



Lymphocele after Renal Transplantation: A Contemporary Review and a Modern Approach for Prevention and Treatment

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Abstract

A lymphocele is a common finding after renal transplantation. The majority of patients are asymptomatic. However, once a lymphocele has become symptomatic, this condition has to be treated. Lymphoceles may originate either from the lymphatic system of the recipient or the transplanted kidney. The most sensible measures to prevent their occurrence therefore seems to be to restrict the transplant bed to the smallest permissible level with careful ligation of the lymphatic vessels in the area of the kidney hilum.

Therapy of a lymphocele after renal transplantation should commence with minimally invasive measures and continue with invasive procedures only if these are unsuccessful, namely, puncture and drainage then sclerotization, and then laparoscopic or open marsupialization.

Keywords: Lymphocele; kidney; transplantation; recipient

Introduction

Lymphocele is a well-known complication of renal transplantation occurring in 0,6% to 22% of the recipients [1-4]. Lymphocele may require surgical intervention because of the complications they cause urinary obstruction, leg edema, deep vein thrombosis, pelvic discomfort, herniation, and lymph leakage through the wound [5]. There are many contributing factors to lymphocele occurrence after kidney transplantation. One of these is donor renal lymphatics. It has been proposed that meticulous ligation of severed lymphatics of the kidney graft in the back table especially in the laparoscopically procured kidneys may decrease the lymphatic complications after transplantation [6].

Although various methods of diagnosis, management, and prevention have been discussed in the literature, the primary focus has been on treatment and no review has summarized all issues

together. The aim of this study was to summarize the current strategies for the prevention and management of lymphoceles.

Etiologies and surgery related factors

The development of lymphoceles after renal transplantation is well documented. The etiology of lymphoceles remains unclear, although they are present in all kidney transplant experiences [7].

The old controversy whether lymphocele is the result of lymph leakage from either the severed recipient iliac lymphatic vessels or the grafted kidney lymphatics seems to favor the latter [8].

A physiological review shows that lymphatic capillaries are more abundant in the kidney cortex compared to the medulla. They run along the intralobular, arcuate and interlobar arteries; not only beside these arteries but also within their walls [9]. At the renal

hilum, 2 to 5 lymphatic ducts are found in close proximity to the main vessels (renal artery and vein).

The well-known and commonly cited contributing factors for lymphocele formation include: the type of immunosuppression used [10], high dose steroid use, use of diuretics, extensive perivascular dissection of the iliac vessels, acute rejection episodes, delayed graft function, source of graft (cadaveric vs living related donor), the etiology of the patient's renal failure such as adult polycystic kidney disease, re transplantation, and some pediatric population [2, 7, 11].

Concerning the pediatric population, in a retrospective single institution review of 241 pediatric kidney transplants performed from 2000 to 2013; Giuliani et al. showed that older age (≥ 11 yr), male gender, BMI percentile for age $\geq 95\%$, and multiple transplantations were Significant risk factors for lymphocele formation [12].

The formation of post-transplant lymphoceles obviously originates in the surgical transection of lymphatic ducts. As demonstrated by lymphangiography two sources of lymphatic leak have been proposed: injured lymphatics in recipient's iliac space and injured lymphatics in the kidney graft [13,14].

A possible distinction between these two origins is feasible by analyzing their composition. In fact, reports showed higher levels of creatine kinase in lower limbs lymphatics vessels compared to renal lymphatics [15-17].

It was believed that the perivascular lymphatics dissection along the iliac vessels was a determining factor for lymphocele development, and that lymphocele could be prevented by ligation of these vessels. Despite many reports showing absence of lymphocele after an accurate ligation of the iliac lymphatics [18], things are still unclear.

Many studies were published concerning the influence of some surgical aspects in decreasing the lymphocele incidence. Indeed, one prospective study suggested a cephalad implantation of the renal graft using vascular anastomoses on the common iliac vessels to minimize lymphocele incidence, but this technique has not yet gained wide exposure [11].

The same concept was reevaluated in another study. This time, a significant reduction of the incidence of lymphocele from 8.5% to 2.1% was noted in 140 patients operated with the new technique versus 140 patients in the control group operated with the standard method [14].

Another retrospective study done by Saidi et al, evaluated the impact of laparoscopic living donor nephrectomy on lymphatic complications after kidney transplantation. They concluded that the incidence of prolonged lymphatic leak is higher in recipients

who received kidney grafts procured laparoscopically. These observations may indicate that the major source of persistent lymphatic leakage is lymphatics of the allograft rather than severed recipient lymphatics. More meticulous ligation of severed lymphatics of the kidney graft in the back table, especially in the laparoscopically procured kidneys, may decrease the lymphatic complications after kidney transplantation [13].

To our date, many researchers are still questioning whether surgical preparation of the kidney with accurate ligation of the hilar lymphatic vessels would effectively reduce its incidence. Hence, a clear answer is reported in our study favoring lymphatic vessels ligation over non preparation of the kidney graft on lymphocele incidence. Indeed, acute rejection rates dropped significantly from 15 to 6.3%, and incidence of symptomatic lymphocele decreased from 17.5% to 0%.

Diagnosis and Clinical Aspects

Ultrasound is currently the preferred method for diagnosis of lymphoceles after the renal transplantation. In complicated cases, radioisotope imaging, computed tomography and magnetic resonance imaging are additional methodologies commonly used[5].

Lymphoceles may lead to deterioration of renal function and the patient with a lymphocele may be inappropriately treated for allograft rejection. Other clinical findings associated with lymphoceles in renal allograft recipients include lower abdominal swelling or mass, edema over the allograft or of the ipsilateral leg, hypertension, drainage from the incision, enlarged allograft, fever without an obvious source of infections, urinary frequency, ipsilateral ileo femoral thrombo phlebitis, and weight gain [4].

Prevention

Prevention of lymphocele formation primarily involves the best method for controlling perivascular lymphatic leaks. A study comparing surgical ties to ultrasonic devices in the surgical dissection technique for control of lymphatics failed to show a statistical advantage to either technique when groups were compared based on patient age, gender, graft source, or repeat transplant [19].

Berardinelli et al. demonstrated the effectiveness of a synthetic polyethylenglycol(PEG) sealant to prevent lymphocele formation after kidney transplantation [20].

Treatment

Lymphoceles are usually asymptomatic and diagnosed incidentally by ultrasound. In most cases, lymphocele disappear spontaneously without any need for a treatment. Several important factors can guide our choice of treatment: severity of the symptoms, lesion size, potential post-therapeutic complications, and the

clinical condition of the patient. For the conservative treatment of posttransplant lymphoceles, percutaneous needle aspiration, continuous drainage over a period of time via various kinds of catheters, and sclerotherapy with various agents have been proposed [21].

Aspiration

Ultrasound-guided aspiration can be used as a diagnostic tool or treatment. to both diagnose and treat a lymphocele. It can be used as the initial treatment modality to relieve urinary obstruction, recover kidney function, and prevent emergency situations. Although simple, safe, and economical, a repeated treatment may be necessary with a low a low risk of infection in each aspiration. A systematic review by Lucewicz et al. [4] looking at over 20 studies, reported that simple aspiration alone has a recurrence rate ranging between 10% and 95% [22].

External drain placement

A lymphocele can also be treated by external drainage by placing a drain. However, this procedure takes a long time and can cause problems related to major fluid loss and secondary infection (particularly in immunosuppressed transplant recipients). External drainage has an efficacy of 50% and a recurrence rate of 20%–60% [23].

Sclerotherapy

The instillation of a sclerosing agent is another treatment approach.

These include povidone iodine, fibrin glue, 95% ethanol, fibrinogen, bovine protease inhibitor, human thrombin, calcium chloride, gentamy sodium tetradecyl sulphate and tetracycline]. The sclerosing agent has been instilled and kept in situ for varying periods ranging from 5 min to 24 h [24,25].

Tasar et al., reported a mean therapy duration of 17 days and a mean alcohol volume of 30 cm³ per session. Out of 18 cases, there was one recurrence, one graft loss, and ten minor complications including local discomfort and low- grade fever. The authors concluded that this method of sclerotherapy was safe and cost-effective [25].

Another analysis of 30 lymphocele patients demonstrated that alcohol injection was a safe and cost-effective treatment, with a success rate of 94%. The authors reported two cases of recurrence and all complications were minor, including catheter-induced infections and catheter displacements [26]. Povidone iodine has been used also as a sclerotherapy agent with a failure rate of less than 11%, but it takes 20–30 days for leaking to cease and iodine-induced acute kidney failure may occur [27]. Limited success has been reported using tetracycline as a sclerosing agent [28].

Instillation of sclerosing agents improves the rate of success of percutaneous management; however, it may cause a dense scar around the renal transplant with potential problems in the long-term [21].

Continuous drainage as well as repeated instilling of sclerosants could be done if needed, by placing a percutaneous drain. However, the main problem encountered during repeated installation of sclerosants is the risk of introducing infection. Furthermore, several case reports have reported direct graft injury and graft loss as a result of sclerosant installation [25]. Hence, with the cost of repetition, it is worthwhile emphasizing that external drainage or sclerosing therapy are not correct options.

Post-transplant lymphoceles have also been treated with a combination of percutaneous aspiration and sclerotherapy. Although this reduced the recurrence rate, recurrences were still reported in 20% of cases [22].

-Surgery: Byron et al. [29] first described open surgical internal drainage in 1966, and these techniques have successfully been used in many patients; however, they still reflect an invasive procedure. The operative strategy is to perform a peritoneal fenestration through a laparotomy, minilaparotomy, or via a laparoscopic approach. Some authors suggest the use of an omentum flap to decrease the risk of lymphocele relapse, but others do not [30].

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).

The open procedure is safe and 100% effective because the lymphocele can be localized accurately. However, the recurrence rate is still 15%. This may be attributed to the high rate of lymph vessel injuries incurred during the open method.

The recurrence rate of the laparoscopic method is lower (0%–10%) because the rate of lymph vessel injuries is lower. Also, the hospitalization period is shorter in this method [31].

In a meta-analysis, Lucewicz et al reported that 12% of laparoscopic operations had to be converted to open surgery, due to technical difficulty in reaching the lymphocele, peritoneal adhesions, thick, impenetrable lymphocele capsule and injury to abdominal viscus [21]. Indeed, it would be helpful in some cases to use an intra-operative ultrasound can avoid organ injury during laparoscopy. Schips et al reported a technique by which the lymphocele was laparoscopically fenestrated under diaphanoscopic guidance and the lymphocele cavity was dilated through the injection of a sterile fluid. Using this approach, the authors were able to determine the exact site of the incision by detecting the light of the cystoscope [32].

Laparoscopic fenestration can cause intestinal herniation into the peritoneal window leading sometimes to strangulation requiring urgent intervention. However, in this era of laparoscopy, open drainage is only of historical importance. In addition, the effectiveness of the laparoscopic approach along with its, low recurrence rate, and low complication rate make it the treatment of choice when other methods fail [28].

Conclusion

Lymphoceles are common and well-known complications that occur in up to 26% of kidney transplant recipients. The cause of lymphocele formation is unclear, but it is believed to result from transection of the lymphatic vessels accompanying the external iliac vessels during transplantation surgery and subsequent lymph accumulation in a nonepithelialized cavity in the extra-peritoneal plane adjacent to the transplanted kidney. In order to prevent the formation of a lymphocele, preparative steps should be kept to the necessary minimum, and lymph vessels in the vicinity of the kidney hilus carefully ligated. Therapy of a lymphocele after renal transplantation should commence with minimally invasive measures and continue with invasive procedures only if these are unsuccessful, namely, puncture and drainage then sclerotization, and then laparoscopic or open marsupialization.

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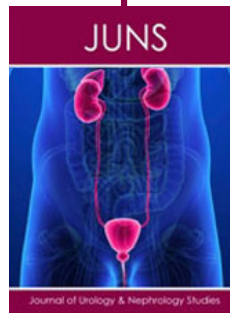
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