

Clinical Significance of Postoperative Lymphoceles Following Pelvic Lymph Node Dissection in Prostate Cancer Disease

Kilian M Gust, Oliver Engel, Ursula Schertl, Rainer Kuefer, Ludwig Rinnab*

Department of Urology, University of Ulm, Ulm, Germany

Abstract

Background and Aims: Pelvic lymph node dissection (pLND) in patients undergoing radical retropubic prostatectomy (rRPE) is often associated with postoperative lymphocele formation. This can lead to consecutive complications such as abscesses and thrombosis. The aim of this study was to evaluate the possible risk of complications due to the lymph node dissection and to identify risk factors being associated with symptomatic lymphoceles.

Methods: Between 02/2002 and 12/2003 all 504 patients who underwent pLND and rRPE were investigated on the 7th postoperative day by pelvic and lower abdominal ultrasound. Volumes of lymphoceles were determined. Complications related to pLND were described and evaluated statistically to explore the role of possible risk factors.

Results: 66 patients (13%) (mean age 63, range 48-75 years) developed a lymphocele. There was no statistically relevant association between size of lymphoceles and age of patients, pre-surgical PSA, T-stage, prostate volume and the number of lymph nodes being removed, the body mass index and duration of surgical procedures. The size of lymphoceles was in 47% of patients < 50 ml, in 15.2 % between 50-100 ml, in 25.8% between 100 and 200 ml and in 12.1% of patients >200ml. The mean volume of the lymphoceles was 111.6 ml (Median 80 ml). 13 patients developed complications such as thrombosis and abscesses. The mean volume of lymphoceles being clinically symptomatic was 227±125ml and in asymptomatic patients it was 87±65 ml. This difference was statistically significant ($p<0.001$).

Conclusions: Because of simple feasibility, universal availability as well as low costs, a pelvic ultrasound should be performed in the clinical setting after removal of all drains. Asymptomatic lymphoceles with a volume less than 100 ml do not need any particular close follow-up. Facing larger lymphoceles invasive means should be planned rather early to avoid complications.

Keywords: Complications, Lymphocele, Pelvic Lymph Node Dissection, Prostate Cancer, Prostatectomy

Introduction

Pelvic lymph node dissection (pLND) in patients undergoing radical retropubic prostatectomy (rRPE) is often associated with postoperative development of lymphoceles (1-5). Besides pain, this can lead to consecutive complications such as peripheral oedema, infection with formation of abscesses and thrombosis (6-11). Lymphoceles are often incidentally found during routine sonographic examination, on the other side they may cause clinical symptoms.

The point of necessary intervention is still not clearly defined and asymptomatic lymphoceles usually need to be observed only. But a restrained

*Correspondence:

Ludwig Rinnab, Assistant Professor of Urology
Department of Urology, University of Ulm, Prittwitzstr. 43,
89075 Ulm, Germany.
Tel: +49 731 500-58030
Fax: +49 731 500-58101
E-Mail: ludwig.rinnab@uniklinik-ulm.de
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approach can lead to serious and avoidable complications. Treatment without serious complications is usually possible in cases of minor pain, moderate changes in blood count (leucocytosis) or increased blood sedimentation with fever as sign of a beginning infection or uncomplicated leg oedema. However, early intervention could preserve cases with thrombosis or abscess formation. There is still no clear strategy, when and if at all clinical asymptomatic lymphocele should be treated.

The aim of this study was to identify influencing parameters and risk factors for the development and severity of lymphoceles as part of an optimised post-surgical management.

Materials and Methods

Between 01/2002 and 12/2003 a total number of 504 radical retropubic prostatectomies (rRPE) with standardised pelvic lymph node dissection (pLND) were performed at the Urological Department of the University of Ulm (Germany). High volume surgeons performed all procedures. Standardised pLND included obturatoric and external iliac lymph nodes (Fig. 1). On day seven after surgery, an abdominal and pelvic ultrasound was performed on all patients after the removal of drains. In 66 patients (13 %) an asymptomatic lymphocele was found. During the

hospitalisation ultrasound was repeated and size of lymphocele, possible occurrence of complications and implemented treatments were documented. Additional clinical and oncological parameters such as age, body mass index (BMI), pre-surgical PSA, as well as histological data with tumour staging, Gleason score, number of removed lymph nodes and weight of the prostate gland were also documented.

Clinical data of all performed rRPEs in stated time period was collected and retrospective statistically analyzed. We evaluated potential risk factors for the development of a lymphocele: patients' age, BMI, pre-surgical PSA, prostate volume, postoperative T-stage and Gleason score, presence of lymph node metastases and the number of removed lymph nodes. Mann-Whitney U-test and unpaired Student's t-test were performed using statistical software SPSS 13.0. The significance level was set to $p < 0.05$.

Results

In 66 of 504 patients (13 %) who underwent surgery in the given time period, lymphoceles were found during routinely performed ultrasound. Detailed patients' data are included in Table 1. The mean age was 63 years. The body mass index (BMI) was between 20.5 and 44.2 kg/m². Mean BMI (27.2 kg/m²) was higher than the normal range of 18.5

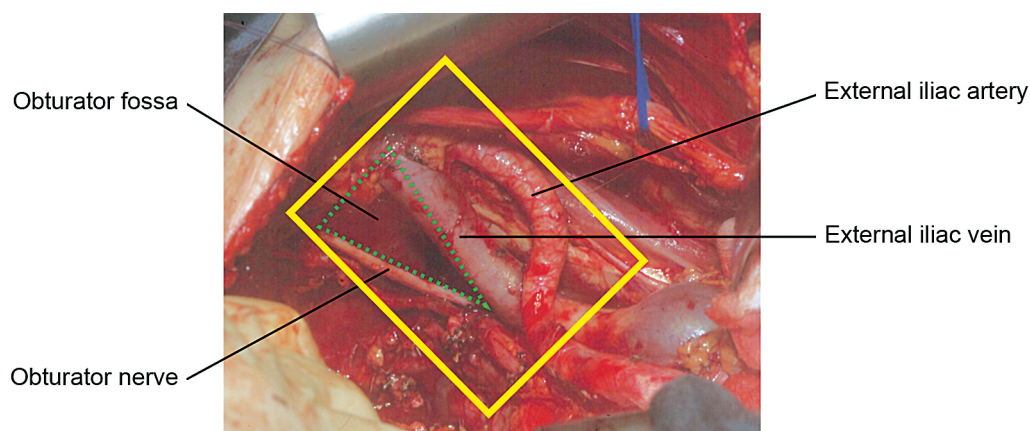


Figure 1. Intraoperative situs after performed standard pelvic lymph node dissection (field marked with yellow square). The whole lymphatic tissue along the external iliac vein, the obturator nerve and the obturator fossa (marked with green triangle) is removed.

to 24.9 kg/m². 28 patients (42 %) were within and 38 patients (58 %) were over the normal range. The pre-surgical PSA value was between 3.9 and 155.0 ng/ml with a mean of 15.6 ng/ml. Mean prostate volume was 56.7 ml. 46 patients (69.7 %) showed a localised disease (pT2). Advanced disease was found in 17 patients (25.8 %) with pT3, and in 3 patients (4.5 %) with pT4 tumours. Sixty-two patients had a lymph node negative disease, lymph node metastases were found in 4 patients (6.1 %). Preoperative distant metastases were excluded with routine staging. Mostafi's tumour grading G2 was found in 51 patients (77.3 %), G3 in 15 patients (22.7 %). Gleason score (GS) of 3 was found in one patient (1.5 %), GS 4 in two patients (3.0 %), GS 5 in 12 patients (18.2 %), GS 6 in nine patients (13.6 %), GS 7 in 33 patients (33 %), GS 8 in eight patients (12.1 %) and one patient showed a Gleason score of 9.

Mean of the removed lymph nodes was 12.8 (2-27). Sonographic sizes of lymphoceles were between 5 and 600 ml. For further analysis, lymphoceles were categorised in steps of 50 ml. Lymphoceles smaller than 50 ml were found in 31 patients (47 %), between 50 and 100 ml in 10 patients (15.2 %). Seventeen patients (25.8 %) showed a lymphocele between

101 and 200 ml and a lymphocele larger than 200 ml was found in 8 patients (12 %). The mean volume of lymphoceles was 111.6 ml and the median, 80.0 ml. In 13 patients complications occurred due to the lymphocele. Three patients developed leg oedema and thrombosis was found in 5 patients. Infected lymphoceles were found in 3 patients, an abscess was found in case and another patient showed a vascular constriction without leg oedema or thrombosis in an implemented CT scan (Fig. 2).

Overall 20 patients (30.3 %), the 13 primary asymptomatic patients and another seven patients with symptoms in the lower abdomen, were treated. 19 patients received sonographic controlled drain insertions, three of these were radiated due to persistent lymphorrhoea. In case of an abscess an open surgical procedure was performed.

Patients were divided into groups by age. Age > 64 years and ≤ 64 years (p=0.556), the preoperative PSA value (p=0.079), even as prostate volume (p=0.161) and the body mass index (p=0.964) showed no statistical significant association to the volume of lymphoceles (Table 1). Similar results were found for tumour staging and Gleason score. Especially the number of removed lymph nodes or



(a)



(b)

Figure 2. a: Contrast enhanced CT scan (10th postoperative day) - bilateral pelvic lymphoceles (LZ). **b:** Left side lymphocele with constriction of iliac vessel und consecutive risk for thrombosis.

Table 1. Description of the study cohort (n=66)

	Mean	Median	Range	SD
Age	63	64	48-75	6.7
Body mass index (kg/m ²)	27.2	25.9	20.5-44.1	N/A
Pre-surgical PSA (ng/ml)	15.6	10.0	3.9-155.0	20.8
Volume of prostate gland (ml)	56.7	55.0	19.0-127.0	27.4
Postoperative Gleason score				
		N	Rate	
	2-6	24	36%	
	7	33	50%	
	8-10	9	14%	
TNM staging				
		N	Rate	
	T2	46	69.7%	
	T3	17	25.8%	
	T4	3	4.5%	
	N-	62	93.9%	
	N+	4	6.1%	
	M0	0	0%	
	R0	58	87.9%	
	R1	8	12.1%	
Type of lymph node dissection				
	Standard field pelvic lymph node dissection			
Number of removed lymph nodes				
	Mean	Median	Range	SD
Number of removed lymph nodes	12.8	12.0	2-27	5.9
Volume of Lymphocele (ml)				
	Mean	Median	Range	SD
Volume of Lymphocele (ml)	111.6	80.0	5-600	129.5
Lymphocele				
	Volume	N	Rate	
	< 50 ml	31	47.0%	
	50-100 ml	10	15.2%	
	101-200 ml	17	25.8%	
	> 200 ml	8	12.1%	
Mean lymphocele size				
	in symptomatic patients			227 ml
	in asymptomatic patients			87 ml
Number of lymphoceles				
	Clinical irrelevant			46
	Clinical relevant			20
Postoperative complications (n=13)				
	Leg oedema			3
	Thrombosis			5
	Infection			3
	Abscess			1
	Vessel constriction without leg oedema or thrombosis			1
Treated lymphoceles (n=20)				
	Sonographic guided percutaneous drain insertion			19
	Surgical drainage			1
	Percutaneous radiation due to persistent lymphorrhea			3

N, Number; SD, Standard Deviation; PSA, Prostate Specific Antigen.

their tumour infiltration showed no relation to the development of lymphoceles.

Statistically significant differences were found for the volumes of lymphoceles getting clinically symptomatic and the need of treatment, as well as occurrence of further complications. Symptomatic lymphoceles (all of them were treated) were compared to the asymptomatic lymphoceles. Mean volume in symptomatic lymphoceles was 227 ml and in asymptomatic lymphoceles, 87 ml and these were significantly different ($p < 0.001$, unpaired student's *t* test). The same applies to the patients that developed complications, compared to the patients without lymphocele-associated complications ($p < 0.001$).

Discussion

The technique of the radical retropubic prostatectomy (rRPE) has remarkably enhanced over the last few years, resulting in a decreased morbidity. One of the most frequent complications due to pelvic lymph node dissection (pLND) is the postoperative development of lymphoceles. This is caused by tissue damage or emission of lymph fluid based on interrupted lymph vessels. The incidence of lymphoceles can be reduced by meticulous surgical preparation and an accurate ligation of lymph vessels.

Subclinical postoperative lymphoceles after pLND and rRPE are frequently observed (27 %). The majority reduces in size; however, up to 44 % need further intervention (2). A German group analysed potential risk factors for occurrence of complications in 1380 patients who underwent pLND and RPE. In 72 patients, a symptomatic lymphocele was found, in 6 of these 72 patients thrombo-embolic events occurred, two additional patients showed secondary infected lymphoceles. Overall, the rate of symptomatic lymphoceles was 5.3 %. These findings correspond with results of other study groups (3, 13, 14). Their results show significant coherences between development of lymphoceles and

dimension of lymph node dissection ($p < 0.0001$), number of removed lymph nodes ($p = 0.0038$) and surgeon's experience ($p = 0.0073$) (15). Pepper *et al* (3) report on subclinical lymphoceles in 30 % of all patients who underwent laparoscopic pelvic lymph node dissections (16). A Scandinavian study shows in postoperative CT scans an overall incidence of lymphoceles of 54 % after performed pLND, with a lower rate of 37% in laparoscopic cases compared to open surgical procedures with 61 %. Despite a high incidence of 27 % large volume lymphoceles after pLND, only three patients needed further intervention (14). This emphasizes the low incidence of clinically relevant lymphoceles. In our study, we found the rate of symptomatic lymphoceles of 5%.

Percutaneous puncture and aspiration with the objective of pressure relief and extraction of a microbiological culture was the former standard of treatment for symptomatic lymphoceles (17-21). Nowadays the therapeutic management of lymphoceles includes percutaneous drains with/without sclerosis, laparoscopic fenestration or open surgical procedures (22-26). Clinical symptoms depend on localization and size of lymphocele as well as the presence of infection. Symptoms can occur as abdominal pain, leg oedema or pain, deep vein thrombosis and hydronephrosis with renal failure (27). The risk of an infected lymphocele is higher in immune compromised patients as found after kidney and pancreas transplantation, despite the fact that usage of steroids lowers the risk of lymphocele development. Therapeutic management depends on the size, localization, infection and the recurrence of lymphoceles.

An American study questioned the routinely postoperative drain insertion after RPE. The study included 552 patients, on 452 patients (82 %) a pLND was performed. In 347 of 452 patients (77 %), no drains were inserted and 105 (23 %) patients were provided with drains. In one of these 105 patients with drain, a lymphocele occurred, that was further drained percutaneously. The authors concluded that a

pelvic drain can often be avoided after RPE (28).

Pelvic lymphoceles can be treated by singular or continuous aspiration of lymph fluid, percutaneous drains, sclerosis or open surgical procedures. Open surgical drainage results in the success rate of 50 to 70 %. The rate can be improved to more than 90 % when carrying out a peritoneal marsupialisation (9). These procedures are unfavourable in view of the need of anaesthesia, longer hospitalization and surgical trauma. However, techniques such as open surgical lymphocele fenestration or marsupialisation with/without pexation of the omentum can be even more effective (29-31).

Complications due to lymphoceles are harmful and should be prevented if possible. The overall percentage of lymphocele related complications in our study was 2.5 %.

Numerous sclerosing agents such as tetracycline, doxycycline, bleomycin, ethanol, povidone-iodine or sodium amidotriozate are also used. These sclerosing substances cause an inflammation and lead to adherence of tissues (32). In a series of patients after renal transplantation the incidence of lymphoceles amounted to 26 %. Singular percutaneous drainage showed a recurrence rate of 33 % in that study, compared to 25 % for a combined treatment of percutaneous drainage and sclerosing therapy with ethanol (33). This may underline the potential use of a sclerosing agent, especially in recurrent lymphoceles before surgical procedures. The advantage in aspiration of lymphoceles consists in the feasibility of local anaesthesia.

The role of heparin as lymphocele promoter is controversially discussed. Different groups (34-36) report an increased risk of developing lymphoceles during low dose application of heparin. However, others couldn't confirm these findings in a randomised, prospective study including 579 patients who underwent pLND and RPE (37). In our study the low dose heparin was administered in the upper arm to prevent lymphocele formation.

Intraoperative fibrin gluing didn't reduce the rate

of lymphoceles in patients that underwent surgery for gynaecological tumours or renal transplantation (38, 39). Fujiwara *et al* (40) investigated the impact of omentoplasty and omentopexy in the prevention of complications after pelvic lymphadenectomy. The authors reported a reduced incidence of lymphoedema, lymphoceles and their complications.

Because of missing symptoms and the fact to be easily missed in routine ultrasound, small lymphoceles are rarely diagnosed. Even with targeted ultrasound as employed in our study, and the inclusion of every small fluid mass (documented volume larger than 5 ml) the rate of detected lymphoceles was only 13 %. In the clinical routine, without ultrasound the rate might be even smaller. The rate of symptomatic lymphoceles that need to be treated is clearly smaller, at about 4%.

Issues of criticism in this retrospective study are for sure the inhomogeneous cohort of patients, the different examiners using ultrasound or colour-duplex ultrasound, and the missing comparative CT scans and standardised vascular flow measurements.

Despite improved diagnostic options like [11C] Cholin PET-CT etc (41-44) the pelvic lymph node dissection is still the method with the highest sensitivity and specificity to confirm or eliminate the presence of lymph node metastases. This additional information, if lymph node metastases exist, has an important prognostic value. In our study, the rate of lymph node metastases was 6.1 % (n=4). The question, if individual patients are at a higher risk for lymphoceles, cannot be conclusively answered. Focusing on our patients' clinical data with age, prostate size, body mass index, TNM classification, Gleason score, preoperative PSA, and number of removed lymph nodes, doesn't show any specific risk factors. These parameters seem to have no influence on lymphocele formation in this cohort. Other groups report that extent of pLND, numbers of removed lymph nodes and the surgeon's experience have a crucial impact on the development of lymphoceles (15). In our study, particularly the

number of removed lymph nodes has no impact on the likelihood of lymphocele formation. Mean number of removed lymph nodes in our cohort was 12.8 (2–27). Heidenreich *et al* (13) investigated the incidence of lymph node metastases in localised prostate cancer disease. In that study the patients that underwent extended (n=103) and standard lymph node dissection (n=100) were compared. Mean numbers of removed lymph nodes were 11 (6-19) for the standard and 28 (21-42) for the extended lymph node dissection. However, in this study, the rate of lymphoceles was the same for both groups (n=9). This shows that the extent of lymph node dissection has no influence on lymphocele formation. Based on these reports and our data, there are no sound arguments against the extended lymph node dissection as recommended by Wawroschek (45) and Bader (5).

In the presence of a lymphocele, the volume has an essential effect on the risk of causing complications. Especially, pain is increasing with lymphocele size. None of the lymphoceles with a volume less than 100 ml were punctured. Serious complications appeared more frequently with increasing lymphocele volumes.

Small asymptomatic lymphoceles don't need to be treated. At volumes notable above 100 ml the risk of complications is increasing significantly. This justifies a prophylactic insertion of drains. In known lymphoceles the occurrence of abscesses or thrombosis should be prevented if possible. Beside the volume of lymphoceles, the localization should also be considered. Lymphoceles localised in the small pelvis have a reduced capability for expansion without producing pressure on neighbouring structures compared to superficial lymphoceles. Particularly emerging pressure on the deep iliac vessels increases the risk of thrombosis. Even small lymphoceles can lead to this type of complication.

Rapidly increasing lymphoceles should be observed more critically than lymphoceles

unaltered in size. But these lymphoceles may get infected, when they persist over a longer period of time. For this reason clinical and sonographic follow-up are recommended for patients with known lymphoceles.

Conclusions

Pelvic lymph node dissection (pLND) during radical retropubic prostatectomy can be associated with a number of postoperative complications.

Nevertheless the pLND remains the best means for accurate lymph node staging. Occurring lymphoceles should be controlled continuously and in the case of adverse events there is need for immediate intervention.

Asymptomatic lymphoceles with a volume larger than 100 ml may be considered for prophylactic treatment to prevent serious complications such as deep vein thrombosis or pelvic abscess formation. In this study we found no association between the volume of lymphoceles and clinical parameters such as patients' age, preoperative PSA, tumour stage, prostate volume, numbers of removed lymph nodes, body mass index or procedure length.

Conflict of interest

There are no potential conflicts of interest.

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