0.007(^1)</td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>18 (16.1)</td>
<td>97 (16.8)</td>
<td>1.24</td>
<td>0.69-2.16</td>
</tr>
<tr>
<td>Parity</td>
<td>2.3</td>
<td>2.4</td>
<td>0.54(^1)</td>
<td></td>
</tr>
<tr>
<td>Cesarean section</td>
<td>7 (7.1)</td>
<td>14 (2.6)</td>
<td>2.32</td>
<td>0.83-5.95</td>
</tr>
<tr>
<td>Climacteric</td>
<td>91 (82.7)</td>
<td>352 (61.4)</td>
<td>1.49</td>
<td>0.76-2.98</td>
</tr>
<tr>
<td>Estrogen treatment (any)</td>
<td>76 (69.1)</td>
<td>315 (55.1)</td>
<td>0.90</td>
<td>0.53-1.60</td>
</tr>
<tr>
<td>Local estrogens</td>
<td>39 (34.8)</td>
<td>112 (19.3)</td>
<td>1.38</td>
<td>0.84-2.24</td>
</tr>
</tbody>
</table>

Chronic constipation was also more common among the women with MUI (n=12, 11.1%) than among the women with SUI (n=26, 4.6%) (OR 2.33, 95% CI 1.07-4.83). There were no other differences in demographic characteristics or medical history. Four patients (3.6%) with MUI needed
surgical correction of the tape, compared to 53 patients (9.2%) of the women with SUI (OR 0.42, 95% CI 0.12-1.06). There were no other significant differences in peri or postoperative characteristics.

The women were grouped according to years since TVT surgery as previously described and asked about changes in their UI. As the mean age gradually increased in the women having TVT surgery, there were only small age differences between the groups by years after the TVT procedure. Of the women with SUI 85% answered “almost cured” or “completely cured”, irrespective of the number of years since surgery. Sixty percent of the women with MUI reported “almost cured” or “completely cured” up to 3 years after surgery. Women that had TVT surgery more than 3 years ago, had a steady decline in outcome to 30% subjective cure 6-8 years after the TVT procedure. (Fig 1)

![Figure 1. Cured or almost cured of stress urinary incontinence or mixed urinary incontinence, grouped by years since TVT surgery.](image)

The difference in cure rate after 2-4 years as compared with 5-8 years in women with MUI was significant (p=0.02). Stress urinary incontinence was subjectively cured at a same level in women with MUI as in women with SUI but the urge symptoms and UUI returned with time in women with MUI. (Fig 2).
Figure 2. Stress urinary incontinence and urgency and urge urinary incontinence in women with the preoperative diagnosis of MUI grouped by years since TVT.

Thirty (27.3%) of the women with MUI reported nocturnal incontinence, as compared to 47 (8.2%) of the women with SUI. Twenty-three (40.4%) of the patients with persistent or recurrent MUI were taking anticholinergic medication, as compared to 2 (5.6%) of the women reporting cure.

Paper II

Women of the study population were asked to report on their present condition and recall their situation prior to TVT surgery. There was a dramatic change in their quality of life. The mean IIQ-7 score before TVT surgery was 43.7, compared to 11.5 at follow-up (p=0.0001). The patients responses to the questionnaire were grouped with “not at all” or “slightly” combined as one variable, while “moderately” or “greatly” were analyzed separately. The majority (75.2%) of the women were moderately or greatly affected by their UI during physical activity preoperatively. Many women were also affected by their UI during entertainment (41.1%) and social activities (39.5%). Nearly half of the women (45.1%) had felt frustration to a moderate or great extent because of their UI before the TVT surgery. At follow-up only 13.2% were moderately or greatly affected by UI during physical activity and only 10% at entertainment or social activities. Frustration because of persisting UI was reported by 9.8%. All comparisons between the situations before and after TVT surgery were highly significant. There were no differences in results when the women were subgrouped in terms of length of time since TVT surgery. The mean UDI-6 score before TVT surgery was 54.2, compared to 24.0 at follow-up (p=0.0001). (Table 2)
Table 2. Quality of life (UDI-6) before and after TVT surgery. p-value <0.0001 for all comparisons between before and after surgery.

<table>
<thead>
<tr>
<th>Bothered by:</th>
<th>Before TVT no. (%)</th>
<th>After TVT no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None/slightly</td>
<td>Moderately</td>
</tr>
<tr>
<td>Frequent urination</td>
<td>237 (31.5)</td>
<td>237 (31.5)</td>
</tr>
<tr>
<td>Urgency incontinence</td>
<td>311 (41.6)</td>
<td>195 (26.1)</td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>93 (12.2)</td>
<td>134 (17.6)</td>
</tr>
<tr>
<td>Drop leakage</td>
<td>264 (35.4)</td>
<td>247 (33.1)</td>
</tr>
<tr>
<td>Difficulty to empty the bladder</td>
<td>484 (64.1)</td>
<td>161 (21.3)</td>
</tr>
<tr>
<td>Lower abdominal/genital discomfort</td>
<td>654 (86.6)</td>
<td>68 (9.0)</td>
</tr>
</tbody>
</table>

There were only minor differences when the women were subgrouped in terms of length of time since TVT surgery. There was a small negative change in mean UDI-6 score later than 6 years after TVT surgery, but the scores were still much more favorable compared to before TVT surgery. (Fig 3)

![Graph showing Quality of life score over years since TVT surgery](image_url)

**Figure 3.** Quality of life after TVT surgery measured with IIQ-7 and UDI-6 as a function of time since surgery.

Highly significant differences at follow-up, with improvement in response to questions in UDI-6, were found. This was also true for women with preoperative MUI. The analyses of IIQ-7 and UDI-6 were adjusted for age, as the older women generally showed less improvement in their QOL score. The size of the study population made it possible to compare QOL between different subgroups of women. The favorable result of TVT surgery on the UDI-6 score in women who smoked and in those suffering from chronic
diseases such as diabetes, bronchitis or constipation, did not differ from that in the rest of the women in the study population. Patients with chronic constipation however, had less improvement in IIQ-7 scores than the remaining women. Postoperatively recurrent urinary infections or dyspareunia was both significantly correlated to worse QOL. Improved sexual life after TVT surgery was significantly correlated to improved QOL.

Paper III

Four hundred and sixty-three women (60.9%) had pure SUI according to the chart review and questionnaire. Sixty-seven women (14.5%) reported persistent de novo urgency and 51 of these women also had de novo UUI. The remaining 396 women served as a comparison group. The frequency of de novo urgency with or without UI was similar irrespective of number of years since TVT surgery (Fig 4).

![Figure 4. Frequency of de novo urgency by duration since TVT surgery. p=0.65.](image)

The mean duration since TVT surgery was 5.2 years. The women developing de novo urgency were significantly older than the control group, (64.7 years versus 60.9 years, p=0.01). They also had a higher BMI than the women of the comparison group (27.8 compared to 26.4, p=0.02), and a history of cesarean section was more frequent, even after adjustment for parity (9.5% versus 2.5%, OR 5.36, 95% CI 1.63-16.85). There were no significant differences between the groups concerning peri or postoperative characteristics. Among the women with de novo urge symptoms 24 (36.4%) had unaltered or worsened UI, as against 9 (2.3%) in the comparison group (OR 22.75, 95% CI 10.13–55.07). The women with de novo urgency had more frequent micturitions and nocturnal incontinence than the comparison
group, and they reported more urinary tract infections and had a feeling of not being able to completely empty their bladder. Nine (14.1%) of the women with de novo urgency were taking medication because of their UI, compared to 7 (1.8%) in the comparison group. (Table 3)

Table 3. Urinary problems in women with de novo urgency after tension-free vaginal tape surgery for SUI. All odds ratios and p-values were adjusted for age.

<table>
<thead>
<tr>
<th></th>
<th>De novo urgency (%) n=67</th>
<th>Comparison group (%) n=396</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unaltered or worsened incontinence</td>
<td>24 (36.4)</td>
<td>9 (2.3)</td>
<td>22.75</td>
<td>10.1-55.1</td>
</tr>
<tr>
<td>Remaining stress incontinence</td>
<td>37 (56.9)</td>
<td>31 (7.9)</td>
<td>15.55</td>
<td>8.4-29.1</td>
</tr>
<tr>
<td>Urgency incontinence</td>
<td>51 (79.7)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Voiding &gt;6 times daily</td>
<td>51 (77.3)</td>
<td>167 (43.4)</td>
<td>4.93</td>
<td>2.7-9.5</td>
</tr>
<tr>
<td>Nocturnal incontinence</td>
<td>19 (31.2)</td>
<td>31 (4.4)</td>
<td>8.97</td>
<td>4.3-19.1</td>
</tr>
<tr>
<td>Medication against incontinence</td>
<td>9 (14.1)</td>
<td>7 (1.8)</td>
<td>8.24</td>
<td>2.9-24.1</td>
</tr>
<tr>
<td>Feeling of not emptying the bladder</td>
<td>34 (53.1)</td>
<td>107 (27.4)</td>
<td>3.16</td>
<td>1.8-5.5</td>
</tr>
<tr>
<td>Recurrent urinary infections</td>
<td>22 (32.8)</td>
<td>65 (16.5)</td>
<td>2.30</td>
<td>1.3-4.1</td>
</tr>
</tbody>
</table>

There was a large difference in QOL between the groups. The women who developed de novo urgency after their incontinence surgery had a mean IIQ-7 score of 28.1 as compared to 5.6 for in the comparison group (p=0.0001). The corresponding figures for UDI-6 were 49.6 and 13.6 respectively (p=0.0001). The results were adjusted for age.

Paper IV

Subjective cure was defined as patients answering “completely cured” or “almost cured”. Women answering the questionnaire were grouped by age as follows, 29-39 years (n=50), 40-49 years (n=179), 50-59 years (n=244), 60-74 years (n=212), 75-91 years (n=61). The mean age of the oldest women was 80 years and the response rate in this group was 79.2%. At the 3-month follow-up, 81.6% of the women aged ≥75 years reported cure compared to 92.8% of the women of ages <75 years (p=0.01). At long-term follow-up the reported cure of SUI or MUI decreased with increasing age (p=0.0008). (Fig 5)
This was particularly evident when subjective cure in women below 60 years of age was compared with that in women of ages ≥75 years (79.7% versus 55.7% p=0.0001). The cure rate was similar irrespective of the number of years since the TVT procedure.

When the women were divided into the age groups, ≥75 and <75 years, the older women were found to be significantly more frequently taking hormonal replacement therapy (69.7% versus 56.1%, OR 1.80, 95% CI 1.18-2.80) and had urinary tract infections more often than the younger women (54.7% versus 20.0%, OR 4.84, 95% CI 2.74-8.65). Of the women aged ≥75 years, 15.5% had former surgery because of UI compared to 5.8% in the younger women (OR 2.27, 95% CI 1.48-5.62). The corresponding figures for pelvic organ prolapse surgery were 27.7% and 6.2% respectively (OR 5.80, 95% CI 3.49-9.53). Regarding urodynamics, the older women were found to have lower urethral closure pressure than the comparison group (34.5 versus 60.4, p=0.0001). There were no other urodynamic parameters that differed significantly between the older and younger women. The maximum urethral closure pressure was not significantly associated with subjective cure after TVT surgery. The mean value for women reporting cure was 39.6 cm of water, compared to 32.6 cm of water in women who did not report cure (p=0.57). A diagnosis of MUI was more common in older than in younger women (29.2% versus 15.2%, OR 2.30, 95% CI 1.47-3.57), and the older women had a longer hospital stay for TVT surgery (2.1 days compared to 0.9 days, p=0.0001). There were no other significant differences in peri or postoperative characteristics between women of ages ≥75 years and <75 years. Adjustment for MUI, former incontinence or prolapse surgery or a history of recurrent urinary tract infections did not alter the less favorable result of TVT surgery among the oldest women (OR 0.38, 95% CI 0.18-0.80).

Women answering the questionnaire were grouped according to BMI as follows, BMI 19-24 (n=239), 25-29 (n=331), 30-34 (n=115), 35-48 (n=48).
The response rate in the latter group was 90.6%. At the 3-month follow-up, 92.7% of the women with a BMI of 19-24 reported cure, compared to 81.6% of those with a BMI ≥35 (p=0.054). At long-term follow-up, 81.2% of the women with BMI <25 reported cure, compared to 52.1% of those with BMI ≥35 (p=0.0005). (Fig 6)

![Figure 6](image)

**Figure 6.** Cure rate of any incontinence after TVT surgery in women with different BMI.

The long-term results were similar irrespective of the length of time since TVT surgery. When a comparison was made between women with a BMI of ≥35 and those with BMI of <25, the following results were obtained: Women with BMI ≥35 were significantly older (60.0 versus 56.1, p=0.03). The very obese women had a higher parity (2.6 versus 2.2 p=0.03) and more commonly had chronic disease such as diabetes (16.7% versus 1.3%, OR 14.53, 95% CI 3.94-69.35) and bronchitis (21.3% versus 3.4%, OR 6.49, 95% CI 2.35-18.41) compared to normal weight women. No significant characteristics were found on urodynamic evaluation before surgery. The women with BMI ≥35 had less favorable result of TVT surgery irrespective of whether they had SUI or MUI preoperatively. Among the very obese women, a subjective feeling of not being able to empty the bladder was more common (35.4% versus 15.8%, OR 2.86, 95% CI 1.41-5.71). But the normal weight women more often had to undergo adjustment of the tape because of high residual urine postoperatively (10.7% versus 1.6%, OR 0.14, 95% CI 0.01-0.69). Adjustment for age, parity, diabetes, chronic bronchitis, chronic constipation or recurrent urinary infections did not alter the poor odds ratio for cure in the very obese women (OR 0.44, 95% CI 0.20-0.95) (Table 4).
Table 4. *Perioperative characteristics and outcome in very obese women and in women of normal weight undergoing TVT surgery.* 1,2. All odds ratios and p-values were adjusted for age. 3. Only those women who reported urgency symptoms preoperatively.

<table>
<thead>
<tr>
<th></th>
<th>BMI ≥35 n=61 (%)</th>
<th>BMI 19-24 N=291 (%)</th>
<th>Odds ratio&lt;sup&gt;1&lt;/sup&gt;</th>
<th>95% CI&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed incontinence</td>
<td>12 (20.0)</td>
<td>35 (12.1)</td>
<td>1.56</td>
<td>0.71-3.23</td>
</tr>
<tr>
<td>Operation time (minutes)</td>
<td>25.0</td>
<td>23.2</td>
<td>0.21&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Bladder perforation</td>
<td>1 (1.6)</td>
<td>11 (3.9)</td>
<td>0.40</td>
<td>0.22-2.15</td>
</tr>
<tr>
<td>Bleeding volume (ml)</td>
<td>52.7</td>
<td>65.8</td>
<td>0.27&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Postoperative residual urine</td>
<td>11.6</td>
<td>25.5</td>
<td>0.02&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Postoperative loosening of the tape</td>
<td>1 (1.6)</td>
<td>31 (10.7)</td>
<td>0.14</td>
<td>0.01-0.69</td>
</tr>
<tr>
<td>Hospitalization (days)</td>
<td>1.2</td>
<td>0.9</td>
<td>0.76&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

**Cure rate**

<p>| | | | | |</p>
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<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Any incontinence problems</td>
<td>25 (52.1)</td>
<td>194 (81.2)</td>
<td>0.28</td>
<td>0.15-0.56</td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>24 (50.0)</td>
<td>201 (83.1)</td>
<td>0.23</td>
<td>0.12-0.44</td>
</tr>
<tr>
<td>Urgency symptoms&lt;sup&gt;3&lt;/sup&gt;</td>
<td>14 (38.9)</td>
<td>96 (66.7)</td>
<td>0.32</td>
<td>0.15-0.69</td>
</tr>
<tr>
<td>De novo urgency symptoms</td>
<td>6 (14.3)</td>
<td>20 (9.5)</td>
<td>1.31</td>
<td>0.44-3.43</td>
</tr>
<tr>
<td>Feeling of not emptying the bladder</td>
<td>17 (35.4)</td>
<td>38 (15.8)</td>
<td>2.86</td>
<td>1.41-5.71</td>
</tr>
</tbody>
</table>
Discussion

Paper I

Some previous studies have shown good short-term effects of TVT surgery on both MUI and SUI. Jeffry et al (55) reported cure in 89% after the TVT procedure in women with SUI and MUI. Rezapour et al (56) reported a cure rate of 85% after TVT surgery in patients with MUI, and Nilsson et al (57) found a cure rate of 81% in patients with MUI and 89% in patients with SUI. In addition Debodinance et al (58) reported 90% cure after TVT surgery in women with MUI.

However some other studies have shown similar, less favorable effects of TVT on MUI, as in the present study. Laurikainen et al (59) had a cure rate of 97% in patients with SUI, but of 69% cure in patients with MUI. Meschia et al (60) found a difference in cure rate, with a rate of 90% in women with SUI but only 50% in women with MUI. Paick et al (61) reported a 96% cure rate in women with SUI compared to 78% in those with MUI. Ducket et al (62) found subjective cure of 63% after TVT surgery in 51 women with MUI and Ankardal et al (63) found a cure rate of 55% in women with MUI as compared to 81% in women with SUI.

Since the definition of MUI varies, it is difficult to compare different studies, and the definition of cure and improvement can also differ. In the present study there was no definition of the lowest bladder capacity required for acceptance for surgery which may explain the relatively low cure rates. In previous studies the length of follow-up was relatively short, 6 months to 2.5 years and thus no decline of the initial positive result of TVT surgery could be detected in women with MUI.

The main finding in the present study was that despite initially promising short-term results, there was a decline with time in the effect of the TVT procedure on MUI. Urgency symptoms and UUI tended to recur in women who had undergone TVT surgery for MUI 4-8 years previously. In the present study the study population was relatively large, all women were operated on at the same clinic and there was a mean follow up of 5.7 years (range 2-8 years). Moreover only a limited number of surgeons were involved and all had been taught by one of the study authors (L.L), and the same technique and tape material were used. Of the women with SUI 85% were cured irrespective of the number of years since surgery, but it is important to emphasize that 67 (14.5%) of the women with SUI had
developed de novo urgency symptoms (51 of these women also had de novo UUI) after surgery, and they were excluded from study 1. The principal aim of study 1 was to evaluate the effect of the TVT procedure on MUI. The effect of TVT on SUI was also presented in the study as subjective cure of SUI symptoms. The results of this study need to be confirmed by other investigators. It is important for women with preoperative MUI to be properly informed about the expected result of TVT surgery.

Other studies have shown an increased frequency of UUI among women who have undergone hysterectomy (64). In the present study we found a strong correlation between cesarean section and MUI, but not SUI, and a possible explanation for this is occurrence of nerve damage when the bladder is dissected from the uterus. The women with MUI were also significantly older and more often used local estrogen, possibly because of symptoms of epithelial atrophy. The women with MUI had a higher BMI, which is known to correlate to UI. The mechanism of this is unclear, but obesity might cause UI through an increase in intraabdominal pressure. There was a correlation between chronic constipation and MUI which could have been due to mechanical factors. The increased need for postoperative correction of the tape in women with SUI as compared to MUI may have been due to hypermobility of the anterior vaginal wall and urethra in the former group, leading to a tendency to overstrecthing of the tape.

Paper II

The main strengths of this study were the large study population, the high response rate, and the long study period. The quality of life instruments specially designed for women with UI and used in the present study, IIQ-7 and UDI-6, were not as widely used at the time of study 2 as they are today. At follow-up the women were asked to recall the situation before TVT surgery and to describe the current situation. This may have introduced a recall bias. However, it is not known whether the women exaggerated or underestimated their preoperative symptoms. At a three-year postoperative evaluation of men with an early stage of prostate cancer, it was found that the men significantly underestimated their preoperative problems when comparing their answers to the same questions pre and postoperatively (65). A recent study suggested that three months after TVT surgery the women had not forgotten the problems caused by UI, (66). Moreover, the magnitudes of improvement in postoperative scores (IIQ-7, 43.7 to 11.5 and UDI-6, 54.2 to 24.0) were very similar to those reported by other researchers (67,68). In a multicenter study of 809 women, Schraffördt Koops et al (69) found a change in mean IIQ-7 score from 58 to 12 and in mean UDI-6 score from 58 to 23 two years after a TVT procedure.
Vasallo et al (70) studied 162 women 9 months after TVT surgery and found favorable changes in IIQ-7 from 39.5 to 10.6 and in UDI-6 from 48.1 to 20.6. Richter et al (71) studied 102 women, 12 months after a similar sling procedure and noted that the IIQ-7 score had declined from 55.1 to 11.0 and the UDI-6 score from 67.1 to 28.0.

The favorable change in QOL in the present study was persistent. Older women (>60 years) showed relatively less improvement in QOL scores compared to younger women. The result might have been biased by a natural decline in QOL with age. The outcome of TVT surgery in women with chronic diseases such as diabetes and bronchitis was analyzed and none of the studied conditions significantly affected the improvement in IIQ-7 or UDI-6 scores, this was also true for women smoking. Women with chronic constipation had a less impaired IIQ-7 score than the comparison group but their UDI-6 score was improved. It is concluded that women with these diseases can successfully undergo TVT surgery for SUI. However, women with recurrent urinary tract infections after TVT surgery showed less improvement in their QOL score at follow-up compared with the remaining study population. The reason of recurrent urinary tract infections in these women is unclear.

In recent years there has been increasing interest in the possible impact of TVT on sexual function. Some studies however, report no change in sexual function (73,73). Ghezzi et al (74) concluded that women reporting cure of coital incontinence after TVT surgery experienced improvement in sexual function. Jha et al (75) studied 54 women undergoing TVT surgery and found that according to the womens answers to the Pelvic organ prolapse / Urinary incontinence Sexual Questionnaire (PISQ), their sexual life was better postoperatively. In a study of Marszalek et al (76) a deterioration of sexual function after TVT was found to be significantly associated with dyspareunia and de novo urgency symptoms.

In the present study women with dyspareunia reported a poorer quality of life (QOL) irrespective of TVT surgery. Women with improved sexual life after a TVT procedure also have improved QOL. It is an important observation that sexual life is an important part of QOL, in both younger and older women.

**Paper III**

In the study 3 the prevalence of de novo urgency was 14.5%, thus within the range of figures found in other studies, 3-30% (77,78). Since the definition of de novo urgency is based on symptoms rather than objective parameters, there is a wide variance in the frequency reported from different studies.
Also in the present study the diagnosis of de novo urgency was symptom based. Another important factor influencing the reported prevalence of de novo urgency is the preoperative diagnosis regarding the type of incontinence. It is well known among clinicians treating women with UI that some women given a diagnosis of SUI can experience urgency symptoms to some extent without being diagnosed as having MUI.

In the present study, 580 women were diagnosed as having SUI when their charts were reviewed. Of these patients, 117 reported urgency symptoms preoperatively in their questionnaires. Thus, eligible for the study were 463 women with pure SUI absolutely free from urgency symptoms, according to both their records and questionnaires. In study 3 some risk factors for developing de novo urgency symptoms after TVT surgery could be identified. Significant risk factors were age and a history of cesarean section. Increasing BMI and parity were also significantly associated with de novo urgency symptoms, but the actual differences in figures were small.

Deval et al (79) reported de novo urgency in 21.3% of 187 patients, but the correlation to age was not statistically significant. Falconer et al (80,81)) found changes in the paraurethral connective tissue after slingplasty and in postmenopausal women. However, a possible association with development of de novo urgency is obscure from their results. Damage to bladder neural control after incontinence surgery has also been suggested as a possible cause of de novo urgency According to some studies there is an increased risk of UUI after abdominal hysterectomy (82), and it is possible that dissection of the bladder from the uterus could lead to nerve damage and trigger bladder instability. This might also be the underlying mechanism after cesarean section.

Obstruction of the bladder after incontinence surgery, leading to bladder instability, could be a possible cause of de novo urgency symptoms. However the diagnosis of obstruction can be challenging. Natale et al (83) conclude that there are no absolute urodynamic criteria for obstruction in women. In many women the voiding dysfunction is transient but 4-22% of women undergoing Burch colposuspension and 3-14% of those treated with the TVT procedure, have persistent voiding dysfunction (longer than 4 weeks) (84). Dietz et al (85) studied 145 women and found a reduction of the maximum flow rate after TVT surgery, but voiding dysfunction seemed to decrease over time. Sander et al (86) found a reduction of the mean average flow rate one year after TVT surgery. There are studies indicating that preoperatively reduced urinary flow rates are a significant risk factor for postoperative obstruction (87,88). Park et al (89) studied 285 women with the aim of identifying risk factors of voiding dysfunction and global dissatisfaction after TVT surgery for SUI. They found that a low postoperative peak urinary flow rate (PFR) significantly compromised global satisfaction.
Patients in whom PFR was already reduced preoperatively were at risk. Cutting of the tape in some patients with signs of obstruction after a TVT procedure can relieve the symptoms of de novo urgency (90,91). In the present study there were no differences in postoperative residual urine between the women developing de novo urgency symptoms and women of the control group.

De novo urgency symptoms after TVT surgery are the most common long-term complication, with a broad negative impact on the patients QOL. The cause of de novo urgency symptoms, with or without UI, is not known. Further research in this area is needed.

Paper IV

There was a decrease in cure rate with increasing age and BMI among our study patients. Even the oldest women reported encouraging results at the 3-month check up (81.6% cure) but at the long-term follow-up the cure rate was decreased (55.7%). The same pattern was seen in the very obese women (81.6% versus 52.1%). However the cure rates at the 3-month follow-up cannot be fully compared with the long-term results, since the women were allowed four alternative answers in the former questionnaire and five in the latter. During the first years of the study period, the short-term follow-up was carried out through appointment with the surgeon and not in a standardized way. A three-month check-up by questionnaire was performed in patients undergoing TVT surgery in 1999-2001. The results stress the importance of long-term follow-up, which in this study was less favorable in the oldest and very obese women but we found the results acceptable, and the TVT procedure was safe and simple also among the oldest and most overweight women.

The menopause is associated with changes in the paraurethral connective tissue that might be associated with UI. The prevalence of UI increases with age. Milson et al (92) showed that 19% of 60-year-old women suffered from UI, compared to 29% of women 80 years old. Symptoms of an overactive bladder (OAB) are also more common in the elderly. The same authors found an OAB prevalence of 31% in women ≥75 years old, compared to 9% in women aged 40. Thus OAB and UI are common in elderly patients and it is of great importance that these women are offered safe and adequate treatment.

Reports have varied concerning results of TVT in the oldest patients. Karantis et al (93) found a significantly lower cure rate 12 months after TVT in women ≥65 years old (45%) as compared to younger women (73%). However, several studies have shown very good results after a TVT procedure even in older women (94). Touloupidis et al (95) reported a significant improvement in bother score, estimated by VAS, after TVT.
surgery in women aged 65-80. Stav et al (96) found a subjective cure rate of 85% after midurethral sling surgery, irrespective of age. Liapis et al (97) found a 76% cure rate after TVT in 55 women aged 65-86 years.

However, intrinsic sphincter deficiency is more common in older women and there are reports from several studies of less favorable results in this group of women, especially in combination with immobile urethra and detrusor overactivity, which also is more common among older women (98-101). Women of ages ≥75 years with or without concomitant chronic disease had less favorable results after TVT surgery in the present study as compared to women aged <75 years. This finding underlines the importance of good preoperative information to give the woman realistic expectations.

There is a strong correlation between intraabdominal pressure and BMI (102). Obesity and UI are also strongly correlated (103). Today there are several studies presenting good results of TVT surgery on obese patients with SUI or MUI. Mukherjee et al (104) reported a cure rate of almost 90% after TVT, regardless of whether BMI was ≥30 or <30. Lovatsis et al (105) found that 88.6% were cured at short-term follow-up in women with BMI ≥35, compared to 91.4% in women with BMI ≤30. Rafii et al (106) did not find any significant difference in cure 6 months after TVT between women with BMI>30 (82%) and those with BMI ≤30 (88.7%). Skriapas et al (107) compared 31 morbidly obese women (BMI >40) with women with BMI <30 and found cure rates of 87% and 92% respectively.

In the present study comparisons of results were made between very obese women (BMI≥35) and normal weight women (BMI<25). The reported cure rate in the very obese women was lower than in the woman of normal weight, but we found the results acceptable if the women were given good preoperative information. There is no other simple and safe method with comparable cure rates.
Conclusions

The main strengths of these studies are the large study population, high response rate and long follow-up. All women who underwent TVT surgery in the region during the study period were included. The women were all operated on at the same clinic, with a standardized technique and no change in tape was required. Subjective cure of SUI was very good. The results of TVT surgery on MUI were relatively good in women who had had surgery up to 3 years previously but with time the urgency and UUI returned, although the SUI was cured to a great extent. There is a need for further studies to confirm these findings.

The TVT procedure had a great impact on QOL in women with a preoperative diagnosis both of SUI and of MUI. The TVT procedure caused a striking positive change in scores of IIQ-7 and UDI-6, in the same range as in other studies, despite another distribution of the questionnaires. Women with UI and chronic diseases such as diabetes, bronchitis, or chronic constipation also had a good result from the TVT surgery.

De novo urgency is a late complication after a TVT procedure for SUI and has a strong negative impact on QOL. There is no large difference between the prevalence of de novo urgency after TVT surgery and that after abdominal incontinence surgery, even though TVT is a minimally invasive operation. The cause of de novo urgency is not known, but in this study increasing age, parity, BMI, and a history of cesarean section were significantly associated with a higher risk of de novo urgency.

Since TVT surgery is a minimally invasive method with relatively few complications even the oldest and the very obese women can be offered surgery when suffering from SUI. However the cure rates are lower in these groups and good preoperative information is important to give the woman reasonable expectations of the result.

de novo urgency med eller utan urinläckage är dock en sen komplikation efter TVT och medför stora bekymmer för de patienter som drabbar.

UUI behandlas konservativt med blåsträning och medicinering med anticholinergika i första hand. Vid MUI finns ofta ett behov av kombinationsbehandling dels för kvinnans UUI men också för hennes SUI.


I enkäten för långtidsuppföljningen delades kvinnorna in i olika grupper beroende av antalet år sedan sin TVT operation. Detaljerade frågor ställdes om resultatet efter TVT operationen, sjukhistoria, utbildning och sexualitet. Kvinnorna fick också fylla i två inkontinensspecifika livskvalitetsformulär. Patienterna med SUI uppgav besvärsfrihet i 85% av fallen och resultatet kvarstod upp till 8 år efter operationen. Kvinnorna med MUI uppgav besvärsfrihet i 60% av fallen upp till 3 år efter operationen, därefter sjönk andelen kvinnor som uppgav besvärsfrihet till 30% för de som opererats för 6-8 år sedan. Dessa patienter uppgav att deras trängningar och trängningsinkontinens, hade kommit tillbaka. Vi använde oss av två urininkontinensspecifika livskvalitetsinstrument, IIE-7 och UDI-6. Svarsalternativen graderades från 0 till 3. Då medelvärdet av svaren multiplicerades med 33.33 gav besvärsfrihet 0 poäng och maximala besvär 100 poäng. Vi fann en kraftig förbättring av patienternas medelvärden för IIE-7 från 43.7 till 11.5 och för UDI-6 från 54.2 till 24.0. Resultaten kvarstod upp till 8 år efter operationen. Kvinnor med kroniska sjukdomar som diabetes, kronisk obstructiv lungsjukdom, kronisk obstipation och recidiverande urinvägsinfektioner, fick en liknande förbättring av sin livskvalitet. Höga ålder hade en negativ inverkan på livskvaliteten. Vid genomgång av
kvinnornas journaler i kombination med deras enkätsvar, fann vi 463 kvinnor med ren SUI utan några som helst trängningar före operationen. Sextiosju (14.5 %) av dessa kvinnor uppgav trängningar, de novo urgency vid långtidsuppföljningen och 51 av dessa hade också ett urinläckage associerat till trängningarna. Signifikanta riskfaktorer för att utveckla de novo urgency var hög ålder, paritet och BMI samt tidigare kejsarsnitt. De subjektiva resultaten för de äldsta kvinnorna (≥75 år) jämfördes med resultaten för kvinnor som var yngre än 75 år. Likaså jämfördes de subjektiva resultaten för överviktiga kvinnor (BMI ≥35) jämfört med resultaten för de normalviktiga kvinnorna (BMI<25). Andelen kvinnor ≥75 år som uppgav besvärfsfrihet var 55.7% jämfört med 79.8% för kvinnor <60 år. Andelen kvinnor med BMI ≥35 som uppgav besvärfsfrihet var 52.1% jämfört med 81.2% av kvinnor med BMI <25.

Konklusion


Vi fann att TVT operationen var enkel och säker men resultatet för de äldsta och de mest överviktiga kvinnorna, var inte lika bra som för de yngre och normalviktiga kvinnorna.
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Appendix

Uppgifter från journalgenomgången

**Medicinska data:**
- diabetes
- neurologisk sjukdom
- kronisk obstipation
- kronisk obstruktiv lungsjukdom
- strålbehandling för gynekologisk cancer
- övrig sjukdom
- BMI
- paritet, vaginal eller sectio
- postmenopausal, östrogenbehandling, lokal eller systemisk
- tidigare gynekologiska operationer:
  - prolapsooperation
  - urininkontinens, vaginal eller abdominell operation, injektionsbehandling

**Utredning:**
- urininkontinens typ, SUI eller MUI
- anamnesformulär
- miktionsschema
- inkontinensprövning
- blöjvägningstest
- cystoskopi
- urodynamisk utredning; cystometri, uretratrycksprofil

**Peri och postoperativa data:**
- poliklinisk eller inneliggande, antal vårddagar
- operatör
- operationstid
- peroperativa komplikationer, perforation urinblåsa, blödning i ml
- postoperativa komplikationer; infektion (lokal, behandling)
  - hematom (lokal behandling)
  - justering eller delning av bandet
  - annan komplikation

Sjukskrivning antal dagar
Enkät för tremånaders uppföljning efter TVT operationen

Hur är dina inkontinensbesvär generellt jämfört med före operationen?
☐ Försämrad  ☐ Oförändrad  ☐ Förbättrad  ☐ Helt bra

Hur är ansträngningsläckaget nu jämfört med före operationen?
☐ Försämrat  ☐ Oförändrat  ☐ Förbättrat  ☐ Helt bra

Hade du urinträngningar före operationen?
☐ Ja  ☐ Nej

Om ja, är trängningarna nu
☐ Försämrad  ☐ Oförändrad  ☐ Förbättrad  ☐ Helt bra

Har du fått nytillkomna trängningar efter operationen?
☐ Ja  ☐ Nej

Har du problem att tömma blåsan efter operationen?
☐ Svåra  ☐ Medelsvåra  ☐ Lätta  ☐ Inga
Enkät för långtidsuppföljning efter TVT operationen:

Utbildning
Grundskola, gymnasium, högskola

Vid tiden för operationen:
röknings, diabetes, neurologisk sjukdom, kronisk förstoppning,
kronisk obstruktiv lungsjukdom, upprepade urinvägsinfektioner

Hur är dina inkontinensbesvär generellt jämfört med före operationen?
☐ Försämrade ☐ Oförändrade ☐ Något förbättrade ☐ Nästan helt bra
☐ Helt bra

Hur är ansträngningsläckaget nu jämfört med före operationen?
☐ Försämrat ☐ Oförändrat ☐ Något förbättrat ☐ Nästan helt bra
☐ Helt bra

Om kvarstående besvär, läckage vid
☐ plötslig ansträngning, hosta nysning, hopp ☐ lyft ☐ promenad på slät mark

Hade du urinträngningar före operationen?
☐ Ja ☐ Nej

Om ja, är trängningarna nu
☐ Försämrade ☐ Oförändrade ☐ Något förbättrade ☐ Nästan helt bra
☐ Helt bra

Har du fått nytillkomna trängningar efter operationen?
☐ Ja ☐ Nej

Om ja
☐ Kvarstående ☐ Övergående

Tar du någon medicin mot trängningarna? Om ja, ange vilken.
☐ Ja ☐ Nej ..................

Har du urinläckage på grund av kraftig urinträngning?
☐ Ja ☐ Nej

Har du nattligt urinläckage?
☐ Ja ☐ Nej
Hur många gånger per dag kisser du?
☐ mer än 6 gånger per dag?  ☐ mindre än 6 gånger per dag

Känns det som om det finns kvar urin efter toalettbesök?
☐ Ja  ☐ Nej

Har du behandlats för upprepade urinvägsinfektioner efter operationen?
☐ Ja  ☐ Nej

Har ditt sexliv förändrats efter operationen?
☐ Nej  ☐ Ja, till det bättre  ☐ Ja, till det sämre

Har du smärtor vid samlag?
☐ Nej  ☐ Ja, lite  ☐ Ja, mycket
UDI 6 - Urogenital Distress Inventory

I vilken grad påverkas du av:

1 Att Du måste kissa ofta?
   □ Inte alls    □ Något       □ Måttlig   □ Mycket

2 Urinläckage på grund av kraftig urinträngning?
   □ Inte alls    □ Något       □ Måttlig   □ Mycket

3 Urinläckage på grund av aktivitet, t ex hosta eller nysning?
   □ Inte alls    □ Något       □ Måttlig   □ Mycket

4 Litet urinläckage (droppar)?
   □ Inte alls    □ Något       □ Måttlig   □ Mycket

5 Känsla av att du inte tömmer urinblåsan när du kissar?
   □ Inte alls    □ Något       □ Måttlig   □ Mycket

6 Smärta eller obehag i underlivet?
   □ Inte alls    □ Något       □ Måttlig   □ Mycket
IIQ 7 – Incontinence Impact Questionnaire

I vilken grad påverkar ditt urinläckage, och/eller dina urinträngningar din:

1 Möjlighet att göra hushållsuppgifter (matlagning, städning, tvätt)?
   □ Inte alls   □ Något   □ Måttlig   □ Mycket

2 Möjlighet till fysiska aktiviteter, t.ex. promenader, simning eller annan aktivitet?
   □ Inte alls   □ Något   □ Måttlig   □ Mycket

3 Möjlighet till nöjen, t.ex. bio, konserter med mera?
   □ Inte alls   □ Något   □ Måttlig   □ Mycket

4 Möjlighet att åka bil eller buss mer än 30 minuter?
   □ Inte alls   □ Något   □ Måttlig   □ Mycket

5 Möjlighet att delta i sociala aktiviteter utanför hemmet?
   □ Inte alls   □ Något   □ Måttlig   □ Mycket

6 Känslomässig hälsa (t.ex. nervositet, depression med mera)?
   □ Inte alls   □ Något   □ Måttlig   □ Mycket

7 Känsla av frustration?
   □ Inte alls   □ Något   □ Måttlig   □ Mycket
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