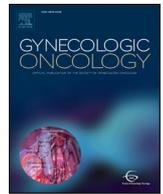




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Review Article

The application of fibrin sealant for the prevention of lymphocele after lymphadenectomy in patients with gynecological malignancies: A systematic review and meta-analysis of randomized controlled trials



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HIGHLIGHTS

- Fibrin sealant agents reduced the duration and volume of drainage after lymphadenectomy for gynecological malignancies.
- They were not associated with difference in the incidence of lymphocele (overall or symptomatic).
- Further studies are required to broaden our knowledge on the impact of those agents in lymphocele prevention.

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ABSTRACT

Purpose. The aim of the present study was to evaluate the correlation between the use of fibrin-collagen sealants on lymph node dissection areas and formation of lymphocele after lymphadenectomy in patients with gynecological malignancies.

Materials and methods. A systematic search of 5 electronic databases for articles published up to November 2018 was performed. All randomized controlled clinical trials (RCTs) which reported outcomes after application of fibrin collagen agents in patients who underwent lymphadenectomy for gynecological malignancies, were finally included in the present meta-analysis. Statistical meta-analysis was performed using the RevMan 5.3 software.

Results. A total of 6 RCTs which recruited 481 patients were included in the present study. Meta-analysis revealed significantly decreased total amount of drained fluid and of mean duration of drainage in fibrin sealant group when compared to control, (187 patients MD −86.40 ml 95% CI −100.2 to −72.60 p < 0.00001 and 113 patients MD −1.00 days 95% CI −1.13 to −0.87 p < 0.00001, respectively). No difference in overall incidence of lymphocele and in the incidence of symptomatic ones among the two groups was observed (592 cases OR 0.61 95% CI 0.36 to 1.05 p = 0.08, and 444 cases OR 0.59 95% CI 0.26 to 1.35 p = 0.22, respectively).

Conclusions. The present meta-analysis supports the safety of the use of fibrin sealants in women undergoing pelvic and/or para-aortic lymphadenectomy due to gynecologic cancer but its benefit remains uncertain. It was found effective in reducing the duration and volume of drainage, but it was not associated with difference in the incidence of lymphocele. Further studies are required to confirm our conclusion and broaden our knowledge about its impact on other parameters.

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1. Introduction

Pelvic and para-aortic lymph node dissection is considered indispensable part of surgery for the management of some cases of gynecological malignancies. The extent and the necessity of this procedure is based on tumor characteristics which are assessed pre- or intraoperatively. It offers surgical staging as well as treatment in case of nodal metastasis. Several studies have reported on the benefits of lymph node dissection on progression free survival and overall survival rates especially in cases of advanced ovarian cancer (OC) when combined with complete cytoreduction [1,2]. Nonetheless, the LION trial reported no survival benefit after lymphadenectomy of clinically negative lymph nodes in patients with advanced epithelial OC [3]. In patients with cervical and endometrial cancer (EC) full lymphadenectomy or selective lymph node sampling is recommended [4]. However, pelvic and/or paraaortic lymphadenectomy have been associated with possible intra- or postoperative complications such as nerve or vessel injury, lymphedema, and asymptomatic or symptomatic lymphocele formation.

The reported incidence of overall lymphocele after lymphadenectomy for gynecological malignancies is estimated in about 20.2%, while symptomatic lymphoceles occur in 5.8% of treated patients [5]. The aforementioned complication is potentially severe and in some cases a surgical intervention is needed. A variety of interventions to reduce the incidence of lymphocele after lymphadenectomy have been proposed. Among them the use of fibrin-collagen coated patches of various origins attached to the area of lymphadenectomy have been proposed. Fibrin-collagen coated patches have been applied as a surgical hemostatic in cardiovascular, hepatic, pulmonary and kidney surgeries [6,7]. Outcomes from studies about the efficacy of this patch in preventing development of lymphocele after lymph node dissection for cancer are controversial; Some presented significant reduction of lymphocele's incidence [8,9], while others did not find differences [10]. According to a recent meta-analysis fibrin-collagen coated patch reduced the incidence of lymphocele after axillary, para-aortic, pelvic or inguinal lymphadenectomy [11]. However, the exact role of fibrin sealants in the prevention of lymphadenectomy after pelvic and/or paraaortic lymphadenectomy for gynecological malignancies still remains elusive. The objective of the present systematic review was to evaluate the correlation between the use of fibrin-collagen coated patch on lymph node dissection areas and formation of lymphocele after lymphadenectomy in patients with gynecological malignancies.

2. Materials and methods

2.1. Search strategy and eligibility of studies

The present meta-analysis was performed in accordance with the guidelines for Systematic Reviews and Meta-analyses (PRISMA) based

on the authors' predetermined inclusion criteria [12]. Selection of abstracts was conducted by three authors (AP, AF and MD) who independently search the literature. No language restrictions were applied. All randomized controlled clinical trials (RCTs) which reported outcomes after application of fibrin collagen sealant agents of different forms of application in patients who underwent pelvic and/or para-aortic lymphadenectomy for gynecological malignancies through open or laparoscopic approach, were finally considered eligible for inclusion in the present meta-analysis. Case reports, reviews and animal studies were excluded from the present meta-analysis. Accordingly, non-randomized (prospective or retrospective) observational studies were excluded from tabulation. Each author independently reviewed the literature; the discrepancies during the data collection were then resolved by consensus of all authors.

2.2. Literature search and data collection

A systematic search of the Medline (1966–2018), Scopus (2004–2018), Google Scholar (2004–2018), Cochrane CENTRAL Register of Controlled Trials and Clinicaltrials.gov databases for articles published up to November 2018 was performed. Reference lists of articles which were retrieved in full text, were systematically searched for relevant articles in the field. The following key words were used for the search: “fibrin sealant”, “fibrin patch”, “tachosil”, “lymphadenectomy”, “pelvic lymphadenectomy”, “para-aortic lymphadenectomy”, “gynecological malignancy”, “lymphocele”, “lymphocele prevention”. The PRISMA flow diagram schematically presents the stages of article selection (Fig. 1).

2.3. Quality assessment

The evaluation of the methodological quality of the included studies was made using the tool of Review Manager 5.3 for the assessment of the “Risk of Bias”, according to Cochrane Collaboration Handbook (Fig. 2) [13]. Two authors independently performed the procedure.

2.4. Statistical analysis

Statistical meta-analysis was performed using the RevMan 5.3 software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011). Confidence intervals (CI) were set at 95%. Mean difference (MD) and odds ratios (OR) were used in the analysis. The results were calculated using the DerSimonian-Laird random effect model (REM) revealing significant heterogeneity in the methodological characteristics of the included studies [14]. The cut-off for statistical significance was set at $p < 0.05$. Mean values and standard deviations were calculated according to the equations proposed by Hozo et al. when not provided by the studies [15]. Publication bias was not tested due to heterogeneity of

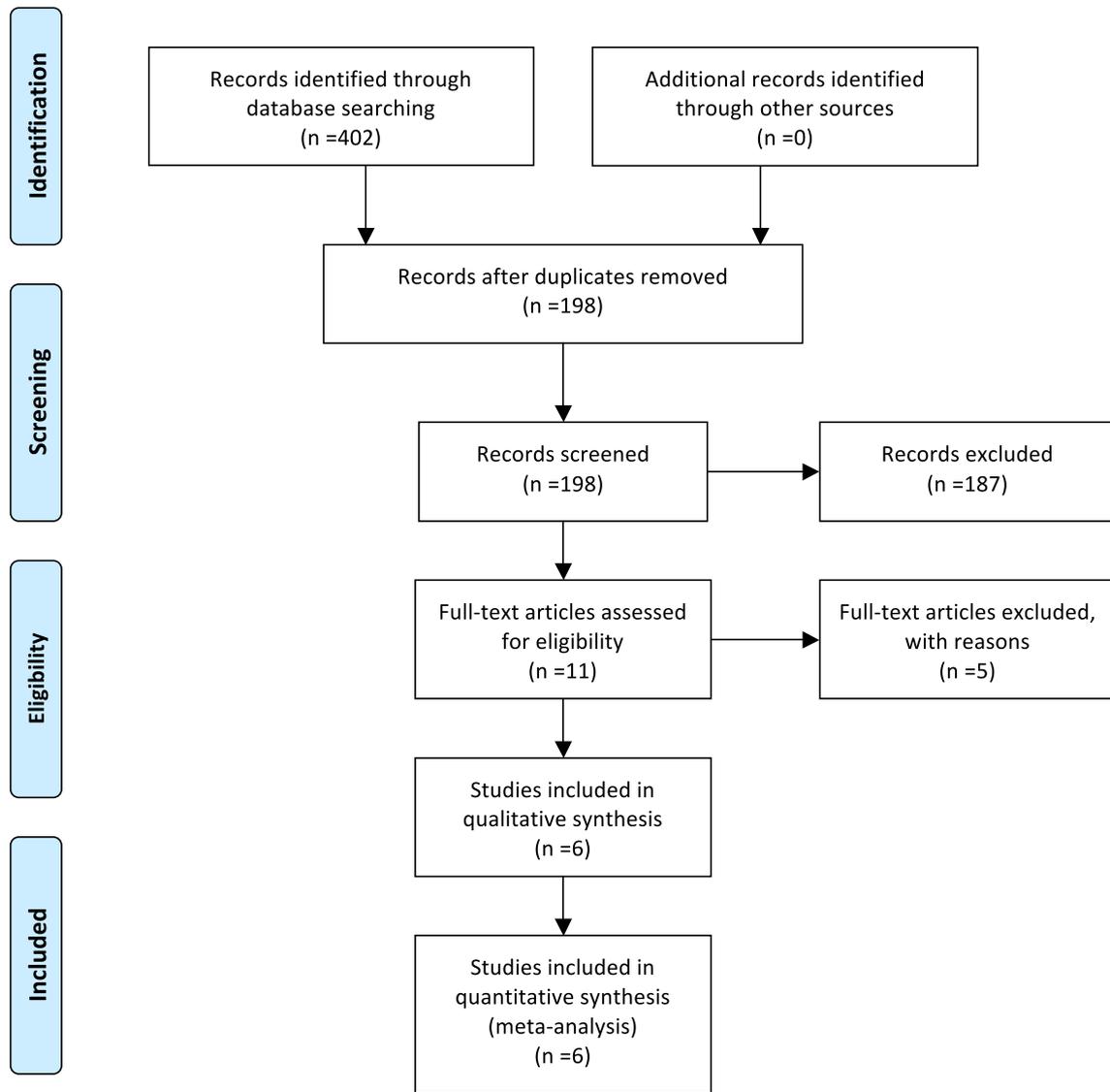


Fig. 1. Search flow diagram.

the included studies, which is a confounder that may influence the methodological integrity of these tests and the limited number of the studies which were included in data analysis.

2.5. Definitions

The presence of lymphocele after surgery was assessed at follow up through imaging including ultrasound, computed tomography or magnetic resonance. Symptomatic lymphocele was defined by the included studies as imaging proved lymphocele which presented with pelvic symptoms such as pelvic discomfort or pain, fever or chills or symptoms from pressure of the surrounding structures and require intervention.

3. Results

3.1. Excluded studies

A total of 5 studies were excluded from the present meta-analysis [10,16–19]. Among them, Carlson et al. despite being RCT, reported outcomes for patients with vulvar carcinoma who underwent inguinal lymphadenectomy and was excluded [16]. Another study was excluded due to heterogeneity among the included groups (fibrin sealant versus drainage) [17]. Furthermore, two studies were excluded since they

were not randomized despite being of interest [10,18]. Finally, another study was a part of an already included study and was excluded [19].

3.2. Included studies

A total of 6 RCTs which included 481 patients with gynecological malignancies who were examined for the impact of application of fibrin sealant enriched agents after lymphadenectomy were included in the present meta-analysis [20–25]. Among them, Kim et al. and Jaunarena et al. utilized and randomized each hemipelvis as treatment and control group and included 37 and 74 patients, respectively [21,22]. For the remaining studies, 178 patients were treated with fibrin sealant (Fibrin sealant group) while the remaining 192 women consisted the control group who underwent lymphadenectomy without application of fibrin sealant (Control group). EC was the primary diagnosis in 232 patients (48.2%) while 113 patients (23.5%) had OC, 126 (26.2%) had cervical cancer and 5 (1.1%) were diagnosed with simultaneous EC and OC. For the remaining patients 2 (0.4%) had fallopian tube cancer, 2 (0.4%) sarcomas and 1 (0.2%) vaginal cancer. All patients underwent lymphadenectomy for staging and/or treatment of their disease; pelvic lymphadenectomy was performed in 271 women whereas the remaining 210 received pelvic and para-aortic lymphadenectomy. The analyzed indices were tabulated in two structured tables as follows:

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
2002; Scholz	+	-	-	-	+	-	+
2011; Tinelli	+	-	-	-	?	-	-
2013; Tinelli	+	-	-	-	?	-	-
2017; Kim	+	+	+	?	+	+	+
2018; Grimm	+	+	?	+	+	?	+
2018; Janarena	+	+	+	?	+	?	+

Fig. 2. RCTs' methodologic quality. Risk of bias summary: “-” represents high risk of bias, “?” represents unclear bias and “+” represents low risk of bias.

methodological and main patients characteristics of the included studies (Table 1), and main postoperative outcomes (Table 2).

3.3. Total volume and duration of drainage

According to the findings of the present meta-analysis, the total amount of drained fluid was significantly decreased in Fibrin sealant group when compared to control, (187 patients MD -86.40 ml 95% CI -100.2 to -72.60 $p < 0.00001$ data derived from 3 studies) Fig. 3. The same was also observed in case of mean duration of drainage (113 patients MD -1.00 days 95% CI -1.13 to -0.87 $p < 0.00001$, data derived from 2 studies).

3.4. Lymphocele rates (overall, symptomatic and intervention) and other complications

Neither total lymphocele rates nor the proportion of symptomatic lymphoceles separately, were found different when fibrin sealant group was compared with control (592 cases, 26% vs 33.7% OR 0.61 95% CI 0.36 to 1.05 $p = 0.08$, data derived from 6 studies and 444 cases, 6.1% vs 9.6% OR 0.59 95% CI 0.26 to 1.35 $p = 0.22$, respectively, data derived from 5 studies) Fig. 4A and Fig. 4B, respectively. Similarly, the two groups did not differ with regards to cases of lymphocele that required intervention (203 patients OR 0.43 95% CI 0.14 to 1.33 $p =$

0.14, data derived from 3 studies). Finally, as shown in Table 2 operative intervention was required only for the patients with symptomatic lymphocele included in the study of Scholz et al. (3 vs 4 cases, in each group) while for the remaining symptomatic lymphocele cases less invasive techniques were applied. Apart from lymphadenectomy-related complications, Jaunarena et al. reported 4 patients who developed vascular complications and Scholz et al. recorded 3 patients from the fibrin sealant group and 8 from the control who developed deep vein thrombosis (Table 2) [21,23].

4. Discussion

Our study aimed to evaluate the efficacy of fibrin sealant patches in prevention of lymphocele formation in areas of pelvic or para-aortic lymphadenectomy in women with gynecological malignancies. Meta-analysis failed to reveal significant effect of application of fibrin sealant after lymphadenectomy with regards to incidence lymphocele (both overall and symptomatic). On the other hand, the total volume and duration of drainage were found significantly reduced in fibrin sealant group.

Fibrin-collagen coated patches and fibrin glue were primarily introduced as hemostatic agents and find clinical application in cardiovascular, liver, lung, gynecological and urological surgery. Furthermore, their role in tissue recovery, regeneration and faster healing has also been investigated [26]. In that setting, they are widely utilized in meningomyelocele closure [27], in microneurosurgery [28], in skull base surgeries [29], in distal pancreatectomy [30] or in gastrointestinal anastomoses [31]. The patch triggers the coagulation process by activating the reaction of fibrinogen and thrombin. Upon contact with a bleeding surface, the fibrinogen-thrombin reaction transforms the active fibrinogen to fibrin and promotes the formation of the fibrin clot. Various types of fibrin sealant patches have been used worldwide. For instance, the fibrin sealant TachoComb comprises a collagen patch coated with human fibrinogen, bovine thrombin and aprotinin. Newer patches use instead of bovine, human thrombin such as TachoSil and Evarrest, in order to avoid potential immunogenic reaction [32] or anaphylaxis caused by bovine aprotinin [33]. Tachosil patch was the most common fibrin agent that was applied in patients from the studies included in the present study, followed by Tissucol and Floseal (Table 1).

The efficacy of fibrin sealant in the prevention of lymphoceles has been investigated in various malignancies. Simonato et al. [8] proposed Tachosil as a useful agent in the prevention of lymphocele in patients who underwent radical prostatectomy and pelvic lymphadenectomy. A systematic review by Marchioni et al. [34] evaluated the effectiveness of these products in incidence of lymphocele after urological procedures but small difference was observed between the groups. The same was also observed by Weber et al. [9], who studied the impact of surgical sealing patches on the drainage of breast cancer patients who underwent axillary dissection. However, an RCT by Dinsmore et al. [35] reported increased drainage volume, duration of drainage and complication rates after fibrin glue application in patients who underwent modified radical mastectomy.

A recent meta-analysis by Gasparri et al. [11] reported outcomes of 720 patients from 10 studies and evaluated the impact of fibrinogen sealant patches on lymphatic reaction after lymphadenectomy for different types of malignancy. They found significantly decreased duration and total volume of lymph drainage, lower lymphocele incidence (symptomatic or not) and less postoperative procedures for drainage. No difference was reported with regards to wound or lymphocele infection and hospital stay. On the contrary, the present meta-analysis proved that despite the fact that fibrin sealant resulted in significant reduction in the volume and the duration of lymph drainage, incidence of lymphocele was not significantly decreased with the use of fibrin sealant. One could argue that the meta-analysis by Gasparri et al. presented significant clinical heterogeneity as it evaluated articles which reported outcomes of patients with various types of malignancies such as breast,

Table 1
Main characteristics of the included studies and patients (Fibrin sealant vs control).

Author (year)	Country	Inclusion criteria	Patient no.	Type of malignancy	Age (years)	Type of LN resection (N) (PLND/P&PaLND/PaLND)	No of resected lymph nodes	Type of patch	Type of patch application	Adjuvant chemo/radio
Jaunarena (2018)	Spain	Laparoscopic surgery for EC, CC, OC and laparoscopic pelvic lymphadenectomy; appropriate bone marrow, kidney and liver function; no previous pelvic RT or CT; no haematological disorders or coagulation defects; no history of thromboembolic disease or lymphatic system disorders; no allergy to aprotinin	74 vs 74 (each hemipelvis)	OC 6/74 EC 50/74 CC 16/74 Sarcoma 2/74	58.8 ± 16.4 ^a	Laparoscopic PLND 15/74 P&PaLND 59/74	Pelvic 7.3 ± 3.6 ^a (right) 7.9 ± 4.9 ^a (left) Paraortic 12.508 ± 7.5 ^a	Tissucol Duo® fibrin sealant	Spray of 5 ml of sealant to the treated hemipelvis	N/A
Grimm (2018)	Germany Czech Republic & Austria	Open or laparoscopic surgery for EC, CC or OC; bilateral PLND; age 18–70	75 vs 89	OC 30 vs 23 EC 17 vs 30 CC 28 vs 36	57.1 ± 12.8 ^a vs 55.4 ± 13.4 ^a	PLND 30 vs 45 P&PaLND 45 vs 44	Pelvic 30.8 ± 15 ^a vs 31 ± 13.9 ^a Paraortic 23.1 ± 13.2 ^a vs 24.4 ± 11.7 ^a	Tachosil collagen fibrin patch	To the obturator fossa and another to the femoral canal bilateral 4.8 × 4.8 each	NA
Kim YH (2017)	Korea	EC, OC, CC; indication for primary laparotomic surgery with PLND for diagnostic and therapeutic purpose; no expected survival <1 year; no anticipation to experience incomplete PLND due to medical conditions	37 vs 37 (each hemipelvis)	OC 15/37 EC 12/37 CC 10/37	52 (34–70) ^a	PLND 2/37 P&PaLND 35/37	Pelvic 29 (12–70) ^b Paraortic 12 (1–45) ^b	Floseal (gelatin-thrombin matrix)	5 ml of Floseal applied to the treated hemipelvis and compression for 2 minutes with wet gauze	RT 9/37
Scholz (2002)	Austria	N/A	47 vs 46	OC 39 EC 10 CC 36 fallopian tube 2 VC 1 EC & OC 5	45 (22–61) ^a vs 47 (32–62) ^a	PLND 32 vs 34 P&PaLND 15 vs 12	44.5 (30–62) vs 40.8 (18–61)	Tissucol fibrin glue	Spray of 4 ml of a thin layer of fibrin glue to the site of the pelvis and 10 ml to paraaortic region	CT 25 vs 22 RT 5 vs 2
Tinelli (2011)	Italy	Surgery for early EC; no evidence of coagulation disorders	30 vs 28	EC 30 vs 28	58.2 ± 2.8 ^b vs 56.7 ± 4.9 ^b	PLND 30 vs 28	15.9 ± 1.8 ^a vs 16.2 ± 1.3 ^a	Fibrin-collaged coated patch (Tachosil)	9.5 × 4.8 × 0.5 cm, subdivided in two equal patches to place both into the obturator fosse	N/A
Tinelli (2013)	Italy	Laparoscopic surgery early EC; no evidence of coagulation disorders	26 vs 29	EC 26 vs 29	55.6 ± 4.5 ^a vs 57.3 ± 2.3 ^a	PLND 26 vs 29	16.5 ± 1.5 ^a vs 17.0 ± 1.5 ^a	Fibrin-collaged coated patch (Tachosil)	9.5 × 4.8 × 0.5 cm, subdivided in two equal patches to place both into the obturator fosse	N/A

EC: endometrial cancer, OC: ovarian cancer, CC: cervical cancer, VC: vaginal cancer, PLND: pelvic lymph node dissection, P&PaLND: pelvic and paraaortic lymph node, PaLND: paraaortic lymph node dissection CR: Chemotherapy, RT: Radiotherapy, N/A: Not available.

^a Mean ± SD.

^b Median (range).

Table 2
Main postoperative outcomes.

Author (year)	Drainage duration (days) mean \pm SD	Total drainage volume (ml)	Daily drainage volume (ml)	Criteria for drainage removal	Postoperative complications (N)	Lymphocele	Symptomatic lymphocele	Therapy for lymphocele (N)/reoperation (yes/no)	Lymphedema
Jaunarena (2018)	N/A	N/A	N/A	N/A	Vascular complications (4)	14/74 vs 17/74	N/A	N/A	N/A
Grimm (2018)	No drainage	No drainage	No drainage	No drainage	N/A	21/75 vs 21/89	5 vs 3	Pain management (5), antibiotics (3) Drainage through US (3) or CT (1)/no	N/A
Kim YH (2017)	N/A	400 (88–1320) ^b 552 \pm 355.7 ^a vs 620 (102–1390) ^b 683 \pm 371.8 ^a for 3 days	N/A	No sign of active bleeding	N/A	8/37 vs 12/37 (1 week) 5 vs 9 (6 month)	0 vs 1	PC drainage and intravenous antibiotics/no	N/A
Scholz (2002)	N/A	Right: 1247 (0–7455) ^c vs 1469 (0–10,500) ^c Left: 1272 (0–7360) ^c vs 1184 (0–5,160) ^c	(Last 24 h) Right: 184 (5–1280) 413.25 \pm 368.1 vs 253 (10–2400) 729 \pm 689.96 Left: 232(0–1660) 531 \pm 479.2 vs 171 (5–1320) 416.75 \pm 379.6	N/A	DVT (3 vs 8)	20/47 vs 21/46	3 vs 4	Operative intervention (3 vs 4)/yes	4 vs 9
Tinelli (2011)	3 \pm 0.4 ^a vs 4 \pm 0.1 ^a	80 \pm 55 ^a vs 170 \pm 60 ^a for up to a max of 3 days	N/A	Until drainage volume < 30 ml	N/A	7/30 vs 16/28	3 vs 9	US drainage and sclerotherapy with a 0.45% lactic acid solution for lymphocele >5 cm (1 vs 4)/no	N/A
Tinelli (2013)	2 \pm 0.5 ^a vs 3 \pm 0.5 ^a	65 \pm 15 ^a vs 150 \pm 40 ^a for up to a max of 3 days	N/A	Until drainage volume < 30 ml	N/A	5/26 vs 15/29	2 vs 5	US drainage and sclerotherapy with a 0.45% lactic acid solution for lymphocele >5 cm (1 vs 3)/no	N/A

^a Mean \pm SD.

^b Median (range).

^c Mean (range), DVT: Deep vein thrombosis.

prostate, EC or melanoma and consequently different types of lymphadenectomies were performed (i.e. axillary, pelvic, inguinal). On the contrary, the present meta-analyses aimed to evaluate cases derived only from RCTs with gynecological malignancies who underwent pelvic and/or paraaortic lymph node dissection.

The impact of fibrin agents in lymphatic reaction after lymphadenectomy in gynecological malignancies was also evaluated by non-randomized observational studies. More specifically, Minig et al. and Kim HC et al. [10] showed no difference with regards to the incidence of lymphocele, both asymptomatic and symptomatic [10,18]. Specifically, Minig et al. reported a decrease of symptomatic lymphocele in patients with application of TachoSil but statistical significance was not reached (7 vs 2 patients, $p = 0.121$) [10]. Concerning the incidence of lymphocele after inguinal lymphadenectomy, Buda et al. reported statistically significant difference in total drainage volume (540 \pm 259 vs 900 \pm 612, $p < 0.0001$) and daily drainage volume (84 \pm 102 vs 143 \pm 107, $p < 0.004$) as well as significant elevated postoperative complication rates in the group without the agent [36]. Nonetheless, a RCT by Carlson et al., reported no difference in drain output, duration of

drains or lymphocele formation in patients who underwent lymphadenectomy for vulvar cancer [16].

Postoperative lymphoceles account for serious morbidity in patients who underwent lymphadenectomy and consequently a number of various agents and techniques for their prevention have been proposed. In that setting, options such as somatostatin analogs [37], synthetic polyethylene glycol (PEG) sealant [38], intraoperative peritoneal fenestration [39,40], povidone iodine application [41] perioperative anticoagulation and placement of pelvic drain electrothermal bipolar vessel sealing device (EBVSD) have been proposed but their exact role still remains elusive. Treatment options consist of percutaneous drainage, injection of sclerosing agents via the percutaneous tube and marsupialization [42,43].

Our study was based on a systematic review of the literature. We have tried to eliminate data losses by setting aside language and data restrictions, and having three authors who independently search the literature which represents a significant strength of the present study. Additionally, the present study is to our knowledge the first which analyzed the outcomes from the existing RCTs on the efficacy of fibrin

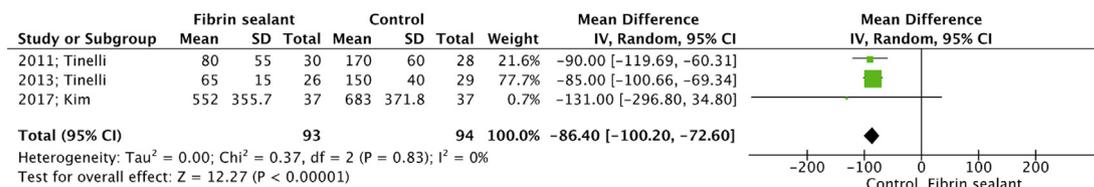


Fig. 3. Forest plot depicting mean total volume of drainage.

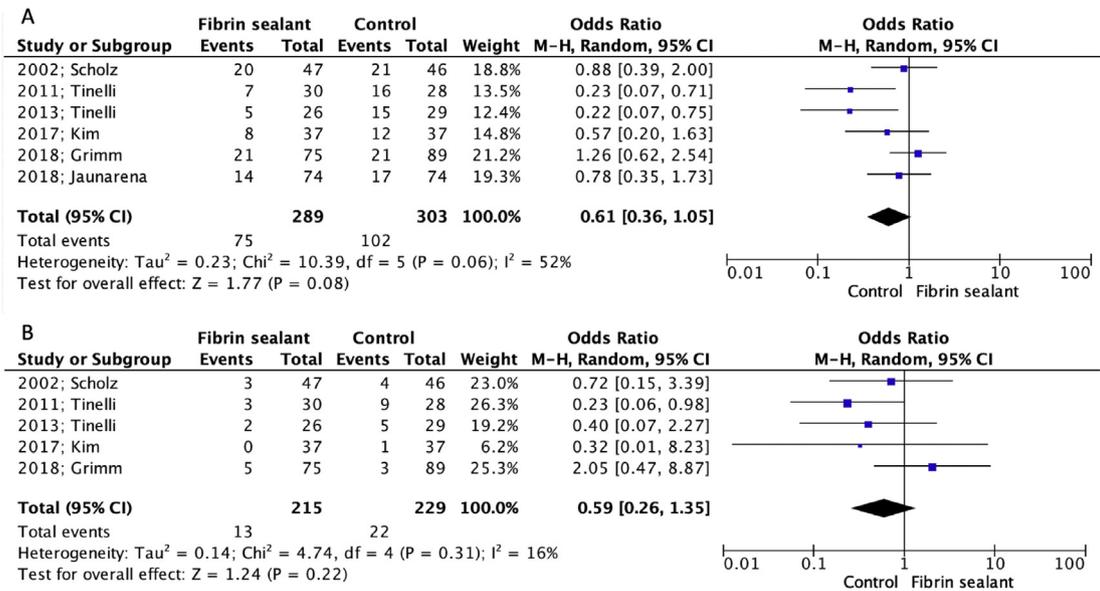


Fig. 4. Forest plot depicting A. incidence of lymphocele. B. incidence of symptomatic lymphocele.

sealant agents in the prevention of lymphocele in patients with gynecological malignancies who underwent pelvic and/or para-aortic lymphadenectomy. Nonetheless, before reaching any conclusion, there are several limitations that should be taken into consideration. The limited number of the existing studies and as a consequence the small number of the included patients cannot allow us to draw any safe conclusion. Our study suggests the planning and design of more multicenter studies, that will reach more efficient conclusions in the field. Furthermore, only published studies were analyzed in our study, therefore the conclusions might be diversified if influenced by ongoing studies. Finally, some significant parameters have not been properly reported by the included studies; The special aspects of management of lymphoceles, the number of postoperative percutaneous drainage procedures or the incidence of infectious and non-lymphadenectomy related complications or furtherly the incidence of late lymphocele formation and the associated complications, should be evaluated. Additionally, the criteria of removal of the drainage were underreported by the included studies. As shown in Table 2, Tinelli et al. removed the drainage in an interval of maximum 3 days until the drainage volume was <30 ml while in the study by Kim et al. the drainage remained for 3 days and was removed if no sign of active bleeding was reported [22,24,25]. For the remaining studies data concerning indication for drainage removal was not available. Another fact that limits reaching to firm results is the heterogeneity in the reported gynecological malignancies and the fact that the included studies did not report separate outcomes concerning each malignancy or incidence of lymphocele with regards to pelvic and para-aortic lymphadenectomy separately. Furthermore, as shown in Table 1 the types of applied fibrin sealants varied among the included studies (i.e. Floseal, Tachosil, Tissucol) as well as the way of application (i.e. spray, patch) of them on the treated area. Further RCTs are needed in order to evaluate the aforementioned parameters.

5. Conclusions

Based on the 6 included studies, our meta-analysis supports the safety of the use of fibrin sealant patches in women undergoing pelvic and/or para-aortic dissection due to gynecologic cancer but its benefit remains uncertain. Despite the fact that it was proven effective in reducing the duration and volume of their lymph drainage, it was not associated with difference in the incidence of lymphocele. More studies are required to confirm our conclusion and broaden our knowledge about its impact on other parameters.

Conflicts of interest

The authors declare they have no conflict of interest.

Author contribution

- A Prodromidou: Data collection and management, data analysis, manuscript writing
- C Iavazzo: Protocol/project development, manuscript writing
- A Fotiou: Data collection and management
- V Psoyiadou: Data collection and manuscript writing
- M Drakou: Data collection and management
- G Vorigias: Protocol/project development, Consultation to the manuscript,
- N Kalinoglou: Protocol/project development, Consultation to the manuscript

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