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2022-09-01

Itkonen Freitas , A-M , Isaksson , C , Rahkola-Soisalo , P , Tulokas , S , Mentula , M & Mikkola , T S 2022 , ' Tension-Free Vaginal Tape and Polyacrylamide Hydrogel Injection for Primary Stress Urinary Incontinence : 3-Year Followup from a Randomized Clinical Trial ' , The Journal of urology , vol. 208 , no. 3 , pp. 658-665 . <https://doi.org/10.1097/JU.0000000000002720>

<http://hdl.handle.net/10138/352328>

<https://doi.org/10.1097/JU.0000000000002720>

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Full-length article available at [auajournals.org/10.1097/JU.0000000000002720](https://doi.org/10.1097/JU.0000000000002720).

Study Need and Importance: Retropubic tension-free vaginal tape (TVT) has been the gold standard treatment for female stress urinary incontinence (SUI). Concerns have been raised about the long-term complications associated with mid urethral mesh slings, and medical authorities in some countries have published warnings and even suspended their use. Transurethral injection of polyacrylamide hydrogel (PAHG) is a minimally invasive alternative; however, the long-term patient satisfaction, safety and efficacy of this treatment in primary SUI are undefined.

What We Found: In this randomized noninferiority trial with 223 randomized patients at 3-year followup the satisfaction score (visual analogue scale 0–100) median was 98.5 in the TVT group and 90.0 in the PAHG group, whereas a score ≥ 80 was reached in 95% and 68%, respectively (see Figure). Thus, PAHG did not meet the noninferiority criteria set in our study. Within the 3-year followup period, any peri- or postoperative complication before crossover between the groups was detected in 44% of women in the TVT group and 24% of women in the PAHG group.

Limitations: According to our normal clinical practice, we did not perform invasive urodynamics in all women after detailed office evaluation for SUI. Although our data cannot be fully generalized to other mid urethral slings or bulking agents, we studied TVT, which is the gold standard for SUI, and PAHG, being currently the most commonly used bulking agent in Europe.

Interpretations for Patient Care: In midterm followup, PAHG did not reach in patient satisfaction

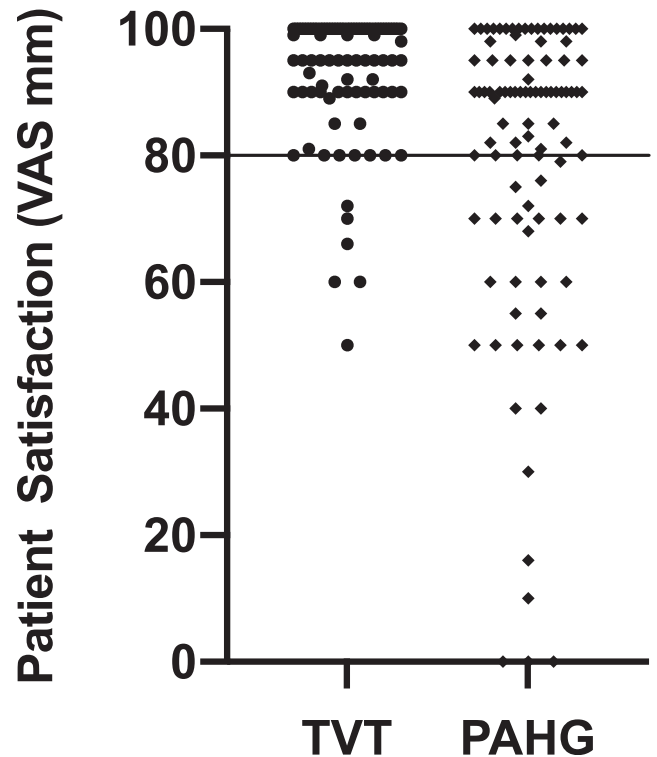



Figure. Patient satisfaction on ITT analysis 3 years after TVT or PAHG treatment.

the noninferiority set in our study. However, since most PAHG-treated women considered themselves cured or improved and the vast majority of women were satisfied without the need for further invasive treatment, PAHG can be offered as a safe and durable alternative treatment for women with SUI.

Tension-Free Vaginal Tape and Polyacrylamide Hydrogel Injection for Primary Stress Urinary Incontinence: 3-Year Followup from a Randomized Clinical Trial

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Purpose: We sought to determine whether polyacrylamide hydrogel (PAHG) is noninferior to tension-free vaginal tape (TVT) in the treatment of women with primary stress urinary incontinence (SUI).

Materials and Methods: In this noninferiority trial, 223 women eligible for operative SUI treatment were randomized for TVT (110) or PAHG (113). Primary outcome was patient satisfaction and the noninferiority margin for the difference was 20%. Secondary outcomes were effectiveness and complications.

Results: At 3 years, 188 (84.3%) women attended the followup. The satisfaction score (visual analogue scale 0–100) median was 98.5 (IQR 90–100) in the TVT group and 90.0 (IQR 70–100) in the PAHG group, whereas a score ≥ 80 was reached in 87 (94.6%) and 65 (67.7%), respectively (difference 26.9%, 95% CI 16.7% to 36.8%). Thus, PAHG did not meet the noninferiority criteria set in our study. The cough stress test was negative in 88 (95.7%) of TVT patients vs 75 (78.1%) of PAHG patients (difference 17.5%, 95% CI 8.6% to 26.9%). Any peri- or postoperative complication before crossover between the groups was detected in 40 (43.5%) women in the TVT group and 23 (24.0%) women in the PAHG group (difference 19.5%, 95% CI 6.8% to 31.4%).

Conclusions: In midterm followup, PAHG did not reach in patient satisfaction the noninferiority set in our study. Furthermore, mid urethral TVT slings show better subjective and objective cure rates than PAHG. However, complications were more often associated with TVT. Since the majority of PAHG treated women were also cured or improved, primary SUI women can be offered PAHG as a safe and durable alternative treatment.

Abbreviations and Acronyms

ITT = intention-to-treat
PAHG = polyacrylamide hydrogel
SUI = stress urinary incontinence
TVT = tension-free vaginal tape
VAS = visual analogue scale

Key Words: suburethral slings, polyacrylamide gels, surgical mesh

Submitted January 21, 2022; accepted April 7, 2022; published August 9, 2022.

This study was funded by a Helsinki University Hospital research grant and an unrestricted research grant from Contura. The funders of the study had no influence in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Support: A-MIF reports grants from the Finnish Society of Gynecological Surgery, Finnish Medical Foundation and Helsinki University Hospital during the conduct of the study. PR-S reports grants from the Finnish Medical Foundation during the conduct of the study. ST reports grants from the Finnish Society of Gynecological Surgery and Helsinki University during the conduct of the study. MM reports grants from the Finnish Cultural Foundation during the conduct of the study.

Conflict of Interest: TSM reports personal lecture fees from Astellas and Mylan outside the submitted work. PR-S reports payment of travel expenses by Intuitive. The remaining Authors have no conflicts of interest to disclose.

Study received Institutional Ethics Committee approval (IRB no. 19/13/03/03/2015).

Trial Registration: ClinicalTrials.gov, number NCT02538991 (<https://www.clinicaltrials.gov/ct2/show/NCT02538991?cond=bulkamid&rank=1>).

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STRESS urinary incontinence (SUI), defined as involuntary leakage on exertion or on sneezing or coughing, is a common and distressing symptom affecting 1 of 3 adult females.¹ Pelvic floor muscle training is the first-line treatment for SUI,² and if this fails, mid urethral sling surgery with retropubic tension-free vaginal tape (TVT) has been the most common surgical option worldwide.³ While the efficacy of TVT is as high as 90%, the safety of mesh implants for SUI has come under scrutiny due to severe complications, and there remains uncertainty on the long-term safety profile of mid urethral slings.³ Thus, medical authorities in some countries have published statements and warnings about the use of mid urethral slings, and in England a national “pause” was announced for mesh slings in July 2018 that continues to date.^{4,5}

Bulking agents are used for SUI treatment to create an artificial mass in the urethral submucosa and improve urethral coaptation and restore continence.^{6,7} Although the efficacy of bulking is traditionally considered to decrease over time, bulking is becoming a popular choice for patients seeking treatment for SUI.⁸ Transurethral polyacrylamide hydrogel (PAHG, Bulkamid®) is a bulking agent that has been used for more than 10 years to treat SUI in women showing high short-term subjective success rates.^{9–11} However, the long-term patient satisfaction, safety and efficacy of this treatment in primary SUI are undefined.

We report here midterm data from a randomized prospective trial comparing TVT and PAHG treatments in women with primary SUI. The aim of this study was to assess the noninferiority of PAHG compared to TVT measured by patient satisfaction (visual analogue scale [VAS] 0–100) in treatment of SUI. Secondary outcomes were subjective and objective efficacy of the treatment and complications.

MATERIALS AND METHODS

Study Design

We conducted at Helsinki University Hospital an investigator-led, prospective, randomized, controlled, parallel-group, non-inferiority trial comparing TVT and PAHG for primary SUI. The study was approved by the Helsinki University Hospital Ethics Committee (IRB no. 19/13/03/03/2015), and patients gave written informed consent prior to enrollment.

Participants and Intervention

We recruited primary SUI patients referred from primary health care and eligible for TVT operation between September 28, 2015 and March 1, 2017, as described before.¹⁰

All procedures were done in an outpatient setting. As a mid urethral sling TVT (TVT-Exact®, Ethicon, Somerville, New Jersey) was used under local anesthesia (70–100 ml 0.25% prilocaine with epinephrine) as originally described.¹² Also, PAHG injections (Bulkamid,

Contura, Denmark) were performed under local anesthesia using periurethral lidocaine (10 ml) injections. Hydrogel was injected under endoscopic control at 1.5 cm from the vesicourethral junction in locations “10, 2, 5 and 7 o'clock.” Both TVT and PAHG patients were discharged after successful micturition and post-void residual <200 ml. Nine urogynecologists with strong background in SUI surgery performed TVT operations, and 2 urogynecologists did PAHG injections.

The study nurse called the patients 1 month after the procedure. As a part of the protocol, after the initial PAHG treatment we offered 1 additional PAHG injection (top up) that was carried out at the 3-month visit for patients describing persisting SUI symptoms. Followup visits performed by a doctor other than the one who had done the surgery took place at 3 months, 1 year and 3 years, and patients with persisting SUI and not satisfied with the given treatment were offered the option to choose an alternative treatment (TVT or PAHG). Patients were, however, encouraged to contact the study nurse at any time if needed.

Outcomes

The primary noninferiority outcome was patient satisfaction with treatment ≥ 80 as measured by a VAS from 0 (extremely unsatisfied) to 100 (extremely satisfied) at followup visits. Secondary outcome measures were effectiveness in reducing urinary leakage and complications. We measured subjective cure with a 5-point Likert scale (symptoms cured, improved, no change, cannot tell or worsened), while a negative cough stress test with a bladder volume of 250–300 ml in a semilithotomy position and a pad stress test were used for objective cure.¹³ Complications were grouped as perioperative, early postoperative (<3 months) and later postoperative (>3 months to 3 years). We also classified complications using the Clavien-Dindo grading system.¹⁴ *De novo* urge was defined as the need for anticholinergic or beta-3 agonist treatment.

Statistical Analyses

All group comparisons are presented with 2-sided 95% confidence intervals using the Newcombe method. In the study protocol calculating 1-sided confidence intervals were planned. However, during the reporting phase it was decided to use 2-sided CIs to help clinical interpretation of the results.

As primary analysis the data are presented on an intention-to-treat (ITT) basis where the results are shown according to the assigned treatment (Fig. 1). Results were based on observed outcomes, and all patients who attended the 3-year followup visit were analyzed for results and complications (188). As a secondary analysis we analyzed primary outcome and efficacy results per protocol (treatment received) excluding women who had received other than the originally randomized treatment. Complications were calculated as before and after any crossover from the originally randomized treatment to the other, aiming to accurately relate the complication with the treatment.

All statistical reporting were calculated with SPSS® Statistics for Windows®, version 24.0 (SPSS Inc., Chicago,

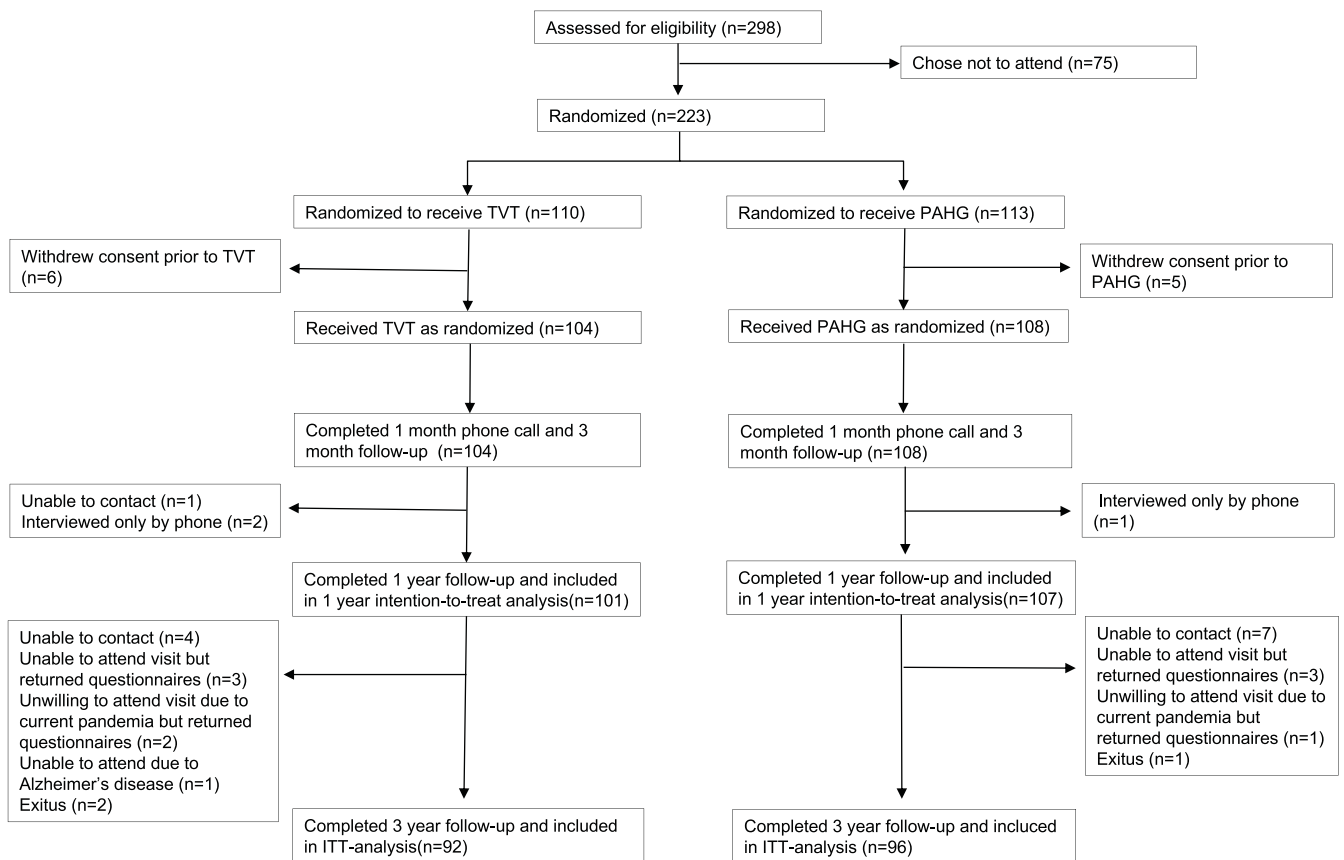


Figure 1. Trial profile.

Illinois). There were no interim analyses planned or carried out.

Sample Size

We estimated that patient satisfaction with the treatment result of ≥ 80 on a VAS from 0 to 100 was a good outcome. The sample size was calculated to test 2 portions for noninferiority, setting the patient satisfaction with the treatment 80% in the TVT group and 75% in the PAHG group based on earlier studies, ie assuming 5% unit predominance for TVT group.^{15–17} The significance level was set at 5%, power at 80% and noninferiority limit (threshold) at 20%. Altogether, 192 patients (96 per group) were required. A 10% dropout rate was assumed, and thus 212 women were planned to be randomized (1:1) for the study. Due to simultaneous recruitment by several doctors at the outpatient clinic, 223 patients were randomized before the study was closed.

RESULTS

A total of 223 women were randomized to the study, and 212 received treatment as randomized (Fig. 1). At 3-year followup 24 women were lost, leaving 188 women (TVT 92 and PAHG 96) for the ITT analysis (Fig. 1). In total 3 women in the TVT group and 30 women in the PAHG group crossed over, leaving 155 women (TVT 89 and PAHG 66) for the per-protocol (treatment received) analysis. In the TVT group 2

women crossed over to PAHG before and 1 after the 1-year followup. In the PAHG group 16 women had received TVT before and 14 after the 1-year followup.

Baseline characteristics of the women did not differ between the groups (Table 1). At 3 years, in the TVT group 3 women (3.3%) had received PAHG after TVT, whereas no woman received a second TVT treatment. In the PAHG group 31 (32.3%) women had received only 1 PAHG injection and 35 (36.5%) women had received 2 PAHG injections, 15 (15.6%) women had received TVT after 1 PAHG injection and 15 (15.6%) women had received TVT after 2 PAHG injections.

Satisfaction median was 98.5 (IQR 90–100) in the TVT group and 90.0 (IQR 70–100) in the PAHG group at 3 years. In the TVT group 87 (94.6%) women and in the PAHG group 65 (67.7%) women scored patient satisfaction VAS ≥ 80 (difference 26.9%, 95% CI 16.7% to 36.8%; Fig. 2). Thus, PAHG did not meet the noninferiority criteria set in our study. More women in the TVT group than PAHG group would come again for the treatment, at 88 (95.7%) vs 78 (81.3%; difference 14.4%, 95% CI 5.9% to 23.4%) or recommend it to a friend, at 91 (98.9%) vs 81 (84.4%; difference 14.5%, 95% CI 7.4% to 23.0%). Subjective and objective cure rates are presented in Table 2.

Table 1. Demographics of the 212 women undergoing TVT or PAHG treatment

	TVT Group		PAHG Group	
No. pts	104		108	
Mean±SD yrs age (range)	50.4±10.4	(32.0–78.0)	51.5±11.0	(31.0–80.0)
Mean±SD kg/m ² BMI (range)	24.5±3.5	(16.1–34.9)	24.8±3.6	(18.9–34.2)
No. socioeconomic status (%):				
White- and blue-collar workers	85	(81.7)	87	(80.5)
Others	19	(18.3)	21	(19.5)
Parity/delivery:				
Mean±SD (range)	2.1±1.0	(0–5)	2.1±0.9	(0–6)
No. 0 (%)	7	(6.7)	4	(3.7)
No. vaginal delivery (%)	93	(89.4)	101	(93.5)
No. cesarean section only (%)	4	(3.8)	3	(2.8)
No. incontinence duration (%):				
>1 and <2 yrs	1	(1.0)	4	(3.7)
2–5 yrs	64	(61.5)	65	(60.2)
>5 yrs	39	(37.5)	39	(36.1)
Mean±SD VAS distress from incontinence (range)*	8.0±1.4	(4–10)	8.1±1.4	(4–10)

ITT data. BMI, body mass index.

*One in PAHG group missing data.

In per-protocol (treatment received) analysis satisfaction median was 99.0 (IQR 90–100) in the TVT group and 85.0 (IQR 69.5–90) in the PAHG group, and 89 (100%) and 56 (84.8%; difference 15.2%, 95% CI 7.7% to 25.7%) considered themselves subjectively cured or improved, respectively. Objective cure measured by negative cough stress and pad test was reached in 74 (83.1%) women in the TVT group and 22 (33.3%) women in the PAHG group (difference 49.8%, 95% CI 34.7% to 61.8%).

Within the 3-year followup period any peri- or postoperative complication was detected in 40 (43.5%) women in the TVT group and 23 (24.0%) women in the PAHG group before crossover (difference 19.5%, 95% CI 6.8% to 31.4%). Complications were detected in the TVT group vs PAHG group perioperatively in 18 (17.3%) vs 2 (1.9%) women, <3 months postoperatively in 13 (12.5%) vs 9 (8.3%) women and >3 months to 3 years 20 (21.7%) vs 14 (14.6%) women, respectively (Table 3). Two or more complications occurred in 10 (10.9%) women in the TVT group and 2 (2.1%) women in the PAHG group (difference 8.8%, 95% CI 1.7% to 16.9%).

Before any crossover, 6 (6.5%) women in the TVT group and 1 woman (1.0%) in the PAHG group (difference 5.5%, 95% CI –0.3% to 12.5%) had reported pain at the tape/implantation site within the 3-year followup period. The numerical rating scale (0–10) median for the patients reporting pain at 3 years was 3 (IQR 2–4). In the TVT group 4 women (4.3%) and in the PAHG group 1 woman (1.0%) reported dysuria before crossover (difference 3.3%, 95% CI –0.2% to 9.7%). One woman requested removal of PAHG due to dysuria and implantation site pain.

After crossover from TVT to PAHG (3), 1 woman had postoperative retention. After crossover from PAHG to TVT (30), 12 women had complications at 3-year followup, including 2 reoperations (hematoma

and loosening of tape), 1 erosion, 1 tape site pain, 3 women with dysuria, 2 women with retention and 3 women with *de novo* urgency.

The Clavien-Dindo classification showed significantly more grade I complications with TVT (11, 12.0%) compared to PAHG (1, 1.0%; difference 10.9%, 95% CI 4.0% to 19.2%), but not in the more severe complications (Table 3). However, complications requiring reoperations occurred in 7 women after TVT surgery, whereas 2 PAHG patients had a complication-related reoperation.

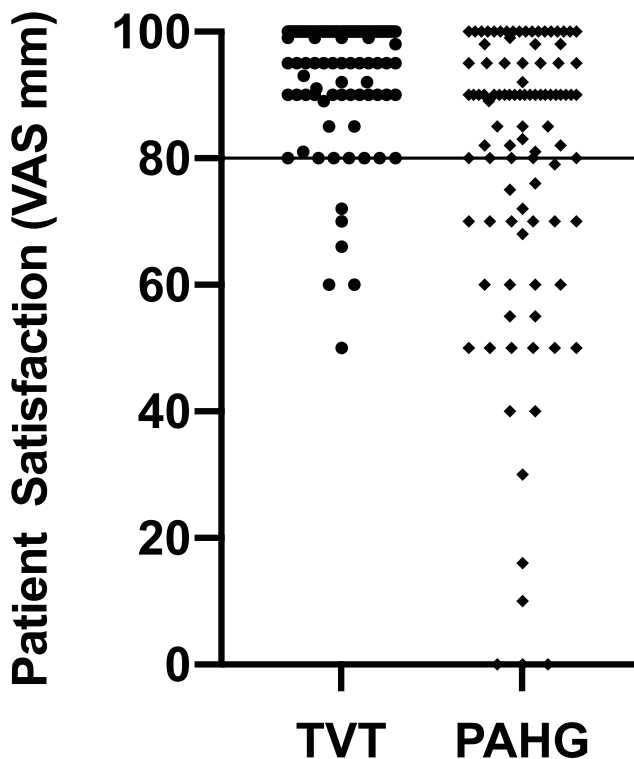
**Figure 2.** Patient satisfaction on ITT analysis 3 years after TVT or PAHG treatment.

Table 2. Subjective and objective cure from ITT analysis at 3 years following TVT or PAHG treatments

	No. TVT Group (%)	No. PAHG Group (%)	% Difference (95% CI)	
Pts	92	96		
Subjective cure:				
Cured	55 (59.8)	24 (25.0)	34.8	(20.8–46.9)
Improved	37 (40.2)	61 (63.5)	–23.3	(–36.3–9.0)
Cured or improved	92 (100)	85 (88.5)	11.5	(5.1–19.4)
Objective cure:				
Cough stress and pad test neg	76 (82.6)	47 (50.0)	33.7	(20.3–45.3)
Cough stress test neg	88 (95.7)	75 (78.1)	17.5	(8.0–27.2)
Pad test neg	76 (83.5)	53 (56.4)	27.4	(14.3–39.2)

DISCUSSION

In a randomized clinical trial, we show that at the 3-year followup VAS satisfaction median in both treatment groups was high, being 99 in the TVT group and 90 in the PAHG group. However, at the primary endpoint in our study, satisfaction VAS ≥ 80 was reached in 95% of the TVT group compared with 68% in the PAHG group, and thus TVT achieved a better outcome. On the other hand, complications were more often associated with TVT than with PAHG.

The long-term durability of the TVT-procedure has been documented consistently,^{18–20} and our current data further support this. Recently, concern has risen about potential long-term complications with mid urethral slings, such as pain, dysuria and mesh erosions.^{21,22} This has also affected new recommendations, eg NICE (National Institute for Health and Care Excellence) guidelines advise that

mid urethral slings should only be considered if alternative surgical procedures are not suitable.²³ Data from routine practice indicate that the risk of mid urethral sling removal for any reason was 2.7% at 5 years and 3.3% at 9 years.²⁴ Another study demonstrated a 2.9% rate of long-term sling-specific surgical intervention.¹⁹ In our study, tape extrusion/impaired healing occurred in 2.9% of women and erosion requiring reoperation in 3.3% of women, but none of the women had the sling removed.

The number of complications in our study was low with both treatments. Since crossover in the PAHG group was more common than in the TVT group, our focus was on complications after the initial treatment in order to accurately relate the complication with the treatment. Major complications such as reoperations were mainly associated with TVT. Furthermore, the difference in

Table 3. Complications before crossover

	No. TVT Group (%)	No. PAHG Group (%)	% Difference (95% CI)	
Pts	104	108		
Periop complications:				
Hematoma	6 (5.8)	0	5.8	(1.1–12.0)
Bladder perforation	7 (6.7)	0	6.7	(1.9–13.2)
Acute urinary retention	10 (9.6)	2 (1.9)	7.8	(1.4–15.1)
Complications occurring <3 mos postop:				
Vaginal tape extrusion	3 (2.9)	0	2.9	(–1.0–8.1)
Reop due to hematoma	1 (1.0)	0	1.0	(–2.6–5.2)
Reop due to retention	3 (2.9)	0	2.9	(–1.0–8.1)
Urinary tract infections	7 (6.7)	9 (8.3)	–1.6	(–9.2–6.0)
Complications occurring >3 mos–3 yrs postop:*				
Vaginal tape erosion	3 (3.3)	0	3.3	(–1.1–9.2)
Reop due to erosion	3 (3.3)	0	3.3	(–1.1–9.2)
Reop due to pain	0	1 (1.0)	–1.0	(–5.7–3.1)
Reop due to fibrotic resistance	0	1 (1.0)	–1.0	(–5.7–3.1)
Tape/implantation site pain	6 (6.5)	1 (1.0)	5.5	(–0.3–12.5)
Dysuria	4 (4.3)	1 (1.0)	3.3	(–2.0–9.7)
Post-void residual >150 ml	1 (1.1)	0	1.1	(–2.9–5.9)
De novo urgency	9 (9.8)	12 (12.5)	–2.7	(–12.0–6.6)
Clavien-Dindo distribution of complications at 3 yrs:*				
None	61 (66.3)	78 (81.3)	–14.9	(–27.0–2.4)
Grade I	11 (12.0)	1 (1.0)	10.9	(4.0–19.2)
Grade II	13 (14.1)	15 (15.6)	–1.5	(–11.8–8.9)
Grade III†	6 (6.5)	2 (2.1)	4.4	(–1.8–11.6)
Grade IV‡	1 (1.1)	0	1.1	(–2.9–5.9)

*Ninety-two patients in TVT group, 96 in PAHG group.

† Acute urinary retention with loosening and ultimately cutting the tape (1 patient), blood transfusion and laparotomy due to hematoma (1), acute urinary retention with loosening the tape using local anesthesia (2), repair of tape extrusion using local anesthesia repeatedly (1), repair of tape erosion (1), after PAHG attempt to aspirate fibrotic resistance at bladder neck using local anesthesia (1), removal of PAHG due to persisting pain in general anesthesia (1).

‡ Ischemic heart symptoms postoperatively possibly related to local anesthesia.

complications between the treatments is also shown by our finding that patients having more than 1 perioperative or postoperative complication were detected more likely after TVT (10) than PAHG (2). The typical TVT-related complications, such as pain, dysuria, and mesh erosions, were also seen in our data, with similar rates as in previous studies.²⁵

Pain has become one of the most feared complications after mesh surgery.²⁵ In our study, within the 3-year followup, 6 patients reported pain after TVT, but none of these patients requested tape removal. One PAHG patient reported pelvic pain and dysuria 20 months after the primary injection and requested PAHG removal that did not affect the pain. She had a history of pelvic pain after delivery, and thus explicit association of the pain and dysuria to PAHG remains uncertain. The other PAHG-related complication requiring intervention (aspiration using local anesthesia) was a vaginal fibrotic resistance below the urethra in an asymptomatic woman. Although the exact etiology is unknown, it could be a PAHG injection-related reaction due to, for example, hematoma and/or local infection. It should be noted that several previously used bulking agents have been associated with more severe complications resulting in the withdrawal of these treatments from the market.²⁶ Our study supports the existing data that with PAHG, complications are mostly mild and/or transient.²⁶

De novo urgency, defined as the need for medication, did not differ between the groups and occurred at a similar rate as seen in previous studies with TVT.^{3,20} The finding that *de novo* urgency was detected after PAHG in a similar manner supports the general mechanism of obstruction for *de novo* urgency. Since urodynamics were not routinely performed, underlying urgency cannot be ruled out.²⁷

Some previous studies with short-term followup have suggested that the efficacy of PAHG in SUI treatment might be transient, thus resulting in inadequate cure and subjective satisfaction.²⁸ In a 12-month randomized clinical trial where PAHG and collagen gel were compared, 77% of the women with PAHG considered themselves cured or improved, despite the fact that only 24% were objectively cured.⁹ In our trial we detected a similar pattern as in the North American study⁹ since although only 54% of the women were objectively cured, 92% considered themselves cured or improved.¹⁰ Importantly, after 3 years this high satisfaction rate was sustained with PAHG, as 89% of the women still considered themselves cured or improved compared to 92% at 1 year, while 50% were objectively cured compared to 54% at 1 year. Thus, in SUI treatment high subjective satisfaction

does not seem to always require complete objective cure. When women were asked about attitudes and expectations with different treatments, 57% preferred a minor procedure with low risk of complications, and they were prepared to accept a lower success rate.²⁹ Thus, health care providers should share both objective and subjective data of the different surgical interventions in order for women to make informed decisions based on their personal goals and expectations.

The main strengths of our trial are comparison of the gold standard surgical SUI treatment with a minimally invasive SUI treatment, and the midterm followup with both subjective and objective outcomes. Furthermore, our recruited participants represent a nonselected population of women considering surgical treatment for primary SUI. In our study, the dropout and loss to followup rates were low. Thus, we provide robust data to inform both health care providers and women considering invasive SUI treatment.

Our study also has limitations. Since our patients were primary SUI patients, we did not perform invasive urodynamics in all women. This is also our normal clinical practice as most guidelines follow the strong evidence that invasive urodynamics do not provide any further benefit after detailed office evaluation in primary SUI patients.³⁰ Neither did we segregate women based on urethral hypermobility or intrinsic sphincter deficiency since each is often present to some extent in typical SUI patients.⁶ Furthermore, we did not include women with clinically significant pelvic organ prolapse or obese women since concomitant prolapse surgery as well as severe obesity could potentially affect the SUI treatment results. Our study was unblinded to the treatment; however, blinding is practically impossible as the treatments were performed with local anesthesia. Although our data cannot be fully generalized to all other mid urethral slings or bulking agents, we studied TVT, which is the gold standard for SUI, and PAHG, being currently the most commonly used bulking agent in Europe. And finally, the study was carried out in a university hospital with urogynecologists who have a strong experience in surgical SUI treatment. This may partially explain our high success rates with both treatments that may not be fully comparable to results at smaller clinical units. However, we believe that with adequate training and similar procedure volumes, comparable results are achievable.

CONCLUSIONS

In this randomized clinical trial with midterm followup, PAHG did not reach the noninferiority criteria in patient satisfaction. However, most

PAHG-treated women considered themselves cured or improved, and most importantly, the vast majority of women were satisfied without the need for further invasive treatment. Although overall complication rates were low in our trial, severe

complications were almost exclusively associated with TVT. These findings will help women make informed decisions based on their personal goals and expectations when considering invasive SUI treatment.

REFERENCES

- Lukacz ES, Santiago-Lastra Y, Albo ME et al: Urinary incontinence in women. *JAMA* 2017; **318**: 1592.
- Hagen S, McClurg D, Bugge C et al: Effectiveness and cost-effectiveness of basic versus biofeedback-mediated intensive pelvic floor muscle training for female stress or mixed urinary incontinence: protocol for the OPAL randomised trial. *BMJ Open* 2019; **9**: e024153.
- Imamura M, Hudson J, Wallace SA et al: Surgical interventions for women with stress urinary incontinence: systematic review and network meta-analysis of randomised controlled trials. *BMJ* 2019; **365**: l1842.
- Powis SMK: Vaginal mesh: high vigilance restriction period; Immediate action required, all cases should be postponed if its clinically safe to do so. Available at https://improvement.nhs.uk/documents/5122/MESH_letter_-_Extension_of_pause_on_the_use_of_vaginal_mesh_29_March_2019.pdf. Accessed September 19, 2018.
- U.S. Food and Drug Administration: Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse. 2011. Available at <https://www.fda.gov/downloads/medicaldevices/safety/alertsandnotices/ucm262760.pdf>. Accessed October 5, 2018.
- Kerr LA: Bulking agents in the treatment of stress urinary incontinence: history, outcomes, patient populations, and reimbursement profile. *Rev Urol, suppl.*, 2005; **7**: S3.
- Kuhn A, Stadlmayr W, Lengsfeld D et al: Where should bulking agents for female urodynamic stress incontinence be injected? *Int Urogynecol J Pelvic Floor Dysfunct* 2008; **19**: 817.
- Dwyer L, Weaver E, Rajai A et al: "Voice your choice": a study of women's choice of surgery for primary stress urinary incontinence. *Int Urogynecol J* 2020; **31**: 769.
- Sokol ER, Karram MM and Dmochowski R: Efficacy and safety of polyacrylamide hydrogel for the treatment of female stress incontinence: a randomized, prospective, multicenter North American study. *J Urol* 2014; **192**: 843.
- Itkonen Freitas A-M, Mentula M, Rahkola-Soisalo P et al: Tension-free vaginal tape surgery versus polyacrylamide hydrogel injection for primary stress urinary incontinence: a randomized clinical trial. *J Urol* 2020; **203**: 372.
- Kasi AD, Pergialiotis V, Perrea DN et al: Polyacrylamide hydrogel (Bulkamid®) for stress urinary incontinence in women: a systematic review of the literature. *Int Urogynecol J* 2016; **27**: 367.
- Ulmsten U, Henriksson L, Johnson P et al: An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct* 1996; **7**: 81.
- Horndalsveen Berild G and Kulseng-Hanssen S: Reproducibility of a cough and jump stress test for the evaluation of urinary incontinence. *Int Urogynecol J* 2012; **23**: 1449.
- Dindo D, Demartines N and Clavien P-A: Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205.
- Leone Roberti Maggiore U, Alessandri F, Medica M et al: Outpatient periurethral injections of polyacrylamide hydrogel for the treatment of female stress urinary incontinence: effectiveness and safety. *Arch Gynecol Obstet* 2013; **288**: 131.
- Heinonen P, Ala-Nissilä S, Rätty R et al: Objective cure rates and patient satisfaction after the transobturator tape procedure during 6.5-year follow-up. *J Minim Invasive Gynecol* 2013; **20**: 73.
- Wai CY, Curto TM, Zyczynski HM et al: Patient satisfaction after midurethral sling surgery for stress urinary incontinence. *Obstet Gynecol* 2013; **121**: 1009.
- Nilsson CG, Palva K, Aarnio R et al: Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. *Int Urogynecol J* 2013; **24**: 1265.
- Tulokas S, Rahkola-Soisalo P, Gissler M et al: Long-term re-procedure rate after mid-urethral slings for stress urinary incontinence. *Int Urogynecol J* 2020; **31**: 727.
- Zhang Y, Song X, Mao M et al: Tension-free vaginal tape for the treatment of stress urinary incontinence: a 13-year prospective follow-up. *J Minim Invasive Gynecol* 2019; **26**: 754.
- Scottish Government: The Scottish Independent Review of the Use, Safety and Efficacy of Transvaginal Mesh Implants in the Treatment of Stress Urinary Incontinence and Pelvic Organ Prolapse in Women: Final Report. Edinburgh; 2017. Available at www.gov.scot/Resource/0051/00515856.pdf.
- Department of Health and Social Care: Update on the Independent Medicines and Medical Devices Safety Review, 2018: Written Statement-HCWS841. London; 2018. Available at <https://questions-statements.parliament.uk/written-statements/detail/2018-07-10/HCWS841>.
- NICE: NICE Guideline Urinary Incontinence and Pelvic Organ Prolapse in Women: Management. 2019. Available at nice.org.uk/guidance/ng123.
- Guroi-Urganci I, Geary RS, Mamza JB et al: Long-term rate of mesh sling removal following midurethral mesh sling insertion among women with stress urinary incontinence. *JAMA* 2018; **320**: 1659.
- Blaivas JG, Purohit RS, Benedon MS et al: Safety considerations for synthetic sling surgery. *Nat Rev Urol* 2015; **12**: 481.
- Kocjancic E, Mourad S and Acar Ö: Complications of urethral bulking therapy for female stress urinary incontinence. *Neurourol Urodyn, suppl.*, 2019; **38**: S12.
- Pergialiotis V, Mudiaga Z, Perrea DN et al: De novo overactive bladder following midurethral sling procedures: a systematic review of the literature and meta-analysis. *Int Urogynecol J* 2017; **28**: 1631.
- Siddiqui ZA, Abboudi H, Crawford R et al: Intraurethral bulking agents for the management of female stress urinary incontinence: a systematic review. *Int Urogynecol J* 2017; **28**: 1275.
- Robinson D, Anders K, Cardozo L et al: What do women want? Interpretation of the concept of cure. *J Pelvic Med Surg* 2003; **9**: 273.
- Clement KD, Lapitan MCM, Omar MI et al: Urodynamic studies for management of urinary incontinence in children and adults: a short version Cochrane systematic review and meta-analysis. *Neurourol Urodyn* 2015; **34**: 407.

EDITORIAL COMMENTS

Synthetic mid urethral slings (MUS) have been the main female surgical procedures globally, with over 80% for the last 20 years.¹ The adverse publicity using synthetic mesh particularly with vaginal prolapse surgery has caused a decline in the use of synthetic MUS and stress incontinence (SI) surgery generally in many countries, so alternative options using native tissue sling options or urethral bulking agents such as transurethral polyacrylamide hydrogel (PAHG, Bulkamid®) will increase. The scientific literature on MUS has been extensive and continues to be positive with long-term followup of effectiveness and safety,² as has medical experience of clinicians worldwide.

This is an important randomized controlled trial comparing what has been the gold standard for the last 20 years against a possible new gold standard, injectable transurethral PAHG. This study does provide important data to enable us to counsel our patients regarding outcomes. Both procedures can be performed under local anesthesia and sedation as day surgery. Satisfaction with surgery was higher in the TVT group compared with the PAHG group, where only 1 in 3 were cured by 1 surgical intervention; complications were more often associated with TVT than with PAHG. There were 30 women who had a TVT after PAHG, and 12 women had complications at 3-year followup, including pain, reoperation and erosion.

Long-term outcome is the holy grail of SI surgery, for which TVT has a good record.² Bulking agents have generally been used in the elderly, those with recurrent SI and the medically infirm, and repeated injections have been necessary. What effect does repeated PAHG have on long-term urethral function and success of other SI operations? This is especially important in this middle-aged group of women (mean age 50 years) with primary SI. There are few long-term studies of any injectables, partly as numerous materials (collagen, fat, silicone) have been tried. In one randomized controlled trial the satisfaction success rates at 1 year were similar following fascial sling and Macroplastique®, but the objective success rate was significantly greater ($p < 0.001$) following the sling (81% vs 9%), but at 5 years the sling group reported better continence success (69% vs 21%).³

Longer followup will be needed to reassure women with primary SI that injectables are their best first option.

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REFERENCES

1. Haya N, Baessler K, Christmann-Schmid C et al: Prolapse and continence surgery in countries of the Organization for Economic Cooperation and Development in 2012. *Am J Obstet Gynecol* 2015; **212**: 755.
2. Karmakar D, Dwyer PL, Murray C et al: Long-term effectiveness and safety of open Burch colposuspension vs retropubic midurethral sling for stress urinary incontinence—results from a large comparative study. *Am J Obstet Gynecol* 2021; **224**: 593.
3. Maher CF, O'Reilly BA, Dwyer PL et al: Pubovaginal sling versus transurethral Macroplastique for stress urinary incontinence and intrinsic sphincter deficiency: a prospective randomized controlled trial. *BJOG* 2005; **112**: 797.

This is a 3-year followup study of a randomized controlled trial comparing tension-free vaginal tape (TVT) to polyacrylamide hydrogel (PAHG) for primary stress urinary incontinence (SUI) in women. This is an important topic to investigate as TVT continues to be controversial—it is the gold standard for SUI treatment in some countries, while other countries have modified patient access to mesh slings due severe complications seen in some patients.^{1,2} A recent U.S. study has highlighted the decreased use of mesh slings over the last several years, likely indicating that patients and providers in the U.S. may be interested in mesh alternatives.³

These data indicate the same pattern at 3 years as at 1 year, mainly confirming the superiority of

the TVT vs PAHG, with the important caveats that both groups reported a high satisfaction rate and a few patients in the sling group had severe complications sometimes requiring reoperation. Regrettably, a nonvalidated visual analogue scale was again used for their primary subjective outcome (patient satisfaction). This is an imprecise measure that can be influenced by many patient and clinical factors. Further, given the absence of a validated questionnaire, it makes it difficult to compare these data with the existing literature. However, a notable effort was made to produce 2 objective outcome measures (cough stress test, pad test). Unfortunately, the severity and type of SUI (specifically, urethral hypermobility

vs intrinsic sphincter deficiency) were not described in the original publication, which somewhat limits the generalizability of these data in clinical practice for patient treatment decision by SUI subtype.

Interestingly, although the numbers are small, the complication rate seems to be slightly higher in the group who underwent TVT after PAHG than in women who received TVT alone, which merits

further investigation. As this data set matures, it will be interesting to see how physicians incorporate this study's findings into their SUI management decision-making algorithms.

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REFERENCES

1. Joint Position Statement on Midurethral Slings for Stress Urinary Incontinence. *Female Pelvic Med Reconstr Surg* 2021; **27**: 707.
2. National Institute for Health and Care Excellence (NICE) Guideline: Urinary incontinence and pelvic organ prolapse in women: management. National Institute for Health and Care Excellence. April 2019. Available at <https://www.nice.org.uk/guidance/ng123>.
3. Chughtai B, Mao J and Matheny ME: Long-term safety with sling mesh implants for stress incontinence. *J Urol* 2021; **205**: 183.