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**ARTÍCULO ORIGINAL**

# EVALUATION OF PATIENTS WITH LYMPOCELE AFTER RENAL TRANSPLANTATION

*EVALUACIÓN DE PACIENTES CON LINFOCELE LUEGO DE TRASPLANTE RENAL*

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## ABSTRACT

**Introduction:** The lymphocele is a common complication following renal transplantation and may cause significant clinical problems especially when reachs to big volumes. The aim of this study is to present the clinical characteristics, diagnostic approaches, and therapeutic strategies of lymphocele formations in a group of Turkish patients. **Methods:** A total of 244 renal transplantations were included in this retrospective study. Data of patients who were diagnosed with lymphocele during the postoperative period were analyzed. **Results:** Ten (2.4%) patients have been diagnosed with lymphocele. There were six males and 4 females, with a mean age of 46 years. The median onset was 19 days posttransplantation. The median size of the lymphoceles was 53 mm. All lymphoceles were localizated between the lower pole of the transplanted kidney and urine bladder. On presentation, one patient had hydronephrosis and three patients had elevated serum creatinine while the remaining six ones were asymptomatic. Five patients were successfully treated by percutaneous aspiration whereas two patients required surgery. Three patients' lymphoceles dissolved spontaneously. **Conclusion:** Preventive strategies including preserving the lymphatics of the recipient, careful organ retrieval and 'back table' work are of great importance to reduce the incidence of lymphocele. Early decision of radiological or surgical intervention should be considered in patients with symptomatic lymphoceles in order to prevent further complications.

**KEYWORDS:** diagnosis; lymphocele; renal transplantation; treatment

## RESUMEN

**Introducción:** El linfocele es una complicación frecuente luego de un trasplante renal y puede ocasionar problemas clínicos importantes, especialmente, cuando alcanza volúmenes elevados. El objetivo de este estudio es presentar las características clínicas, métodos de diagnóstico y estrategias para el tratamiento del linfocele en un grupo de pacientes turcos. **Material y métodos:** Se incluyeron 244 pacientes en este estudio retrospectivo. Se analizaron los datos de pacientes diagnosticados con linfocele durante el período postoperatorio. **Resultados:** Se diagnosticó linfocele a diez pacientes (2,4%). Eran seis hombres y cuatro mujeres con una edad promedio de 46 años. El comienzo promedio fue 19 días luego del trasplante. El tamaño medio de

los linfoceles fue de 53 mm. Todos se encontraban entre el polo inferior del riñón trasplantado y la vejiga urinaria. En la consulta, un paciente presentó hidronefrosis, y tres pacientes, creatinina sérica elevada, mientras que los seis restantes eran asintomáticos. Cinco pacientes fueron tratados con éxito por aspiración percutánea; en cambio, otros dos pacientes requirieron cirugía. Tres pacientes mostraron disolución espontánea de los linfoceles. **Conclusión:** Las estrategias preventivas, que incluyen la preservación de los vasos linfáticos del receptor, la extracción cuidadosa de los órganos y la preparación de estos antes de realizar el trasplante, son de gran importancia para reducir la incidencia de linfocele. Debe considerarse tempranamente la intervención radiológica o quirúrgica en pacientes con linfoceles sintomáticos para prevenir complicaciones adicionales.

**PALABRAS CLAVE:** diagnóstico; linfocele; trasplante renal; tratamiento

## INTRODUCTION

The lymphocele is defined as a lymphatic collection around the renal graft and urinary bladder, covered by a pseudomembrane. It is one of the most common complication following kidney transplantation, with a reported incidence of up to 40%.[1-4] It can arise from either the lymph that drains through the lymphatic vessels in the sinus of the transplanted kidney or the lymphatic vessels surrounding the iliac vessels of the recipient.

Although most of the lymphoceles are asymptomatic, it may cause significant clinical problems such as ureteral obstruction or compression, venous thrombosis, unilateral leg edema, abdominal discomfort, infection, and deterioration of graft function, especially when reachs to big volumes.[2-3, 5-6] Therefore, early diagnosis of this annoying complication is of great importance to prevent potential unwanted situations. In this context, regular and detailed patient follow-up and appropriate radiological examinations such as sonography are the first step tools in the diagnosis. Management of lymphocele varies according to the location and amount of the collection, and its clinical manifestations. Large and/or complicated lymphoceles requires surgical interventions while small lesions are often treated conservatively.[7-8]

In this study, we aimed to present the clinical characteristics, diagnostic approaches, and therapeutic strategies of lymphocele formations in a group of Turkish patients, and to discuss the outcomes with the relevant literature.

## MATERIAL AND METHODS

### Study design

Between January 2006 and June 2018, a total of 244 renal transplantations were performed at the Gazi University Transplantation Center, Ankara, Turkey. Among those, renal transplant recipients who developed lymphocele during the postoperative period were included in this retrospective study. Postoperative haematomas, urinomas and abscesses were excluded from the analysis. Data of the patients were obtained from the hospital records and personnel charts.

### Transplant surgery

All transplantations were performed by a single surgeon through an extraperitoneal approach in the iliac fossa. All patients were received prophylactic antibiotic treatment with 1 gr intravenous ceftriaxone twice a day until the removal of drain. We have been using modified version of the Lich-Gregoir method with Haberal's anastomosis technique for ureteroneocystostomy anastomosis with DJS since January 2006. Pelvic drain and urinary catheter were usually removed at the second and fifth postoperative day, retrospectively.

### Postoperative course

All patients were followed up at regular intervals. Rutinary detailed physical examination and biochemical tests were done in all cases. All recipients were received trimethoprim/sulfamethoxazole prophylaxis for

three months after transplantation. Appropriate immunosuppressive therapy (Prograf-based triple immunosuppression) was given to all patients for an appropriate period. Double J catheter was removed on postoperative 4th week under sedation by the department of Urology. Ultrasonography was the primary imaging method in patients with symptoms and signs indicating lymphocele. The treatment decision was made according to the size and localization of the lymphocele, patient's complaints, and biochemical values. In general, conservative approach was preferred in small and asymptomatic lymphoceles, whereas large and symptomatic ones were treated by radiological intervention or surgery.

**Statistical analysis**

Data analyses were done by using the Statistical package for social science (SPSS 21.0 software, IL-Chicago- USA) standard version. Descriptive analyses were presented as number/ percentage for categorical variables and mean ± SD/percentages for continuous variables.

## RESULTS

A total of 244 patients who underwent renal transplantation were included in this study. Renal transplantations were done in 89 recipients from deceased donor and the remaining 155 from living related donor (first degree 121, spouse 25 and 9 donors were up to $4^{th}$ degree relative).

Ten (2.4%) kidney recipients have been diagnosed with lymphocele during the postoperative period. Six out of 10 were male and four were female. Among those, transplantation was done from decease donor in five patients and from living related in five donors. The mean age of these patients in our study was 46 (ranging from 23 to 61) years old. The median onset was 19 days (range 5-32) after transplantation. The median size of the lymphoceles was 53 mm (range 15-100 mm), all of which were located at the lower pole of the transplanted kidney. The basic characteristics of the patients with lymphoceles were summarized in **Table 1**.

**Table 1.** Basic characteristics of patients with lymphocele after renal transplantation

| **Patients** | **Age** (y) | **Gender** (F/M) | **donor** | **Onset** (day) | **presentation** | **Size** (mm) | **treatment** |
|---|---|---|---|---|---|---|---|
| **Patient 1** | 42 | F | deceased | 42 | elevated cr | 30 | fenestration |
| **Patient 2** | 28 | M | living | 5 | asymptomatic | 15 | conservative |
| **Patient 3** | 61 | F | deceased | 11 | asymptomatic | 30 | conservative |
| **Patient 4** | 45 | M | living | 9 | asymptomatic | 30 | conservative |
| **Patient 5** | 57 | M | deceased | 14 | asymptomatic | 60 | percutaneous |
| **Patient 6** | 55 | F | deceased | 32 | hydronephrosis | 100 | open drainage |
| **Patient 7** | 41 | F | living | 22 | asymptomatic | 40 | percutaneous |
| **Patient 8** | 23 | M | living | 29 | asymptomatic | 50 | percutaneous |
| **Patient 9** | 33 | M | living | 15 | elevated cr | 80 | percutaneous |
| **Patient 10** | 23 | M | living | 14 | elevated cr | 90 | percutaneous |

**Abbreviations: Y,** *year*; **F,** *female;* **M,** *male*; **cr,** *creatinine*; **mm,** *milimeter*

Diagnosis of lymphoceles after kidney transplantation included clinical examination and an initial sonographic imaging in all patients. Biochemical analysis of the collecting fluids' electrolyte and retention parameters were also performed in order to make a differential diagnosis of lymphocele from a urinoma formation. In this study group, all collections

referred to a lymphocele was named after biochemical analysis of the collecting fluids.

One patient had hydronephrosis on presentation while three patients had elevated serum creatinine at the onset of lymphocele. On the other hand, two patients' lymphoceles were diagnosed at routine follow-up, without any complaints. All were on Prograf based triple immunosuppression.

Five patients' lymphoceles were successfully treated percutaneously in the interventional radiology unit. Surgery (fenestration in one and open drainage in one) was required in two patients. Three patients' lymphoceles were dissolved spontaneously. There was neither graft nor patient loss due to lymphocele in this study group.

## DISCUSSION

Because of the rising global trend in renal transplantation over the past decades, lymphocele formation has become a common problem that may lead to serious clinical situations when treated lately or inadequately. In this regard, the present study focused on the clinical features, diagnostic approaches, and the treatment options of lymphocele formation following renal transplantation. In our cohort, the incidence of lymphocele was found to be 2.4%. This ratio was lower than those reported in the majority of similar studies, probably due to the higher experience of our transplantation center on renal transplantation.[9-11]

As known, lymphocele formation can be a complication of any surgery involving the lymphatic system. In renal transplantation, various surgical and medical risk factors have been determined for the development of this entity. Dissection of the lymphatics around the iliac vessels of the recipient and dissection of renal lymphatics of the donor during the time of organ procurement surgery or during 'back table' work are the most common accused surgical risk factors.[7] In a recent study by Joosten et al, multiple heterogeneous predictors including venous anastomosis on the external iliac vein, concomitant peritoneal dialysis catheter removal, perfusion defects, shorter operating time, splint over seven days, double J stenting, discharge with drain, low initial drain production and ureteral obstruction were found to be associated with the development of symptomatic lymphocele after renal transplantation.[11] However, as the authors mentioned, those results are needed to confirm by multicenter or larger scale studies. Besides, several non-surgical factors such as older age, obesity, primary diagnosis of autosomal dominant polycystic kidney disease, and presence of peritoneal dialysis catheter have been also reported as potential predictors of lymphocele formation.[7, 11-13] The use of some immunosuppressive drugs, such as m-TOR inhibitors or MMF (14) or steroids may be associated with lymphoceles and delayed wound healing.[15] It was also confirmed in our material that the use of m-TOR inhibitors (Everolimus, Sirolimus) was more common in patients operated on because of lymphocele; however, m-TOR inhibitors use was not a risk factor of LRT in the univariate and multivariate model of logistic regression.[15] The lymphocele formation can be attributed to the anti-lymphoangiogenic effects of m-TOR inhibitors during tissue regeneration, m-TOR inhibitors interfere with the intracellular pathway activation of LECs by vascular endothelial growth factor-C, the main initiator of lymphangiogenesis. However, in the literature there are reports suggesting that de novo kidney transplant patients receiving an initial Everolimus dose of 1.5 mg do not appear to have a pronounced increased risk of wound healing complications versus patients receiving mycophenolic acid.[15]

Although most of the lymphoceles are clinically silent, edema in the inguinal regions and/or legs and impaired graft function have been reported as the most common clinical manifestations.[7, 10, 16] In accordance, sixty percent of patients were asymptomatic in our cohort whereas only one case presented with hydronephrosis.

Ultrasound evaluation is the key diagnostic tool in the evaluation of suspected cases.

Sonography can easily distinguish lymphocele from hematoma or urinoma, and show any urinary obstruction that leads hydronephrosis. Moreover, ultrasonography-guided aspiration allows biochemical and cytologic analysis.[7] Additional radiological imagen such as dynamic renal Tc 99m scintigraphy, intravenous urography, and computed tomography are not necessary in typical cases, but they are required in complicated ones.[17] Early recognition of the lymph reservoir may facilitate the diagnosis, and prevent kidney failure, because even a small lymphocele can lead to graft dysfunction. In our material, the smallest symptomatic lymphocele was 4 ml. Although in the majority of cases small lymphoceles containing <100 mL of lymph are asymptomatic, and resolve spontaneously with time, larger collections may become apparent clinically about several months after transplantation.[16] In our center, two cases with symptomatic lymphoceles were qualified to fenestration after transplantation. In the literature, lymphocele has been reported as long as 3.7 years after transplantation.[18]

Lymph fluid can accumulate in different locations. Lymphocele located near the upper part of the graft is usually low pressure and asymptomatic. In such cases, the size of the lymph reservoir is not of crucial importance. In contrast, the increasing pressure in the lymphocele placed near the upper part of the graft can cause difficulties in wound healing and result in eventration, cutaneous fistula, or abdominal hernia. When lymph fluid accumulates in the area of vessels, both in the recipient and the transplanted kidney, it can cause increasing pressure in the limited spaces, and influence on the deterioration of renal graft function.

When asymptomatic, a lymphocele does not require treatment; it resolves spontaneously. In symptomatic cases, ultrasonography-guided simple aspiration is mostly used as an initial treatment because of its both diagnostic and therapeutic properties. It can also allow relief of urinary obstruction and recovery of renal functions and can be repeated in appropriate cases. If complications occur, treatment is not standardized, and most often involves laparoscopic drainage or open surgical marsupialization. In our study group only two patients required surgical treatment due to failure of the radiological treatment. Other treatment modalities including sclerotherapy with ethanol, povidone iodine, and tetracycline have been used for this purpose; however, higher recurrence rates or potential complication risks limited their widespread use.[19-20]

## CONCLUSION

Lymphocele still remains an important complication after renal transplantation. Considering its serious complications that may lead to graft rejection, preventive approaches including preserving as much as possible the lymphatics of the recipient and careful organ retrieval and 'back table' work are of great importance to reduce the incidence of lymphocele. Additionally, early decision of radiological or surgical interventions should be considered in patients with symptomatic lymphoceles, so as to shorten hospital stay and prevent further complications.

**Conflict of interest:** Authors declare no conflict of interest.

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