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The impact of previous inguinal mesh hernioplasty on oncological and patient-reported outcomes following radical prostatectomy

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Abstract

Background: The impact of previous inguinal mesh hernioplasty (MH) with non-resorbable mesh prostheses on surgical performance of radical prostatectomy (RP) has been controversially discussed, with unknown impact of MH on oncologic outcomes and health-related quality of life (HRQOL) following RP. We therefore aimed to assess the influence of previous MH on metastasis-free survival (MFS), biochemical recurrence-free survival (BRFS), and HRQOL following RP.

Methods: We identified 344 patients with previous MH prior RP within our prospectively assessed institutional database of 6275 patients treated with RP for PC (2008–2019). A 1:3 propensity-score matched analysis of 1345 men ($n = 319$ previous MH, $n = 1026$ no previous MH) was conducted. Primary endpoint was MFS and secondary endpoints were BRFS and HRQOL (based on EORTC QLQ-C30). Binary logistic regression, Kaplan–Meier, and Cox regression models tested the effect of previous MH on MFS, BRFS, and HRQOL ($p < 0.05$).

Results: Median follow-up was 47 months. Patients with previous MH had significantly lower 5-year MFS (72% vs. 85%, $p < 0.001$) and 5-year BRFS estimates (43% vs. 57%, $p < 0.001$). In multivariate analysis, previous MH was confirmed as an independent predictor for impaired MFS (hazard ratio [HR]: 3.772, 95% CI 1.12–12.64, $p = 0.031$) and BRFS (HR: 1.862, 95% CI: 1.22–2.85, $p = 0.004$). These results held true if stratified for surgical approach or limited to patients with successful PLND. We found significantly shorter median time to continence recovery for patients without previous MH ($p = 0.001$) without significant differences in total continence recovery rates, erectile function recovery, and HRQOL.

Conclusions: Our findings show an impaired oncologic outcome for patients with previous MH following RP with no significant differences regarding continence recovery, erectile function recovery, and general HRQOL.

KEYWORDS

biochemical recurrence-free survival, EORTC QLQ-C30, health-related quality of life, high-risk prostate cancer, radical prostatectomy

1 | INTRODUCTION

There has been an open debate about the impact on previous inguinal hernia repair with implantation of a non-resorbable mesh prothesis ("mesh") on outcomes following radical prostatectomy (RP), especially since preperitoneal inguinal hernia repair using mesh has become increasingly popular, offering earlier return to regular daily activities, less postoperative pain, and less operating time.[1,2] Several reports have shown general feasibility of open retropubic RP (ORP)[3,4] as well as laparoscopic robotic RP (RALP)[5] and endoscopic extraperitoneal RP[6] after previous inguinal hernioplasty. However, the effect of hernioplasty on functional and oncological outcomes following RP remains uncertain, since current evidence is based on small historic case series with limited follow-up periods and varying primary endpoints.

Encouraged by this paucity of data, we conducted this first propensity-score matched analysis of a large contemporary cohort of prostate cancer (PCa) patients that underwent ORP or RALP with or without previous mesh hernioplasty. Hereby, we tested the hypothesis that a more technically challenging RP procedure after previous mesh hernioplasty will lead to subpar oncological and functional outcomes.

2 | MATERIAL AND METHODS

2.1 | Patient population, study design, and data assessment

Following approval by a local ethics committee (#20-1022), 6236 patients from a prospective institutional database who underwent RP for PCa between January 2008 and December 2019 ($n = 4609$ ORP, $n = 1627$ RALP) were identified. Surgical techniques in our department have been described before.[7] Inclusion criteria for the current study encompassed: surgery performed by high-volume surgeons with more than 200 previous RP. Patients with preoperative imaging suspicious for metastatic disease, or neoadjuvant treatment prior RP were excluded. Prospective assessment of HRQOL prior surgery (baseline HRQOL) was performed using a validated translation of the standardised European Organisation for Research and Treatment of Cancer (EORTC) quality of life questionnaire (QLQ)-C30 and its prostate-specific QLQ-PR25 add-on.[8] As per previously established cut-off values, good general HRQOL was defined as a global health status (GHS) of ≥70.[9] Urinary continence was assessed using the International Consultation of Urinary Incontinence questionnaire in its short-form (ICIQ-SF),[10] as well as daily pad usage. Continence recovery was defined by use of up to one security pad per 24 h. Erectile function was assessed using the simplified International Index on Erectile Function (IIEF-5) questionnaire.[11] According to institutional standards, questionnaires were handed out to patients 1–3 days prior RP.

Propensity score matching (PS-matching) limited to eligible patients with complete follow-up was created applying matching variables age, BMI, PSA-value, prostate volume (PV), pT-stage Gleason grade, and lymph node involvement. PS-matching was conducted in a 1:3 manner, applying nearest neighbor matching with a matching tolerance of 0.0001, resulting in a matched cohort of 1345 patients ($n = 319$ [previous mesh hernioplasty], $n = 1026$ [no previous hernioplasty]). A flow chart illustrating the patient selection process is provided in Figure 1.

2.2 | Outcomes

Primary endpoint was metastasis-free survival (MFS) based on conventional or PSMA PET-based imaging and calculated from the date of the RP. Patients were censored at the last follow-up including imaging or death. Secondary endpoints encompassed biochemical recurrence-free survival (BRFS), defined as the time from RP to biochemical recurrence defined as PSA ≥0.2 ng/mL following current guidelines,[12] and functional outcome parameters including HRQOL based on validated questionnaires.

2.3 | Follow up

Follow-up of eligible patients was performed at 3-month intervals within the first postoperative year, followed by annually intervals thereafter. Hereby, validated questionnaires were sent via mail to eligible patients. Additionally, oncological outcomes were retrieved directly from patients, referring urologists, and primary physicians.

2.4 | Statistical analysis

Statistical analyses and reporting and interpretation of the results were conducted according to Guidelines for Reporting of Statistics for Clinical Research in Urology.[13] Statistical analysis was performed using MedCalc Statistical Software version 20.011 (MedCalc Software) and R software environment for statistical computing and graphics (version 4.1.3; R Foundation for Statistical Computing).

The balance of covariates before and after propensity score matching is tested by applying standardized mean differences (SMD). An SMD value of greater than 0.1 is considered the sign of important covariate imbalance.[14] To test for the normal distribution of variables, the Shapiro–Wilk test was performed. For descriptive statistics, median and means were used to present continuous variables and percentages or absolute numbers to present noncontinuous variables. The chi-square test and Mann–Whitney *U* test were applied for univariate analyses of categorical variables and continuous variables, respectively. Survival- and continence recovery probabilities were estimated by applying the Kaplan–Meier method and compared using the log-rank test. Uni- and multivariable Cox regression analyses were used to identify potential relations between previous mesh hernioplasty and MFS as well as BRFS. A p value of <0.05 was considered statistically significant.

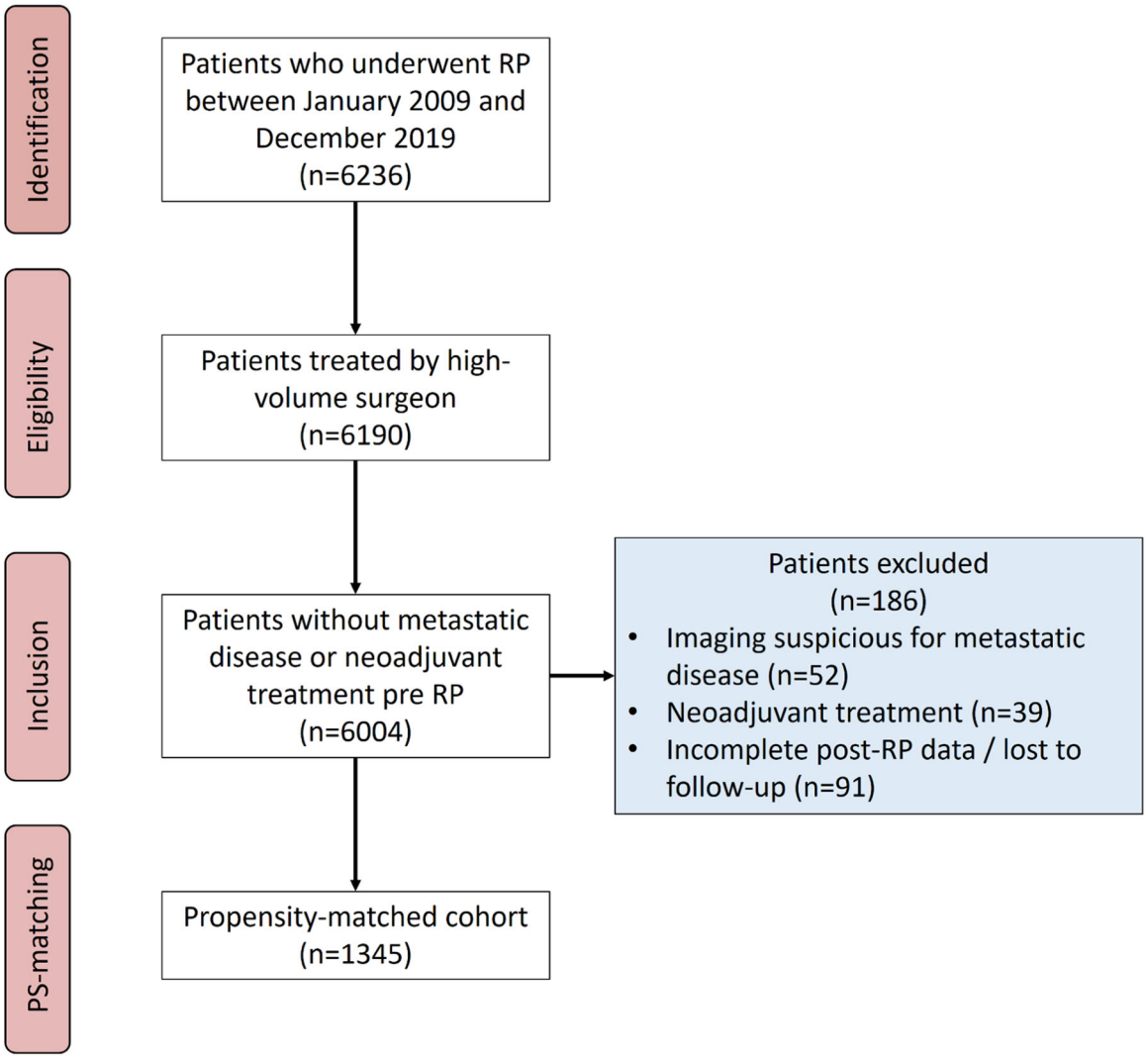

FIGURE 1 Flow chart summarizing the inclusion process for eligible subjects including the propensity score (PS) matched cohorts of the current study. RP, radical prostatectomy. [Color figure can be viewed at wileyonlinelibrary.com]

3 | RESULTS

3.1 | Perioperative patient characteristics

Patient characteristics of the unmatched and matched cohorts are provided in Table 1. Applying PS-matching, we generated a well-balanced cohort of 1345 patients ($n = 319$ [previous mesh hernioplasty], $n = 1026$ [no previous hernioplasty]). Median follow-up was 47 months. Following PS-matching, lymph node involvement did not show important covariate imbalance between cohorts (SMD = 0.096) with a similar ratio of patients without intraoperative pelvic lymph node dissection (PLND) (31.0%. vs. 26.5%). The median number of lymph nodes removed showed an important covariate imbalance with higher mean LN-count for patients without hernioplasty (10 vs. 7 nodes, SMD = 0.203); however, the median number of positive lymph nodes showed no important covariate imbalance (SMD = 0.023).

3.2 | Impact of previous mesh hernioplasty on MFS

At the time of analysis, 28 patients with previous mesh hernioplasty had experienced distant metastasis with a median MFS of 18.5 months, compared to 55 patients without previous hernioplasty and a median MFS of 29.7 months. Figure 2 displays the Kaplan–Meier plots with the estimates of MFS of both subgroups. Patients with previous mesh hernioplasty had significantly lower 5-year-MFS estimates of 72% compared to 85% for patients without previous hernioplasty ($p < 0.001$; Figure 2).

These results were confirmed in multivariate Cox regression analyses, stratified for locally advanced disease (>pT2c), ISUP high-risk features, preoperative PSA level, positive surgical margins, lymph node involvement, number of LN removed, adjuvant radiotherapy, age and surgical approach (HR: 3.772, 95% CI: 1.12–12.64, $p = 0.031$). Results of the multivariate Cox regression models are summarized in Table 2.

TABLE 1 Baseline characteristics of the unmatched and matched cohorts included in the current study.

	Baseline characteristics					
	Unmatched cohort			Matched cohort		
	Mesh hernioplasty	No hernioplasty	SMD	Mesh hernioplasty	No hernioplasty	SMD
No. of patients	344	5660		319	1026	
Date of surgery	2008–2019	2008–2019		2010–2019	2008–2019	
Hernioplasty without mesh, *n* (%)	–	338 (6.0)		–	55 (5.4)	
Age, years [median, IQR][a]	68 [63, 73]	66 [60, 71]	**0.120**	68 [63, 73]	67 [62, 73]	0.094
BMI (kg/m^2) [median, IQR][a]	25.9 [24.1, 28.4]	26.5 [24.5, 29.1]	**0.129**	25.8 [24.1, 28.4]	26.3 [24.3,28.4]	0.068
PSA preop. (ng/mL) [median, IQR][a]	8.6 [5.9, 12.9]	7.9 [5.4, 12.7]	0.036	8.6 [5.9, 12.7]	8.5 [5.6, 14.3]	0.007
Prostate volume (mL) [median, IQR][a]	52 [41, 67]	51 [41, 65]	0.015	52 [41, 67]	51 [41, 65]	0.035
Gleason grade, *n* (%)[a]						
6	33 (9.7)	1104 (19.5)	**0.178**	30 (9.4)	96 (9.4)	0.023
7a	135 (39.3)	2026 (35.8)		124 (38.9)	409 (39.9)	
7b	71 (20.5)	1132 (20)		66 (20.7)	214 (20.8)	
8	42 (12.3)	611 (10.8)		40 (12.5)	136 (13.3)	
9	60 (17.3)	713 (12.6)		56 (17.6)	153 (14.9)	
10	3 (0.9)	74 (1.3)		3 (0.9)	18 (1.7)	
pT stage, *n* (%)[a]						
pT2a	20 (5.9)	419 (7.4)	0.075	18 (5.6)	53 (5.2)	0.001
pT2b	8 (2.3)	96 (1.7)		4 (1.3)	20 (1.9)	
pT2c	168 (48.7)	3017 (53.3)		156 (48.9)	498 (48.5)	
pT3a	77 (22.3)	1087 (19.2)		72 (22.6)	239 (23.3)	
pT3b	71 (20.8)	1041 (18.4)		69 (21.6)	216 (21.1)	
Lymph node involvement, *n* (%)[a]						
pN0	195 (56.7)	3956 (69.9)	**0.156**	188 (58.9)	646 (63.0)	0.096
pN1	33 (9.6)	526 (9.3)		32 (10.0)	108 (10.5)	
pNx	116 (33.7)	1183 (20.9)		99 (31.0)	272 (26.5)	
Number of LN removed [median, IQR]	8 [5, 12]	10 [7, 14]	**0.199**	7 [5, 12]	10 [6, 14]	**0.203**
Numer of postive LN [median, IQR]	1 [1, 3]	2 [1, 3]	**0.454**	1 [1, 3]	1 [1, 4]	0.023
PSA-persister, *n* (%)	45 (13.1)	809 (11.1)	0.030	28 (11.7)	94 (12.7)	0.041
Robot assisted RP, *n* (%)	97 (28.2)	1477 (26.1)	**0.253**	96 (30.1)	366 (35.7)	**0.119**
Nerve sparing, *n* (%)	281 (81.7)	5094 (90.0)	**0.130**	265 (83.1)	891 (86.8)	0.091
Positive surgical margin, *n* (%)	101 (29.4)	1557 (27.5)	0.085	84 (26.3)	285 (27.8)	0.033
Radiation, *n* (%)	64 (18.6)	1596 (28.2)	**0.271**	59 (18.5)	240 (23.4)	0.097

Note: Bold values indicate SMD > 0.1 (important covariate imbalance).

Abbreviations: BMI, body mass index; IQR, interquartile range; PSA, prostate-specific antigen; RALP, robot-assisted laparoscopic radical prostatectomy; RP, radical prostatectomy; SD, standardized mean differences.

[a]Propensity score matched variables.

3.3 | Impact of previous mesh hernioplasty on BRFS

At the time of analysis, 88 patients with previous mesh hernioplasty had experienced biochemical failure with a median time-to-recurrence of 10 months, compared to 322 patients without previous hernioplasty with a median time-to-recurrence of 25 months. Figure 3 displays the Kaplan–Meier plots with the estimates of BRFS of both subgroups. Patients with previous mesh hernioplasty had significantly lower 5-year-BRFS estimates

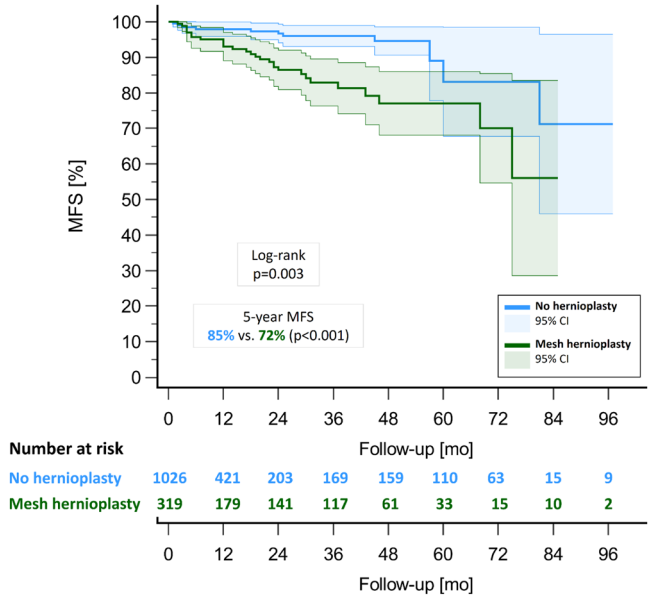

FIGURE 2 Metastasis-free survival (MFS) for patients with previous mesh hernioplasty (green) and patients without previous hernioplasty (blue). CI, confidence interval; mo, months. [Color figure can be viewed at wileyonlinelibrary.com]

of 43% compared to 57% for patients without previous hernioplasty ($p < 0.001$; Figure 3).

These results were confirmed in multivariate Cox regression analyses, stratified for locally advanced disease (>pT2c), ISUP high-risk features, preoperative PSA level, positive surgical margins, lymph node involvement, number of LN removed, adjuvant radiotherapy, age and surgical approach (HR: 1.862, 95% CI 1.22–2.85, $p = 0.004$). Results of the multivariate Cox regression models are summarized in Table 2.

3.4 | Subgroup analyses

In a separate model, we excluded patients without PLND. In this PLND-only subgroup, 5-year MFS rates (85% vs. 55%) and 5-year BRFS rates (51% vs. 28%, $p < 0.001$, respectively) were significantly higher for patients without previous mesh hernioplasty (Supporting Information: Figure 1). In multivariate Cox regression analysis, we confirmed previous mesh hernioplasty as an independent predictor for impaired MFS (HR: 3.971, 95% CI: 1.14–13.82, $p = 0.030$) and BRFS (HR: 2.091, 95% CI: 1.35–3.23, $p = 0.001$). Multivariate Cox regression analyses for patients who underwent PLND are summarized in Supporting Information: Table 1.

Finally, we tested the impact of previous mesh hernioplasty for patient subcohorts stratified for surgical approach (ORP vs. RALP). Hereby, we found significantly impaired 5-year MFS and BRFS rates for patients with previous mesh hernioplasty after ORP (90% vs. 74%, $p = 0.03$ [MFS]; 56% vs. 47%, $p = 0.002$ [BRFS]; Supporting Information: Figure 2) as well as after RALP (74% vs. 66%, $p = 0.02$ [MFS]; 62% vs. 34%, $p = 0.002$ [BRFS]; Supporting Information: Figure 3).

TABLE 2 Multivariate Cox regression analyses for the endpoints metastasis-free survival (MFS) and biochemical recurrence-free survival (BRFS).

Multivariate Cox regression analysis				
		95% CI		
Parameter	HR	Lower	Upper	p
Impact of previous mesh hernioplasty on MFS				
Previous mesh hernioplasty	3.772	1.13	12.64	**0.031**
Locally advanced PCa (≥pT3)	2.445	1.07	6.26	**0.042**
ISUP high-risk (Gleason grade ≥8)	1.781	0.54	5.86	0.343
iPSA	1.012	1.00	1.03	0.147
Positive surgical margin	0.810	0.25	2.61	0.724
Lymph node involvement	0.734	0.31	1.74	0.483
Number of LN removed	1.003	0.94	1.07	0.937
Adjuvant radiotherapy	1.210	0.38	3.84	0.746
Age (years)	1.020	0.94	1.11	0.647
RALP	1.239	0.40	3.88	0.713
Impact of previous mesh hernioplasty on BRFS				
Previous mesh hernioplasty	1.862	1.22	2.85	**0.004**
Locally advanced PCa (≥pT3)	0.845	0.48	1.50	0.566
ISUP high-risk (Gleason grade ≥8)	1.327	0.82	2.15	0.253
iPSA	1.012	1.00	1.02	**0.001**
Positive surgical margin	1.243	0.80	1.92	0.326
Lymph node involvement	0.554	0.40	0.77	**<0.001**
Number of LN removed	1.021	0.99	1.05	0.129
Adjuvant radiotherapy	1.880	1.18	2.99	**0.008**
Age (years)	1.016	0.99	1.05	0.319
RALP	1.180	0.77	1.81	0.448

Note: Bold values indicate $p < 0.05$.

Abbreviations: CI, confidence interval; HR, hazard ratio; ISUP, International Society of Urological Pathology; iPSA, initial prostate-specific antigen; LN, lymph node; RALP, robot-assisted laparoscopic radical prostatectomy.

3.5 | Functional outcomes

Functional outcomes at baseline and after a median follow-up of 47 months, including urinary continence, erectile function, and HRQOL are displayed in Table 3. Briefly, we found no significant difference in mean ICIQ-SF scores between both cohorts ($p = 0.183$). In line, continence recovery rates did not differ significantly between both

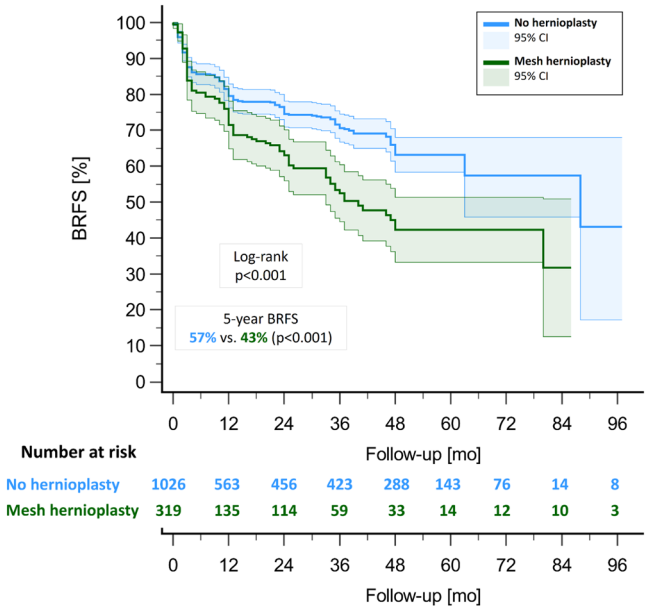

FIGURE 3 Biochemical recurrence-free survival (BRFS) for patients with previous mesh hernioplasty (green) and patients without previous hernioplasty (blue). CI, confidence interval; mo, months. [Color figure can be viewed at wileyonlinelibrary.com]

cohorts (74.6% vs. 78.8%, $p = 0.21$). However, median time-to-continence-recovery was significantly shorter for patients without previous hernia repair compared to patients with previous mesh hernioplasty (6 vs. 12 months, $p = 0.001$; Figure 4).

Regarding erectile function, we found no significantly different rates in good erectile function (IIEF-5 score 18 or more) between both cohorts at baseline (42.2% vs. 39.0%, $p = 0.45$) and at follow-up (15.7% vs. 22.2%, $p = 0.06$).

For HRQOL, we found significantly worse mean fatigue- and constipation-symptom scores for patients with previous mesh hernioplasty (p: 0.025–0.049). Social function scores were increased for patients without previous mesh hernioplasty (82.5 vs. 78.2, $p = 0.028$). QLQ-PR25 subdomains showed significantly worse mean scores of urinary symptoms, incontinence aid, bowel symptoms, and treatment symptoms for the subgroup with previous mesh hernioplasty (each $p < 0.001$, respectively), sexually active and sexual functioning subdomains did not differ between both cohorts (p: 0.088–0.241). Notably, there were no significant differences in general HRQOL based on the QLQ-C30 GHS ($p = 0.138$). Net baseline changes of the respective QLQ-C30 and QLQ-PR25 subdomains are summarized in Supporting Information: Table 2.

4 | DISCUSSION

Even though RP is a standard treatment option for localized PCa and inguinal hernioplasty is one of the most common surgeries performed worldwide, current evidence of outcomes following RP after previous inguinal hernioplasty with mesh prostheses is still subpar and based on small historic case series.

The present study is the first to evaluate the impact of previous mesh hernioplasty in a large and contemporary cohort, with focus equally on oncologic as well as patient-reported outcomes.

We hereby confirmed previous findings that ORP and RALP are generally feasible in the setting of previous inguinal mesh hernioplasty, with comparable duration of surgery and estimated blood loss between subcohorts.[3,4,6,15] By conducting PS-matching for patient age, BMI, PSA-value, PV, pT-stage, Gleason-grade, and lymph node involvement we aimed to eliminate previously confirmed confounders resulting in a well-balanced cohort.[16]

To date, evidence regarding the impact of previous mesh hernioplasty on oncologic outcomes following RP is scarce. Vijan et al. conducted a small retrospective analysis of perioperative morbidity and oncologic outcomes following ORP and matched nine patients with previous preperitoneal mesh implantation with 26 case controls. The authors found no increase in morbidity and no differences regarding recurrence rates.[3] Do et al. analyzed 92 patients with previous inguinal hernia repair and, in line with the aforementioned results, observed no significant increases in positive surgical margin rates and low PSA recurrence rates within a limited maximum follow-up of 12 months. However, it has to be emphasized that the study included an extraperitoneal laparoscopic approach for RP, which is not common elsewhere.[6]

In the current study, we provide data from a large well-balanced contemporary cohort with a median follow-up of 47 months. In this matched cohort, we did not find statistically significant differences in PSM- and PSA-persistence rates. Contrary to previous findings, survival analysis revealed a significantly impaired MFS and BRFS for patients following RP after previous mesh hernioplasty. In line, 5-year MFS and BRFS-estimates were significantly lower for the aforementioned patient subgroup.

One possible explanation of this finding focuses on the impaired PLND in patients with non-resorbable mesh prostheses. Saint-Elie and Marshall[4] identified 21 patients with previous laparoscopic hernia repair who underwent consecutive ORP and described impossible PLND due to scarring in 28.6% ($n = 6$). In the largest case-matched analysis on the impact of previous preperitoneal mesh hernia repair on RP outcomes to date, Peeters et al.[17] included 60 patients per subgroup and observed that significantly fewer lymph nodes were excised in the subgroup with previous hernia repair in intermediate- and high-risk patients. Those results are supported by a large nationwide survey of experienced surgeons that reports RP with prior mesh hernioplasty to be considered more difficult with less adequate PLND.[18] In line, we found significantly lower total number of lymph nodes removed in our matched subcohort of 338 patients with previous MH, indicating a more difficult PLND in patients with previous MH with a potential risk for occult nodal micrometastases.[19] Notably we included pN-status to our matching process, and balanced our multivariable analysis by pN-status as well as number of lymph nodes removed, to eliminate the bias of impossible PLND.

TABLE 3 Patient-reported outcomes at baseline (T0) and after a median follow-up of 48 months.

	T0			Follow-up		
	Hernia repair MESH	no Hernia repair	*p*	Hernia repair MESH	no hernia repair	*p*
Erectile function						
IIEF-5 score [mean, SD]	11.6 (9.8)	11.7 (10.1)	0.909	4.6 (6.8)	4.5 (7.1)	0.129
IIEF-5 score 18 or more [%]	42.2	39	0.449	15.7	22.2	0.060
Urinary continence						
ICIQ-SF score [mean, SD]	1.2 (2.8)	1.1 (2.7)	0.67	6.8 (5.4)	7.6 (5.7)	0.183
Daily pad usage [mean, SD]	n.a.	n.a.	n.a.	1.9 (2.3)	1.4 (1.9)	**0.005**
Continence recovery [%]	n.a.	n.a.	n.a.	74.6	78.8	0.21
Health related Quality of life						
EORTC QLQ-C30						
Symptom scale						
Dyspnea	7.1 (17.8)	5.2 (16.1)	0.083	10 (26.9)	9.7 (28.0)	0.518
Pain	11.5 (22.4)	7.4 (18.5)	**0.002**	11.2 (27.3)	10.2 (26.3)	0.250
Fatigue	14.1 (17.7)	11.0 (18.6)	**0.002**	19.7 (28.4)	15.3 (26.8)	**0.025**
Insomnia	10.4 (23.9)	9.7 (21.6)	0.722	15.5 (32.8)	17.2 (33.8)	0.575
Appetite loss	3.0 (13.5)	3.2 (13.5)	0.871	2.9 (22.5)	0.8 (15.5)	0.628
Nausea/vomiting	0.5 (4.0)	0.6 (4.3)	0.444	0.3 (14.1)	0.2 (11.7)	0.639
Constipation	6.9 (19.6)	4.4 (15.8)	0.053	8.0 (24.0)	4.3 (18.4)	**0.049**
Diarrhea	8.6 (18.5)	4.3 (14.9)	**<0.001**	10.0 (25.5)	11.1 (26.9)	0.687
Financial difficulty scale	3.8 (16.2)	2.3 (13.2)	0.215	24.6 (53.5)	29.4 (60.0)	0.706
Functioning scale						
Physical	94.9 (10.6)	95.2 (10.2)	0.501	91.6 (22.0)	92.8 (18.8)	0.375
Role	89.4 (20.7)	93.1 (20.9)	**<0.001**	80.8 (31.7)	85.4 (27.4)	0.100
Cognitive	89.5 (17.4)	92.0 (16.1)	**0.010**	86.3 (25.6)	87.1 (25.4)	0.152
Emotional	76.1 (24.9)	77.5 (24.4)	0.591	79.9 (28.2)	80.5 (27.9)	0.451
Social	86.8 (21.0)	89.7 (19.9)	**0.024**	78.2 (31.9)	82.5 (30.5)	**0.028**
Global health status	72.4 (20.9)	72.8 (20.6)	0.723	65.4 (21.4)	62.3 (22.5)	0.095
Global health status ≥70 (%)	53.6	60.5	0.068	44.0	38.2	0.138
EORTC QLQ-PR25						
Urinary symptoms				29.7 (20.3)	23.6 (20.7)	**<0.001**
Incontinence aid				36.4 (33.5)	24.6 (35.9)	**<0.001**
Bowel symptoms				7.1 (11.9)	4.2 (10.0)	**<0.001**
Treatment symptoms				17.2 (14.7)	11.7 (15.0)	**<0.001**
Sexually active				38.9 (32.6)	36.1 (34.5)	0.241
Sexual functioning				56.5 (23.1)	61.1 (24.6)	0.088

Note: Bold values indicate $p < 0.05$.

Abbreviations: ICIQ-SF, International Consultation on Urinary Incontinence Questionnaire short-form; IIEF-5, International Index on Erectile Function; n.a., not applicable.

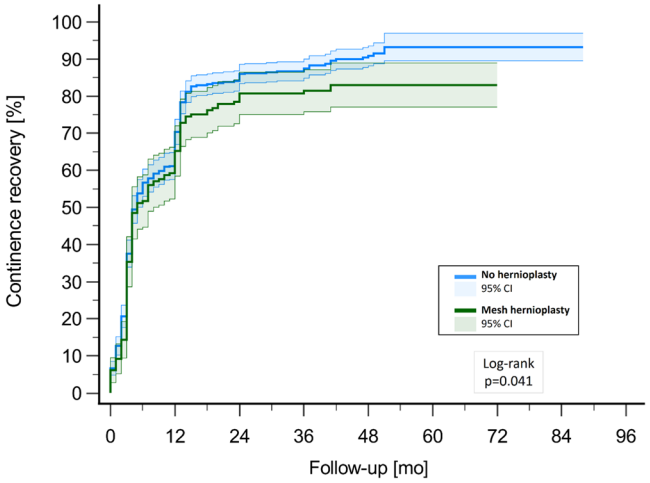

FIGURE 4 Continence recovery (%) for patients with previous mesh hernioplasty (green) and patients without previous hernioplasty (blue). CI, confidence interval; mo, months. [Color figure can be viewed at wileyonlinelibrary.com]

However, the role of intraoperative PLND in intermediate- and high-risk patients remains controversial. A recent meta-analysis did not demonstrate significant improvements in oncological outcomes by performance of PLND.[20] In addition, extended PLND did not show benefits over standard PLND in a recent randomized controlled trial.[21] As stated by current guidelines, it is generally accepted that extended PLND provides more accurate staging compared to any other modality.[22] It has to be emphasized that we performed a separate subgroup analysis excluding patients who did not undergo PLND and were able to confirm previous mesh hernioplasty as an independent predictor of impaired BRFS and MFS even if PLND was successfully performed. However, a potential impact of possible nodal under-staging due to more difficult surgical conditions cannot be ruled out entirely.

Another potential explanation for impaired oncological outcomes following mesh implantation focuses on the chronic inflammation that might be induced by non-resorbable mesh prostheses. It has been shown that implantation of polypropylene mesh biomaterials is commonly associated with inflammatory foreign body reaction, even if the patient is asymptomatic. This foreign body reaction provokes rapid and continuous infiltration of transient bone marrow-derived monocytes.[23] Furthermore, in patients with localized PCa peripheral blood monocyte count have recently been shown to be a predictive factor for tumor progression and prognosis.[24,25] Finally, elevated monocyte counts were associated with more aggressive tumor features and poor survival outcomes in patients with metastatic hormone-resistant PCa treated with docetaxel chemotherapy.[26]

There is also a lack of evidence regarding functional outcomes following RP after previous MH. Do et al.[6] found no significant impact of previous inguinal hernia repair on continence and potency recovery rates using the rather uncommon extraperitoneal laparoscopic approach for RP. Previous analyses from our institution showed similar continence and potency outcomes assessed via daily pad usage and IIEF-5 scores. However, this analysis included only a non-matched cohort of 51 patients with previous inguinal hernioplasty with or without mesh and was based on a historic cohort that underwent RP between 2004 and 2008.[27]

In the current study, assessment of patient-reported outcomes was based on validated questionnaires, including ICIQ-SF, IIEF-5, QLQ-C30, and QLQ-PR25. Hereby, we did not observe statistically significant differences regarding continence and potency rates. However, time-to-continence recovery was significantly prolonged in patients with previous MH. This could indicate that the more challenging surgical procedure in these patients might lead to a longer postoperative continence rehabilitation process. We furthermore assessed HRQOL in our matched patient cohort. We found significantly increased social function scores for patients without previous MH, indicating better social functioning in this cohort. Notably, general HRQOL, assessed via the QLQ-C30 global health status did not differ between both subcohorts. These results underline the notion that RP can be performed with satisfying functional and HRQOL outcomes after previous MH.

The current study is not devoid of limitations. First and foremost are the limitations that are inherent to the retrospective study design, which also did not allow to differentiate between previous total extraperitoneal and transabdominal extraperitoneal hernioplasties. By conducting propensity-score matching for previously confirmed confounders patient age, BMI, PSA-value, prostate volume, pT-stage, Gleason-grade, and lymph node involvement, we aimed to compensate this limitation and improve generalizability of the data.[16] Although our study lacks data on overall survival (OS), a recent meta-analysis has shown MFS to meet the standards for valid surrogate parameters for OS and has consequently been included as the primary endpoint in the current study.[28] Finally, since biochemical recurrence following RP is frequently followed by salvage radiotherapy, superior HRQOL outcomes of delayed salvage therapies have to be considered when increased BRFS outcomes are discussed.[29]

5 | CONCLUSION

In this propensity score-matched analysis of patients who underwent RP with or without previous mesh hernioplasty, we found significantly impaired MFS and BRFS for patients with previous implantation of a non-resorbable mesh prothesis. There were no differences regarding definitive postoperative functional outcomes including HRQOL with a longer time to continence recovery for patients with previous mesh hernioplasty.

AUTHOR CONTRIBUTIONS

Thilo Westhofen: Protocol/project development, study design, data collection, data analysis, and manuscript writing/editing. **Moritz Bensel**: Data collection and manuscript editing. **Boris Schlenker**: Data collection and manuscript editing. **Armin Becker**: Data collection and manuscript editing. **Christian G. Stief**: Protocol/project development, coordination

of study, and manuscript editing **Alexander Kretschmer**: Protocol/project development, study design, data collection, data analysis, and manuscript writing/editing. **Alexander Buchner**: Study design, data collection, data analysis and manuscript editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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