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INDEKS REZISTENCIJE ARTERIJE RENALIS MEREN DOPPLER ULTRAZVUKOM KAO PREDIKTOR FUNKCIJE TRANSPLANTIRANOG BUBREGA

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Abstract

Background / Aim. As an optimal treatment of choice for the patients with the latest stage of chronic renal failure (CKD), renal transplantation is performed. The resistance index (RI) of 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. Goal to determine the correlation between the values of the RI index and the function of the transplanted kidney. Methods. in whom the Doppler of renal blood vessels were made in the first month after the renal transplant. In addition to standard demographic data, all patients were analyzed the RI We analyzed retrospectively 63 patients at the Clinic for Nephrology and Clinical Immunology in KC Vojvodina in the period from 2013 to 2017. In the study were included all patients index and its relationship to the function of the transplanted kidney. Results. Out of 63 patients, men were 63.5%, and women 26.5%, with an average age of 47.67 years. +/- 13.62. The primary diseases in patients which led to the terminal CKD stage were hypertension (HTA) at 33.3% and different forms of glomerulonephritis (GN); while other diseases (diabetes mellitus (DM), chronic pyelonephritis (chr PN), eclampsia, polycystic kidneys, kidney agenesis and unknown cause) were present in a smaller percentage. RI <0.75 was present in 73% of patients, and RI> 0.75 in 27%. According to the data, there is no statistically significant association between the resistance index and serum creatinine or creatinine clearance at a given time, and there is no connection to gender and length on HD. There is statistically significant association between RI and age of kidney recipient, as well as Tx type. Conclusion. In the observed group of patients, the resistance index 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: transplantation; doppler ultrasonography; resistance index.

Apstrakt

Uvod / Cilj. Transplantacija bubrega (Tx) je metoda izbora prilikom lečenja pacijenata sa petim stadijumom hronične bubrežne bolesti (HBB). Indeks rezistencije arterije renalis (RI) se meri prilikom doppler ultrasonografskog pregleda bubrega i može se koristiti za
procenu stanja renalnog grafa. Vrednosti RI > 0,75 smatraju se patološkim. Cilj rada bio je da se utvrdi postojanje korelacije između vrednosti RI indekса i funkcije transplantiranog bubrega kod bolesnika lećenih transplantacijom bubrega u Kliničkom centru (Kc) Vojvodine. Metode. Retrospektivno smo analizirali 63 bolesnikakod kojih je urađena transplantacija bubrega u Kc Vojvodine u periodu od 2013. do 2017. godine. U ispitivanje su uk lučeni svi bolesnici kod kojih je u prvih mesec dana nakon transplantacije bubrega urađen doppler renalnih krvnih sudova. Pored standardnih demografskih podataka, svim pacijentima je analizirana vrednost kreatinina u serumu, kreatinin klirensa i RI indeks i njegova povezanost ovog indeksa sa funkcijom transplantiranog bubrega neposredno nakon transplantacije, kao i u 6., 12., 18. mesecu, a kod određenog broja bolesnika i u 24 i 48. mesecu nakon transplantacije. Rezultati. U ispitivanoj grupi bolesnika, muškaraca je bilo 63,5%, a žena 26,5%, sa prosečnom starošću 47,67 god. +/- 13,62. Osnovna oboljenja koja su dovela do terminalnog stadijuma HBB su hipertenzija (HTA) i različiti oblici glomerolonefritisa (GN) sa po 33,3%; dok su ostale bolesti (šećerna bolest (DM), hronični pijelonefritis (chr PN), eklampsija, policistična bolest bubrega, agenesija bubrega i nepoznat uzrok) zastupljene u manjem procentu. RI<0.75 je bio prisutan kod 73% pacijenta, a RI>0.75 kod 27%. Nije utvrđena značajna povezanost RI i kreatitina u serumu, klirensa kreatninina, kao ni povezanost sa polom I dužinom prethodnog lećenja hemodijalizom (HD). Dokazali smo značajnu povezanost izmedju RI i starosti primaoca bubrega, kao ivrste Tx. Zaključak. U posmatranoj grupi pacijenata indeks RI se nije pokazao kao dobar prediktor funkcije transplantiranog bubrega ni u ranom, niti u kasnijem postrasplantacionom periodu. Ovaj indeks bi mogao imati veću prediktivnu vrednost ukoliko bi se merenje vršilo neposredno nakon završene transplantacione procedure.

Ključne reči: transplantacija; doppler ultrasonografija; indeks rezistencije.

Introduction

Terminal stage of CKD (Chronic kidney disease) 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 the treatment of patients in stage five CKD regardless of its etiology, because in addition to excretory, it replaces all other function that a healthy
kidney has. In addition to improving health, kidney transplantation reduces mortality, improves patient quality of life, and increases survival rates relative to hemodialysis and retroperitoneal dialysis methods. [1-3] Tx is complex surgical procedure which replaces nonfunctional organ with a new one in order to compensate tissue or organ function. During kidney transplantation, organ is usually placed ileocecaly. The donor/donor is the person who gives the spool or transplant. Donors can be living related donors, living unrelated donors and a 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 renal transplantation can be determined in the most rapid and non-invasive manner is Doppler ultrasonography. It is an imaging method for monitoring the condition after renal transplantation. [4, 5]

By calculating 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 Resistance 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), so the resistance index 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 the resistance index greater than 0.75 is interpreted as pathological peripheral resistance. Values> 0.7 and <0.75 are considered borderline elevated. The physiological resistance index shows maintenance of high perfusion throughout the kidney. [8]

An elevated resistance index in comparison with a decreased resistance index 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 index values and renal transplant function in patients treated with renal transplant at the Clinical Center (Cc) of Vojvodina.

Methods

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

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 termination of transplant operation and/or death in the immediate postoperative period. In addition to standard demographics, all patients were analyzed for and RI index and its association with renal transplant function (serum creatinine, creatinine clearance). We used MDRD formula to determine creatinine clearance. The data obtained were analyzed statistically using the statistical software MedCalc and Microsoft Excel. Numerical data are presented by means of 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, Mann Whitney test. Statistical significance was defined by \( p \leq 0.05 \).
Results

General demographic data

The study included 63 patients. Patients were followed for 18 to 48 months after kidney transplantation. Median time of follow up was 24 months. Main demographic characteristics of our patients were shown in table 1.

The main cause that lead to end-stage of chronic kidney disease, also to the need for kidney transplantation, were hypertension in 21 patients (33,3%) and glomerulonephritis in 21 (33,3%). Other causes were shown in chart 1.

Function of 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. Last control of kidney function was within 3 months before analysis. As insufficient transplant function we considered creatinine values greater than 200 µmol/l and this was found in the last control in 6 patients (9.5%). Creatinine values in this group were from 206 to 583 µmol / l, median value was 216,5 µmol / l. Median value of creatinine clearance in this group was 29,4 ml/min/1,73m².

In the group of patients with creatinine values less than 200 µmol/l, range of creatinine was from 68 to 199 µmol/l, median value was 116,0 µmol/l. Median value of creatinine clearance in this group was 54,2 ml/min/1,73m². In the observed group of 63 patients, one (1.6%) required active replacement of renal transplant function by hemodialysis method, 4 years after kidney transplantation.

Resistance index

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

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

The pathological RI value> 0.75 was detected in 27% (17 patients). RI values were from 0.75 to 0.97. 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. Results were shown in table 3.

**Discussion**

Kidney transplantation is a method that replaces not only excretory but also all other kidney functions. Therefore, it is of great importance to maintain adequate function of the transplanted organ for as long as possible. Numerous complications can occur after Tx kidney. Over the years, research has focused on the detection of non-invasive 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 resistance index over a longer period is a predictor for the early detection of chronic nephropathy. [1,4]

Our retrospective study included 63 patients treated with kidney transplantation in Cc 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 finding in developed countries. [12]

Cessation of graft function, ie the transfer of patients to another form of active treatment in our study sample was determined in one patient four years after transplantation. Similar results were obtained by Nessens et al. [6]. Therefore, according to the literature, we took a creatinine value greater than 200 µmol / l as a value indicating inadequate graft function. In our study, these creatinine levels at the last control of the nephrologist were observed in 9.5% of patients, which is slightly better than 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 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 trial. 

RI in our patients is most commonly measured at the first outpatient check-up of the nephrologist during the first month after kidney transplantation, 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 subjects. According to the literature data, 20% of patients had pathological resistance index 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. It is possible that such data are 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 which include doppler ultrasound of transplanted kidney on the day of the transplantation. This procedure is performed by a radiologist, specialized in this field, so measurements were done when radiologist was available. Data from the work of Cano et al., 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 this association has not been established. [1,3,4]

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

We did not demonstrate an association between RI and gender of patients, whereas in other literature we found no correlation, which is consistent with the literature data. [1,3,4,5,6,9,12]

According to the literature data, a statistically significant correlation of 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 significant statistical correlation was shown between RI and type of transplantation, which coincides with research in papers already published. [1,11]
In the study, we proved that there is no statistically significant correlation between RI and the length of previous dialysis treatment, as confirmed by the available literature data. [11]

**Conclusion**

In the observed group of patients, resistance index of renal arteries was not proven to be a good predictor of renal transplant function 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.

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Table 1: Demographic characteristics

| Characteristic                                                   | N (%)      |
|-----------------------------------------------------------------|------------|
| Male gender                                                     | 40 (63.5)  |
| Age at the time of transplantation (median)                     | 48 (20-73) |
| Body mass index (kg/m²) (median)                                | 24.49 (18.9-29.1) |
| Patients on hemodialysis before transplantation                 | 60 (95.2)  |
| Preemptive kidney transplantation                               | 3 (4.8)    |
| Time on HD in years (median)                                    | 5 (0.1-17) |
| Cadaveric kidney transplantation                                | 54 (85.7)  |
| Living related transplantation                                  | 9 (14.3)   |
| Age of kidney donor (median)                                    | 52 (28-69) |
| Gender of kidney donor same as recipient                        | 4 (44.4)   |
| Immunosuppressive drugs (Calcineurin inh/mTOR inh)              | 61 (96.8)/2 (3.2) |
| Immunosuppressive drugs (corticosteroids)                       | 100        |
| Immunosuppressive drugs (mycophenolic acid)                    | 100        |
Chart 1. The main cause of chronic kidney disease.

![Chart showing the main cause of chronic kidney disease](chart.png)

Table 2: Values of serum creatinine and creatinine clearance in the 1\textsuperscript{st}, 12\textsuperscript{th}, 18\textsuperscript{th}, 24\textsuperscript{th} and 48\textsuperscript{th} posttransplantation month

|                                | Number of patients | Mean value | Standard deviation |
|--------------------------------|--------------------|------------|--------------------|
| Serum creatinine 1 month (µmol/l) | 63                 | 192.89     | ± 164.45           |
| Serum creatinine 6 months (µmol/l) | 63                 | 140.75     | ± 49.45            |
| Serum creatinine 12 months (µmol/l) | 63                 | 132.61     | ± 57.02            |
| Serum creatinine 18 months (µmol/l) | 63                 | 137.81     | ± 59.90            |
| Serum creatinine 24 months (µmol/l) | 38                 | 135.39     | ± 66.57            |
| Serum creatinine 48 months (µmol/l) | 22                 | 165.14     | ± 101.27           |
| Creatinine clearance 1 month (ml/min/1.73m\textsuperscript{2}) | 63                 | 45.08      | ± 25.96            |
| Creatinine clearance 6 months (ml/min/1.73m\textsuperscript{2}) | 63                 | 46.14      | ± 24.53            |
| Creatinine clearance 12 months (ml/min/1.73m\textsuperscript{2}) | 63                 | 49.92      | ± 24.64            |
| Creatinine clearance 18 months (ml/min/1.73m\textsuperscript{2}) | 63                 | 47.13      | ± 25.36            |
| Creatinine clearance 24 months (ml/min/1.73m\textsuperscript{2}) | 38                 | 50.39      | ± 24.06            |
| Creatinine clearance 48 months (ml/min/1.73m\textsuperscript{2}) | 22                 | 49.90      | ± 25.60            |
Table 3: Correlation of RI with various factors

| Correlation of RI with:                        | Value  | CI 95%         |
|-----------------------------------------------|--------|----------------|
| Serum creatinine 1 month after Tx             | p=0.9925 | -0.191 to 0.215 |
| Serum creatinine 6 months after Tx            | p=0.5404 | -0.160 to 0.246 |
| Serum creatinine 12 months after Tx           | p=0.6786 | -0.228 to 0.160 |
| Serum creatinine 18 months after Tx           | p=0.6445 | -0.259 to 0.143 |
| Serum creatinine 24 months after Tx           | p=0.572  | -0.259 to 0.170 |
| Serum creatinine 48 months after Tx           | p=0.596  | -0.385 to 0.206 |
| Creatinine clearance 1 month after Tx         | p=0.0791 | -0.201 to 0.251 |
| Creatinine clearance 6 months after Tx        | p=0.1893 | -0.224 to 0.157 |
| Creatinine clearance 12 months after Tx       | p=0.1582 | -0.251 to 0.188 |
| Creatinine clearance 18 months after Tx       | p=0.1542 | -0.261 to 0.194 |
| Creatinine clearance 24 months after Tx       | p=0.1761 | -0.253 to 0.185 |
| Creatinine clearance 48 months after Tx       | p=0.1598 | -0.259 to 0.198 |
| Gender of kidney recipient                    | p=0.486  | -0.292 to -0.166 |
| Age of kidney recipient in the time of Tx     | p=0.0104 | 0.0333 to 0.382 |
| **Type of Tx**                                | **p=0.0499** | **0.000439 to 0.467** |
| Period on HD                                  | p=0.3853 | -0.189 to 0.354 |