


# Endovascular treatment for transplant renal artery stenosis

## A retrospective cohort study

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### Abstract

Transplant renal artery stenosis (TRAS) is the most common (1%–23%) vascular complication following kidney transplantation. The aim of this study was to review our experience with an endovascular approach to treat TRAS.

We retrospectively reviewed kidney transplant recipients who underwent percutaneous transluminal angioplasty (PTA) due to TRAS in our institute from January 2009 to December 2015. We analyzed the patient's baseline characteristics, postoperative renal function, blood pressure evolution, and the number of pre- and post-procedure antihypertensive drugs.

A total of 21 patients (15 men, 6 women) were treated with the endovascular technique. The predominant presentation was graft dysfunction (76.2%). Stenosis or hemodynamic kinking was located at the anastomosis in 7 (33.3%) patients, proximal to the anastomosis in 13 (61.9%) patients, and distal the anastomosis in 1 (4.8%) patient. PTA without stent placement was performed in 7 patients (33.3%), and PTA with stent placement was performed in 14 patients (67.7%). Serum creatinine levels demonstrated no difference between the pre-procedure level and that on discharge day (1.61 mg/dl [0.47–3.29 mg/dl] vs 1.46 mg/dl [0.47–3.08 mg/dl];  $P = .33$ ). The glomerular filtration rate also showed no difference between the pre-procedure value and that on discharge day (53.6 ml/min [22.4–145.7 ml/min] vs 57.0 ml/min [17.56–145 ml/min];  $P = .084$ ). Systolic blood pressure and diastolic blood pressure (DBP) varied from 137 mm Hg (120–160 mm Hg) and 84 mm Hg (70–100 mm Hg) pre-procedure to 129 mm Hg (90–150 mm Hg) and 79 mm Hg (60–90 mm Hg) at discharge, respectively ( $P = .124$  and  $P = .07$ ). The number of antihypertensive medications significantly decreased from 1.5 (0–6) pre-procedure to 0.5 (0–2) at discharge ( $P = .023$ ). In our study, there were no technical failures, procedure-related complications or deaths. During the follow-up period, the free-from-reintervention rate was 100%, and graft failures occurred in 2 patients (9.5%) due to rejection.

Endovascular procedures for TRAS show a high technical success rate with a low complication rate and a low reintervention rate. PTA showed a trend toward a positive impact on lowering serum creatinine, systolic blood pressure, and diastolic blood pressure and improving estimated glomerular filtration rate, and the number of antihypertensive medications could be significantly reduced after this procedure.

**Abbreviations:** CIN = contrast-induced nephropathy, DBP = diastolic blood pressure, DGF = delayed graft function, DUS = Doppler ultrasonography, eGFR = estimated glomerular filtration rate, EIA = external iliac artery, IIA = internal iliac artery, MRA = magnetic resonance angiography, POBA = plain old balloon angioplasty, PSV = peak systolic velocity, PTA = percutaneous transluminal angioplasty, SBP = systolic blood pressure, TIT = total ischemic time, TRAS = transplant renal artery stenosis.

**Keywords:** kidney transplantation, percutaneous angioplasty, transplant renal artery stenosis

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## 1. Introduction

Transplant renal artery stenosis (TRAS) is a rare but the most common vascular complication after kidney transplantation ranging from 1% to 23%, the variabilities owing to institutional variations in screening protocols, different strategies for treating TRAS, and underlying patient demographics.<sup>[1–4]</sup> Patients with TRAS may be asymptomatic for a long time or present with refractory hypertension, new-onset hypertension, allograft dysfunction without evidence of rejection, or even graft loss.<sup>[5]</sup> TRAS is a potentially curable cause of refractory hypertension and allograft dysfunction that accounts for approximately 1% to 5% of cases of post-transplant hypertension<sup>[2]</sup> and at least 75% of all post-transplant vascular complications.<sup>[6]</sup>

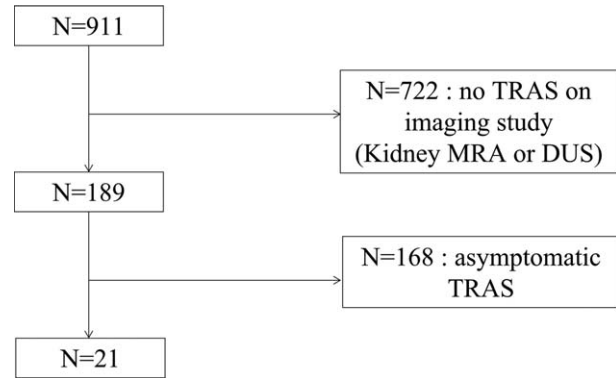
Although TRAS usually arises close to the surgical anastomosis, pre- or post-anastomotic stenosis may also occur, and different locations and timings of disease onset may demonstrate particular etiologies.<sup>[2]</sup> Anastomotic stenosis is commonly related to trauma to the donor or recipient vessels during surgical manipulation and usually arises early after transplantation; on the other hand, late stenosis, which appears several years after transplantation, usually reflects atherosclerotic disease in either the transplant renal artery or the adjacent proximal iliac artery.<sup>[1,2,4,7]</sup>

Noninvasive imaging, such as Doppler ultrasonography (DUS) and magnetic resonance imaging, can be useful in diagnosing TRAS. Nevertheless, angiography provides a definitive diagnosis that assists subsequent endovascular therapy. Most physicians regard percutaneous transluminal angioplasty (PTA) as the treatment of choice for TRAS,<sup>[8,9]</sup> and this method plays a significant role in preserving graft function and graft survival. Reported results after PTA are heterogeneous, and a relatively high restenosis rate has been reported without stenting, ranging from 16% to 62%, however, restenosis rate decreased to 10% after stent placement.<sup>[10,11]</sup> In this study, we retrospectively reviewed our experiences with endovascular treatment for TRAS and evaluated its outcomes.

## 2. Materials and methods

This study was approved by the institutional review board of clinical research coordinating center of our institute (KC16RISI0027). From January 2009 to December 2015, 911 allograft kidney transplantation were performed (including living and deceased donors). There were 189 cases (20.7%) of TRAS, among which 21 patients (11.1%) underwent endovascular procedures due to symptomatic TRAS (Fig. 1). In our institute, we schedule follow-up DUS of the graft kidney on postoperative days 7 and 14 (before discharge) and renal magnetic resonance angiography (MRA) on postoperative days 7<sup>§</sup> or 14<sup>§</sup> (multiple donor renal arteries or hostile conditions of the donor renal artery or recipient iliac artery). TRAS was considered significant when the graft renal artery peak systolic velocity (PSV) was  $>2$  m/s or when there was an increase in PSV by  $>50\%$  within the stenotic lesion diagnosed by DUS or renal MRA and when  $>50\%$  luminal narrowing was suspected (Fig. 2A, B).<sup>[2,12–14]</sup>

Data was collected from the electronic medical records and operation records concerning recipients' and donors' characteristics, number of donor renal arteries, number of anastomoses, clinical symptoms, time to presentation, type of procedure (PTA with or without stent placement), serum creatinine level, estimated glomerular filtration rate (eGFR) (calculated by the modified modification of diet in renal disease [MDRD] equation).



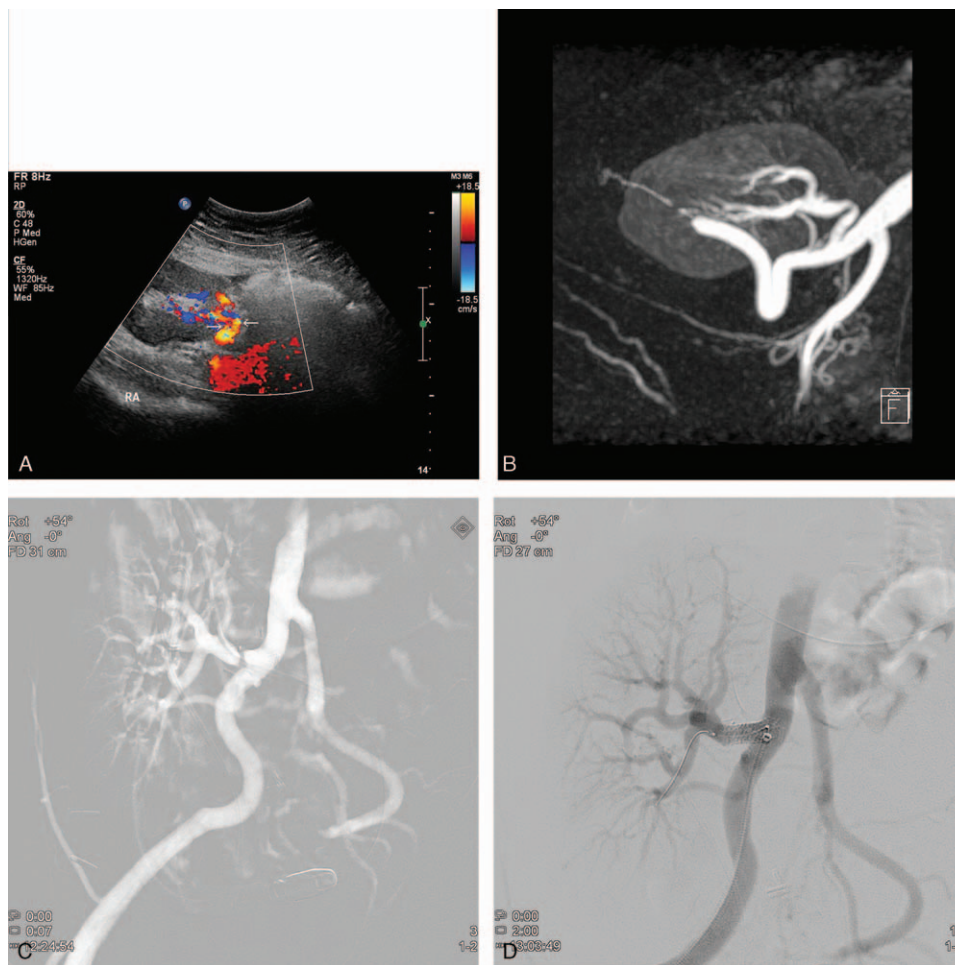
**Figure 1.** Flow sheet of patients' selection. DUS=Doppler ultrasonography, MRA=magnetic resonance angiography.

Hypertension was defined as a systolic blood pressure (SBP) of 140 mm Hg or higher, or a diastolic blood pressure (DBP) of 90 mm Hg or higher, lasting more than 3 days.<sup>[15]</sup> Oral nifedipine (calcium-channel blocker) was given as primary anti-hypertensive drug, and carvedilol (nonselective beta adrenergic blocker) was given additionally if hypertension persisted. For each patient, the number and the dose of anti-hypertensive medications taken before the procedure and on the day of discharge were noted. During the study period, the target BP was less than 140/90 (mm Hg). Decreased renal function was defined as more than 20% increase in creatinine level compared to nadir, and increased PSV of 2.5 m/s or more on DUS was considered abnormal.

After discharge, patients were scheduled for follow-up evaluation; laboratory tests were done at 1, 2, 4 weeks and at 3, 6, 12 months, while DUS was performed at 1, 3, 6, 12 months. Regardless of scheduled follow-ups, if a patient presented to the outpatient clinic with symptoms related to graft dysfunction (e.g., decreased urine output, edema, weight gain, etc) or increased creatinine level, DUS was performed to check the flow of the graft kidney, presence of abnormal fluid collections or hydronephrosis. If there were no abnormal findings upon DUS, patients received hydration as primary treatment. If creatinine level did not decrease even after sufficient hydration, graft kidney biopsy was performed and the patients were immediately started on high-dose steroid pulse therapy for 3 days on the assumption of graft rejection. Delayed graft function (DGF) was defined as a need for dialysis in the first 7 days after transplant and expanded criteria donor (ECD) was defined as any deceased donor over the age of 60, or a donor over the age of 50 with 2 of the following: a history of hypertension, a creatinine  $\geq 1.5$ , or death resulting from a stroke.<sup>[16,17]</sup> Clinical outcomes were evaluated by reduction of serum creatinine, increment of eGFR, reduction of mean SBP and DBP, reduction of the number of anti-hypertensive medications at before and after procedure.

### 2.1. Operative technique

Kidney transplantation was performed by 2 highly experienced surgeons according to the standard surgical protocol. After making a Rutherford–Morison incision, transversalis fascia was divided, and the peritoneum was reflected anteromedially to expose the iliac fossa. Arterial dissection was performed from the iliac bifurcation to the distal external iliac artery (EIA), while loose connective tissue and vasa vasorum were left undisturbed



**Figure 2.** A 55-yr-old female showed (A) high PSV on a follow-up duplex scan ( $>220$  cm/s) with stenosis lesion (arrow) at POD #7. (B) On MR angiography, severe stenosis was demonstrated at the anastomosis site. (C) CO<sub>2</sub> angiography was performed initially to reduce the amount of contrast media. (D) PTA with stent placement was successful with any complications. MR=magnetic resonance, POD=postoperative day, PSV=peak systolic velocity, PTA=percutaneous angioplasty.

except for a 2-cm segment at the site of the anticipated anastomosis. No arterial branches were ligated, even when the internal iliac artery (IIA) was used. In such cases, the proximal IIA was divided to its first branch and the iliolumbar artery was preserved. Detailed operation technique of our center has been described in a previous study.<sup>[18]</sup>

In case of single renal artery, end-to-side anastomosis to EIA with continuous 6-0 monofilament suture was the preferred method. Given that the contralateral IIA is patent, end-to-end anastomosis to IIA was performed for following circumstances: short donor renal artery, EIA deemed incompetent for anastomosis due to calcification or tortuosity, or the surgeon's preference. In case of multiple renal arteries, either anastomoses were performed separately to EIA and/or IIA or a common trunk was formed by spatulating arteries together prior to anastomosis to EIA or IIA.<sup>[14,18]</sup>

## 2.2. Endovascular procedure

All interventions were performed in the intervention room by an interventional radiologist and vascular surgeon. Under local anesthesia, the ipsilateral or contralateral common femoral artery

to the graft was cannulated using ultrasound. Initially, nonselective iliac arteriography was performed to confirm the stenotic lesion, and 0.035 inch-wire was inserted into the transplant renal artery through 5-Fr sheath of common femoral artery. Selective angiography was conducted, road-mapping images were captured, and stenotic lesions were measured by analyzing the ratio between the narrowed segment and the normal segment of the renal artery. The size of the balloon and stent was matched to the diameter of the adjacent normal renal artery. Balloon angioplasty was performed on the stenotic segment, and a stent was deployed if remnant stenosis ( $>25\%$ ) or recoil was identified. Selection of stent was made based on the type of the arterial lesion: balloon-expandable stents were used for lesions with short segment and heavy calcification which require precise placement, and self-expandable stents were used for lesions with long segment and tortuosity. During the procedure, to minimize contrast-induced nephropathy (CIN), CO<sub>2</sub> angiography and road mapping properly applied (Fig. 2C). Technical success of PTA was defined as a residual stenosis of  $<30\%$  after angioplasty with flow-limiting intimal dissection (Fig. 2D). The patients were started on oral aspirin (100 mg) or clopidogrel (75 mg) the day before the procedure, which was maintained daily for at least 30 days.

### 2.3. Statistics

Pre-procedure and post-procedure serum creatinine levels, eGFR and BP were compared by paired *t* test. The Wilcoxon signed rank test was performed to compare the number of antihypertensive medications. Continuous variables are expressed as mean and range. Statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC). Two-sided *P* values <.05 were considered statistically significant.

### 3. Results

A total of 21 patients were enrolled in this study, of which 15 were male and 6 were female, 16 had living donors while 5 had deceased donors. The mean age was 49 years (range, 31–65 years), and the mean follow-up duration was 41 months (range, 5–72 months). The predisposing causes of renal disease were diabetic nephropathy (*n*=7), chronic glomerular nephritis (*n*=5), hypertensive nephropathy (*n*=4), and unknown origins (*n*=5) (Table 1). The clinical symptoms were decreased renal function in 14 cases, DGF in 2 cases, and abnormal findings on duplex ultrasound and MRA without any clinical symptoms in 5 cases. None of the patients had hypovolemia, calcineurin inhibitor toxicity or CMV infection that could affect renal function during study periods. The mean time from transplantation to presentation was 45 days (range, 4–230 days) (Table 1). After procedure, all patients were discharged within 3 days. During the follow-up period, the free-from-reintervention rate was 100%. Three patients developed rejection: 1 case of antibody-mediated rejection and 2 cases of acute cellular rejection; graft failure occurred in 2 patients, who had active T-cell mediated rejection at 9 and 11 months postoperatively.

The allograft renal artery was anastomosed to the EIA by the end-to-side method in 9 cases, and the allograft renal artery was anastomosed to the IIA by the end-to-end method in 12 cases. During the operation, 10 recipients (47.6%) demonstrated diseased conditions of the iliac artery around the anastomosis site, such as intimal hyperplasia (*n*=4), atherosclerotic changes or severe calcifications (*n*=6), and in 4 patients with atheroma, we performed endarterectomy concurrently before anastomosis. The number of allograft renal arteries was 1 in 11 cases (52.4%) more than 1 in 10 cases (47.6%) (2 [*n*=8], 3 [*n*=2]). In case of multiple renal arteries, we performed ex vivo pantaloon (side-to-side) anastomosis to create a common channel (*n*=3) and directly anastomosed to iliac arteries, and the rest of each renal artery was anastomosed separately (*n*=7) to iliac arteries (Table 2). The mean number of artery anastomoses were 1.57 (range, 1–3), and the mean total ischemic time (TIT) was 99.1 minutes (range, 38–278 minutes) and the mean TIT was longer in the multiple renal artery group, which was not a significant difference (83.9 vs 115.8 minutes, *P*>.05). There were no operation related complications.

The stenotic lesion was confirmed by selective angiography in all patients. Pre-anastomotic stenosis occurred in 7 patients (33.3%), anastomotic stenosis occurred in 13 patients (61.9%), and post-anastomotic stenosis occurred in 1 patient (4.8%). Among the 13 anastomotic stenoses, multiple renal arteries were anastomosed in 5 (38.5%) cases, and the renal artery was anastomosed to the IIA in 8 cases (61.5%); among the 7 pre-anastomotic stenoses, multiple renal arteries were anastomosed in 4 (57.1%) cases, and the renal artery was anastomosed to the IIA in 3 (42.9%) cases. Severe donor iliac artery calcifications were observed in 4 (57.1%) case (Table 1). In 1 case of post-

**Table 1**

#### Demographics of the recipients and donors and operation-related factors.

Demographic	Value
<b>Recipient</b>	
Age (yr)	49.2 ± 9.3
Sex (male)	15 (71.4%)
BMI (kg/m <sup>2</sup> )	24.1 ± 2.8
Obesity (BMI > 25 kg/m <sup>2</sup> )	5 (23.8%)
Cause of ESRD	
DM	7 (33.3%)
HBP	4 (19.1%)
CGN	5 (23.8%)
Unknown	5 (23.8%)
Number of KT (1st)	20 (95.2%)
Number of mismatched HLA	3.9 ± 1.7
History of	
HBP	15 (71.4%)
DM	7 (33.3%)
IHD	3 (14.3%)
CVD	1 (4.8%)
PAD	4 (19.0%)
Hyperlipidemia	6 (28.6%)
Induction immunosuppression	
Basiliximab	20 (95.2%)
Antithymocyte globulin	1 (4.8%)
Diseased iliac artery	
Severe calcification	6 (28.5%)
Intimal hyperplasia	4 (19.1%)
<b>Donors</b>	
Age (yr)	42.3 ± 12.7
>50 yr	6 (28.6%)
Sex (male)	11 (52.4%)
Type of donor (live)	16 (76.2%)
Multiple renal artery transplantation (>1)	10 (47.6%)
ECD	3 (14.3%)
<b>Operation related factors</b>	
Total ischemic time (min)	99.1 ± 75.2
Number of arterial anastomoses	1.57 ± 0.68
Combined procedures during the operation	10 (47.6%)
Arterioplasty	5 (23.8%)
Endarterectomy	5 (23.8%)

Values are presented as mean ± standard deviation or number (%).

BMI = body mass index, CGN = chronic glomerular nephritis, CVD = cerebral vascular disease, DM = diabetes mellitus, ECD = expanded criteria donor, ESRD = end stage renal disease, HBP = high blood pressure, HLA = human leukocyte antigen, IHD = ischemic heart disease, KT = kidney transplantation, PAD = peripheral artery disease.

anastomosis stenosis, 3 arteries were affected, and we performed ex vivo pantaloon (side-to-side) anastomosis to create a common channel and anastomosed the artery to the IIA (Table 2). In 7 patients (33.3%), only plain old balloon angioplasty (POBA) was performed, and 14 other patients underwent stent placement due to residual stenosis. All of the stents used were bare-metal stents; 8 were balloon-expandable stents, 6 were self-expanding stents, the mean stent diameter was 6.1 mm (range, 5–12 mm), and the length was 20.2 mm (range, 14–40 mm). The overall technical success rate of PTA with or without stent placement was 100%, and there were no periprocedural complications.

The nadir creatinine level after transplantation was 1.21 mg/dl (range, 0.30–3.21 mg/dl). The day before the procedure, the creatinine was increased to 1.61 mg/dl (range, 0.47–3.29 mg/ml); it decreased to 1.54 mg/dl (range, 0.47–3.08 mg/dl, *P*>.05) and 1.46 mg/dl (0.47–4.34 mg/dl, 9.3% reduction, *P*>.05), on the day after

**Table 2**  
Summary of reviewed cases.

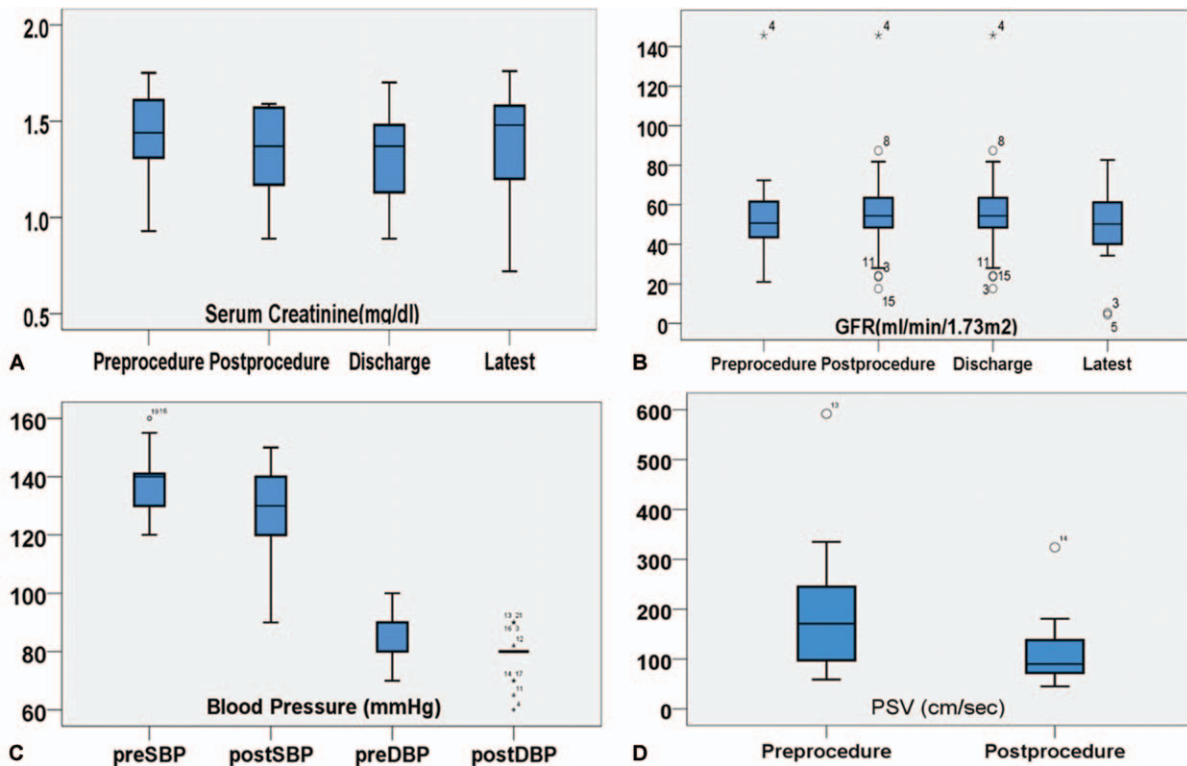
Pt	Age	Sex	CP	Days from KT to CP	Stenosis location	RA-Anastomosis to	Number of renal a.	Condition of iliac a.
1	53	M	Increased sCr	32	Pre-anastomosis	IIA	Single (E-to-E)	Atheroma on IIA → endarterectomy
2	35	M	Increased sCr	22	Anastomosis	IIA	Double (Pantaloon E-to-E)	Favorable
3	31	F	Increased sCr	171	Anastomosis	EIA	Double (E-to-S, each)	Favorable
4	56	F	Abnormal DUS criteria	14	Pre-anastomosis	EIA	Double (E-to-S, each)	Favorable
5	58	M	Increased sCr	230	Anastomosis	EIA	Double (E-to-S, each)	Favorable
6	53	M	Increased sCr	105	Pre-anastomosis	IIA	Single (E-to-E)	Heavy calcific stenosis on IIA → endarterectomy
7	37	M	Increased sCr	15	Anastomosis	IIA	Single (E-to-E)	Short length of IIA
8	37	M	Abnormal DUS criteria	11	Anastomosis	IIA	Single (E-to-E)	Short length of IIA
9	48	F	Increased sCr	15	Anastomosis	①IIA ②EIA	Double ①E-to-E ②E-to-S	Atheroma on IIA → endarterectomy
10	49	F	Abnormal DUS criteria	79	Anastomosis	IIA	Single (E-to-E)	Atheroma on IIA → endarterectomy
11	53	M	DGF	5	Pre-anastomosis	①EIA ②Inferior epigastric a.	Double ①E-to-S ②E-to-E	Favorable
12	49	M	Increased sCr	50	Pre-anastomosis	EIA	Double (Pantaloon E-to-S)	EIA Calcified
13	63	M	Increased sCr	14	Anastomosis	EIA	Single (E-to-S)	EIA Calcified
14	50	M	Increased sCr	50	Anastomosis	IIA	Single (E-to-E)	IIA Calcified * RA aneurysm (1 cm) → aneurysm repair
15	43	F	DGF	4	Pre-anastomosis	①IIA ②EIA ③Inferior epigastric a.	Triple ① E-to-E ② E-to-S ③ E-to-E	Calcified EIA, IIA
16	55	M	Increased sCr	14	Pre-anastomosis	EIA	Single (E-to-S)	EIA calcified
17	65	M	Abnormal DUS criteria	11	Anastomosis	EIA	Single (E-to-S)	Favorable
18	56	M	Increased sCr	13	Anastomosis	EIA	Single (E-to-S)	EIA calcified
19	58	M	Increased sCr	66	Anastomosis	IIA	Single (E-to-E)	Atheroma on IIA → endarterectomy
20	44	F	Abnormal DUS criteria	13	Anastomosis	EIA	Double (E-to-S, each)	Favorable
21	40	M	Increased sCr	6	Post-anastomosis	IIA	Triple (Pantaloon E-to-E)	Favorable

a. = artery, CP = clinical presentation, DGF = delayed graft function, DUS = Doppler ultrasonography, EIA = external iliac artery, E-to-E = end to end anastomosis, E-to-S = end to side anastomosis, F = female, IIA = internal iliac artery, KT = kidney transplantation, M = male, Pt. = patients, RA = renal artery, sCr = serum creatinine.

the procedure and at the day of discharge, respectively, even though the difference did not reach significance (Fig. 3A). After transplantation, the mean eGFR was initially restored to 81.1 ml/min (range, 21.6–244.6 ml/min). Prior to procedure, mean eGFR decreased to 53.6 ml/min (range, 22.4–145.7 ml/min), which slightly increased to 57.0 ml/min (range, 17.6–145.0 ml/min) after receiving intervention; the latest follow-up results showed some improvement to 59.9 ml/min (range, 11.8–145.7 ml/min). However, none of the results were statistically significant (Fig. 3B).

The mean SBP before the procedure, after the procedure and on discharge day were 145 mm Hg (range, 110–180 mm Hg), 127 mm

Hg (range, 90–160 mm Hg) and 127 mm Hg (range, 90–160 mm Hg), respectively ( $P > .05$ ) which was decreased 15%. The mean DBP also decreased from 85 mm Hg (range, 60–100 mm Hg) before the procedure to 77 mm Hg (range, 60–90 mm Hg) after the procedure and 75 mm Hg (range, 60–90 mm Hg) on discharge day ( $P > .05$ ) which was decrease 9.5% (Fig. 3C). The mean number of antihypertensive medications significantly decreased from 1.67 (range, 0–6) pre-procedurally to 0.57 (0–2) on discharge day ( $P < .05$ ). Follow-up duplex ultrasound was performed within 7 days after the procedure, and the blood flow rate significantly decreased from 188.4 cm/s (range, 59–592 cm/s) to 109.1 cm/s (range, 45–324 cm/s) within 1 week ( $P < .05$ ) (Fig. 3D).



**Figure 3.** Clinical outcome after endovascular treatment: (A) serum creatinine ( $P > .05$ ); (B) eGFR ( $P > .05$ ); (C) SBP ( $P > .05$ ) and DBP ( $P > .05$ ); (D) PSV ( $P < .05$ ). DBP=diastolic blood pressure, eGFR=estimated glomerular filtration rate, PSV=peak systolic velocity, SBP=systolic blood pressure.

#### 4. Discussion

TRAS is the most common vascular complication in kidney transplantation, and the clinical features of TRAS include refractory hypertension, new-onset hypertension, allograft dysfunction, and presence of bruit over the graft; most events occur during the early period of transplantation (within 6 months). Early presentations of TRAS are mostly due to traumatic intimal or adventitial injury during harvesting or vessel manipulation, kinking of the artery (longer than necessary), technical problems during vascular anastomosis, and diseased condition of the anastomosed artery (severe calcifications, tortuosity, atheroma, etc).<sup>[12,19]</sup> However, late-appearing TRAS with diffuse, multiple and concentric stenosis is associated with an immune response after transplantation, such as graft rejection and cytomegalovirus infection.<sup>[1,20]</sup> In addition, DGF and prolonged cold ischemia time are other known risk factors in recipients of cadaveric grafts, ECDs, patients with obesity, and patients with ischemic heart diseases.<sup>[16,17,20]</sup> Hurst et al reported that major predictors of TRAS include recipient age ( $>65$  years), ECD (18.5%), DGF (23.0%), IHD (12.3%), and induction immunosuppression (86.6%).<sup>[17]</sup> In this study, only 1 recipient was older than 65 year and 2 cases (9.5%) DGF was observed, however, ECD (14.3%), IHD (14.3%), and use of induction immunosuppression (100%) were comparable to previous data.<sup>[17]</sup>

The most frequent clinical symptoms were decreased renal function (57.1%), delayed allograft function (9.5%), and refractory hypertension (4.8%), and the proportion of asymptomatic patients with abnormal findings on duplex ultrasound and MRA were 28.6%. The mean time from transplantation to

presentation was 45 days (range, 4–230 days), which was the early period after transplantation. During the operation, 10 patients (47.6%) were observed to have a diseased iliac artery (severe calcifications or stenosis due intimal hyperplasia), which was a relatively high prevalence, and all of these recipients required concomitant surgical procedures during transplantation, such as angioplasty ( $n=5$ ) or endarterectomy ( $n=5$ ).

Most transplantation surgeons prefer end-to-side anastomosis to the EIA or end-to-end anastomosis to the IIA with a single renal artery, as multiple renal arteries increase the risk of vascular and urological complications.<sup>[21,22]</sup> Several comparison analysis studies of multiple versus single renal artery transplantation reported that there was no significant difference in the occurrence of TRAS between the 2 groups<sup>[23,24]</sup>; however, Benedetti et al<sup>[25]</sup> reported that multiple renal arteries/1 anastomosis demonstrated a significantly higher rate of TRAS than single renal artery/1 anastomosis, and there was no difference compared with cases of multiple renal arteries/multiple anastomosis. Nicholson et al<sup>[22]</sup> reported that the TRAS group underwent multiple renal artery transplantation more often than the no-TRAS group (47% vs 18.1%), and TIT was an independent factor for TRAS. In our study, 10 (47.6%) allograft kidneys required multiple renal artery transplantation, including double ( $n=8$ ) and triple ( $n=2$ ) artery transplantations, and the mean number of arterial anastomoses was 1.57; the mean TIT was longer in the multiple renal artery group, which was not a significant difference (83.9 vs 115.8 minutes,  $P > .05$ ).

The location of stenosis is also an important issue, as it is related to its etiology. Anastomotic stenosis and transplant renal artery kinking are thought to be primarily caused by anatomical

and surgical technical issues and occur in larger vessels near the anastomosis, or these issues are secondary to incompatible artery or vein length.<sup>[12]</sup> On the other hand, post-anastomotic stenosis has been associated with immunologic factors, such as de novo DSA class II donor-specific antibodies,<sup>[26]</sup> and pre-anastomotic stenosis is related to the iliac artery condition of the donors or kinking after anastomosis. In this study, the incidence of anastomotic stenosis was 61.9%, and the incidences of pre- and post-anastomotic stenosis were 33.3% and 4.8%, respectively. Among the anastomotic stenosis cases, anastomosis to the IIA was performed in 61.8% of the cases, and this result is probably related to the end-to-end anastomosis technique; however, among pre-anastomosis cases (n=7), 57.1% of the iliac arteries of donors were heavily calcified.

Endovascular treatment for TRAS is known as first-line therapy, with a high technical success rate of nearly 100%<sup>[19,27]</sup> and a high clinical success rate of 65.5 to 94%.<sup>[26]</sup> However, the reported results are heterogeneous; PTA alone has been associated with restenosis rates of 16% to 62% in some studies, whereas restenosis rates with PTA with stenting are typically <10%.<sup>[11]</sup> In this study, 7 patients (33.3%) were treated with only POBA. However, 14 patients (66.7%) underwent stent placement due to residual stenosis after POBA; the technical success rate was 100%, and there was no restenosis during the study period. There are several complications of endovascular treatment, such as bleeding, puncture site pseudoaneurysm/hematoma, anastomotic rupture, arterial dissection, thrombosis, and CIN, and the reported complication rates are as high as 10%.<sup>[3,12]</sup> There were no observed periprocedural complications in our study and to minimize the incidence of CIN, we alternatively performed CO<sub>2</sub> angiography with conventional angiography.

To assess the clinical outcomes, several reported studies measured and analyzed the alterations in serum creatinine, glomerular filtration rate, BP, number of antihypertensive drugs taken by patients, and PSV before and after the procedure.<sup>[2,12,19,26,27]</sup> Most of the study cohorts were too small and the results showed heterogeneity; however, these parameters showed trends of improvement following the procedure. In our study, we observed a trend toward a positive impact on lowering serum creatinine, SBP and DBP and improving eGFR after the procedure, but these differences were not significant, which may also be due to the small sample size and different follow-up periods in each study. However, the mean number of antihypertensive drugs taken by patients was significantly reduced from 1.67 pre-procedure to 0.57 on the discharge day, and the PSV measured by DUS decreased to 188.4 to 109.1 cm/s within 1 week after the procedure, which was a significant change. These results support the findings of a previous study that the PSV is a reliable, reproducible, and efficient DUS parameter for screening, monitoring, and selecting patients suspicious of TRAS.<sup>[14]</sup> Also, another study reported that increased PSV could potentially serve as a predictive measure of TRAS recurrence. Standardized screening protocol using DUS may enable early detection of recurrence following endovascular procedure.<sup>[28]</sup>

There are several drawbacks to this study: this was a retrospective single-center study with a small sample size and the absence of control groups, such as those who had no TRAS or those who had no symptoms or signs of TRAS. Similar to the sample of another study, the dataset was heterogeneous, and the lack of standard methodology and reporting systems are also limitations of this study.

This study was different from previous studies in that it was conducted in the perspective of transplant surgeons and concerns

surgical aspects of TRAS including the number of graft arteries, the number of anastomoses, and the condition of recipient iliac artery. Therefore, we believe that the results of this study can provide basis to future studies related to surgical aspects of post-transplant complications. Also, further study with a larger sample size may provide deeper insight into the subject.

## 5. Conclusion

This study supports that endovascular procedures for TRAS show a high technical success rate with a low complication rate and a low reintervention rate. These methods show a trend toward a positive impact on lowering serum creatinine, SBP and DBP and improving eGFR, but the differences were not significant; however, the number of antihypertensive medications could be significantly reduced after these procedures.

Although TRAS may affect a small portion of the renal transplant population, it has significant complications such as refractory hypertension and graft dysfunction or loss, so early suspicion and diagnosis are warranted. In this study, there was a relatively high rate of multiple renal artery transplantation and diseased conditions in recipients with TRAS, and those who have these factors require more cautious monitoring during and after transplant surgery. However, to clarify these results, more large cohorts and more long-term graft survival results are required in further investigations.

## Author contributions

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## References

- [1] Ardalan MR, Shoja MM, Tubbs RS, Ghabili K. Transplant renal artery stenosis associated with acute cytomegalovirus infection: resolution following ganciclovir administration. *Ren Fail* 2009;31:982–4.
- [2] Bruno S, Remuzzi G, Ruggenenti P. Transplant renal artery stenosis. *J Am Soc Nephrol* 2004;15:134–41.
- [3] Fervenza FC, Lafayette RA, Alfrey EJ, Petersen J. Renal artery stenosis in kidney transplants. *Am J Kidney Dis* 1998;31:142–8.
- [4] Patel NH, Jindal RM, Wilkin T, et al. Renal arterial stenosis in renal allografts: retrospective study of predisposing factors and outcome after percutaneous transluminal angioplasty. *Radiology* 2001;219:663–7.
- [5] Trompeter RS, Bewick M, Haycock GB, Chantler C. Renal transplantation in very young children. *Lancet* 1983;1:373–5.
- [6] Aguera Fernandez LG, Zudaire JJ, Isa WA, et al. Vascular complications in 237 recipients of renal transplant from cadaver. *Actas Urol Esp* 1992;16:292–5.

- [7] Patel U, Khaw KK, Hughes NC. Doppler ultrasound for detection of renal transplant artery stenosis-threshold peak systolic velocity needs to be higher in a low-risk or surveillance population. *Clin Radiol* 2003;58:772–7.
- [8] Chen W, Kayler LK, Zand MS, Muttana R, Chernyak V, DeBoccardo GO. Transplant renal artery stenosis: clinical manifestations, diagnosis and therapy. *Clin Kidney J* 2015;8:71–8.
- [9] Greenstein SM, Verstandig A, McLean GK, et al. Percutaneous transluminal angioplasty. The procedure of choice in the hypertensive renal allograft recipient with renal artery stenosis. *Transplantation* 1987;43:29–32.
- [10] Naghavi M, Wang H, Lozano R, et al. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;385:117–71.
- [11] Henning BF, Kuchlbauer S, Böger CA, et al. Percutaneous transluminal angioplasty as first-line treatment of transplant renal artery stenosis. *Clin Nephrol* 2009;71:543–9.
- [12] Braga AF, Catto RC, Dalio MB, et al. Endovascular approach to transplant renal artery stenosis. *Ann Transplant* 2015;20:698–706.
- [13] Nikolic B, Rose SC, Ortiz J, et al. Standards of reporting for interventional radiology treatment of renal and pancreatic transplantation complications. *J Vasc Interv Radiol* 2012;23:1547–56.
- [14] Li Marzi V, Campi R, Sessa F, et al. Standardized duplex ultrasound-based protocol for early diagnosis of transplant renal artery stenosis: results of a single-institution retrospective cohort study. *Biomed Res Int* 2018;2018: Article Id 2580181, 9 pages.
- [15] Perloff D, Grim C, Flack J, et al. Human blood pressure determination by sphygmomanometry. *Circulation* 1993;88:2460–70.
- [16] Kamali K, Abbasi MA, Behzadi AH, Mortazavi A, Bastani B. Incidence and risk factors of transplant renal artery stenosis in living unrelated donor renal transplantation. *J Ren Care* 2010;36:149–52.
- [17] Hurst FP, Abbott KC, Neff RT, et al. Incidence, predictors and outcomes of transplant renal artery stenosis after kidney transplantation: analysis of USRDS. *Am J Nephrol* 2009;30:459–67.
- [18] Kim MH, Jun KW, Hwang JK, Moon IS, Kim JI. Characteristics of femoral motor neuropathies induced after kidney transplantation: a case series. *Transplant Proc* 2016;48:933–7.
- [19] Touma J, Costanzo A, Boura B, Alomran F, Combes M. Endovascular management of transplant renal artery stenosis. *J Vasc Surg* 2014;59:1058–65.
- [20] Audard V, Matignon M, Hemery F, et al. Risk factors and long-term outcome of transplant renal artery stenosis in adult recipients after treatment by percutaneous transluminal angioplasty. *Am J Transplant* 2006;6:95–9.
- [21] Zorgdrager M, Krikke C, Hofker SH, Leuvenink HG, Pol RA. Multiple renal arteries in kidney transplantation: a systematic review and meta-analysis. *Ann Transplant* 2016;21:469–78.
- [22] Nicholson ML, Yong C, Trotter PB, Grant L, Hosgood SA. Risk factors for transplant renal artery stenosis after live donor transplantation. *Br J Surg* 2019;106:199–205.
- [23] Hwang JK, Kim SD, Park SC, et al. The long-term outcomes of transplantation of kidneys with multiple renal arteries. *Transplant Proc* 2010;42:4053–7.
- [24] Taghizadeh Afshari A, Mohammadi Fallah MR, Alizadeh M, Makhdoomi K, Rahimi E, Vossoghian S. Outcome of kidney transplantation from living donors with multiple renal arteries versus single renal artery. *Iran J Kidney Dis* 2016;10:85–90.
- [25] Benedetti E, Troppmann C, Gillingham K, et al. Short- and long-term outcomes of kidney transplants with multiple renal arteries. *Ann Surg* 1995;221:406–14.
- [26] Ngo AT, Markar SR, De Lijster MS, Duncan N, Taube D, Hamady MS. A systematic review of outcomes following percutaneous transluminal angioplasty and stenting in the treatment of transplant renal artery stenosis. *Cardiovasc Intervent Radiol* 2015;38:1573–88.
- [27] Beecroft JR, Rajan DK, Clark TW, Robinette M, Stavropoulos SW. Transplant renal artery stenosis: outcome after percutaneous intervention. *J Vasc Interv Radiol* 2004;15:1407–13.
- [28] Roustan FR, Lareyre F, Bentellis I, et al. Endovascular treatment of transplant renal artery stenosis: evaluation of postoperative outcomes and risk factors for recurrence. *Angiology* 2019;70:249–56.