Ultrasound features of kidney transplants and their use in assessing rejection

Abstract

Nowadays, kidney transplants are the surgical procedure of choice for patients with chronic kidney disease (CKD) because it increases life expectancy and health related quality of life. Given that the need for transplants has increased worldwide, but organ donation has not, it is vital that organ rejection be prevented. Follow up through ultrasound imaging has been established as a vital post-surgical tool. Nevertheless, their findings, aside from pathological ones, have yet to be linked with organ rejection.

Objective: To determine morphological, pathological and arterial characteristics of transplanted kidneys through gray scale and color Doppler ultrasonography and to associate factors predicting transplant rejection.

Methods: This is an analytical, observational, transversal and retrospective study of 88 patients that underwent kidney transplant during 2012 to 2016 in a second-level hospital. Through the collection and analysis of data obtained from medical records, we sought to establish which factors might predict renal graft rejection.

Results: Yearly, transplant procedures averaged 32.4; majority of recipients were male (58%). Most transplants came from living donors (93.2%). Complications were present in 12.5% and renal artery stenosis and lymphoceles were the most common.

Kidney rejection occurred in 9 patients. Gender, renal artery resistance index, shape, diameter, cortical echogenicity, corticomedullary differentiation and complications were associated with rejection.

Conclusion: Male gender, high renal artery resistance index, lobulated kidneys, changes in diameter and cortical echogenicity, presence of corticomedullary differentiation and renal complications are associated with kidney transplant rejection. The relationship of non-pathological findings requires further study to determine whether these are independent predictors of rejection.

Keywords: chronic kidney disease, kidney transplantation, rejection, ultrasonography, predictors

Introduction

Kidney transplantation has extended and improved the quality of life for patients with kidney disease. Worldwide, the need for transplants has risen, as shown by a 35.6% increase in waiting lists.¹ The 2016 estimates of the Mexican National Transplant Center (Centro Nacional de Trasplantes, CENETRA) determined that 61% of patients in the national transplant registry were in need of a kidney transplant, despite 43,429 transplant procedures being performed that same year.² Nowadays, kidney transplants are the surgical procedure of choice for patients with chronic kidney disease (CKD) because it not only increases life expectancy, but it also entails a mean in which patients can reinstate their activities, improving their health related quality of life.³,⁴ In Mexico, the most common causes of CKD include diabetes (48.5%), hypertension (19%), and chronic glomerulopathies (12.7%).³

Given that organ donations have yet to fulfill the increasing need for kidney transplants, it is vital that organ rejection be prevented. A thorough postsurgical monitoring must be employed in order to give an early and accurate diagnosis of complications.⁵ Transplant complications are commonly attributed to three major causes: infectious, surgical (urological, perinephric collections, vascular), or immunological reasons. The first tests that should be performed in patients with decreasing renal function are a two-dimensional and Doppler ultrasound, since they constitute a non-invasive, highly sensitive diagnostic tool.⁶ Since transplant dysfunction is likely to be produced by vascular complications (frequently by renal artery stenosis), gray scale and color Doppler ultrasound imaging are a great choice for diagnosis, since they evaluate kidney complications as well as structural and vascular anatomy.⁷ This radiological modality contributes in three major aspects: appropriate complication treatment, transplant preservation and health related quality of life increase.⁸ That’s why it has become a necessary instrument for patient follow up. Multiple studies have proven ultrasonography’s (US) primary role in kidney transplant care, yet none have linked findings (other than complications) with organ rejection.⁹-¹⁲ Thus, the present study sought to assess the morphological, arterial and pathological characteristics of transplanted kidneys through gray scale and color Doppler ultrasonography and to associate factors predicting transplant rejection.

Material and methods

The present work is an analytical, observational, transversal and retrospective study of patients that underwent kidney transplant during
2012 to 2016 in the Regional General Hospital No.1 of the Mexican Institute of Social Security (Instituto Mexicano del Seguro Social, IMSS). Enrollment criteria included the following: first-time kidney recipients, absence of surgical complications and post-surgical follow up through grey scale and Doppler ultrasounds. Patients that did not comply with inclusion criteria (history of ≥2 kidney transplants, presence of surgical complications) nor had incomplete medical records were excluded. All procedures performed in this study were in accordance with the ethical standards of the Helsinki declaration, Mexico’s General Health Law, and their later amendments, as well as the local institutional research committee guidelines. Written consent was waived given that this is a retrospective study. With previous authorization by the Local Research Committee and hospital director, we reviewed each patient’s file and collected the following data: age, gender, type of donor, transplanted kidney characteristics (anatomical position, diameter, cortical echogenicity, corticomedullary differentiation, complications, and renal artery resistive index) obtained via grey scale and Doppler US, and the absence/presence of renal rejection (and whether it was acute or chronic). Ultrasounds were performed using a Philips (SONOS 45000 model) equipment, in conjunction with a 5 MHz linear transducer and a 2.5MHz convex transducer, using real time tracking in grey scale and color Doppler. Ultrasound findings were previously established by a radiologist.

Statistical analysis
A descriptive analysis was performed by calculating the means and standard deviations for quantitative variables and absolute frequencies and percentages for qualitative variables. Additionally, contingency tables were created in order to study the association between variables and organ rejection using the Chi-squared test. The level of significance was set at 0.05. All information was input in a data file and analyzed with the statistical package IBM® SPSS version 22.0.

Results
A total of 159 patients underwent kidney transplant during the years 2012-2016. During this time frame, there was a great variation of transplants performed per year (29 in 2012, 13 in 2013, 74 in 2014, 29 in 2015 and 14 in 2016); it averaged 32.4 yearly transplants. Male patients were more prevalent (58%) than women (42%). Patients aged 36-45 years were the most likely age group to receive a transplant. The rest of patient distribution can be seen in Table 1. A total of 71 patients had incomplete medical records; therefore, only 88 patients were included in the study.

Table 1 Patient distribution by age

| Age (years) | Number of patients (percentage) |
|-------------|---------------------------------|
| 5-Jan       | 2 (1.3)                         |
| 10-Jun      | 1 (0.6)                         |
| 15-Nov      | 9 (5.7)                         |
| 16-25       | 28 (17.6)                       |
| 26-35       | 34 (21.4)                       |
| 36-45       | 47 (29.6)                       |
| 46-55       | 30 (18.9)                       |
| 56-65       | 8 (5.0)                         |
| Total       | 159 (100)                       |

Surgical and transplant characteristics
Living donors were the most common (n=82, 93.2%), while deceased donors were unusual (n=6, 6.8%). Most transplants were placed in the right iliac fossa (n=86, 97.7%) and only two were placed in the left iliac fossa. Morphologically, transplanted kidneys were classified in one of three categories: oval (n=65, 73.8%), round (n=13, 14.7), and multi lobulated (n=10, 11.3%). Most transplants retained their pre-surgical diameter (n=76, 86.3%), 8 (7.9%) decreased and 4 (4.5%) increased their size. Cortical echogenicity was preserved in 64 kidneys (72.7%), while it increased in 15 patients (17%), and decreased in 9 patients (10.2%). Corticomedullary differentiation was present in 78 patients (88.6%). A high renal artery resistance index was found in 8 patients (9.1%).

Transplant outcomes
Complications were recorded in 11 patients (12.5%); lymphocele and renal arty stenosis was the most common, whereas pseudoaneurysms and arteriovenous fistula was the least common. The frequency of these and other complications can be seen in Table 2. Kidney rejection was present in 9 patients (10.2%). Statistically significant findings are in bold.

Variable association with kidney rejection
In order to find possible link between variables and graft rejection, data was evaluated in different contingency tables. Table 2 demonstrates the univariate analysis of predictors of transplant rejection. Clinical, morphological and pathological characteristics (specifically gender, resistance index, shape, diameter, cortical echogenicity, corticomedullary differentiation and complications) were significantly associated with rejection (P <0.05). Age and type of donor were proven to be uncorrelated with rejection.

Table 2 Univariate predictors for kidney transplant rejection

| Kidney transplant rejection | Yes n (%) | No n (%) | P-value |
|-----------------------------|-----------|----------|---------|
| Age (years)                 |           |          |         |
| 1-10                        | 1 (1.1)   | 3 (3.4)  | 0.757   |
| 11-15                       | 0          | 6 (6.8)  |         |
| 16-25                       | 2 (2.3)   | 8 (9.1)  |         |
| 26-35                       | 3 (3.4)   | 15 (17)  |         |
| 36-45                       | 2 (2.3)   | 25 (28.1)|         |
| 46-55                       | 1 (1.1)   | 19 (21.6)|         |
| 56-65                       | 0          | 3 (3.4)  |         |
| Gender                      | <0.05     |          |         |
| Female                      | 2 (2.3)   | 34 (38.7)|         |
| Male                        | 7 (8)     | 45 (51.1)|         |
| Type of donor               | 0.59      |          |         |
| Live                        | 8 (9.1)   | 74 (84.1)|         |
| Cadaver                     | 1 (1.1)   | 5 (5.7)  |         |
| Resistance index            | <0.05     |          |         |
| Normal                      | 1 (1.1)   | 79 (89.8)|         |
| Abnormal                    | 8 (9.1)   | 0        |         |
Table Continued...

| Kidney transplant shape | Kidney transplant rejection |
|-------------------------|-----------------------------|
| Oval                    | 0.05                        |
| Round                   | 11 (12.5)                   |
| Multi lobulated         | 3 (3.4)                     |
| Kidney diameter         | <0.05                       |
| Preserved               | 76 (86.4)                   |
| Increased               | 11 (12.5)                   |
| Decreased               | 5 (5.7)                     |
| Cortical echogenicity   | <0.05                       |
| Preserved               | 63                          |
| Increased               | 11 (12.5)                   |
| Decreased               | 5 (5.7)                     |
| Corticomedullary diffusion | <0.05                     |
| Present                 | 78 (88.6)                   |
| Not present             | 1 (1.1)                     |
| Complications           | <0.05                       |
| Pseudo aneurism         | 0                           |
| Arteriovenous fistula   | 0                           |
| Arterial stenosis       | 0                           |
| Urethral stenosis       | 1 (1.1)                     |
| Lymphocele              | 1 (1.1)                     |
| None                    | 77 (87.5)                   |

**Discussion**

Recently, the need for kidney transplants has skyrocketed in Mexico and Latin America, mainly due to the increased prevalence of chronic and degenerative diseases. \(^{1-10}\) CENATRA’s records show a rise of 11% in kidney transplants from 2012 to 2017, \(^{17}\) yet the Regional General Hospital No. 1 in Tijuana had a 12% decrease in transplants during this same time period. Gender wise, the study yielded comparable results with what was previously described, having 1:4:1 men to women ratio while Gómez and his group reported a 1.2:1 ratio. \(^{18}\) In Latin America, in 2013, 70.4% of kidneys came from deceased donors. \(^{16}\) More recently, 2018 CENATRA estimates state that 33% of kidney grafts originated from dead patients. \(^{11}\) Both outcomes contrast sharply with the present study, since majority of kidneys came from living (related) donors, and only 6.8% were attributed to cadaveric donors. \(^{19}\) As per usual, 98.1% of kidneys were placed in the right iliac fossa, since this placement allows easier dissection for vascular anastomosis. \(^{14}\) While complication rates were previously estimated at 59.7%, this study found a 12.5% rate. \(^{11}\) As stated before, this may be because, since transplants are somewhat rare procedures in Mexico, their prevention has become imperative. Vascular and perinephric liquid collections were the most frequent (3.4% prevalence for both types of complications). Its frequency differed from a prior study by Quevedo and cols. which found that lymphoceles and renal artery stenosis were present in 9.1% and 1.3% respectively in their cohort. \(^{11}\) Kidney rejection (n=9, 10.2%) was less prevalent than other Mexican studies, which varies from 11% to 18.2%. \(^{11,18}\) Yet, it was more frequent than what is estimated in the United States (3% and 4% in living and deceased donors correspondingly, within a year after transplant). \(^{30}\) As Palomar and her group formerly stated, donor age and type did not influence transplant outcomes significantly. \(^{1}\) As expected, reduced cortical echogenicity and presence of corticomedullary differentiation were linked with renal rejection, since both can be seen in patients with diminished renal function. \(^{21}\) Interestingly, different cortical echogenicity changes were also found in patients with rejection. A high renal artery resistance index was associated with transplant complications and rejections. This comes as no surprise, since it has been recognized as a, albeit nonspecific, parameter of renal dysfunction. \(^{9,22}\) No studies correlating kidney shape or diameter with organ rejection were found to compare this study’s findings. Finally, the presence of complications was established as a preceding factor to renal rejection. Altogether, the analyzed variables reveal new parameters that physicians, especially radiologists, should take into consideration during patient follow up in order to avoid transplant rejection in a timely manner. We suggest that these factors be revised in future studies in order to corroborate or reject their statistical significance.

**Conclusion**

This study has described the clinical, arterial and pathological features in kidney transplant patients, suggesting that all of them can be predictors for graft rejection. Gender, high renal artery resistance index, lobulated kidneys, changes in diameter and cortical echogenicity, presence of corticomedullary differentiation and renal complications are associated with kidney rejection. This study supports the fact that ultrasound imaging is a key method of postsurgical monitoring in kidney transplantation patients.

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None.

**Conflict of interest**

The author declares there is no conflict of interest.

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