Management of non-vascular complications following renal transplantation using percutaneous approach

Ann. Ital. Chir., 2018 89, 1: 86-91
pii: S0003469X18026933

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OBJECTIVE: *Non-vascular complications following renal transplantation can cause graft failure. In this study, we present our two-year experience with percutaneous treatment for non-vascular complications following renal transplantation.*
PATIENTS AND METHODS: *A total of 30 patients who underwent percutaneous radiological treatment between March 2014 and July 2016 were included in the study.*
RESULTS: *Following renal transplantation, a total of 36 percutaneous radiological procedures which includes hydronephrosis secondary to ureteral stricture (n. 15), clinical symptom-producing lymphocele due to pressure (14) and creatinine elevated nondilated grafts (n. 7) after excluding other reasons of creatinine elevation, were performed. Six patients received percutaneous treatment for both ureteral stricture and lymphocele. The patients underwent balloon dilatation and double-J ureteral stent due to ureteral stricture. The mean pre- and post-procedural creatinine levels were 4.36 ± 2.84mg/dL and 2.17 ± 1.24 mg/dL respectively (p=0.004), indicating a significant difference. For lymphocele treatment, sclerosing agents were injected and lymphatic leakage areas were injected with percutaneous glue. The mean pre- and post-procedural creatinine values were 2.97 ± 1.78 mg/dL and 1.75 ± 1.18 respectively (p=0.002), indicating a significant difference. Nephrostomy catheters were placed for patients with elevated creatinine levels and non-dilated collecting system. The mean pre- and post- nephrostomy creatinine levels were 3.55 ± 2.36 mg/dL and 2.57 ± 1.82 mg/dL respectively (p>0.05), indicating no statistically significant difference.*
CONCLUSION: *The results of our study suggest that percutaneous treatment is an effective method for the treatment of non-vascular complications following renal transplantation, and, therefore, should be the first option for the preservation of graft functions.*

KEY WORDS: Percutaneous treatment, Renal transplantation

Introduction

With the recent improvements in surgical treatments, perioperative assessment tools and immunosuppressive therapies, survival rates following renal transplantation has increased, and renal transplantation has become the preferred treatment of choice for most patients with renal failure [1]. Nonetheless, vascular and non-vascular complications are frequently seen following renal transplantation [2]. Post-transplantation urological complications have an incidence ranging from 3 to 10% while ureteral stricture is the most common urological complication of renal transplantation [3] In addition, non-vascular complications including urinary incontinence, lymphoceles, and abscess can cause poor urination, elevated serum creatinine levels, and hypotension [4]. The incidence of post-transplantation lymphocele is approximately 1 to 18%,

Pervenuto in Redazione Ottobre 2016. Accettato per la pubblicazione Febbraio 2017
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and the development of lymphoceles has been associated with the allograft and surgical bed [5].
In this study, we present our two-year experience with the percutaneous radiological interventions in the treatment of non-vascular complications following renal transplantation.

Material and Methods

A written informed consent was obtained from each patient. The study protocol was approved by the institutional Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.
A total of 30 patients who underwent percutaneous radiological intervention between March 2014 and July 2016 were included in the study. These patients were a subgroup of 186 patients who had renal transplantation at the Inonu University, Renal Transplantation Unit between March 2010 and July 2016. The medical data of the patients were retrospectively analyzed.

Radiological Imaging

Radiological analysis was performed to detect vascular or non-vascular complications in patients who had an elevated creatinine level following renal transplantation. The initial radiological evaluation was performed by a 10-year experienced specialist using Doppler ultrasonography (USG) (Logiq S8 GE Healthcare, USA). Antegrade pyelographies were obtained from the patients with urinary obstruction using fluoroscopy (Artis zee, Siemens Inc., Germany).
Each week, a team consisting of a general surgeon, nephrologist, and radiologist, who have experience in renal transplantation at the Renal Transplantation Council, evaluated all available data. The planning of percutaneous treatment was based on a consensus. Two radiologists with 5 and 20 year experience in the interventional radiology performed the radiological interventions.

Percutaneous Treatment

All percutaneous treatments were done under intravenous sedation. Changes in electrocardiography and blood pressure were monitored during the procedure.
Nephrostomy was the first procedure applied to all ureteral complications. Lower and mid-pole calyces were accessed with a 21-gauge needle under the Doppler USG guidance to minimize the vascular damage to the transplanted kidney. Antegrade pyelographies were taken and the diagnosis was confirmed (Fig. 3a). A coaxial introducer (AccuStick Introducer System; Boston Scientific, Natick, MA, USA) was placed over an 0.018-in. nitinol guide wire. Then, over a stiff guide wire (Amplatz Super Stiff Guide wires; Boston Scientific), we placed a 8-Fr

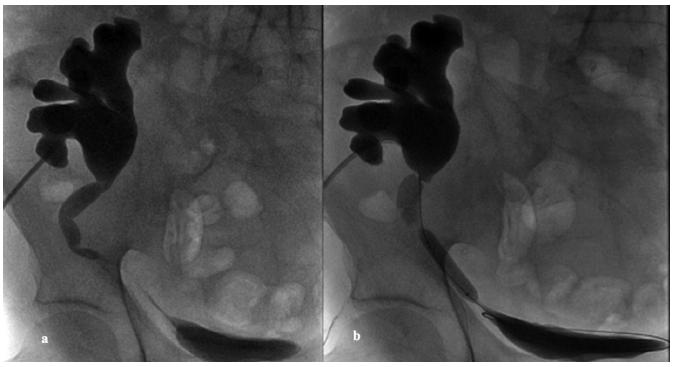


Fig. 1: (A) A long-segment distal ureteral stricture shown in the antegrade pyelography. (B) Balloon dilatation procedure following the ureteral stricture passed over by the guidewire.

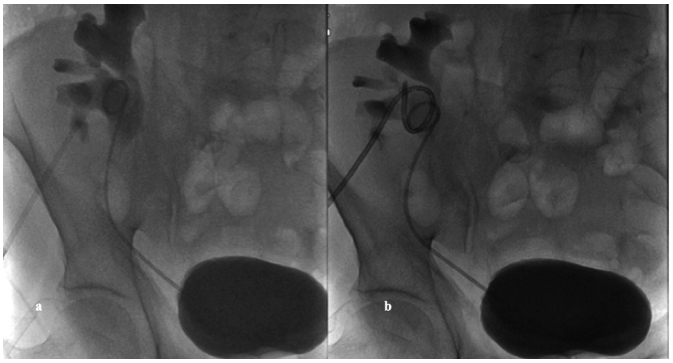


Fig. 2: (A) showing Double-J stenting following balloon dilatation. (B) showing nephrostomy catheter, which is routinely applied following double stent to prevent intraluminal clotting, cleaning minor bleeding during procedure, and cleaning collecting tubules with saline irrigation.

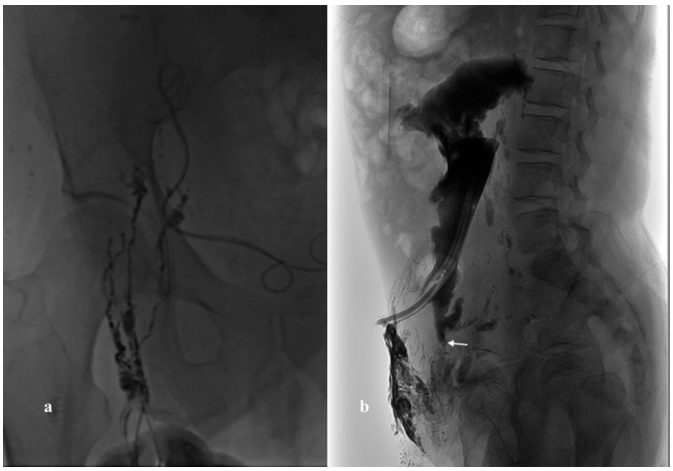


Fig. 3: (A) showing normal lymphangiogram of under fluoroscopy. Two double-J stent placed previously. No sign of lymphatic leakage seen. (B) white arrow showing area of Lipiodol accumulation, indicating lymphatic leakage from lymphatic duct.

nephrostomy drainage catheter (Flexima; Boston Scientific) into the renal pelvis.
A decline in creatinine levels was seen two to seven days following nephrostomy, and the patients underwent balloon dilatation and double-J stent placement. Ureteral stenosis were passed antegradely using a 5F vertebral catheter (Cordis, USA) and 0.035-in guide wire (Terumo, Tokyo) manipulations. A microcatheter (Fast Tracker; Boston Scientific) and 0.014-in guide wires (Pointer, Angiotech Denmark) were used in case of more severe stenosis. For the ureteral obstructions, a 5 to 8-mm high-pressure balloon catheter (Renma, Terumo Tokyo) was used for five min under 10 ATM pressure. Following balloon dilatation, all patients were placed a 6F double-J stent (Percuflex, Boston Scientific, USA). After double stenting, nephrostomy catheters were re-applied, which is routinely used to prevent intraluminal clotting, to remove minor bleeding during the procedure, and to remove the collecting tubules with saline irrigation. Antegrade pyelographies were taken within one to two days. Once double-J stents were confirmed to work properly, nephrostomy catheters were removed (Figgs. 1, 2).
For lymphocele treatment, the collection was accessed with an 18-gauge needle under the USG guidance and a sufficient amount of fluid was aspirated. After the positioning of the guide wire, an 8F drainage catheter was placed (Flexima, Boston Scientific, USA). After draining all the fluid, sclerosing agents (i.e., ethanol and fibrin glue) were injected. Ethanol injection was repeated once within two days, until the drainage amount decreased below 20cc per day. The patients with unchanged fluid levels were administered fibrin glue (Tisseel Kit, Baxter Australia).

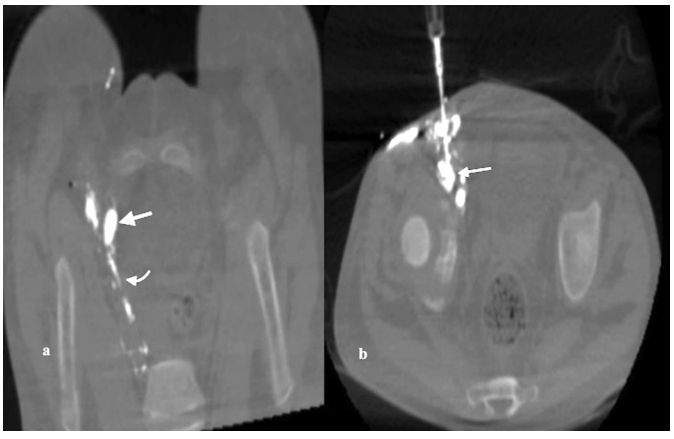


Fig. 4: (A) showing cone-beam computed tomography images taken in the same session. The curved arrow indicates the lymphatic duct. The bold arrow indicates Lipiodol extravasation from the lymphatic duct in the inferior region of the transplanted kidney. (B) The arrow showing area of glue injection with 18-gauge needle under cone-beam computed tomography guidance to coverage lymphatic leakage percutaneously.

In addition, lymphatic leakages were checked with a 22-gauge needle, accessing the inguinal lymph nodes under the USG guidance. Post-injection of Lipiodol (Lipiodol Ultra-fluid Guerbet, France) lymphatic leakages were located under fluoroscopy (Fig. 3). In the same session, cone-beam computed tomography (CT) (Syngo DynaCT Siemens Inc., Germany) was used and images were transferred to the workstation to confirm the localization of lymphatic leakage (Fig. 4a). Under cone-beam CT, the percutaneous glue (Histoacryl, Braun UK) was injected into lymphatic leakages (Fig. 4b).

Statistical Analysis

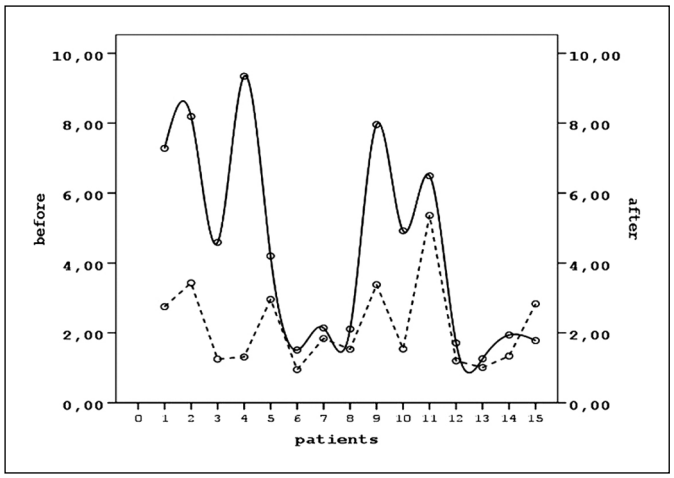
Statistical analysis was performed using SPSS v15.0 software (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed in numeric values. Paired sample t-test was performed to compare creatinine levels before and after the percutaneous treatment. A p value of< 0.05 was considered statistically significant.

Results

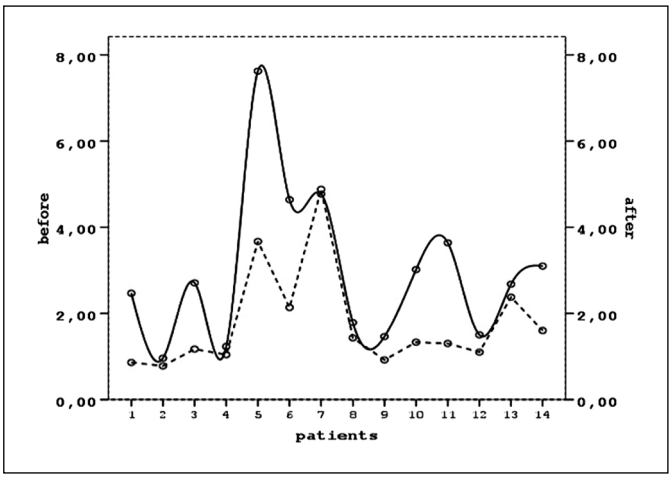
Following renal transplantation, 30 patients underwent interventional procedures. A total of 36 percutaneous radiological procedures which includes hydronephrosis secondary to ureteral stricture (n=15), clinical symptom-producing lymphocele due to pressure (n=14) and creatinine elevated nondilated grafts (n=7) after excluding other reasons of creatinine elevation like rejection, dehydration, impaired graft blood perfusion and serious grade of ATN were performed. Six patients received percutaneous treatment for both ureteral stricture and lymphocele. The patient group consisted of 23 males and seven females. The median age was 34.5 years (range, 16 to 64 years). Transplanted kidneys were taken from 23 living donors and six cadaver donors.

Ureteral Stricture

Ureteral stenosis in 15 patients was detected within 243 days (range, 25 to 1,080 days) following renal transplantation. Ureteral stenosis was located in the distal ureter (n=14) and in proximal ureter (n=1). All patients had pelvicalyceal dilatation. The double-J stent removal time was average 97.8 days after the placement of the balloon dilatation and double-J stenting. In three patients, pelvicalyceal dilatation and creatinine levels did not improve after the placement of the balloon dilatation and double-J stenting. Therefore, an 8-mm cutting balloon dilatation was applied. Following the procedure, two double-J stents were placed into the stenotic area to improve the intraluminal patency. Radiological and clinical improvements were seen in one patient. Two patients responded poorly



Graphic 1: Creatinine values of patients undergoing balloon dilatation and double-J stenting before and after procedure.



Graphic 2: Creatinine values of lymphocele patients before and after percutaneous treatment.

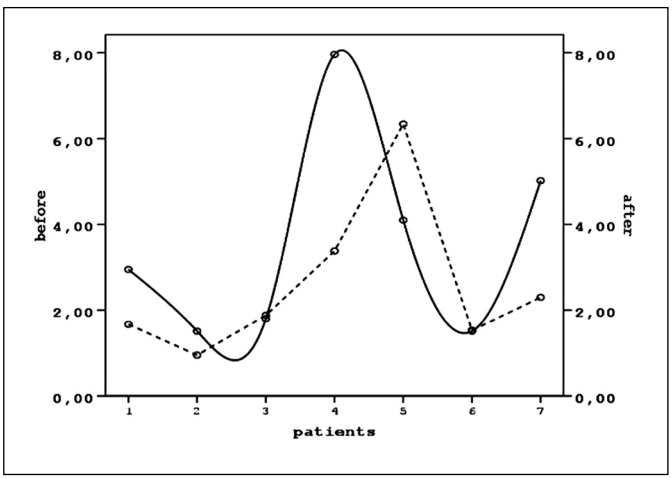
to treatment, and, then, underwent surgery. One of the patients with recurrent distal ureteral stenosis re-underwent balloon dilatation and double-J stenting.
Before and after the application of balloon dilatation and double-J stenting, creatinine levels of all patients were examined. The mean pre- and post-procedural creatinine levels were 4.36 ± 2.84 and 2.17 ± 1.24 mg/dL indicating a significant difference (p=0.004) (Graph 1).

Lymphocele

Lymphocele in 14 patients had increased creatinine levels due to urinary obstruction, as assessed by USG or pressure onto the transplanted kidney. Lymphocele was treated within 72 days (range, 6 to 311 days), following renal transplantation. The mean of the longest axis of the collection cavity was 9.8 cm and all patients initially had an ethanol injection into the cavity. The mean number of applications was 2.5 (range, 1 to 5), while the mean duration of treatment was 5 days (range, 1 to 10 days).
The size of lymphocele cavity was measured following ethanol sclerosis (mean 2.2 cm). A reduction in size of lymphocele cavity was not seen in three patients, and the total volume of drained fluid was approximately 50 to 100 cc/day. The existing catheters were removed, and two-way catheters were placed into the cavities. Tetracycline (5cc) injection through the first-way and fibrin glue (mixture of calcium cryoprecipitate plasma and thrombin) injection through the second-way was performed. During follow-up, lymphocele cavity was disappeared in only one of these three patients, while the remaining two patients had excessive lymphatic leakage. To confirm lymphatic leakage, Lipiodol was injected into the inguinal lymph node under guidance USG, and the location of lymphatic leakages was, then, detected under fluoroscopy. Next, CT-guided percutaneous glue injections were performed.
During follow-up, lymphocele cavity disappeared in one of two patients. The other patient, however, did not respond to percutaneous treatment, and underwent surgery. There was a significant difference between the mean pre- (2.97 ± 1.78 mg/dL and post-procedural (1.75 ± 1.18 mg/dL) creatinine levels (p=0.002) (Graph 2).

Non-Dilated Collecting System with Elevated Creatinine

After excluding rejection, dehydration, impaired graft perfusion, and all phases of ATN, nephrostomy catheters were placed in seven patients with normal USG and Doppler findings and elevated creatinine levels. Nephrostomy procedure was performed within 19 days (range, 8 to 35 days) following renal transplantation. Following nephrostomy, a decline in creatinine levels was seen in four patients, while creatinine levels did not



Graphic 3: Creatinine values of non-dilated grafts before and after nephrostomy.

improve in three patients. There was no significant difference between the mean pre- (3.55 ± 2.36 mg/dL and post-procedural (2.57 ± 1.82 mg/dL creatinine levels (p> 0.05) (Graph 3).

Discussion

The incidence of urological complications following renal transplantation is approximately 3 to 10% (3) Non-vascular complications such as ureteral obstructions, urinary incontinence, perigraft fluid, abscess, and lymphocele are serious conditions which may cause graft loss [6]. Open surgery is the traditional treatment method for these complications, although it may cause other complications, which may induce graft loss [7]. Therefore, interventional percutaneous method is applied in our center in the first-line setting, as in many other centers.

Following transplantation, the incidence of lymphocele is about 50% and symptomatic patients is about 18% (8). It is of utmost importance to consider that patients become clinically symptomatic due to serious pressure on the collecting system or kidney. The collection pressures to the collecting system, vascular system, or iliac veins and affects the function of the transplanted kidney. Previous studies have shown that different sclerosing agents are remedial to treat lymphoceles; even the application of drainage without any sclerosing agent has a remedial effect, as well [9]. The success rate of sclerosing agents such as ethanol, povidone-iodine, doxycycline, bleomycin, and fibrin glue ranges between 80 and 100% [10-14] In this study, we first used ethanol thanks to its effectiveness and low-cost. We found that ethanol had 78,5% clinical and radiological effectiveness, and treatment was unsuccessful in three patients. For these patients, we used fibrin glue as a second sclerosing agent, which produced clinical and radiological success in one patient. In the remaining two patients, Lipiodol was injected into the inguinal lymph nodes to identify the amount lymphatic leakage. In the same session, the location of lymphatic leakage was confirmed and percutaneous glue was injected into the area to overlap the leakage externally. During follow-up, clinical and radiological recovery was successful in one patient, while the other patient underwent surgery. In our center, the application of ethanol drainage usually results in a positive clinical and radiological impact on lymphocele treatment. In addition, we believe that fibrin glue injection can increase the success rate of continuous collection treatment. Based on these findings, we suggest that lymphangiography of an inguinal lymph node can be helpful to locate the lymphatic leakage and percutaneous treatment.

Following renal transplantation, percutaneous treatment of ureteral stenosis is done by balloon dilatation or double-J stent alone. Balloon dilatations can be repeated, if necessary. Particularly for refractory fibrotic stenosis (when balloon dilatation fails), a cutting balloon can be used [15]. We used cutting balloon in three patients who did not respond to standard balloon dilatation. To ensure better intraluminal patency, two double-J stents were placed. One of the patients recovered following percutaneous treatment, while two patients underwent surgery. After surgery, relapse of ureteral stenosis was seen in one patient, and the patient underwent balloon dilatation, and a double-J stent was re-placed. Review of the literature using a cutting balloon with standard balloon dilatation and double-J stenting can increase the efficacy of ureteral stenosis treatment [15-17]. In the present study, clinical and radiological success rate of percutaneous treatment was 93.3%, and only one of 15 patients needed surgery for clinical and radiological improvement. Furthermore, we had another experimental group in this study consisting of the patients with elevated creatinine levels after rejection, dehydration, impaired graft perfusion, and all phases of ATN were ruled out. Radiological, these patients had a normal collecting system following renal transplantation. Peregrin et al. [18] reported that, in 10 of 13 patients, early implantation of nephrostomy catheter into the non-dilated collecting system had beneficial effects on the renal graft functions. They claim that the pressure developing immediately post transplant in the renal pelvis due to ureteral obstruction can be higher than the filtration capacity of the newly kidney transplant which means that the graft stops (or does not start) urine production and it prevents renal collecting system dilatation

Moreover, we observed periodical creatinine increases in this patient group and we did not observe any dilatations in the kidney pelvis in USG examinations. Therefore, the Renal Transplantation Council decided to use antegrade pyelography initially and apply balloon dilatation and double-J stenting to the patients who had periodical elevations of creatinine and rare pelvic dilatations under USG, if the patient had any detectable ureteral obstruction. Using antegrade pyelography, none of seven patients had dilatation in the collecting system, whereas three had massive accumulation in the renal pelvis, which was detected following the injection of the contrast agent through the lower pole calyx. Following pelvic dilatation, the cumulant moved to the ureteral system and vesica urinaria. We did not observe any stenosis in the ureteral track, although the contrast agent dilated the pelvis and moved to the ureteral system and vesica urinaria under certain pressure. A nephrostomy catheter was, then, placed to exclude possible obstructive problems. Although we did not find any significant difference between pre- and post-procedural creatinine levels, a decline in creatinine levels was seen in four of these seven patients. Based on these findings, we conclude that the initial evaluation needs to be followed closely, and the functional obstruction findings can develop, even if fluoroscopy does not indicate any mechanical strictures. However, further large-scale studies are required to establish a conclusion.

Conclusion

In conclusion, our study results suggest that percutaneous treatment is an effective method for the treatment of non-vascular complications following renal transplantation, and, therefore, should be the first option for the preservation of graft functions. In addition, surgical treatment should be performed, when percutaneous treatment methods fail.

Riassunto

Le complicanze non vascolari del trapianto renale possono determinarne il fallimento. In questo studio si presenta la nostra esperienza di due anni del trattamento percutaneo di tali complicanze.
Esso riguarda un totale di 30 pazienti sottoposti a trattamento radiologico percutaneo tra il marzo 2014 e luglio 2016 compresi nello studio. Si è trattato dell'esecuzione di un totale di 36 procedimenti radiologici percutanei comprendenti 15 casi di idronefrosi secondaria a stenosi ureterale, 14 casi di linfocele sintomatico dovuto a compressione, 7 casi di creatinina aumentata in trapianti non dilatati dopo esclusione di altre cause di ipercreatininemia.
Sei pazienti sono stati trattati per via percutanea per stenosi ureterale e linfocele. Si è proceduto con dilatazione con palloncino della stenosi e doppio J-stent ureterale. I livelli medi di creatininemia pre- e post-trattamento sono stati rispettivamente 4.36 ± 2.84 mg/dL e 2.17 ± 1.24 mg/dL (p=0.004), ad indicare una differenza significativa.
Per il trattamento dei linfocele si è proceduto con l'iniezione di agenti sclerosanti e le brecce linfatiche con l'iniezione percutanea di colla. I livelli medi di creatininemia pre- e post-trattamento sono stati rispettivamente 2.97 ± 1.78 mg/dL e 1.75 ± 1.18 (p=0.002), indicative di una differenza significativa.
Nei pazienti con elevati livelli di creatinina e sistema collettore non dilatato sono stati collocati cateteri nefrostomici. I livelli medi di creatininemia pre- e post-trattamento sono stati rispettivamente 3.55 ± 2.36 mg/dL e 2.57 ± 1.82 mg/dL (p>0.05), indicando differenze statisticamente significative.
In conclusione questi risultati del nostro studio indicano come efficace il trattamento percutaneo per il trattamento delle complicanze non vascolari del trapianto renale, e dunque dovrebbe costituire la prima opzione per ottenere di preservare la funzione dell'organo trapiantato.

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