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Resistance index of the renal artery measured by doppler ultrasound as a predictor of graft function after kidney transplantation

Indeks rezistencije bubrežne arterije meren dopler ultrazvukom kao pokazatelj funkcije transplantiranog bubrega

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Abstract

Background/Aim. As an optimal treatment of choice for patients with the latest stage of chronic kidney failure (CKD), renal transplantation (Tx) is performed. The resistance index (RI) of the renal artery is measured by Doppler ultrasonography routinely at certain time intervals to show the condition of the renal graft. The value of RI > 0.75 is considered abnormal. The aim of the study was to determine the correlation between the values of the RI index and the function of the transplanted kidney. **Methods.** We analyzed retrospectively 63 patients in whom kidney transplant was done at the Clinic for Nephrology and Clinical Immunology, the University Clinical Center of Vojvodina, Novi Sad, Serbia, in the period from 2013 to 2017. Doppler of renal blood vessels was made to all examined patients in the first month after the renal transplantation. In addition to standard demographic data, all patients had the RI index and its relationship to the function of the transplanted kidney analyzed immediately after transplantation, as well as in the 6th, 12th, and 18th month, and in a certain number of patients in the 24th and 48th month after transplantation. **Results.** Out of 63 patients, 63.5% were men, and 26.5% were women, with an average age of 47.67 ± 13.62 years. The primary diseases in patients which led to the terminal CKD stage were hypertension in 33.3% and different forms of glomerulonephritis; while other diseases (diabetes mellitus, chronic pyelonephritis, eclampsia, polycystic kidneys, kidney agenesia, and unknown cause) were present in a lower percentage. RI < 0.75 was present in 73%, and RI > 0.75 in 27% of patients. There was no statistically significant association between RI and serum creatinine or creatinine clearance at a given time, and there was no connection between RI and gender, as well as length of previous treatment by HD. There was a statistically significant association between RI and age of kidney recipient, as well as Tx type. **Conclusion.** In the observed group of patients, RI of renal arteries did not prove to be a good predictor of the function of the transplanted kidney either in the early or later post-transplant periods. RI might have greater predictive significance if it were determined on or immediately after the transplantation procedure.

Key words:
graft survival; kidney transplantation; postoperative complication; prognosis; renal artery; ultrasonography; doppler.

Apstrakt

Uvod/Cilj. Transplantacija bubrega (Tx) je metoda izbora za lečenja bolesnika sa finalnim stadijumom hronične bubrežne bolesti (HBB). Indeks rezistencije (RI) bubrežne arterije meri se prilikom dopler ultrasonografskog pregleda bubrega i može se koristiti za procenu stanja renalnog grafta. Vrednosti RI > 0,75 smatraju se patološkim. Cilj rada bio je da se utvrdi korelacija između vrednosti RI indeksa i funkcije transplantiranog bubrega kod bolesnika lečenih Tx. **Metode.** Retrospektivno smo analizirali 63 bolesnika kod kojih je urađena Tx u Univerzitetskom kliničkom centru Vojvodine, Novi Sad, Srbija u periodu od 2013. do 2017. godine. U ispitivanje su bili uključeni svi bolesnici kod kojih je u prvih mesec dana nakon Tx urađen dopler renalnih krvnih sudova. Pored standardnih demografskih podataka, svim bolesnicima su analizirane vrednosti kreatinina u serumu, kreatinin klirensa i RI indeks i povezanost tog indeksa sa funkcijom transplantiranog bubrega neposredno nakon tranplantacije, kao i u 6, 12. i 18. mesecu, a kod određenog broja bolesnika i u 24. i 48. mesecu nakon Tx. **Rezultati.** U ispitivanoj grupi

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bolesnika, muškaraca je bilo 63,5%, a žena 26,5%, prosečne starosti 47,67 ± 13,62 godine. Osnovna oboljenja koja su dovela do terminalnog stadijuma HBB bila su hipertenzija i različiti oblici glomerolonefritisa sa zastupljenošću od po 33,3%, dok su ostale bolesti (dijabetes melitus, hronični pijelonefritis, eklampsija, policistična bolest bubrega, agenezija bubrega i nepoznat uzrok) bile zastupljene u nižem procentu. Indeks RI < 0,75 bio je prisutan kod 73%, a RI > 0,75 kod 27% bolesnika. Nije utvrđena značajna povezanost RI i kreatinina u serumu, klirensa kreatinina, kao ni povezanost RI sa polom i dužinom prethodnog lečenja hemodijalizom. Dokazana je značajna povezanost između RI i starosti primaoca bubrega, kao i vrste Tx. **Zaključak.** U posmatranoj grupi bolesnika indeks RI se nije pokazao kao dobar pokazatelj funkcije transplantiranog bubrega ni u ranom, niti u kasnijem postransplantacionom periodu. Taj indeks bi mogao imati veću prediktivnu vrednost ukoliko bi se merenje vršilo neposredno nakon završene transplantacione procedure.

Ključne reči:
graft, preživljavanje; transplantacija bubrega; postoperativne komplikacije; prognoza; *a. renalis*; ultrasonografija, dopler.

Introduction

The terminal stage of chronic kidney disease (CKD) requires active treatment by replacement of renal function. Methods available to do this are hemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation (Tx).

Tx is the method of choice for treating patients in stage five CKD regardless of its etiology because, in addition to excretory, it replaces all other functions that a healthy kidney has. In addition to improving health, Tx reduces mortality, improves patient quality of life, and increases survival rates relative to HD and retroperitoneal dialysis methods [1–3]. Tx is a complex surgical procedure that replaces a nonfunctional organ with a new one in order to compensate for the tissue or organ function. During Tx, the organ is usually ileocecal. The donor is the person who gives the spool or transplant. Donors can be living-related donors, living-unrelated donors and cadaveric donors, that is, a person who has been diagnosed with brain death with the consent of the family [2].

There is a spectrum of complications that may occur after Tx. Vascular complications include hematoma, hemorrhage, renal vein, and artery thrombosis, lymphocele, pseudoaneurysm, renal artery stenosis. Urological complications are urine leakage and hydronephrosis [3].

The diagnostic method by which the occurrence of complications after Tx can be determined in the most rapid and noninvasive manner is Doppler ultrasonography. It is an imaging method for monitoring the condition after Tx [4, 5].

By calculating the resistance index (RI) at certain time intervals, the function of the renal graft can be monitored. The first examination is performed shortly after the transplant, and then after examination according to the appropriate protocols [6]. Arterial RI is a measure of pulse blood flow that shows resistance to blood flow caused by a microvascular bed distal to the site of measurement. It is usually measured in three places: the upper, middle, and lower poles of the kidney.

Doppler ultrasonography measures maximum systolic value (Vmax) and minimum diastolic value (Vmin), thus the RI is measured as 100x [1- (Vmin / Vmax)] [7]. The physiological value of RI, that is, the upper limit, is taken to be 0.7, while RI greater than 0.75 is interpreted as pathological peripheral resistance. Values > 0.7 and < 0.75 are considered borderline elevated. The physiological RI shows maintenance of high perfusion throughout the kidney [8].

An elevated RI, in comparison with a decreased RI, is a significant predictor of progressive renal dysfunction. RI can show different types of graft rejection, but it cannot distinguish between them [4].

The aim of this study was to investigate the correlation between RI values and transplanted kidney function in patients treated with Tx at the University Clinical Center (UCC) of Vojvodina, Novi Sad, Serbia.

Methods

We retrospectively analyzed the medical records of 63 patients undergoing kidney transplantation at the UCC of Vojvodina from 2013 to 2017. The study included all patients who underwent renal blood vessel Doppler in the first month after Tx. Color Doppler examination was performed with a 3.5 MHz convex-array transducer (Toshiba Ultrasound) in a supine position, at the angle of 30–60°. In interlobar and segmental renal arteries, RI was calculated from the Doppler spectra using the system software, according to the following formula: RI = (peak systolic frequency shift − minimum diastolic frequency shift)/peak systolic frequency shift.

This method was done sporadically in our Center from 2013 to 2015, after which it became a routine method. The study did not include patients whose surgical complications or cardiovascular comorbidities resulted in the termination of transplant operation and/or death in the immediate postoperative period. In addition to standard demographics, all patients were analyzed for RI and its association with renal transplant function (serum creatinine, creatinine clearance). We used the Modification of Diet in Renal Disease (MDRD) formula to determine creatinine clearance. The data obtained were analyzed statistically using the statistical software MedCalc and Microsoft Excel. Numerical data are presented using arithmetic means and standard deviations and median. Spearman's and Kendall's correlation coefficients were used in the analysis of one-way correlations. Comparisons were made by Student's *t*-test and the Mann-Whitney test. Statistical significance was defined by $p \leq 0.05$.

Results

General demographic data

The study included 63 patients who were followed for 18 to 48 months after Tx. The median time of follow-up was 24 months. The main demographic characteristics of our patients are shown in Table 1.

The main causes that lead to the end-stage of CKD, as well as the need for Tx, were hypertension in 21 (33.3%) patients and glomerulonephritis in 21 (33.3%) of patients. Other causes were shown in Figure 1.

The function of the transplanted kidney

Mean values of serum creatinine and creatinine clearance in the 1st, 12th, 18th, 24th, and 48th posttransplantation month are shown in Table 2. The last control of kidney function was within 3 months before

Table 1

Demographic characteristics

Characteristic	Values
Male gender, n (%)	40 (63.5)
Age at the time of transplantation (years), median (min–max)	48 (20–73)
Body mass index (kg/m^2), median (min–max)	24.49 (18.9–29.1)
Patients on hemodialysis before transplantation, n (%)	60 (95.2)
Preemptive kidney transplantation, n (%)	3 (4.8)
Time on HD (years), median (min–max)	5 (0.1–17)
Cadaveric kidney transplantation, n (%)	54 (85.7)
Living related transplantation, n (%)	9 (14.3)
Age of kidney donor (years), median, n (%)	52 (28–69)
Gender of kidney donor same as the recipient, n (%)	4 (44.4)
Immunosuppressive drugs (calcineurin inhibitor/mTOR inhibitor), n (%)	61 (96.8)/2 (3.2)
Immunosupressive drugs (corticosteroids), n (%)	100
Immunosupressive drugs (mycophenolic acid), n (%)	100

min – minimum; max – maximum; HD – hemodialysis.

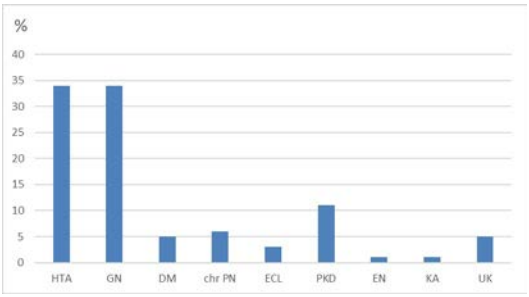


Fig. 1 – The main causes of chronic kidney disease.
HTA – hypertension arterials; GN – glomerulonephritis;
DM – diabetes mellitus; chr PN – chronic pyelonephritis;
ECL – eclampsia; PKD – polycystic kidney disease;
EN – endemic nephropathy; KA – kidney agenesis;
UK – unknown.

Table 2

Values of serum creatinine and creatinine clearance in the 1st, 12th, 18th, 24th, and 48th posttransplantation month

Parameter	Number of patients	Mean ± SD
Serum creatinine (μmol/L)		
1 month	63	192.89 ± 164.45
6 months	63	140.75 ± 49.45
12 months	63	132.61 ± 57.02
18 months	63	137.81 ± 59.90
24 months	38	135.39 ± 66.57
48 months	22	165.14 ± 101.27
Creatinine clearance (mL/min/1.73m^2)		
1 month	63	45.08 ± 25.96
6 months	63	46.14 ± 24.53
12 months	63	49.92 ± 24.64
18 months	63	47.13 ± 25.36
24 months	38	50.39 ± 24.06
48 months	22	49.90 ± 25.60

SD – standard deviaton.

analysis. As insufficient transplant function, we considered serum creatinine values greater than 200 μmol/L and they were found in the last control in 6 (9.5%) patients. Serum creatinine values in this group were from 206 μmol/L to 583 μmol/L; the median value was 216.5 μmol/L. The median value of creatinine clearance in this group of patients was 29.4 mL/min/1.73 m^2.

In the group of patients with serum creatinine values less than 200 μmol/L, they were in range from 68 μmol/L to 199 μmol/L; the median value was 116.0 μmol/L. The median value of creatinine clearance in this group of patients was 54.2 mL/min/1.73 m^2. In the observed group of 63 patients, one (1.6%) patient required active replacement of renal transplant function by HD 4 years after Tx.

Resistance index

Doppler ultrasound and RI measurement time range from 1 to 24 days after transplantation.

The physiological value of the RI < 0.75 was present in 46 (73%) patients, RI values were from 0.51 to 0.71. The median value was 0.63.

The pathological RI value > 0.75 was detected in 17 (27%) patients. RI values were from 0.75 to 0.97. The median value was 0.80.

Correlation of the pathological resistance index

We examined the correlation of the value of RI with the serum creatinine and creatinine clearance value in the 1st, 12th, 18th, 24th, and 48th posttransplantation month, as well as the correlation with gender and age of kidney recipients, type of transplantation, and previous dialysis duration time. The results are shown in Table 3.

Discussion

Tx is a method that replaces not only excretory but also all other kidney functions. Therefore, it is of great importance to maintain the adequate function of the transplanted organ for as long as possible. Numerous complications can occur after Tx. Over the years, research has focused on the detection of noninvasive diagnostic techniques that could allow early detection of complications and graft rejection [9].

RI is useful for showing different types of graft dysfunction, which can be: acute tubular necrosis (ATN), acute graft rejection, renal vein thrombosis, ureteral obstruction, and pyelonephritis but cannot differentiate between diseases [4].

Measuring RI over a longer period is a predictor for the early detection of chronic nephropathy [1, 4].

Our retrospective study included 63 patients treated with Tx at the UCC of Vojvodina from 2013 to 2017. Gender and age of patients were consistent with the literature [1, 6, 9].

The most common underlying disease leading to CKD was hypertension and some form of glomerulonephritis, which is similar to the findings in developed countries [10].

Cessation of graft function, i.e., the transfer of patients to another form of active treatment, in our study sample was determined in one patient four years after Tx. Similar results were obtained by Naesens et al. [6]. Therefore, according to the literature, we took a serum creatinine value greater than 200 μmol/L as a value indicating inadequate graft function. In our study, these serum creatinine levels at the last control of the nephrologist were observed in 9.5% of patients, which is slightly better than in the literature, where the incidence of inadequate renal transplant function was 23% [1]. A possible explanation for these results would be the rigorous selection of recipients due to the relatively small number of transplants

Table 3

Correlation of Resistance index (RI) with various factors

Correlation of RI with:	*p*	CI 95%
Serum creatinine after Tx		
1 month	0.9925	-0.191 to 0.215
6 months	0.5404	-0.160 to 0.246
12 months	0.6786	-0.228 to 0.160
18 months	0.6445	-0.259 to 0.143
24 months	0.572	-0.259 to 0.170
48 months	0.596	-0.385 to 0.206
Creatinine clearance after Tx		
1 month	0.0791	-0.201 to 0.251
6 months	0.1893	-0.224 to 0.157
12 months	0.1582	-0.251 to 0.188
18 months	0.1542	-0.261 to 0.194
24 months	0.1761	-0. 253 to 0.185
48 months	0.1598	-0.259 to 0.198
Gender of kidney recipient	0.486	-0.292 to -0.166
Age of kidney recipient in the time of Tx	0.0104	0.0333 to 0.382
Type of Tx	0.0499	0.000439 to 0.467
Period on HD	0.3853	-0.189 to 0.354

Tx – kidney transpantation; HD – hemodialysis; CI – confidence interval. Statistical significance was considered as values $p \leq 0.05$.

in our Center, as well as the fact that patients who had a permanent loss of graft function or death due to surgical complications in the immediate postoperative course were not included in the study.

RI in our patients is most commonly measured at the first outpatient check-up of the nephrologist during the first month after Tx, or in patients with delayed graft function, during hospitalization, also during the first month after transplantation. A pathological value of RI higher than 0.75 was present in 27% of our patients. According to the literature data, 20% of patients had pathological RI values, that is, RI > 0.75 [3–5].

In our study, we found no statistically significant association of RI with serum creatinine values at all time intervals tested. Such data may be due to the time of measurement of the RI, that is, the RI might have greater predictive significance if it were determined on or immediately after the transplantation procedure. In our center, we do not have a standard protocol that includes a Doppler ultrasound of a transplanted kidney on the day of the transplantation. This procedure is performed by a radiologist who is specialized in this field. Therefore, measurements were done when the radiologist was available. Data from the study of Cano et al. [4] show an association when measuring RI in the early period after transplantation as a valid marker for determining renal graft function, whereas in other literature data, this association has not been established [1, 3, 4].

According to other studies, we can conclude that a statistically significant association between the RI and serum creatinine values is shown over a period of 12 to 18 months [1, 4].

We did not demonstrate an association between RI and the gender of patients, which is consistent with the literature data [1, 3–6, 9, 10].

According to the literature data, a statistically significant correlation of the RI was found with recipient years, confirming that RI depends on the vascular characteristics of the recipient. We have reached the same conclusions in our research [1, 4].

A statistically significant correlation was shown between RI and type of transplantation, which coincides with results of studies already published [1, 11].

In the study, we proved that there is no statistically significant correlation between the RI and the length of previous dialysis treatment, as confirmed by the available literature data [11].

Conclusion

In the observed group of patients, the RI of renal arteries was not proven to be a good predictor of renal transplant function in the early or later posttransplant periods.

The RI might have greater predictive significance if it was determined on or immediately after the transplantation procedure.

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