

## Artery Stenosis of the Renal Graft: Experience of a Center of Northeastern Brazil

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### ABSTRACT

**Background.** Transplant renal artery stenosis (TRAS), the most common vascular complication after transplant (Tx), leads to resistant hypertension, impaired renal function, and even loss of the graft. The purpose of the study was to investigate the prevalence and factors associated with TRAS in northeastern Brazil.

**Methods.** The study was conducted as a retrospective case-control study in a population of Tx recipients in a renal Tx center in northeastern Brazil. Demographic and clinical characteristics of the recipients and donors, data related to the surgery, laboratory data, and number of anti-hypertensive drugs were assessed. Statistical analysis was performed with the use of SPSS 17.0.

**Results.** A total of 494 of 529 recipients were assessed, of which 24 had TRAS. The prevalence of TRAS was 4.8%. Twelve patients (50%) were men with a mean age of  $46.7 \pm 13.5$  years. The mean time of diagnosis was 89.9 days after Tx. The risk factors associated with TRAS were number of anti-hypertensive drugs  $\geq 2$  (odds ratio, 17.0; confidence interval, 4.1 to 70.4;  $P = .001$ ) and grafting with 2 or more arteries (odds ratio, 8.9; confidence interval, 1.4 to 56.6;  $P = .021$ ). There was a significant reduction in mean systolic blood pressure ( $147.1 \pm 23.7$  to  $127.8 \pm 15.2$  mm Hg,  $P = .001$ ) and diastolic blood pressure ( $86.6 \pm 13.0$  to  $77.6 \pm 9.4$  mm Hg,  $P = .001$ ) after TRAS repair and in serum creatinine ( $2.8 \pm 2.4$  to  $1.9 \pm 1.8$  mg/dL,  $P = .04$ ).

**Conclusions.** Grafts with 2 or more arteries are associated with TRAS, as well as patients who use a higher number of anti-hypertensive drugs. TRAS repair was associated with improved blood pressure control and renal function.

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**T**RANSPLANT RENAL ARTERY STENOSIS (TRAS) is the most common vascular complication after transplantation (Tx), representing 75% of these complications. The incidence reported in the literature varies from 1% to 23%, being an important cause of hypertension, renal function deterioration, and/or graft loss [1–11].

TRAS can be diagnosed at any time after renal transplantation, but it usually becomes apparent between the third month and the second year after Tx, being of multifactorial origin [2,4,5]. Regarding the location of the renal transplant arterial anastomosis, the stenosis may be proximal as the result of atherosclerotic disease in the recipient, at the anastomosis, or distal, in the donor's renal artery. Regarding stenosis involvement, it may be diffuse or

multiple [11,12,31]. Early anastomosis stenosis is generally associated with trauma during surgery and/or postoperative fibrosis. The etiology of the distal TRAS is less clear but may be due to mechanical or immunological damage. Regardless of the stenosis location, early diagnosis is important to reduce morbidity and mortality [12].

The gold standard for the diagnosis of TRAS is still renal arteriography. Different, less invasive methods are available

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to confirm the diagnosis, such as Doppler ultrasonography (US), magnetic resonance imaging, computed tomography, or scintigraphy with captopril. The use of these methods depends in part on the center's experience. The graft Doppler US is the test of choice for recipients with graft dysfunction [13–15].

TRAS treatment modalities include surgical and interventional radiological treatments. Percutaneous transluminal angioplasty (PTA), with or without stenting, is the main therapy because it is less invasive, with a reduced number of severe complications and little chance of failure. An adequate clinical response to PTA of renal artery stenosis is the return of renal function and blood pressure control [4,16].

Technical success and complication rates of PTA of renal artery stenosis are 60% to 94% and 0% to 8.3%, respectively, with graft loss rarely occurring [17]. Pillot et al [4] found 100% efficacy in TRAS repair with the endovascular procedure. Surgical treatment is reserved for patients with anastomosis stenosis or severe distal artery stenosis that is inaccessible through PTA [5,17].

Consequently, because this is the most common vascular complication after renal transplantation and because there are few available data in Brazil, the aim of this study was to identify the prevalence and factors associated with TRAS in a referral center for kidney transplantation in northeastern Brazil.

## METHODS

All patients submitted to renal transplantation at Hospital Universitário Walter Cantídio, Fortaleza, Ceará, Brazil, from January 2008 to March 2014 were included in the study, whereas those lost to follow-up because of being transferred to another renal transplant unit were excluded. A retrospective, case-control study was carried out with patients with suspected TRAS at the Doppler US. A control group of patients submitted to renal Tx who did not have TRAS was chosen in this transplant center in the same study period, being matched according to the type of donor and age/sex of the recipient and donor, with 2 control patients for each TRAS case.

The criteria used at the Doppler US to diagnose TRAS were peak systolic velocity (PSV) >250 cm/s and/or *parvus-tardus* waveform (acceleration time >0.07 seconds, acceleration index <3 m/s<sup>2</sup>) and intrarenal artery pattern represented by the Pourcelot resistive index (RI; normal range, 0.5 to 0.7), which is the result of dividing the difference at the maximum PSV and minimum diastolic velocity (MDV) by the maximum PSV ( $RI = PSV - MDV / PSV$ ) was used as an additional parameter. All patients with suspected TRAS at Doppler US underwent renal graft arteriography, with TRAS being confirmed when there was a greater narrowing of the arterial lumen >50%, a significant stenosis diameter [12,13].

We analyzed the following recipient variables: age at transplant; sex, weight, and height; body mass index (BMI; kg/m<sup>2</sup>); cause of primary kidney disease; systemic arterial hypertension (SAH) and diabetes (diabetes mellitus, DM); serology for cytomegalovirus; and serum levels of calcium, phosphorus, uric acid, cholesterol, LDL-cholesterol, and triglyceride levels at the diagnosis of TRAS. We also assessed variables such as the type of donor (deceased or living), age, sex, renal function at the time of organ donation

(creatinine), cause of death if the donor was deceased, and cold ischemia time.

The anastomosis site (common iliac artery, external iliac artery), number of graft arteries, lateralization of the kidney used in surgery (right or left), and presence of technical problems during surgery were evaluated. Regarding the post-transplant evolution, the following data were evaluated: induction therapy (anti-thymocyte rabbit immunoglobulin; Thymoglobulin or Basiliximab), initial immunosuppression (with or without prednisone), presence of delayed graft function (DGF), acute rejection diagnosis before stenosis, and diagnosis of cytomegalovirus infection.

Data directly related to TRAS, such as post-Tx time of diagnosis, with early TRAS being defined as that diagnosed within less than 90 days and late TRAS after 90 days or more, were also analyzed, in addition to serum creatinine levels, number of anti-hypertensive used, and mean systolic and diastolic blood pressure levels at TRAS diagnosis. All patients underwent Doppler US, and those suggestive of TRAS were compared with the gold standard, that is, arteriography. The comparison of the mean systolic and diastolic factors associated with stenosis of the renal graft artery blood pressure and creatinine levels, as well as the number of anti-hypertensive drugs before and after TRAS repair, was also performed. It was also assessed whether there was graft loss or death related to TRAS; clinical and laboratory data of patients with and without TRAS were taken to investigate the factors associated with stenosis development.

## Statistical Analysis

At statistical analysis, continuous variables were expressed as mean ± standard deviation and categorical variables as percentage or frequency. The comparison of continuous and categorical variables between the 2 patient groups (control and study) was carried out with the use of the Student *t* test (for continuous variables) and Fisher exact test (for categorical variables), respectively. The correlation analysis between TRAS and possible risk factors was performed through Fisher exact test,  $\chi^2$  test, and Pearson correlation. We calculated the adjusted measures of association (odds ratios, OR) with 95% confidence intervals (CI). Univariate and multivariate analyses were performed. In the univariate analysis, the variables that reached a probability value of <15% were included in a multivariate logistic regression model. Descriptive values <5% ( $P < .05$ ) were considered statistically significant. Statistical analysis was performed with the use of SPSS 17.0 for Windows (SPSS Inc., Chicago, Ill, United States).

## RESULTS

A total of 529 patients submitted to renal transplantation during the study period were assessed. Of these, 35 were excluded because of being transferred to other transplant units. All patients were evaluated for suspected stenosis of the renal artery graft by Doppler US. Thirty-seven patients were selected for having US Doppler results suggestive of TRAS, and 24 of these had TRAS confirmed by arteriography, as shown in Fig 1.

The prevalence of TRAS was 4.8% (24 patients), of which 23 had a deceased donor. Twelve patients (50%) were men with a mean age of  $46.7 \pm 13.5$  years (range, 17 to 78 years) and mean BMI of  $23.3 \pm 3.6$  kg/m<sup>2</sup> (range, 16.3 to 31.1 kg/m<sup>2</sup>). The cause of chronic kidney disease was SAH

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