



The retropubic tension-free vaginal tape procedure (TVT) – efficacy, risk factors for recurrence and long-term safety

Journal:	<i>Acta Obstetrica et Gynecologica Scandinavica</i>
Manuscript ID	AOGS-18-0835.R1
Wiley - Manuscript type:	Original Research Article
Date Submitted by the Author:	n/a
Complete List of Authors:	Holdø, Bjørn; Nordland Hospital, Department of Obstetrics and Gynecology Skjeldestad, Finn; UiT The Arctic University of Norway, Department of Community Medicine; Svenningsen, Rune; Oslo universitetssykehus Ulleval, Department of Obstetrics and Gynecology Milsom, Ian; Institute of Clinical Sciences, Obstetrics & Gynecology Verelst, Margareta; Universitetssykehuset Nord-Norge, Division of Surgery, Oncology and Women's Health
Keywords:	Incontinence, Urogynaecology

SCHOLARONE™
Manuscripts

1
2
3 **The retropubic tension-free vaginal tape procedure (TVT) –**
4 **efficacy, risk factors for recurrence and long-term safety**
5
6
7
8

9 Bjørn Holdø¹, Margareta Verelst², Rune Svenningsen³, Ian Milsom⁴, Finn Egil Skjeldestad⁵.
10
11

12
13 ¹Department of Obstetrics and Gynecology, Nordland Hospital, Bodø, Norway ²Division of
14 Surgery, Oncology and Women's Health, University Hospital of North Norway, Tromsø,
15
16 Norway; ³Department of Obstetrics and Gynecology, Oslo University Hospital, Ullevål, Oslo,
17
18 Norway; ⁴Department of Obstetrics and Gynecology, Sahlgrenska Academy, Gothenburg
19
20 University, Gothenburg, Sweden and the ⁵Institute of Community Medicine, UiT The Arctic
21
22 University of Norway, Tromsø, Norway
23
24
25
26
27
28
29

30 **Corresponding author:**

31
32 Bjørn Holdø

33
34 Nordland Hospital, Prinsensgate 164, 8092 Bodø

35
36 E-mail: bjorn.holdo@yahoo.no

37
38
39 Phone: +4791773015
40
41
42
43

44 **Funding:** The study has received funding from Northern Norway Regional Health Authority
45
46 and Nordland Hospital, Bodø, Norway
47
48
49

50 **Potential conflicts of interest:**

51
52 B Holdø: none

53
54 M Verelst: none

55
56 R Svenningsen: Advisory board Astellas and speaker fees from Astellas

57
58
59 I Milsom: none
60

1
2
3 FE Skjeldestad: none
4
5
6
7

8 **Authorship contributions**

9
10 B Holdø: Protocol/project development, data collection, data analysis, manuscript
11 writing/editing
12
13

14 M Verelst: Protocol/project development, data collection, manuscript writing
15
16

17 R Svenningsen: Manuscript writing/editing
18

19 I Milsom: Manuscript writing/editing
20

21 FE Skjeldestad: Protocol/project development, data collection and management, data
22 analysis, manuscript writing, main supervisor for first author
23
24
25
26
27

28 **Word count:**

29
30 Main body text: 3127
31

32
33 Abstract: 251
34
35
36
37

38 **Key words (Tape-terms):** Complications; Long-term results; Midurethral slings; Mixed
39 urinary incontinence; Stress urinary incontinence.
40
41
42
43

44 **Brief summary:** TVT has high long-term safety and efficacy. Mixed urinary incontinence is
45 a risk factor for long-term recurrence.
46
47
48
49
50

51 **Abbreviations**

52 TVT – tension-free vaginal tape
53

54 SUI – stress urinary incontinence
55

56 MUI – mixed urinary incontinence
57
58
59
60

1
2
3 UI – urinary incontinence
4

5 UR – urinary retention
6
7
8
9

10 **Key message:**
11

12 TVT is a surgical method with high safety and efficacy with low risk of serious long-term
13
14 tape complications. However, mixed urinary incontinence predicts lower long-term cure.
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For Peer Review

Abstract

Introduction: The retropubic tension-free vaginal tape has been the preferred method for primary surgical treatment of stress urinary incontinence and stress dominated mixed urinary incontinence in women for more than 20 years. This study presents long-term safety and efficacy data and assesses risk factors for long-term recurrence.

Material and methods: In a case-series design we assessed a historical cohort of primary surgeries performed with the tension-free vaginal tape procedure in 596 women from 1998 to 2012 with follow-up through 2015. Information from the medical records was transferred to a case report form comprising data on early and late complications and recurrence of urinary incontinence defined as bothersome stress urinary incontinence symptoms. All analyzes were performed with SPSS using Pearson Chi-Square, survival and Cox regression analyzes.

Results: After a 10-year follow-up mixed urinary incontinent women (HR 2.1, 95% CI; 1.4-3.0) had a significant increased risk of recurrence of stress urinary incontinence symptoms compared to women with pure stress urinary incontinence as indication for surgery. Overall cumulative cure rates after one, five and 10 years were 92% (95% CI; 90-94%), 79% (95% CI; 75-83%) and 69% (95% CI; 63-75%), respectively. Recurrent surgery (0.3%) and serious tape complications needing major surgical treatment (0.3%) were rare. Six patients (1.0%) had the tape cut due to urinary retention, and nine patients (1.5%) reported urinary retention more than three months after surgery.

Conclusion: The tension-free vaginal tape procedure has a high long-term durability. Mixed urinary incontinence as indication for surgery predicted long-term recurrence. Long-term complications were rare.

Word count: 251

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For Peer Review

Introduction

Within a few years after the introduction of the retropubic tension-free vaginal tape (TVT) in 1996, several studies demonstrated excellent short-term clinical outcomes, making this minimally invasive method the gold standard in the surgical treatment of women with stress (SUI) and stress-dominated mixed (MUI) urinary incontinence.¹⁻² From 2005 and onwards, the number of women undergoing midurethral sling surgery increased rapidly.³ Probable explanations are an increased awareness of urinary incontinence (UI), a lower symptom threshold for surgery, as the surgical method is considered less invasive, and a possible increase in prevalence of UI.⁴

To date, several studies assessing clinical outcomes and risk factors for failure have demonstrated excellent long-term clinical outcomes after midurethral sling surgery. However, patient selection varies according to indication for surgery, the inclusion of women with repeat UI surgery and women with previous and/or concomitant prolapse surgery.⁵⁻¹⁰ Most long-term follow-up studies do not have sample sizes large enough for risk factor analysis.⁵⁻⁷ The highest long-term subjective cure rates of 77-90% apply only to primary surgery on pure SUI women,^{5,11} whereas subjective cure rates of 75-80% are reported for heterogeneous populations of women with both SUI and MUI.^{6,12} Long-term studies including women with previous/concomitant pelvic surgery have reported lower subjective cure rates (65-76%).⁷⁻⁸ Subjective cure rates as low as 37-55% have been reported for MUI women, only.¹³⁻¹⁴ Therefore, study population characteristics are crucial when comparing studies and may explain why clinical outcomes and risk factor patterns for recurrence vary.

MUI as an independent risk factor for recurrence is well established,¹³⁻¹⁵ but across studies age, body mass index and diabetes are inconsistently reported.^{6,9,13,15} The possible impact of

1
2
3 perioperative complications on long-term efficacy has only been evaluated in a few studies.⁹
4
5

15

6
7
8
9
10 The aims of this study were to investigate clinical long-term outcomes, and to assess
11 demographic, clinical and perioperative risk factors for recurrence within 10 years after
12 primary retropubic TVT surgery.
13
14
15

21 **Material and methods**

22
23 The Department of Gynecology at Nordland Hospital, Bodø, Norway, introduced the
24 retropubic TVT procedure in 1998. Within a year, TVT had replaced the Burch
25 colposuspension as the preferred method. We identified all patients having undergone a
26 possible UI-related surgical procedure during 1994-2012 either as primary or recurrence
27 surgery, in total 895 women (Figure 1). After exclusions of women having had Burch
28 procedures on solely prolapse indication, past pelvic surgery, concomitant prolapse surgery,
29 primary incontinence surgery other than TVT, and women with no follow-up, the final study
30 population comprised 596 women having had TVT as primary surgery for SUI or MUI. The
31 TVT surgery was performed as originally described by Ulmsten.¹ All patients received
32 prophylactic antibiotics, and we used the surgical kits from Johnson & Johnson.
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48

49 We screened the electronic medical records retrospectively and transferred the information to
50 a case report form especially designed for the study. The following preoperative data were
51 included: type of UI (SUI/MUI), age at time of surgery (≤ 49 , 50-59, ≥ 60 years), parity (0-1, 2,
52 3+), body mass index, past hysterectomy (total and subtotal) and relevant comorbidities
53 (cardiovascular disease/diabetes (0/1), pulmonary disease (0/1) and neurological disease
54
55
56
57
58
59
60

1
2
3 (0/1)). From the preoperative examination prior to primary surgery, we collected the
4
5 following information: previous conservative treatment for UI (pelvic floor muscle training
6
7 and electrical stimulation), uroflowmetry assessments (including the shape of the curve and
8
9 the estimate of maximum flow rate ($<$ or \geq 15 ml/s)). In addition, the results from two
10
11 standardized stress-tests (coughing during gynecological examination with 300 ml saline in
12
13 the bladder and/or pad weight before and after three forceful coughs and 20 jumping jacks
14
15 (sideways splits)) and cystometry as well as measurement of residual urine (ml) were
16
17 included.¹⁶⁻¹⁷
18
19
20
21
22

23
24 The classification of the type of incontinence was based on a combination of symptoms
25
26 documented in the medical record, outcome of stress tests and/or urodynamic examinations
27
28 and a standardized validated short-form UI disease-specific questionnaire used from 2002 and
29
30 onwards.¹⁸ We defined SUI as bothersome symptoms of SUI as described in the medical
31
32 record and/or in the standardized questionnaire in combination with a positive stress test. MUI
33
34 was defined as a combination of a dominant SUI component and urgency urinary
35
36 incontinence defined as description of bothersome symptoms of involuntary leakage of urine
37
38 after sudden urgency to void in the medical record and/or in the standardized questionnaire. A
39
40 positive cystometry was not mandatory for a diagnosis.
41
42
43
44
45

46
47 Primary outcome was recurrence of UI defined as the presence of any bothersome symptoms
48
49 of SUI reported by the patient and/or by a stress urinary incontinence index score > 0
50
51 indicative of bothersome symptoms of SUI on the validated questionnaire, and/or a positive
52
53 standardized stress test at follow-up. Neither de novo urgency urinary incontinence in women
54
55 with pure SUI before surgery nor recurrence of urgency urinary incontinence in women with
56
57 preoperative MUI was defined as recurrence.
58
59
60

1
2
3
4
5 Secondary outcomes were urinary retention (UR), other perioperative complications and late
6
7
8 tape complications.
9

10
11
12 UR was defined as the need for catheterization more than one week after primary surgery
13
14 and/or in need of traction and/or surgical correction necessitating cutting of the tape. Traction
15
16 was performed non-invasively by stretching the urethra with a Hegar dilator in gel anesthesia.
17
18
19

20
21 Other perioperative complications comprised bladder injury defined as perforation by the
22
23 trocar or by the tape, hematoma defined as clinical significant and/or ultrasonographically
24
25 identified hematomas of any size and other complications. We chose not to include urinary
26
27 infections as complication as the prevalence will be underestimated when these infections
28
29 most often are treated post discharge by general practitioners.
30
31
32

33
34
35 We defined late tape complications as symptomatic or asymptomatic erosions, fistulas, and
36
37 symptoms of dyspareunia and/or chronic pain/discomfort diagnosed three months or later
38
39 after primary surgery. Recurrent urinary infections without any other complaints were not
40
41 considered to be a late complication, and de novo urgency urinary incontinence in SUI
42
43 women was not included in the study.
44
45
46

47
48
49 All patients were offered a follow up after 6-12 months with an interview and a clinical
50
51 examination, followed by urodynamics, if bothersome symptoms. In the interview the women
52
53 were asked about their satisfaction with the treatment, and from 2002 and onwards the
54
55 department used a standardized questionnaire including the categories “very satisfied”,
56
57
58
59
60

1
2
3 “satisfied”, “neither satisfied nor dissatisfied”, “dissatisfied” and “very dissatisfied”. For
4
5 patients residing far from our hospital, we performed an interview by post or phone.
6
7
8
9

10 Later follow-up data was based on consultations at our outpatient clinic after referral from
11
12 general practitioners or private gynecologists. For patients not residing in our hospital’s local
13
14 catchment area (n = 166), we retrieved follow-up data from the medical records at relevant
15
16 local hospitals from in- and/or outpatient visits. As the department introduced a standardized
17
18 3-year follow-up using the validated short-form UI disease-specific questionnaire from 2009
19
20 and onwards, we assessed changes in outcomes in three different time periods (1998-2003,
21
22 2004-2008 and 2009-2012).
23
24
25
26
27

28 ***Statistical analysis***

29
30 In this case-series, the data were analyzed using SPSS version 25. Pearson Chi-Square test
31
32 was used when comparing SUI and MUI, survival analysis (life tables) when estimating
33
34 cumulative cure rates of TVT and Cox regression analysis in the risk factor analysis of
35
36 recurrence. In the survival analysis and the Cox regression analysis of recurrence, UI was
37
38 recorded at the date of the first visit for bothersome symptoms of SUI following primary
39
40 surgery, or censored at the date of last visit being continent as documented in the medical
41
42 record, or at the date of repeat surgery due to complications or prolapse, when repeat surgery
43
44 occurred prior to debut of SUI symptoms. All analyzes stopped for any outcome at 10 years of
45
46 follow-up due to few observations thereafter. Medical records were screened through
47
48
49
50
51 November 1st, 2015.
52
53
54
55
56
57
58
59
60

1
2
3 The Regional Committee for Medical and Health Research Ethics (REC-North ref. number
4 2012/1238/REK nord; date of approval: 8 April 2013), and the Patient Ombudsman, Nordland
5 Hospital, Bodø, have reviewed and approved the study protocol.
6
7
8
9
10
11
12
13

14 **Results**

15
16 Women with MUI as indication for surgery were significantly older, had higher body mass
17 index and parity order, and had more often co-morbidities compared to women having pure
18 SUI as indication for surgery (Table 1). Before surgery, women with MUI more often
19 practiced electrostimulation alone or in combination with pelvic floor muscle training
20 compared to women with SUI ($p < 0.001$), while women with SUI more frequently performed
21 pelvic floor muscle training, only (Table 2). The preoperative evaluations of the stress-test,
22 uroflowmetry, cystometry and measurement of residual urine were performed in almost 100%
23 of the women (Table 2).
24
25
26
27
28
29
30
31
32
33
34
35
36
37

38 The surgeries were performed as day surgery procedures from 2005 and onwards. Mean
39 postoperative hospital stay was 1.0 day (range 0-15). 10 patients (1.7%) had a protracted
40 postoperative hospital stay of > 7 days due to infection and UR.
41
42
43
44
45
46

47 499/596 patients (83.7%) had their first follow-up within 12 months, 454 (76.2%) visited the
48 outpatient clinic, and 45 patients (7.6%) responded to a standardized questionnaire either by
49 post or phone. From interview and questionnaire data at the first postoperative follow-up,
50 95.7% of SUI women and 82.1% of MUI women were “satisfied” or “very satisfied” ($p <$
51 0.01). UR and/or recurrence were significantly associated with not being satisfied.
52
53
54
55
56
57
58
59
60

1
2
3 18 patients (3.0%), residing in Nordland County at the time of surgery, moved later to other
4 regions of Norway, while 39 patients (6.5%) died during follow-up. These patients were
5 censored at last follow-up visit if no prior outcome.
6
7
8
9

10 11 12 *Efficacy and risk factor analysis* 13

14 Table 3 summarizes time to last observation for recurrence-free women, events leading to
15 premature discontinuation (censoring) and recurrence rates by study group. In total, 54
16 (13.8%) SUI women and 52 (25.2%) MUI women had recurrence of SUI symptoms within
17 10 years of surgery ($p = 0.001$). There was no difference in the number of cases censored by
18 study group (Table 3). Mean recurrence-free follow-up time in SUI and MUI women were
19 53.8 and 46.0 months ($p = 0.02$), respectively.
20
21
22
23
24
25
26
27
28
29

30 In the assessment of complications as a risk factor for recurrence, perioperative complications
31 except UR applied to women with SUI, only. Whereas none of 8 MUI women with other
32 perioperative complications had recurrence, 11 out of 25 (44%) SUI women with the above
33 mentioned complications had recurrence. Women with other perioperative complications had
34 a HR for recurrence of 2.5 (95% CI; 1.3-4.7) relative to women without such complications,
35 whereas mixed incontinent women had a HR for recurrence of 2.1 (95% CI; 1.4-3.0)
36 compared to stress incontinent women. Neither age, overweight, parity, previous
37 hysterectomy, comorbidities listed in Table 1 nor UR were independent risk factors for
38 recurrence and had only minor confounding effects ($< 4\%$) on the primary outcome. In the
39 same model the HR for recurrence was 4.0 (95% CI; 2.4-6.7) in the 3rd compared with the 1st
40 time period. Cumulative cure rates after one, five and 10 years by indication for surgery and
41 in total are shown in Table 4, whereas Figure 2 displays continuous cumulative recurrence
42 rates by indication for surgery.
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5 Two patients (0.3%) had recurrent surgery 17 and 68 months after primary surgery,
6
7 respectively.
8
9

10 11 12 ***Complications*** 13

14 5.2% of the patients had UR (Table 5), 22 out of these 31 patients recovered within three
15 months after surgery (10 recovered spontaneously after a period with self-catheterization, 10
16 after traction of the tape, and two after the tape was cut). Four out of the remaining nine
17 patients reporting UR more than three months after surgery had the tape cut. All patients with
18 UR > 3 months after surgery were after a clinical examination offered cutting of the tape.
19 However, as cutting the tape entails a risk of recurrent UI, these five patients preferred, after
20 extensive counseling, to continue self-catheterization .
21
22
23
24
25
26
27
28
29
30

31
32
33 Other perioperative complications remained stable by study groups (Table 5) and over the
34 time periods apart from seven bladder perforations observed during the first time period vs.
35 one in the third period ($p < 0.04$). Among patients with other perioperative complications, one
36 needed evacuation of an infected hematoma and two patients needed repeat surgery with total
37 removal of the tape because of pain or graft-related problems. Three patients had the tape
38 removed at primary surgery due to bladder perforation.
39
40
41
42
43
44
45
46
47
48

49 17 (2.9%) women had late tape complications within 10 years after primary surgery (Table 5).
50
51 Two women developed a fistula, one vesico- and one urethro-vaginal. Seven of the 12
52 patients with erosions had neither symptoms nor recurrence at the time of diagnosis. The rate
53 of surgery due to late complications was 1.3% ($n = 8$); partial resection of the tape due to
54 erosion ($n = 6$), fistula ($n = 1$) and pain ($n = 1$). The second patient with fistula
55
56
57
58
59
60

1
2
3 (vesicovaginal) recovered with conservative treatment. Six patients with erosion were also
4
5 treated conservatively with local estrogens without surgery. Mean time from primary surgery
6
7 to surgery for late complication was 52 months (range 5-120 months).
8
9
10
11
12
13

14 **Discussion**

15 *Main findings*

16
17 MUI predicted recurrence 10 years after primary TVT surgery. We did not find any
18
19 association between age, overweight, parity, comorbidities, UR and recurrence of SUI.
20
21
22
23
24
25

26 *Efficacy and risk factor analyzes*

27
28 Among patients not satisfied with the treatment, recurrence and UR within one year impacted
29
30 on dissatisfaction. Already at the first follow-up visit we found a significantly lower
31
32 satisfaction rate in MUI-operated compared to SUI-operated women. As there were
33
34 differences in follow-up time across the study period, with a shorter observation time in the
35
36 3rd time period relative to the previous periods, we performed a Cox regression analysis of
37
38 recurrence through four years of observation in order to avoid attrition bias. The overall HR
39
40 for recurrence in the 3rd compared to the 1st time period dropped from 4.0 to 2.2 (95% CI: 1.2-
41
42 4.0) indicating that attrition bias may account for 45% of the difference in HR for recurrence
43
44 between the 3rd and the 1st time period. At the start of the 3rd time period our department
45
46 initiated a systematic 3-year follow-up by a postal questionnaire. A larger proportion of
47
48 women were below 50 years of age (47.8% vs. 35.4%) in the 3rd compared to the 1st time
49
50 period. We ascribe this to increasing awareness of TVT as an improved method for treatment
51
52 of female incontinence. Furthermore, a higher expectation for cure after surgery may have led
53
54 some women in the 3rd period to seek medical advice for UI at a threshold that may have
55
56
57
58
59
60

1
2
3 differed to women in the 1st period. These circumstances may have led to a reporting bias
4
5 important for interpretation of the increased HR for recurrence in the 3rd versus the 1st period.
6
7
8
9

10 The overall cumulative subjective cure rate after 10 year follow-up (69%) was somewhat
11
12 lower than results from comparable studies (75-80%).⁷⁻⁸ When we stratified our results into
13
14 pure SUI and MUI, the cumulative subjective cure rate after 10 year follow-up was 74% for
15
16 the women with pure SUI (95% CI; 66-82%) and 58 % for the MUI women. The long-term
17
18 SUI cure rate was thus lower in our study compared to what has been reported by others (77-
19
20 90%),⁵⁻⁶ while the mixed incontinent women had a higher cumulative subjective cure rate
21
22 compared to other studies (37-55%).¹¹⁻¹² In line with other reports we found that the effect of
23
24 surgery decreased more with time in mixed incontinent women than SUI women (Figure 2).¹⁹
25
26 As our study analyzed cure rates using survival analyses, we expected the estimates of cure
27
28 rates to be lower, as recurrence is estimated only among patients remaining in the study at the
29
30 different time intervals. This differs significantly from most other studies in which time most
31
32 often is not taken into account when estimating recurrence using the total number of patients
33
34 having surgery as the denominator.^{5-6, 9-10}
35
36
37
38
39
40
41

42 In studies showing an association between overweight, advanced age and lower cure rates, the
43
44 results may be influenced by including in the study populations women with past UI surgery
45
46 and/or past or concomitant prolapse surgery, which is not the case in our study.
47
48
49

50
51 The rates of repeat surgery due to recurrence vary in the literature from 0-4%.^{5-6, 9-10} Studies
52
53 reporting “no” repeat surgery often comprise low-risk populations having included only
54
55 primary surgeries on pure SUI women.⁵⁻⁶
56
57
58
59
60

1
2
3 Only a few studies have demonstrated perioperative complications as an independent risk
4 factor for recurrence.^{9, 15} Our study finds a possible association between recurrence and non-
5 UR perioperative complications. However, due to low number of cases with such
6 UR perioperative complications. However, due to low number of cases with such
7 complications and inconsistency between SUI and MUI women, this finding has to be
8 interpreted with caution.
9
10
11
12
13
14
15
16

17 ***Complications***

18
19 Most studies assessing UR include the need for catheterization resolving spontaneously within
20 one week after surgery, leading to large variations in published rates of women with
21 postoperative UR.²¹⁻²³ In our study, only nine patients (1.5%) reported serious problems with
22 bladder emptying more than three months after surgery. Other studies assessing UR after TVT
23 report 1.2% rate of “very disturbing UR” more than one year after TVT.²²⁻²⁴
24
25
26
27
28
29
30
31
32

33 In 2015, an editorial from the Cochrane library questioned the safety of sub-urethral slings.²⁵

34 In this editorial, the authors referred to a report from the UK Medicines and Healthcare
35 Products Regulatory Agency (MHRA), claiming serious and debilitating problems reported
36 by women operated for UI with vaginal tape implants.²⁶ However, in our study, only 2.9% of
37 the patients had experienced long-term tape-related problems. Of these less than 50% were in
38 need of repeat surgery due to complications, and only two patients needed major surgery, one
39 due to fistula, and one with resection of the tape due to pain. This is in accordance with most
40 other long-term studies stating an incidence of tape complications varying from < 1% to
41 3.5%.^{10, 27}
42
43
44
45
46
47
48
49
50
51
52
53
54
55

56 ***Strengths and limitations of the study***

57
58
59
60

1
2
3 Compared to most studies reporting outcome of incontinence surgery, our study has a large
4 sample size, long follow-up time and a high follow-up rate (596/621) as we included
5 information from neighboring hospitals in follow-up. In order to avoid any confounding effect
6 of earlier pelvic floor surgery on the efficacy, we have included only primary surgeries, and in
7 our analysis of recurrence, patients were censored at the date of surgery due to prolapse or
8 complications. Over the years surgeries and postoperative follow-up have been performed in
9 our department in a standardized manner and by a limited number of surgeons.
10
11
12
13
14
15
16
17
18
19
20

21 The most important weaknesses of this study are the retrospective design, the possibility for
22 bias due to changes in quality of reporting across the study periods and the possible loss to
23 follow-up by women having repeat surgery at hospitals in other parts of Norway. However, a
24 report from Auditor General of Norway stated that Norwegian patients have high loyalty to
25 their local hospitals, especially in the rural areas in northern and western Norway.²⁸ This
26 report supports that escape of patients out of the catchment area of our hospital is of limited
27 magnitude.
28
29
30
31
32
33
34
35
36
37
38
39
40
41

42 **Conclusion**

43
44 Retropubic TVT is a surgical method with high long-term safety and efficacy with low risk of
45 long-term serious tape complications. MUI is a risk factor for long-term recurrence.
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. **Ulmsten U, Henriksson L, Johnson P, Varhos G.** An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence. *Int Urogynecol J.* 1996;7:81-86.
2. **Ulmsten U, Johnson P, Rezapour M.** A three year follow-up of tension-free vaginal tape for surgical treatment of female stress urinary incontinence. *BJOG.* 1999;106:345-350.
3. **Withington J, Hirji S, Sahai A.** The changing face of urinary continence surgery in England: a perspective from the Hospital Episode Statistics database. *BJU Int.* 2014;114:268-277.
4. **Ebbesen MH, Hunnskaar S, Rortveit G, Hannestad YS.** Prevalence, incidence and remission of urinary incontinence in women: longitudinal data from the Norwegian HUNT study (EPINCONT). *BMC Urol.* 2013;13/27:1-10.
5. **Serati M, Ghezzi F, Cattoni E, et al.** Tension-free Vaginal Tape for the Treatment of Urodynamic Stress Incontinence: Efficacy and Adverse Effects at 10-Year Follow-Up. *Eur Urol.* 2012;61:939-946.
6. **Han JY, Park J, Choo MS.** Long-term durability, functional outcomes, and factors associated with surgical failure of tension-free vaginal tape procedure. *Int Urol Nephrol.* 2014;46:1921-1927.
7. **Groutz A, Rosen G, Cohen A, Gold R, Lessing JB, Gordon D.** Ten-year subjective outcome results of the retro-pubic tension-free vaginal tape for treatment of stress urinary incontinence. *J Minim Invasive Gynecol.* 2011;18:726-729.
8. **Svenningsen R, Staff AC, Schiøtz HA, Western K, Sandvik L, Kulseng-Hanssen S.** Long-term follow-up of the retropubic tension-free vaginal tape procedure. *Int Urogynecol J.* 2013;24:1271-1278.
9. **Stav K, Dwyer PL, Rosamilia A, Schierlitz L, Lim YN, Lee J.** Risk factors of treatment failure of midurethral sling procedures for women with urinary stress incontinence. *Int Urogynecol J.* 2010;21:149-155.
10. **Houwert RM, Venema PL, Aquarius AE, Bruinse HW, Kil PJ, Vervest HA.** Predictive value of urodynamics on outcome after midurethral sling surgery for female stress urinary incontinence. *Am J Obstet Gynecol.* 2009;200(6):649 e 1-12.
11. **Nilsson CG, Palva K, Rezapour M, Falconer C.** Eleven years prospective follow-up of the tension-free vaginal tape procedure for treatment of stress urinary incontinence. *Int Urogynecol J.* 2008;19:1043-1047.
12. **Costantini E, Kocjancic E, Lazzeri M, et al.** Long-term efficacy of the trans-obturator and retropubic mid-urethral slings for stress urinary incontinence: update from a randomized clinical trial. *World J Urol.* 2016;34:585-593.
13. **Ankardal M, Heiwall B, Lausten-Thomsen N, Carnelid J, Milsom I.** Short- and long-term results of the tension-free vaginal tape procedure in the treatment of female urinary incontinence. *Acta Obstet Gynecol Scand.* 2006;85:986-992.

- 1
2
3 14. **Deffieux X, Donnadiou AC, Porcher R, Gervaise A, Frydman R, Fernandez H.** Long-term results of
4 tension-free vaginal tape for female urinary incontinence: Follow up over 6 years. *Int J Urol.*
5 2007;14:521-526.
6
7
8 15. **Svenningsen R, Staff AC, Schiøtz HA, Western K, Sandvik L, Kulseng-Hanssen S.** Risk Factors for
9 Long-Term Failure of the Retropubic Tension-Free Vaginal Tape Procedure. *Neurourol Urodyn.*
10 2014;33:1140-1146.
11
12
13 16. **Wall LL, Wiskind AK, Taylor PA.** Simple bladder filling with a cough stress test compared with
14 subtracted cystometry for the diagnosis of urinary incontinence. *Am J Obstet Gynecol.*
15 1994;171(6):1472-1477.
16
17
18 17. **Berild GH, Kulseng-Hanssen S.** Reproducibility of a cough and jump stress test for the evaluation
19 of urinary incontinence. *Int Urogynecol J.* 2012;23:1449-1453.
20
21
22 18. **Kulseng-Hanssen S, Borstad E.** The development of a questionnaire to measure the severity of
23 symptoms and the quality of life before and after surgery for stress incontinence. *BJOG.*
24 2003;110:983-988.
25
26
27 19. **Bing MH, Gimbel H, Greisen S, Paulsen LB, Soerensen HC, Lose G.** Clinical risk factors and
28 urodynamic predictors prior to surgical treatment for stress urinary incontinence: a narrative review.
29 *Int Urogynecol J.* 2015;26:175-185.
30
31
32 20. **Petros PEP, Ulmsten UL.** An Integral Theory of Female Urinary Incontinence. *Acta Obstet Gynecol*
33 *Scand.* 1990;69:7-31.
34
35
36 21. **Cetinel B, Demirkesen O, Onal B, Akkus E, Alan C, Can G.** Are there any factors predicting the
37 cure and complication rates of tension-free vaginal tape? *Int Urogynecol J.* 2004;15:188-193.
38
39
40 22. **Duckett JRA, Patil A, Papanikolaou NS.** Predicting early voiding dysfunction after tension-free
41 vaginal tape. *J Obstet Gynaecol.* 2008;28:89-92.
42
43
44 23. **Madhuvrata P, Ford J, Merrick K, Boachie C, Abdel-Fattah M.** Voiding dysfunction following
45 suburethral tape. *J Obstet Gynaecol.* 2011;31:424-428.
46
47
48 24. **Reich A, Kohorst F, Kreienberg R, Flock F.** Voiding Dysfunction after the Tension-Free Vaginal
49 Tape Procedure. *Gynecol Obstet Invest.* 2011;72:79-84.
50
51
52 25. **Glazener, CMA.** What is the role of mid-urethral slings in the management of stress incontinence
53 in women? *Cochrane Database of Systematic Reviews.* 2015;7:1-3.
54 <https://doi.org/10.1002/14651858.ED000101>.
55
56 26. **Medicines and Healthcare Products Regulatory Agency (MHRA).** *A summary of the evidence on*
57 *the benefits and risks of vaginal mesh implants.*
58 <Http://www.gov.uk/government/publications/vaginal-mesh-implants-summary-of-benefits-and-risks>
59 (accessed 25 May 2015).
60

1
2
3 27. **Kokanali MK, Doganay M, Aksakal O, Cavkaytar S, Topcu HO, Özer I.** Risk factors for mesh
4 erosion after vaginal sling procedures for urinary incontinence. *Eur J Obstet Gynecol Reprod Biol.*
5 2014;177:146-150.
6
7

8 28. **Auditor General of Norway.** *The Office of the Auditor General's investigation into the free choice*
9 *of hospital system.* Auditor General of Norway. 2011-2012.

10 [Http://www.riksrevisjonen.no/en/Reports/Pages/free](http://www.riksrevisjonen.no/en/Reports/Pages/free) (accessed 28 Sept 2018)
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For Peer Review

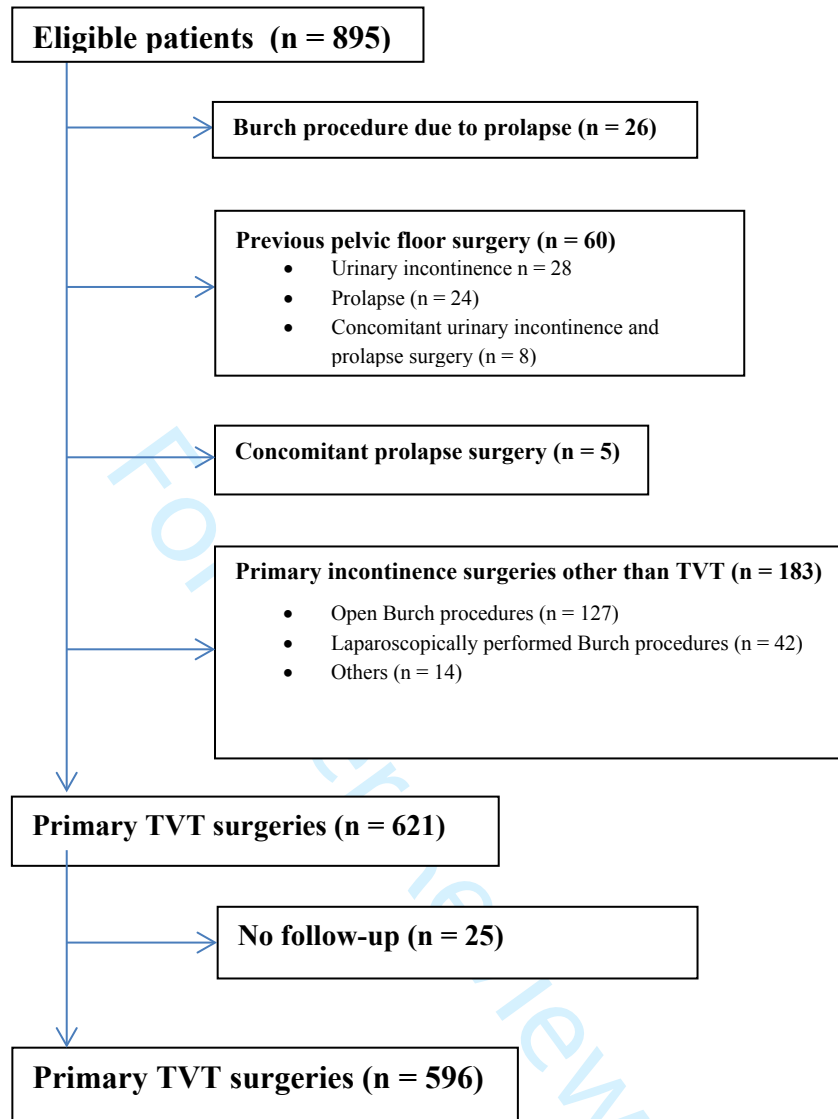
Figure 1 Flowchart of study participation

Table 1. Preoperative baseline characteristics by indication for surgery (%).

		SUI N = 390	MUI N = 206	P-value
		%	%	
Age (yrs.)	28-49	51.3	26.7	< 0.001
	50-59	24.6	31.6	
	60-93	24.1	41.7	
Body mass index (kg/m²)	Missing	1.3	1.0	< 0.001
	18.29-24.99	38.5	28.2	
	25.00-29.99	45.4	43.7	
	30.00-42.15	14.9	27.2	
Parity	Para 0-1	11.8	12.6	0.01
	Para 2	42.8	29.6	
	Para ≥ 3	45.4	57.8	
Hysterectomy (yes)		12.8	14.1	= 0.67
Comorbidity	Cardiovascular (yes)	18.5	33.0	< 0.01
	Pulmonal (yes)	9.7	16.5	< 0.02
	Neurological (yes)	7.9	11.2	= 0.19

Tabell 2. Preoperative conservative treatment and clinical examinations performed by indication for surgery (%).

	SUI N = 390	MUI N = 206
	%	%
Treatment		
Electrical stimulation	3.6	14.6
Pelvic floor muscle training	49.0	24.3
Both electrical stimulation and pelvic floor muscle training	5.9	16.0
Neither electrical stimulation nor pelvic floor muscle training/data missing	41.5	45.1
Clinical assessments performed		
Stress test	100.0	99.0
Measure of residual urine	99.2	98.1
Uroflowmetry	94.9	92.7
Cystometry	93.0	97.6

Table 3. Summary for recurrence and events leading to censoring by indication for surgery (%).

Outcomes	SUI	MUI	In total
	N = 390	N = 206	N = 596
	%	%	%
Time to last observation among recurrence-free women			
Follow-up < 1 year	18.7	15.0	17.4
Follow-up 1-5 years	28.5	28.6	28.5
Follow-up ≥ 5 years	33.8	25.2	30.9
Events leading to censoring			
Removal of tape immediate perioperatively (n = 5)	0.8	1.0	0.8
Other surgery due to other periop. compl. (n = 1)	0.3	-	0.2
UR with cutting of tape (n = 5)	0.5	1.5	0.8
Late tape complications with resection of the tape (n = 3)	0.8	-	0.3
Prolapse surgery (n = 18)	2.8	3.4	3.0
Recurrence	13.8	25.2	17.8

Table 4. Cumulative cure rates after one, five and 10 years by indication for surgery and in total.

TVT surgery risk group	1 year (95% CI)	5 years (95% CI)	10 years (95% CI)
SUI	94% (92-96%)	85% (81-89%)	74% (66-82%)
MUI	88% (84-92%)	67% (59-75%)	58% (48-68%)
Overall cumulative cure rate	92% (90-94%)	79% (75-83%)	69% (63-75%)

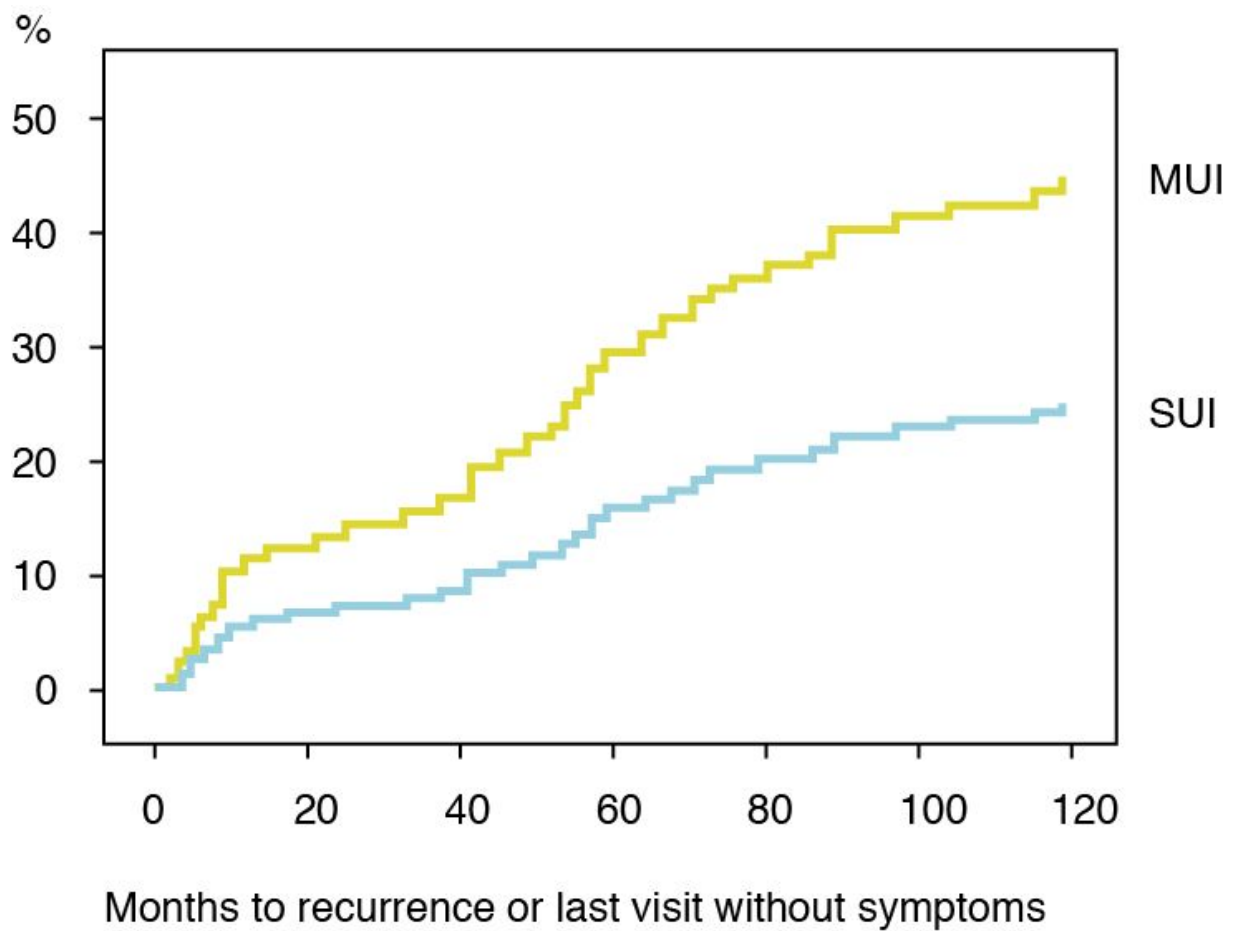
For Peer Review

Table 5. Complications by indication for surgery (%).

	SUI		MUI	
	N = 390		N = 206	
	N	%	N	%
Urinary retention (UR)	22	5.6	9	4.4
Other perioperative complications	25	6.4	8	3.9
Bleeding/hematoma	10	2.6	3	1.5
Bladder perf./injury	10	2.6	2	1.0
Others*	5	1.3	3	1.5
Late tape complications within 10 years	13	3.3	4	1.9
Erosion	10	2.6	2	1.0
Pain	1	0.3	2	1.0
Fistula	2	0.5	0	0

*Five patients with superficial surgical site infection and four with other complications.

Figure 2 Cumulative rates of recurrence of stress incontinence after TVT surgery by indication for surgery.



view

Table 1. Preoperative baseline characteristics by indication for surgery (%).

		SUI	MUI	P-value
		N = 390	N = 206	
		%	%	
Age (yrs.)				
	28-49	51.3	26.7	< 0.001
	50-59	24.6	31.6	
	60-93	24.1	41.7	
Body mass index (kg/m²)				
	Missing	1.3	1.0	< 0.001
	18.29-24.99	38.5	28.2	
	25.00-29.99	45.4	43.7	
	30.00-42.15	14.9	27.2	
Parity				
	Para 0-1	11.8	12.6	0.01
	Para 2	42.8	29.6	
	Para ≥ 3	45.4	57.8	
Hysterectomy (yes)		12.8	14.1	= 0.67
Comorbidity				
	Cardiovascular (yes)	18.5	33.0	< 0.01
	Pulmonal (yes)	9.7	16.5	< 0.02
	Neurological (yes)	7.9	11.2	= 0.19

Tabell 2. Preoperative conservative treatment and clinical examinations performed by indication for surgery (%).

	SUI N = 390	MUI N = 206
	%	%
Treatment		
Electrical stimulation	3.6	14.6
Pelvic floor muscle training	49.0	24.3
Both electrical stimulation and pelvic floor muscle training	5.9	16.0
Neither electrical stimulation nor pelvic floor muscle training/data missing	41.5	45.1
Clinical assessments performed		
Stress test	100.0	99.0
Measure of residual urine	99.2	98.1
Uroflowmetry	94.9	92.7
Cystometry	93.0	97.6

Table 3. Summary for recurrence and events leading to censoring by indication for surgery (%).

Outcomes	SUI	MUI	In total
	N = 390	N = 206	N = 596
	%	%	%
Time to last observation among recurrence-free women			
Follow-up < 1 year	18.7	15.0	17.4
Follow-up 1-5 years	28.5	28.6	28.5
Follow-up ≥ 5 years	33.8	25.2	30.9
Events leading to censoring			
Removal of tape immediate perioperatively (n = 5)	0.8	1.0	0.8
Other surgery due to other periop. compl. (n = 1)	0.3	-	0.2
UR with cutting of tape (n = 5)	0.5	1.5	0.8
Late tape complications with resection of the tape (n = 3)	0.8	-	0.3
Prolapse surgery (n = 18)	2.8	3.4	3.0
Recurrence	13.8	25.2	17.8

Table 4. Cumulative cure rates after one, five and 10 years by indication for surgery and in total.

TVT surgery risk group	1 year (95% CI)	5 years (95% CI)	10 years (95% CI)
SUI	94% (92-96%)	85% (81-89%)	74% (66-82%)
MUI	88% (84-92%)	67% (59-75%)	58% (48-68%)
Overall cumulative cure rate	92% (90-94%)	79% (75-83%)	69% (63-75%)

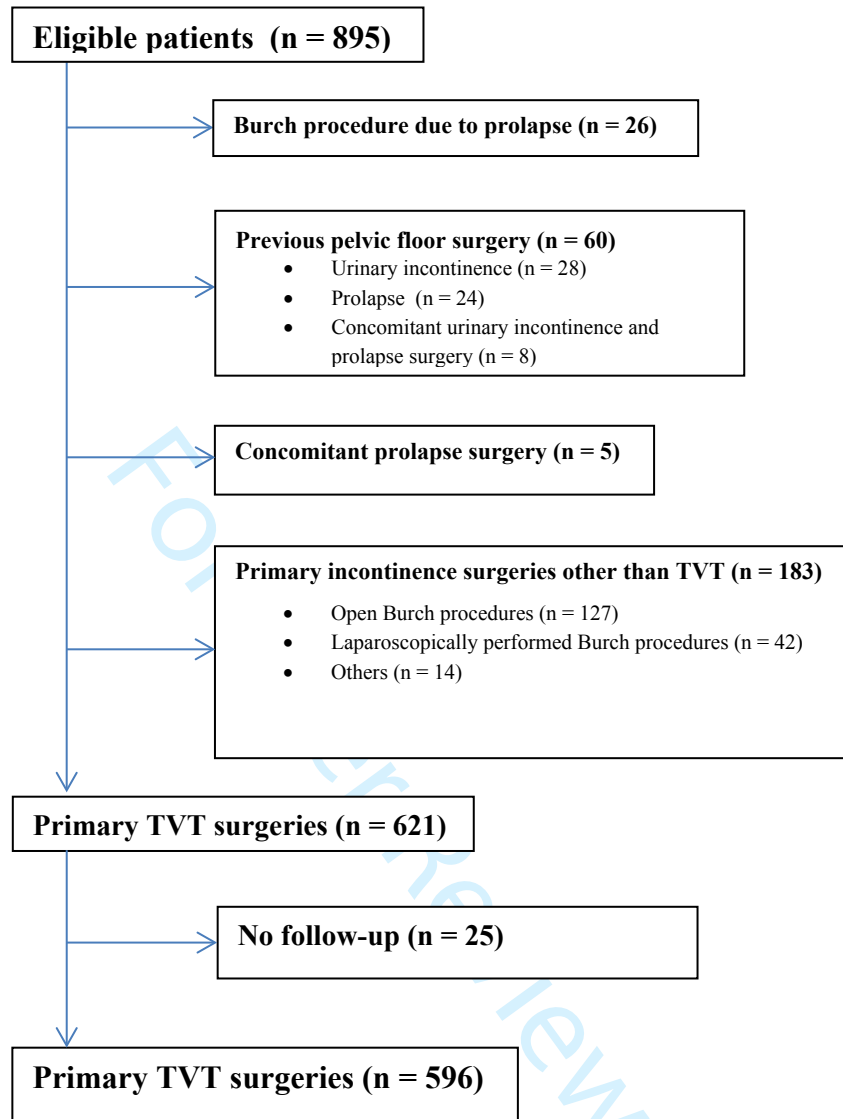
For Peer Review

Table 5. Complications by indication for surgery (%).

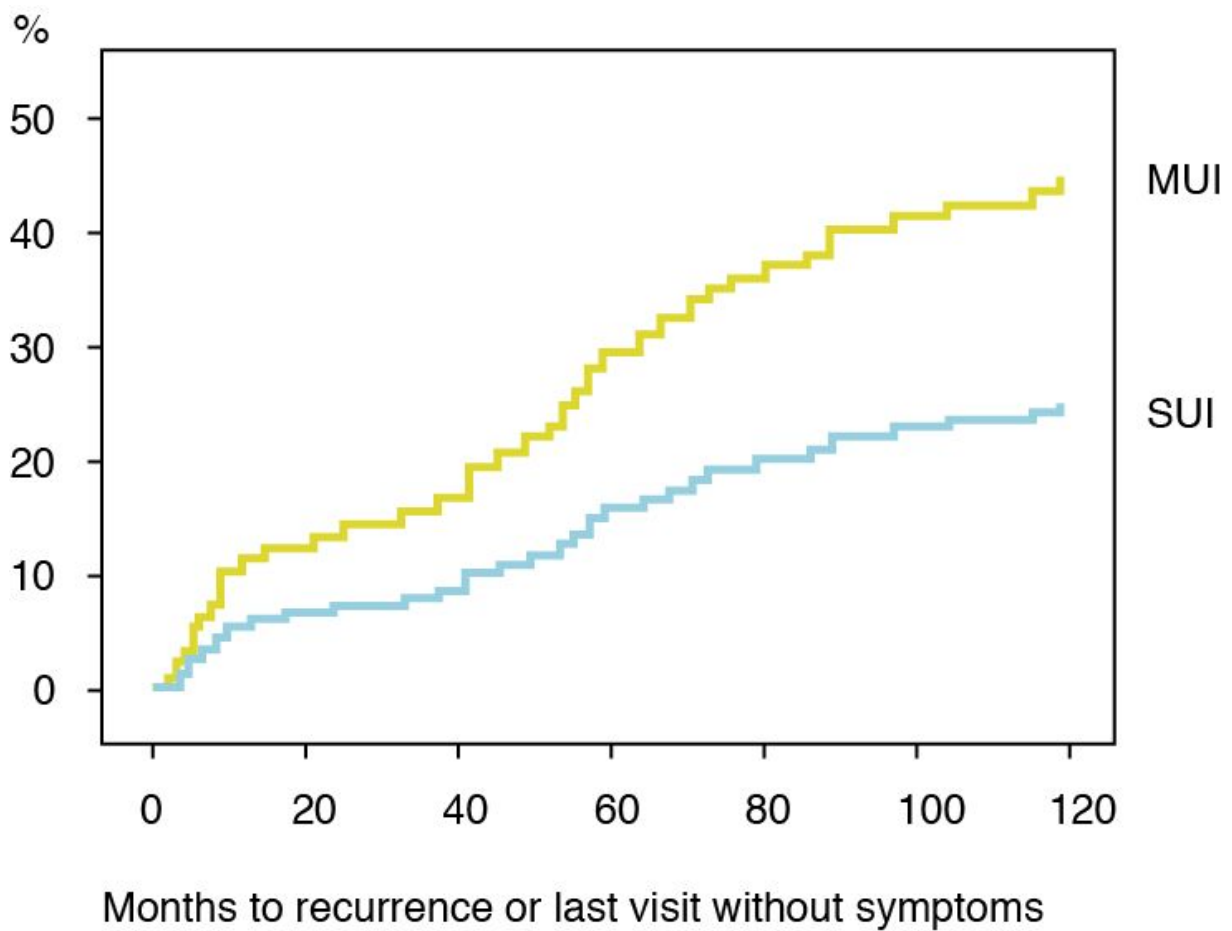
	SUI		MUI	
	N = 390		N = 206	
	N	%	N	%
Urinary retention (UR)	22	5.6	9	4.4
Other perioperative complications	25	6.4	8	3.9
Bleeding/hematoma	10	2.6	3	1.5
Bladder perf./injury	10	2.6	2	1.0
Others*	5	1.3	3	1.5
Late tape complications within 10 years	13	3.3	4	1.9
Erosion	10	2.6	2	1.0
Pain	1	0.3	2	1.0
Fistula	2	0.5	0	0

*Five patients with superficial surgical site infection and four with other complications.

1
2
3 **Figure 1 Flowchart of study participation**
4
5
6
7



1 **Figure 2 Cumulative rates of recurrence of stress incontinence after TVT surgery by**
2 **indication for surgery.**



4
5