Comparison Between Bipolar Lymphatic Vessels Cautery and Suture Ligature in Prevention of Postrenal Transplant Lymphocele Formation: A Randomized Controlled Trial

Nasser Simforoosh,[1] Ali Tabibi,[1] Hamed Mohseni Rad,[2] Hamid Reza Gholamrezaie[2]

Abstract

Objectives: **In this randomized controlled trial, our aim was to compare bipolar cautery of lymphatic vessels with standard silk-tie ligation in renal transplant procedures for prevention of lymphocele formation.**

Materials and Methods: **Sixty end-stage renal disease patients were enrolled in a prospective randomized controlled trial. The mean age of recipients in the suture ligature group was 41.6 years (range, 6-65 years) and 40.9 years in the bipolar cautery group. Patients were assessed by symptoms; however, ultrasonography was also used as the primary diagnostic procedure in all patients to find lymphocele collection within 5 months.**

Results: **Of 60 patients, 25 received living-donor kidney transplant and 35 received deceased-donor kidney transplant. Fifty-threeprocedures were first-time kidney transplants, 6 were retransplants, and 1 was for athird-time transplant. No lymphocele collection (symptomatic or asymptomatic) was diagnosed by ultrasonography at the 5-month follow-up. Postoperative pain was not significantly different between the 2 groups (*P*= .245). The time for ligation or cauterization of lymphatic vessels was similar between the 2 groups. Mean duration of operative field drainage was 5.6 days in the suture ligature group and 6.07 days in the bipolar cautery group (not significantly different; *P*= .547).**

Conclusions: **Bipolar cautery of lymphatic vessels to prevent lymphocele formation in kidney transplant seems to be an effective, easy, and safe method.**

Key words: *End-stage renal disease, Kidney transplant, Ultrasonography*

Introduction

Lymphocele formation after renal transplant is a complication that may cause pain, place pressure on the allograft, and sometimes result in reoperation. Therefore, prevention of lymphocele formation is important. The incidence of symptomatic lymphocele has been reported to be about 5.2%,whereas 0.04% to 14.6% of lymphoceles need some kind of intervention.[1] The peak time of lymphocele formation is 6 weeks posttransplant, but it may emerge from 2 weeks to 6 months posttransplant.[2]

Electrothermal bipolar cautery spreads less thermal energy than monopolar cautery, which may decrease the retroperitoneal lymphocele after pelvic lymphadenectomy in gynecologic cancers.[3] Although conventional bipolar cautery has become popular in pelvic laparoscopic lymphadenectomy,[4] this method has not been considered in renal transplant to prevent lymphocele formation.To our knowledge, this is the first trial to evaluate the use of bipolar cautery in prevention of lymphocele formation in kidney transplant recipients.

This randomized controlled trial aimed to compare the efficacy of bipolar cautery versusstandard silk-tie ligation in renal transplant procedures for lymphocele prevention.

Materials and Methods

Sixty end-stage renal disease patients were enrolled in a prospective randomized controlled trial. Recipients of living or deceased kidney donations were randomized into 2 groups for suture (silk-tie) ligature or bipolar cautery treatment. Patient age

From the [1]Department of Urology, Shahid Beheshti Medical University, Tehran, Iran; and the [2]Department of Kidney Transplantation, Labbafinezhad Hospital, Tehran, Iran

Acknowledgements: *The authors have no sources of funding for this study and have no conflicts of interest to declare.*

Corresponding author: *Hamed Mohseni Rad, Fellowship of Kidney Transplantation in Labbafinezhad Hospital, Tehran, Iran*

Phone: *+98 9125847866* ***E-mail:*** *Sirhamed2@gmail.com*

Experimental and Clinical Transplantation (2018)

DOI: 10.6002/ect.2017.0207

ranged from 6 to 65 years with a mean age of 41.6 years in the suture ligature group and 40.9 years in the bipolar cautery group. The suture ligature group comprised 15 male and 15 female patients, and the bipolar cautery group comprised 18 male and 12 female patients. Written, informed consent was signed by all of the patients before study participation.

Our study also included multiple vessel kidneys. A standard right or left lower pararectal incision was made in every recipient, and the renal bed was prepared extraperitoneally. External iliac vein and common iliac or internal iliac artery were selected for allograft anastomosis. Lymphatic vessels were tied by 3-0 and 2-0 silk suture without any cautery in the suture ligature group; vessels were cauterized in the bipolar cautery group.

Our study had no inclusion or exclusion criterion except for the informed consent of the patients. Study investigators were blinded to patient randomization. Two closed-suction Hemovac drains, one in the upper pole of the allograft and another near the bladder, were inserted in all patients. The drain was removed when discharge was less than 50 cm^3 over 24 hours. All ureterocystostomy Gregoir-Lich antireflux anastomosis was done with Vicryl 5-0 suture associated by stent connected to a Foley catheter, which was extracted on day 7 after surgery. All patients were evaluated for pain on a scale of 0 to 10, with 0 being no pain and 10 being the worst pain imaginable.

All patients received triple immunosuppression regimens with cyclosporine or tacrolimus, mycophenolate mofetil, and steroids. High-risk patients received thymoglobulin as induction therapy. Patients were observed for pain, drainage length, and lymphocele formation. Ultrasonography was performed to assess lymphocele formation at 5 months posttransplant.

Results

Our study involved 60 kidney recipients seen in our hospital in 2017 (Table 1). End-stage renal disease was due to polycystic kidney disease in 6 patients, renal stone in 2 patients, tuberous sclerosis in 1 patient, congenital factors in 2 patients, diabetes mellitus in 11 patients, urinary reflux in 4 patients, glomerulonephritis in 11 patients, hypertension in 12 patients, and unknown or unclear causes in 11 patients. Preemptive transplant was performed in 10 patients; of 50 patients who underwent dialysis, 5 were on peritoneal dialysis and 45 were on hemodialysis (duration of 1 to 60 mo). Twenty-five patients received allografts from living donors, and 35 received allografts from deceased donors.

Table 1. Patient Data

	Silk Ligature Group	Bipolar Cautery Group	*P* Value
Male/female	15/15	18/12	
Age	41.6 y (range, 6-62 y)	40.93 (range, 8-65 year)	.874
Body mass index	24.13 kg/m^2	25.25 kg/m^2	.202
Ultrasonographiccollection atmonth 5	No collection	No collection	
Vessel preparationtime	15.73 ± 3.65 min (range, 10-21 min)	mean 15.73 ± 3.17 min (range, 9-23 min)	<.001
Postoperative pain			.245
1-3	5	6	
4-5	20	21	
6-8	3	2	
9-10	2	1	
Drainage duration	5.6 ± 2.2 d (range 3-12 d)	6.07 ± 1.8 d) (range, 3-10 d)	.547
Surgery site infection	1 patient	0 patients	.236
End-stage renal disease cause			.406
Glomerulonephritis	7	4	
Diabetes mellitus	5	6	
Hypertension	6	6	
Congenital	0	2	
Reflux nephropathy	1	3	
Renal stone	2	0	
Polycystic kidney disease	5	1	
Tuberous sclerosis	0	1	
Unknown	4	7	
Donor type			.462
Living	13	12	
Deceased	17	18	
Transplant number			.327
1st	25	28	
2nd	4	2	
3rd	1	0	

Of the 60 patients, 53 patients had received a first-time kidney transplant, 6 had received a second-time transplant, and 1 had received a third-time transplant. Seven patients encountered delayed graft function. Body mass index was 24.13 kg/m^2 for the silk ligature group and 25.25 kg/m^2 for the bipolar cautery group (no significant difference). Two patients were excluded from the study because of graft nephrectomy due to vein thrombosis and infection. Both of these patients had been enrolled in the silk ligature group. There were no symptomatic and asymptomatic lymphocele collections in the remaining 58 patients, as checked by ultrasonography at 5-month follow-up. Postoperative pain was also not significantly different between the 2 groups (P = .245). Duration of lymphatic vessel clearance and preparation for anastomosis was similar between the 2 groups, ranging from 9 to 23 minutes (average of 15.73 min in both groups). Mean duration of drainage in the silk ligature group was 5.6 days and 6.07 days in the bipolar cautery group (not significant, P = .547).

It was interesting that no lymphocele formation or any collection was detected in any of the 58 patients seen at the 5-month follow-up.

Discussion

Box and associates reported that bipolar cautery can effectively seal a porcine thoracic duct during laparoscopy.[5] Farouk and associates showed that electrocoagulation of lymphatic vessels in kidney transplant is comparable with use of silk ligature.[6] Simforoosh and colleagues established the safety of bipolar electrocoagulation of lymphatic vessels in laparoscopic retroperitoneal dissection.[7] The group also reported that laparoscopic donor nephrectomy can be safely accomplished with bipolar cautery.[8,9] Bipolar cautery has lower thermal current propagation compared with monopolar electrocoagulation and is better than silk ligature for closure of delicate vessels. Our study reported efficacy of lymphatic vessel bipolar electrocoagulation in renal transplant surgery as a first randomized controlled trial.

Lymphocele is a lymph-filled collection in the retroperitoneum without epithelial lining that could result in hydronephrosis and graft dysfunction.[10] If the iliac vessels in recipient lymphatics are not sealed off securely with sutures during dissection, lymphocele formation can occur.[11] The lymphocele usually has a fibrous dense capsule; other causes include steroid therapy and heparin use, retransplant surgery, and incomplete lymphatic occlusion during transplant.[12,13]

In our hospital, kidney transplant is usually performed by anastomosis of allograft vein to external iliac vein and artery to internal or common iliac artery. It has been reported that the external iliac artery can be surrounded by lymphatic vessels.[14] Presently, kidney recipients are more likely to be affected by diabetes mellitus than immunosuppressive medications that negatively affect vessel repair. Extraperitoneal surgical procedures also augment lymphocele formation. Lymphorrhea is a minor kidney transplant complication that could lead to lymphocele formation.[7] A nonsuction surgical drain placement or peritoneal aperture at surgery can decrease perinephric collection.[3]

Lymphoceles may cause lower limb and inguinal edema, urgency, abdominal discomfort, ileus, deep vein thrombosis, and infection.[10] Inferior vena cava compressive syndrome after kidney transplant has also been reported.[15] Biochemical analysis of perinephric collection to differentiate seroma and lymph from urine could be examined by creatinine, sodium, potassium, total protein, and albumin.[16]

The lymphatic system is pivotal in homeostasis of interstitial body fluid temperance and immunologic cell recruitment.[17] The kidney has a capsular and hilar lymphatic system, in which the hilar system is predominant but that can reverse underpathologic circumstances.[18] Smooth muscle cells in the lymphatic vessel wall and their one-way valves contribute to lymph pump toward the blood system.[19] Lymphatic vessels are affluent around interlobar and arcuate vessels but rare around glomeruli and medulla.[20]

Medications like sirolimus, antithymocyte globulin, high-dose mycophenolate mofetil, and diuretics can interfere with tissue regeneration and thus increase lymphocele formation.[11,21,22] Diabetes mellitus, obesity, senescence, acute rejection, and acute tubular necrosis-delayed graft function have been also reported to be associated with lymphocele complications.[23] Longer warm ischemia time of the kidney and long-term dialysis have also been shown as reasons for lymphoceles.[13]

Lymphoceles may cause considerable morbidity. Symptomatic pelvic lymphoceles have been reported in 1.6% to 3.5% of patients after prostate cancer

lymphadenectomy, with rate of 34% for patients with gynecologic lymphadenectomy. High body mass index and postoperative radiotherapy have been associated with increased occurrence of pelvic lymphoceles. Meticulous surgical manipulation and exact lymphatic closure, especially around the external iliac artery, prevent pelvic lymphocele formation.[24] The effects of open or closed drain and intraoperative fibrin glue application on lymphocele formation has not been elucidated.[3]

Anastomosis of renal vessels to the common iliac vein and artery because of lower lymphatic wrenching has been shown to decrease lymphocele formation from 8.5% to 2.1%.[14] One study showed that lymphatic drainage was longer in kidney recipients of laparoscopic donor transplant (8.6±2.5 days) than in recipients of deceased-donor transplant (5.4±2.5 days) ($P < .05$).[25] Another study showed that single renal artery kidney transplant has a lower incidence of lymphocele formation than multiple renal arteries, which may be because of insufficient lymphatic ligature (3.1% vs 12.5%; $P < .05$).[26] However, some studies have not shown differences in lymphocele rate according to surgical technique or surgeon experience.[27,28] Pacovsky and associates proposed that a perinephric collection creatinine kinase level of higher than 210 U/L meant that the source of drain was > 85% from recipients. This may be because creatine kinase is produced by the skeletal muscle, with drain from the iliac vessel into collection. A creatine kinase concentration below 35 U/L meant that <30% is from a recipient source.[29]

Ultrasonography has increased the ability to diagnose asymptomatic lymphocele collection incidence from 0.6% to 18.1% or 33.9%.[30,31] Lymphoceles are usually asymptomatic in patients, and ultrasonography and computed tomography scans can detect asymptomatic lymphoceles. Aspiration of collections should be done under ultrasonographic guidance if larger than 2 cm or more than 140 cm^3 and symptomatic. Large symptomatic lymphoceles may require open or laparoscopic surgery.[32]

Large kidneys in recipients with autosomal dominant polycystic kidney disease can compress the inferior vena cava, interfering lymphatic flow and increasing lymphocele rate.[33] Anticoagulation and uremia-induced coagulopathy impair lymphatic vessel repair.[34]

Because of the association between lymphoceles and rejection, patients with lymphoceles have been shown to have <10-year graft survival. It is interesting to note that, during rejection associated with hemodynamic changes, graft lymphatic flow increased 20- to 50-fold.[35] Nuclear factor-kappa B during inflammation induces vasoendothelial growth factor-C, resulting in lymphatic vessel growth, which can be treated with mammalian target of rapamycin inhibitors. However, long intervals between surgery and mammalian target of rapamycin inhibitor treatment may not decrease lymphocele formation. It has been shown that greater lymphatic vessel density in grafts is accompanied by greater graft survival, perhaps due toexiting mononuclear cells from graft that reduces inflammation.[36]

We introduced bipolar cautery in kidney transplant as an easier technique to prevent postoperative lymphocele formation compared with silk ligature. Bipolar cautery may be added as a surgical tool to improve delicate vascular and transplant surgery. During surgery, there are many subtle vessels that make ligation with silk ligature impossible, whereas these could be managed easily and swiftly with bipolar cautery.[6] Silk ligature as a foreign body may precipitate infection. Although monopolar cautery is ineffective in lymphatic vessel occlusion,[37] bipolar energy melts proteins in vessel walls and seals them permanently.[38] Monopolar cautery produces electrical spread from cautery pen toward grounding skin pad, desiccating tissues. In the bipolar cautery device,an electrical current is established between 2 cautery tips, making the current more efficient with less heat and electricity.[9] Because lymphatic vessels have less smooth muscle cells and lymphoid modest clotting factors without thrombocytes, it is recommended to involve perilymphatic tissue into bipolar blades for effective sealing.

Conclusions

Our findings suggest that bipolar cautery to occlude lymphatic vessels and prevent lymphocele formation in kidney transplant is feasible, safe, and easy to perform. Therefore, bipolar cautery could be a valuable tool with the use of silk suture ligature.

References

1. Lucewicz A, Wong G, Lam VW, et al. Management of primary symptomatic lymphocele after kidney transplantation: a systematic review. *Transplantation.* 2011;92(6):663-673.

2. Samhan M, Al-Mousawi M. Lymphocele following renal transplantation. *Saudi J Kidney Dis Transpl.* 2006;17(1):34-37.
3. Tsuda N, Ushijima K, Kawano K, et al. Prevention of lymphocele development in gynecologic cancers by the electrothermal bipolar vessel sealing device. *J Gynecol Oncol.* 2014;25(3):229-235.
4. Gallotta V, Fanfani F, Rossitto C, et al. A randomized study comparing the use of the Ligaclip with bipolar energy to prevent lymphocele during laparoscopic pelvic lymphadenectomy for gynecologic cancer. *Am J Obstet Gynecol.* 2010;203(5):483.e1-6.
5. Box GN, Lee HJ, Abraham JB, et al. Comparative study of in vivo lymphatic sealing capability of the porcine thoracic duct using laparoscopic dissection devices. *J Urol.* 2009;181(1):387-391.
6. Farouk K, Bano U. Electrocoagulation versus suture-ligation of lymphatics in kidney transplant recipients surgery. *J Postgrad Med Inst.* 2011;20:398-403.
7. Simforoosh N, Nasseh H, Masoudi P, et al. Clipless laparoscopic retroperitoneal lymph node dissection using bipolar electrocoagulation for sealing lymphatic vessels: initial series. *Urol J.* 2012;9(2):480-485.
8. Simforoosh N, Basiri A, Tabibi A, Shakhssalim N, Hosseini Moghaddam SM. Comparison of laparoscopic and open donor nephrectomy: a randomized controlled trial. *BJU Int.* 2005;95(6): 851-855.
9. Simforoosh N, Sarhangnejad R, Basiri A, et al. Vascular clips are safe and a great cost-effective technique for arterial and venous control in laparoscopic nephrectomy: single-center experience with 1834 laparoscopic nephrectomies. *J Endourol.* 2012;26(8): 1009-1012.
10. Heidenreich A, Varga Z, Von Knobloch R. Extended pelvic lymphadenectomy in patients undergoing radical prostatectomy: high incidence of lymph node metastasis. *J Urol.* 2002;167(4): 1681-1686.
11. Ranghino A, Segoloni GP, Lasaponara F, Biancone L. Lymphatic disorders after renal transplantation: new insights for an old complication. *Clin Kidney J.* 2015;8(5):615-622.
12. Lundin C, Bersztel A, Wahlberg J, Wadstrom J. Low molecular weight heparin prophylaxis increases the incidence of lymphocele after kidney transplantation. *Ups J Med Sci.* 2002;107 (1):9-15.
13. Zagdoun E, Ficheux M, Lobbedez T, et al. Complicated lymphoceles after kidney transplantation. *Transplant Proc.* 2010;42(10):4322-4325.
14. Sansalone CV, Aseni P, Minetti E, et al. Is lymphocele in renal transplantation an avoidable complication? *Am J Surg.* 2000; 179(3):182-185.
15. Naselli A, Andreatta R, Introini C, Fontana V, Puppo P. Predictors of symptomatic lymphocele after lymph node excision and radical prostatectomy. *Urology.* 2010;75(3):630-635.
16. Heyman JH, Orron DE, Leiter E. Percutaneous management of postoperative lymphocele. *Urology.* 1989;34(4):221-224.
17. Karpanen T, Alitalo K. Molecular biology and pathology of lymphangiogenesis. *Annu Rev Pathol.* 2008;3:367-397.
18. Holmes MJ, O'Morchoe PJ, O'Morchoe CC. The role of renal lymph in hydronephrosis. *Invest Urol.* 1977;15(3):215-219.
19. Aukland K. Arnold Heller and the lymph pump. *Acta Physiol Scand.* 2005;185(3):171-180.
20. Ishikawa Y, Akasaka Y, Kiguchi H, et al. The human renal lymphatics under normal and pathological conditions. *Histopathology.* 2006;49(3):265-273.
21. Ebadzadeh MR, Tavakkoli M. Lymphocele after kidney transplantation: where are we standing now? *Urol J.* 2008;5(3):144-148.
22. Lima ML, Cotrim CA, Moro JC, Miyaoka R, D'Ancona CA. Laparoscopic treatment of lymphoceles after renal transplantation. *Int Braz J Urol.* 2012;38(2):215-221; discussion 221.
23. Ulrich F, Niedzwiecki S, Fikatas P, et al. Symptomatic lymphoceles after kidney transplantation - multivariate analysis of risk factors and outcome after laparoscopic fenestration. *Clin Transplant.* 2010;24(2):273-280.
24. Vetere PF, Lazarou G, Apostol R, Khullar P, Okonkwo L, Nezhat F. Postoperative adhesion formation in a rabbit model: monopolar electrosurgery versus ultrasonic scalpel. *JSLS.* 2015;19(2). pii: e2015.00018.
25. Saidi RF, Wertheim JA, Ko DS, et al. Impact of donor kidney recovery method on lymphatic complications in kidney transplantation. *Transplant Proc.* 2008;40(4):1054-1055.
26. Mazzucchi E, Souza AA, Nahas WC, Antonopoulos IM, Piovesan AC, Arap S. Surgical complications after renal transplantation in grafts with multiple arteries. *Int Braz J Urol.* 2005;31(2):125-130.
27. Ekser B, Furian L, Broggiato A, et al. Technical aspects of unilateral dual kidney transplantation from expanded criteria donors: experience of 100 patients. *Am J Transplant.* 2010;10(9):2000-2007.
28. Cash H, Slowinski T, Buechler A, et al. Impact of surgeon experience on complication rates and functional outcomes of 484 deceased donor renal transplants: a single-centre retrospective study. *BJU Int.* 2012;110(8 Pt B):E368-E373.
29. Pacovsky J, Hyspler R, Navratil P, Ticha A, Brodak M. The estimation of post-transplant lymphocele origin using creatine kinase activity. *Ups J Med Sci.* 2010;115(3):187-192.
30. Dubeaux VT, Oliveira RM, Moura VJ, Pereira JM, Henriques FP. Assessment of lymphocele incidence following 450 renal transplantations. *Int Braz J Urol.* 2004;30(1):18-21.
31. Zietek Z, Sulikowski T, Tejchman K, et al. Lymphocele after kidney transplantation. *Transplant Proc.* 2007;39(9):2744-2747.
32. Orvieto MA, Coelho RF, Chauhan S, Palmer KJ, Rocco B, Patel VR. Incidence of lymphoceles after robot-assisted pelvic lymph node dissection. *BJU Int.* 2011;108(7):1185-1190.
33. Martinez-Ocana JC, Lauzurica R, Castellote E, et al. Adult polycystic kidney disease: a risk factor for lymphocele formation after renal transplantation? *Transplant Proc.* 1995;27(4):2246-2247.
34. Zietek Z, Iwan-Zietek I, Sulikowski T, et al. The outcomes of treatment and the etiology of lymphoceles with a focus on hemostasis in kidney recipients: a preliminary report. *Transplant Proc.* 2011;43(8):3008-3012.
35. Veeramani M, Mishra S, Kurien A, Ganpule A, Sabnis R, Desai M. Does rejection have a role in lymphocele formation post renal transplantation? A single centre experience. *Indian J Urol.* 2010;26(2):193-195.
36. Ristimaki A, Narko K, Enholm B, Joukov V, Alitalo K. Proinflammatory cytokines regulate expression of the lymphatic endothelial mitogen vascular endothelial growth factor-C. *J Biol Chem.* 1998;273(14):8413-8418.
37. Landman J, Kerbl K, Rehman J, et al. Evaluation of a vessel sealing system, bipolar electrosurgery, harmonic scalpel, titanium clips, endoscopic gastrointestinal anastomosis vascular staples and sutures for arterial and venous ligation in a porcine model. *J Urol.* 2003;169(2):697-700.
38. Kennedy JS, Stranahan PL, Taylor KD, Chandler JG. High-burst-strength, feedback-controlled bipolar vessel sealing. *Surg Endosc.* 1998;12(6):876-878.