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Cumulative 5-year Results of a Randomized Controlled Trial Comparing Biological Mesh With Primary Perineal Wound Closure After Extralevator Abdominoperineal Resection (BIOPEX-study)

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Objective: To determine long-term outcomes of a randomized trial (BIO-PEX) comparing biological mesh and primary perineal closure in rectal cancer patients after extralevator abdominoperineal resection and preoperative radiotherapy, with a primary focus on symptomatic perineal hernia.

Summary Background Data: BIOPEX is the only randomized trial in this field, which was negative on its primary endpoint (30-day wound healing).

Methods: This was a posthoc secondary analysis of patients randomized in the BIOPEX trial to either biological mesh closure (n = 50; 2 dropouts) or primary perineal closure (n = 54; 1 dropout). Patients were followed for 5 years. Actuarial 5-year probabilities were determined by the Kaplan-Meier statistic.

Results: Actuarial 5-year symptomatic perineal hernia rates were 7% (95% CI, 0–30) after biological mesh closure versus 30% (95% CI, 10–49) after primary closure ($P = 0.006$). One patient (2%) in the biomesh group underwent elective perineal hernia repair, compared to 7 patients (13%) in the primary closure group ($P = 0.062$). Reoperations for small bowel obstruction were necessary in 1/48 patients (2%) and 5/53 patients (9%), respectively ($P = 0.208$). No significant differences were found for chronic perineal wound problems, locoregional recurrence, overall survival, and main domains of quality of life and functional outcome.

Conclusions: Symptomatic perineal hernia rate at 5-year follow-up after abdominoperineal resection for rectal cancer was significantly lower after biological mesh closure. Biological mesh closure did not improve quality of life or functional outcomes.

Keywords: abdominoperineal resection, biological mesh closure, perineal hernia, perineal wound healing, primary perineal wound closure, quality of life, sexual function, urinary function

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Perineal infection and wound dehiscence often complicate the postoperative course of patients undergoing abdominoperineal resection (APR) for rectal cancer. The published incidence of perineal wound complications generally varies around 30% to 50%,[1–3] and depends on several factors such as the extent of the resection and whether preoperative (chemo)radiotherapy was given.[4–7] Many perineal wounds will take several weeks or months to heal, but some wounds may never heal. The incidence of chronic perineal sinuses after APR can even be as high as 10%.[1,2] In addition, perineal hernia is a late complication after APR that might become symptomatic or require surgical repair.[2,8–10]

The perineal wound after APR can be closed primarily, or with a biological mesh or tissue flap.[11,12] Retrospective cohort series suggested better wound healing after biological mesh closure than after primary closure,[7] but the randomized controlled BIOPEX-study revealed identical wound healing rates between the 2 closure techniques at any time point within 1 year after APR.[3] Quality of life was neither found to be significantly different. A promising secondary finding of the BIOPEX study was the lower 1-year perineal hernia

rate in favor of biological mesh closure. Establishing whether biological mesh closure prevents or simply delays the occurrence of perineal hernia needs longer follow-up. In addition, other long-term outcomes of the BIOPEX study could be of interest, including chronic perineal wound problems, small bowel obstruction, oncological outcomes, health related quality of life, and functional outcomes.

Therefore, this study aimed to determine long-term outcomes of the BIOPEX study after 5-year follow-up, with primary focus on symptomatic perineal hernia rate.

METHODS

Patients and Study Design

Between February 2013 and September 2014, a total of 104 primary rectal cancer patients were enrolled in the BIOPEX-study, of which the primary outcome and 1 year follow-up has been published previously.[3,13] Main inclusion criteria were preoperative radiotherapy and planned extralevator APR. Patients were recruited in 11 Dutch hospitals and 1 hospital in the United Kingdom, and were randomly allocated to biological mesh closure (6 x 10 cm, Strattice, LifeCell Corporation, Branchburg, USA) and primary layered perineal wound closure in a 1:1 ratio.

The present study was an unplanned prospective extension of the BIOPEX study, in which patients were followed for 5 years after APR according to a study protocol amendment that was approved by the local ethical committee. Clinical examinations were performed every 3 months for the first year, half-yearly until 2 years postoperatively, and annually thereafter until 5 years after surgery. The participating surgeons received reminders before each outpatient visit with the request to fill out the case report form. At each visit, all perineal wound complications, presence of perineal hernia, small bowel obstruction at the level of the pelvis, related readmission, reintervention, and oncological outcomes were recorded. Quality of life and functional outcome questionnaires were sent once to all patients still alive at 3 to 5 years postoperatively. Radiological imaging included CT scan as part of the oncological follow-up. Some patients were prepared and signed informed consent for pelvic MRI without dynamic imaging after 3 to 5 years follow-up. Central data management was done at the Department of Surgery of the Amsterdam University Medical Centers (Amsterdam UMC), location Academic Medical Center (AMC), the Netherlands. Reporting adhered to the CONSORT statement (see Table, Supplemental Digital Content 1).[14]

Clinical Outcome Measurements

The primary outcome of this update of the BIOPEX-study was symptomatic perineal hernia during 5-year follow-up. Perineal hernia was defined as bulging or clearly noticeable swelling in a standing position at the perineal scar and/or radiological imaging in supine position that revealed intraabdominal contents descending beyond the pubococcygeal line during rest.[15,16] Perineal hernia were considered symptomatic if any degree of perineal pain or discomfort was reported, either at time of diagnosis or thereafter, whereas absence of any symptoms was defined as asymptomatic perineal hernia.

Other outcome measures included the presence of a persistent perineal or presacral sinus (perineal wound that failed to heal for more than 1 year after APR), chronic nonspecific perineal pain (perineal pain or discomfort beyond 1 year postoperatively without presence of a perineal sinus or perineal hernia), long-term incidence of small bowel obstruction located in the pelvis (not caused by recurrent cancer), related need for readmission and reintervention (surgical or percutaneous), and locoregional recurrence rate, distant metastasis-free survival, disease-free survival and overall survival at 5-years after surgery.

Generic quality of life was assessed using the Short Form-36 version 2 and the 5-dimensional EuroQol (EQ-5D-5L), and gastro-intestinal quality of life was assessed using the EORTC (QLQ-C30/CR29) before the operation and 3 to 5 years postoperatively. Male participants completed the International Index of Erectile Function (IIEF), and female participants completed the Female Sexual Function Index (FSFI) and Female Sexual Distress Scale (FSDS) regarding postoperative sexual function. Urinary function was assessed using the Urogenital Distress Inventory (UDI-6) and Incontinence Impact Questionnaire (IIQ-7).

Cost Differences

Mean marginal costs were evaluated for the experimental group (biological mesh closure) and control group (primary perineal wound closure). A description of the analysis is included in the appendix (Supplemental Digital Content 2, http://links.lww.com/SLA/C935).

Statistical Analysis

All the data were analyzed in accordance to the intention-to-treat principle. According to distribution, descriptive data were reported as mean with standard deviation (SD) or median with interquartile range (IQR). The χ^2 test or Fischer exact test was applied to evaluate differences in proportions, and the *t*-test or Mann-Whitney *U* test to evaluate differences in continuous measurements. Perineal hernia and survival rates were reported as 5-year probabilities using Kaplan-Meier analysis, and compared using the log-rank test. Omentoplasty was imbalanced among the 2 study arms, and was included into a posthoc multivariable logistic regression model to account for its potential effect on symptomatic and overall perineal hernia rates. All questionnaires were analyzed according to the manuals, and presented as domain and summarized scores. Established cut-off scores of sexual function were used to characterize patients in either the dysfunctional or functional range.[17−21] For women, sexual dysfunction was defined as an FSFI score below 26.55 and an FSDS score higher or equal to 11, and for men, erectile dysfunction was defined as an IIEF score below 22. Impact of urinary incontinence was categorized as none to mild (IIQ-7 score below 50), moderate (IIQ-7 score between 50 and 70), and severe (IIQ-7 score above 70).[22] A *P*-value of 0.05 was considered significant. All analyses were performed with IBM SPSS statistics, version 26.0.0 (IBM Corporation, Armonk, NY).

RESULTS

From 104 patients that were initially randomized, 48 patients (12 female and 36 male) in the biological mesh group and 53 patients (14 female and 39 male) in the primary closure group were available for analysis. Initial randomization was stratified for age, sex, and laparoscopic surgery. Details on the pretreatment and surgery characteristics, as well as the 1-year results, have been described previously.[3] Follow-up continued until December 2019. Median follow-up was 4.7 years (IQR 3.4−5.1) and did not differ between the 2 groups (*P* = 0.380).

Perineal Hernias

During complete follow-up, 18 patients developed a symptomatic perineal hernia (Table 1). Median time to diagnosis of symptomatic perineal hernia was 9 months (IQR 5−17). Actuarial 5-year symptomatic perineal hernia rates were 7% (95% CI, 0−30) after biological mesh closure and 30% (95% CI, 10−49; *P* = 0.006) after primary perineal wound closure. Rate of omentoplasty was 61% (11/18) for patients with a symptomatic perineal hernia, compared

TABLE 1. Perineal Hernia

Variables		Primary Closure (n = 53)	Biological Mesh (n = 48)	*P*-value
Follow-up duration	*Median in years (IQR)*	4.8 (3.8–5.1)	4.7 (2.6–5.1)	0.380
Perineal hernia				
Symptomatic	*5-year actuarial rate[†] (95% CI)*	30% (10–49)	7% (0–30)	0.006
	Cumulative incidence, n (%)	15/53 (28)	3/48 (6)	0.004
	Perceptible by clinical examination, n (%)	13/15	3/3	—
	Detected by radiological imaging only, n (%)	2/15	0/3	—
*Overall**	*5-year actuarial rate[†] (95% CI)*	51% (31–70)	24% (1–47)	0.004
	Cumulative incidence, n (%)	21/53 (40)	6/48 (13)	0.002
	Perceptible by clinical examination, n (%)	17/21	5/6	—
	Detected by radiological imaging only, n (%)	4/21	1/6	—
Surgical repair	*5-year actuarial rate[†] (95% CI)*	14% (0–34)	2% (0–25)	0.053
	Cumulative incidence, n (%)	7/53 (13)	1/48 (2)	0.062

*Any symptomatic or asymptomatic bulge or noticeable swelling at the perineal level detected by clinical examination and/or radiological imaging.
†As estimated by the Kaplan-Meier statistic, and compared with the log-rank test.

with 60% (50/83) for patients not having a symptomatic perineal hernia (*P* = 0.945). If corrected for omentoplasty in multivariable analysis, biomesh closure resulted in an adjusted odds ratio for symptomatic hernia of 0.157 (95% CI 0.041–0.602; *P* = 0.007). There were no significant sex differences in occurrence of symptomatic perineal hernia (*P* = 0.775). In total, 8 patients (30%) underwent surgical repair of a perineal hernia: one in the biomesh group versus 7 in the primary closure group (*P* = 0.062). The remaining 10 symptomatic patients opted for conservative treatment. Based on physical examination and available radiological imaging, an additional 9 patients were diagnosed with an asymptomatic hernia (3 after biomesh and 6 after primary closure). After adding these numbers to the symptomatic hernias, the overall actuarial 5-year rates were 24% (95% CI, 1–47) and 51% (95% CI, 31–70) (*P* = 0.004; Table 1; Fig. 1), respectively.

Chronic Perineal Wound Morbidity

At 1-year follow-up, 3 of 97 patients still alive demonstrated a persistent sinus: 2 patients with clear discharge from a superficial perineal wound, and 1 patient with purulent discharge from a presacral sinus. Beyond 1 year, a chronic wound problem was observed in another 6 patients: 2 superficial dehiscences, 1 vaginal fistula, and 3 perineal sinuses. This resulted in an overall chronic sinus rate of 9% (9/97), which was 11% (5/44) after biomesh and 8% (4/53) after primary closure (*P* = 0.727). Additionally, 7/44 (16%) and 6/53 (11%) patients reported some degree of nonspecific perineal pain or discomfort during daily activities beyond 1 year, respectively

(*P* = 0.509). One patient with chronic perineal wound problems was readmitted. None of the total 9 patients underwent a surgical or percutaneous intervention. Two chronic sinuses were still not completely healed at last follow-up, 2.5 and 5 years from index surgery. There were no biomesh-related complications observed, and none of the meshes needed explantation.

Small Bowel Obstruction

Overall incidence of small bowel obstruction in the pelvic cavity was 8% (8/101), which was 4% (2/48) after biomesh and 11% (6/53) after primary closure (*P* = 0.274). Causes of obstruction were pelvic adhesions (n = 5), omental band (n = 2), and internal herniation underneath the uterus (n = 1). Reoperations for small bowel obstruction were necessary in 1/48 patients (2%) and 5/53 patients (9%), respectively (*P* = 0.208). No obstructions were related to the biomesh. One patient (primary closure group) had multiple episodes of obstruction, requiring laparotomy twice.

Long-term Oncological Follow-up

Oncological outcomes are shown in Table 2 and Supplementary Figure 1 (see figure, Supplemental Digital Content 3, http://links.lww.com/SLA/C936). Five-year locoregional recurrence rate was 9% after biomesh and 8% after primary perineal closure (*P* = 0.890), with an identical 62% 5-year disease-free survival in both arms (*P* = 0.984). Five-year overall survival was 76% and 80%, respectively (*P* = 0.621).
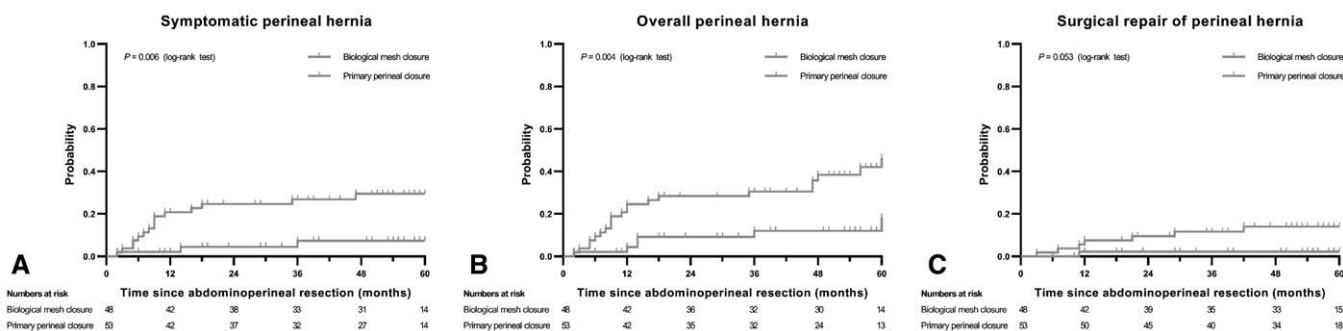

FIGURE 1. Kaplan-Meier survival curves of A. symptomatic perineal hernia, B. overall perineal hernia (including asymptomatic), and C. surgical repair of perineal hernia following abdominoperineal resection with biological mesh closure (green line) and primary closure of the perineal wound (pink line).

TABLE 2. Long-term Oncological Outcomes After Abdominoperineal Resection

Variables	Primary Closure (n = 53)	Biological Mesh (n = 48)	*P*-value
Follow-up duration			
Median in years (IQR)	4.9 (4.0–5.2)	4.7 (2.8–5.1)	0.235
Locoregional recurrence*			
1-yr actuarial rate	8% (0–15)	0% (0–0)	
3-yr actuarial rate	8% (0–15)	5% (0–12)	
5-yr actuarial rate	8% (0–15)	9% (0–18)	0.890
Distant metastasis-free survival*			
1-yr actuarial rate	85% (75–95)	87% (77–97)	
3-yr actuarial rate	73% (61–85)	78% (65–90)	
5-yr actuarial rate	69% (56–81)	75% (62–88)	0.564
Disease-free survival*			
1-yr actuarial rate	85% (75–95)	83% (72–94)	
3-yr actuarial rate	70% (57–82)	68% (54–81)	
5-yr actuarial rate	62% (48–75)	62% (47–76)	0.984
Overall survival*			
1-yr actuarial rate	98% (94–100)	94% (87–100)	
3-yr actuarial rate	90% (82–98)	84% (73–95)	
5-yr actuarial rate	80% (69–91)	76% (63–89)	0.621

*As estimated by the Kaplan-Meier statistic, and compared with the log-rank test.

Quality of Life

The response rate for the long-term health-related quality of life assessment was 87% (73/84) (Fig. 2). Quality of life as assessed by the SF-36 and EQ-5D-5L showed no statistical differences when comparing biological mesh versus primary closure. Neither did the EQ-5D-5L show any statistical differences when comparing patients who experienced a symptomatic perineal hernia to those who did not (data not shown). Similarly, no significant differences were found in any scale of the EORTC QLQ-C30/CR29 questionnaires, except for 2 symptom scales of the CR29: biological mesh group had lower stool frequency (*P* = 0.042) and less urinary incontinence (*P* = 0.028). The responses and subscales are shown in Table 3 and Supplemental Digital Content 4, http://links.lww.com/SLA/C937.

Urinary and Sexual Function

In total, 62 patients completed the urinary function assessment questionnaires, with a total response rate of 79% (49/62) for the male patients, and 59% (13/22) for the female patients (Fig. 2). Corresponding response rates for sexual function were 50/62 (81%) and 12/22 (55%).

The median scores on the urinary function questionnaires are shown by method of perineal wound closure and sex (see table, Supplemental Digital Content 5, http://links.lww.com/SLA/C938). No significant group differences were recorded on urinary incontinence symptoms (UDI-6; *P* = 0.362) or impact of urinary incontinence (IIQ-7; *P* = 0.508). Most patients (57/62) reported no or only mild impairment of urinary incontinence-related quality of life, while 3 and 2 patients reported a moderately and severely impaired urinary incontinence-related quality of life, respectively. Women tended to report more stress incontinence symptoms (*P* = 0.017) and irritative symptoms (*P* = 0.072), and also more impact on quality of life (*P* = 0.087) compared to men. No other differences were found.

Median scores on sexual function for men and women were not statistically different between the 2 study groups. Most patients had no partnered sexual activity. According to the FSFI and FSDS, 4 of 12 (33%) women were sexually active, all of whom were classified as dysfunctional (FSFI < 26.55). Two sexually active women reported that intercourse was impossible since chemoradiation and surgery. All 12 women reported decreased sexual desire.

Three of 4 women (75%) with partnered sexual activity were bothered by their sexual function (FSDS). Of the women with no sexual activity, 3 of 6 (50%) participants were unhappy with their sexual life. According to the IIEF, 15 of 50 (30%) male participants attempted sexual activity and intercourse. In those with intercourse, erectile dysfunction was reported in 87% (13 of 15). Orgasmic dysfunction was reported in 12 of 21 (57%) patients. Based on the IIEF, most men had decreased sexual desire (41 of 50 (80%)). The majority of men were unhappy with their sexual life (35 of 46 (75%): 8 of 15 (53%) for the sexually active and 27 of 31 (87%) for nonactive men.

Cost Differences

Mean marginal costs related to preventive biological mesh use and surgical repair of symptomatic perineal hernia were € 1130 to € 2430 per patient in the experimental group, and € 545 per patient in the control group (see Supplemental Digital Content 2, http://links.lww.com/SLA/C935 and 6, http://links.lww.com/SLA/C939).

DISCUSSION

Five-year results of the BIOPEX trial revealed that biological mesh closure after APR resulted in a significantly lower symptomatic perineal hernia rate (7% vs 30%). Persistent perineal wound problems occurred in 11% after biological mesh closure and 8% after primary perineal closure. Unplanned reoperations for small bowel obstruction were not statistically different (9% vs 2%, *P* = 0.208). Biological mesh use did not affect the quality of life, urogenital function, or oncological outcomes of evaluable patients at 5-year follow-up.

The incidence of perineal hernia after APR with varying perineal closure techniques is poorly investigated, and reported to be somewhere between 1 and 21%.[7,23–26] All these studies had a retrospective design, which may explain the considerable differences with the current study, especially regarding primary closure. Furthermore, most of these studies did not provide long-term follow-up, calculated only cumulative incidences (not Kaplan-Meier estimates), and used varying definitions for perineal hernia, which all complicate direct comparisons. A recent well documented cohort study including 100 patients demonstrated a 4-year cumulative perineal hernia
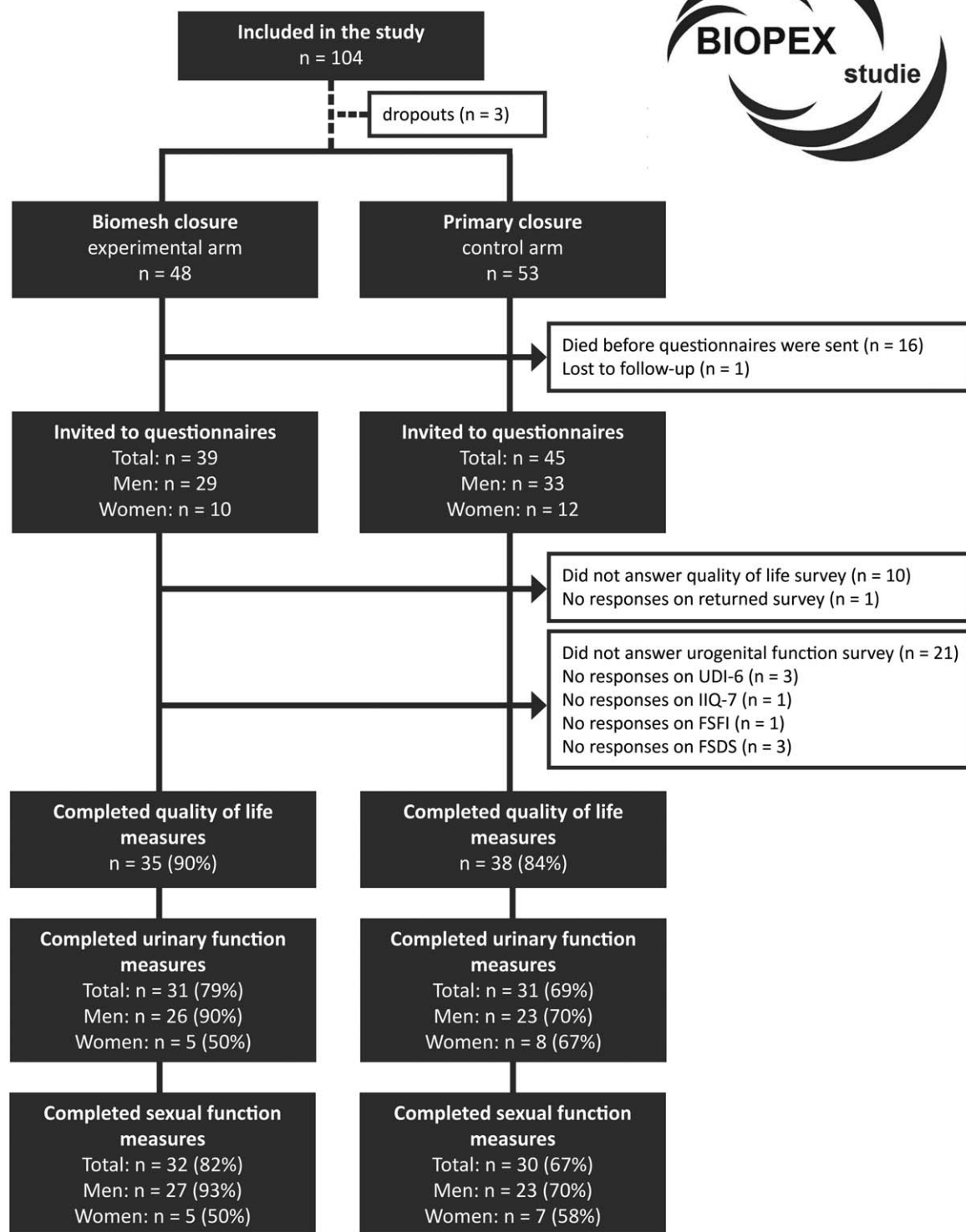
FIGURE 2. Flow chart of the randomized controlled trial.

TABLE 3. Long-term Generic Quality Of Life

	Primary (n = 38)	Biological (n = 35)	
	Mean (SD)	Mean (SD)	*P*-value
Short Form-36			
Physical functioning	68.0 (29.1)	72.1 (26.2)	0.526
Role functioning/physical	61.1 (44.1)	56.6 (44.1)	0.671
Role functioning/emotional	71.2 (40.9)	80.8 (36.4)	0.304
Energy/fatigue	66.1 (20.4)	61.3 (20.0)	0.318
Emotional wellbeing	77.8 (18.6)	77.7 (14.3)	0.985
Social functioning	78.9 (25.8)	79.3 (24.1)	0.954
Pain	71.7 (29.2)	78.2 (27.7)	0.333
General health	60.1 (19.7)	56.7 (24.0)	0.507
Health change	56.6 (24.4)	47.9 (16.5)	0.076
EQ 5D-5L			
Total health state	8.1 (4.1)	7.6 (3.4)	0.573
Mobility	1.7 (1.1)	1.7 (0.9)	0.915
Self-care	1.4 (1.0)	1.2 (0.5)	0.288
Activity	1.8 (1.1)	1.7 (1.1)	0.710
Pain	1.8 (0.9)	1.6 (1.0)	0.473
Anxiety	1.5 (0.8)	1.4 (0.7)	0.732
EQ VAS	74.3 (20.0)	70.7 (17.9)	0.415

N = total number of patients returning the questionnaire, but may differ per item. Data are mean scores with standard deviation (SD). Note, high scores for SF-36 = better function, whereas high EQ 5D scores = more problems (except for EQ VAS). *P*-values are calculated using *T*-tests.

rate of 8% after biomesh closure, which is in line with the present results of the BIOPEX study.[27]

We have previously conducted a meta-analysis showing that omentoplasty was associated with an increased risk of developing a perineal hernia after APR.[23] In the current trial, the application of omentoplasty was left at the discretion of the surgeon, which resulted in imbalance between the 2 study arms (50% after biomesh and 70% after omentoplasty; $P = 0.04$), but the proportions of omentoplasty were comparable in those who did and did not develop a symptomatic hernia during follow-up. Therefore, the imbalance in omentoplasty is likely not an explanation for the observed results.

Costs should be taken in consideration when thinking about implications of the reduced symptomatic perineal hernia rate for clinical practice. Routine use of a relatively expensive biological mesh with prolonged operative time in all patients must be weighed against more surgical hernia repairs using a less costly synthetic mesh after initial primary closure, as suggested by the observed differences in marginal costs. On the other hand, the decision to repair a perineal hernia is complex, and not necessarily reflective of the severity of a hernia. Many factors such as patient and surgeon preference, experience with hernia repair surgery, resource availability, and patient comorbidities may influence the decision on elective surgical repair. Furthermore, conservative treatment of symptomatic hernia's is also associated with costs of T bandages or specific pairs of underpants. As no proper cost-effectiveness studies are available yet – including reasons for elective hernia repair and indirect medical costs – perhaps both strategies are acceptable, and may best be determined by hospital's policy or preferences of surgeons and patients. Of note, biological mesh use in APR appears safe, without increase in late perineal or mesh-related complications.

Chronic perineal sinus was observed in 9% of patients, with 2% of wounds that did not heal during the study period. There were, however, no percutaneous or surgical reinterventions beyond 1 year post-APR, which probably means the complications gave rise to only mild complaints. Interestingly, some of the sinuses were not mentioned at the 1-year clinical visit, but presented later during follow-up.

Measuring the patients' quality of life to evaluate the outcome of surgical care is a topic with increasing importance, particularly in conditions with such high survival rates. Despite the clear reduction of symptomatic perineal hernias, mesh use did not affect the quality of life in the present study. This might be explained because of the low and insignificant impact of a perineal hernia on the several domains of questionnaires that were used for this purpose. Furthermore, our study might also be underpowered to distinguish differences between the 2 study groups. On the other hand, a perineal hernia might not cause that much trouble for a patient considering the mainly elderly population with reduced physical activity.

Functional complaints related to urinary and sexual problems might probably be more important determinants of long-term quality of life of rectal cancer survivors.[28] Patients across both sexes often experience urinary and sexual dysfunction after treatment for rectal cancer,[29–31] especially after APR.[32–35] In the present cohort, sexual dysfunction was difficult to evaluate due to high rates of sexual inactivity among both men (70%) and women (67%). This is in accordance with previous studies[34,36] and can in large part be explained by increased age and partner status. Among respondents who were sexually active, only 47% of men and 25% of women experienced their present sex life as satisfying.

The etiology of sexual dysfunction is multifactorial. Risk factors have been suggested to be increased age, presence of stoma, chemoradiotherapy, and direct nerve injury during dissection along the pelvic floor.[29,37–40] Mechanical factors after APR may also play a role, but have not gained much attention in the current literature. Dorsal angulation of the vagina might compromise sexual intercourse or cause dyspareunia. In the present study, 2 sexually active women reported sexual intercourse being impossible since APR (1 biomesh patient). Prolapse of the bladder, especially in case of a perineal hernia, might result in urinary retention and incontinence. Interestingly, a significant difference in urinary incontinence was found in favor of the biomesh group based on a subscale of the QLQ-CR29. However, this was not confirmed by the specific urinary function questionnaire scores. At present, there are no studies suggesting any beneficial effect of pelvic floor reconstruction on urinary or sexual function, neither for filling of the presacral cavity after APR.[41–43] Theoretically, an omentoplasty or tissue flap might provide some support to the urogenital organs, but whether this

translates into better function is unknown and should be explored in future studies.

The strength of the present study lies in the fact that this is still the only published randomized study on perineal morbidity after APR for rectal cancer, but there are also some limitations. This study was not originally designed to detect a reduction in perineal hernia rate, and results have to be judged with care. Radiological imaging to confirm the presence or absence of perineal hernia was not routinely performed, and the used imaging protocols were not state-of-the-art (dynamic MRI), for which reason the actual overall incidence might be even higher. However, one may wonder about the clinical relevance of finding asymptomatic perineal hernia. Unfortunately, some patients were lost to follow-up, and some data were unavailable for certain outcome measures. This may have introduced some recording bias but is probably inherent to the long-term follow-up of an oncological patient population. Furthermore, the trial was not powered for investigation of sex-specific differences. Given the differences in pelvic anatomy this may be useful in future trials. Finally, mortality was slightly skewed in favor of the primary closure group, unlikely being related to the intervention, but which might have influenced observed perineal hernia rates.

Considering the clinical implications, there is a need for alternative closure techniques, mainly because a biomesh fails to improve perineal wound healing. Small gluteal transposition flaps that eliminate the perineal dead space are promising new interventions,[44–46] but more high-quality data is required. We have therefore launched a second international multicenter randomized controlled trial (BIOPEX-2),[47] comparing a gluteal turnover flap with primary closure of the perineal wound, the latter being still considered standard of care by our study group.

CONCLUSIONS

We conclude that biological mesh closure is associated with a significantly lower risk of symptomatic perineal hernia in patients undergoing APR for rectal cancer with preoperative radiotherapy when compared to primary perineal closure. The study was not designed and powered for this endpoint, which makes it difficult to conclude on superiority of biomesh closure. Prophylactic biomesh or synthetic mesh repair at time of herniation seem both acceptable strategies for daily practice. Future study should include formal cost-effectiveness analysis.

Ackknowledgments

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