Endarterectomy for Iliac Occlusive Disease during Kidney Transplantation: A Multicenter Experience

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Abstract

Little is known about the surgical challenges and outcomes of kidney transplantation (KT) in the face of severe iliac occlusive disease (IOD). We aim to examine our institution's experience and outcomes compared with all KT patients. Retrospective review of our multi-institutional transplant database identified patients with IOD requiring vascular surgery involvement for iliac artery endarterectomy at time of KT from 2000 to 2018. Clinical data, imaging studies, and surgical outcomes of 22 consecutive patients were reviewed. Our primary end-point was allograft survival. Secondary end-points included mortality and perioperative complications. A total of 6,757 KT were performed at our three sites (Florida, Arizona, and Minnesota); there were 22 (0.32%) patients receiving a KT with concomitant IOD requiring iliac artery endarterectomy. Mean patient age was 61.45 ± 7 years. There were 13 (59.1%) male patients. The most common etiology of renal failure was diabetic nephropathy in 10 patients (45.5%) followed by a combination of hypertensive/diabetic nephropathy in five patients (22.7%), and hypertensive nephrosclerosis in three patients (13.6%). The majority ($n = 16$, 72.7%) of patients received renal allografts from deceased donors and six (27.3%) were recipients from living donors. Mean time from dialysis to transplantation was 2.9 ± 2.9 years. Mean follow-up was 3.5 ± 2.5 years. Mean length of hospital stay was 6.3 ± 4.3 days (range: 3–18 days). Graft loss within 90 days occurred in two (9.1%) patients, one due to renal vein thrombosis and another due to acute tubular necrosis. Overall allograft survival was 90.1% at 1-year and 86.4% at 3-year follow-up. Overall mortality occurred in 6 (27.3%) patients. Perioperative complications (Clavien-Dindo Grade 2–4) occurred in 13 (59.1%) patients, including 10 (45.5%) with acute blood loss anemia requiring transfusion, 2 (9.1%) reoperations for hematoma evacuation, 1 (4.5%) ischemic colitis requiring total abdominal colectomy, and 1 (4.5%) renal

Keywords

► peripheral arterial disease
► renal failure
► transplant

vein thrombosis requiring nephrectomy. IOD patients selected for KT are not common and although challenging, they have similar outcomes to our standard KT patients. The 1- and 3-year allograft survivals were 90.1 and 86.4% versus 96.0 and 90.3% in the general KT patient population. With these excellent outcomes, we recommend expanding the criteria for KT to include patients with IOD with prior vascular surgery consultation to prevent progression of IOD or prevention of wait list removal in select patients who are otherwise good candidates for KT.

Atherosclerosis is frequent in patients with end-stage renal disease awaiting kidney transplantation (KT).[1] The increasing incidence of iliac occlusive disease (IOD) in KT patients is related to the advanced age of recipients and the increased incidence of atherosclerosis in chronic renal failure.[2] Furthermore, there is increased incidence of atherosclerotic comorbidities including diabetes, hypertension, and hypercholesterolemia.[3] Cardiovascular events are a primary cause of mortality in these patients and often preclude KT.[3–6] Despite preoperative preparations, IOD is commonly encountered at KT that requires concomitant treatment of the vascular lesion to assure proper allograft vascular in- and outflow.[4] Current literature demonstrates a range from 1.3 to 13% incidence of significant IOD at the time of KT.[5,6] We sought to review our institutional experience for this significant risk factor for renal allograft survival.

Methods

We identified all patients from our three transplant centers at our regional sites (Florida, Arizona, and Minnesota) with IOD requiring iliac artery endarterectomy undergoing KT between January 1, 2000 and November 30, 2018. Data collection included details of each patient's clinical presentation, comorbidities, KT evaluation, surgical management, and follow-up through a retrospective chart review. This study was approved by the Mayo Clinic Institutional Review Board (IRB#17–007736). Informed consent was waived by the IRB as this study was deemed minimal risk to patients.

Our primary end-point was allograft survival. Our secondary end-points included mortality and perioperative complications. Data are reported using means and standard deviations for continuous variables or as frequencies for categorical variables. Differences between categorical variables were tested using χ^2 test and differences between continuous variables were tested using Student's t-test when deemed appropriate. Long-term outcomes were performed descriptively due to the relatively few patients in our cohort. Analyses were performed using JMP 14 (SAS Institute, Cary, NC).

Kidney Transplantation Selection

Evaluation of KT candidates at the Mayo Clinic is based on a multidisciplinary patient care approach standardized across all Mayo Clinic sites (Florida, Arizona, and Minnesota). All patients considered for transplantation undergo a multipart evaluation with the following objectives: (1) to confirm severely limited kidney function, (2) to assess the patient's ability to tolerate operative intervention, (3) to ensure that there is good long-term allograft and patient survival, and (4) to ensure that there is a good social and financial support to successfully sustain the transplanted organ.

A transplant committee comprised of a transplant nurse coordinator, nephrologist, surgeon, pharmacist, psychiatrist, social worker, and nutritionist is involved in the evaluation process for potential KT recipients based on the following criteria:

1. The transplant recipient should meet the medical indications of the United Network of Organ Sharing
2. The transplant recipient must be younger than 80 years of age. Should he/she be older than 80 years, the recipient is evaluated on a case-by-case basis.
3. The transplant recipient must have kidneys with severely diminished function. The glomerular filtration rate should be less than or equal to 20 mL/min/m^2.
4. The transplant recipient should have a body mass index (BMI) of less than or equal to 40 kg/m^2. Those individuals with BMIs between 40 and 45 kg/m^2 will be considered on a case-by-case basis.
5. The transplant recipient should be able to comply with transplant-related management and medical follow-up.
6. The transplant recipient should have a good social support system. There should be no psychiatric/psychological barriers for transplantation.
7. The transplant recipient should have adequate financial resources including health care insurance with medication coverage.

Once the recipient starts the evaluation process, a myriad of tests and consultations is prompted, which is included in ►Table 1. Based on these evaluations, the decision to proceed with transplantation is reached. Absolute contraindications for transplantation include active infection, active malignancy, active substance use/abuse, reversible renal failure, uncontrolled psychiatric disorders, documented treatment nonadherence, and/or short life expectancy. A relative contraindication for KT has included severe calcifications of the iliac arteries observed on noncontrast computed tomography.

Table 1 Laboratory, cardiovascular, pulmonary, imaging studies, and consultations required for kidney transplantation (KT) evaluation

Laboratory testing	
Metabolic panel	**Serologies**

Total and direct bilirubin
Aspartate aminotransferase (AST)
Alanine aminotransferase (ALT)
Alkaline phosphatase
Albumin and total protein
Total cholesterol
High-density lipoprotein (HDL) cholesterol
Triglycerides, low-density lipoprotein (LDL) cholesterol
Albumin
Blood urea nitrogen
Calcium
Chloride
Potassium
Sodium
Phosphorus
Creatinine
Glucose
Bicarbonate
Rheumatologic workup as indicated
If patient has good pastures, order anti-glomerular basement membrane (GBM) antibody
ABO blood group testing drawn on two separate occasions
Human leukocyte antigen (HLA) typing
Single antigen bead
Troponin T
Hemoglobin A1C
C peptide (if diabetic)
Thyroid-stimulating hormone (TSH)
Parathyroid hormone (PTH)
Pregnancy testing in females under 60 (unless they have had a hysterectomy)
Serum protein electrophoresis (SPEP) with reflex for age > 50, history of Monoclonal gammopathy of undetermined significance (MGUS), myeloma, amyloid considered in patients with history of proteinuric kidney disease of unknown etiology
	For all patients
	  Cytomegalovirus (immunoglobulin G [IgG] only)
	  Herpes simplex virus ½ (IgG only)
	  Varicella zoster virus (IgG only)
	  Measles and rubella (IgG only)
	  Ebstein–Barr virus (antibody profile—Epstein–Barr virus viral capsid antigen IgG/IgM and Epstein–Barr nuclear antigen)
	  HIV ½ antibody
	  Syphilis IgG
	  HBsAb, HBs antigen, HBcAb
	  Hepatitis C virus (HCV) antibody (Ab)
	  HCV RNA if suspected to have recent HCV infection
	  Hepatitis A virus (HAV)—total antibody
	For selected candidates (any candidate at risk for infection by virtue of residency or travel):
	  Coccidioides immitis serology (EIA—enzyme immunoassay, ID—immunodiffusion, and CF—complement fixation)
	  Strongyloides serology
	  Schistosoma serology
	  Trypanosoma cruzi serology
	Hematology
	Prothrombin time (PT)/international normalized ratio (INR)
	Complete blood count (CBC) with differential
	Urine tests
	Urinalysis
	Random urine protein and creatinine
	Gram stain (reflex urine culture)

Cardiovascular and pulmonary testing	
Electrocardiogram (EKG) Echocardiogram to evaluate valves and pulmonary pressures Stress test for patients with diabetes, age >59, prior coronary artery disease (CAD), or tobacco use Carotid duplex ultrasound for all patients with a history of CAD, stroke, transient ischemic attack (TIA), diabetes, or severe peripheral arterial disease (PAD) Thrombophilia workup: for history of lupus, clotting of access, miscarriages or prior clotting, consider thrombophilia clinic or order the following tests/thrombophilia profile	

Antithrombin activity plasma
  Cardiolipin (phospholipid) antibody
  Coagulation survey, lupus like anticoagulants
  Protein C activity
  Protein A free plasma
  Prothrombin G20210A nucleotide
  Beta 2 glycoprotein 1 antibodies (IgG, IgM, and IgA)	

Radiology imaging studies	
Chest X-ray posterior–anterior and lateral views Duplex scan of kidneys to evaluate for kidney size and presence of cysts Computed tomography (CT) of the abdomen/pelvis without contrast in patients who are older than 65 years of age or with diabetes mellitus (DM), PAD, and if they have been on hemodialysis or peritoneal dialysis for more than 3 years. If complex renal cysts are present, then abdominal CT with contrast should be done annually with urology evaluation Magnetic resonance angiography (MRA) of the brain without contrast should be obtained for all autosomal dominant polycystic kidney disease (ADPKD) patients, who have not had one completed	

(*Continued*)

Table 1 (Continued)

Laboratory testing	
Metabolic panel	Serologies
Cancer screening	
Usual screening according to the American Cancer Society guidelines	
Consultations	
Transplant nephrology Transplant surgery Transplant nurse coordinator Transplant pharmacist Transplant nutrition Transplant financial coordinator Infectious diseases (if indicated) Psychology and psychiatry consultation (if indicated) Cardiology, if patient has history of cardiac problems or abnormal echocardiogram/stress test Other consultations and tests, as indicated	

Table 2 Patient characteristics of our kidney transplant (KT) cohort

Age at the time of transplant (years)	61.5 ± 7 years
Male sex	13 (59.1%)
Race/ethnicity	**n (%)**
Caucasian	11 (50)
African American	9 (40.1)
Latino	2 (9.1)
Body mass index (BMI, in kg/m^2)	29.5 ± 4.5
Comorbidities	**n (%)**
Peripheral artery disease	22 (100)
Hypertension	21 (95.5)
Diabetes mellitus	14 (63.6)
Coronary artery disease	10 (45.5)
Hyperlipidemia	7 (31.8)
Chronic pulmonary obstructive Disease	2 (9.1)
Medication	**n (%)**
Acetylsalicylic acid	19 (86.4)
Beta blockers	15 (68.2)
Statins	10 (45.5)
Calcium channel blockers	10 (45.5)
Clopidogrel	6 (27.3)
Anticoagulation medications	4 (18.2)
Etiology of end-stage renal disease	**n (%)**
Diabetes mellitus	10 (45.5)
Diabetes/hypertension	5 (22.7)
Hypertension	3 (13.6)
Lupus nephritis	1 (4.5)
Interstitial nephritis	1 (4.5)
Proteinuric kidney disease	1 (4.5)
Focal segmental Glomerulosclerosis	1 (4.5)

Table 2 (Continued)

Type of kidney donor	n (%)
Deceased donor	16 (72.7)
Living donor	6 (27.3)
Preoperative computed tomography	13 (59.1)
Preoperative serum creatinine (mg/dL)	7.4 ± 2.6

Results

There was a total of 6,757 KT at our three sites (Florida, Arizona, and Minnesota). From these, 22 (0.32%) patients had concomitant IOD requiring iliac artery endarterectomy at the time of transplantation. The demographic data, comorbidities, and the etiology of kidney failure are presented in ►**Table 2**. Thirteen (59.1%) patients were male and the mean age at KT was 61.5 ± 7 years. The most common etiology of kidney failure was diabetic nephropathy in 10 patients (45.5%) followed by a combination of hypertensive/diabetic nephropathy in five patients (22.7%) and hypertensive nephrosclerosis in three patients (13.6%). The mean time from dialysis to transplantation was 2.9 ± 2.9 years. Sixteen patients (72.7%) received renal allografts from deceased donors and six (27.3%) were recipients from living donors.

Preoperative cross-sectional imaging in the form of non-contrast CT was performed in 13 (59.1%) patients as part of their routine transplant evaluation, which includes only patients over the age of 65 years, with complex renal cysts, history of peripheral arterial disease, and diabetes mellitus and hemo- or peritoneal dialysis of over 3 years duration (►**Fig. 1**). There was one (4.5%) patient with planned endarterectomy in our cohort. The rest of our patients required intraoperative consultations with vascular surgery.

Immunosuppression is achieved by administration of induction medication followed by maintenance therapy to prevent acute rejection and renal allograft loss. Long-term follow-up after transplantation was managed by our
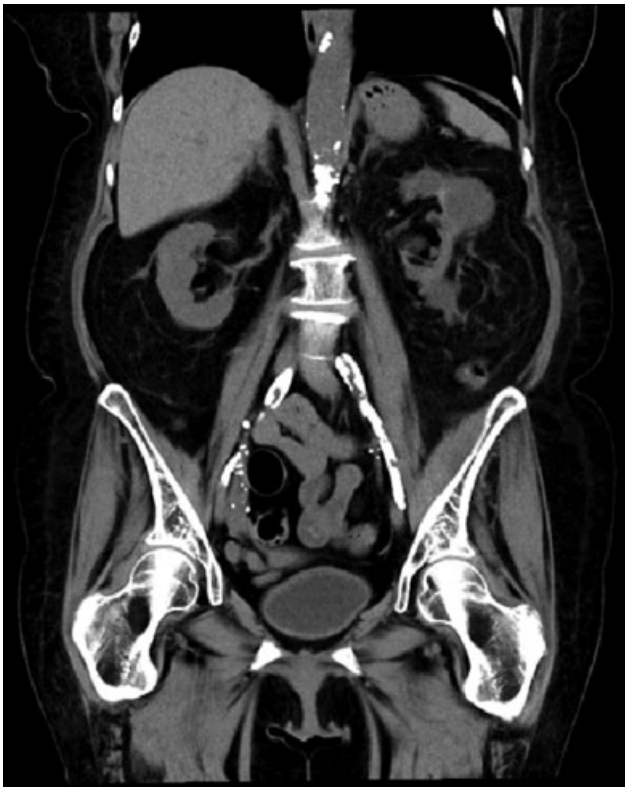
Fig. 1 Coronal view of a noncontrast computed tomography scan of the abdomen and pelvis in a patient with significant Iliac occlusive disease (IOD) prior to kidney transplantation.

Fig. 2 Primary kidney transplantation are performed in the iliac fossa (Used with permission of Mayo Foundation for Medical Education and Research. All rights reserved).

Table 3 Postoperative complications

Postoperative complications	n (%)
Acute blood loss anemia, requiring transfusion	10 (45.5)
Perinephric hematoma requiring reoperation	2 (9.1)
Ischemic colitis requiring colectomy	1 (4.5)
Graft thrombosis requiring nephrectomy	1 (4.5)

transplant team in 19 (86.4%) patients and in 3 (13.6%) patients by external providers. Follow-up is rigorous and requires good patient adherence: visits every 2 weeks in the first 2 to 4 months; then, monthly visits until the 6th month. Subsequently, visits every 2 months in the first year and every 3 to 4 months until the third year and lastly one visit per semester thereafter. During each follow-up visit, laboratory data are obtained for medication adjustments, if needed. If acute rejection is noted, plasma exchange and/or corticosteroids and/or immunosuppressant medication is initiated depending on the histologic grade of the rejection.

Operative Procedure

In 19 (86.4%) of 22 patients, a right lower quadrant Gibson incision was made to obtain access to the iliac vessels in the retroperitoneal space in the standard fashion.[7] The other three (13.6%) kidney allografts were placed in the left iliac fossa, two of those secondary to advanced peripheral arterial disease in the right iliac vessels (►**Fig. 2**). There were five patients who required iliac artery patching (two with bovine pericardium and three with renal vein from the donor kidney). A single patient required a distal external iliac artery stent. In all 22 patients, an end-to-side anastomosis was performed from the renal artery and vein directly to the external iliac artery and vein, respectively. The ureter was anastomosed directly into the bladder using a Lich-gregoir technique Mean operative time was variable at 225.1 ± 104.9 minutes (range: 137–560 minutes).
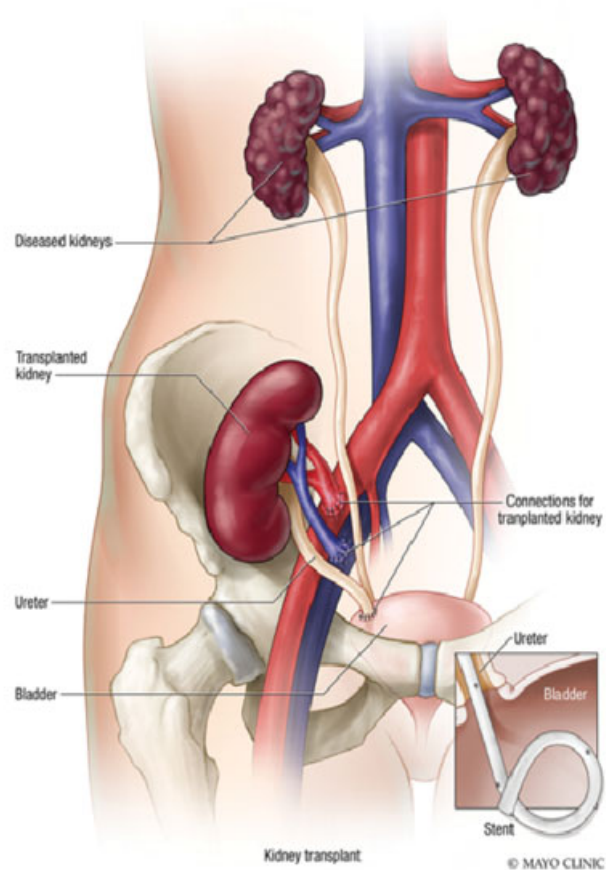
Postoperative and Long-Term Management

Mean length of hospital stay was 6.3 ± 4.3 days (range: 3–18 days). All patients were placed on oral aspirin 81 mg. The significant discrepancy in hospitalization was predominantly due to those patients who suffered from postoperative complications. Complications were graded using the Clavien-Dindo system[8,9] (Clavien-Dindo Grade 2–4) and occurred in 13 (59.1%) patients, including 10 (45.5%) with acute blood loss anemia requiring transfusion, 2 (9.1%) reoperations for hematoma evacuation, 1 (4.5%) ischemic colitis requiring total abdominal colectomy, and 1 (4.5%) renal vein thrombosis requiring nephrectomy (►**Table 3**). Nine (40.9%) patients required hemodialysis in the first week following transplantation.

The perinephric hematoma evacuations were on patients with significantly large hematomas. They measured 13 × 3.7 × 7.8 cm and 14 × 11 × 4 cm in size. The patient

who developed ischemic colitis was slow to recover following KT. She later developed a leukocytosis of up to 40×10^9/L on postoperative day 9 along with significant abdominal pain. On postoperative day 11, she underwent a flexible sigmoidoscopy that revealed colonic ischemia. She then underwent total abdominal colectomy with end ileostomy.

There were two graft losses (9.1%) that occurred within 90 days of transplant. The first one was described as a "difficult" vascular anastomosis during the transplantation. This patient became oligoanuric within 24 hours and a duplex ultrasound on postoperative day 1 revealed no blood flow to the new transplanted kidney. He underwent allograft nephrectomy on this same day. The pathology report revealed extensive venous thrombosis with cortical and medullary necrosis. The second patient with allograft loss had initially delayed graft function of 7 days. His postoperative course was then unremarkable. However, 30 days later, he was readmitted with acute renal injury. He was treated for acute rejection with steroids, and underwent ultrasound and carbon dioxide angiogram to no avail. The allograft function did not recover and his renal biopsy revealed dense acute tubular necrosis of unknown etiology.

Mean follow-up was 3.5 ± 2.5 years. Overall allograft survival was 90.1% at 1-year and 86.4% at 3-year follow-up. Overall mortality occurred in six (27.3%) patients. Information regarding cause of death could only be found for one patient, who expired from cardiac arrest; all others have unknown causes of death.

Discussion

Little is known about the surgical challenges and outcomes of KT in the face of IOD. As the population continues to age and as more patients present with diabetes, hypertension, and longstanding smoking history, the incidence of kidney transplant recipients presenting with significant IOD should be expected to increase.[10,11] In this study, we have identified 22 patients (0.32%) with extensive IOD at the time of KT. While the safety of simultaneous reconstruction has been questioned previously,[8,9] Clavien et al[9] have demonstrated that concurrent interventions are both safe and feasible.

The primary end-point of our study was graft survival, which we demonstrated to be 90.1% at 1-year and 86.4% at 3-year follow-up, which is consistent with the national means for any high-volume transplant center.[10] Comparatively, our three-site allograft survival is 96.0 and 90.3% at 1- and 3 years post-KT, respectively. Two renal allografts were lost within 90 days secondary to renal vein thrombosis on postoperative day 1 and acute tubular necrosis on postoperative day 30. Despite this being a substantial loss, our early allograft loss is lower than what has been previously reported.[4] This further reaffirms that endarterectomy at the time of KT is both safe, effective, and may lead to long-term allograft survival. Of those patients requiring endarterectomy, only one case was identified and planned in the preoperative setting. This may be due to the infrequent use of cross-sectional imaging (59.1% of patients had preoperative CT) to screen for IOD in our KT population. Since the conduction of the current study, we have

included a noncontrast CT as required preoperative assessment and a vascular surgery consultation in those patients with significant IOD in our KT patient population. We believe this highlights the importance of standardizing preoperative screening protocols and the vital role of multidisciplinary approach to patient care in this complex patient population.

Patients undergoing endarterectomy at the time of renal transplant are at increased risk of complications. We recommend baseline surveillance of renal allografts on postoperative day 0 utilizing Doppler ultrasound. Doppler ultrasound should be repeated for any change in renal function, significant ultrasound abnormalities, or delayed allograft function beyond expectations of the specific donor allograft. Doppler ultrasound represents a noninvasive, low-cost screening tool in these complex patients. A low index of suspicion should be maintained for the need to pursue CO_2 contrast or traditional angiography versus early return to the operating room in cases of atypical allograft function. It is worthwhile mentioning that in the current endovascular era of managing many vascular diseases, this option has been mostly used in the post-transplantation setting. Glebova et al[11] illustrate both a renal artery and an iliac artery stenosis managed with balloon angioplasty. In a second review of 10-year data from the University of Michigan, 25 of their 34-patient cohort required endovascular balloon angioplasty due to renal artery and iliac artery stenosis.[12]

Mortality on dialysis far exceeds our reported transplant mortality. The United States Renal Data System reports 3-year survival on hemodialysis is only 57%; 3-year survival on peritoneal dialysis is 70%.[13] In contrast, our patients requiring iliac intervention at the time of renal transplant demonstrated 86.4% 3-year survival. This demonstrates significant survival benefit in those patients eligible for combined vascular surgery and transplant over starting/remaining on dialysis. Carefully selected patients have significant potential improvement in both quality of life and overall survival by considering combined endarterectomy and KT.

Limitations

Our review is a single-center retrospective review and as such, several limitations need to be acknowledged. First, our limited number of KT patients with concomitant IOD that required endarterectomy at the time of transplantation. Second, we believe that although this cohort is limited, most likely many of the KT candidates were not considered in the selection process due to the extensive IOD. In light of our current findings, several practical changes have been introduced that include a noncontrast CT as required preoperative assessment and a vascular surgery consultation in those patients with significant IOD on imaging. Furthermore, we are unable to generalize our outcomes to other transplant practices. Therefore, larger studies with multicenter data are necessary.

Conclusion

IOD patients selected for KT are not common and although challenging, they do have the same outcomes as our standard KT patients. The 1- and 3-year allograft survivals were 90.1

and 86.4% versus 96.0 and 90.3% in the general KT patient population. With these excellent outcomes, we recommend expanding the criteria for KT to include patients with IOD with prior vascular surgery consultation to prevent progression of IOD or prevention of wait list removal in select patients who are otherwise good candidates for KT.

Note
Poster Presentation at the 2019 Annual Vascular Meeting on June 12–15 2019 in Washington DC.

Conflict of Interest
None.

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