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Renal Transplant Artery Stenosis: Clinical Manifestations, Diagnosis and Treatment

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Abstract

Introduction: Renal transplant artery stenosis (RTAS) is a common and early complication of renal transplantation, which can lead to severe post-transplant hypertension, as well as significant morbidity and mortality, particulary graft loss. The aim of this study is to determine the prevalence, clinico-radiological characteristics and evaluate the outcomes of luminal angioplasty as a first-line treatment for RTAS, through the analysis of medical records of 27 kidney transplant patients. **Material and Methods:** This is a retrospective, single-center, and descriptive study conducted at the Nephrology department of the Ibn-Sina Hospital in Rabat, including 27 renal transplant patients with RTAS during the period from 1998 to 2023. All patients with clinically suspected RTAS and confirmed by Doppler ultrasound of the transplanted renal artery were included in the study. **Results:** The mean age of donors was 48.66 ± 13.55 years, with a female predominance (65%). The donor was deceased in 15% of cases. The mean age of the recipients was 39 ± 16 years with a male-to-female ratio of 4.4. The median onset of RTAS was 3.6 ± 3.4 months after renal transplantation. Seven patients (26%) had high blood pressure (HBP) before their transplantation. Six patients (22%) had hypertriglyceridemia and 7 patients (26%) had pure hypercholesterolemia. The main clinical signs were worsening of preexisting HBP, de novo HBP and acute renal failure (ARF). Stenosis was confirmed by renal Doppler ultrasound in all patients. It was severe in 63%, with a stenosis degree greater than 70%. Six patients underwent angioplasty, resulting in the stabilization of graft function with a nadir of 15 mg/l creatinine and blood pressure control with dual therapy in 5 patients. No graft loss cases were noted. **Conclusion:** RTAS is a significant vascular complication of renal transplantation that predicts unfavorable outcomes for both the patient and the graft. Early diagnosis is crucial to successfully restore graft function and prevent complications.

Keywords

RTAS, Post Transplant Hypertension, Graft Function, Luminal Angioplasty

1. Introduction

Introduced several decades ago, kidney transplantation today represents the most effective treatment for end-stage chronic kidney failure, restoring normal kidney function and patient autonomy. It provides better long-term survival and quality of life than hemodialysis or peritoneal dialysis [1]. Despite significant progress in surgical techniques, several post-operative complications may arise, notably vascular complications, with the most frequent being graft artery stenosis [2]. RTAS affects 1% to 23% of kidney recipients [3]-[5] and accountsfor approximately 75% of vascular complications post-transplant. It typically occurs early, usually between 3 months and 2 years after kidney transplantation, with a higher frequency in the first 6 months post-transplant [6]-[9]. RTAS can be completely asymptomatic or responsible for 1% to 5% of post-transplant hypertension [5] [10] [11]. It can lead to graft dysfunction and loss, hence the widespread use of echo-Doppler in routine renal graft surveillance. This examination allows for the detection of asymptomatic stenosis or stenosis causing hypertension, thereby avoiding serious complications. The aim of this study is to determine the prevalence, clinico-radiological characteristics, and to evaluate the outcomes of luminal angioplasty as the first-line treatment for RTAS, through the analysis of record from 27 kidney transplant patients.

2. Material and Methods

2.1. Study Objectives and Outcome Measures

The main objectives of this study are:

- To determine the prevalence of RTAS and the clinical and radiological characteristics of our patients.
- To evaluate the results of luminal angioplasty as the first choice treatment for RTAS by analyzing the graft survival rate and function, the percentage of restenosis and graft loss. Secondary outcome measures included analyzing improvement in blood pressure readings and reduction in the number of antihypertensive medications.

2.2. Definitions

Severe RTAS was defined as an obstruction exceeding 70% of the arterial lumen.

Early RTAS was defined as stenosis occurring within 3 months post-transplant and late RTAS as stenosis occurring after 12 months of kidney transplantation [12].

Hypertriglyceridemia was defined by a triglyceride level > 2 g/l, hypercholesterolemia as total cholesterol levels > 2.4 g/l and LDL cholesterol levels > 1.6

g/l [13].

HBP was defined by blood pressure > 140/90 mmHg and refractory hypertension as e uncontrolled blood pressure despite taking at least 3 antihypertensive agents [14].

2.3. Study Design

This is a retrospective, single-center and descriptive study conducted within the Nephrology department of Ibn-Sina Hospital in Rabat, including 27 renal transplant patients with RTAS during the period from 1998 to 2023.

2.4. Inclusion Criteria

The study includes all patients in whom RTAS was clinically suspected due to worsening ambulatory blood pressure measurements, becoming refractory to antihypertensive medications, requiring additional therapeutic classes, or the onset of de novo hypertension or the presence of a murmur on clinical examination and/or unexplained graft dysfunction in the absence of rejection, obstruction or infection, leading to the performance of echo-Doppler of the transplanted renal artery. We diagnosed RTAS based on two echo-Doppler examinations with velocities > 190 cm/s, disturbance of downstream flow and >50% significant stenosis with clinical repercussions. RTAS was differentiated by its location: ostial, trunk or ostial-trunk.

2.5. Methodology

Demographic data, initial nephropathy, donor and recipient characteristics, blood pressure profile, graft function, immunosuppressive treatment, biological data including lipid and glucose profiles, arteriography and angio-MRI data and therapeutic modalities were collected from medical record and reported on a predefined form (see appendix). This form was completed for each selected file. We have retrieved descriptive results. Statistical analysis could not be conducted due to the small sample size of patients.

3. Results

Among the 181 renal transplant patients during this period, 27 patients had graft artery stenosis, representing 14.9%, after a median delay of 3.6 ± 3.4 months post-transplant. Twenty-two patients were male and 5 were female with a male-to-female ratio of 4.4. The mean age of recipients was 39 ± 16 years. The mean body mass index was 24 +/− 2 kg/m^2 with extremes of 19 to 27.5 kg/m^2. The mean total cholesterol level was 1.98 +/− 0.32 g/l and the mean LDL cholesterol level was 1.5 +/− 0.33 g/l. The mean triglyceride level was 1.85 +/− 0.66 g/l. Six patients had hypertriglyceridemia and 7 patients had pure hypercholesterolemia. The mean age of donors was 48.66 ± 13.55 years, with a predominance of females (65%). The donor was deceased in 15% of cases. Initial nephropathy was mainly represented by undetermined nephropathy (48%), vascular (15%), glo-

merular (12%), and diabetic (4%). Seven patients had hypertension before transplantation, accounting for 26% of patients. All patients were on calcineurin inhibitors, 85% (23) were on cyclosporin. The residual rate was within target for all patients (see Table 1).

Table 1. The demographic, clinical, biological and ultrasound characteristics of our patients are as follows.

Characteristics	Results
The average age of the recipients	39 +/− 16 years
The Sex of the recipients	
Male (N)	22
Female (N)	5
Average age of the donors	48.66 ± 13.55 years
Sex of the donor	
Male (N)	10
Female (N)	17
Type of donor	
Cadaveric donor (N)	4
Living donor (N)	23
Average BMI of recipients (kg/m²)	24 +/− 2 (19 - 27.5)
Average GFR of recipients	18.5 ± 3.2 ml/min/1.73m²
Initialnephropathy (in percentage)	
Indeterminate	48%
Vascular	15%
Glomerular	12%
Diabetic	4%
Immunosuppressive treatment	
Ciclosporine (N)	23
Tacrolimus (N)	4
Location of stenosis (in percentage)	
ostial	88.9%
truncular	7.4%
ostio-truncular	3.7%
Average total cholesterol of recipients (g/l)	1.77 +/− 0.32
Average LDL cholesterol of recipients (g/l)	de 1.24 +/− 0.33
Average triglyceride levels in recipients (g/l)	1.52 +/− 0.66

N = number; GFR = Glomerular Filtration Rate; LDL: low-density lipoprotein.

The diagnosis was early, within the first 3 months post-renal transplantation in 92.6% of cases (25 patients) and late at 12 and 18 months respectively in 2 patients. The main clinical signs included worsening of pre-existing hypertension in 6 patients, de novo hypertension in 10 cases, acute renal failure in 4 cases with an average creatinine level of 18.5 ± 3.2 mg/l, and the presence of vascular murmur in 1 patient, while 6 patients remained asymptomatic and the stenosis was discovered during routine screening.

Stenosis was diagnosed by renal echo Doppler in all patients. It was primarily located ostially (88.9%) (n = 24), trunk (7.4%) and ostial-trunk (3.7%). The stenosis was significant in 17 cases (63%) with clinical repercussions and a degree of stenosis greater than 70%. The maximum systolic velocity was greater than 300 cm/s in 13 cases (48%). Stenosis was confirmed by angio-MRI in 3 cases and by arteriography in 1 case.

Endovascular treatment indications were selected for six patients with severe hypertension (n = 5), four of whom were on ≥ 3 antihypertensive medications, and/or for graft involvement (n = 4) with an average creatinine level of 18.5 mg/l, and for severe stenosis > 80% (n = 1) and its intraparenchymal repercussions on the graft. Only one patient underwent angioplasty with stent placement. Endovascular management resulted in stabilization of graft function at a nadir of 15 mg/l creatinine level with controlled hypertension on dual therapy in 5 patients. These patients achieved controlled blood pressure 3 to 6 months after endovascular treatment with only 2 antihypertensive medications, including a calcium channel blocker. Systolic blood pressure decreased from an average of 170 mm Hg to 126 mm Hg and diastolic blood pressure from 90 mm Hg to an average of 72 mm Hg (see Table 2). No cases of graft loss were noted among our patients.

Table 2. The evolution of the blood pressure profile in patients 3 to 6 months after endovascular treatment.

	Average blood pressure at the time of diagnosis (mmHg)	Average blood pressure after endovascular treatment (mmHg)	Antihypertensive treatment
Patient 1	160/80	130/60	ACE inhibitors/CCB
Patient 2	180/100	120/70	CCB/thiazide diuretic
Patient 3	160/90	130/70	CCB/Beta-Blocker
Patient 4	180/100	120/80	CCB/Beta-Blocker
Patient 5	170/80	130/80	CCB/ACE inhibitors

Angiotensin-converting enzyme (ACE) inhibitors; Calcium channel blocker: CCB.

The remaining patients are under systematic clinical, biological and radiological surveillance. It's worth noting that 9 patients have been put on antiplatelet therapy.

4. Discussion

RTAS represents about 75% of vascular complications post-transplantation and accounts for 1% to 5% of post-transplant hypertension [5] [10] [11]. Its incidence varies from 1.3% to 12.5% according to different series [3] [15]-[17] and its prevalence ranges from 1% to 23% of cases [3]-[5]. It typically occurs between 3 months and 2 years after renal transplantation, with a higher frequency in the first 6 months post-transplantation [6]-[9]. In our series, RTAS was observed in 14.9% of cases with an average delay of 3.6 ± 3.4 months.

RTAS was clinically suspected in 21 of our patients either by impact on graft function or hemodynamic repercussion (HBP), consistent with existing literature [3] [5] [15] [18]. It was significant in 17 cases (63%) of our series with clinical repercussion and a stenosis degree exceeding 70%. However, stenoses can be incidentally discovered by Doppler ultrasound, as was the case with 6 of our patients. The widespread use of Doppler ultrasound controls allows the discovery of asymptomatic stenoses [18]-[21].

RTAS may result from defective surgical technique, curvature or angulation of the renal artery, size discrepancy between donor and recipient renal arteries and atherosclerosis of the donor's or recipient's renal arteries [22]-[24]. Several risk factors are associated with the occurrence of SAG including extended criteria donors, advanced age of recipient and donor, hypertensive nephropathy, delayed graft function and prolonged cold ischemia time [8] [25]. Some studies have found a higher prevalence of RTAS in the case of deceased donors [15]-[17] [26]. In our series, donors were living in 85% of cases. End-to-end anastomoses are also associated with a lower incidence of RTAS than end-to-side anastomoses in some studies [27]. It is also noteworthy that calcineurin inhibitor toxicity should be sought due to its preglomerular vasoconstriction mechanism affecting blood pressure and graft function [22].

Endovascular treatment is indicated if the stenosis is symptomatic, hemodynamically significant or if the risk of thrombosis is high. Stenosis is treated by percutaneous transluminal angioplasty (PTA) with or without stenting. Angioplasty with or without stent has a success rate of approximately 70% to 90% [15] [28]-[30]. It allows control of systolic and diastolic blood pressure, a decrease in the number of anti-hypertensive medications and creatinine. However, the risks are not negligible: Thromboembolic events, pseudoaneurysms, traumatic arteriovenous fistulas, hematomas and nephrotoxicity of iodinated products used. Six of our patients underwent endovascular treatment, with successful results manifested by stabilization of graft function at a nadir of 15 mg/l of creatinine with well-controlled hypertension under dual therapy in 5 of them. Surgery also yields good results but with a high risk of surgical complications that can lead to graft loss and high mortality. It is indicated in case of angioplasty failure and recurrent lesions [31].

It is important to recognize renal graft artery stenosis in patients with hypertension after transplantation because it is associated with graft loss and high

mortality, and most importantly, because it is potentially treatable.

5. Limitations

Given the small sample size of our study, we were unable to conduct an analytical study identifying the different risk factors present in our patients. Moreover, some data were missing in our records such as the type of surgical anastomosis.

6. Conclusion

RTAS is a significant vascular complication of renal transplantation that predicts adverse outcomes for both the patient and the graft. Renal Doppler ultrasound represents a sensitive and non-invasive means to detect it. It should be suspected in the presence of refractory and/or progressive hypertension and/or acute renal failure. Angioplasty is an excellent treatment modality for stenosis in cases of refractory hypertension and allograft dysfunction. However, therapeutic strategies still warrant further investigation through prospective trials. Early diagnosis is therefore crucial to successfully restore graft function and prevent complications.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abreviations

- Renal transplant artery stenosis (RTAS)
- High blood pressure (HBP)
- Acute renal failure (ARF)

Appendix

Reference sheet:

Kidney recipient:

Name:

Sex: *female *Male:

Date of birth:

Medical history before the kidney tranplant:

- Diabetes: *Yes *No
- Hypertension: *Yes *No
- Dyslipidemia: *Yes *No
- Alcoholisme: *Yes *No
- Smoking: *Yes *No

Initial nephropathy:

*Indeterminate: *Diabetic: *Glomerular: *Vascular: *Other:

Kidney Donor:

Living donor: Donor in a state of brain death:

Date of birth

Body masse index:

Medical history:

- Diabetes: *Yes *No
- Hypertension: *Yes *No
- Smoking: *Yes *No
- Alcoholisme: *Yes *No
- Dyslipidemia: *Yes *No
- Vascular atheromatosis: *Yes *No

Transplantation date:

End-to-end anastomosis: End-to-side anastomosi:

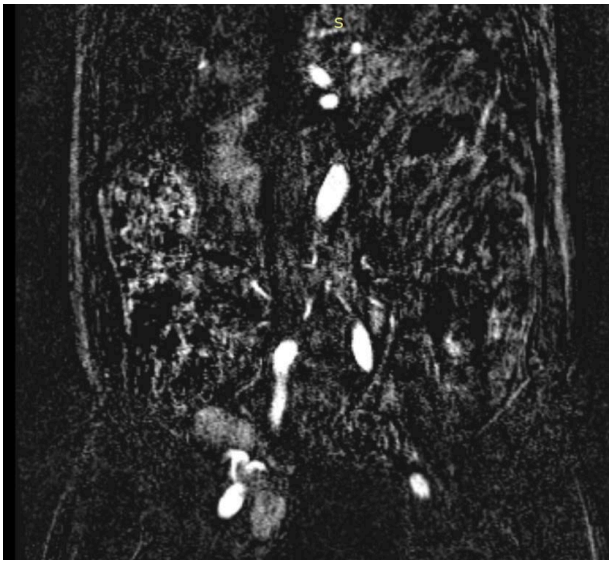
Surgical trauma: *Yes *No

Arterial plication *Yes *No

		Month 1	Month 3	Month 6	Year 1	Year 2	Year 4	Time period after tranplantation
Asymptomatic	Yes No							
Systolic blood pressure mmhg	>130 <130							
Diastolic blood pressure mmhg	> 80 <80							
Body mass index	In numbers							
Vascular murmur	Yes No							
Sodium and water retention	Yes No							
Cardiac decompensation	Yes No							
Blood creatinine	In numbers							
Filtration glomerular rate	In numbers							
Total cholesterol	Rate							
LDL cholesterol	Rate							
Triglycerides	Rate							
Proteinuria	Negative Positive							
Diuretic	Yes No							
Angiotensin-converting enzyme inhibitor	Yes No							
Angiotensin receptor antagonist	Yes No							
Calcium channel blocker	Yes No							
Beta-blocker	Yes No							
Cyclosporine	Yes No							
Tacrolimus	Yes No							
Mycophenolate mofetil	Yes No							

Continued

Azathioprine	Yes No
Doppler	Completed Carried out
MR Angiography	Completed Carried out
CT Angiography	Completed Carried out
Arteriography	Completed Carried out
Site of stenosis	Ostium Truncular Truncular ostium
Number of stenoses	One Two Multiples
Degree of stenosis	<70% >70%
Resistance index	<0.7 >0.7
Maximum systolic velocity cm/s	<240 240 - 300 >300
Dietary measures	Yes No
Angioplasty+stent	Yes No
Therapeutic abstention	Yes No
Surgery trauma	Yes No
Good evolution	Yes No
Restenosis	Yes No
Complication	Yes No
Graft loss	Yes No
Death	Yes No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