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The value of Doppler ultrasound in predicting delayed graft function occurrence after kidney transplantation

Grzegorz Mocny[1*], Piotr Bachul[2*], Ea-sle Chang[3], Piotr Kulig[1]

[1]1st Department of General, Oncological and Gastroenterological Surgery, Jagiellonian University Medical College
ul. Kopernika 40, 31-501 Kraków, Poland
[2]Department of Anatomy, Jagiellonian University Medical College
ul. Kopernika 12, 31-034 Kraków, Poland
[3]Saint Louis University Hospital, Saint Louis, MO, USA
*These authors contributed equally to this work.

Corresponding author: Piotr Bachul, Department of Anatomy, Jagiellonian University Medical College
ul. Kopernika 12, 31-034 Kraków
Phone/fax: +48 12 422 95 11; E-mail: piotrbachul@gmail.com

Abstract: The aim of this study was to assess the predictive value of blood flow velocity and vascular resistance measured by Doppler ultrasound in terms of pulsatility index (PI) and resistive index (RI) respectively, in the occurrence of delayed graft function (DGF) after kidney transplantation.
This prospective study enrolled kidney transplant recipients operated from January 2005 to April 2009 in the 1st Department of General, Oncological and Gastroenterological Surgery, Jagiellonian University Medical College, Kraków, Poland. The medical records of 53 kidney transplant recipients from deceased donors were reviewed. PI and RI values of the graft arcuate artery were calculated immediately after blood flow restoration and on the 1st, 2nd, 4th and 8th post-operative day.
DGF was observed in 20 patients (37.7%), while 33 patients (62.3%) had immediate restoration of the kidney function. The mean intraoperative values of RI and PI from patients with DGF were significantly higher in comparison to patients without DGF (0.9 vs. 0.74, $p < 0.001$; 1.76 vs. 1.54, $p = 0.019$, respectively). Post-operatively, the RI and PI values remained stable and significantly higher in DGF group. The highest sensitivity of RI to predict DGF occurrence was observed intraoperatively and on the first postoperative day, with values of 77.8% and 72.2%, respectively. The risk of DGF occurrence with intraoperative RI value ≥0.9 increased by 13-fold, and with intraoperative PI value ≥1.9 by 12-fold. This increase was even more prominent during the first post-operative day with RI value ≥0.9 or PI value ≥1.9 with 19-fold increase in the risk of DGF occurrence.

According to our study, the utilization of Doppler ultrasound with measurement of hemodynamic parameters (PI, RI), play a crucial role in predicting the outcomes of kidney transplantation.

Key words: kidney transplantation, renal graft, delayed graft function (DGF), Doppler ultrasonography, resistive index (RI), pulsatility index (PI).

Introduction

Since the 1970s when Doppler ultrasound was introduced for organ imaging and measuring hemodynamic parameters i.e. blood flow velocity and direction, accurate and quantitative analysis of decreasing blood flow in kidney graft microcirculation and the rejection rate has been possible. Objective methods for the assessment were introduced later on, and were based on calculating the Gosling pulsatility index (PI) and Pourcelot resistive index (RI). These two parameters enabled quantitative reflection of the velocity flow and vascular renal resistance, respectively, also during comparative assessment at subsequent follow-up visits [1, 2].

Delayed graft function (DGF) is a state of acute renal graft failure, which manifests with postoperative oliguria, and increased biochemical markers, such as creatinine or urea. It is defined as a number of hemodialysis needed to restore kidney function, or a time period between the transplantation and final dialysis and has been found to be correlated with increased risk of acute transplant rejection and shortening of graft survival time [3–6]. The prevalence of DGF after renal transplantation from a deceased donor varies from 20% to 30%, however some studies report a frequency of DGF to be as high as 50% [6–10]. According to the data from the Organ Procurement and Transplantation Network (USA), approximately 50% of transplanted kidneys sufficiently recover its function on the 10th post-operative day. Between the 10th and 20th post-transplantation day, kidney function returns to normal in 33% of patients with DGF, while 10-15% of renal grafts regains its function after the 20th postoperative day.

Methods

This was an observational prospective study of allogenic renal transplant recipients performed from January 2005 to April 2009 at the 1st Department of General, Oncological and Gastroenterological Surgery, Jagiellonian University Medical College, Krakow. The study group comprised of 53 graft recipients with end-stage renal disease. Characteristics of the study group is presented in Table 1.

Blood flow was analyzed by Doppler ultrasound (Siemens Logic 7.0) in order to detect vessel abnormalities of the transplanted kidney intraoperatively and on 1st, 2nd, 4th and 8th post-operative day (Fig. 1–4). RI and PI values were automatically

Table 1. Characteristics of the study group (53 recipients of the kidney graft).

		Number of the kidney recipients	%
Age (years)	≤30 years	9	1.0
	31–40 years	12	22.6
	41–50 years	15	28.3
	≥50 years	17	32.1
Sex	men	16	30.2
	women	37	69.8
DGF occurrence	with DGF	20	37.7
	without DGF	33	62.3

calculated by the computer software, which allowed to present both parameters in an objective and comparable manner. For objectivity of the study, the Doppler ultrasound was performed by single experienced ultrasonographer.

Potassium, urea and creatinine serum concentrations were measured and used as biochemical markers of restoration of kidney graft function. In the following study, delayed graft function was defined as the need for hemodialysis according to post-transplant oliguria and elevated biochemical markers in kidney graft recipients.

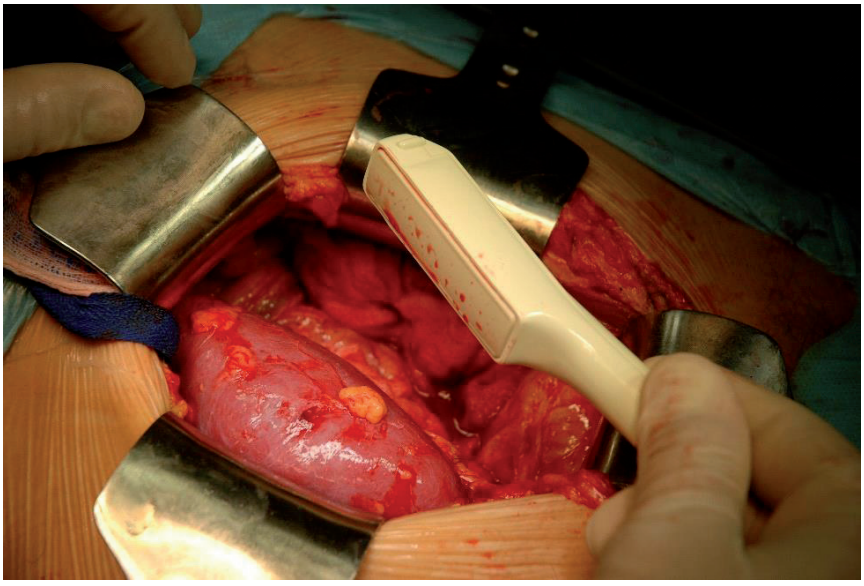

Fig. 1. Doppler ultrasound examination — intraoperative view.

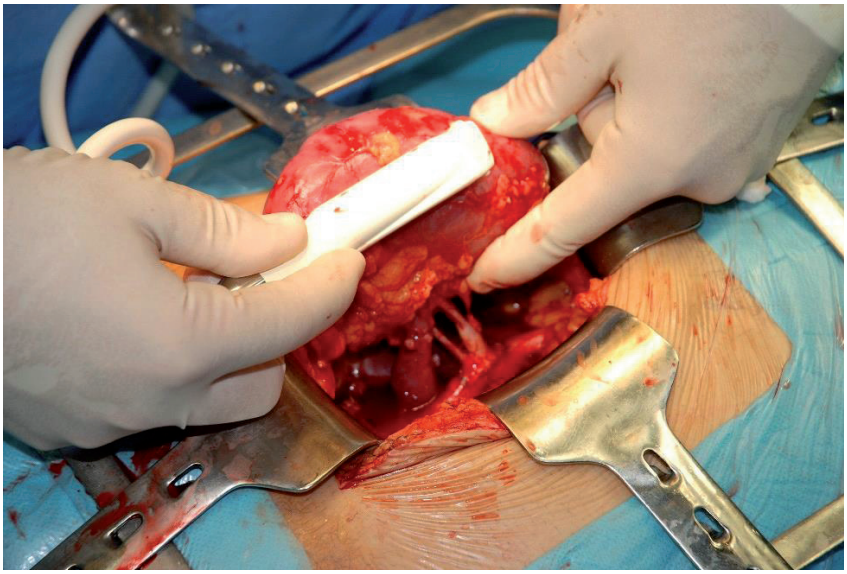

Fig. 2. Doppler ultrasound examination — intraoperative view.

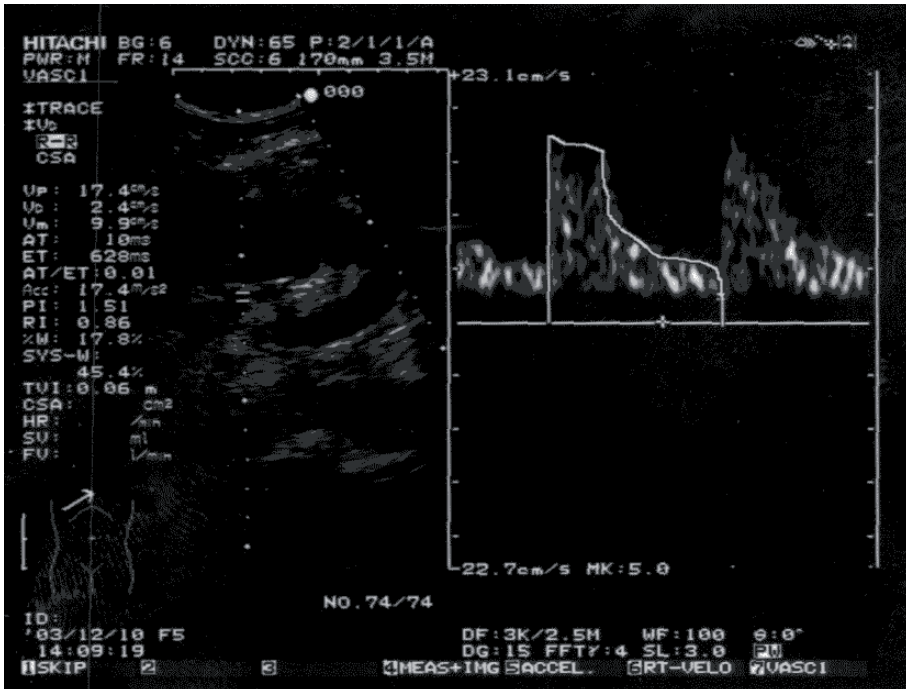

Fig. 3. View of intraoperative Doppler ultrasound examination — RI and PI value measurements.

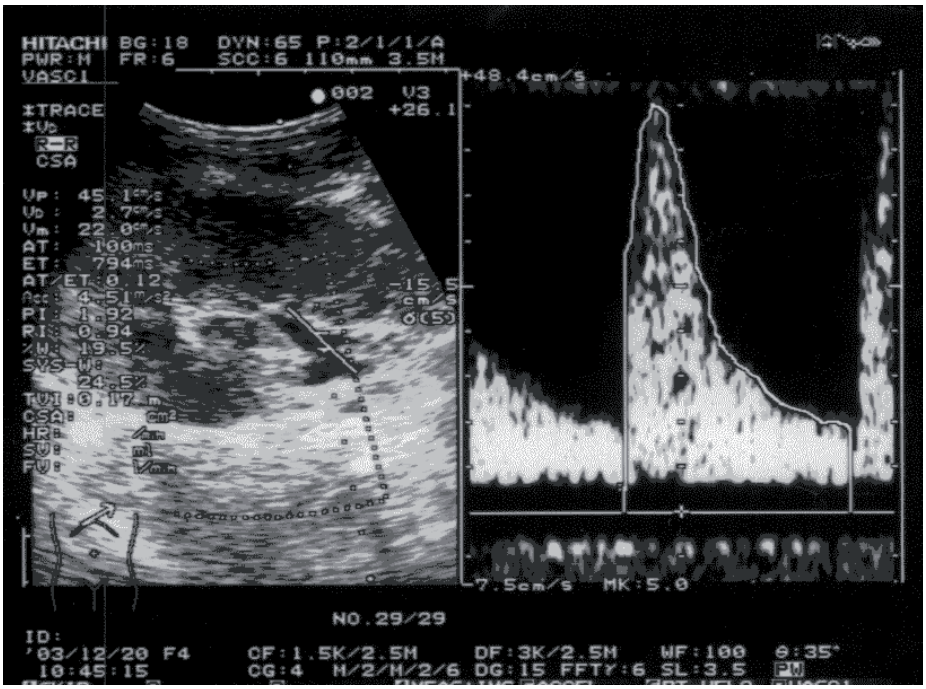

Fig. 4. View of intraoperative Doppler ultrasound examination — RI and PI value measurements.

Statistical analysis

All statistical analyses were performed with Statistica version 10 (StatSoft, Inc). Student's t-test was used to compare the mean values of quantitative parameters in the studied groups. All reported P values are two-sided and P values <0.05 were considered statistically significant.

Results

Delayed graft function was observed in 20 patients (37.7%), while 33 patients (62.3%) had immediate restoration of kidney function.

The mean RI and PI values obtained from Doppler ultrasound, performed immediately after restoration of blood flow to the graft, were found to be positively correlated with the occurrence of DGF. In the group of patients with DGF, the mean intraoperative RI and PI values were 0.9 and 1.76, respectively. These results were significantly higher when compared to the values of RI and PI in the group of patients who did not develop DGF (0.74 vs. 1.54, p <0.05). During the 1st, 2nd, 4th and 8th post-operative day, the RI and PI values were also correlated to the incidence of DGF. The

group of patients who developed DGF had significantly higher mean values of RI and PI postoperatively than the group of patients who did not experience DGF ($p < 0.05$). Cumulative changes in the RI value and cumulative changes of PI value during the subsequent measurements were depicted in Figures 5 and 6, respectively.

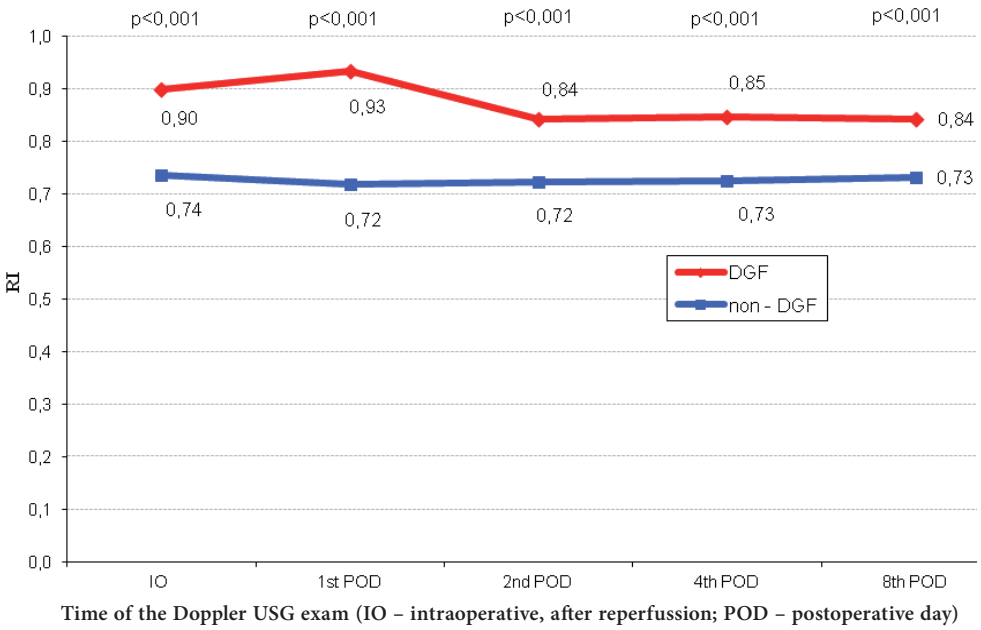

Fig. 5. RI value changes after reperfussion and during postoperative period in the non-DGF and DGF group of kidney recipients.

The sensitivity of RI and PI values in predicting the occurrence of DGF was calculated and presented in Figure 7. The sensitivity of mean intraoperative RI value was 77.7%. The sensitivity slightly decreased to 72.2% on the first post-operative day ($p = 0.353$). However, on the 2nd post-operative day, there was a significant drop in the RI sensitivity to 53.8% ($p = 0.04$). The mean intraoperative PI sensitivity in predicting DGF occurrence was 66.7%. At first, this increased to 72.2% during the first post-operative day ($p = 0.361$) but then decreased to 69.2% on the 2nd post-operative day ($p = 0.428$). It is imperative to recognize that the sensitivity of RI and PI values are the same on the first post-operative day, with a value of 72.2%.

The odds ratio for DGF occurrence was obtained according to the RI and PI values (Fig. 8). In patients whose intraoperative RI was higher or equal to 0.9, the risk of DGF occurrence increased by 13-fold, when compared to patients with RI below 0.9. This was even more prominent, with a 19-fold increase, when the RI value was higher or equal to 0.9 during the first post-operative day. In patients whose

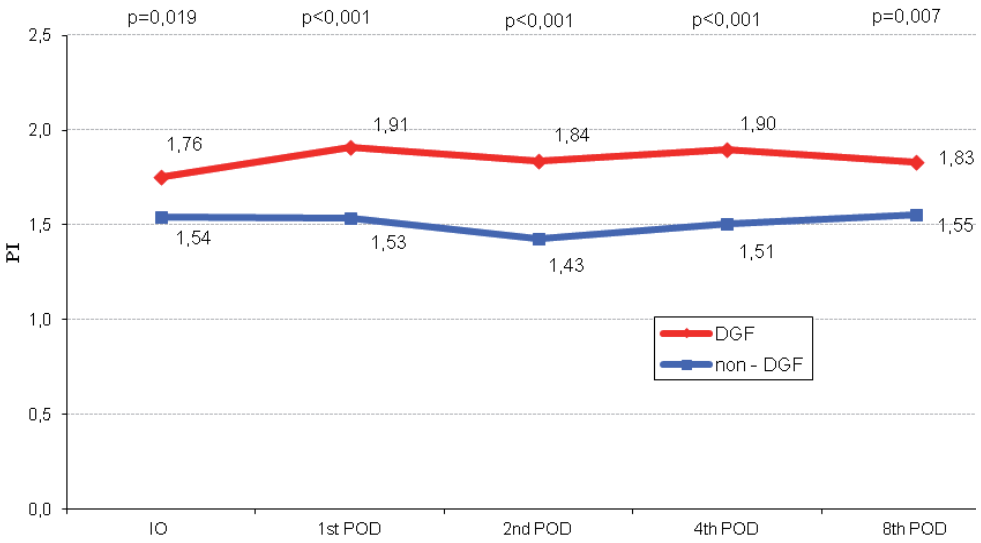

Fig. 6. PI value changes after reperfussion and during postoperative period in the non-DGF and DGF group of kidney recipients.

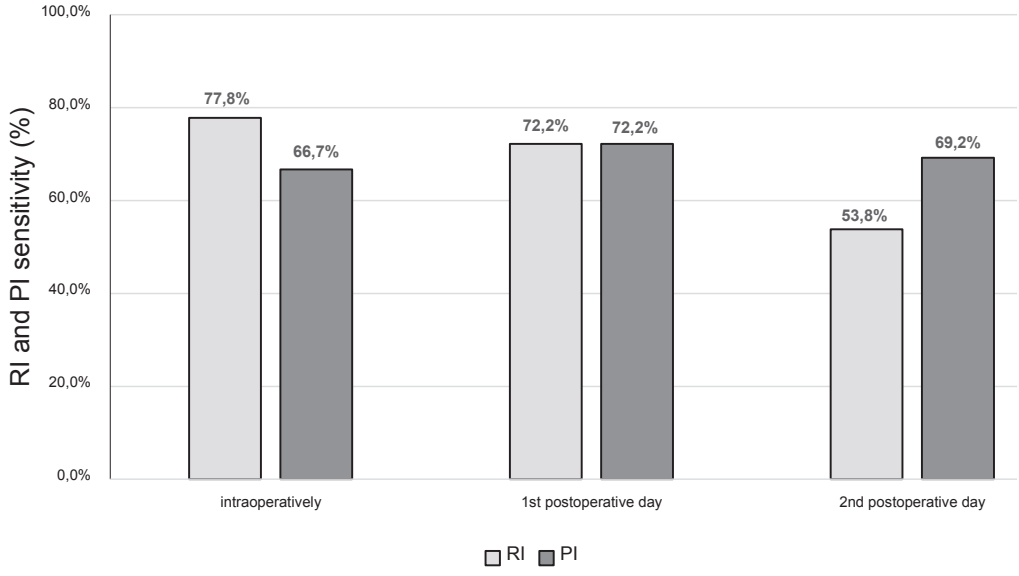

Fig. 7. RI and PI sensitivity in predicting DGF occurrence.

intraoperative PI was higher or equal to 1.9, the risk of DGF occurrence increased by 15-fold, when compared with patients with an intraoperative PI below 1.9. Moreover, in patients whose PI on the first post-operative day was higher or equal to 1.9, the risk of DGF occurrence increased by 19-fold (Fig. 8).

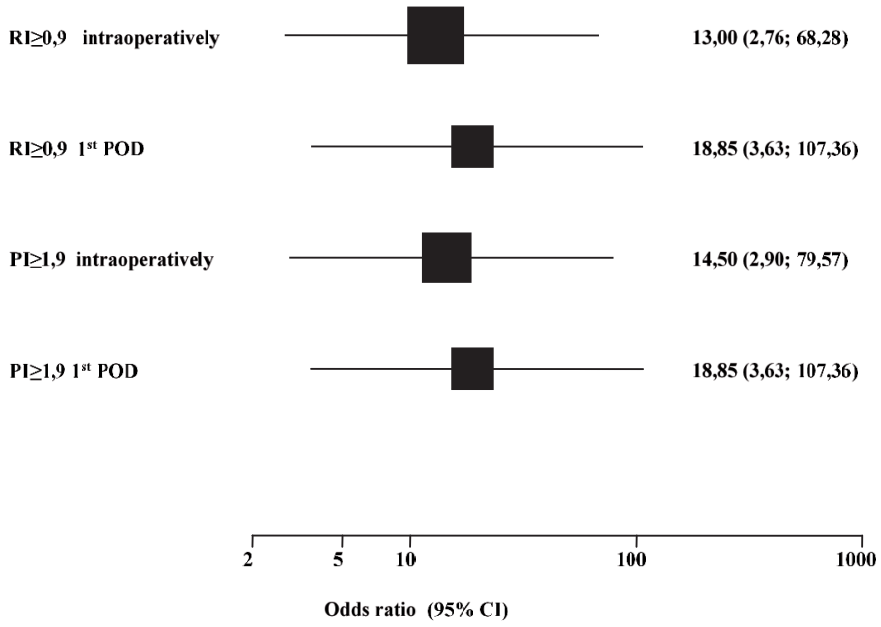

Fig. 8. Odds ratio of DGF occurrence in patient with RI ≥0.9 and PI ≥1.9 intraoperatively and 1st postoperative day (1st POD).

Discussion

Doppler ultrasound is an essential imaging tool for monitoring graft blood flow after kidney transplantation. It obtains not only the anatomical image of the renal graft but also supplies hemodynamic data of the blood flow velocity and direction. Doppler ultrasound is also a valuable clinical tool in predicting the occurrence of DGF. RI and PI values obtained from the ultrasound are standardized measurements that can be used to compare assessments objectively. The RI parameter is widely used in determining vascular resistance of the transplanted kidney, and the normal value is considered to be below 0.8 [11]. One of the aims of post-transplantation graft assessment is early identification of patients with renal dysfunction. In the case of abnormality found in Doppler ultrasound, it is crucial to define and eliminate the cause underlying the graft failure.

According to the literature, the value of RI and PI in diagnosing episodes of graft rejection, acute tubular necrosis (ATN) or obstruction of the urinary tract is still under

discussion due to their low specificity [12, 13]. Herz *et al.* and Skjoldbye *et al.* concluded that RI increase during the reperfusion period suggests incorrect kidney graft placement or vessel kinking, which may lead to thrombosis [11, 14]. Microcirculation impairment in the renal cortex immediately after reperfusion, assessed by thermodiffusion, increases the risk of acute tubular necrosis (ATN) or episodes of graft rejection [15]. In a study by Raiteri, all intraoperative RI values measured by Doppler ultrasound were found to be normal, and had no value in predicting early post-operative complications. However, 24 hours after transplantation, RI values were predictive of the occurrence of surgical vascular complications, and were also statistically significant different from the intraoperative RI values. This suggest an increase in RI sensitivity in the 24 hour post-transplantation period. The delay in sensitivity can be accredited to the time required for developing changes in the renal microcirculation by immunologic and non-immunologic factors [16]. As observed in our study, the sensitivity of the mean RI value to predict DGF occurrence was the highest on the day of the transplantation and slightly less on the 1st post-operative day. By the second post-transplantation day, the reduction in RI sensitivity decreased its diagnostic importance in predicting the incidence of DGF. The sensitivity of PI was the highest during the first 24 hours after the procedure, without any significant difference in its sensitivity when compared to the intraoperative and 2nd post-operative day ($p = 0.442$).

Radmehr demonstrates that the maximal RI and PI value calculated on the 5th post-operative day has a better efficacy in assessing graft dysfunction. The RI and PI values assessed between the 1st and 5th post transplantation day were higher in the group of patients who developed complications, compared with the group of patients without complications. According to Radmehr, a sequential increase in RI and PI values is an important diagnostic marker of graft dysfunction. With various cut-off points for RI and PI, it was found that the higher value for RI and PI was associated with increased specificity but, at the same time, decreased sensitivity. A sequential assessment of RI and PI during Doppler ultrasound examinations is characterized by increased sensitivity and specificity in comparison to a single assessment [17]. Hollenbeck *et al.* also found that sequential increase in RI and PI is a good indicator of acute graft rejection compared to absolute values [18]. Hollenbeck *et al.* and Sharma *et al.* found that sensitivity of a single high RI and PI value is lower comparing with sensitivity of a series of high RI and PI values [18, 19].

Radmehr found that the increase in RI and PI values between the 1st and 5th post-transplantation day contributed to acute rejection as the cause of kidney graft failure.

When RI and PI values are high from the 1st post-transplantation day, the underlying cause of DGF was non acute graft rejection. Moreover, in his study there was no statistically significant difference between RI and PI values in the assessment of graft dysfunction in early post-transplantation period [17]. This finding supports the observation in the current study and leads to a conclusion that it is not necessary

to assess both indices, specifically on the first post-operative day. Choi assessed the sensitivity and specificity of RI in the 24 hours post-transplantation to be 88% and 58%, respectively, with a RI cut-off point of 0.6 [20]. Radmehr used a cut-off point of 0.62 for RI, and calculated the sensitivity of 83% and a specificity of 54% on the first post-transplantation day. On the 3rd post-operative day, sensitivity and specificity were 87% and 61% respectively, with a RI cut-off point of 0.63. Radmehr concluded that the specificity of RI values increased with longer period after the transplantation [17]. As supported in the current study, Angelescu demonstrated that both intraoperative and early post-operative assessments of transplanted renal cortex microcirculation are sensitive tools for graft function evaluation [15]. The reduction of blood flow in the renal cortex during and shortly after the operation has high predictive value in diagnosing DGF. Tublin confirms the usefulness of Doppler ultrasound by demonstrating the prognostic value of RI assessments from the 1st and 3rd post-operative day on the short-term renal graft function [21]. Saracino suggests that early evaluation of RI can predict short-term renal DGF outcome [22]. Splendiani also supports the usefulness of RI measurements in anticipating renal graft function [23]. Ikee presents the relationship between RI values and the histopathological finding of the graft biopsy. The increase in RI correlated with increasing incidence of graft failure, manifesting as vessel fibrosis (sensitivity 75%, specificity 85.7%) [24]. In Radermacher's study, RI values greater than 0.8 measured for at least three months after the transplant was a strong predictor in the occurrence of both graft impairment and host death with functioning graft. Since there is a correlation between RI and cardiovascular risk factors such as age, coronary disease, hypertension, and impaired graft function, it does not come as a surprise that the increase of renal vascular resistance has a predictive role in the occurrence of not only impaired graft function but also host death due to cardiovascular complications [25]. Don and Drudi used the RI for diagnosing graft failure in long-term follow-up [26, 27]. According to Anderson, the renal blood flow (RBF) is a predictive factor of immediate renal function and absence of ATN occurrence in 87% of recipients. However, no correlation was observed between RBF with the time of ATN occurrence, warm ischemia time (WIT) or cold ischemia time (CIT) [28]. In an animal study, Aryian found a correlation between RBF measured one hour post-transplantation and the occurence of IGF [29]. Numerous studies conclude that Doppler ultrasound with RI and PI values have no predictive value or correlation with graft function [30, 31]. However, after excluding recipients with post-operative complications such as ATN, DGF, acute graft rejection and calcineurin inhibitors toxicity, the correlation between RI and PI with graft function is observed. Kahraman found that Doppler ultrasound performed within the first week of post-transplant were predictive of one year allograft function. By identifying early markers that can predict the renal function prognosis will greatly benefit kidney recipients by early detection of long-term graft failure [32].

Conclusions

Doppler ultrasound, with resistive index (RI) and pulsatility index (PI), is a significant diagnostic method to predict delayed graft function (DGF) occurrence after kidney transplantation. The results demonstrate that the patients who developed DGF had significantly higher RI and PI values when compared to patients without DGF. The increase in RI and PI values is an essential indicator of diminished blood flow to the graft, which consequently leads to the increased risk of DGF development.

Limitations

Limitations of this study include the single center design and low number of patients. These factors may contribute to reduce the potential of this study.

Conflict of interest

None declared.

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