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ORIGINAL ARTICLE

Periurethral injection with polyacrylamide after previous TVT surgery

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Abstract

Introduction and hypothesis The aim of this registry study was to assess the clinical utility of using periurethral bulking with polyacrylamide hydrogel in women with stress urinary incontinence (SUI) after previous midurethral sling surgery.

Methods The study period was 2007 through 2019. Using data from the Norwegian Female Incontinence Registry we included 57 women who had received Bulkamid® because of insufficient improvement or recurrent SUI after previous retropubic TVT surgery. The primary outcome was cure of SUI, and secondary outcomes were patient satisfaction, degree of leakage, change in urgency incontinence (UUI), free flow rate, postvoid residual volume, and complications. Descriptive statistics were used to characterize data and Wilcoxon signed-rank test to compare pre- and postoperative results for pairs, with level of significance at $p < 0.05$.

Results Pure SUI was seen in 19 (33.3%) while 38 (66.7%) had mixed incontinence. Postoperatively 72.9% had a negative stress test and 73.7% were satisfied with treatment. There was only 1 complication in 67 injections (1.5%). De novo UUI occurred in five patients, corresponding to 8.8% of the whole study group, but 26.3% among those with no preoperative UUI problems. Among the patients with preoperative UUI, 39.5% were cured of this problem and a further 36.8% were improved.

Conclusions The cure rate and satisfaction rate of periurethral bulking with polyacrylamide after previous MUS are favorable and complications are rare. There seems to be a risk of overactive bladder symptoms developing in women with no such symptoms preoperatively.

Keywords Female · Incontinence · Periurethral injection · Polyacrylamide · Surgery

Introduction

Mid-urethral-sling (MUS) has been the first-line surgical treatment for female stress urinary incontinence (SUI) since the 1990s. However, up to 20% of patients are not primarily cured or they later develop recurrent stress incontinence, and the best method for those women needing a new surgical procedure has not been established. The 2019 Cochrane report "*Interventions for treating recurrent stress urinary incontinence after failed minimally invasive synthetic midurethral tape surgery in women*" concluded that there was insufficient evidence to recommend any one of the various possible surgical treatment strategies available [1]. However, periurethral injection therapy has commonly been employed in this situation [2], but only four studies using injection therapy as a secondary procedure have so far been published. These are shown in Table 1. In our study we report the results of 57 women treated with periurethral injection with polyacrylamide hydrogel (Bulkamid®) who had previously undergone a TVT procedure in our department.

Materials and methods

In this registry study we included 57 women who had received Bulkamid® after previous retropubic TVT surgery because of insufficient improvement or recurrent SUI at the Vestfold Hospital Trust, Norway. The inclusion period was from January 2007 through December 2019 (13 years). During the study period 1756 women were operated on with TVT and 328 with injection of polyacrylamide. A total of 64 women had repeat incontinence surgery, 5 with a new TVT and 59 with injection of polyacrylamide. Of these 59 women 2 were lost to follow-up, leaving 57 available for analysis (Fig. 1). Using an application that extracted anonymous data from the hospital's local Norwegian Female Incontinence Registry

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Table 1 Published studies with bulking procedures as secondary treatment

Author [reference]	Patients (N)	MUI* (%)	Follow-up (months)	Cured (%)	Cured + improved (%)	De novo OAB** (%)	OAB** resolved (%)
Gaddi 2014 [3] [a]	67	–	≥ 12	61.2	79.1	–	–
Clark 2018 [4] [b]	17	71	10–40	–	70.6	–	–
Martan 2015 [5] [c]	34	17.6	29	11.8	41.2	–	–
Zivanovic 2017 [6] [d]	55	31.7	12	25.4	83.6	3.6	41.2

*MUI, mixed urinary incontinence

**OAB, overactive bladder

[a] Gaddi 2014 [3]: Comparison of midurethral slings and injection therapy after failed midurethral sling using Contigen, Coaptite, or Macroplastique. Polyacrylamide not used

[b] Clark 2018 [4]: Polyacrylamide after a great variety of failed primary incontinence procedures

[c] Martan 2015 [5]: Polyacrylamide after failed midurethral sling; 74% of subjects had also had another previous incontinence procedure

[d] Zivanovic 2017 [6]: Polyacrylamide after failed midurethral sling

database, we analyzed their subjective and objective results. There were no exclusion criteria except missing from postoperative follow-up. For ethical reasons we were only allowed to use anonymous data from the registry. The study was approved by The Norwegian Center for Research and the hospital's data protection officer. The Ethics Committee of Southeast Norway considered the study to represent quality assurance for treatment given and without need for formal committee approval. Prior to treatment all patients had given written consent for their data to be entered into the registry and used for research.

All procedures were performed by a urogynecologist under local or a short total i.v. anesthesia. The patients were given oral antibiotic prophylaxis (ciprofloxacin or trimethoprim-sulfamethoxazole tablets). Under endoscopic control three to four deposits of Bulkamid® were injected transurethrally into the submucosa near the middle of the urethra, aiming to just close the lumen. The bladder was then emptied. After successful voiding with PVR < 100 ml, they were discharged.

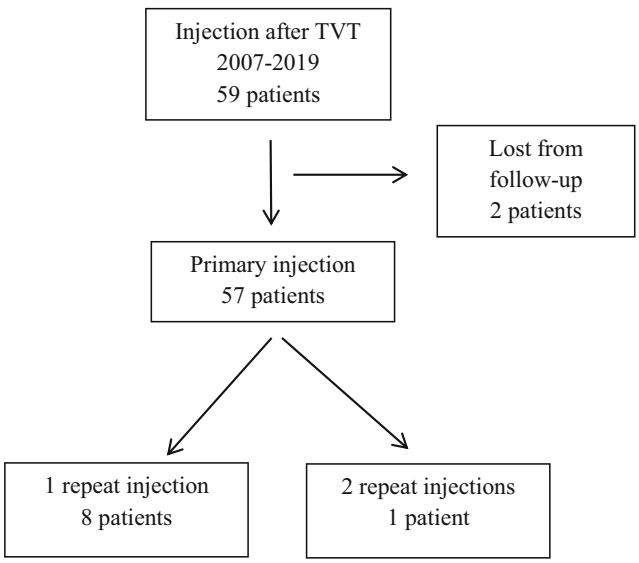

Fig. 1 Patients and injections

In Norway pre- and postoperative evaluation is standardized in women undergoing a surgical procedure for SUI, and reporting to the national Norwegian Female Incontinence Registry is compulsory. The hospital departments report pre- and postoperative patient-reported data as well as clinical and urodynamic data to the registry, including type of incontinence procedure and complications. Subjective data are collected using a validated disease-specific urinary incontinence questionnaire [7]. The pre- and postoperative evaluation includes a 24-h voiding diary and pad test, the questionnaire, a standardized stress test consisting of 20 jumping jacks and 3 forceful coughs with 300 ml bladder content, urinary free flow rate and postvoid residual volume. The stress test has been shown to be reproducible [8]. Urethral pressure measurement is done at the discretion of the individual department. From the questionnaire [7] the stress incontinence index score (0–12), urgency incontinence index score (0–8), and quality of life index score (0–16) are calculated to quantify the degree of symptom bother. A higher score signifies more bother and 0 indicates no bother. Clinical follow-up is after 6–12 months using the same evaluation. Postoperatively the patient also states her degree of satisfaction on a scale from 0 to 4 where 0 means very satisfied and 4 very dissatisfied. If the patient was not satisfied, another injection was offered.

The primary outcome was objective cure of SUI as evaluated by the stress test. Secondary outcomes were subjective cure rate, 24-h leakage, degree of satisfaction, reinjection rate, postvoid residuals, and changes in urgency incontinence (UUI). The effect of increasing age or BMI as well as low urethral closure pressure was also analyzed. Objective cure of SUI was defined as no leakage on the postoperative stress test while subjective cure of SUI was defined as postoperative SUI index score ≤ 2. Cure of UUI was defined as a postoperative index score of ≤ 2 in those with a preoperative score > 2,

while improvement in UUI was defined as a > 2 point reduction in the UUI index score. De novo UUI was defined as preoperative UUI score ≤ 2 and postoperative score > 2.

Statistics

Descriptive statistics were used to characterize data, which are presented as mean, median, range and standard deviation. Wilcoxon signed-rank test was used to compare pre- and postoperative results for pairs with level of significance at $p < 0.05$. Statistical analyses were performed using SPSS® Statistics, version 26.0.

Results

Patient characteristics are presented in Table 2. Pure stress incontinence was seen in 19 (33.3%) while 38 (66.7%) had mixed incontinence (MUI). Time since TVT was 5 months to 15 years (mean 5.4 years) with only ten patients earlier than 12 months. Mean follow-up time was 11.7 months (range 1–84, SD 11.7) post injection. Nine (15.8%) of the patients received more than one injection (Fig. 1) after a mean of 23.3 months, range 5–41 months. The mean volume injected was 1.2 ml at both primary and repeat injections (range 0.5–3.0 ml and 0.5–1.8 ml, respectively). Postoperative results are presented in Tables 3 and 4. All variables of clinical interest showed statistically highly significant improvement. The only complication in 67 injections was one case (1.5%) of transient urinary retention which resolved spontaneously after 1 week of intermittent self-catheterization. Objective cure of SUI was seen in 35/48 patients (72.9%), subjective cure in 13/57 (22.8%), while 42/57 (73.7%) were satisfied with their treatment result. Among the 38 patients with preoperative MUI, cure of UUI was seen in 15 (39.5%) while 14 (36.8%) experienced improvement. De novo UUI was diagnosed in five patients (8.8%) and eight (14.0%) with preexisting UUI experienced worsening of UUI. There was no effect of age over or under 50 or 60 years, BMI over or under 25, preoperative low urethral closure pressure (< 20 cm water), or time since the TVT operation (over or under 5 years).

Discussion

Not all patients are cured by an MUS procedure, and some require repeat surgical treatment. However, there is currently no consensus on the ideal surgical method for these women [1], but a repeat MUS or periurethral injection therapy is commonly used. Repeat MUS has relatively good results with success rates around 62–78% [9–12] and has fewer failures than injection therapy [3], but repeat MUS is a more invasive method with a higher risk of complications and is associated with a higher risk of postoperative OAB symptoms than primary MUS [9].

Urethral bulking as a primary procedure for SUI or stress dominant MUI has fair results, but is inferior to MUS [13–16], and about one third receive repeated injections [15, 17]. Urethral bulking as a secondary procedure after a previous MUS has not been well researched, and there are only four studies in the literature, reporting success rates from 41 to over 80% (Table 1). Bulking procedures have a lower risk of complications than a new MUS [15, 16] and can also address any intrinsic sphincter deficiency that might remain after the primary MUS has improved urethral hypermobility. Our department's routine has been to usually recommend this treatment first, before considering a new MUS to those with an indication for further surgical SUI treatment after a previous MUS.

In our study, 73.7% of the patients were satisfied, 72.9% had a negative postoperative stress test, all relevant clinical variables were statistically significantly improved (Tables 3 and 4), and there was only one complication, a case of self-limiting urinary retention.

Any SUI procedure may lead to overactive bladder (OAB) symptoms improving, being unchanged or developing de novo. After MUS more patients experience improvement than those who experience worsening or de novo UUI [18]. However, not much has been published on postoperative OAB after bulking procedures. In a study comparing retropubic TVT and periurethral bulking using data from the British Society of Urogynecology (BSUG) database (56% primary and 39% secondary bulking procedures, 67% SUI and 33% MUI), only 0.8% of bulking patients reported having developed de novo OAB while 25.7% experienced cure or improvement of OAB symptoms [16]. In another study

Table 2 Patient characteristics

	N	Mean	Median	Range	SD
Age at bulking (years)	57	59.7	57	36–88	13.47
Body mass index at bulking	57	27.5	27.5	19.5–42.0	5.07
Volume injected (ml)	57	1.2	1	0.5–3.0	0.49
Years since TVT operation	57	5.4	5.1	0.4–16.2	4.01
Follow-up after injection (months)	57	11.7	7	1–84	11.74
Preoperative urethral closure pressure (cmH_2O)	38	25.8	44.2	7–100	25.78

Table 3 Postoperative results I

	Preoperative					Postoperative					
	N	Mean	Median	Range	SD	N	Mean	Median	Range	SD	P *
Pads/24 h (N)	57	2.7	3	0–4	0.90	57	1.8	3	0–4	1.5	0.0001
Micturitions/24 h (N)	56	8.8	8	5–20	2.9	39	8.1	8	5–13	2.1	0.026
Mean voided volume (ml)	55	217	205	71–500	84.8	39	211	194	41–408	80.0	0.632
24-h leakage (gram)	53	82.4	25	0–1490	209.1	51	21.1	0	0–284	50.9	0.0001
Stress test (gram)	55	35.0	24	0–221	41.1	48	3.9	0	0–50	10.0	0.0001
Postvoid residual (ml)	57	15.4	2	0–100	25.3	53	12.1	0	0–145	29.0	0.416
Maximal flow (ml/s)	56	21.5	20	4–63	10.5	40	15.5	15	3–36	8.6	0.003
Stress index	57	7.8	8	3–11	2.0	57	4.5	4	0–11	3.0	0.0001
Urgency incontinence index	57	3.9	4	0–8	2.5	57	2.6	2	0–8	2.3	0.001
Quality of life index	57	7.9	8	0–15	4.0	57	4.4	4	0–16	3.9	0.0001
Degree of satisfaction						57	0.9	0	0–4	1.2	

*Statistical calculations on paired samples only

Zivanovic reported at 12 months that de novo urgency had developed in 3.6% but without UUI, while 41.2% with preoperative MUI were cured of their UUI [6]. A recent Finnish study reported that 9.3% developed postoperative de novo urgency, defined as a need for medical treatment [15].

In the literature postoperative de novo UUI is generally reported as a percentage of the whole data set and not limited to those without preoperative MUI. In our study five patients reported de novo UUI, i.e., 8.8% of the whole study group. However, if we look at only the 19 patients who had no preoperative OAB problems, 26.3% developed postoperative de novo UUI. Their diagnoses have not been urodynamically confirmed, and one cannot read too much into such small numbers, but our study indicates that the risk of UUI developing with injection therapy as repeat surgery after previous MUS is not insignificant and the patients must be informed of this risk. On the other hand, among the patients with preoperative UUI 39.5% were cured of this problem and a further 36.8% were improved for a total of 76.3%. However, an increased risk of OAB after repeat surgery is not limited to bulking; it has also been reported after repeat MUS [9].

Table 4 Postoperative results II

	N total	N (%)
Objective cure of SUI (postop stress test 0 g)	48	35 (72.9)
Subjective cure of SUI (postop stress index ≤ 2)	57	13 (22.8)
Cure of UUI (postop urge index ≤ 2)	38	15 (39.5)
Improved UUI (urge index reduced by < 2)	38	14 (36.8)
De novo UUI (postop urge index > 2)	57	5 (8.8)
Satisfied with treatment (satisfaction score≤1)	57	42 (73.7)

SUI stress urinary incontinence

UUI urgency urinary incontinence

Increasing age and BMI are generally associated with somewhat poorer results after MUS surgery [19–21], but there is little published information on the impact of age or BMI on the results after periurethral injection. In our study we found no effect. Only two other studies have addressed this. Lose reported no effect of age or BMI on primary bulking procedures [22], and Gaddi found with repeat injections that failure was not associated with age, BMI, vaginal parity, or menopausal status. [3]. In patients with low urethral closure pressure/incompetent urethra, Gaddi found poorer results after bulking procedures than after MUS [3], while Zivanovic did not [6]. In our study the eight patients with low urethral closure pressure actually had slightly better results than those with normal urethral closure ($p = 0.72$). Periurethral injection with polyacrylamide hydrogel is known to be a safe procedure with few complications [14, 23]. Only one complication occurred in our material, supporting this view.

Strengths

There were no confounding surgical procedures, and all the patients had previously undergone retropubic TVT. Very few patients were lost to follow-up, only 3.4%. With only two surgeons doing the procedures a standardized and consistent placement of the bulking material was ensured. The study had no exclusion criteria except missing from follow-up. In many other studies various patient groups have been excluded (e.g., related to high BMI, high age, low urethral pressure, low bladder capacity, low free flow rate, high postvoid volume, UUI [i.e., patients with MUI]). Our results therefore represent the real-life situation and have high external validity. We present both subjective and objective outcomes as is recommended by the International Continence Society and the International Urogynecological Association [24, 25].

Weaknesses

Using registry data always entails the risk of missing data and inaccuracies in individual entries that may potentially impact results. Postoperative urodynamic investigation involving cystometry was not routinely done in our study, and the diagnosis of OAB/UUI was made from the patient's questionnaire with the inherent imprecision of this diagnostic method. The study is from one department only. The 11.7-month follow-up time is relatively short. A known complication to bulking procedures is UTI, but we have not reported on postoperative UTI as the data from the registry are considered to be too uncertain.

Conclusions

As a secondary procedure, periurethral injection with polyacrylamide, is a safe surgical treatment option with good results in women with SUI or stress dominant MUI after a previous MUS. The cure rate was 72.9% and the satisfaction rate 73.7% in our study.

Age, high BMI, or low urethral closure pressure did not impact the results. There was a risk of OAB symptoms developing in women with no such symptoms preoperatively, but as a group many more women experienced OAB symptom improvement than those developing OAB symptoms.

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Author contributions SS Myhr: Protocol development, data collection and analysis, manuscript writing
M Rakovan: Data analysis, manuscript editing
HA Schiotz: Protocol development, data collection and analysis, manuscript writing

Declarations

Financial disclaimers/Conflict of interest None.

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