#### ORIGINAL ARTICLE

# Simultaneous recipient external iliac endarterectomy and renal transplant – a propensity score matched analysis

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#### **SUMMARY**

Patients with end-stage renal disease and severe iliac atherosclerosis are frequently denied renal transplant due to technical challenges, and risk of potential steal syndrome in the allograft, or ipsilateral limb. Few studies have evaluated the safety and efficacy of performing an endarterectomy in this setting. A single-center retrospective review of renal transplant patients from 1/2013 to 12/2017 was performed. Patients requiring endarterectomy at the time of transplant were matched to a nonendarterectomized cohort in a 1:2 fashion using propensity score matching. Patients were followed for a minimum of 12 months. Simultaneous endarterectomy and renal transplant were performed in 23 patients and subsequently matched to 42 controls. Ankle-brachial index was lower in the endarterectomized group (P = 0.04). Delayed graft function (26.1% vs. 19%, P = 0.54), graft loss (8.7% vs. 7.1%, P = 0.53), 1-year mortality (8.7% vs. 4.8%, P = 0.53), and renal function at 12 months were comparable in both groups. There were no incidents of ipsilateral limb loss in the endarterectomized population. This is the first matched study investigating endarterectomy and renal transplant. Longterm follow-up of limb and graft function is indicated. Despite the small sample size, our findings suggest that a combined procedure can safely provide renal transplantation access to a previously underserved population.

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#### **Key words**

endarterectomy, peripheral vascular disease, renal transplantation

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#### Introduction

Renal transplant is the treatment of choice for patients with end-stage renal disease (ESRD). Presently, it offers the most potential for improving patient survival and quality of life, compared to patients on dialysis [1]. The prevalence of chronic kidney disease in the US adult population is reported at 14.8%, with ESRD projections estimated to steadily increase by 2030 [2]. Due to the

organ shortage, waiting lists continue to grow steadily, with increasing number of deaths on the waiting list [3]. At the time of publication, there are 94 933 patients currently on the kidney transplant waiting list [4].

The combination of chronic kidney disease, long-term use of hemodialysis, and the prevalence of diabetes in this population has been linked to the development of intimal and medial calcifications in arterial walls [5,6]. This clinical picture translates to a higher risk of

cardiovascular and peripheral vascular disease in patients with CKD. As a consequence, patients are screened for cardiovascular and peripheral vascular disease sequelae that may negatively impact surgery prior to transplant. The presence of severe atherosclerosis of the iliac arteries is not a contraindication to surgery; however, countless CKD patients are denied access to renal transplant from multiple transplant centers annually for this reason [7,8], limiting these patients to a lower quality of life, and higher mortality risk. The safety and outcomes of combining a revascularization procedure such as an endarterectomy, with renal transplant remains unclear. With the exception of case reports, and case series, there are very few research publications addressing this clinical question [9-11]. Our transplant center is unique as we serve as a referral center for a large urban multiethnic metropolis, with a high prevalence of comorbidities such as morbid obesity, diabetes, cardiovascular, and peripheral vascular disease. Over the years, patients with severe atherosclerotic disease involving the aortoiliac distribution have been evaluated at the center and benefitted from our expertise. This study aims to report on our experience and compare the outcomes to a matched cohort.

#### **Methods**

After Institutional review board (IRB) approval was obtained, the records of all renal transplant patients over a 5-year period beginning January 2013 and ending December 2017 were reviewed. Patient follow-up was documented for up to 1 year. Patients undergoing multi-visceral organ transplant were excluded from this analysis.

# Vascular screening

Per protocol, all patients undergoing renal transplant were screened for cardiovascular risk [12], and prior clearance obtained if indicated. Peripheral vascular screening was performed using carotid duplex ultrasound, ankle-brachial index (ABI) on lower extremity arterial Doppler ultrasound, and computed tomography angiography (CTA) of the abdomen/pelvis with bilateral iliac artery run-off to rule out occlusive disease. An abnormal ABI indicates the presence of pathology, but does not necessarily identify the location of the defective anatomy. CTA images are essential in our decision tree, and upon review, target iliac vessel disease is classified as either patent, partially occlusive, or occlusive depending on the severity of calcifications. Patients with patent

vessels would proceed to transplant once a suitable donor was available, while asymptomatic patients with partially occlusive iliac disease were offered endarterectomy and renal transplant at the same setting. Calcifications precluding safe clamp application for subsequent anastomosis, or situations where suturing is not technically feasible are absolute contra-indications to endarterectomy at our institution. Patients with concomitant aortic aneurysms, descending aorta calcific stenosis, symptomatic peripheral vascular disease, or occlusive iliac calcifications were referred to the vascular surgery service for evaluation and therapy as indicated. At our institution, patients with intermittent claudication, rest pain, or tissue loss secondary to peripheral arterial disease were considered symptomatic.

#### **Patients**

Demographic details such as age, gender, ethnicity, and body mass index were obtained. Information on comorbidities, preoperative dialysis requirements, prior renal transplant surgery, and postoperative immune suppression regimen were also obtained. Perioperative metrics such as duration of surgery, warm, and cold ischemia times, renal allograft anomalies, and use of ureteral stents were acquired from operative records.

# Surgical technique/approach

This entailed an abdominal lower quadrant hockey stick incision (usually right-sided, except when precluded by prior surgical intervention, and scar tissue), followed by division of the underlying musculature, and exposure of the retroperitoneum. Occasionally, a midline approach was utilized to evaluate iliac vessels on both sides prior to endarterectomy. The external iliac arteries and veins are mobilized, and a 5 cm length of vessel skeletonized prior to the anastomosis to the donor vessels. In patients requiring an endarterectomy, the arterial anastomosis is performed first. This approach minimizes the warm ischemia time during organ reperfusion. Donor renal artery was anastomosed to the external iliac artery in patients with minimal plaque along the anterior iliac artery wall. Appropriate organ reperfusion was ascertained from visual inspection, and audible handheld Doppler signals on the implanted kidney. In cases where perfusion was deemed to be insufficient, the organ would be removed, flushed with custodial solution, returned to cold storage and an endarterectomy performed prior to re-implantation. In living donor cases, both donor and recipient procedures are performed

simultaneously. The donor surgery proceeds as usual, without making modifications for any delay with the recipient surgery. Ureteroneocystostomy is performed using monofilament absorbable suture, with or without the placement of a double-J stent.

#### External iliac artery endarterectomy

Conventional endarterectomy with primary repair of the vessel wall, patch angioplasty with a variety of grafts, or eversion endarterectomy is utilized depending on the surgeon's preference and vascular anatomy. Proximal and distal control of the iliac artery is achieved using atraumatic vascular clamps. In vessels with circumferential calcific disease at the distal landing zone, the artery is amputated proximally, and distal occlusion achieved with an appropriately sized Fogarty balloon catheter. The donor renal artery is implanted onto the patched or repaired external iliac artery after reconstruction. A handheld Doppler probe is used to document adequate perfusion of the implanted kidney and the ipsilateral extremity at the end of the procedure in each case.

# Conventional endarterectomy with primary closure

A longitudinal incision is made along the anterior wall of the iliac artery after proximal and distal control has been secured using atraumatic vascular clamps. The arterial wall plaque is elevated circumferentially from the underlying media using a Freer elevator. The distal margin of the vessel plaque is tacked down using interrupted fine monofilament nonabsorbable suture. The vessel wall is partially closed using a running nonabsorbable monofilament, and an aortic patch graft implanted at the termination of the suture line.

# Patch angioplasty

The endarterectomy is performed as above; however, closure is achieved using prosthetic material. Bovine patch grafts were frequently used at our institution; however, an aortic (Carrel) patch may be used if available. The choice of one over the other depends on the length of the incision and surgeon preference. The bovine pericardial patch has the advantage of being biologic material, available in a variety of sizes, free of plaque and resistant to contamination even in infected fields. An appropriately sized graft is selected and sutured onto the edges of the arteriotomy using a continuous suture technique. Following confirmation of adequate distal perfusion using handheld Doppler, the

vessel clamps are reapplied, and an arteriotomy made on the anterior surface of the patch for subsequent anastomosis to the donor renal artery.

#### Eversion endarterectomy

Proximal and distal control is obtained as in the conventional approach. The vessel is transected distally, and a cleavage plane around the plaque developed. The distal vessel wall is everted circumferentially around the plaque using vascular forceps. Gentle traction is applied to the atheroma using forceps, until the plaque is detached like a cast. Copious irrigation of the lumen is performed with heparinized saline to remove any residual debris. The vessel ends are then re-approximated and closed posterior wall first, using a fine continuous monofilament suture.

# Statistical analysis

Patients who received external iliac artery endarterectomy were identified from the operative notes. These patients were matched to using propensity score matching technique in a 1:2 ratio to similar cohort based on age, gender, ethnicity, body mass index, comorbidities, duration of dialysis, and donor organ type. Matches were sourced from the institutional transplant database using a sampling without replacement technique, with match tolerance set at 0.05.

The outcome variables studied were delayed graft function (defined as need for hemodialysis within the first week following transplant), acute rejection (biopsy confirmed, or empirical therapy for presumed rejection), graft loss (return to maintenance hemodialysis), and patient death. Secondary outcomes analyzed were blood transfusions, intraoperative blood loss, duration of hospitalization, surgical complications, surgical site infections, 30-day readmission rates, serum creatinine, and estimated glomerular filtration rate (eGFR) at the 1-year mark.

Continuous variables were tested for normality using the Shapiro–Wilk test. Categorical variables were described as proportions of the denominator population and reported as percentages. Normally distributed continuous variables were reported as mean  $\pm$  standard deviation, while non-normally distributed data are presented as median (interquartile range). Univariate analyses were performed using Fisher's exact test for categorical variables, and the Mann–Whitney U test for continuous variables. To address uncontrolled confounding, sensitivity analyses were performed using the

renal transplant database for the same period. Graft and patient survival after 1 year were explored with Cox regression models including all potential confounding variables. Time-to-event analyses using Cox regression analysis stratified by matched pairs were performed for the study population. For these analyses, patients were considered to have graft failure if they returned to maintenance hemodialysis or died during the 1-year follow-up period. A two-sided *P* value < 0.05 was considered significant. All statistical analyses were performed using IBM SPSS Statistics for Macintosh, Version 25.0 (Armonk, NY, USA: IBM Corp).

#### Results

Over the study period, simultaneous renal transplant and external iliac endarterectomy procedures were performed in 23 patients (EP). The median age was 62 years (IOR: 59-69), with male gender preponderance (65%), and median BMI of 30.8 kg/m<sup>2</sup> (26.8-34). All of the patients (100%) were hypertensive, 14 (61%) were diabetic, and 13 (57%) had a personal history of coronary artery disease. The patients were all on routine maintenance dialysis at the time of surgery, with majority (87%) of patients on hemodialysis. Two-thirds of patients (57%) were self-reported nonsmokers, 9 (39%) were former smokers, and one patient was a current smoker at the time of surgery. Seven patients (30%) carried a prior diagnosis of peripheral vascular disease, five of whom had prior intervention for symptomatic disease. The median ABI was 1.05 (0.8-1.2), and none of the patients had active symptoms at the time of surgery.

A matched cohort of patients was identified from the institutional renal transplant database (n = 512) using propensity score matching. These patients were statistically matched on age, gender, ethnicity, BMI, comorbidities (diabetes, hypertension, coronary artery disease, peripheral vascular disease), tobacco use, PRA (panel reactive antibody), prior transplant, EPTS (estimated post-transplant survival), donor type, KDPI (kidney donor profile index), dialysis usage, and duration of dialysis prior to transplantation. Appropriate 1:2 matches could not be obtained for four patients using the set parameters. Comparisons of the transplant patient demographics prior to and after the match are presented in Table 1. The median ABI in the nonendarterectomy patients (NEP) group was significantly higher than in the EP group [1.2 (1.03-1.25) vs. 1.05 (0.8-1.2), P = 0.036]. Operative time was longer in EP

[255 min (241–333) vs. 214 (174–273) min, P=0.008] in the NEP group; however, the warm ischemia time [23.5 (20.7–30.7) vs. 35 (27.5–44) min, P=0.004] was significantly lower. Ureteral stents were used more frequently in the EP group (95.5% vs. 69%, P=0.023) (Table 2).

Standard immune suppression was provided using Basiliximab as induction agent in low-risk patients, and thymoglobulin in high-risk patients. Other induction agents used include Alemtuzumab and Eculizumab, as part of clinical trials, and Methylprednisolone in a patient with recurrent HCV to avoid antibody induction, and subsequent disease progression. There were no significant differences in the choice of induction and maintenance immune suppression agents (see Table 2). There were higher rates of delayed graft function (26.1% vs. 19%, P = 0.54), acute graft rejection (13%vs. 2.4%, P = 0.123), and graft failure (8.7% vs. 7.1%, P = 0.53), none of which were statistically significant (see Table 3). Similarly, there was no statistical difference in serum creatinine levels (1.57  $\pm$  0.57 vs.  $1.4 \pm 0.85$  mg/dl, P = 0.435) or glomerular filtration rate (50.4  $\pm$  16.9 vs. 59.7  $\pm$  19.1, P = 0.062) after 1 year.

One-year graft survival and patient survival analyses were calculated using a Cox regression stratified by matched pairs and adjusting for significant postoperative variables identified in the univariate analysis. The variables included in this model were the duration of surgery, warm ischemia time, and the use of ureteral stents. These variables were considered either clinically and statistically significant to the outcome of the renal transplantation. There was no significant difference in 1-year graft survival [21 EP patients (91.3%) vs. 39 NEP patients (92.9%), HR: 2.4 (0.2–35.6), P = 0.530], or 1-year patient survival [21 EP patients (91.3%) vs. 40 NEP patients (95.2%), HR: 2.4 (0.2, 35.2), P = 0.531]. Given the wide confidence intervals, and the potential for uncontrolled confounders, time-toevent outcomes were also evaluated using the renal transplant database adjusting for all potential confounding variables. Variables included in this model were patient age, gender, ethnicity, BMI, comorbidities (diabetes, hypertension, coronary artery disease, peripheral vascular disease), tobacco use, PRA, prior transplant, EPTS, donor type, KDPI, dialysis usage, duration of dialysis prior to transplantation, the use of hypothermic machine perfusion, duration of surgery, warm ischemia time, and the use of ureteral stents. This yielded 1-year survival data as follows: graft survival [21 EP patients (91.3%) vs. 477 NEP patients (97.5%),

 Table 1. Patient characteristics before and after propensity score matching.

512) Rest of sample (N = 489)  50 (21)  292 (59.7%)  229 (46.8%)  105 (21.5%)  118 (24.1%)  107 (21.9%)  91 (18.6%)  67 (13.7%)  106 (21.7%)  30.2 (13)  205 (41.9%)  206 (42.1%)  18 (3.7%)  18 (3.7%)  468 (95.7%)  3 (0.6%)		5							
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Apertension 228 (44.5%) abetes mellitus 220 (43%) AD 239 (46.7%) AD 164 (32%) 1.3 (0.4) acco use 31 (6%) ormer smoker 477 (93.2%) urrent smoker 470 (93.2%) e of dialysis 13 (6.8%)	Si								
abetes mellitus 220 (43%)  AD 239 (46.7%)  AD 164 (32%)  1.3 (0.4)  acco use 31 (6%)  onsmoker 31 (6%)  urrent smoker 477 (93.2%)  e of dialysis 13 (2.5%)		28 (44.5%)	205 (41.9%)	23 (100%)	0.40	(%6.96)	40 (95.2%)	23 (100%)	0.54
AD 239 (46.7%)  164 (32%)  164 (32%)  1.3 (0.4)  acco use  31 (6%)  ormer smoker  477 (93.2%)  urrent smoker  4 (0.8%)  e of dialysis  13 (2.5%)		20 (43%)	206 (42.1%)	14 (60.9%)	0.20	31 (47.7%)	17 (40.5%)	14 (60.9%)	0.13
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er 477 (93.2%) er 4 (0.8%) 13 (2.5%)		31 (6%)	18 (3.7%)	13 (56.5%)	<0.001	38 (58.5%)	25 (59.5%)	13 (56.5%)	0.90
er 4 (0.8%) 13 (2.5%)		77 (93.2%)	468 (95.7%)	9 (39.1%)		25 (38.5%)	16 (38.1%)	9 (39.1%)	
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(0/ 0:3) 01		13 (2.5%)	13 (2.6%)	0	0.10	5 (7.7%)	5 (11.9%)	0	0.22
Hemodialysis 475 (92.8%) 455 (93%)		75 (92.8%)	455 (93%)	20 (87.0%)		53 (81.5%)	33 (78.6%)	20 (87.0%)	
Peritoneal dialysis 24 (4.7%) 21 (4.3%)		24 (4.7%)	21 (4.3%)	3 (13.0%)		7 (10.8%)	4 (9.5%)	3 (13.0%)	
Duration of dialysis 68 (78) 66 (75)		68 (78)	66 (75)	72 (80)	0.88	49 (68)	46 (62)	72 (80)	0.75

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ABI, Ankle-brachial index; BMI, body mass index; CAD, coronary artery disease; EP, endarterectomy patient; IQR, interquartile range; NEP, nonendarterectomy patient; PVD, peripheral vessel disease.

Table 2. Perioperative details.

	Matched patients ( $N = 65$ )	NEP $(N = 42)$	EP (N = 23)	Р
PRA (%), median (IQR)	0 (21)	0 (20)	0 (41)	0.672
Prior transplant, n (%)	8 (12.3%)	3 (13.0%)	5 (11.9%)	1.000
EPTS, median (IQR)	76 (45)	87 (50)	69 (43)	0.116
Donor type				
Deceased, n (%)	32 (49.2%)	11 (47.8%)	21 (50%)	0.867
Living, <i>n</i> (%)	33 (50.8%)	12 (52.2%)	21 (50%)	
KDPI, mean $\pm$ SD	$42.7 \pm 29.6$	$41.9 \pm 32.5$	$43.1 \pm 28.3$	0.882
Induction medication				
Thymoglobulin, n (%)	36 (55.4%)	22 (52.4%)	14 (60.9%)	0.634
Basiliximab, n (%)	23 (35.4%)	15 (35.7%)	8 (34.8%)	
Other, <i>n</i> (%)	6 (9.2%)	5 (11.9%)	1 (4.3%)	
Maintenance medication				
Tacrolimus/MMF, n (%)	61 (93.8%)	39 (92.9%)	22 (95.7%)	0.481
Other, <i>n</i> (%)	4 (6.2%)	3 (7.1%)	1 (4.3%)	
Perioperative details				
Duration of surgery (min), median (IQR)	230 (132)	214 (99)	255 (92)	0.008
Renal allograft variant, n (%)	16 (24.6%)	13 (31%)	3 (13%)	0.139
Ureteral stent, n (%)	50 (78.1%)	29 (69%)	21 (95.5%)	0.023
Warm Ischemia time (min), median (IQR)	30 (17)	35 (17)	23.5 (10)	0.004
Cold Ischemia time (min), median (IQR)	342 (677)	450 (794)	273 (628)	0.735

EPTS, estimated post-transplant survival; IQR, interquartile range; KDPI, kidney donor profile index; MMF, Mycophenolate mofetil; PRA, panel reactive antibodies; SD, standard deviation.

Table 3. Patient outcomes.

	Matched patients $(N = 65)$	NEP (N = 42)	EP (N = 23)	Р
Outcomes				
Operative metrics				
Estimated blood loss, median (IQR)	200 (300)	200 (238)	250 (250)	0.301
Red cell transfusion, n (%)	19 (29.2%)	10 (23.8%)	9 (39.1%)	0.194
Length of stay, median (IQR)	8 (6)	8 (6)	8 (6)	0.809
Surgical complications, n (%)	19 (29.2%)	13 (31%)	6 (26.1%)	0.780
30-day readmission, n (%)	24 (36.9%)	19 (45.2%)	5 (21.7%)	0.106
Surgical site infections, <i>n</i> (%)	7 (10.8%)	6 (14.3%)	1 (4.3%)	0.406
Delayed graft function, n (%)	14 (21.5%)	8 (19%)	6 (26.1%)	0.540
Acute rejection, n (%)	4 (6.2%)	1 (2.4%)	3 (13.0%)	0.123
1-year graft failure, n (%)*	5 (7.7%)	3 (7.1%)	2 (8.7%)	0.530
1-year mortality, n (%)*	4 (6.2%)	2 (4.8%)	2 (8.7%)	0.610
1-year serum creatinine ( $n=59$ ), mg/dl, mean $\pm$ SD	$1.45\pm0.76$	$1.40\pm0.85$	$1.57 \pm 0.57$	0.435
1-year estimated GFR ( $n=58$ ), ml/min per 1.73 m <sup>2</sup> , mean $\pm$ SD	$56.5 \pm 18.7$	$59.7 \pm 19.1$	$50.4 \pm 16.9$	0.062

GFR, glomerular filtration rate; IQR, interquartile range; SD, standard deviation.

Missing values: NEP serum creatinine n = 3, EP serum creatinine n = 3, NEP GFR n = 4, EP GFR n = 3.

HR: 3.0 (0.5, 15.7), P = 0.189) and patient survival (21 EP patients (91.3%) vs. 462 NEP patients (94.5%), HR: 1.4 (0.3, 6.1), P = 0.683].

Majority of endarterectomies were performed using a standard longitudinal incision, and patch angioplasty completed using bovine pericardium (Table 4; Fig. 1). In

<sup>\*</sup>P values estimated using Cox regression analysis.

**Table 4.** Procedures performed on endarterectomy patients.

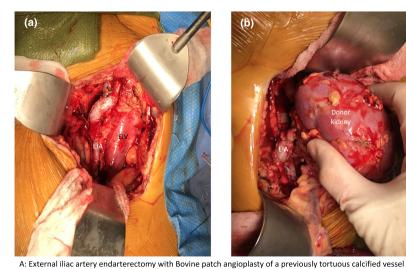
	N (%)
Endarterectomy	
With primary vessel repair	1 (4.3%)
With aortic patch angioplasty	2 (8.7%)
With bovine pericardium patch angioplasty	20 (87%)
Common iliac artery extension	5 (21.7%)
Femoral artery extension	6 (26%)
Eversion endarterectomy	
External iliac artery	2 (8.7%)
Profunda femoris artery	1 (4.3%)
lliofemoral bypass using PTFE graft	1 (4.3%)
Vascular surgeon involvement	3 (13%)

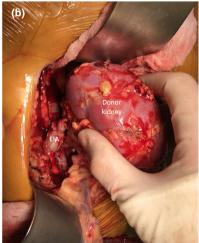
PTFE, Polytetrafluoroethylene.

two patients with extensive calcifications sparing the anterior wall, arterial anastomoses were initially performed without endarterectomy, but the organ perfusion proved to be unsatisfactory. Following completion of the endarterectomy, the donor organs pinked up appropriately, and audible Doppler signals were demonstrable. The external iliac artery was the target vessel for the intervention in all situations, with proximal and distal extension in 22% and 26% of cases, respectively. Eversion endarterectomy was used in conjunction with the standard approach in three cases, and one case required an iliofemoral bypass to maintain perfusion in the ipsilateral lower extremity following the procedure. One patient had an associated abdominal aortic aneurysm which was treated with an endovascular stent graft 72 h prior to renal transplant and external iliac endarterectomy.

Despite advances in health care, the widening gap between organ demand and supply remains, leaving a large number of patients with suboptimal care. In this article, we present the outcomes following renal transplantation and revascularization surgery in the same setting. Predictably, the ABIs were lower and operative times longer in patients requiring endarterectomy; however, these findings did not result in added morbidity, neither were graft or patient survival negatively impacted. Using a variety of approaches, vascular inflow to the extremity was preserved while maintaining perfusion to the kidney graft. None of the patients undergoing endarterectomy required additional peripheral vascular interventions or required amputations in the ipsilateral limb during follow-up. Comparison to a matched patient cohort without severe aortoiliac disease requiring endarterectomy or other vascular reconstruction demonstrated similar outcomes after 1-year.

At present, guidelines do not recommend exclusion of any patients based on their vascular status [13]. Furthermore, reconstruction prior to transplant or at the same setting is advocated in patients with symptomatic disease [14]. Survival benefit has been reported following transplant in patients with combined peripheral artery disease and end-stage renal disease [15]. The routine screening of prospective candidates with computed tomography angiography varies with center, due to variable incidence of severe atherosclerosis requiring reconstruction in this population [7,16]. Our center does not perform routine screening with angiography. Screening





of external iliac artery. (a) Following endarterectomy and bovine patch angioplasty. (b) Following

Figure 1 Intraoperative photograph

anastomosis of donor renal artery.

B: Same vessel following renal transplant \* EIV: External iliac vein

\* EIA: External iliac artery

of potential renal transplant candidates with the ABI, supplemented with toe-brachial pressures has been shown to be just as effective [17,18]. In fact, worse outcomes have been reported in patients with low ABIs following renal transplant [19]. In our population, screening with ABIs was performed routinely on all patients with no reports of lower extremity ischemic symptoms after 1 year of follow-up. This result is similar to the findings in Northcutt's retrospective review of ischemic symptoms in the ipsilateral limb of renal transplant patients with peripheral arterial disease; however, none of the patients required endarterectomy [20]. Sagban et al reported on their experience with an extensive preoperative screening approach with duplex studies, and angiograms when indicated [21]. A hundred-ten patients were identified and benefitted from thromboendarterectomy at least 6-months prior to planned transplant. An additional 29 patients (20%) were however missed during screening and required thrombo-endarterectomy at the time of transplant. Tsivian reported on ESRD patients requiring concomitant aortoiliac surgery [22]. Of the 30 patients in his cohort, 24 (80%) were determined to need vascular intervention intraoperatively despite the routine use of screening in their facility.

The use of bovine pericardial patch for angioplasty has long been indispensable in cardiovascular surgery. The advantages of this material include superior biocompatibility, ease of handling, and lower incidence of suture line bleeding, and infection resistance [23]. The latter has been exploited in our center for vascular reconstruction in infected fields, without complication [24]. In one of our patients, a segment of artery was resected due to extensive atherosclerosis and replaced with a tube graft fashioned out of pericardial patches stitched to one another on the back table. Other materials used in vascular reconstruction during renal transplant include donor vessels [25] and synthetic grafts [26] despite infectious concerns [27].

At the 1-year mark, both the graft and patient survival of the EP patients in our study were 91.3%. In Tsivian's study, 15 of the patients ultimately proceeded to endarterectomy with 1-year graft survival reported at 80% and patient survival 86.6%. Galazka reviewed 25 patients who underwent iliac endarterectomy and renal transplant in the same setting and reported 1-year graft and patient survival rates of 88% and 93%, respectively [28]. The results from our study compare favorably with the reported literature; moreover, results from EP patients were comparable to their matched NEP patients.

The study has several limitations, of which the most apparent is the retrospective design. We adopted meticulous chart review to address the problem of missing variables common in database studies. The lack of a suitable comparison group has plagued previous authors investigating this topic. Ideally, our cohort would be compared to patients with severe iliac atherosclerosis disease not undergoing transplant. In lieu of this, we utilized propensity score matching to generate a closely matched cohort based on clinically relevant factors and performed survival analysis adjusting for statistically significant variables in the univariate analysis. Follow-up ABI postendarterectomy was only performed in three patients, as clinical follow-up was deemed appropriate in the absence of symptoms. The reported long-term follow-up is limited to 1-year graft and patient survival. Our sample size is relatively small and limits the interpretation of some of our results.

In this study, patients with severe iliac atherosclerotic disease underwent endarterectomy and renal transplant at the same setting, without a significant difference in outcomes when compared to a matched cohort of identical patients without atherosclerosis requiring intervention. Our findings suggest that patients with aortoiliac disease amenable to vascular reconstruction should not be excluded from renal transplant. Knowledge of vascular surgery techniques should be incorporated into transplant surgeon's skill set.

# **Author contributions**

Spaggiari, Almario, Tzvetanov, Benedetti involved in study conception and design; Okoye, Tulla, Di Cocco involved in acquisition of data; Okoye, Tulla, Spaggiari involved in analysis and interpretation of data; Okoye, Di Cocco drafted the manuscript; Spaggiari, Almario, Tzvetanov, Benedetti involved in critical revision.

# Financial disclosure

The authors have no financial or proprietary interest in the subject matter or materials discussed in the manuscript, including but not limited to employment, consultancies, stock ownership, honoraria, and paid expert testimony.

# **Conflicts of interest**

The authors by this submission declare that all financial and material support is identified in the manuscript, that all affiliations and financial involvement over the past 5 years and foreseeable future with any organization or entity with financial interest in financial conflict with the subject matter or materials mentioned in the manuscript are completely disclosed below or in an attachment, and certify that over the past few years, they have had, and for the foreseeable future, they have no commercial association or financial involvement, including the categories cited above that might pose a conflict of interest with regard to the submitted manuscript.

#### REFERENCES

- Meier-Kriesche HU, Ojo AO, Port FK, Arndorfer JA, Cibrik DM, Kaplan B. Survival improvement among patients with end-stage renal disease: trends over time for transplant recipients and wait-listed patients. J Am Soc Nephrol 2001; 12: 1293.
- McCullough KP, Morgenstern H, Saran R, Herman WH, Robinson BM. Projecting ESRD incidence and prevalence in the United States through 2030. J Am Soc Nephrol 2019; 30: 127.
- 3. Leichtman AB, Cohen D, Keith D, et al. Kidney and pancreas transplantation in the United States, 1997–2006: the HRSA breakthrough collaboratives and the 58 DSA challenge. Am J Transplant 2008; 8(4 Pt 2): 946.
- 4. Organ Procurement and Transplantation Network. National data on Kidney website. https://optn.transplant.hrsa.gov/data/view-da ta-reports/national-data/. Updated Feb 1, 2019. Accessed Feb 2, 2019.
- Lindner A, Charra B, Sherrard DJ, Scribner BH. Accelerated atherosclerosis in prolonged maintenance hemodialysis. N Engl J Med 1974; 290: 697.
- 6. Covic A, Vervloet M, Massy ZA, *et al.*Bone and mineral disorders in chronic kidney disease: implications for cardiovascular health and ageing in the general population. *Lancet Diabetes Endocrinol* 2018; **6**: 319.
- 7. Brekke IB, Lien B, Sodal G, *et al.*Aortoiliac reconstruction in preparation for renal transplantation. *Transpl Int* 1993; **6**: 161.
- 8. Galazka Z, Grochowiecki T, Jakimowicz T, Kowalczewski M, Szmidt J. Is severe atherosclerosis in the aortoiliac region a contraindication for kidney transplantation? *Transplant Proc* 2011; **43**: 2908.
- Codd JE, Anderson CB, Graff RJ, Gregory JG, Lucas BA, Newton WT. Vascular surgical problems in renal transplantation. *Arch Surg* 1974; 108: 876.

- Basic D, Hadzi-Djokic J, Milutinovic D, Basic M, Djokic M. Renal allograft implantation in respect of atypical vascular procedures. *Acta Chir Iugosl* 2003; 50: 73.
- 11. Gill R, Shapiro R, Kayler LK. Management of peripheral vascular disease compromising renal allograft placement and function: review of the literature with an illustrative case. *Clin Transplant* 2011; 25: 337.
- Guidelines for assessing and managing the perioperative risk from coronary artery disease associated with major noncardiac surgery. American College of Physicians. Ann Intern Med 1997; 127: 309.
- 13. Kasiske BL, Cangro CB, Hariharan S, *et al.* The evaluation of renal transplantation candidates: clinical practice guidelines. *Am J Transplant* 2001; **1**(Suppl 2): 3.
- 14. Pampaloni F, Sanchez LJ, Bencini L, Taddei G. Simultaneous aortoiliac reconstruction and renal transplantation: is it safe? *Chir Ital* 2002; **54**: 115.
- Cassuto J, Babu S, Laskowski I. The survival benefit of kidney transplantation in the setting of combined peripheral arterial disease and end-stage renal failure. Clin Transplant 2016; 30: 545.
- Smith D, Chudgar A, Daly B, Cooper M. Evaluation of potential renal transplant recipients with computed tomography angiography. *Arch Surg* 2012; 147: 1114.
- 17. Garimella PS, Hart PD, O'Hare A, DeLoach S, Herzog CA, Hirsch AT. Peripheral artery disease and CKD: a focus on peripheral artery disease as a critical component of CKD care. Am J Kidney Dis 2012; 60: 641.
- 18. Shishehbor MH, Aksut B, Poggio E, Flechner SM. Presence of peripheral artery disease in renal transplant outcomes don't throw the baby out with the bath water. *Vasc Med* 2017; 22: 231.
- 19. Patel SI, Chakkera HA, Wennberg PW, et al. Peripheral arterial disease

- preoperatively may predict graft failure and mortality in kidney transplant recipients. *Vasc Med* 2017; **22**: 225.
- 20. Northcutt A, Zibari G, Tan TW, Coulter AH, Zhang WW. Does kidney transplantation to iliac artery deteriorate ischemia in the ipsilateral lower extremity with peripheral arterial disease? *Vascular* 2015; 23: 490.
- Sagban TA, Baur B, Schelzig H, Grabitz K, Duran M. Vascular challenges in renal transplantation. Ann Transplant 2014; 19: 464.
- Tsivian M, Neri F, Nardo B, et al.
   Aortoiliac surgery concomitant with kidney transplantation: a single center experience. Clin Transplant 2009; 23: 164.
- 23. Li X, Guo Y, Ziegler KR, *et al.* Current usage and future directions for the bovine pericardial patch. *Ann Vasc Surg* 2011; **25**: 561.
- 24. Garcia Aroz S, Spaggiari M, Jeon H, Oberholzer J, Benedetti E, Tzvetanov I. The use of bovine pericardial patch for vascular reconstruction in infected fields for transplant recipients. *J Vasc Surg Cases Innov Tech* 2017; **3**: 47.
- 25. Coleman S, Kerr H, Goldfarb D, Krishnamurthi V, Rabets JC. Utilization of vascular conduits to facilitate renal transplantation in patients with significant aortoiliac calcification. Urology 2014; 84: 967.
- Anan G, Nanmoku K, Shimbo M, et al. Renal transplantation with simultaneous aortoiliac reconstruction using a polytetrafluoroethylene vascular graft for severe atherosclerosis.
   Case Rep Transplant 2018; 2018: 8959086.
- 27. Koskas F, Goeau-Brissonniere O, Nicolas MH, Bacourt F, Kieffer E. Arteries from human beings are less infectible by Staphylococcus aureus than polytetrafluoroethylene in an aortic dog model. J Vasc Surg 1996; 23: 472.
- Galazka Z, Szmidt J, Nazarewski S, et al. Kidney transplantation in recipients with atherosclerotic iliac vessels. Ann Transplant 1999; 4: 43.