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CLINICAL STUDY

Cardiovascular risk assessment prior to kidney transplantation

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ABSTRACT

OBJECTIVES: The objective was to find out risk factors indicating the patients directly to selective coronarography (SCG) to avoid unnecessary non-invasive testing and in their absence to asses low cardiovascular risk and faster inclusion on the waiting list.

BACKGROUND: Cardiovascular diseases (CVD) are the most frequent cause of death in dialysed patients. The aim of our retrospective analysis was to identify risk factors for coronary artery disease (CAD) before kidney transplantation (KTx).

METHODS: Our retrospective analysis consisted of 55 dialysed patients (46 males, 9 females, $p < 0.0001$), undergoing SCG before KTx. We divided the patients according to SCG results (negative, n = 40, positive finding, n = 15).

RESULTS: We confirmed a significantly lower incidence of diabetic nephropathy ($p = 0.0484$), ischaemic heart disease ($p = 0.0174$) and CAD ($p = 0.0001$) in patients without percutaneous coronary intervention (PCI; negative finding). Haemodynamically significant coronary stenosis correlated with the occurrence of stroke in a patient's history ($p = 0.0104$). We identified predictors for performing PCI (positive result): type 2 diabetes mellitus (DM) ($p = 0.0472$), high-density lipoprotein cholesterol ≤ 1.03 mmol/l ($p = 0.0359$), total calcium level ≤ 2 mmol/l ($p = 0.0309$), phosphate level ≥ 1.45 mmol/l (OR 0.2034; $p = 0.0351$).

CONCLUSION: In our analysis, patients with DM and poorly managed chronic kidney disease/mineral bone disease were the riskiest subset of the patients with a positive SCG finding *(Tab. 4, Fig. 2, Ref. 30)*. Text in PDF *www.elis.sk*

KEY WORDS: kidney transplantation, coronary artery disease, selective coronarography, cardiovascular risk.

Abbreviations: ACC/AHA – American College of Cardiology/American Heart Association, ACEi – angiotensin converting enzyme inhibitor, ACS – acute coronary syndrome, AGEP – advanced glycated end products, ARB – angiotensin II receptor blockers, ASA – aminoacyl salicylic acid, BMI – body mass index, CAD – coronary artery disease, CKD – chronic kidney disease, CKD/MBD – chronic kidney disease/mineral bone disease, CVD – cardiovascular diseases, DM – diabetes mellitus, DSE – dobutamine stress echocardiography, ECG – electrocardiogram, ESC – European Society of Cardiology, ESRD – end stage renal disease, HD – haemodynamically, HDL – high-density lipoprotein, IVS – interventricular septum, KTC – kidney transplant candidate, KTx – kidney transplantation, LDL – low-density lipoprotein, MET – metabolic equivalent, PCI – percutaneous coronary intervention, PTH – parathormone, SCG – selective coronarography, TAG – triacylglycerides, TIA – transitory ischaemic attack, TTE – transthoracic echocardiogram, WL – waiting list

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Introduction

Patients with chronic kidney disease (CKD) have a very high incidence of acute cardiovascular events that result from the presence of traditional and non-traditional risk factors. The prevalence of CKD is increasing by 8% annually worldwide, and patients with CKD have a predisposition to cardiovascular diseases (CVD) that manifest in different forms (coronary artery disease, stroke, etc.). The main cardiovascular risk factors are diabetes mellitus (DM), arterial hypertension, albuminuria, dyslipidaemia, and smoking (1). Herzog described a 44.4 % incidence of typical chest pain in the group of dialysed patients in comparison with 68.3 % incidence in the general population without CKD (2).

Non-invasive stress tests are the cornerstone in diagnosing coronary artery disease (CAD) in asymptomatic patients; sensitivity and specificity varies from test to test. ECG stress testing was commonly used because the available, meta-analysis of multiple studies showed a different sensitivity (23–100 %, mean 68 %) and specificity (17–100 %, mean 77 %) (4). Dialysed patients often cannot achieve an optimal heart rate, and thus pharmacologic stress testing should be performed. Dobutamine stress echocardiography (DSE) has a sensitivity from 75 to 95 % and specificity from 76 to 94 %, with a CAD diagnosis accuracy of 90 % (5). A negative DSE result identifies the low-risk population, with 97 % absence of acute cardiovascular events or sudden cardiac death in 12 ± 6

Tab. 1. Basic characteristics of the patients in this study.

n = 55	
Age at time of SCG (years)	60.3±9
Gender (males)	83.6
BMI at time of SCG (kg/m2)	27.6±4.6
Smoking (%)	16.4
Duration of haemodialysis (months)	48.4±36.8
Diabetic kidney disease (%)	32.7
Glomerulonephritis (%)	18.2
Tubulointerstitial nephritis (%)	16.4
Polycystic kidney disease (%)	12.7
Nephrosclerosis (%)	7.3
Other (%)	7.3
Main diagnosis unknown (%)	5.5
Arterial hypertension in anamnesis (%)	94.5
Diabetes mellitus in anamnesis (%)	45.5
- Diabetes mellitus type 1 (%)	9.1
- Diabetes mellitus type 2 (%)	34.5
Secondary diabetes mellitus (%)	1.8
Stroke in anamnesis (%)	5.5
Ischaemic heart disease in anamnesis (%)	78.2
Chronic heart failure in anamnesis (%)	3.6
Peripheral artery disease in anamnesis (%)	12.7
Cholesterol at time of SCG (mmol/l)	4.8±1.2
HDL at time of SCG (mmol/l)	1.2±0.4
LDL at time of SCG (mmol/l)	2.7±1
TAG at time of SCG (mmol/l)	2±1.3
Haemoglobin at time of SCG (g/l)	110.6±10.6
PTH at time of SCG (ng/l)	280±238
Calcium level at time of SCG (mmol/l)	2.2±0.3
Phosphate level at time of SCG (mmol/l)	1.7±0.4
Use of ACEi/ARB at time of SCG (%)	56.4
Use of beta-blockers at time of SCG (%)	83.6
Use of statins at time of SCG (%)	52.7
Use of ASA at time of SCG (%)	74.5
Treatment of CKD/MBD at time of SCG (%)	58.2
Left ventricle ejection fraction (%)	56.9±6
IVS (mm)	12.4±1.8
Treatment with PCI (%)	27.3
Coronary artery disease (%)	58.2
Haemodynamically significant stenosis (%)	29.1
Haemodynamically insignificant stenosis (%)	45.5

SCG – selective coronarography; BMI – body mass index; HDL – high-density lipoprotein; LDL – low-density lipoprotein; TAG – triacylglycerides; PTH – parathormone; ACEi – angiotensin converting enzyme inhibitor; ARB – angiotensin II receptor blockers; ASA – aminoacyl salicylic acid, CKD/MBD – chronic kidney disease/mineral bone disease; IVS – interventricular septum

months (6). According to the ACC/AHA, in the general population, there is no need to perform stress testing in the patients with functional capacity > 10 metabolic equivalents (METs). According to the European Society of Cardiology (ESC)/ European Society of Hypertension (ESH) guidelines, non-invasive stress testing should be performed in patients with poor functional capacity (< 4 METs) with the presence of two or more risk factors (DM, anamnesis of cardiovascular disease, haemodialysis > 1 year, age > 60 years, arterial hypertension, left ventricular hypertrophy, dyslipidaemia) (7). In the patients with end stage renal disease (ESRD) and a low functional capacity, only one risk factor is needed to perform non-invasive stress testing. If there are three or more risk factors, patients should undergo non-invasive stress testing regardless of the functional capacity (3). Coronary revascularisation should not be performed for the purpose of decreasing cardiovascular risk. The CARP study did not confirm differences in the survival between the patients treated pharmacologically and revascularized patients (8). Although the presence of haemodynamically (HD) significant stenosis of the coronary artery (lumen occlusion > 70 %) was a predictor of acute cardiovascular events in post-transplant period in the study of 126 kidney transplant candidates, 94 % of the patients without CAD did not experience an acute cardiovascular event within 48 months. On the other hand, 54 % of the patients with CAD did not experience an event in the same time frame (9).

Ramphul et al created a diagnostic algorithm for stratifying the patients into the risk groups: high risk patients are older than 60 years or younger than 60 years with at least one risk factor (DM, CAD, peripheral artery disease, heart failure), low risk patients are 40–60 years old and minimal risk patients are younger than 40 years. Based on the risk group, they chose to examine the modality. This stratification indicated that the patients with minimal risk have a 0.7 % incidence of acute cardiovascular events annually, while the patients in very high-risk group have 8.9 % (10). The recent study by Tabriziani stratified the patients into the risk groups based on the presence of risk factors, gender and age. A specific group with stricter criteria and diagnostic tests are the patients with DM with respect to duration and type of DM (11).

Kidney transplantation (KTx) is the best option for renal replacement therapy in the patients with ESRD. This modality improves survival, reduces associated complications, and improves the quality of life (12). When KTx is successful, patient´s mortality is reduced. However, pre-existing CVD determine overall patient survival after KTx. For patients with low or medium cardiovascular risk, KTx is beneficial during the early post-transplant period, while the benefit of KTx in the patients with high cardiovascular risk is apparent from 6 to 12 months post-KTx (13). Therefore, it

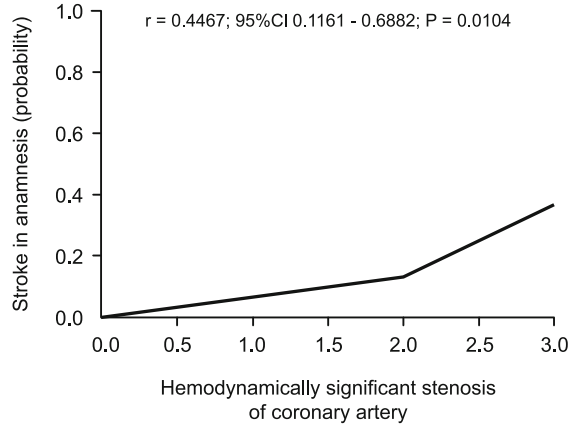

Fig. 1. Correlation between stroke and haemodynamically significant stenosis of the coronary arteries.

Tab. 2. Comparison of the percutaneous coronary intervention (PCI) and control groups.

	Control group n = 40	PCI group n = 15	p
Age at time of SCG (years)	60±9,5	61.2±7.7	0.6662
Gender (males)	82.5	86.7	0.7102
BMI at time of SCG (kg/m2)	27.7±4.6	27.3±4.8	0.7776
Smoking (%)	12.5	26.7	0.2091
Duration of haemodialysis (months)	50.3±40	43.3±27.5	0.5359
Diabetic kidney disease (%)	**25**	**53.3**	**0.0484**
Glomerulonephritis (%)	17.5	20	0.8320
Tubulointerstitial nephritis (%)	15	20	0.6583
Polycystic kidney disease (%)	17.5	0	0.0857
Nephrosclerosis (%)	10	0	0.2076
Other (%)	10	0	0.2076
Main diagnosis unknown (%)	5	6.7	0.8066
Arterial hypertension in anamnesis (%)	97.5	86.7	0.1193
Diabetes mellitus in anamnesis (%)	40	60	0.1887
Stroke in anamnesis (%)	7.5	0	0.2798
Ischaemic heart disease in anamnesis (%)	**70**	**100**	**0.0174**
Chronic heart failure in anamnesis (%)	5	0	0.3820
Peripheral artery disease in anamnesis (%)	12.5	13.3	0.9347
Cholesterol at time of SCG (mmol/l)	4.8±1.2	4.8±1.1	1.0000
HDL at time of SCG (mmol/l)	1.3±0.4	1.1±0.4	0.1046
LDL at time of SCG (mmol/l)	2.7±1	2.8±1	0.7425
TAG at time of SCG (mmol/l)	2±1.4	2.1±1.3	0.8110
Haemoglobin at time of SCG (g/l)	111±10.2	109.7± 12.1	0.6908
PTH at time of SCG (ng/l)	302±264	224±151	0.2867
Calcium level at time of SCG (mmol/l)	2.2±0.2	2.1±0.4	0.2228
Phosphate level at time of SCG (mmol/l)	1.8±0.5	1.6±0.3	0.1531
Use of ACEi/ARB at time of SCG (%)	60	46.7	0.3801
Use of beta-blockers at time of SCG (%)	85	80	0.6583
Use of statins at time of SCG (%)	50	60	0.5121
Use of ASA at time of SCG (%)	70	86.7	0.2095
Treatment of CKD/MBD at time of SCG (%)	60	53.3	0.6567
Left ventricle ejection fraction (%)	57.1±6.3	56.3±5.5	0.6666
IVS (mm)	12.5±2	12.2±1.5	0.6005
Coronary artery disease (%)	**42.5**	**100**	**0.0001**

PCI – percutaneous coronary intervention; SCG – selective coronarography; BMI – body mass index; HDL – high-density lipoprotein; LDL – low-density lipoprotein; TAG – triacylglycerides; PTH – parathormone; ACEi – angiotensin converting enzyme inhibitor; ARB – angiotensin II receptor AT1 blockers; ASA – 5-aminoacyl salicylic acid; IVS – interventricular septum

is crucial to assess the cardiovascular risk prior to kidney transplantation to anticipate or prevent acute cardiovascular events and maximize KTx benefits.

The primary aim for our study was to identify risk factors for CAD in the patients with ESRD prior to KTx. The secondary aims were to identify the effect of pharmacotherapy in developing CAD, identify low-risk patients that would allow a swift inclusion on the waiting list (WL) and recognize the risk factors that would contraindicate the patient listing on the WL or KTx.

Materials and methods

Our study was a retrospective analysis of the patients after KTx in the transplant centre in Martin, Slovakia. They underwent a diagnostic algorithm for CVD prior to KTx by undergoing a selective coronarography (SCG). At the time of coronarography, we obtained necessary information such as: age, gender, body mass index (BMI), smoking status, duration of haemodialysis, type of haemodialysis, cause of ESRD, other comorbidities (arterial hypertension, type of DM, stroke, ischaemic heart disease, chronic heart failure, peripheral artery disease), medication used (aminoacyl salicylic acid [ASA], statins, type of beta-blockers, drugs for CKD/mineral bone disease (MBD)). At the time of SCG, a blood sample was taken, and we monitored the levels of high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triacylglycerides (TAG), total cholesterol, haemoglobin and serum levels of total calcium, phosphate and parathormone (PTH). The patients underwent transthoracic echocardiogram (TTE) prior to coronarography. We monitored the following echocardiographic parameters: width of interventricular septum (IVS) and left ventricle ejection fraction with the biplane Simpson's method.

According to coronarography results, patients were divided into two groups: patients requiring revascularisation because of HD significant stenosis of the coronary artery, which was defined as arterial lumen occlusion > 75 % (percutaneous intervention (PCI) group) and group of patients without HD significant stenosis of the coronary arteries (control group).

We used a certified statistical program, namely MedCalc version 13.1.2 (MedCalc Software VAT registration number BE 0809 344,640, Member of International Association of Statistical Computing, Ostend, Belgium). Comparisons of continuous variables between the groups were performed using parametric (*t*-test) or non-parametric (Mann–Whitney) tests; associations between the categorical variables were analysed using the $\chi 2$ test and Fisher's exact test, as appropriate. Logistic regression was used for multivariate analysis for independent predictors of CAD. A p value < 0.05 was considered to be statistically significant.

Results

A total of 55 patients (46 men and 9 women) were involved in this study. There were significantly more men than women (p < 0.0001). The mean patient age was 60.3 ± 9 years (41–76, median 61 years). A positive ECG stress test occurred in 10.9 % of the patients, while 32.7 % had a negative result and stress testing

was not performed in 56.4 % of the patients. HD significant stenosis of the coronary arteries was presents in 16 patients (29.1 %): one vessel CAD (10 patients), two-vessel CAD (4 patients) and multiple-vessel CAD (2 patients). The basic characteristics of the patients in our study are shown in the Table 1.

There were no differences between the PCI and control groups with regards to age, gender, BMI or smoking status. In the PCI group, there was a statistically significant difference in the incidence of diabetic kidney disease (p = 0.0484), ischaemic heart disease in anamnesis (p = 0.0174) and CAD (p = 0.0001). There were no differences in biochemical parameters (lipid profile, calcium-phosphate metabolism, level of haemoglobin), pharmacotherapy or echocardiographic parameters (left ventricular ejection fraction and IVS width) between the groups (Tab. 2).

We confirmed a positive correlation between the presence of stroke or transitory ischaemic attack (TIA) in personal anamnesis and incidence of HD significant stenosis of the coronary arteries (Fig. 1).

By using a logistic regression, we confirmed independent risk factors for HD significant stenosis of the coronary arteries (Tab. 3). Independent risk factors were: DM in the patient's history (odds ratio (OR) 2.3492; 95% confidence interval (CI) = 1.0105–5.4615; p = 0.0472), and levels of HDL cholesterol < 1.03 mmol/l (OR 4.3276; 95% CI = 1.1009–17.0123; p = 0.0359), calcium ≤ 2.0 mmol/l (OR 2.4935; 95% CI 1.0926–5.6905; p = 0.0309) and phosphate ≥ 1.45 mmol/ (OR 0.2034; 95% CI 0.0462–0.8946; p = 0.0351).

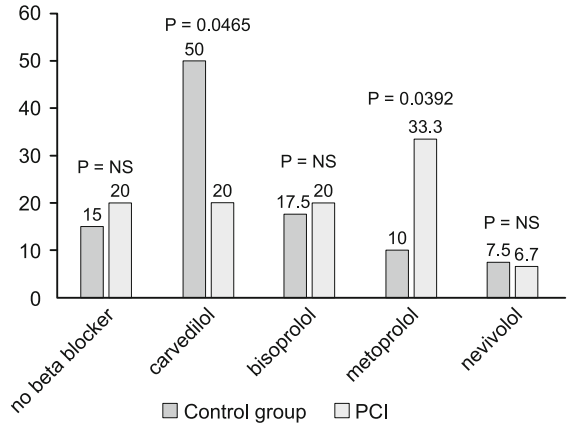

Fig. 2. Types of beta-blocker used in percutaneous coronary intervention (PCI) and control group patients.

There were significant differences between the groups with regards to the type of beta-blocker. Metoprolol use was significantly higher in the PCI group (p = 0.0392), while carvedilol was used more often in the control group (p = 0.0465) (Fig. 2).

At the end of our study, we confirmed several risk factors that were potentially contraindicative for placement on the WL or for KTx. They included: smoking (p = 0.0079), type 2 DM (p = 0.0087) and use of statins (p = 0.0025). HD significant stenosis of the coronary arteries was not a statistically significant risk factor that contraindicated patients for KTx or not listing them on the WL (Tab. 4).

Tab. 3. Independent risk factors for haemodynamically significant coronary artery stenosis (logistic regression).

PCI	Odds ratio	95% CI	p
Age at time of SCG ≥ 60 years	1.1244	0.3337–3.7879	0.8500
Gender (males)	2.0264	0.3056–13.4391	0.4644
BMI at time of SCG ≥ 30 kg/m2	1.4966	0.3692–6.0661	0.5723
Smoking	2.5048	0.5049–12.4267	0.2612
Duration of haemodialysis ≥ 60 months	0.5870	0.1202–2.8675	0.5104
Diabetic kidney disease	5.2276	0.4684–58.3489	0.1790
Arterial hypertension in anamnesis	0.1277	0.0093–1.7490	0.1232
Diabetes mellitus in anamnesis	**2.3492**	**1.0105–5.4615**	**0.0472**
Stroke in anamnesis	0.3456	0.01684–7.0948	0.4908
Ischemic heart disease in anamnesis	13.5965	0.7529–24.5386	0.0771
Chronic heart failure in anamnesis	0.4968	0.02253–10.9519	0.6575
Peripheral artery disease in anamnesis	1.1234	0.1349–9.3582	0.9143
Cholesterol at time of SCG ≥ 5,17 mmol/l	2.6385	0.6589–10.5666	0.1705
HDL at time of SCG ≤ 1,03 mmol/l	**4.3276**	**1.1009–17.0123**	**0.0359**
LDL at time of SCG ≥ 3,3 mmol/l	2.2197	0.4771–10.3270	0.3094
TAG at time of SCG ≥ 1,7 mmol/l	1.1556	0.3499–3.8163	0.8125
Haemoglobin at time of SCG < 110 g/l	2.1725	0.5679–8.3114	0.2571
PTH at time of SCG > 300 ng/l	0.4130	0.1016–1.6785	0.2164
Ca at time of SCG ≤ 2 mmol/l	**2.4935**	**1.0926–5.6905**	**0.0309**
P at time of SCG ≥ 1,45 mmol/l	**0.2034**	**0.0462–0.8946**	**0.0351**
Ejection fraction of left ventricle < 50 %	0.8630	0.1645–4.5281	0.8617
IVS > 12 mm	1.4562	0.3653–5.8041	0.5942

PCI – percutaneous coronary intervention; SCG – selective coronarography; BMI – body mass index; HDL – high-density lipoprotein; LDL – low density lipoprotein; TAG – triacylglycerides; PTH – parathormone; Ca – calcium; P – phosphate; IVS – interventricular septum

Discussion

CVD are the most common cause of mortality and complications after KTx. The risk of death in kidney transplant candidates (KTC) is 10-times higher, when they have CVD. Furthermore, this risk is 50-times higher than the mean nonfatal acute cardiovascular events, when compared to the general population. Notably, approximately one third of KTC have a significant stenosis of the coronary arteries (14, 15) Our study confirmed this fact because this dysfunction was present in 29.1 % of the patients.

Our study confirmed independent risk factors for severe CAD. One of those risk factors was altered calcium-phosphate metabolism (serum level of calcium ≤ 2 mmol/l and serum level of phosphate ≥ 1.45 mmol/l). Hyperphosphatemia is associated with increased risk of acute cardiovascular events in the patients with known CAD (16). In the observational retrospective study by Shin et al (17), the authors confirmed an association between hyperphosphatemia and

Tab. 4. Comparison of patients on the kidney transplantation waiting list (Tx/WL – yes) and patients contraindicated transplantation (Tx/WL – no).

	Tx/WL – yes n=43	Tx/WL – no n=12	p
Age at time of SCG (years)	59.5±9.3	63.3±7.2	0.9168
Gender (males)	83.7	83.3	0.9738
BMI at time of SCG (kg/m2)	27.1±4.7	29.4±4.1	0.1301
Smoking (%)	**2.3**	**25**	**0.0079**
Duration of haemodialysis (months)	49.3±39	45.3±29.4	0.7433
Diabetic kidney disease (%)	30.2	41.7	0.4569
Glomerulonephritis (%)	16.3	25	0.4937
Tubulointerstitial nephritis (%)	18.6	8.3	0.3980
Polycystic kidney disease (%)	11.6	16.7	0.6422
Nephrosclerosis (%)	7	8.3	0.8793
Other (%)	9.3	0	0.2770
Main diagnosis unknown (%)	7	0	0.3503
Arterial hypertension in anamnesis (%)	93	100	0.3503
Diabetes mellitus in anamnesis (%)	39.5	66.7	0.0973
- Diabetes mellitus type 1 (%)	11.6	0	0.2202
- Diabetes mellitus type 2 (%)	**25.6**	**66.7**	**0.0087**
Secondary diabetes mellitus (%)	2.3	0	0.5994
Stroke in anamnesis (%)	2.3	16.7	0.0540
Ischaemic heart disease in anamnesis (%)	74.4	91.7	0.2037
Chronic heart failure in anamnesis (%)	2.3	8.3	0.3289
Peripheral artery disease in anamnesis (%)	9.3	25	0.1528
Cholesterol at time of SCG (mmol/l)	4.9±1.1	4.7±1.4	0.6023
HDL at time of SCG (mmol/l)	1.3±0.4	1.1±0.3	0.1142
LDL at time of SCG (mmol/l)	2.8±1	2.6±1.1	0.5428
TAG at time of SCG (mmol/l)	1.9±1.4	2.3±1	0.3600
Haemoglobin at time of SCG (g/l)	111±11.5	108.8±6,6	0.5304
PTH at time of SCG (ng/l)	308±259	184±107	0.1130
Calcium level at time of SCG (mmol/l)	2.2±0.2	2.1±0.5	0.2942
Phosphate level at time of SCG (mmol/l)	1.7±0.5	1.7±0.4	1.0000
Use of ACEi/ARB at time of SCG (%)	60.5	41.7	0.2499
Use of beta-blockers at time of SCG (%)	79.1	100	0.0862
Use of statins at time of SCG (%)	**41.9**	**91.7**	**0.0025**
Use of ASA at time of SCG (%)	76.7	66.7	0.4861
Treatment of CKD/MBD at time of SCG (%)	55.8	66.7	0.5024
Left ventricle ejection fraction (%)	56.8±5.6	57.2±7.6	0.8408
IVS (mm)	12.4±1.9	12.7±1.8	0.6270
Treatment with PCI (%)	55.8	66.7	0.5024
Coronary artery disease (%)	27.9	25	0.8433
Haemodynamically significant stenosis (%)	30.2	33.3	0.8386
Haemodynamically insignificant stenosis (%)	44.2	50	0.7237

PCI – percutaneous coronary intervention; SCG – selective coronarography; BMI – body mass index; HDL – high-density lipoprotein; LDL – low density lipoprotein; TAG – triacylglycerides; PTH – parathormone; Ca – calcium; P – phosphate; ACEi – angiotensin converting enzyme inhibitor; ARB – angiotensin II receptor AT1 blockers; ASA – 5-aminoacyl salicylic acid; IVS – interventricular septum

increased coronary calcification in patients with CKD as well as in patients with a preserved renal function. This study confirmed independent risk factors (serum levels of calcium, phosphate, and calcium-phosphate products) for coronary atherosclerosis, particularly in patients with DM, where advanced glycated end products (AGEP) enhanced mineralisation and CAD incidence on the background of mineral imbalance (17).

HDL-C particles enzymatically remove oxidised LDL particles (which increase atherogenicity). CAD development increases, when LDL-C levels are increased concomitant with reduced HDL-C (18). Our study revealed that HDL-C $\leq$ 1.03 mmol/l was an independent risk factor of HD significant stenosis of the coronary arteries (p = 0.0359). Patients with low HDL-C have increased risk of CAD, in stent re-stenosis after PCI and mortality of cardiovascular causes, particularly if the patients are males and have DM (19). The retrospective study of Kashayar and Mohagehi demonstrated that even with effective LDL-C decrease to therapeutic levels, in the long term, elevating HDL-C should be a priority to prevent cardiovascular mortality (20).

Our study revealed that DM was an independent risk factor for severe CAD (p = 0.0359). The presence of DM worsened cardiovascular prognosis 3-fold compared with the non-diabetic population (21). According to the NHANES study, the prevalence of diabetic kidney disease (DKD) is increasing, and it is one of the most common causes of ESRD. Our data confirmed this finding because DKD was the most common cause of ESRD (32.7 %) with a significantly increased incidence in the PCI group (53 % versus 25 % in the control group, p = 0.0484). This difference can be explained by the DM duration. In the study of 175 patients, the authors confirmed macrovascular complications, including coronary artery calcification and number and degree of affected coronary arteries were time dependent with its stabilization over 5 to 10 years (22).

In our analysis, there was a positive link between stroke (or TIA) in anamnesis and HD significant stenosis of the coronary arteries (p = 0.0104). Risk factors for both diseases (stroke and CAD) were similar, but not the same. Patients with anamnesis of stroke and severe intracranial atherosclerosis also had an increased incidence of dyslipidaemia, metabolic syndrome, and type 2 DM (23). Hypothetically, if the severity of coronary artery atherosclerosis is analogous with cerebral artery atherosclerosis, in our study type 2 DM (p = 0.0472) and dyslipidaemia (low HDL-cholesterol, p = 0.0359) would contribute to the development of severe CAD in the PCI group. In the AMISTAD study, authors observed an association between a $\geq$ 50 % occurrence of coronary artery stenosis (verified by coronarography) in 26 % of the patients

with asymptomatic CAD and stroke of different aetiologies; 62 % of the patients had borderline insignificant atherosclerotic changes of coronary arteries (24). In the AMISTAD substudy, the authors revealed a 2-fold higher risk of acute cardiovascular events in the patients, who had suffered non-fatal ischaemic stroke and had asymptomatic CAD diagnosed by coronarography (25).

Our retrospective analysis found a difference between beta-blockers used in the PCI and the control groups. In the PCI group (with more severe CAD), the cardio selective beta-blocker (metoprolol) was used more often (33.3 versus 10 % for the control, p = 0.0392). Metoprolol increases insulin resistance and causes hyperinsulinemia. This dysregulation leads to functional and structural changes in coronary arteries (26). In the control group, carvedilol was used more often (50 % versus 20 % for the PCI group, p = 0.0465). In the COMET study, type 2 DM development was reduced by 22 % in the patients using carvedilol compared to metoprolol in 5-year follow-up (27). In the randomised, double-blind study, the authors compared the effect of metoprolol and carvedilol in the patients with type 2 DM and arterial hypertension and observed a significant reduction in the risk of albuminuria progression and better compensated DM with lower levels of glycated haemoglobin in the patients using carvedilol (28). These data are consistent with the finding in our study: low levels of HDL-C and type 2 DM are risk factors for HD significant stenosis of the coronary arteries.

In our study, smoking was identified as a risk factor that might potentially contraindicate patients for placement on the KTx WL (p = 0.0079). Smoking is not an absolute contraindication for KTx. It is a traditional risk factor for CVD: smokers have a higher risk of generalised atherosclerosis that affects carotid or lower limb circulation. An increased risk of incidence of comorbidities delays listing KTC on the KTx WL due to diagnostic and therapeutic interventions. Myriad studies confirmed the negative effect of smoking on graft survival and survival of the patients (29).

Type 2 DM is the most common type of DM. Its associated micro- and macrovascular complications lead to functional and structural changes of vessels. Its presence prolongs the time for placing a patient on the KTx WL because it is necessary to perform diagnostic methods to unmask asymptomatic comorbidities. In our study, a significant number of patients were contraindicated or not listed for KTx due to the presence of type 2 DM (p = 0.0087).

Type 2 DM – along with dyslipidaemia – is part of metabolic syndrome. It is an independent risk factor for developing acute cardiovascular events, which was confirmed in the study of 337 patients after KTx, with 32 % prevalence of metabolic syndrome (p = 0.002) (30). Statins were more often used in the risk group for KTx (p = 0.0025), meaning that patients in this group were more often treated for dyslipidaemia. Although there was no difference in LDL-C levels (for which statins are used to decrease), patients listed on the KTx WL, who already underwent KTx did not have at least two risk factors of metabolic syndrome.

Conclusion

Patients with ESRD have a very high risk for developing cardiovascular events. KTx is the most beneficial type of renal replacement therapy, and it improves patient survival. To maximally benefit from KTx, clinicians must identify potential asymptomatic comorbidities and risk factors. CVD represent the most common cause of complications and mortality of the patients after KTx, which can compromise the maximal benefit from KTx. Diagnosis of CAD in ESRD is complicated due to incoherent signs and symptoms in anamnesis, physical findings, echocardiographic abnormalities, and low prediction value of stress testing. Potential revascularization in the patients with suspected CAD is sometimes a long and complicated process. A prolonged time spent in dialysis worsens the prognosis of patient and graft function after KTx. Thus, the goal of transplantation centres is to shorten the time interval between beginning of dialysis and listing patients on the WL. For this purpose, it is necessary to identify high-risk groups of the patients by analysing the presence of risk factors with incidence of comorbidities directly with SCG. On the other hand, identifying low risk patients with a low probability of CAD can quicken their placement on the WL without having to perform unnecessary stress testing.

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