

## Lymphocele after Renal Transplantation: A New Look at an Age-Old Problem!

Nalaka Gunawansa<sup>1,2\*</sup>, Ajay Sharma<sup>2,3</sup> and Ahmed Halawa<sup>2,4</sup>

<sup>1</sup>National Institute on Nephrology and Transplantation, Colombo, Sri Lanka

<sup>2</sup>Faculty of Health and Life Science, Institute of Learning and Teaching, University of Liverpool, UK

<sup>3</sup>Royal Liverpool University Hospitals, Liverpool, UK

<sup>4</sup>Sheffield Teaching Hospitals, Sheffield, UK.

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### ABSTRACT

Post-transplant lymphocele has a reported incidence of 0.6-34%. While numerous surgical and non-surgical risk factors have been described, the incidence remains fairly constant among different transplant settings. The majorities of such lymphoceles are asymptomatic and are incidental findings on routine imaging of the allograft. Large volume lymphoceles and those in relation to the graft hilum may exert pressure effects causing potential graft dysfunction. Local symptoms may develop if venous or lymphatic outflow of gonads or lower limb is impinged. Such symptomatic lymphoceles require definitive treatment. This review looks at the risk factors for lymphocele formation along with different management options and their outcomes.

**Keywords:** Renal transplant, Lymphocele, Lymph leak, Fluid collections, Laparoscopic fenestration

### INTRODUCTION

A lymphocele is an abnormal collection of lymphatic fluid that lacks an epithelialized cover, usually occurring at a site of extensive surgical dissection. In renal transplantation, a lymphocele may occur adjacent to the graft, due to multiple factors including damage to host retroperitoneal lymphatics as well as donor lymphatics accompanying the allograft. A peri-graft lymphocele is well-recognised morbidity following renal transplantation and can manifest in a broad spectrum of clinical presentations. This can range from indolent collections detected merely as incidental findings on or those that cause graft dysfunction, vascular compromise or sepsis.

The reported incidence of lymphocele is variable as the majority are asymptomatic and detected only on surveillance imaging. True incidence depends up on the presence of symptoms, size, as well as the duration of follow up and frequency of post-transplant imaging. As such, the reported incidence shows a wide variation ranging from 0.6% to 34% [1-3]. The incidence of symptomatic lymphocele is much lower and has been reported at a mean of 5.2% (range 0.03-26%) [4,5]. The peak incidence of lymphoceles has been reported at 6 weeks post-transplant. However, it may occur

as early as 1-2 weeks after transplant and may occur several months to years after transplantation.

### PATHOPHYSIOLOGY AND RISK FACTORS

#### Surgery related risk factors

The etiology of lymphoceles may be categorised broadly based on surgical or medical risk factors. Among these, the most common are the surgical risk factors involving the donor and recipient operation. During donor kidney procurement, hilar lymphatics may be damaged either at the time of nephrectomy or during 'back-table' dissection. These damaged lymphatics continue to leak lymph after

**Corresponding author:** Dr. Nalaka Gunawansa, Consultant Vascular and Transplant Surgeon, National Institute of Nephrology and Transplant, Colombo, Sri Lanka, Tel: +94 773737644; E-mail: vascular@dmalakagunawansa.com

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reperfusion and can contribute to lymphocele formation. If dissected lymphatics around iliac vessels are ligated or clipped, it would leak lymph. Diathermy does not close lymph vessels unlike causing thrombosis of blood vessels that are diathermised for haemostasis. Furthermore, the presence of the allograft and associated inflammatory processes increase lymph flow from the renal hilum as well as from the lymphatics around iliac vessels, resulting in lymphocele formation due to lymph leakage [3].

Several other factors surrounding the recipient and donor operation have also been recognized as potential risk factors for the incidence of lymphocele. Laparoscopic donor nephrectomy has been implicated with a higher incidence of lymphocele compared to open nephrectomy. Saidi et al. [6] reported a significantly higher incidence of lymphocele with laparoscopic live donor nephrectomy compared to deceased donor transplants. Mazzucchi et al. [7] reported that donor kidneys with complex arterial anatomy carried a higher risk of lymphocele (12.5%) compared to grafts with single renal artery (3.1%).

Sansalone et al. [8] demonstrated that the ipsilateral placement of the kidney and implantation to the common iliac vessels compared to contralateral iliac fossa placement and implantation to external iliac vessels was associated with a lower incidence of lymphocele (2.1% vs. 8.5%). The authors postulated that there is higher lymphatic disruption associated with dissection around the external iliac compared to common iliac vessels. However, other studies that compared the incidence of lymphocele based on different surgical approaches, the degree of iliac dissection and level of surgeons' experience failed to show any significant difference [9,10]. Minimal disruption of lymphatics is the key.

#### Non-surgical risk factors

Multiple non-surgical factors have also been implicated as possible risk factors in the formation of lymphocele. Ulrich [11] studied the potential non-surgical risk factors for lymphocele in over 420 transplants performed over five years. Use of tacrolimus, the incidence of acute rejection and diabetes in the recipient were all found to be significant in univariate analysis. However, during the multivariate analysis, only diabetes in the recipient proved to be an independent risk factor.

Adult polycystic kidney disease in the recipient has also been described as a potential risk factor [12]. The possible explanation has been the external pressure on the inferior vena cava by the polycystic kidney resulting in impaired lymphatic drainage from the allograft and iliac region. Obesity in the donor (BMI>30) has also been described as an independent risk factor for the occurrence of lymphocele [13].

The correlation between the incidence of lymphocele and the use of different immunosuppressive agents is controversial.

Goel et al. [13] demonstrated a significantly higher incidence of lymphocele with the use of sirolimus, mycophenolate and prednisolone combination. Furthermore, Langer [14] also demonstrated that the use of sirolimus was an independent risk factor for lymphocele formation. However, a subsequent study by Tondolo et al. [15] failed to show any correlation based on different immunosuppressive agents including sirolimus. Benavides [16] described the higher incidence of lymphocele with the use of rabbit anti-thymocyte globulin induction.

Lundin et al. [17] demonstrated a significantly higher incidence of lymphocele with the use of low molecular weight heparin after transplantation. The authors postulated that the increased anticoagulant effect impaired sealing of damaged lymphatics resulting in higher incidence of lymphocele. This is difficult to accept because the suggestion that anti-coagulation would affect patency of opened up lymphatics, does not sound a logical argument. Other risk factors implicated with lymphoceles in different studies include: increased recipient age, increased warm ischaemia time [18], acute tubular necrosis and delayed graft function [19], prolonged pre-transplant dialysis [20] and re-transplantation [21].

Goel et al. [13], Khauli [19] and many authors have independently described the acute rejection of the graft as an independent risk factor for the incidence of lymphocele. Veeramani et al. [22] also demonstrated that patients with symptomatic lymphoceles had a significantly higher incidence of acute rejection compared to those who had no lymphoceles (51% vs. 20%). The intense inflammatory process during an episode of acute rejection is involved with increased lymphangiogenesis and lymph flow, possibly explaining its association with lymphocele.

#### CLINICAL PRESENTATION

The vast majority of lymphoceles are asymptomatic and are detected as an incidental finding on imaging. Depending on the size, extent and location in relation to the allograft, lymphoceles may exert pressure effects causing symptomatic presentation. Pressure on the hilar vessels can lead to impaired graft function and may even lead to catastrophic renal artery or vein thrombosis in rare instances where it goes undetected. Pressure on the ureter may lead to hydronephrosis or hydronephrosis of the graft. Pressure on the recipient iliac vein or compression of lymph drainage may lead to unilateral limb oedema, scrotal or vulval oedema and deep vein thrombosis of the iliac veins.

Large lymphoceles may cause abdominal discomfort, pain, urgency (due to bladder compression) and backache (sacral nerve compression). Association with wound dehiscence can lead to sepsis or lympho-cutaneous fistula. The latter presentation requires careful assessment to differentiate from urinary leakage and needs prompt intervention to prevent septic complications.

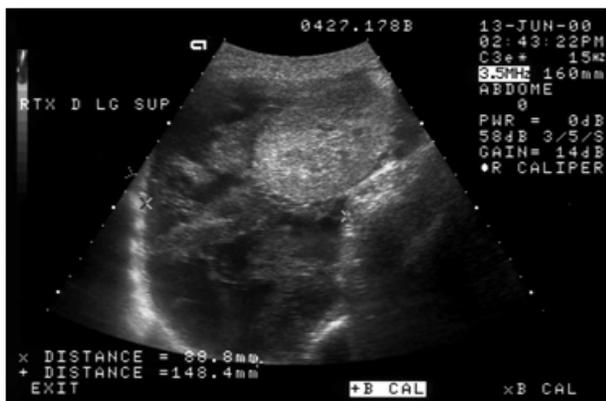
## DIAGNOSIS

The primary modality in diagnosis is imaging. USS can determine the collection as well as its dimensions, location in relation to the graft and possible effects on the graft vessels and ureter (**Figure 1**). USS guided aspiration, and biochemical analysis of contained fluid allows differentiation from urinary leak and urinoma. The biochemical analysis should be done for creatinine, electrolytes, protein content, gram stain and culture. Comparison with simultaneous samples taken from serum and urine for creatinine and electrolytes often become invaluable in differentiating from urinoma.



**Figure 1.** Large lymphocele related to the lower pole of the kidney.

USS appearance can also indicate the possible presence of infection within the collection. Complex echo pattern with internal debris within the collection is more indicative of complicated infected lymphocele (**Figure 2**) [23]. An uncomplicated lymphocele appears hypoechoic or anechoic compared to the hyper-echoic appearance of an infected lymphocele. Further imaging with computerised tomography can also assist in differentiating innocuous lymphoceles from infected ones and other collections such as hematomas.



**Figure 2.** Infected lymphocele with internal echo pattern.

Once a lymphocele has been confirmed by the above tests, some authors have recommended further testing to evaluate the origin of the lymph; donor or recipient. Pacovsky et al. [24] described distinct difference in the creatine kinase (CK) levels of the fluid based on its source, with recipient origin lymph demonstrating higher levels of CK. However, the clinical utility of this analysis from a management perspective remains unproven.

## TREATMENT

The vast majority of asymptomatic lymphoceles are self-limiting and do not require specific treatment. Once they are detected, further testing is done to establish any pressure effects on the vasculature or ureter. In the absence of any demonstrable pressure effects or evidence of infection, such lymphoceles can be safely left alone with periodic imaging surveillance. Notably, small lymphoceles located cephalad to the graft, away from the vasculature and ureter are unlikely to cause pressure effects and rarely need intervention. The decision to intervene depends on definitive pressure effects causing symptoms, graft dysfunction, evidence of sepsis or fistula formation. The reported incidence of lymphoceles requiring definitive intervention varies between 0.04-14.6% [4,5].

### Intra-operative drain placement

The placement of retroperitoneal drains adjacent to the graft at the time of transplantation is a practice performed by many surgeons. These are usually removed once the drainage becomes negligible or before hospital discharge. Some studies have shown that drains placed intra-operatively decrease the incidence of lymphocele [25]. However, other authors have reported contrary outcomes where drain placement showed no benefit in reducing post-transplant lymphocele [26]. Hence, this practice remains an individual choice of the surgeon based on individual practice and patient characteristics.

### Percutaneous aspiration and sclerotherapy

Symptomatic lymphoceles can be aspirated under USS guidance and remain the safest mode of intervention where needed. It also allows for sampling of the collection to establish its true nature and rule out infection. Percutaneous aspiration can, at the best, be a diagnostic step that helps in differentiation from urinoma. Seroma may not appear again, if aspiration is really indicated. However, lymphocele would not be treated just by aspiration. Some clinicians recommend placement of a percutaneous drain to minimise re-accumulation, but external drainage always get infected. Furthermore, some studies have documented the advantage of performing percutaneous drainage followed by sclerotherapy to sclerose open lymphatics, but it is mentioned here only for condemnation.

A systematic review by Lucewicz et al. [4] looking at over 20 studies, reported that simple aspiration alone was

associated with a recurrence rate between 10-95% (mean 59%), compared to 50% with percutaneous drain placement. The eventual success rate also depends on the size and volume of lymphocele. Krol et al. [25] demonstrated that lymphoceles with a volume >140 ml were symptomatic and those >500 ml were unlikely to resolve with percutaneous aspiration, sclerotherapy or drain placement.

Different sclerosing agents have been described in various studies with varying degrees of success. These include; povidone iodine, fibrin glue, 95% ethanol, fibrinogen, sodium tetradecyl sulphate and tetracycline [4,27,28]. The sclerosing agent has been instilled and kept *in situ* for varying periods ranging from 5 min to 24 h. The review by Lucewicz et al. [4] reported the recurrence rate after sclerotherapy was 31% over 14 studies. Placement of a percutaneous drain allows for continuous drainage as well as repeated instilling of sclerosants if needed. However, the chief drawbacks of repeated installation of sclerosants are the risk of introducing infection. Furthermore, several case reports have reported direct graft injury and graft loss as a result of sclerosant installation [27,29]. At the cost of repetition, it is worthwhile emphasizing that external drainage or sclerosing therapy are not correct options.

#### Laparoscopic fenestration

Large lymphoceles can be opened into the peritoneal cavity by making fenestrations in the lymphocele capsule. This allows for lymph to be internally drained to the peritoneal cavity whereby the peritoneal lymphatics would drain it into thoracic duct. In patients who are fit to undergo general anesthesia, this can be performed by laparoscopic fenestration. However, the presence of infection in the lymphocele needs to be carefully excluded before this procedure. Laparoscopic fenestration has shown high rates of success with a minimal rate of recurrence (4-8%) [30,31]. It carries lower procedure-related morbidity, and reduced overall hospital stay compared to open surgical drainage. In the review by Lucewicz et al. [4], (total of 322 patients), 26 patients (12%) required conversion to open drainage. The indications for conversion included technical difficulty in reaching the lymphocele, peritoneal adhesions, thick, impenetrable lymphocele capsule and injury to abdominal viscus.

#### Open surgery

Open surgical drainage of lymphocele is required in the presence of infection (external drainage) or where laparoscopic fenestration is not possible (internal drainage to the peritoneum). In this era of laparoscopy, open drainage is only of historical importance. Lymphoceles located in relation to the lower pole of the graft or complex lymphoceles causing vascular compromise is best treated by open de-roofing. However, open drainage carries a significantly higher risk of ureteric damage and needs to be performed with the utmost care in order to minimise

additional morbidity. The reported recurrence rate following open surgical drainage to the peritoneal cavity is 16% [3].

#### CONCLUSION

Peri-graft lymphocele is fairly common morbidity following renal transplantation. However, the vast majority of these remains asymptomatic and is self-limiting. Nevertheless, close surveillance is required to rule out pressure effects on the graft and possible secondary infection. Multiple risk factors have been described which helps in identifying patients at a higher risk of lymphocele. Symptomatic or complicated lymphoceles require prompt intervention with minimal morbidity to the graft as well as the patient. Small volume collections, only if there is clinical indication, may be treated with percutaneous techniques to allow resolution. Recurrent collections or large volume lymphoceles are best treated by laparoscopic fenestration into the peritoneal cavity. Open surgical de-roofing is of historical importance.

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