

The role of pelvic lymphocele in the development of early postoperative complications

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Abstract

With the increasing incidence of gynecologic malignancy, radical hysterectomy represents an important part of the adequate treatment of these patients. The pelvic lymphocele is a known side effect of pelvic and para-aortic lymphadenectomy. The aim of our study was to assess the role of the lymphocele in the development of early postoperative complications.

A single-center, retrospective analysis between January 2000 and May 2017 revealed 1867 patients with cervical and endometrial cancer, treated through radical or modified radical hysterectomy and pelvic lymphadenectomy. Postoperative complications and the occurrence of pelvic lymphocele were evaluated.

Approximately 47.6% of patients were diagnosed with pelvic lymphocele, with only 5.2% being symptomatic. Early postoperative complications rate recorded an incidence of 8.1%, occurring more frequent if lymphocele were present ($P < .001$). The pelvic lymphocele represented, in univariate analysis, a risk factor for the development of pelvic abscesses, but not for deep vein thrombosis, lymphedema, or bowel obstruction. Hydronephrosis was found to be significantly correlated with the pelvic lymphocele, but we believe this urological complication to have a different underlining mechanism. Neoadjuvant radiotherapy represented in both uni- and multivariate analysis a risk factor for the occurrence of postoperative complications.

In the postoperative context of oncogynecological surgery, pelvic lymphocele occur at high rates, representing a statistical risk factor for hydronephrosis and pelvic abscesses, with neoadjuvant radiotherapy being an independent risk factor for early postoperative complications.

Abbreviations: BMI = body mass index, DVT = deep vein thrombosis, US = ultrasound.

Keywords: cervical cancer, endometrial cancer, hysterectomy, lymphadenectomy, lymphocele, postoperative complications

1. Introduction

Gynecologic cancers record a high incidence at a global level, particularly cervical and endometrial cancer, ranking third and fifth, respectively worldwide.^[1] In our region, this high incidence includes, in considerable proportion, patients with advanced stages of disease, due to late diagnosis.^[2,3] Treatment modalities comprise a combination to different extent of surgery, radiotherapy, and chemotherapy depending on stage and according to current treatment guidelines.^[4,5]

Following radical surgery such as radical hysterectomy with pelvic lymphadenectomy, the incidence of pelvic lymphocele has been reported at varying percentages, between 1% and 58%, with only 5% to 18% being reported as symptomatic.^[6–9]

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Radical oncogynecological surgery has been reported to associate a high rate of postoperative complications, with incidence rates varying greatly depending on author. Among these, some of the most common complications are represented by hydronephrosis (23%–55%),^[10,11] deep vein thrombosis (DVT 0.8%–25%),^[12–14] pelvic, or inferior limb lymphedema (0–70%).^[14–19]

Weinberger et al,^[6] in an analysis of the mechanisms and secondary morbidity following pelvic lymphocele, suggested a direct link between pelvic lymphocele and postoperative complications after radical hysterectomy with pelvic/para-aortic lymphadenectomy, highlighting the total number of lymph nodes, number of positive lymph nodes, type of primary tumor, radiotherapy and body mass index (BMI) as risk factors.

The purpose of our study was to analyze the link between postoperative pelvic lymphocele and early postoperative morbidity, respectively which of these complications have radiotherapy and/or pelvic lymphocele as a risk factor.

2. Materials and methods

This was a single-center, retrospective analysis of data collected from patients that presented with cervical or endometrial cancer between January 2000 and May 2017 at the Second Department of General Surgery and Surgical Oncology, Emergency City Hospital. Approval for this study was obtained from the Ethical Committee and the research was performed in accordance with the World Medical Association Declaration of Helsinki, revised in 2000, Edinburgh.

Patient inclusion criteria comprised diagnosis of cervical or endometrial cancer, surgical treatment consisting radical or

modified radical hysterectomy with uni- or bilateral anexectomy and pelvic \pm para-aortic lymphadenectomy performed through an open approach, with or without neoadjuvant radiotherapy. Patients with multivisceral pelvic resections, macroscopic residual tumor (R2), postoperative pelvic hematomas, as well as patients presenting with preoperative complications consisting of pelvic collections, DVT, hydronephrosis, pelvic venous or lymphatic stasis, or bowel obstruction were excluded from the present study. Data were extracted from patients' private medical records and hospital database and included demographic information, diagnosis at admission, surgical procedure type, oncologic treatment, pathology report, and follow-up reports. Overall, 2209 patients were identified during the selected time period. After inclusion and exclusion criteria were applied 1867 eligible patients were selected for the evaluation of the role of lymphocele in early postoperative complications.

All patients were diagnosed through imaging studies [ultrasound (US) and/or computed tomography and/or magnetic resonance imaging] with pelvic lymphocele, either early—secondary to a complication or due to an independent symptomatology; or late, as part of follow-up investigations.

Early complications were considered those postoperative morbidities that occurred in the first 30 days after surgery, patients presenting with clinical manifestations that required evaluation and in some cases treatment. Early complications were considered uni- or bilateral hydronephrosis, DVT, pelvic abscess, pelvic or inferior limb lymphedema, and bowel obstruction.

Statistical analysis was performed using SPSS software for Windows version 20 (IBM Corp, Armonk, NY). Descriptive analysis of continuous data was presented as mean range and standard deviation. Pearson chi square test, Student *t* test, Fisher exact test, and logistic regression models were used for the evaluation of correlation between the presence of pelvic lymphocele and postoperative complications. A *P* value of $<.05$ was considered statistically significant.

3. Results

The study series comprised 1867 patients. Cervical cancer was seen in a significantly higher percentage, with a cervical/endometrial cancer ratio of 18.9. Mean age for the whole group was 54.7 ± 14.7 years, with a minimum of 24 years and a maximum of 85 years. Differences in age average were also seen when comparing mean age by type of cancer, with higher age average for endometrial cancer patients, as shown in Table 1.

Surgical treatment comprised radical or modified radical hysterectomy with pelvic lymphadenectomy for all patients with cervical cancer included in study group: patients with stages IB2 and higher received neoadjuvant radiotherapy. The endometrial cancer group included patients who underwent modified radical hysterectomy with pelvic \pm para-aortic lymphadenectomy, with only a small number receiving neoadjuvant radiotherapy. Study group distribution by disease stage is shown in Table 1.

Pelvic lymphocele was seen in a large number of patients ($N=890$), being present in almost half of the study group (47.6%). Early diagnosis was made in 116 cases (6.2%), whereas late diagnosis was seen in 774 cases (41.4%). The pelvic lymphocele was predominantly asymptomatic, with only 5.2% of patients presenting symptoms. Distribution of patient group diagnosed with lymphocele by cancer type can be seen in Table 2.

Overall early postoperative complications recorded a value of 8.1%, most commonly seen were hydronephrosis, followed by pelvic abscess and DVT. Almost twice as many early complications

Table 1

Distribution of patients according to cancer type, disease stage, and neoadjuvant radiotherapy.

	Cervical cancer	Endometrial cancer
No. patients	1773 (94.9)	94 (5.1)
Age (mean \pm SD)	49.2 ± 17.2	63.1 ± 16.9
Neoadjuvant radiotherapy	1620 (91.3)	6 (6.3)
Staging		
I		
A2	14 (0.8)	26 (27.6)
B1	139 (7.8)	
B2	574 (32.4)	
II		
A	56 (3.2)	48 (51.1)
B	982 (55.4)	
III	8 (0.4)	20 (21.3)

Values are shown as n (%). SD = standard deviation.

occurred in the group of patients presenting with pelvic lymphocele (11.0% in lymphocele group vs 5.5% in the group of patients without lymphocele), suggesting a strong correlation between the presence of lymphocele and the development of postoperative complications ($P < .001$). Univariate analysis of the main postoperative complications revealed the pelvic lymphocele as a risk factor only in the case of hydronephrosis and pelvic abscess; as for DVT significance level was close but did not reach a value <0.05 and in the case of lymphedema and bowel obstruction, neither were found significant (Table 3). Univariate analysis included several other parameters, such as age, type of surgery, etc, but none have shown statistical significance (Table 4).

Neoadjuvant radiotherapy has shown in both univariate and multivariate analysis to be an independent risk factor for the development of early postoperative complications (Table 3).

4. Discussion

The occurrence of pelvic lymphocele after lymphadenectomy procedures is well-known, occurring not only after gynecologic surgery, but also after surgical treatment of urological malignancy or renal transplantation.^[6,20] A few risk factors for the development of lymphatic collections have been proposed, such as number and positivity of removed lymph nodes, postoperative radiotherapy, BMI, and type of surgical procedure (open vs laparoscopic approach).^[6–9] However, consensus has not been reached in this matter as several studies fail to confirm these findings.^[6,8,16]

In our study we recorded an overall incidence of postoperative lymphocele of 47.6%, with only 5.2% being symptomatic. The diagnostic incidence of lymphocele values ranges between 1% and 58% as reported by Weinberger et al.^[6] Similar to our findings, values of symptomatic lymphocele have been presented by Pan et al.^[21] (5%), Ghezzi et al.^[7] (5.7% following an open

Table 2

Distribution of patients with pelvic lymphocele by symptomatology and cancer type.

Pelvic lymphocele	Cervical cancer	Endometrial cancer	Whole series
Asymptomatic	758 (42.7)	34 (36.2)	792 (42.4)
Symptomatic	95 (5.4)	3 (3.2)	98 (5.2)

Values are shown as n (%).

Table 3**Distribution of early postoperative complications by presence of lymphocele and radiotherapy.**

Overall early postoperative complications	With lymphocele		Without lymphocele		P lymphocele <0.001	P RT <0.001	
	+ RT	– RT	+ RT	– RT			
Hydronephrosis	59 (3.2)	31	9	16	3	.001	.001
DVT	25 (1.3)	9	7	4	5	.09	<.001
Lymphedema	16 (0.8)	7	2	6	1	.49	<.001
Pelvic abscess	31 (1.7)	14	9	4	4	.002	<.001
Bowel obstruction	21 (1.1)	6	4	8	3	.99	<.001

Values are shown as n (%).

+RT = with neoadjuvant radiotherapy, –RT = without neoadjuvant radiotherapy, DVT = deep vein thrombosis.

approach), and Zikan et al^[8] (5.8%), but with rates being reported as high as 35%.^[16,22] These large differences in reported incidence may be explained by a considerable variability in postoperative surveillance and detection of lymphocele and by how a symptomatic lymphocele is defined.

The physiopathological pathway of postoperative complications comprises a multifactorial problem and not a single or bifactorial cause. In the postoperative context a sum of factors favor the rigidity of pelvic tissues from both a mechanical and metabolic point of view, being accentuated by the cumulative effect.^[14,16,23]

Fibrous tissue formation can be seen as a response to intraoperative mechanic injury affecting not only tissue, but also vascularization. These lesions favor the occurrence of fibrosis either direct—through exudation and collagen formation—or indirect through acute, subacute, and chronic ischemia.^[14,20,23,24] Therefore, this hypothesis could explain the occurrence of rigidity at the level of ureteral and venous walls, amplification of Virchow triad, the partial or total lymphatic insufficiency, as well as the involvement of neighboring tissues in the fibrosis process, with potential secondary malposition. In this context, structural and metabolic remodeling may account for tissue distortion or stenosis phenomena, affecting a large variety of structures, such as ureters with secondary hydronephrosis; main venous trunks with secondary DVT; lymphatic vessels, generating defective regeneration and secondary lymphedema; and peritoneum with defective peritoneal healing and pelvic visceral adhesion formation, with secondary bowel obstruction episodes.^[6,12,16,23,24]

Postoperative pelvic collection development—with or without septic contamination—cannot be fully explained through the previously mentioned mechanisms, except in the case of tissue distortion and defective lymphatic healing leading to lymphatic

collections, that may evolve to a septic or inflammatory state, representing mechanical or inflammatory amplification factors.^[7,8,16,21,23] Thus, a lymphocele may exert a direct mechanical effect on adjacent structures, with progressive compression and impairing normal flux flow leading to hydronephrosis or DVT. Under different conditions, septic contamination of the lymphocele amplifies the locoregional effect, the mechanical role of the lymphocele being intensified by the septic process, either by adding new elements to Virchow triad, by adding inflammatory elements to the initial mechanical deficit or by an independent expression.^[7,9,22,23,25]

Analyzing each complication in part, in our study it can be observed that the presence of pelvic lymphocele, regardless of septic contamination, does not represent a risk factor in the appearance of DVT, lymphedema, or bowel obstruction, and therefore not representing a risk factor for this kind of complications. Thus the obvious mechanoinflammatory effects secondary to the presence of the lymphocele do not constitute a statistically sufficient element for the possibility of determining early venous, lymphatic, or bowel complications.^[14,20] Similar to our results, Biglia et al^[15] and Achouri et al,^[16] in 2 independent studies, have found no statistically significant evidence to suggest that the presence of pelvic lymphocele causes lower limb lymphedema. In contrast, Kuroda et al,^[22] in a series of 264 patients with gynecologic malignant pathology, with a 35.2% incidence of lymphocele, reported lymphocyst formation to be an independent risk factor for lymphedema.

Understandably, the presence of a pelvic lymphatic collection may participate and favor the occurrence of a secondary septic process, supporting thus the role of pelvic lymphocele in the development of postoperative pelvic abscesses.^[7,8,16,23,24] In a series of 397 patients surgically treated for endometrial cancer, Pan et al^[21] reported 76 patients being diagnosed with pelvic lymphocele, among which 26.3% developed a secondary abscess, suggesting that a size >5 cm of the lymphocele represented an independent risk factor for septic contamination. Zikan et al,^[8] in a report of 800 patients with gynecologic malignancy, indicated that secondary abscesses represented the most serious complication of pelvic lymphocele, presenting a diameter of >6 cm as a factor for presence of symptomatology. In this study the size of the lymphocele was not evaluated, as from 116 cases (6.2%) that have been diagnosed in an early phase, 98 (84.5%) were symptomatic. In this context the size of lymphocele could be obtained in an early phase in only 13% from all cases diagnosed with lymphocele; the rest (87%) being diagnosed at a later stage, after various postoperative time periods, in a nonstandardized manner. Therefore, in this retrospective evaluation, size quantification was not performed.

Table 4**Other parameters included in univariate analysis of early postoperative complications.**

Evaluated parameter	P
Age	.48
Type of surgery (radical hysterectomy vs modified radical hysterectomy)	.61
Extent of nodal clearance (pelvic lymphadenectomy vs pelvic + para-aortic lymphadenectomy)	.27
Laboratory parameters (WBC, RBC, PLT)	.56

PLT = platelet count, RBC = red blood cell count, including hemoglobin values, WBC = white blood cell count.

The discussion comprises also the role of lymphocele in the development of early postoperative hydronephrosis. The problem resides in the possibility of early hydronephrosis having 2 completely different evolutions—transitory evolution and a secondary mechanoinflammatory evolution.^[10,23,26,27] From a clinical point of view, although the statistical data suggest lymphocele as a favorizing factor for secondary hydronephrosis after radical total hysterectomy with pelvic lymphadenectomy for uterine cancers, in our opinion, we do not believe the lymphocele to represent a urologic mechanoinflammatory factor of such impact, as long as it does not reproduce the same effect for venous and lymphatic complications.

The shortcoming of this article lies in that we cannot specify which of the hydronephrosis, although symptomatic and receiving treatment, would have had a naturally spontaneous resolution, and which hydronephrosis, symptomatic or not, would have had a chronic, progressive evolution. Only patients with chronic hydronephrosis represent true urologic complications in need of therapy and, in our opinion, only these should have been statistically analyzed for the correlation with pelvic lymphocele. The problem lies in that the interval of transitory hydronephrosis overlaps with the period of early postoperative complication occurrence.^[6,7,20] Also, the mechanical factor represented by the lymphocele cannot prove a direct role in the development of hydronephrosis, as the hydronephrosis does not recede or attenuate (without stenting) after the clearance/evacuation of the lymphocele (as could be seen in DVT). The role of lymphocele is rather secondary to the perilesional mechanoinflammatory phenomena, events that are present postoperatively to various degrees, even in the absence of an adjacent collection. In a different perspective, according to a previous personal study, hydronephrosis developed after oncogynecological surgery may persist even after extensive urinary reconstruction procedures are performed^[28]; histopathological reports showing extensive and not focal wall lesions, stenosis being caused by parietal loss of elasticity and not by extrinsic compression.^[23]

In this sense a more detailed study that would clearly exclude these possible biases would prove useful in determining the correlation between hydronephrosis and pelvic lymphocele.

In this study, the management for all postoperative complications followed the same direction from conservative, to minimally invasive and finally surgical, when required: DVT treatment was conservative, with US-guided transparietal or transvaginal aspiration being performed only for patients not responding to a sole conservative approach; for *pelvic abscess* antibiotic therapy and US-guided aspirations were followed by laparotomy only if both clinical and imagistic acute inflammation signs were persistent; conservative treatment was applied for *lymphedema*; *bowel obstructions* were surgically treated as soon as a certainty diagnosis was established; patients with *hydronephrosis* that did not remit under anti-inflammatory and antispastic treatment were offered endoscopic ureteral stenting, with urinary diversion procedures being performed for patients presenting with recurrent hydronephrosis after ureteral stent removal or in whom ureteral stents could not be placed.

Neoadjuvant radiotherapy has shown to be both a global and individual risk factor (and not a causatory factor, as in patients receiving exclusive radiotherapy the same rate of post-treatment complications are not seen) for early postoperative complications. It is understandable why regional fibrosis and post-therapy pelvic tissue ischemia account for the parietal dysfunction at the level of the ureteral wall and also for the venous or lymphatic

walls, explaining complications such as DVT, bowel obstruction, hydronephrosis, or lymphedema, being directly proportional to the amount of aggression.^[6,12,13,15,22,23] A study done by Kim et al^[9] showed that a lower incidence of pelvic lymphocele can be seen if postoperative radiotherapy is not applied, suggesting a more cautious choice of adjuvant treatment. In only 1 study, performed by Achouri et al,^[16] did adjuvant radiotherapy have a beneficial effect, by significantly reducing number of symptomatic pelvic lymphocele, but this study does not mention whether radiotherapy lowers the number of lymphocele altogether.^[16]

In conclusion, the presence of pelvic lymphocele represents a statistical risk factor for the development of postoperative hydronephrosis and pelvic abscess, but not for DVT, lymphedema, or bowel obstruction, with the observation that the mechanism of urological complications remains an open book for further studies. Radiotherapy has been seen to represent a risk factor for postoperative complications both at an individual and global level.

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