Original article

Pelvic floor related quality of life after vaginal mesh implantation. Secondary endpoint of a prospective randomized trial

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Abstract: Objective: To evaluate the impact of mesh implantation and the type of mesh used on pelvic floor related quality of life (QoL). Mesh implantation is commonly used for prolapse repair, but mesh exposure and chronic pain are risks. *Material and methods:* Pre- and postoperative QoL was evaluated as secondary endpoint of a prospectively randomized multicenter open-label trial; primary endpoint was the difference of exposure rates between a nonabsorbable and a partially absorbable mesh. QoL was evaluated after 3, 12, and 36 months using a validated pelvic floor questionnaire, together with visual analogue scales on pelvic floor pain and satisfaction with surgery and compared to baseline by paired t-tests. Mean scores within treatment groups at 36 months were compared adjusting for baseline values in a linear regression model. *Results:* Between 2007 and 2008, 200 patients with cystocele ≥ stage 2 were centrally randomized to the nonabsorbable (n=102) or the partially absorbable (n=98) mesh. QoL improved significantly after 3 months, remaining constant: mean±SD 8.3±3.2 preoperatively (n=193) to 3.9±2.9 (3 months, n=188), 3.6±2.5 (12 months, n=186), 3.8±2.7 (36 months, n=181). Change from baseline was significant ($p \leq 0.002$). There were no relevant differences among study arms; at 36 months, QoL improved by 0.6 points more for the partially absorbable (n=85) than for the nonabsorbable mesh (n=84; 95%, CI: -0.2 to 1.4). *Conclusions:* We demonstrate a clinically relevant improvement of pelvic floor related QoL together with improved pelvic floor pain and high satisfaction after 3 years, with an equal improvement in both study arms.

Key words: Quality of life; Pelvic organ prolapse; Sexuality; Polypropylene mesh; Pelvic floor pain.

Abbreviations: POP pelvic organ prolapse, QoL Quality of life, PP nonabsorbable mesh, PA partially absorbable mesh, FDA US Food & Drug Administration, ICS International Continence Society.

INTRODUCTION

Pelvic organ prolapse (POP) is a health condition that virtually never affects patients´ life expectancy but has a significant impact on the quality of life of women. Almost one third of women suffer from POP during their lifetime, and the lifetime risk for POP and incontinence surgery at the age of 80 is approximately 11%.[1,2] Quality of life is reduced because women feel ashamed or due to impaired bladder and bowel function. Women may refrain from sexual intercourse because they are afraid that POP could worsen or because they do not want to present themselves to their partner in this condition.[3] Considering that many POP patients are active women with many more years of life expectancy they need an operation that a) produces long-lasting results and b) does not impair their quality of life.

There are several techniques of native tissue repair for anterior vaginal wall prolapse, colporrhaphy being the most frequently used. For this procedure a recurrence rate of up to 40% is known.[4] Classical surgery techniques have been partially replaced by vaginal mesh repair due to better anatomical outcomes.[5] Unfortunately, there are few randomized trials directly comparing native tissue repair with vaginal mesh implantation.[6] However, only recently the ongoing discussion of risks of mesh repair has been renewed after the second warning of the US Food & Drug Administration (FDA).[7] A well-considered reply to the FDA warning has been authored by Murphy et al. on behalf of the Pelvic Surgeons Network.[8] In 2013 another update on the Cochrane analysis on mesh repair was published. This update emphasizes the need for more data on quality of life after mesh repair, as the anatomic results are superior compared to native tissue repair.[5]

With the increasing number of patients treated using vaginal meshes, new postoperative problems have emerged. While native tissue repair also has specific problems, mesh implantation is under discussion for the risk of mesh exposure, dyspareunia and chronic pelvic pain. Mesh exposure is the most common problem and the risks have not been completely understood. Both simultaneous hysterectomy and younger age seem to play an important role.[9] Dyspareunia and chronic pelvic pain are difficult problems, because often the exact cause is unknown and treatment may be difficult. Pain may be due to shrinking of the mesh or compression of pudendal nerves or scarring. Possible treatments are partial excision of the mesh, pelvic floor exercises or infiltration with local anesthetics.[10,11]

In order to evaluate the long-term subjective and objective outcome of vaginal mesh repair this prospectively randomized study was initiated (PARETO-trial, German Clinical Trials Register DRKS00004566). Patients were randomized either for a nonabsorbable or a partially absorbable mesh. The primary endpoint was the effect of the type of mesh used on the mesh exposure rate; as secondary endpoints the effect of POP repair on quality of life and whether the type of mesh used made any difference were tested. The hypothesis was that the lighter mesh would cause less mesh exposures compared to the nonabsorbable meshes. Furthermore, less pain was expected after implantation the partially absorbable mesh. Whether there would be a difference regarding QoL between the treatment groups could not be forecast.

MATERIAL AND METHODS

Patient randomization, the mesh, surgical technique

After approval of the local ethics committee, 200 patients were included in this two-arm prospective open-label study. Surgery was performed in one of six urogynecologic centers in Germany between 2007 and 2008. All patients eligible had a cystocele stage 2 or above in combination with a lateral defect and risk factors for POP (e.g. obesity, constipation). The exclusion criteria were as follows: age <18 yrs, imcompleted family planning, allergy to polypropylene, previous malignancy of the urinary tract, genital organs or rectosigmoid, previous mesh implantation, missing informed consent, life expectancy <3 yrs or patients who could not ensure follow-up visits over 3 years. The prolapse was classified according to the International Continence Society (ICS) definition.[12]

After informed consent, patients were randomized for either a nonabsorbable prolypropylene mesh (PP group) or a partially absorbable mesh of the same size and shape (PA group) (Seratom®, Serag Wiessner, Germany). The threads of the partially absorbable mesh are made of polypropylene filaments with an absorbable coating of polyglycolic acid and caprolactone. Following absorption after approx. 120 days, a light and soft mesh remains. Patient characteristics, the exact features of the mesh and the surgical technique, which was identical in both groups, have been described before.[13] For treatment concealment, block randomization with a 1:1 allocation ratio and variable block size, stratified for center, was performed by the study's main office. There was no blinding to group assignment. For reasons of practicability and feasibility a sample size of 100 patients per group was chosen, as mesh exposure rates vary from 2% up to 25%.[4, 14-15]

Primary and secondary outcomes

The primary end point of the study was to evaluate mesh exposure rates at 12 months after surgery. As secondary endpoints, risk factors for mesh exposure, the influence of the mesh used on POP recurrence and, as reported here, the effect on pelvic floor related quality of life were evaluated.

Quality of life data

For evaluation of pelvic floor related quality of life the German version of a validated pelvic floor function questionnaire was used.[16, 17] It was completed by the patients on paper before the operation and at follow-up visits. Patients unable to come for follow-up were contacted by mail and asked to fill out the questionnaire in order to achieve a low drop out rate.

This questionnaire comprises 15 questions on bladder and 12 questions on bowel function, 9 on sexual activity and 5 on prolapse sensation. The four resulting scores of each domain range from 0 to 10, with 0 representing no problems and 10 representing high dysfunction. Furthermore, a summary score including bladder and bowel function and prolapse symptoms, ranging from 0 to 30, can be calculated. In accordance with the recommendation of the questionnaire´s author the sexual function score was not included in the total score, as approximately one half of the study population was not sexually active. Regarding clinical relevance, an improvement of the subdomains was considered significant if change from baseline was >1, regarding the total score >2-3 points.[17]

Visual analogue scales

Apart from the validated questionnaire, patients filled out a visual analogue scale regarding satisfaction with the operation (range 0 to 10; 0 meaning no satisfaction, 10 highest satisfaction) and pelvic floor related pain (range 0 to 10; 0 meaning no pain, 10 corresponding to strong pain).

Follow-up visits

Follow-up was scheduled at 3, 12 and 36 months at the operating hospital. Apart from quality of life data, mesh exposure rates and other clinical data (further surgeries etc.) were obtained. Mean follow-up time of the study population was 3.3, 13.7 and 39.1 months.

Statistical analysis

Distributions of score values at follow-up time points were compared to baseline by paired t-tests. Mean scores within treatment groups at 36 months were compared adjusting for baseline values in a linear regression model. Satisfaction with surgery and pelvic floor pain were compared between treatment groups in a cumulative logit model. The model for pelvic floor pain was adjusted for baseline pain measurements. Throughout, complete case analyses were performed, and two-sided p-values <5% were considered statistically significant. SPSS version 19 and SAS version 9.2 were used for statistical calculations.

RESULTS

Patient characteristics and follow-up

From 02/2007 to 07/2008, 200 women with POP were included in the study. Patient characteristics of the two treatment groups regarding surgery and medical history were similar.[13] Follow-up was performed between April 2007 and December 2011. 198 patients were treated according to the study protocol, with 101 patients in the PP group and 97 in the PA group. In 120 patients, additional sacrospinous suspension was performed in view of a central defect, using arms 5 and 6 of the mesh.

Quality of life data could be obtained from 196, 188, 186, and 181 patients at baseline and after three, twelve and 36 months of follow-up. There were various reasons for missing follow-up mainly that women were too sick or too old to come to the hospital or that the contact address had changed. The CONSORT-PRO flowchart is shown in fig. 1.

Quality of life data: Questionnaire

Preoperative QoL scores were compared to values at 3, 12 and 36 months of follow-up. The overall score including bladder, bowel and prolapse sensation improved significantly: the mean score ±SD was 8.3±3.2 preoperatively (n=193), 3.9±2.9 after 3 months (n=188), 3.6±2.5 after 12 months (n=186) and 3.8±2.7 after 36 months (n=181). Change from baseline was of a clinically relevant order of magnitude and also statistically significant at all three time points (mean improvement 4.6±3.5, p <0.001 at 3 months (n=180); 4.7±3.5, p= 0.001 at 12 months (179); 4.8±3.7, p= 0.002 at 36 months (n=170). This improvement was mainly due to the subdomain covering prolapse sensation.

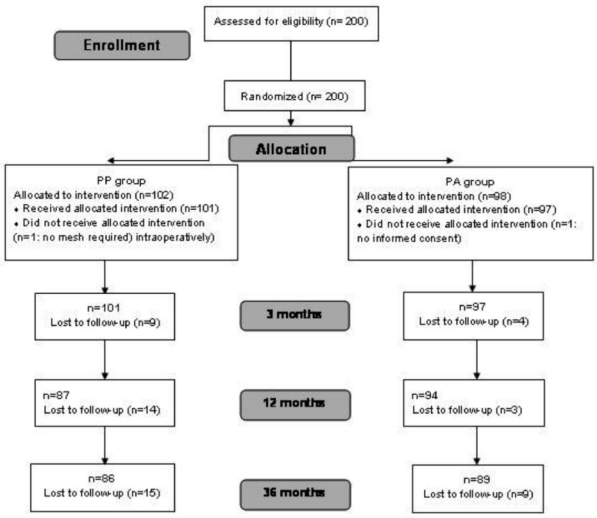

Figure 1. - CONSORT-PRO statement.

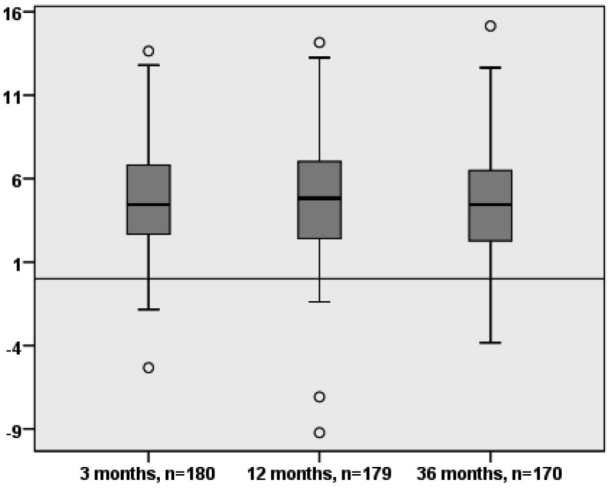

Figure 2a. - Total score change (bladder, bowel, prolapse).

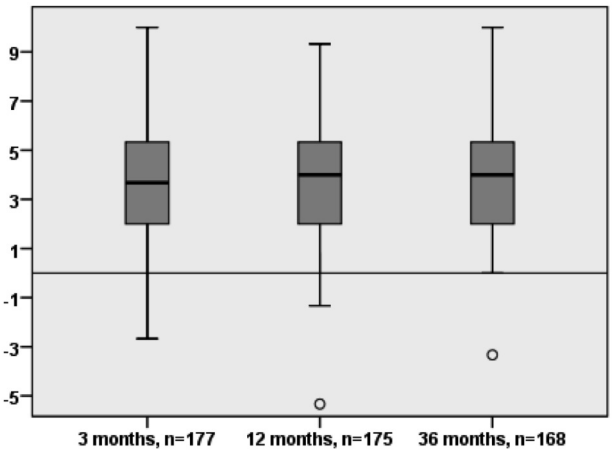

Figure 2b. - Prolapse score change.

Sexual function did improve, however not significantly (mean score 1.9±1.6 preoperatively (n=93) vs. 0.9±1.3 after 3 months (n=78), 1.1±1.4 after 12 months (n=91) and 1.1±1.6 after 36 months (n=74). Looking at the mean age of our patients being 67 years (range 35-88 yrs), only part of them were sexually active: 47.7% (93/195, missing n=3) preoperatively vs. 42% (76/181, missing n=17) at 3 months, 50.6% (89/176, missing n=22) at 12 months and

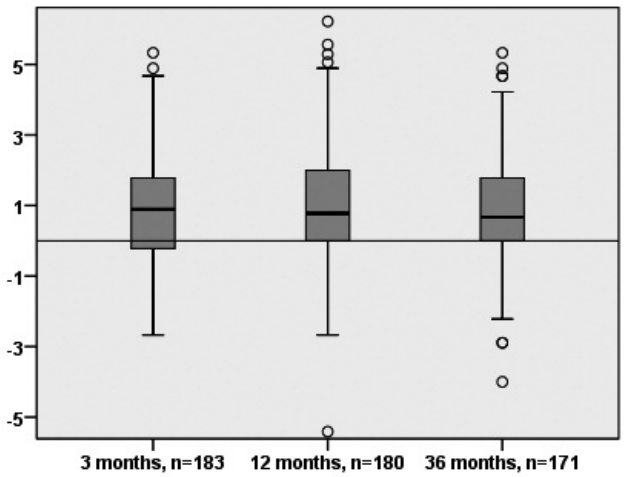

Figure 2c. - Bladder score change.

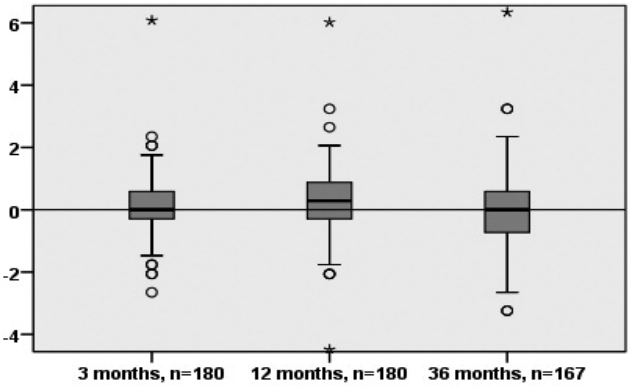

Figure 2d. - Bowel score change.

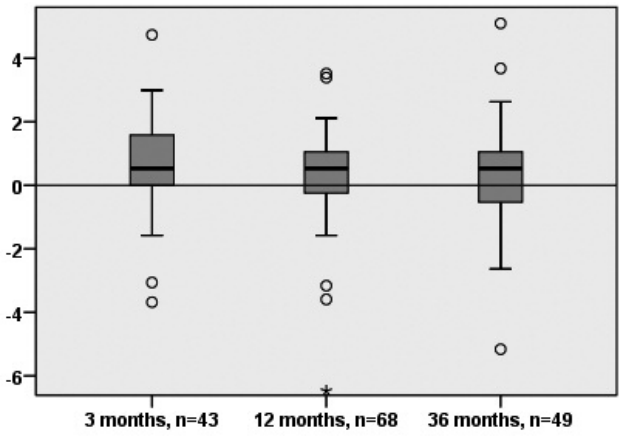

Figure 2e. - Sexuality score change (within the sexually active).

43% (74/172, missing n=26) at 36 months. Among the sexually inactive women, the main reason was "missing partner" or "sickness of partner" (60% (63/105) preoperatively vs. 61.3% (57/93) after 36 months). Only 49 patients answered the questions on sexual activity both at baseline and at 36 months. For details, see Figures 2 a-e. Bowel function did not show a relevant change after surgery (1.6±1.2 preoperatively (n=193) vs. 1.6±1.2 at 3 months (n=188), 1.4±1.2 at 12 months (n=184) and 1.7±1.3 after 3 years (n=174). Also in patients who had a simultaneous posterior repair by colporrhaphy or using mesh, the bowel function score did not change relevantly (n=93, data not shown).

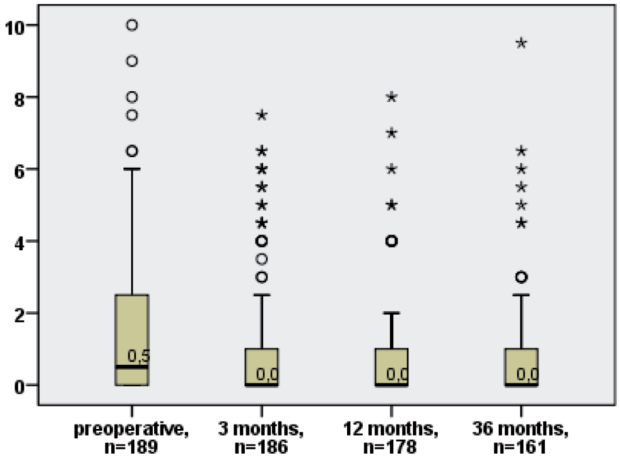

Figure 3a. - Pelvic floor related pain (0= no pain, 10= strong pain).

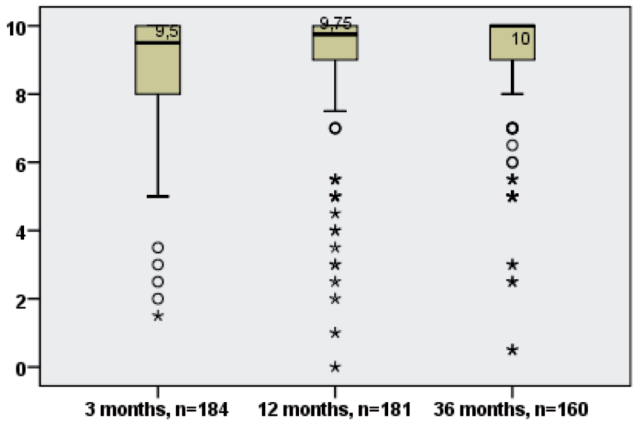

Figure 3b. - Satisfaction with the operation (0= not satisfied, 10= very satisfied).

Visual analogue scales

Preoperatively, the mean score of pelvic floor related pain was 1.5±2.1 (n=189) on a scale ranging from 0 to 10 (10 meaning strong pain). This was improved after 3 months to 1.1±2.0 (n=186), to 0.9±2.0 after 12 months (n=178) and after 36 months to 0.7±1.5 (n=161); see figure 3. Change from baseline was statistically significant at all three follow-up visits ($p < 0.05$, data not shown).

Satisfaction with the operation on a scale ranging from 0 to 10 (10 meaning very satisfied) was very high at all three time points (8.7±2.0 at 3 months (n=184), 8.7±2.2 at 12 months (n=181) and 8.7±2.2 after 3 years (n=160), (Figure 3).

Influence of mesh type on QoL data after 3 years

Apart from the primary outcome of mesh exposure rates,[13] the influence of randomized mesh type used on pelvic floor related QoL after 3 years was evaluated. All quality of life data were compared between the two study groups (Table 1). Changes from baseline of the QoL total score and subscores were similar in both study arms. Clinically relevant differences between them could be excluded for all scales, based on confidence intervals for the treatment effects (Table 1). Similarly, the visual analogue scale regarding pain showed comparable results in both arms, and also satisfaction with the operation was at the same level. However, the confidence intervals for the effect of treatment on pain and satisfaction with the

TABLE 1. – Difference in QoL data among nonabsorbable (PP) and partially absorbable (PA) mesh.

Score (range: best to worst)	**Baseline scores**		**Change from baseline (baseline-month 36) unadjusted means**		**Difference adjusted for baseline**	**95% CI**	**p-value**
	PP	**PA**	**PP**	**PA**	**PA - PP[1]**		
Total score (0 to 30) n	8.6 99	8.1 92	4.3 84	4.4 85	0.6	-0.16 to 1.4	0.1220
Bladder (0 to 10) n	3.0 100	2.4 96	0.7 83	0.8 86	0.4	-0.02 to 0.79	0.0624
Prolapse (0 to 10) n	3.9 99	3.7 92	3.8 84	3.7 84	0.1	-0.15 to 0.31	0.4880
Bowel (0 to 10) n	1.5 100	1.6 93	-0.2 84	0.0 85	0.2	-0.18 to 0.50	0.3432
Sexuality (0 to 10) n	2.3 43	1.6 50	0.6 20	0.2 29	0.0	-0.80 to 0.88	0.9297
Visual analogue scales (range: best to worst)			**Change from baseline (baseline-month 36) medians [unadjusted means]**		**Odd ratio for greater pain (>1 pt.), adjusted for baseline, PA vs. PP[2)]**		
	PP	**PA**	**PP**	**PA**	**PA - PP[1]**		
Pain (0 to 10) n	1.7 95	1.3 94	0 [0.8] 73	0 [0.9] 73	0.98	0.54 to 1.79	0.9469
			Month 36, medians		**Odd ratio for greater satisfaction PA vs. PP[3)]**		
Satisfaction (10 to 0) n	n.a.	n.a.	10 76	10 84	1.1	0.63 to 2.04	0.6729

[1)] A value above 0 favours PA; [2)] A value below 1 favours PA; [3)] A value above 1 favours PA
PA, nonabsorbable polypropylene mesh; PP, partially absorbable mesh; CI, confidence interval

operation were too wide to exclude a potential difference of clinically relevant magnitude (Table 1).

DISCUSSION

It has become clear in recent years that POP needs to be seen and treated in all its complexity, taking into account all effects it has on affected women's quality of life. In this prospectively randomized trial on 200 women, a positive course of patients´ quality of life after vaginal mesh implantation could be demonstrated. All patients underwent surgery mainly for cystoceles. As expected, bladder function and prolapse sensation improved after the operation. Furthermore, sexual function improved, however not at a statistically significant level. Bowel function did not show a relevant change. This is also true for patients with additional surgery for posterior compartment prolapse.

Overall, pelvic floor related quality of life improved significantly. These effects could already be seen at 3 months´ follow-up, but remained constant after 3 years. In the comparison of the two meshes, the absorbable -meshes showed a negligible benefit compared to the non-absorbable meshes for the four domains and for the total score. Since all confidence intervals exclude clinically irrelevant differences, we conclude that both treatments worked equally well with respect to pelvic floor related QoL (Table 1). To our knowledge, there are no other prospectively randomized studies on the quality of life after mesh implantation with a similarly long follow-up.

Furthermore, the effect of the partially absorbable mesh on patients' pain was under investigation, as one could assume that a lighter mesh causes less pain. At all three follow-up intervals we observed less pelvic floor related pain in the group which had received the lightweight mesh, but the difference in change from baseline was not statistically significant between the treatment groups. The lower pain score may be due to the special features of the partially absorbable mesh, supplying good support without rendering the tissue too firm to yield. On the other hand, the mesh must not be too thin as this could cause more recurrent prolapse.[13]

As for the risks of vaginal mesh implantation, the two most relevant risks are mesh exposure and chronic pelvic pain. According to the most recent Cochrane data, the risk of mesh exposure is 11.4% on average, with surgical interventions being necessary in 6.8%.[5] In the majority of cases, mesh exposure causes minor or no problems for the patients even in long term follow-up and can mostly be handled by local estrogen application or partial excision of the mesh.[18] An adequate patient selection and profound surgical training is important for successful mesh-based repair.[19]

Chronic pelvic pain originating from the operation is something that surgeons using vaginal meshes dread. An operation causing chronic pain is a severe problem. Therefore, the reasons of chronic pelvic pain after mesh implantation need to be studied further on in order to improve surgical techniques and also to identify patients who are at special risk. In this trial, we compared pre- and postoperative pain. Interestingly, the change from baseline in pelvic floor related pain was statistically significant, with improvement after the operation.

In order to evaluate patients' satisfaction with the operation, a visual analogue scale on this topic was included in the questionnaire. Patients' satisfaction was very high and consistently remained at this level. Patients with mesh exposure did not have a higher pain score than those patients with complete wound healing. Amrute et al. could also show high patient satisfaction after mesh augmented surgery.[20]

As a limitation of the study, we cannot draw any conclusion whether the improvement in QoL is comparable to patients treated with native tissue repair. This has been investigated in a trial by Nieminen et al., showing better relief of bulge symptoms after mesh implantation compared to native tissue repair.[21] Furthermore, not all our patients were available for follow-up, especially after 3 years.

In summary, in this multicenter, prospective and randomized study we describe a relevant improvement of QoL in patients after mesh augmented POP surgery. After a follow-up time of three years, no difference between treatment groups was observed. Patients' satisfaction was very high over the course of time. Pelvic floor related pain decreased significantly after surgery compared to preoperative data. Being conscious of the risks of mesh surgery, we hereby present data emphasizing good quality of life after mesh augmented POP repair.

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