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CARDIOVASCULAR RISK FACTORS AND ECHOCARDIOGRAPHIC FINDINGS IN PATIENTS ON WAITING LIST FOR CADAVERIC KIDNEY TRANSPLANTATION

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Summary. *Cardiovascular (CV) disease is the main cause of morbidity and mortality in dialysis patients, as well as in the kidney transplant recipient population. Assessing the prevalence of CV diseases and CV risk factors is an essential step in developing risk profiles and individualizing interventions to reduce the cardiovascular morbidity and mortality of kidney transplant recipients. Evaluating the CV organs of cadaveric kidney transplant potential recipients on the waiting list is very important for prevention of developing the post-transplant CV diseases.*
The aim of this study was to determine prevalence of CV diseases and risk factors of patients registered on the waiting list. We performed a retrospective study on patients (pts) registered as waiting for cadaveric kidney transplantation and evaluated their CV status concerning the ECG abnormality and echocardiographic finding. We also discussed CV risk factors in this population.
During the period October 2000-November 2003, 96 potential recipients (42 females, 54 males) were evaluated for cadaveric kidney transplantation at the Institute for Nephrology and Hemodialysis, Clinical Center-Niš. All the patients had sinus ritham, with no registered extra-systole and no conduction abnormality in ECG. 67 pts (69.4%) had EF >50%. The main echocardiography characteristics were left ventricular hypertrophy (LVH) observed in 55 pts (56.9%) and LVH with left ventricular dilatations (LVD) observed in 21 pts (22.2%). Arterial hypertension, hyperlipidemia, smoking and, particularly, anemia were the most frequent risk factors among the dialysis population.
Dialysis doctors should attempt at providing optimal diagnostic procedures and treatment for CV diseases and CV risk factors, even if this generally fails to prevent the CV diseases. Recognition of CV diseases, CV risk factors, and their treatment is essential for better post-transplant surviving in the kidney transplant recipient population.

Key words: *Cardiovascular disease, dialysis, echocardiography, left ventricular hypertrophy, kidney transplantation, hypertension*

Introduction

Patients with end-stage renal disease (ESRD) are at a much higher risk of CV disease than the general population. Evaluating the CV organs of potential recipients for the purpose of preventing or, at least, delaying the development of cardiac abnormalities, understanding the determinants of CV disease, and careful preparation of interventions aimed at correcting them is very important in the management of ESRD patients, particularly those on the waiting list for cadaveric kidney transplantation. There is growing evidence suggesting that prevalence of CV disease among ESRD patients is already high by the time renal replacement treatment is initiated (1, 5, 6). The results of a number of studies suggest that factors leading to the development of CV abnormalities begin to operate very early in the progression of chronic kidney disease, well before patients reach ESRD (Table 1).

Table 1. Multiple risk factors for CV disease in ESRD patients

Traditional risk factors	Risk factors related to ESRD
Hypertension	Hemodynamic overload
Diabetes	Anemia
Dislipidemia	Calcium-phosphate disorders
Smoking	Fluctuation in blood pressure and electrolyte during dialysis
Overweight	Chronic inflammation and oxidative stress
Hyperhomocystenemia	Uremic state

CV disease is the leading cause of death in renal transplant recipients (6). During the evaluation of potential candidates for kidney transplantation, a special attention should be paid to the presence of CV morbidity. Among the diagnostic procedures, ECG and different types of echocardiography (2-D, stress echocardiography) findings should provide the most important details. Coronarography is not a standard diagnostic

procedure for evaluation of CV status of patients registered on the waiting list for cadaveric kidney transplantation (Fig. 2). The aim of this study was to determine the prevalence of CV diseases and risk factors in patients registered on the waiting list.

Patients and Methods

The study involved 96 potential cadaveric kidney recipients (42 females, 54 males) registered on the waiting list for cadaveric kidney transplantation during the period October 2000-November 2003 at the Institute for Nephrology and Hemodialysis, Clinical Center-Niš. The clinical history data included: history of angina pectoris and myocardial infarction, smoking, hypertension, and diabetes. Cholesterol and body mass index were detected in all patients. Standard ECG was done before a dialysis session and categorized into one of the three groups concerning the ritham, conductions, and rhythm disturbances. During trans-thoracic echocardiography, performed the day after the dialysis session using a Toshiba system, a 2.5 MHz transducer in M-mode, and 2D projections, the following data were being observed: percentage of ejection fraction (EF %), presence of left ventricular hypertrophy (LVH), LVH with left ventricular dilatation, right ventricular hypertrophy, and valvular disorders.

Analysis

Standard statistical analyses were calculated in the study group. All data were analyzed using the statistical package NCSS 97. The overall survival (OS) curve was calculated according to the Kaplan and Meier method. OS was calculated from the date of initiation of hemodialysis until death from any cause or the date of the kidney transplantation or the date of the last contact for living patients. The univariate association between individual clinical features and overall survival were determined with the log-rank test. The limit of significance for all analyses was defined as p=0.05.

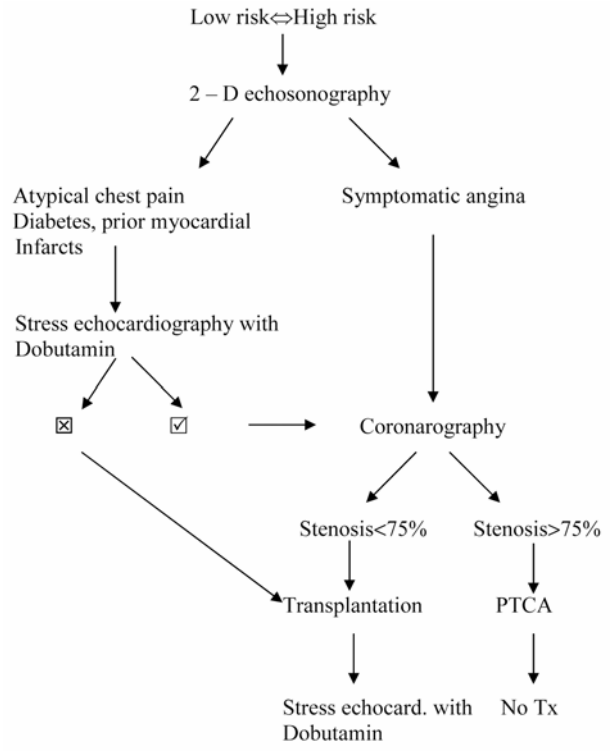

Fig. 1. Algorithm in evaluation of the CV status

Results

During the period from October 2000 until November 2003, 96 potential recipients (42 females, 54 males) were evaluated for cadaveric kidney transplantation at the Institute for Nephrology and Hemodialysis, Clinical Center-Niš. The main demographic finding is shown in Table 2. Vesicouretheral reflux (VUR) was the second cause of developing CRF, and others are shown in Table 3.

Table 2. Demographic data

Females		Males	
42 Pts.	(34.8%)	54 Pts.	(65.2%)
Age (X±SD):	43.96±10.53 yr	Age (X±SD):	48.44±9.12 yr
Time on HD (X±SD):	81.3±39.74 mo	Time on HD (X±SD):	104.8±51.5 mo.*

* P=0,048

Table 3. Main causes of developing CRF

Kidney disease	∑ pts. (%)
GN chr.	53 (54.40)
VUR	11 (11.10)
ADPKD	9 (9.70)
PN chr.	5 (5.50)
DM	4 (4.27)
SLE	3 (2.70)
Sy. Alport	1 (1.40)
Unknown	9 (9.70)

Cardiovascular risk factors

The frequency of CV risk factors is shown in Table 4. Of the total of 96 patients, there were 60 smokers (62.5% of the total population) and 63 patients (65.2% of the total population) had a history of hypertension (HTA). On the other hand, there were only 4 patients with diabetes (DM) (4.27% of the total population) and there were no patients with a history of angina pectoris or other CV diseases.

Table 4. Frequency of cardiovascular risk factors

CV risk factor	∑ pts. (%)
HTA	63 (65.2)
Smoking	60 (62.5)
Lipid disorders	53 (55.0)
BMI < 25	24 (25.0)
DM	4 (4.27)

ECG findings

A very low prevalence of ECG abnormality was registered in patients prior to renal transplantation. There were 84 normal ECG tracings (87.5%). Simple LVH was present in 12 patients (12.5%). All of these patients had sinus ritham, with no registered extra-systole and no conductions abnormality in ECG.

Echocardiographic findings

Ejection fraction (EF %) higher than 50% was found in 67 patients (69.4%). The most frequent finding was LVH, which was seen in 55 patients (56.9%) and accompanied with dilatation of the left ventricle in 21 patients (22.2%). There was a very low rate of aortal (1 patient) and mitral (3 patients) regurgitation. The frequency of echocardiographic disorders is shown in Table 5.

Table 5. Echocardiographic findings

Echocardiographic findings	∑ pts. (%)
EF>50%	67 (69.4)
LVH	55 (56.9)
LVH+LVD	21 (22.2)
Septal hypertrophy	8 (8.3)
Right ventricular dilatation	7 (6.9)
Mitral regurgitation	3 (2.7)
Aortic regurgitation	1 (1.3)

Patient survival

OS was calculated from the date of the initiation of hemodialysis until death from any cause or the date of the kidney transplantation or the date of the last contact for living patients. Of the total population, 50% spent more than 160 months on hemodialysis (Fig. 2).

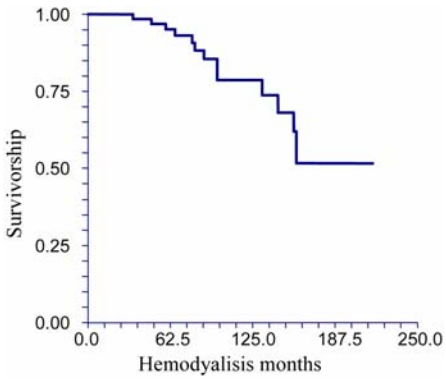

Fig. 2. Total survival of patients on the waiting list

In the univariate survival analysis, the strongest association was found with EF% (Log Rank for EF% P=0.001249 – Fig. 3) and with dilatation of LV (Log Rank for DLV P=0.045979 – Fig. 4). There was no significant correlation with HTA (P=0.6007), smoking (P=0.5187) and lipid disorders (P=0.1253).

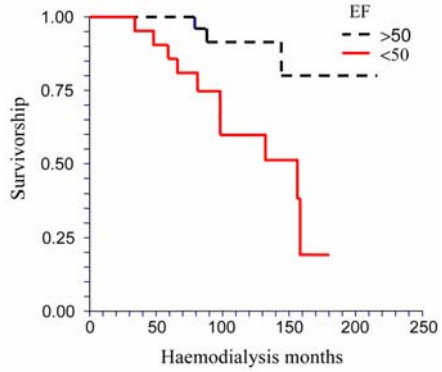

Fig. 3. Univariate survival analysis concerning EF%

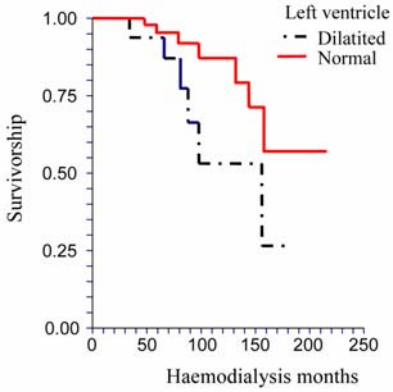

Fig. 4. Univariate survival analysis concerning LVD

Discussion

The aim of this study was to identify the prevalence and predictive importance of CV risk factors prior to renal transplantation. The design is retrospective and must be interpreted with caution, because the study group was chosen among dialysis population to meet the criteria for safe transplantation (much younger, in good condition, without serious concomitant diseases, etc). Despite these considerations, the prevalence of risk factors compares well with other related populations (7, 8, 9, 10, 11, 12) and we have demonstrated that a good systolic function, absence of echocardiographic disorders, strict control of arterial hypertension and smoking are associated with the survival rate in this group.

Arterial hypertension was present in almost 70% of the patients in the current study, which is consistent with the findings in transplant recipients (8, 9) and with the data in other studies of the dialysis population (13). More than 60% were cigarette smokers, which is significantly higher than the reported rate of current smokers in other studies (14). Cigarette smoking at the time of transplantation was associated with a two-fold increased risk of death during follow-up (14).

Lack of ECG abnormalities, history of myocardial infarction or stoke or a history of angina were probably a consequence of the selected group (younger population, in good condition, without serious concomitant diseases, etc.).

Left ventricular hypertrophy is a very often finding during the echocardiographic evaluation of patients undergoing hemodialysis (15). LVH with dilatation and EF were one of the strongest independent risk factors in the univariate analysis (Figures 3-4), thus supporting some recent studies (10) that echocardiographic abnormalities are strong, readily accessible predictors of outcome in renal transplant recipients (14).

Arterial hypertension is one of the basic factors governing pathogenic changes in the circulatory system in patients with a chronic renal disease (16, 17, 18). Autonomic nervous system dysfunction may be among the factors playing a crucial role in systolic function impairment. Chronic end-stage renal disease is accompanied by secondary hyperparathyreoidism. Excessive parathormone concentration, acting directly on cardiomyocytes, leads to cardio-hypertrophy. This mechanism is considered to be one of a number of factors leading to uremic cardio-myopathy.

Conclusion

Cardiovascular (CV) disease is the main cause of morbidity and mortality in dialysis patients, as well as in the kidney transplant recipient population. The significant prevalence of patients undergoing dialysis with signs of well-established CV abnormalities serves as indirect evidence that CV risk factors are present from the early stages of chronic kidney disease. In this context, the early detection and treatment of modifiable risk factors must be seen as a primary challenge for the nephrologist in everyday management of this group of patients. Particular care must be taken to provide optimal treatment for those expecting kidney transplantation.

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KARDIOVASKULARNI FAKTORI RIZIKA ZA NASTAJANJE OBOLENJA SRCA I EHOKARDIOGRAFSKI NALAZ KOD BOLESNIKA NA LISTI ČEKANJA ZA KADAVERIČNU TRANSPLANTACIJU BUBREGA

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Kratak sadržaj: *Kardivaskularne bolesti su najčešći uzrok smrtnosti i obolevanja u populaciji bolesnika koji se leče ponavljanim dijalizama. Veoma slične rezultate vidimo i u studijama koji se bave morbiditetim i mortalitetom bolesnika kod kojih je presadjen bubreg. Pažljivo ispitivanje stanja kardivaskularnog sistema potencijalnih recipijenata kadaveričnog bubrega od velike je važnosti u prevenciji razvoja postransplantacionih kardiovaskularnih bolesti.*
Cilj rada je da se odredi prevalenca kardiovaskularnih bolesti kod bolesnika na listi čekanja za kadaveričnu transplantaciju bubrega.
Uradili smo retrospektivnu studiju kod bolesnika sa liste čekanja za kadaveričnu transplantaciju i odredili kardiovaskularni status u odnosu na EKG promene i ehokardiografski nalaz. Takodje smo ispitivali najvažnije faktore rizika za nastajanje kardiovaskularnih bolesti.
U vremenskom periodu od oktobra 2000. do novembra 2003. godine ispitali smi 96 potencijalnih recipijenata (♀:♂=42 bol.: 54 bol.) kadaveričnog bubrega u Institutu za nefrologiju i hemodijalizu u Nišu. Kod ove grupe bolesnika nismo registrovali značajnije EKG promene. Najznačajnija ehokardiografska promena bila je hipertrofija leve komore koju smo našli kod 55 bolesnika (56,9%), a sledi dilatacija leve komore kod 21 bolesnika (22,2%). Ejekciona frakcija iznad 50% nadjena je kod 67 bolesnika (69,4%). Arterijska hipertenzija, hiperlipidemija, pušenje, a pogotovo sekundarna anemija su najznačajniji faktori rizika kod ove populacije bolesnika.
U toku dijaliznog perioda bolesnicima koji se nalaze na listi čekanja neophodno je obezbediti optimalni dijagnostički i terapijski pristup koji bi obezbedio prevenciju kardiovaskularnih bolesti. Takvim pristupom bi sigurno obezbedili bolje preživljavanje u posttransplantacionom periodu.

Ključne reči: *Kardiovaskularne bolesti, dijaliza, ehokardiografija, hipertrofija leve komore, transplantacija bubrega, arterijska hipertenzija*