ORIGINAL ARTICLE

Surgery versus Physiotherapy for Stress Urinary Incontinence

Julien Labrie, M.D., Bary L.C.M. Berghmans, Ph.D., Kathelijn Fischer, M.D., Ph.D., Alfredo L. Milani, M.D., Ph.D., Ileana van der Wijk, M.D., Dina J.C. Smalbraak, M.D., Astrid Vollebregt, M.D., Ph.D., René P. Schellart, M.D., Giuseppe C.M. Graziosi, M.D., Ph.D., J. Marinus van der Ploeg, M.D., Joseph F.G.M. Brouns, M.D., Ph.D., E. Stella M. Tiersma, M.D., Ph.D., Annette G. Groenendijk, M.D., Ph.D., Piet Scholten, M.D., Ph.D., Ben Willem Mol, M.D., Ph.D., Elisabeth E. Blokhuis, M.D., Albert H. Adriaanse, M.D., Ph.D., Aaltje Schram, M.D., Ph.D., Jan-Paul W.R. Roovers, M.D., Ph.D., Antoine L.M. Lagro-Janssen, M.D., Ph.D., and Carl H. van der Vaart, M.D., Ph.D.

ABSTRACT

BACKGROUND

Physiotherapy involving pelvic-floor muscle training is advocated as first-line treatment for stress urinary incontinence; midurethral-sling surgery is generally recommended when physiotherapy is unsuccessful. Data are lacking from randomized trials comparing these two options as initial therapy.

METHODS

We performed a multicenter, randomized trial to compare physiotherapy and midurethral-sling surgery in women with stress urinary incontinence. Crossover between groups was allowed. The primary outcome was subjective improvement, measured by means of the Patient Global Impression of Improvement at 12 months.

RESULTS

We randomly assigned 230 women to the surgery group and 230 women to the physiotherapy group. A total of 49.0% of women in the physiotherapy group and 11.2% of women in the surgery group crossed over to the alternative treatment. In an intention-to-treat analysis, subjective improvement was reported by 90.8% of women in the surgery group and 64.4% of women in the physiotherapy group (absolute difference, 26.4 percentage points; 95% confidence interval [CI], 18.1 to 34.5). The rates of subjective cure were 85.2% in the surgery group and 53.4% in the physiotherapy group (absolute difference, 31.8 percentage points; 95% CI, 22.6 to 40.3); rates of objective cure were 76.5% and 58.8%, respectively (absolute difference, 17.8 percentage points; 95% CI, 7.9 to 27.3). A post hoc per-protocol analysis showed that women who crossed over to the surgery group had outcomes similar to those of women initially assigned to surgery and that both these groups had outcomes superior to those of women who did not cross over to surgery.

CONCLUSIONS

For women with stress urinary incontinence, initial midurethral-sling surgery, as compared with initial physiotherapy, results in higher rates of subjective improvement and subjective and objective cure at 1 year. (Funded by ZonMw, the Netherlands Organization for Health Research and Development; Dutch Trial Register number, NTR1248.)

From the University Medical Center Utrecht (J.L., K.F., C.H.V.) and Diakonessenhuis (P.S.), Utrecht; University Medical Center Maastricht, Maastricht (B.L.C.M.B.); Reinier de Graaf Gasthuis, Delft (A.L.M.); Groene Hart Ziekenhuis, Gouda (I.W.); Amphia Ziekenhuis, Breda (D.J.C.S.); Spaarne Ziekenhuis, Hoofddorp (A.V.); Kennemer Gasthuis, Haarlem (R.P.S.); Antonius Ziekenhuis, Nieuwegein (G.C.M.G.); Martini Ziekenhuis (J.M.P.) and University Medical Center Groningen (A.S.), Groningen; Zaans Medisch Centrum, Zaandam (J.F.G.M.B.); Vrije Universiteit Medisch Centrum (E.S.M.T.), Onze Lieve Vrouwe Gasthuis (A.G.G.), and Academic Medical Center (B.W.M., J.-P.W.R.R.), Amsterdam; Hofpoort Ziekenhuis, Woerden (E.E.B.); Medisch Centrum Alkmaar, Alkmaar (A.H.A.); and University Medical Center Nijmegen, Nijmegen (A.L.M.L.-J.) — all in the Netherlands. Address reprint requests to Dr. Labrie at University Medical Centre Utrecht, Heidelberglaan 100, P.O. Box 85500, Room F05.121, Utrecht, the Netherlands, or at j.labrie@umcutrecht.nl.

N Engl J Med 2013;369:1124-33.
DOI: 10.1056/NEJMoa1210627

Stress urinary incontinence is a common health problem among women that negatively affects quality of life.[1-3] The International Consultation on Incontinence defines stress urinary incontinence as an involuntary loss of urine on physical exertion, sneezing, or coughing.[4] Pelvic-floor muscle training (physiotherapy) is generally regarded as first-line management for the condition.[5] However, physiotherapy is associated with broad variation in the rates of subjective success (53 to 97%) and objective success (5 to 49%), and more severe symptoms are associated with worse outcomes.[6,7] After 3 to 15 years, 25 to 50% of women initially treated with physiotherapy have proceeded to surgery.[7-9] Midurethral-sling surgery is a minimally invasive surgical technique for the treatment of stress urinary incontinence,[10] with subjective cure rates between 75% and 94% and objective cure rates between 57% and 92%.[1,11,12] The procedure is regarded as effective, with minimal complications.[11]

The difference in the reported frequencies of a successful outcome between surgery and physiotherapy raises the question of whether all women with moderate-to-severe stress-predominant urinary incontinence should initially be treated with physiotherapy or should immediately undergo surgery as initial treatment. Midurethral-sling surgery and physiotherapy have not been directly compared. We therefore conducted a multicenter, pragmatic, randomized trial to compare initial midurethral-sling surgery with initial physiotherapy in women with moderate-to-severe stress urinary incontinence, using standardized outcome measures at 12 months.

METHODS

STUDY DESIGN

We performed our randomized trial at 4 university medical centers and 19 general hospitals (24% of Dutch hospitals). The study protocol and inclusion and exclusion criteria have been published previously.[13] In brief, eligible women were 35 to 80 years of age and had been referred to an outpatient gynecology or urology clinic after presenting with stress urinary incontinence classified as moderate or severe according to the severity index developed by Sandvik et al.[14] (see Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). In women presenting with mixed incontinence (involuntary loss of urine associated with urgency [urge incontinence] and also on physical exertion, sneezing, or coughing), stress incontinence was classified as predominant if there were more episodes of stress than urge incontinence, as reported on the validated Dutch version of the Urogenital Distress Inventory.[13] Women included in the study either had not received treatment or had undergone physiotherapy more than 6 months before randomization. The diagnosis of stress urinary incontinence was based on a demonstration of leakage of urine on straining or coughing at a bladder volume of at least 300 ml. Urodynamic testing to confirm the diagnosis was not mandatory for eligibility.[15] Women who had undergone previous incontinence surgery or who had concomitant pelvic-organ prolapse of stage 2 or higher (according to the Pelvic Organ Prolapse Quantification system) were excluded.[4]

The ethics committee of the Utrecht Medical Center and the institutional review boards at the individual sites approved the study protocol (available at NEJM.org). The last author assumes responsibility for the completeness and accuracy of the data and analyses and for the fidelity of the study to the protocol. The trial was initiated and performed without the support or involvement of manufacturers of midurethral slings.

After written informed consent was obtained, research nurses on site performed computerized randomization on a central server. An independent data manager designed the randomization table. Women were assigned in a 1:1 ratio to the surgery group or the physiotherapy group, with blocks of four per center, stratified according to the severity of incontinence (moderate or severe). The treatment assignments were not concealed.

Surgical procedures were performed by 49 gynecologists and urologists. Before participating in this trial, each surgeon had performed a minimum of 20 procedures. Both retropubic and transobturator midurethral-sling surgical techniques were allowed.[10,16]

Physiotherapy was performed by 83 (17%) of the 478 certified pelvic physiotherapists in the Netherlands. Pelvic-floor muscle training for stress urinary incontinence was performed according to the Dutch guidelines.[17] Women were educated about the function of the pelvic-floor muscles, bladder function, and how to perform a correct pelvic-floor muscle contraction. They were also taught to perform a short muscle contraction before an increase in intraabdominal pressure, such as that associated with sneezing.[18]

A supervised program to help women build up to 8 to 12 maximal contractions three times per day was provided. Treatment was given at 1-week or 2-week intervals, depending on the severity of symptoms, treatment goals, adherence, and the ability of the women to learn to perform the muscle contractions. The physiotherapist determined the number of sessions, with an intended number of nine sessions in 9 to 18 weeks (the standard number at the time). If a woman was unable to contract her pelvic-floor muscles, touch, tapping, and massage were applied to increase awareness of these muscles. Biofeedback-assisted or functional electrostimulation therapy could be used. If a woman was dissatisfied with the result of the assigned treatment, she was allowed to cross over to the alternative treatment, which is consistent with usual clinical practice, but data were analyzed according to the intention-to-treat principle.

OUTCOMES

The primary outcome was subjective improvement in symptoms of stress urinary incontinence at 12 months, measured with the use of the Patient Global Impression of Improvement (PGI-I) instrument, a 7-point Likert scale that ranks the response to a single question from "very much worse" to "very much better." The PGI-I response has been shown to correlate significantly with the frequency of incontinence episodes, cough-test results, pad-test results, and scores on several Incontinence Quality of Life questionnaires.[19,20] In concordance with other studies, improvement was considered to be clinically significant if the patient's response was "much better" or "very much better."[21-23] The PGI-I response was also assessed at 2, 4, 6, and 18 months to monitor changes.

The secondary outcomes included urogenital symptom improvement; disease-specific quality of life; objective and subjective cure of stress urinary incontinence; and adverse events, including new urinary symptoms. Urogenital symptoms and disease-specific quality of life were measured with the validated Dutch versions of the Urogenital Distress Inventory (UDI) and the Incontinence Impact Questionnaire (IIQ), respectively.[24,25] The domain scores range from 0 to 100, with lower scores indicating less distress caused by urogenital symptoms (UDI) and better quality of life (IIQ). The Patient Global Impression of Severity (PGI-S) index was used to assess changes in the perceived severity of incontinence on a 4-point Likert scale. Responses were dichotomized into no symptoms and symptoms (mild, moderate, or severe).[19]

Subjective cure of stress urinary incontinence was defined as a negative response to the question, "Do you experience urine leakage related to physical activity, coughing, or sneezing?" Objective cure was defined as no incontinence observed during a cough stress test at a bladder volume of at least 300 ml.

A standardized case-report form was used to record adverse events perioperatively for women undergoing surgery and at each follow-up visit for all women. Data were collected at baseline (either the day of surgery or the first physiotherapy session) and at 2, 4, 6, 12, and 18 months by 13 research nurses covering all clinical sites. Data collection was performed on a standardized, computerized, secured case-record form accessible online and was controlled by an independent data-management center. The cough test was performed at the clinical evaluation at 12 months.

STATISTICAL ANALYSIS

On the basis of the assumption that 80% of women in the surgery group and 65% of women in the physiotherapy group would report subjective improvement,[13] we calculated that 197 women were needed in each group to achieve a power of 90% (at a two-sided significance level of 5%). Anticipating a 15% loss to follow-up, we planned to include 460 women.

We performed a modified intention-to-treat analysis, which included all women who underwent initial surgery as the assigned treatment or who started initial physiotherapy as the assigned treatment. In cases of crossover between treatment groups, the data were analyzed according to the assigned treatment. The main analysis was performed with the original data and was repeated after imputation of missing data (sensitivity analysis). To impute missing data, a multiple-imputation model with 10 iterations using predictive mean matching was applied.[26]

Descriptive statistics were used to analyze baseline characteristics. Treatment effects on binary variables (PGI-I [improvement], PGI-S [no symptoms], subjective cure, and objective cure) are presented as the absolute change in percentage points between groups. The 95% confidence intervals were calculated with the use of the

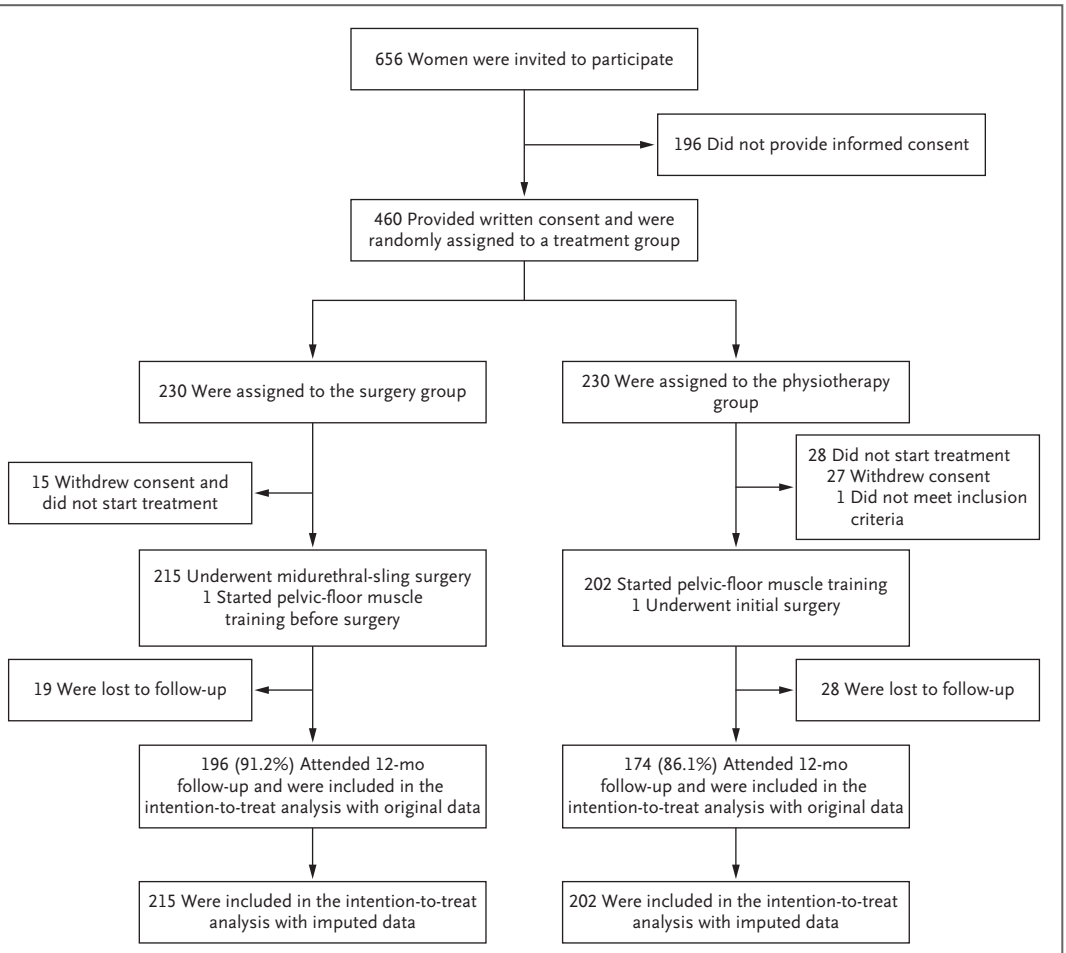

Figure 1. Randomization and Follow-up.

Newcombe–Wilson method for interval estimation, and Fisher's exact test was used for calculating the significance level.[27]

Student's t-test was used to compare continuous data between groups. Changes in UDI and IIQ domain scores over time were analyzed with the use of a paired-samples Student's t-test. To facilitate interpretation of changes in UDI and IIQ scores, effect sizes were calculated with the use of Cohen's D test. An effect size of 0.3 or less was considered small, more than 0.3 to 0.8 moderate, and more than 0.8 large.[28]

A post hoc per-protocol analysis of outcomes among women who underwent physiotherapy only, women who underwent surgery after physiotherapy, and women who underwent initial surgery was performed with the use of one-way analysis of variance and paired t-tests with Holm's Bonferroni correction for multiple comparisons. All statistical analyses were performed with the use of SPSS Statistics for Windows, version 17.0 (SPSS).

RESULTS

STUDY POPULATION

During the period from March 2008 through May 2010, a total of 656 women with stress urinary incontinence or mixed urinary incontinence in which stress incontinence was predominant were asked to participate in the study, of whom 460 gave written informed consent. These women were randomly assigned to the surgery group (230) or the physiotherapy group (230) (Fig. 1).

Analyses were performed for 215 women assigned to the surgery group and 202 women assigned to the physiotherapy group; at 12 months, outcome data were available for 196 (91.2%)

and 174 (86.1%) of these women, respectively (P=0.11). In the physiotherapy group, 99 women (49.0%) crossed over to the surgery group, after a mean (±SD) time of 31.7±12.7 weeks.

The frequency of crossover to the surgery group was similar among women who had undergone specialized physiotherapy before enrollment and women who had not received previous treatment (47.4% [18 of 38] vs. 49.4% [81 of 164], P=0.86). Twenty-two women (11.2%) received additional physiotherapy after surgery; these women had symptoms related to pelvic-floor muscle hyperactivity, such as obstructive micturition, and underwent training to relax the pelvic-floor muscles.

INTENTION-TO-TREAT ANALYSIS

Baseline characteristics and UDI and IIQ domain scores were similar in the two groups (Table 1). Primary and secondary outcomes according to

Table 1. Baseline Characteristics of the Study Population.*

Characteristic	Surgery Group (N=215)	Physiotherapy Group (N=202)
Age — yr	50.2±9.8	50.0±8.2
College or university degree — no./total no. (%)	56/211 (26.5)	49/199 (24.6)
Parity		
Median	2	2
Range	0–4	0–7
Current smoker — no./total no. (%)	36/207 (17.4)	37/191 (19.4)
Body-mass index†	26.4±5.0	26.9±5.0
Postmenopausal — no./total no. (%)	78/209 (37.3)	67/196 (34.2)
Previous vaginal surgery — no./total no. (%)	41/213 (19.2)	38/202 (18.8)
No. of voidings in 24-hr period‡		
Median	8	8
Range	3–22	3–17
Physiotherapy >6 mo before study — no./total no. (%)	34/215 (15.8)	38/202 (18.8)
PGI-S: not severe — no./total no. (%)	9/213 (4.2)	12/196 (6.1)
UDI domain score§		
Urinary incontinence	42.8±19.1	41.1±19.2
Overactive bladder	22.8±21.3	18.4±20.3
Obstructive micturition	14.8±20.6	11.3±18.7
Discomfort or pain	11.0±14.2	9.9±14.1
Genital prolapse	3.9±11.6	2.6±10.5
IIQ domain score§		
Physical functioning	15.3±17.5	15.4±17.3
Mobility	28.7±19.4	27.3±20.6
Emotional health	17.7±16.5	18.7±18.6
Social functioning	9.8±16.0	11.9±20.6
Embarrassment	30.4±22.6	29.1±24.1

* Plus–minus values are means ±SD. No significant between-group differences were observed for any characteristic. PGI-S denotes Patient Global Impression of Severity.
† The body-mass index is the weight in kilograms divided by the square of the height in meters. Data were available for 212 women in the surgery group and 193 women in the physiotherapy group.
‡ Data were available for 202 women in the surgery group and 177 women in the physiotherapy group.
§ Domain scores on the Incontinence Impact Questionnaire (IIQ) and the Urogenital Distress Inventory (UDI) scores range from 0 to 100, with higher scores indicating more distress caused by urogenital symptoms (UDI) or a more negative effect on health-related quality of life (IIQ).[24,25] Data were available for 212 women in the surgery group and 199 women in the physiotherapy group.

the assigned treatment group, for both original and imputed data, are presented in Table 2. The PGI-I and PGI-S responses for all follow-up assessments, including the assessment at 18 months, are shown in Table S2 in the Supplementary Appendix. At 12 months, a significantly higher proportion of women assigned to the surgery group reported improvement, as compared with women assigned to the physiotherapy group; the difference between the groups was 26.4 percentage points (95% confidence interval [CI], 18.1 to 34.5; P<0.001) for the original data and 26.5 percentage points (95% CI, 18.5 to 34.2; P<0.001) when the imputed data were included. Of the 99 women who crossed over from physiotherapy to surgery, 90 (90.9%) reported no improvement on the last PGI-I assessment before surgery was performed. Subjective cure and objective cure of stress urinary incontinence were significantly more frequent in the surgery group than in the physiotherapy group (objective cure, P=0.001; subjective cure, P<0.001). Treatment effects are shown in Table 2.

Both treatment groups had significant improvement in UDI and IIQ domain scores, as compared with baseline values (Table 2). Improvements in the UDI scores for incontinence and overactive bladder were significantly greater in the surgery group than in the physiotherapy group (P<0.001 and P=0.02, respectively, for the original data), but with only moderate effect sizes; the effect sizes were 0.50 (95% CI, –1.6 to 2.6) for incontinence and 0.36 (95% CI, –1.0 to 1.7) for overactive bladder. In the comparison of IIQ

Table 2. Primary and Secondary Outcomes in the Surgery and Physiotherapy Groups at 12 Months.*

Outcome	Surgery Group (N=196)	Physiotherapy Group (N=174)	Original Data	Imputed Data
			Treatment Effect (95% CI)†	
			percentage points	
PGI-I: improvement — no./total no. (%)	177/195 (90.8)	112/174 (64.4)	26.4 (18.1–34.5)	26.5 (18.5–34.2)
PGI-S: no symptoms — no./total no. (%)	167/195 (85.6)	114/174 (65.5)	20.1 (11.4–28.6)	19.7 (11.4–27.8)
Subjective cure — no./total no. (%)‡	167/196 (85.2)	93/174 (53.4)	31.8 (22.6–40.3)	29.2 (20.5–37.4)
Objective cure — no./total no. (%)§	140/183 (76.5)	94/160 (58.8)	17.8 (7.9–27.3)	15.5 (6.4–24.2)
			P Value¶	
Change in UDI domain score‖				
Urinary incontinence	–37.3±20.9**	–26.9±20.6**	<0.001	<0.001
Overactive bladder	–15.5±20.5**	–10.6±19.5**	0.02	0.01
Obstructive micturition	–7.9±22.4**	–3.8±20.1	0.06	0.06
Discomfort or pain	–7.4±13.8**	–5.4±11.6**	0.15	0.18
Genital prolapse	–1.8±11.6	–1.9±10.8	0.97	0.77
Change in IIQ domain score‖††				
Physical functioning	–13.2±17.2	–10.3±17.0	0.11	0.12
Mobility	–24.6±19.9	–17.5±21.8	0.001	0.004
Emotional health	–15.1±15.7	–11.8±18.1	0.07	0.24
Social functioning	–8.5±16.6	–9.7±19.3	0.54	0.55
Embarrassment	–26.6±23.2	–19.3±24.5	0.004	0.006

* Plus–minus values are means ±SD. PGI-I denotes Patient Global Impression of Improvement.
† P≤0.001 for all four outcomes in the analyses of both the original data and the imputed data.
‡ Subjective cure was measured with the UDI question, "Do you experience urine leakage related to physical activity, coughing, or sneezing?"
§ Objective cure was defined as a negative provocative cough stress test.
¶ P values are for comparisons between the physiotherapy group and the surgery group.
‖ Data were available for 193 women in the surgery group and 171 women in the physiotherapy group.
** P<0.001 for the change in the domain score over time in the analyses of both the original data and the imputed data.
†† P<0.001 for changes in all domain scores over time for both groups in the analyses of both the original data and the imputed data.

Table 3. Adverse Events.*

Adverse Event	Physiotherapy Group (N=202)†	Surgery Group (N=215)
	no. of events (%)	
Serious adverse events		
Bladder perforation‡	0	6 (2.8)
Vaginal epithelial perforation	2 (1.0)	8 (3.7)
Reoperation for tape exposure	1 (0.5)	5 (2.3)
Reoperation to loosen tape	0	1 (0.5)
Postoperative bleeding	1 (0.5)	0
Hematoma§	4 (2.0)	16 (7.4)
Blood loss ≥500 ml	1 (0.5)	2 (0.9)
New urge urinary incontinence	5 (2.5)	13 (6.0)

* Adverse events occurred in 41 women in total.
† All adverse events in the physiotherapy group occurred in women who crossed over to the surgery group.
‡ P=0.03.
§ P=0.01.

domain scores between groups, improvements in mobility and embarrassment scores were significantly greater in the surgery group than in the physiotherapy group (P=0.001 and P=0.004, respectively), but again with only moderate effect sizes; effect sizes were 0.34 (95% CI, –1.8 to 2.5) for mobility and 0.31 (95% CI, –2.1 to 2.7) for embarrassment.

ADVERSE EVENTS

Table 3 summarizes adverse events in both groups. A total of 65 adverse events occurred in 41 (9.8%) of 417 women; all adverse events were related to surgery. Intraoperative bladder perforation and vaginal epithelial perforations were successfully treated during surgery without further clinical implications. Three women had a recorded blood loss of 500 ml or more. One woman needed reoperation to loosen the synthetic sling because of persistent voiding problems, and six reoperations were performed for tape exposure.

POST HOC PER-PROTOCOL ANALYSIS

Table 4 shows the results of the post hoc per-protocol analysis comparing women who underwent only physiotherapy (103), those who underwent surgery after physiotherapy (99), and those who underwent initial surgery (215). At 12 months, the proportion of women who reported improvement was lower among women who underwent only physiotherapy than among women in the physiotherapy group who crossed over to the surgery group (absolute difference, 61.8 percentage points) or women who underwent initial surgery (absolute difference, 59.1 percentage points). Women who underwent only physiotherapy also had lower frequencies of subjective and objective cure, as compared with both groups of women who underwent surgery. Outcomes were similar between the women who underwent surgery after physiotherapy and those who underwent surgery initially. The mean number of physiotherapy sessions attended was 9.1±4.9 among women who did not cross over to the surgery group and 7.4±4.4 among women who did cross over (P=0.06). When we considered the last PGI-I assessment for women who underwent physiotherapy alone and were lost to follow-up, we found that 76% of women (16 of 21) reported no improvement (Table S3 in the Supplementary Appendix).

DISCUSSION

In this Dutch nationwide, multicenter trial, we compared strategies of initial surgery and initial physiotherapy, with an option to cross over to surgery, in the treatment of women with moderate-to-severe stress-predominant urinary incontinence. Women randomly assigned to undergo initial surgery were significantly more likely to have improvement at 12 months than were those assigned to receive initial physiotherapy. Surgery also resulted in greater improvement than did physiotherapy on all secondary end points. The benefits of surgery persisted in analyses involving multiple imputation of missing data. In a subsequent per-protocol analysis, women in the physiotherapy group who crossed over to the surgery group had outcomes that were similar to those among women who underwent initial surgery, whereas women who underwent only physiotherapy had significantly less favorable outcomes.

Our study has some limitations. Selection bias may have occurred. Women with a preference for surgery may have been more likely to participate in the study, because they otherwise would have received initial physiotherapy according to Dutch guidelines. In addition, women who had undergone physiotherapy more than 6 months before entering the trial were allowed to participate, although they represented only one fifth of the study population; a negative experience with prior

Table 4. Per-Protocol Analysis of Primary and Secondary Outcomes at 12 Months.*

Outcome	Physiotherapy Only (N=103)	Surgery after Physiotherapy (N=99)	Initial Surgery (N=215)	P Value		
				Physiotherapy Only vs. Surgery after Physiotherapy	Surgery after Physiotherapy vs. Initial Surgery	Physiotherapy Only vs. Initial Surgery
PGI-I: improvement — no./total no. (%)	26/82 (31.7)	86/92 (93.5)	177/195 (90.8)	<0.001	0.68	<0.001
PGI-S: no symptoms — no./total no. (%)	30/82 (36.6)	84/92 (91.3)	167/195 (85.6)	<0.001	1.00	<0.001
Subjective cure — no./total no. (%)	13/82 (15.9)	80/92 (87.0)	167/196 (85.2)	<0.001	1.00	<0.001
Objective cure — no./total no. (%)	33/75 (44.0)	61/85 (71.8)	140/183 (76.5)	<0.001	1.00	<0.001
Physiotherapy sessions — no.	9.1±4.9	7.4±4.4	0.6±1.9	0.06	<0.001	<0.001
Change in UDI domain score						
Urinary incontinence	−10.9±20.8	−41.3±20.6	−37.3±20.9	<0.001	0.42	<0.001
Overactive bladder	−6.4±18.2	−14.4±19.9	−15.5±20.5	0.03	1.00	0.002
Obstructive micturition	−0.21±20.3	−7.0±19.4	−7.9±22.4	0.11	1.00	0.02
Discomfort or pain	−4.0±10.4	−6.7±12.5	−7.4±13.8	0.50	1.00	0.15
Genital prolapse	−1.3±6.4	−2.4±13.5	−1.8±11.6	1.00	1.00	1.00
Change in IIQ domain score						
Physical functioning	−5.6±13.0	−14.5±19.1	−13.2±17.2	0.002	1.00	0.002
Mobility	−8.8±18.9	−25.4±21.3	−24.6±19.9	<0.001	1.00	<0.001
Emotional health	−6.4±16.2	−16.7±18.4	−15.1±15.7	<0.001	1.00	<0.001
Social functioning	−5.6±14.7	−13.3±22.1	−8.5±16.6	0.01	0.10	0.65
Embarrassment	−10.7±18.4	−27.1±26.7	−26.6±23.2	<0.001	1.00	<0.001

* Plus–minus values are means ±SD.

physiotherapy may have negatively affected their adherence to the study regimen and the number of sessions they attended, which could have resulted in a lower efficacy of physiotherapy.[29] However, this possibility is not supported by our data; in the physiotherapy group, prior physiotherapy was similarly frequent among those who crossed over to surgery and those who did not.

The high crossover rate (49.0%) among women assigned to the physiotherapy group complicates the interpretation of results, because we used a modified intention-to-treat analysis. To address this problem, we performed a post hoc per-protocol analysis, which showed a favorable effect of additional surgery in the physiotherapy group.

Strengths of our study include our randomized design and inclusion of a variety of centers (24% of Dutch university and general hospitals), as well as many gynecologists, urologists, and certified pelvic physiotherapists (17% of certified Dutch pelvic physiotherapists). Because we allowed both the transobturator and retropubic techniques for the placement of polypropylene tape, the range of typical clinical practice was represented in the surgery group. Complications of surgery were limited and were consistent with those seen in prior studies of sling surgery.[11,12] We used patient-reported outcomes because clinicians' assessments have often been shown to underestimate the degree of symptom-related distress perceived by women.[30,31] In our study, both subjective and objective outcomes in the surgery group were superior to those in the physiotherapy group.

The frequency of improvement in the surgery group (90.8%) was slightly higher than that reported in the literature (68 to 87%).[20-23,32-34] Heterogeneity in the study design, patient population, interventions, and outcome measures may account for this difference.[11] The improvement rate (64.4%) we observed in the physiotherapy group, which included women who crossed over to surgery, was higher than the rates in two other physiotherapy studies, which did not allow crossover (33% and 43%).[35,36] Our high crossover rate is the most likely explanation; the frequency of improvement among women who did not cross over to surgery (31.7%) is similar to the frequencies in the other studies.

In contrast to the findings in another prior study,[5] the rate of subjective cure among women in the physiotherapy group in our study was lower than the rate of objective cure (15.9% vs. 44.0%). It is possible that women who underwent physiotherapy were able to control their pelvic-floor muscles during the clinical provocative cough test yet still had stress urinary incontinence in everyday life in response to unexpected events.

In summary, the results of our trial show that women with moderate-to-severe stress urinary incontinence have significantly better subjective and objective outcomes at 12 months after surgery than after physiotherapy. Our findings suggest that women with this condition should be counseled regarding both pelvic-floor muscle training and midurethral-sling surgery as initial treatment options. Information on expected outcomes with both interventions, as well as on the potential, albeit infrequent, complications of surgery, will allow for individualized decision making by each woman and her health care provider.

Supported by a grant from ZonMw, the Netherlands Organization for Health Research and Development (80-82310-98-08203).

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

REFERENCES

1. Novara G, Artibani W, Barber MD, et al. Updated systematic review and meta-analysis of the comparative data on colposuspensions, pubovaginal slings, and midurethral tapes in the surgical treatment of female stress urinary incontinence. Eur Urol 2010;58:218-38.
2. van der Vaart CH, de Leeuw JRJ, Roovers JPWR, Heintz APM. The effect of urinary incontinence and overactive bladder symptoms on quality of life in young women. BJU Int 2002;90:544-9.
3. Coyne KS, Zhou Z, Thompson C, Versi E. The impact on health-related quality of life of stress, urge and mixed urinary incontinence. BJU Int 2003;92:731-5.
4. Haylen BT, de Ridder D, Freeman RM, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. Neurourol Urodyn 2010;29:4-20.
5. Dumoulin C, Hay-Smith J. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. Cochrane Database Syst Rev 2010;1:CD005654.
6. Imamura M, Abrams P, Bain C, et al. Systematic review and economic modelling of the effectiveness and cost-effectiveness of non-surgical treatments for women with stress urinary incontinence. Health Technol Assess 2010;14:1-188, iii-iv.
7. Cammu H, Van Nylen M, Blockeel C, Kaufman L, Amy J-J. Who will benefit from pelvic floor muscle training for stress urinary incontinence? Am J Obstet Gynecol 2004;191:1152-7.
8. Lamers BHC, van der Vaart CH. Medium-term efficacy of pelvic floor muscle training for female urinary incontinence in daily practice. Int Urogynecol J Pelvic Floor Dysfunct 2007;18:301-7.
9. Bø K, Kvarstein B, Nygaard I. Lower urinary tract symptoms and pelvic floor muscle exercise adherence after 15 years. Obstet Gynecol 2005;105:999-1005.
10. Ulmsten U, Henriksson L, Johnson P, Varhos G. An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 1996;7:81-5.
11. Ogah J, Cody JD, Rogerson L. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev 2009;4:CD006375.
12. Latthe PM, Singh P, Foon R, Toozs-Hobson P. Two routes of transobturator tape procedures in stress urinary incontinence: a meta-analysis with direct and indirect comparison of randomized trials. BJU Int 2010;106:68-76.
13. Labrie J, van der Graaf Y, Buskens E, Tiersma SE, van der Vaart HC. Protocol for Physiotherapy Or TVT Randomised Efficacy Trial (PORTRET): a multicentre randomised controlled trial to assess the cost-effectiveness of the tension free vaginal tape versus pelvic floor muscle training in women with symptomatic moderate to severe stress urinary incontinence. BMC Womens Health 2009;9:24.
14. Sandvik H, Hunskaar S, Seim A, Hermstad R, Vanvik A, Bratt H. Validation of severity index in female urinary incontinence and its implementation in an epidemiological survey. J Epidemiol Community Health 1993;47:497-9.
15. Nager CW, Brubaker L, Litman HJ, et al. A randomized trial of urodynamic testing before stress-incontinence surgery. N Engl J Med 2012;366:1987-97.
16. de Leval J. Novel surgical technique for the treatment of female stress urinary incontinence: transobturator vaginal tape inside-out. Eur Urol 2003;44:724-30.
17. Berghmans L, Bernards A, Bluyssen A, et al. KNGF-richtlijn Stress Urine-Incontinentie. Ned Tijdschr Fysiother 2003;115: Suppl 1:1-24. (In Dutch.)
18. Miller JM, Perucchini D, Carchidi LT, DeLancey JO, Ashton-Miller J. Pelvic floor muscle contraction during a cough and decreased vesical neck mobility. Obstet Gynecol 2001;97:255-60.
19. Yalcin I, Bump RC. Validation of two global impression questionnaires for incontinence. Am J Obstet Gynecol 2003; 189:98-101.
20. Padmanabhan P, Nitti VW. Female stress urinary incontinence: how do patient and physician perspectives correlate in assessment of outcomes? Curr Opin Urol 2006;16:212-8.
21. Biggs GY, Ballert KN, Rosenblum N, Nitti V. Patient-reported outcomes for tension-free vaginal tape-obturator in women treated with a previous anti-incontinence procedure. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:331-5.
22. Ballert KN, Rose AE, Biggs GY, Rosenblum N, Nitti VW. Outcomes of patients lost to followup after mid urethral

synthetic slings — successes or failures? J Urol 2010;183:1455-8.
23. Abdel-Fattah M, Ramsay I, Pringle S, et al. Randomised prospective single-blinded study comparing 'inside-out' versus 'outside-in' transobturator tapes in the management of urodynamic stress incontinence: 1-year outcomes from the E-TOT study. BJOG 2010;117:870-8.
24. Shumaker SA, Wyman JF, Uebersax JS, McClish D, Fantl JA. Health-related quality of life measures for women with urinary incontinence: the Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Qual Life Res 1994;3:291-306.
25. van der Vaart CH, de Leeuw JRJ, Roovers JPWR, Heintz AP. Measuring health-related quality of life in women with urogenital dysfunction: the Urogenital Distress Inventory and Incontinence Impact Questionnaire revisited. Neurourol Urodyn 2003;22:97-104.
26. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ 2009;338:b2393.
27. Newcombe RG. Interval estimation for the difference between independent proportions: comparison of eleven methods. Stat Med 1998;17:873-90. [Erratum, Stat Med 1999;18:1293.]
28. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale, NJ: Lawence Erlbaum, 1988.
29. Dumoulin C, Glazener C, Jenkinson D. Determining the optimal pelvic floor muscle training regimen for women with stress urinary incontinence. Neurourol Urodyn 2011;30:746-53.
30. Staskin DR, Kelleher C, Avery K, et al. Patient-reported outcome assessment. In: Abrams P, Cardozo L, Khoury S, Wein A, eds. Incontinence. 4th ed. Paris: Health Publication, 2009:363-412.
31. Black NA, Downs SH. The effectiveness of surgery for stress incontinence in women: a systematic review. Br J Urol 1996;78:497-510.
32. 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 Pelvic Floor Dysfunct 2008;19:1043-7.
33. Foglia G, Mistrangelo E, Lijoi D, Alessandri F, Ragni N. Transfascial vaginal tape (TFT): a simple, safe and cost-effective procedure for stress urinary incontinence: a preliminary study. Arch Gynecol Obstet 2007;276:59-63.
34. Jelovsek JE, Barber MD, Karram MM, Walters MD, Paraiso MFR. Randomised trial of laparoscopic Burch colposuspension versus tension-free vaginal tape: long-term follow up. BJOG 2008;115:219-25.
35. Richter HE, Burgio KL, Brubaker L, et al. Continence pessary compared with behavioral therapy or combined therapy for stress incontinence: a randomized controlled trial. Obstet Gynecol 2010;115:609-17.
36. Tannenbaum C, Brouillette J, Corcos J. Rating improvements in urinary incontinence: do patients and their physicians agree? Age Ageing 2008;37:379-83.