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Peritoneal interposition flap reduces symptomatic lymphocele following transperitoneal robot-assisted radical prostatectomy and pelvic lymph node dissection: An updated meta-analysis

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Abstract

Background: Robot-assisted radical prostatectomy with intraoperative pelvic lymph node dissection is the criterion standard for surgical treatment of nonmetastatic intermediate- and high-risk prostate cancer. However, this method is associated with symptomatic lymphocele (SLC), which is an important morbidity factor. To overcome this complication, several modifications of the technique have been developed, including the peritoneal interposition flap (PIF). We performed an updated systematic review and meta-analysis to investigate the efficacy and safety of this technique for preventing SLC and lymphocele (LC) formation.

Materials and methods: Searches were performed using databases and references from included studies and previous systematic reviews. Only randomized controlled trials and nonrandomized cohorts were included. Primary outcomes were the incidence of SLC and LC formation, and safety outcomes were defined as operation time, estimated blood loss, length of hospital stay, and urinary incontinence. Quality assessment was performed using the Newcastle-Ottawa Scale and Cochrane Collaboration's tool. Pooled treatment effects were estimated using odds ratios with 95% confidence intervals (CIs) for binary endpoints. Heterogeneity was examined using Cochran's *Q* test and I^2 statistics; *p* values < 0.10 and $I^2 > 25\%$ were considered significant for heterogeneity. We used Mantel-Haenszel fixed-effect models in the analyses with low heterogeneity. Otherwise, the DerSimonian and Laird random-effects model was used.

Results: The initial search yielded 510 results. After the removal of duplicate records and application of the exclusion criterion, 9 studies were fully reviewed for eligibility. Three randomized controlled trials and 5 retrospective cohorts met all the inclusion criteria, comprising 2261 patients, of whom 1073 (47.4%) underwent PIF. Six studies reported a significant reduction in SLC in the PIF group, and 3 of the 4 studies reported LC formation yielded significant results in preventing this complication. The incidence of SLC and LC formation in a follow-up of ≥3 months was significantly different between the PIF and no PIF group (odds ratio, 0.34 [95% CI, 0.16–0.74; $p = 0.006$] and 0.48 [95% CI, 0.31–0.74; $p = 0.0008$]), respectively. The safety outcomes did not differ significantly between the 2 groups.

Conclusions: These results suggest that PIF is an effective and safe technique for preventing LC and SLC in patients undergoing transperitoneal robot-assisted radical prostatectomy and pelvic lymph node dissection.

Keywords: Robot-assisted radical prostatectomy; Lymphocele; Peritoneal reapproximation; Peritoneal interpolated flap; Meta-analysis

1. Introduction

Robot-assisted radical prostatectomy (RARP) has emerged as the new standard of care for surgical treatment of nonmetastatic prostate cancer because of its adequate oncological and functional results.[1,2] Intraoperative pelvic lymph node dissection (PLND) may be required, depending on the preoperative risk profile of the patient. Current guidelines recommend that extended PLND should be performed in intermediate- and high-risk patients.[3,4] The most common complication following PLND is lymphocele (LC) formation, with an incidence of 2% to 61%.[5,6] In most cases, LC is clinically asymptomatic,[7] and the rate of symptomatic lymphocele (SLC) is 2% to 10%.[8–10] Symptomatic lymphocele is an important morbidity factor after RARP owing to its association with infection, pelvic pain, lower limb edema, lower urinary tract symptoms, and venous thromboembolism.[11]

In recent years, modifications of extended PLND techniques have been examined for their potential to prevent SLC. Specifically, for transperitoneal RARP, Lebeis et al.[12] introduced the peritoneal interposition flap (PIF) in 2015. After this, several studies have evaluated the reapproximation of peritoneal flaps following extended PLND and RARP in the prevention of SLC. In a previous meta-analysis of retrospective studies, the role of PIF in preventing SLC remained unclear, as data from retrospective studies conflicted with the only clinical trial published at the time.[13] However, new studies have been conducted, including randomized trials that may strengthen the power of the pooled outcomes. Furthermore, a prior meta-analysis did not specifically investigate the

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Table 1

Characteristics of included studies and data extraction for meta-analysis.

Study	Study design	Surgical approach	Surgeons (learning curve)	No. patients, PIF/no PIF	SLC (%) PIF/no PIF	LC formation, PIF/no PIF, %	No. lymph nodes removed,* PIF/no PIF	BMI,* PIF/no PIF, kg/m^2	Age,* PIF/no PIF, yr	PSA,* PIF/no PIF, ng/mL	Gleason >7 (ISUP GG 4 or 5), PIF/no PIF, %	Operation time,* PIF/no PIF, min	Estimated blood loss,* PIF/no PIF, mL	Length of hospital stay,* PIF/no PIF, d	Mean follow-up between groups, mo
Lebeis et al.,[12] 2015	Retrospective cohort	RARP + PLND	2 (RARP ≥400)	77/77	0/11.6†	NA	3.81/4.19	28.89/29.33	60.41/60.74	7.12/7.08	NA	NA	235.36/201.3	1.14/1.25	12.7
Dal Moro and Zattoni,[17] 2017	Retrospective cohort	RARP + PLND	1 (NA)	176/195	0.6/4.1†	NA	10/5†	NA	NA	NA	NA	NA	NA	NA	44.7
Stolzenburg et al.,[18] 2018	Retrospective cohort	RARP or LRP + ePLND	4 (NA)	193/193	1.0/4.7†	3.1/12.9†	15/15	26.85/27.13	64/64	8.7/9	23.3/30	180/183.9	210/250	NA	3
Brundl et al.,[19] 2020	RCT	RARP + PLND	9 (NA)	108/124	8.3/9.7	82.4/85.5	15/16	27.4/27.2	64.5/66	8.1/8.3	15.7/17.8	160/172	180/150	8/8	3
Lee et al.,[20] 2020	Retrospective cohort	RARP + PLND	1 (RARP ≥1000)	117/201	0/6.0†	NA	19/14.7	28.6/29.4	63.6/63.4	9.4/8	25.6/16.4	196.9/178.5†	257.2/219	1.2/1.3	10.6‡
Gloger et al.,[21] 2022	RCT	RARP + PLND	19 (RARP ≥100)	239/236	3.3/8.1†	22/33†	14/14	26/27	65/66	6.9/7.4	16.5/14.7	159/168	150/150	7/7	3
Student et al.,[22] 2022	RCT	RARP + ePLND	2 (RARP ≥500)	123/122	2.4/11.5†	22/41†	17/17	28.1/28.9	66/66	7.2/7.6	39/29.5	145/146	200/200	NA	20
Yılmaz et al.,[23] 2022	Retrospective cohort	RALP + ePLND	2 (RARP ≥100)	40/40	12.5/5	NA	14/15.5	26.47/27.25	65.35/66.2	11.76/16.4	20/20	240/215	200/150†	4.5/3†	16.3

BMI = body mass index; ePLND = extended pelvic lymph node dissection; ISUP GG = International Society of Urological Pathology grade group; LC = lymphocele; LRP = laparoscopic radical prostatectomy; NA = not available; no PIF = no peritoneal interposition flap; PIF = peritoneal interposition flap; PLND = pelvic lymph node dissection; PSA = prostate-specific antigen; RALP = robot-assisted laparoscopic prostatectomy; RARP = robot-assisted radical prostatectomy; RCT = randomized controlled trial; SLC = symptomatic lymphocele.

*Mean or median.

†Reported statistical difference between PIF and no PIF groups.

‡Significant difference in follow-up time reported between the 2 groups.

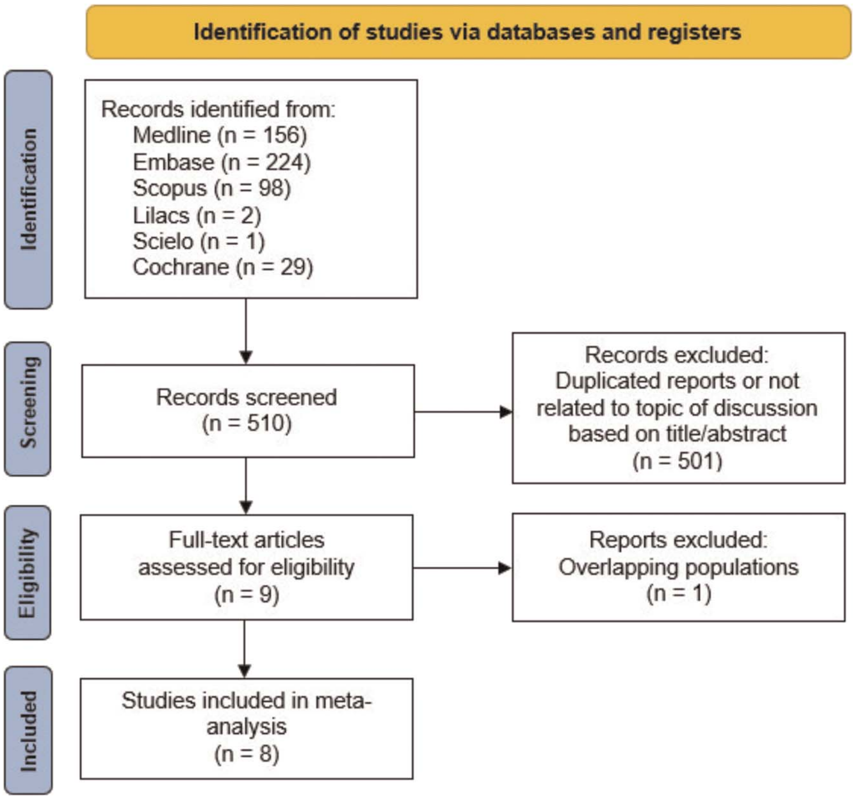

Figure 1. PRISMA flow diagram of the studies identified, excluded, and included in the meta-analysis. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

impact of PIF on LC formation and safety outcomes, such as operation time, estimated blood loss, and length of hospital stay. Therefore, we performed an updated systematic review and meta-analysis to investigate the efficacy and safety of PIF in the prevention of SLC and LC formation following transperitoneal RARP and extended PLND.

Table 2

Systematization of the definition of symptomatic lymphocele used by each study.

Study	Lymphocele measurement method	Definition for symptomatic lymphocele
Lebeis et al.,[12] 2015	Cystography, ultrasound, and computed tomography	Lymphocele with lower abdominal pain, lower urinary tract symptoms, fever, lower extremity swelling, or deep vein thrombosis
Dal Moro and Zattoni,[17] 2017	Ultrasound, computed tomography, or magnetic resonance	Patients with pelvic symptoms such as pelvic fullness, fever, or lower abdominal pain, even if mild, with ultrasound, computed tomography, or magnetic resonance imaging feedback showing a lymphocele
Stolzenburg et al.,[18] 2018	Ultrasound	Patients with a urinary catheter who presented with lower abdominal pain, even if slight, late-onset fever, or lower extremity swelling with concomitant ultrasound feedback showing a lymphocele. Following catheter removal, symptomatic lymphocele was considered in patients who presented with lower abdominal pain, even if slight, late-onset fever, lower urinary tract symptoms, or lower extremity swelling with concomitant ultrasound feedback showing a lymphocele
Brundl et al.,[19] 2020	Ultrasound	Patients with a pelvic collection of lymphatic fluid detected by ultrasound with newly developed voiding abnormalities due to lymphocele formation adjacent to the bladder, deep vein thrombosis, lymphatic drainage disorder, leg swelling, fever, sepsis, and/or abdominal pain in regional relation to the lymphocele (after exclusion of other possible causes)
Lee et al.,[20] 2020	Computed tomography	Symptomatic lymphocele was defined as a lymphocele causing fever, abdominal pain, lower extremity pain and/or swelling, lower urinary tract symptoms, deep vein thrombosis, or pulmonary embolism. Patients with clinical symptoms of symptomatic lymphocele underwent computed tomography scans of the abdomen and pelvis to confirm the diagnosis
Gloger et al.,[21] 2022	Ultrasound	Patients with lymphocele on ultrasound who presented with pain, subsequent deep vein thrombosis with compression of the ipsilateral iliac vein, ipsilateral leg swelling, fever, and hydronephrosis
Student et al.,[22] 2022	Computed tomography	Patients with lymphocele on computed tomography that caused severe pain (visual analog scale score 8–10, located in the area of the lymphocele, and following exclusion of other potential causes), infection, and deep vein thrombosis with/without swelling of the extremities
Yılmaz et al.,[23] 2022	Cystography, ultrasound, and computed tomography	Lymphocele that causes fever, abdominal pain, lower extremity pain, and/or swelling, and/or lower urinary tract symptoms, and/or as a lymphocele associated with a deep vein thrombosis, and/or pulmonary embolism. Patients with clinical symptoms of symptomatic lymphocele were administered lymphocele cystography, ultrasonography, and a computed tomography scan to confirm the diagnosis of symptomatic lymphocele

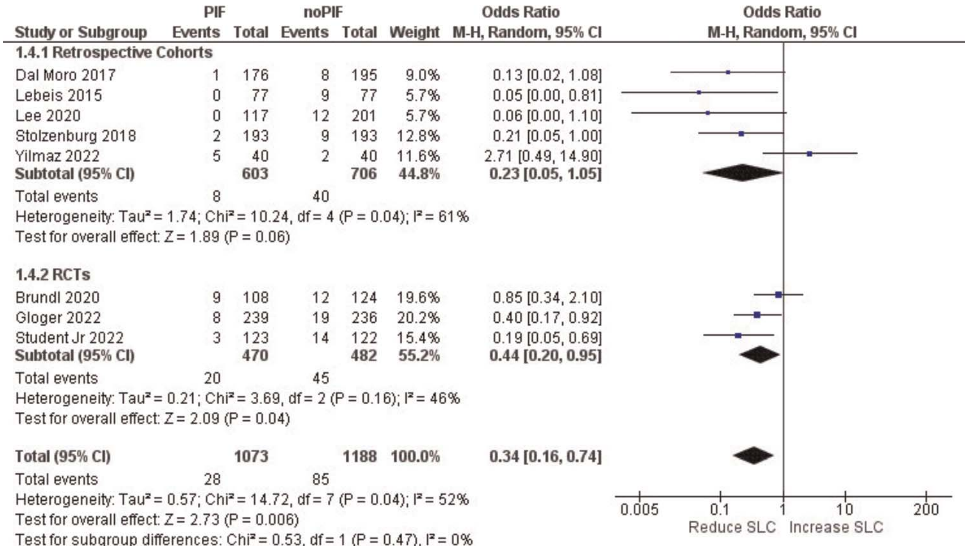

Figure 2. The incidence of symptomatic lymphocele was significantly lower in the PIF group (p = 0.006). CI = confidence interval; M-H = Mantel-Haenszel method; PIF = peritoneal interposition flap; RCTs = randomized controlled trials; SLC = symptomatic lymphocele.

2. Materials and methods

2.1. Search strategy and selection criteria

The present systematic review and meta-analysis was performed in accordance with the recommendations of the Cochrane Collaboration and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement guidelines.[14] We systematically searched the MEDLINE, EMBASE, Scopus, LILACS, SciELO, and Cochrane databases for studies published until December 2022 using the following combination of medical subject heading terms: ((Peritoneal Flap) OR (peritoneal) OR (interposition) OR (fixation) OR (reapproximation)) AND ((robot-assisted radical prostatectomy) OR (RARP) OR (laparoscopic radical prostatectomy) OR (LRP)) AND ((Symptomatic Lymphoceles) OR (Lymphocele) OR (Complications)). References from the included studies and previous systematic reviews were also manually searched.

Inclusion in this meta-analysis was restricted to studies that met all the following eligibility criteria: (1) randomized controlled trials (RCTs) or nonrandomized cohorts; (2) studies comparing peritoneal flap interposition with no peritoneal flap interposition; (3) those in patients undergoing transperitoneal RARP or transperitoneal laparoscopic radical prostatectomy; and (4) those reporting SLC as an outcome. The exclusion criteria were as follows: studies with (1) no control group, (2) extraperitoneal approach, (3) open radical prostatectomy, (4) conference abstracts, (5) study protocol, and (6) overlapping patient populations. In the last case, only the most recent study was included.

2.2. End points and quality assessment

The primary outcomes of interest were the incidence of SLC and LC formation, as defined in each study. The safety outcomes included operation time, estimated blood loss, length of hospital stay, and urinary incontinence. The Newcastle-Ottawa Scale (NOS) was used for the quality assessment of cohort studies.[15] Using this scale, each study received a total of 0 to 9 stars, which reflected the methodological quality of participant selection, comparability of groups, and outcome assessment. We considered high-quality studies as those with NOS ≥7. The quality assessment of RCTs was performed using the Cochrane Collaboration tool for assessing the risk of bias in randomized trials.[16] Publication bias was assessed using a funnel

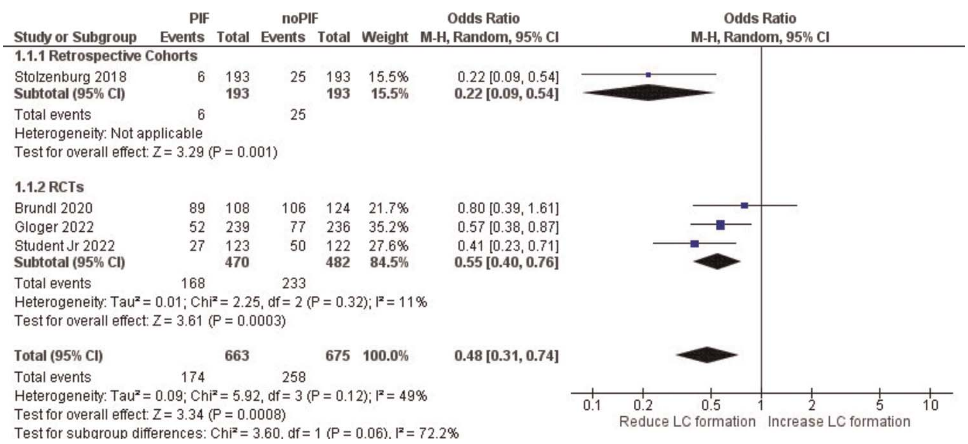

Figure 3. The incidence of lymphocele formation was significantly lower in the PIF group (p = 0.0008). CI = confidence interval; LC = lymphocele; M-H = Mantel-Haenszel method; PIF = peritoneal interposition flap; RCTs = randomized controlled trials.

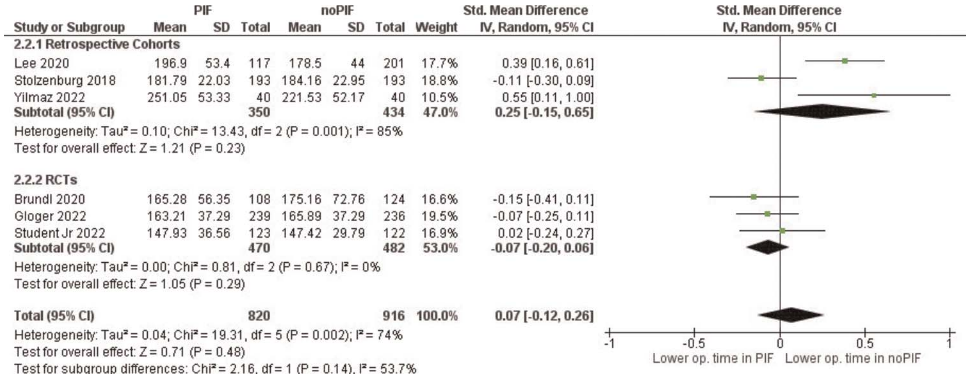

Figure 4. Operation time was not significantly different between groups (p = 0.48). CI = confidence interval; IV = inverse variance method; Op. time = operation time; PIF = peritoneal interposition flap; RCTs = randomized controlled trials.

plot analysis of the primary outcome and evaluation of symmetrical distribution of trials with similar weights. A pooled analysis of confounding factors, body mass index (BMI), and number of lymph nodes removed was performed to assess group comparability.

2.3. Data extraction and statistical analysis

Two authors (J.H.S.P. and L.V.S.R.) independently extracted the baseline characteristics (Table 1) and outcome data using prespecified criteria for search, data extraction, and quality assessment. Disagreements were resolved by consensus among 3 authors (J.H.S.P., L.V.S.R., and J.P.M.). Pooled treatment effects were estimated using odds ratios (ORs) with 95% confidence intervals (CIs) for binary endpoints. Weighted mean differences were used to pool continuous outcomes. Heterogeneity was examined using Cochran's Q test and I^2 statistics. $p < 0.10$ and $I^2 > 25\%$ were considered significant for heterogeneity. We applied the Mantel-Haenszel fixed-effect models in the analyses with low heterogeneity. Otherwise, the DerSimonian and Laird random-effects model was used. Review Manager 5.4 (Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark) was used for statistical analysis.

3. Results

3.1. Study selection and characteristics

As illustrated in Figure 1, the initial search yielded 510 results. Nine studies were fully reviewed for eligibility after the removal of duplicate records and of studies with an exclusion criterion based on title/abstract review. Of these, 1 study was excluded because of a population overlap. Finally, 8 published articles,[12,17–23] including 3 RCTs[19,21,22] and 5 retrospective cohorts,[12,17,18,20,23] met all the inclusion criteria for this systematic review and meta-analysis. Ultimately, a nonoverlapping population of 2261 patients was included, of whom 1073 (47.4%) underwent PIF. The study's characteristics are presented in Table 1. The median number of surgeons was 2, and among studies reporting a learning curve, the minimum value was 100 RARPs. In all studies, the mean or median age was 60 to 70 years, and the mean or median BMI was in the overweight range. Among the studies reporting the Gleason score, approximately 20% of patients had a Gleason score >7.

The majority of studies used ultrasound or computed tomography to assess the presence of LCs. There was no significant heterogeneity in the definition of SLC, as all studies defined it as an LC confirmed by imaging examination resulting in lower abdominal pain, lower urinary tract symptoms, fever, lower extremity swelling, or deep vein thrombosis (Table 2). Overall, 6 studies reported a significant reduction in SLC in the PIF group, and 3 of the 4 studies that reported LC formation had significant results in preventing this complication. Several studies showed significant differences between the PIF and no PIF groups regarding the number of lymph nodes removed, operation time, estimated blood loss, length of hospital stay, and follow-up time. The mean follow-up period between studies was 14.2 months with a minimum of 90 days.

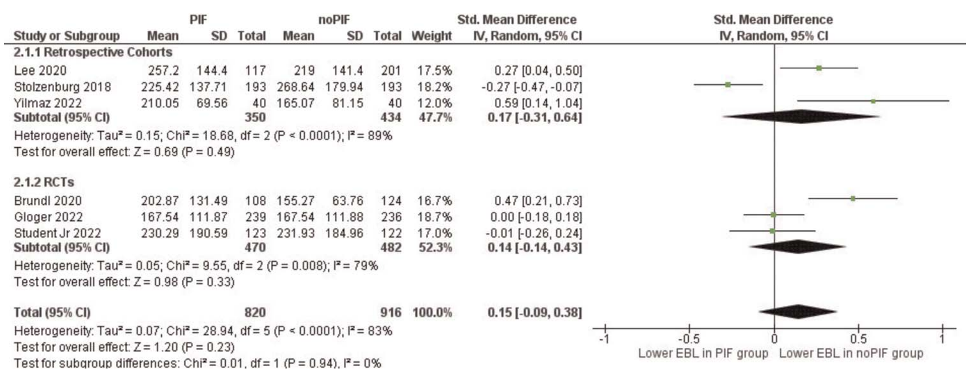

Figure 5. Estimated blood loss was not significantly different between groups (p = 0.23). CI = confidence interval; EBL = estimated blood loss; IV = inverse variance method; PIF = peritoneal interposition flap; RCTs = randomized controlled trials.

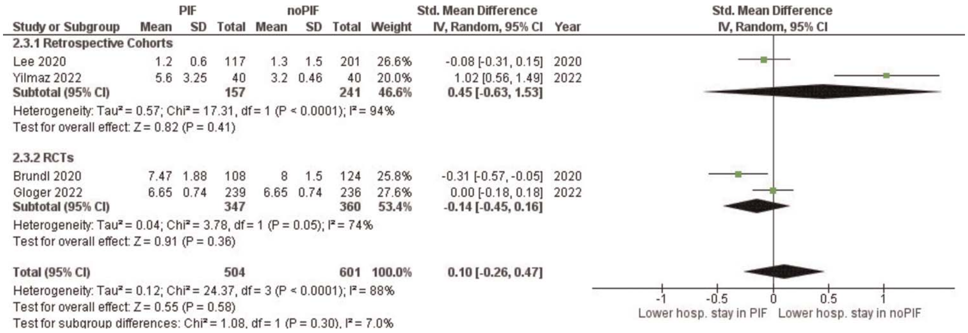

Figure 6. Length of hospital stay was not significantly different between groups (p = 0.58). CI = confidence interval; Hosp. stay = hospital stay; IV = inverse variance method; PIF = peritoneal interposition flap; RCTs = randomized controlled trials.

3.2. Primary outcomes

The incidence of SLC in the follow-up ≥3 months was significantly different between the PIF and no PIF groups (OR, 0.34; 95% CI, 0.16–0.74; p = 0.006; Fig. 2). The separate results for retrospective cohorts and RCTs were as follows: OR of 0.23 (95% CI, 0.05–1.05; p = 0.06; Fig. 2) and OR of 0.44 (95% CI, 0.2–0.95; p = 0.04; Fig. 2), respectively. The incidence of LC formation in a follow-up ≥3 months was significantly different between the PIF and no PIF group in the pooled analysis of 4 studies that reported LC formation (OR, 0.48; 95% CI, 0.31–0.74; p = 0.0008; Fig. 3). We found heterogeneity across all studies in terms of these analyses of primary outcomes, although I^2 statistics were equal (I^2, 52% [p = 0.04; Fig. 2] and I^2, 49% [p = 0.12; Fig. 3], respectively). Therefore, a random-effects analysis was applied.

3.3. Safety outcomes

Operation time, estimated blood loss, and length of hospital stay did not statistically differ between the 2 groups, with standardized mean differences of 0.07 (95% CI, −0.12 – 0.26; p = 0.48; Fig. 4), 0.15 (95% CI, −0.09 – 0.38; p = 0.23; Fig. 5), and 0.10 (95% CI, −0.26 – 0.47; p = 0.58; Fig. 6), respectively. Because of the heterogeneity between studies in all these analyses, I^2 statistics were equal (I^2, 74% [p = 0.002; Fig. 4], I^2, 83% [p <.0001; Fig. 5], and I^2, 88%; p <.0001 [Fig. 6]). Therefore, a random-effects model was applied. Between the 2 studies that reported urinary incontinence, there was no significant difference between patients who underwent PIF or not (0.81; 95% CI, 0.56–1.16; p = 0.24; Fig. 7). Although 1 study used the Ingelman-Sundberg scale and another the number of daily pads to assess incontinence, there was no significant heterogeneity in the analysis of the effect (I^2 = 0%; p = 0.61; Fig. 7). Therefore, the fixed-effects model was used.

3.4. Quality assessment

Overall, 3 of the 5 retrospective cohorts were of high quality.[12,18,23] The mean NOS score was 7. All cohorts lost 1 point in the selection domain of the NOS because of the retrospective design. Other studies lost points in the comparability domain of the NOS because the groups did not match baseline characteristics (Table 3). The risk of selection, performance, detection, attrition, and reporting biases was considered low in the 3 RCTs according to the Cochrane Collaboration tool for assessing the risk of bias. Furthermore, one of the RCTs[19] had an unclear risk of bias as it did not report the learning curve of the 9 surgeons in the study (Table 4). The funnel plot analysis of the primary outcome revealed an asymmetric distribution with publication bias in small studies (Fig. 8). Among the predictive factors of LC, there was no significant difference in the number of lymph nodes removed between the groups (0.09; 95% CI, −0.18 – 0.37; p = 0.51; Fig. 9). Although all studies included mean or median BMI in the overweight range, in the pooled analysis of standardized mean differences, patients undergoing PIF had a significantly lower BMI (−0.21; 95% CI, −0.41 – −0.01; p = 0.04; Fig. 10).

4. Discussion

The systematic review and meta-analysis of 8 studies and 2261 patients was performed to compare the interposition of the peritoneal flap in patients undergoing extended PLND and RARP. The main findings from the pooled population analysis were as follows: (1) the incidence of SLC was significantly lower in the PIF group at a follow-up of ≥3 months; (2) the incidence of LC formation was significantly lower in the PIF group at a follow-up of ≥3 months; (3) the operation time, estimated blood loss, and length of hospital stay were lower in the no PIF group, although the difference was not statistically significant; and (4) there was no significant difference in the 90-day postoperative urinary incontinence rate between the 2 groups.

Although the first finding was demonstrated in a previous meta-analysis,[13] the present study has several unique characteristics

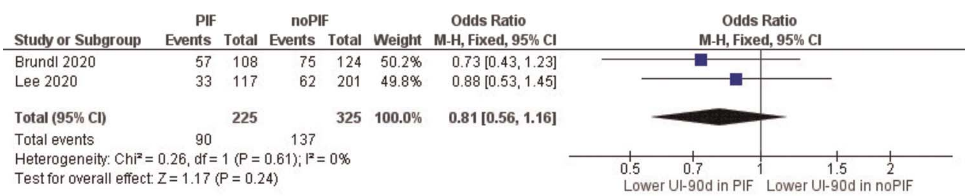

Figure 7. Urinary incontinence was not significantly different between groups (p = 0.24). CI = confidence interval; M-H = Mantel-Haenszel method; PIF = peritoneal interposition flap; UI-90d = 90-day urinary incontinence rate.

Table 3

Newcastle-Ottawa Scale for cohort studies.

	Selection				Comparability		Outcome			
Study	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Demonstration that the outcome of interest was not present at the start of the study	Comparability of cohorts based on the design or analysis		Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up of cohorts	Score
Lebeis et al.,[12] 2015	1	1	1	0	1	1	1	1	1	8
Dal moro 2017	1	1	1	0	0	0	1	1	1	6
Stolzenburg et al.,[18] 2018	1	1	1	0	1	1	1	1	1	8
Lee et al.,[20] 2020	1	1	1	0	0	0	1	1	1	6
Yılmaz et al.,[23] 2022	1	1	1	0	1	0	1	1	1	7

that strengthen the evidence supporting this conclusion. First, the overall population in the previous study was approximately 58% of the size of our study. Second, we included 3 RCTs in the pooled effect analysis. Third, we found a significantly lower incidence of LC in the PIF group, which corroborates the lower incidence of SLC in these patients.

Preventing LC after extended PLND remains an interesting challenge, for which various solutions have been proposed. Hemostatic agents, such as FloSeal, TachoSil, fibrin glue, and octreotide, were investigated, but no significant results were reported.[24–27] Certain studies showed a lower incidence of LC following RALP with extended PLND using a transperitoneal approach instead of traditional open or extraperitoneal approaches. Therefore, surgeons have started to investigate the peritoneal action in the prevention of LC.[5,28,29] The first technique was bilateral peritoneal fenestration for extraperitoneal radical prostatectomy, which was developed in 2008 by Stolzenburg et al.[30] Analysis of this technique showed that the incidences of LC formation and SLC were significantly lower in the fenestrated group.

Peritoneal interposition flap was first described by Lebeis et al.[12] in 2015. They performed reperitonealization of the anterior and lateral parts of the bladder to optimize drainage of the lymphatic fluid by creating a larger drainage area from the PLND bed toward the intraperitoneal cavity. Excellent results were achieved with 0% SLC incidence among 77 patients compared with 11.6% in the control group. External validation of Lebeis and colleagues'[12] technique was performed by Lee et al.[20] in a retrospective study that noted a significantly lower incidence of SLC in the PIF group. Variations of Lebeis and colleagues'[12] technique have been described by Stolzenburg et al.[18] and Dal Moro and Zattoni,[17] achieving significant results in preventing LC formation and SLC.

On the other hand, Boğa et al.[31] in 2020 and Yılmaz et al.[23] in 2022 concluded that PIF does not affect the incidence of SLC and reported a higher number of SLC in the PIF group. An important limitation of these studies was that the surgeons differed between groups. Moreover, the group undergoing PIF exhibited significantly higher intraoperative bleeding and a longer hospitalization time. As these studies were conducted with the same patients, we included only the most recent one. The study by Yılmaz et al.[23] was the only one to have a negative effect in our analysis and was the largest source of heterogeneity. This study included 3 groups of patients: a control group, a PIF group, and a half PIF group. However, as none of the other studies evaluated unilateral PIF, we included only the PIF group and the control group in our analysis.

The effect of PIF has recently been investigated by Brundl et al.[19] (PIANOFORTE) and Gloger et al.[21] (ProLy) in RCTs. The studies had a similar design using the same technique described by Lebeis et al.[12] and an ultrasound-based investigation at a 90-day follow-up. Although the sample size from the ProLy study (475 patients) was more than double that of the PIANOFORTE study (232 patients), both reported a lower incidence of LC formation and SLC in the PIF group. Nonetheless, these differences were statistically significant only in the ProLy study. Differences in the sample sizes and exclusion rates may explain the divergent findings between the 2 trials. Student et al.[22] published the most recent RCT (PerFix) that evaluated the impact of PIF on LC formation on 245 patients and found a significantly lower incidence of SLC in the group undergoing PIF ($p = 0.011$).

The main predictors of LC described in the literature are high BMI, high-grade tumors, and the number of lymph nodes removed.[32–34] Among the studies included in our analysis that reported the mean or median BMI of each group, all were overweight. Although the difference between the standardized means was significant, the difference between the final means of the 2 groups was only 0.51 points. As all groups in all studies were within a similar BMI range, we hypothesize that this factor did not influence the lower incidence of LC and SLC in the PIF group.

We found no difference in the number of high-grade tumors between the groups in the included studies. Regarding the number of lymph nodes removed, in the pooled analysis of this predictive factor, we found no significant difference between the groups. Only Dal Moro and Zattoni[17] showed a significant difference in the number of lymph nodes removed; however, the control group had

Table 4

Cochrane Collaboration's tool for assessing risk of bias.

Study	Selection bias	Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias
Brundl et al.,[19] 2020	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear
Gloger et al.,[21] 2022	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Student et al.,[22] 2022	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

"Other bias" column was based on reported surgeon experience and the balance of surgical outcomes (lymph node count, estimated blood loss, operation time, and length of hospital stay) between study groups.

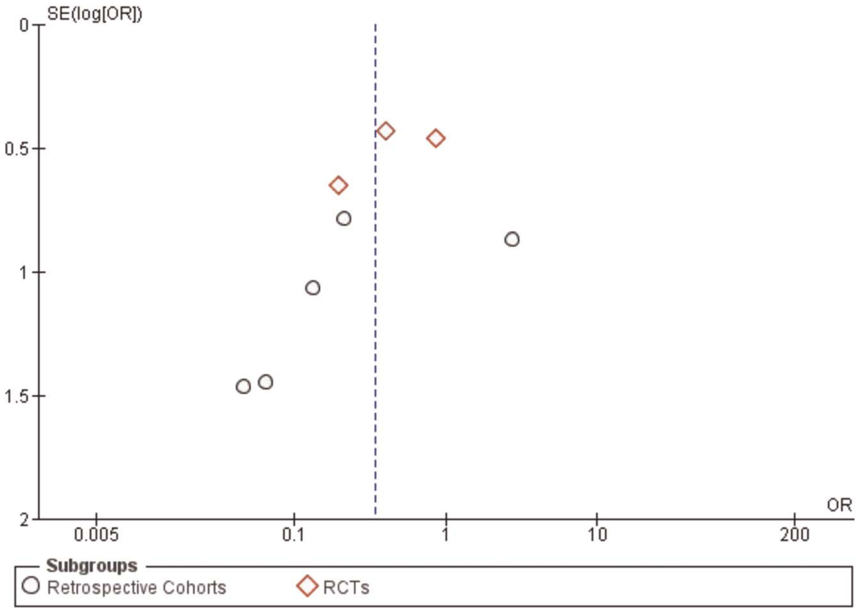

Figure 8. The funnel plot analysis shows an asymmetric distribution with publication bias among small studies. OR = odds ratio; RCTs =randomized controlled trials; SE = standard error.

the lowest number of lymph nodes removed. Therefore, this difference did not influence the result, as the control group presented more LC even with a more conservative PLND.

Other risk factors for LC are a long operative time and the use of low-molecular-weight heparin.[33,34] Only Lebeis et al.[12] reported a significantly longer operative time in the PIF group; however, as none of the patients undergoing PIF had SLC, this did not influence this outcome. Except for Stolzenburg et al.[18] and Brundl et al.,[19] all studies used heparin antithrombotic prophylaxis in both groups. According to the European Association of Urology guidelines on thromboprophylaxis in urological surgery,[35] antithrombotic prophylaxis is recommended for RARP, with PLND in patients at high risk for thromboembolism and for RARP with extended PLND in patients at medium or high risk of thromboembolism.

The safety of the technique was evaluated among the studies that investigated the impact of PIF on urinary continence or complications unrelated to LC, and unfavorable results were not observed.[19,20] In the pooled analysis of the 2 studies that reported the 90-day urinary incontinence rate, we found less incontinence in patients undergoing PIF, although the difference was not significant. Nevertheless, PIF did not have a negative impact on continence in this meta-analysis. Although the operation time, estimated blood loss, and length of hospital stay were shorter in patients with no PIF (control group) in the pooled analysis, these differences were not statistically significant. The shortest follow-up time in the included studies was 90 days. This is adequate for LC-related outcomes as the median time for SLC onset reported in the literature is 22 to 63 days.[36]

Limitations

This study has several limitations. First, 5 of the 8 included studies were nonrandomized. Despite the adequate quality of the retrospective studies, 2 studies[17,20] had a NOS score lower than 7 as they included groups with significant differences in at least 1 LC predictor. The bias of the retrospective studies was confirmed by

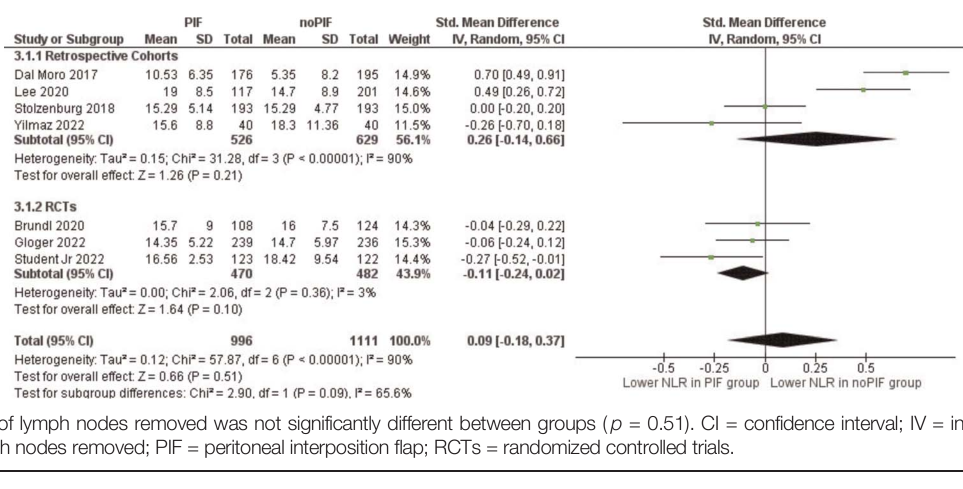

Figure 9. The number of lymph nodes removed was not significantly different between groups (p = 0.51). CI = confidence interval; IV = inverse variance method; NLR = number of lymph nodes removed; PIF = peritoneal interposition flap; RCTs = randomized controlled trials.

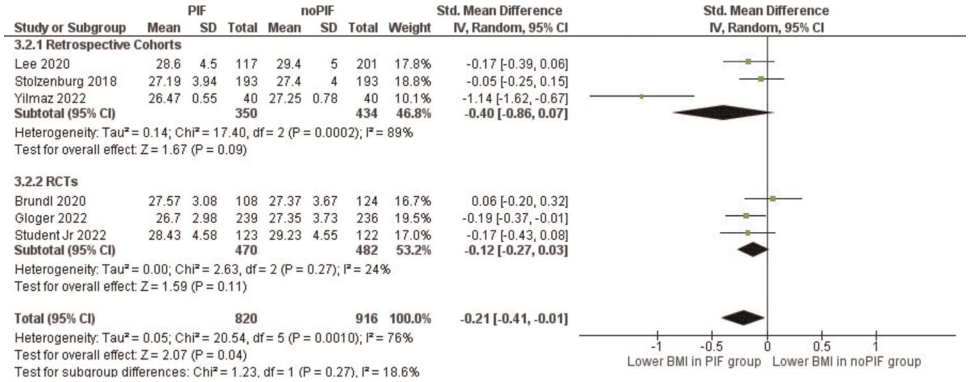

Figure 10. Body mass index was significantly lower in the PIF group (p = 0.04). BMI = body mass index; CI = confidence interval; IV = inverse variance method; PIF = peritoneal interposition flap; RCTs = randomized controlled trials.

asymmetric distribution in the funnel plot analysis. Second, most studies started with the presence of LC symptoms to perform imaging confirmation with methods that varied between studies (cystography, ultrasonography, and computed tomography). Only 4 studies[18,19,21,22] reported LC formation as an outcome, which reduced the power of our analysis. Third, to enable the analysis of safety outcomes and confounding factors, we estimated through statistical tools the mean and SD from the median and interquartile range reported by several of the included studies.[37–39] Data from Lebeis et al.[12] were not included in the safety outcomes and confounding factors, as a measure of the variance of outcomes was not reported. Finally, the statistically significant result of SLC reduction in the PIF group appeared only in the pooled result of all included studies and in the RCT subgroup. However, it was not significant among the retrospective cohorts. Although the 3 RCTs[19,21,22] included in our meta-analysis had a low risk of bias, they represented only 42% of the total number of patients in this study. In the future, the results of another ongoing RCT (Pelycan) should clarify the benefits of PIF in preventing SLC.[40]

5. Conclusions

In conclusion, the results of the present meta-analysis, which included 2261 patients, suggest that PIF is an effective and safe technique for the prevention of LC and SLC in patients undergoing transperitoneal RARP and extended PLND. However, this result is predominantly based on retrospective data. Therefore, further multicenter, randomized prospective studies are needed to strengthen these observations.

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None

Statement of ethics

The present systematic review and meta–analysis was performed in accordance with the recommendations of the Cochrane Collaboration and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement guidelines.

Conflict of interest statement

No conflict of interest has been declared by the authors.

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Author contributions

JHSP: Research design, writing of the paper, performance of the research, data collection, analysis, and interpretation;
LVSR: Writing of the paper, performance of the research and data collection;
JPM: Writing of the paper, analysis and interpretation;
All authors: Critical revision of the article and final approval.

Data availability

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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