

DIAGNOSTIC ACCURACY OF COLOR DOPPLER SONOGRAPHY IN EVALUATION OF RENAL TRANSPLANT REJECTION

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PJR January - March 2017; 27(1): 24-29

ABSTRACT

BACKGROUND: Despite the introduction of new immunosuppressive agents, the incidence of allograft rejection after renal transplantation is still high. Color Doppler Sonography (CDS) is the imaging technique which is safe for the evaluation of a renal allograft. It provides rapid recovery room examination. If warranted, the patient can immediately return to surgery, be referred for testing, or undergo other interventional procedures. **OBJECTIVE:** It is aim of present study to determine diagnostic accuracy of color doppler sonography in acute renal transplant rejection with support of histopathological findings as gold standard. **METHODS:** Total 88 patients of either gender with age 20 years or more and suspected of renal transplant rejection within one week to one month after transplantation were included in this study. Color doppler sonography was performed and abdominal, serial longitudinal and transverse images were assessed. Resistive index >0.8 was considered graft rejection. Sensitivity, specificity, PPV, NPP, and diagnostic accuracy were calculated taking histopathology as gold standard. The data were analyzed using SPSS and p values of >0.05 were considered as significant. **RESULTS:** Male patients were 51.1% and female were 48.9%. Mean age was 36.5 ± 10 years. Acute renal transplant rejection was diagnosed in 46.5% patients using color doppler sonography and on histopathology it was observed in 55.6% patients. The sensitivity of CDS was 79.2%, while we observed 95% specificity and diagnostic accuracy was found 86.3%. **CONCLUSION:** We propose that color doppler sonography (CDS) is an accurate test for diagnosis of acute renal transplant rejection. It is non-invasive and helps to avoid unnecessary surgeries in such patients. **Key words:** Diagnostic Accuracy, Color Doppler Sonography, Renal Transplant Rejection, Histopathology

Introduction

Kidney transplant is the treatment of choice for patients with end-stage renal disease. There are approximately 12 major centers (0.08) per million populations in Pakistan¹⁻² performing an estimated 400 transplants every year. Although there are many immuno suppressive agents used in clinical practice, but incidence

of allograft rejection after renal transplantation still around 24%.³

Ultrasound is the principal imaging modality for the evaluation of a renal allograft; it is a safe imaging technique to assess the structure of allograft as well as its perfusion.⁴ Color doppler technology permits

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Submitted 5 October 2016, Accepted 30 November 2016

rapid assessment of the entire renal arterial perfusion and venous patency. It also allows visualization of the main renal artery with its anterior and posterior divisions, segmental, interlobar and arcuate arteries and corresponding veins within the graft. The main renal artery shows normally biphasic waveform with flow velocity ranging 180-200 cm/sec.⁵ Resistance index (RI) is used as a measurement of resistance to arterial flow within the renal vascular bed. Generally, RI value of 0.7 to 0.8 is considered normal.⁶⁻⁷ RI value of > 0.8 is an indicator of transplant dysfunction and in previous studies its sensitivity and specificity was found up to 90% and 76% respectively.⁸ This study is designed to determine the role of resistive index (RI) on color doppler sonography to aid in diagnosis of transplant rejection and limit the role of invasive procedure like biopsy. Significant results may therefore provide a cost effective, non invasive and easily available method without radiation burden.

Material & Methods

This cross sectional study was conducted in Sindh Institute of Urology and Transplantation on patients who underwent living donor renal transplantation between 1st February and 30th September 2011. 88 patients of both genders with age 20 years or above were included in this study. Included patients were suspected for acute transplant rejection and had one or more of following sign and symptoms; blood pressure $>140/90$ mmHg, serum creatinine level $>20\%$ above base line, serum urea $>20\%$ above base line, bruit over the graft site, and urine output <1000 ml / 24 hours. Color doppler Sonography was performed on Toshiba Aplio 5.0 and GE Voluson 730 PRO V using 3.75 MHz convex probe per-abdominally, serial longitudinal and transverse images and doppler parameters were obtained and assessed for any change or abnormal findings. All patients with previous abnormal biochemical findings, who already underwent some interventional procedure and have known cause of transplant dysfunction were excluded from this study.

The resistance index (RI) 0.7 to 0.8 was considered as normal RI which was further evaluated and correlated with histopathological findings. RI of >0.8

was considered as graft rejection. We compared findings of color doppler sonography and resistance index values with histopathological findings suggestive of acute transplant rejection.

Data compilation and analysis was performed on SPSS version 21. Descriptive statistics were calculated. Quantitative variables were expressed as mean \pm SD and qualitative variables were presented in terms of frequency and percentages. Sensitivity, specificity, positive predictive value (PPV), negative predictive values (NPV), diagnostic accuracy of color doppler sonography were calculated taking histopathological findings as gold standard. (Fig.1 & 2).

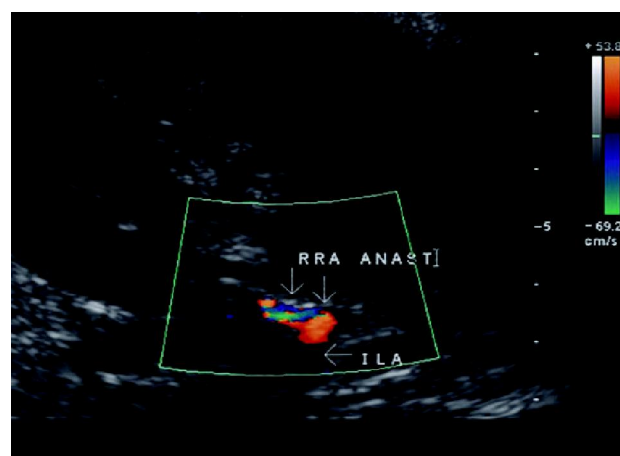


Figure 1: Renal artery stenosis. Color doppler image of the transplant renal artery near anastomosis with the iliac artery (ILA) shows aliasing and heterogeneous signal compatible with the turbulent, high-velocity blood flow at the site of stenosis.

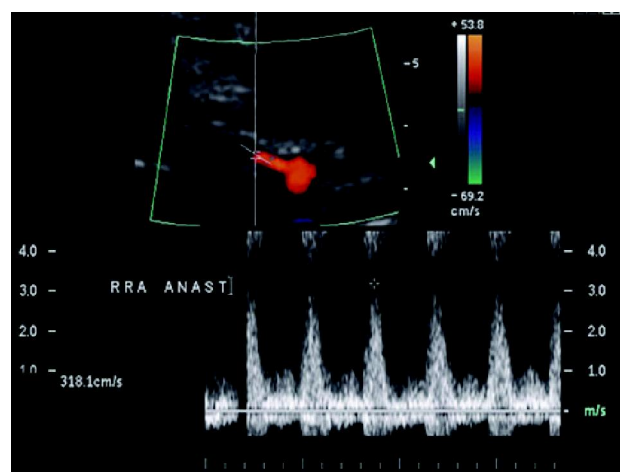
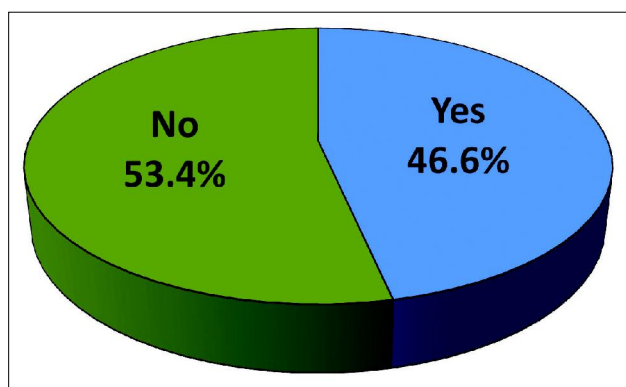


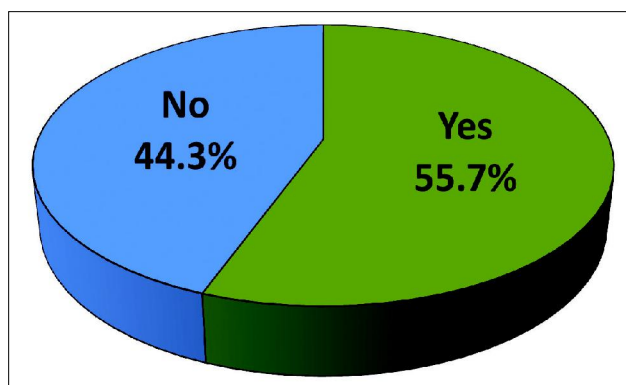
Figure 2: Renal artery stenosis. Color doppler image, Peak systolic velocity (PSV) of the renal artery in the region of anastomosis.

Results

In this study, male were 51.1% and female were 48.9% and male to female ratio was 1.01:1. The mean age was 36.5 ± 10 years. Age of 41(46.5%) patients was ≤ 40 years and rest of the patients were aged >40 year. Using color Doppler ultrasound, renal transplant rejection was diagnosed in 41 patients where as it was not diagnosed in 47 patients (Graph-1). In histopathology rejection was observed in 49 patients and was not observed in 39 patients (Graph-2). The frequency of distribution of allograft rejection is shown in (Tab. 1).



Graph 1: Percentage of renal transplant rejection in color Doppler ultrasound



Graph 2: Percentage of renal transplant rejection in Histopathology

n=88		Frequency	%
Color Doppler U/S Findings	Reject	41	46.6%
	Not Reject	47	53.4%
Histopathology Findings	Reject	49	55.7%
	Not Reject	39	44.3%

Table 1: Frequency distribution of renal transplant rejection between two procedures

In both procedures renal transplantation rejection was observed in 38 patients (True positive, correctly diagnosed) and it was also not rejected in 38 patients (True negative, correctly diagnosed) in both procedures. The overall sensitivity of color Doppler ultrasound was 79.2%, specificity 95% and diagnostic accuracy was 86.3% (Tab. 2).

n=88		Histopathological Findings		Total
		Reject	Not Reject	
Color Doppler U/S Findings	Reject	38 (79.2%)*	2	40
	Not Reject	10	38 (95.0%)**	
Total		48	40	88

*Sensitivity

PPV= 95.0%

**Specificity

NPP=79.2%

Diagnostic accuracy=86.3%

Table 2: Diagnostic accuracy of color Doppler ultrasound for detection of renal transplant rejection.

Effect modifiers i.e. gender and age were stratified. Post stratification analysis based on male gender showed that sensitivity of color doppler sonography was 84%, specificity was 95.2% and diagnostic accuracy was 87.2%. Among females, sensitivity was 73.9%, specificity was 94.7% and diagnostic accuracy was 83.3% (Tab. 3).

(n=88)	Male	Female
Sensitivity	84.0%	73.9%
Specificity	95.2%	94.7%
Positive Predictive Value	95.5%	94.4%
Negative Predictive Value	83.3%	75.0%
Diagnostic Accuracy	87.2%	83.3%

Table 3: Diagnostic accuracy of color Doppler ultrasound for detection of renal transplantation rejection according to gender.

Post stratification results of age ≤ 40 years showed that sensitivity of color doppler sonography among these patients was 80.8%, specificity was 95.2%, and diagnostic accuracy was 87.2%. Among patients whose age was ≥ 40 years the sensitivity was 77.3%, specificity was 94.7% and diagnostic accuracy was 85.3% (Tab. 4).

Discussion

Kidney transplantation is therapy of choice in end stage renal disease (ESRD) which results in improved survival and quality of life. Advancements in surgical

(n=88)	≤ 40 years	≥ 40 years
Sensitivity	80.8%	77.3%
Specificity	95.2%	94.7%
Positive Predictive Value	95.5%	94.4%
Negative Predictive Value	80.0%	78.3%
Diagnostic Accuracy	87.2%	85.3%

Table 4: Diagnostic accuracy of color Doppler ultrasound for detection of renal transplant rejection according to age.

techniques and immunosuppression therapy provided improved transplant survival. In United Kingdom, 5 years renal graft survival rate is 83% for deceased donor organs and 89% of living donor organs.⁹ Despite the introduction of new immunosuppressive agents, the incidence of allograft rejection after transplantation still ranges around 24%.³ For proper therapy early diagnosis plays a vital role that impact patient's life. Sonography and serum creatinine screening are commonly used to assess the function and conditions of renal transplant. Kidney biopsy provides histological information consider as gold standard in diagnosis of transplant dysfunction and acute transplant rejection. But it is an invasive, contraindicated in coagulopathy and can result in complications such a perinephric hematoma, vascular aneurysm or fistula which eventually lead to or worsen renal failure.¹⁰ Color doppler sonography (CDS) provides information of renal morphology such as urinary tract obstruction or perinephric collection as well as about graft vasculature, blood flow and hemodynamic state. It is useful in early diagnosis of kidney allograft vascular thrombosis and RAS.¹¹⁻¹⁵ It is reliable noninvasive tool readily available for identifying patients who may benefit from kidney allograft revascularization and for assessing the effectiveness of the procedure.¹⁶⁻¹⁹ Hence, patients with renal vessels thrombosis and RAS could be diagnosed noninvasively and timely.²⁰⁻²³ Doppler parameter measurement at inter-lobar artery include; PSV, EDV, PI and RI which reflect the changes in blood flow and correlate with certain histological type. Resistive Index (RI) assess the hemodynamic state like renal vascular resistance which has been vastly used to assess renal allograft dysfunction.^{9,10,11,24} RI > 0.8, is an indicator of transplant dysfunction.²⁴ In previous studies the sensitivity and specificity of RI reached 90% and 76% respectively, in diagnosis of renal transplant dysfunction.⁸

This study aims to investigate correlation between CDS and acute rejection of renal allograft in particular clinical setting and to define RI cut off in this diagnosis. Some researcher did not support the correlation between doppler parameters and function of trans-planted kidney,²⁵ however, there are many studies which show acceptable correlation between doppler parameters and transplant function. Kahrman et al showed that measurement of RI in the first post-transplant week can predict one month and one year function of non-complicated renal allograft.¹¹ Radar-marchar et al reported RI the best predictor for kidney transplant failure and recipient's death. In their prospective study they reported sensitivity of 56% and specificity of 96% in measurement of RI = 0.80 in renal allograft 3 months post-transplantation.²⁴ Mc Arther et al in retrospective study reported a significant correlation between RI and PI levels measured in first week to 3 month post transplantation and renal allograft function 1 year after transplantation. He argued that patients with PI >1.49 and RI >0.74 measured between first week and 3 months post transplantation are at high risk of graft dysfunction first year after transplantation.⁹

In current study it was found that overall diagnostic accuracy color doppler sonography was 86.3%. As of age stratification results showed that diagnostic accuracy of color doppler sonography was 87.2% in age <40 years. On gender stratification it was found that male patients had diagnostic accuracy 87.2%. We used specific clinical setting and time frame in early post transplantation period, thereby increasing the prognostic relevance and providing more accurate relationship between RI and transplant rejection.


The strength of this study is stratified analysis. Most of the other studies have reported overall diagnostic accuracy. There are also some limitations in this study. First, in this study diagnosis of renal graft rejection based on single reading but it may require serial ultrasound. Though SIUT is the largest public sector hospital in Pakistan for renal diseases, however, the results of this study may not be generalized. For generalization multicenter study should be done in order to get more valid results that can be generalized to population.

Conclusion

The results of the study concluded that the color doppler sonography is sensitive, specific and accurate test in the diagnosis of acute transplant rejection. This procedure is non-invasive and helps to avoid unnecessary surgeries in patients underwent renal transplantation.

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