Chronic kidney disease in patients with significant left main coronary artery disease qualified for coronary artery bypass graft operation

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According to the guidelines and experts' opinion, chronic kidney disease can be diagnosed when estimated glomerular filtration rate (eGFR) is lower than 60 ml/min/1.73 m^2 and such a filtration rate lasts for more than 3 months. Impaired kidney function accelerates the progress of atherosclerosis, significantly increases the risk of adverse cardiovascular events and worsens prognosis in patients with cardiac diseases. This risk increases in patients with slightly decreased renal function but increases drastically in patients on regular dialysis [1–3].

According to epidemiological data, the rate of chronic kidney disease is growing steadily. About 11% of the population in the United States and Australia have eGFR < 60 ml/min/1.73 m^2. In Poland, 10–13% of the general population suffer from chronic kidney disease [4–7].

Among the patients hospitalized due to coronary artery disease (CAD), 5–7% are diagnosed with left main disease (LMD), the most severe form of CAD. Patients with LMD require urgent revascularization, either a coronary artery bypass graft (CABG) operation or percutaneous coronary intervention (PCI) [8]. Presence of chronic kidney disease in these patients may increase the risk of complications and mortality connected with cardiac operation. After coronary angiography and PCI contrast-induced acute kidney injury (CI-AKI) is more frequently observed. It was also observed that in-hospital and late mortality are higher in patients with CI-AKI [9, 10]. Cardiac operation in the group with chronic kidney disease correlates with higher mortality and higher risk of acute kidney injury which requires dialysis [11].

All popular surgical scores take into account serum concentration of creatinine as a factor influencing operative risk. Nevertheless, the correlation between concentration of creatinine and eGFR is not linear. Patients with impaired renal function may have normal creatinine concentration in serum. Estimated glomerular filtration rate is crucial in precise assessment of kidney function, especially in high cardiovascular risk patients such as individuals with LMD treated with CABG [12].

The aim of the study was to assess the prevalence of chronic kidney disease evaluated by eGFR in patients with LMD and its impact on 30-day prognosis after CABG.

During 2 years (2006–2008) 5000 patients underwent coronary angiography in the Department of Invasive Cardiology in Bialystok, Poland. We investigated 257 consecutive patients with significant LMD. Left main disease was recognized when the lumen of coronary artery disease was < 50%. The majority of the group was treated invasively. One hundred and seventy-two (67%) of the patients underwent CABG, 19 (7%) underwent PCI without left main stem protection, 30 (12%) of the group had CABG previously. The remaining 36 (14%) persons were treated conservatively.

The study inclusion criteria were 1) confirmed left main coronary artery stenosis, 2) informed consent obtained from each patient. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the local ethics committee. The exclusion criterion was life-limiting non-cardiac disease. No upper age limit was used.

Coronary angiography was performed by injection of contrast medium (low osmolarity, low viscosity) via 6 Fr catheters after 200 µg of intracoronary glyceryl trinitrate (ICGTN), filmed at 12.5 frames/s. The procedure was done via the radial or femoral route by the standard Judkins technique. Contrast flow through the epicardial vessel was graded with the standard Thrombolysis In Myocardial Infarction trial (TIMI trial) flow scale of 0 to 3. All angiograms were analysed by 2 observers blinded to clinical and echocardiographic results.

Eventually we enrolled 163 patients with LMD treated with CABG and with known body mass. We used the Cockcroft-Gault (C-G) formula to assess creatinine clearance [13] and modified Modification of Diet in Renal Disease (MDRD) [14] and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations to calculate eGFR [15]. We also evaluated creatinine clearance according to the Cockcroft-Gault formula using calculated lean body mass.

The patients were divided into 2 groups according to eGFR estimated by the MDRD formula: with eGFR < 60 ml/min/1.73 m^2 and with eGFR ≥ 60 ml/min/1.73 m^2.

Follow-up was done for 161 patients treated with CABG 30 days after the procedure. We gathered information either from the patients or from their families by telephone contact. Missing information was obtained from the Polish population registry (Ministry of the Interior and Administration) in Bialystok, Poland.

Complications after CABG were assessed in 161 patients operated on in the Department of Cardiac Surgery of the Medical University of Bialystok, Poland. Only 2 patients underwent operations in other cardiac centres. We analysed perioperative mortality, mortality after the procedure and the following complications: stroke, pneumonia or pleuritis, atrial fibrillation, cardiac tamponade, reoperation due to bleeding or low cardiac output, difficulties with healing of wounds after sternotomy and saphenectomy and dehiscence of the sternum.

The prognosis was assessed by 5 scores of cardiac surgical risk: EuroSCORE (numerical and logistic model), Parsonnet's score, Cleveland score and the Polish Score of Surgical Risk [16–20].

The patients were treated with the following drugs: acetylsalicylic acid, β-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, statins, unfractionated heparin or low molecular weight heparin.

The results were analysed using statistical methods from the GRETL (Gnu Regression, Econometrics and Time-series Library) set and Statistica 10. Differences in means of continuous variables were compared using Student's *t* test or the Mann-Whitney *U* test. Additional analysis of correlations between non-categorical variables was performed using Pearson or Spearman tests, where applicable. Multivariate logistic regression was used to test associations between variables (age, sex, diabetes, body mass index (BMI), acute coronary syndrome, ejection fraction, glycaemia, cholesterol fractions, eGFR assessed by various methods and others) and outcomes. Data are expressed as means and 95% confidence intervals (95% CI). Relative frequencies are used to present categorical variables. These variables were assessed with the χ^2 test. A p value of less than 0.05 was considered as statistically significant.

Values of eGFR/creatinine clearance were calculated according to three different formulae and also according to the Cockcroft-Gault formula taking into account lean body mass. The results are shown in Figure 1.

There were 42 (26%) patients with eGFR < 60 ml/min/1.73 m^2 and 141 (74%) persons with eGFR ≥ 60 ml/min/1.73 m^2 according to the MDRD equation. The patients with lower eGFR were older. Women made up over half of the group (54.8%). Patients with eGFR < 60 ml/min/1.73 m^2 had lower left ventricular ejection fraction. There were fewer smokers in this group but more patients with diabetes. More patients with LMD and eGFR < 60 ml/min/1.73 m^2 than in the other group were hospitalized due to acute coronary syndromes (Table I). Higher surgical risk was assessed in the group with impaired kidney function according to all cardiac surgical scores used by us (Table I).

In the group with eGFR < 60 ml/min/1.73 m^2 we found significantly lower haemoglobin concentration (Table I). Kidney function also influenced the type of operations. The patients with lower eGFR were more frequently operated on with off-pump cardiopulmonary bypass (Table II). This group also

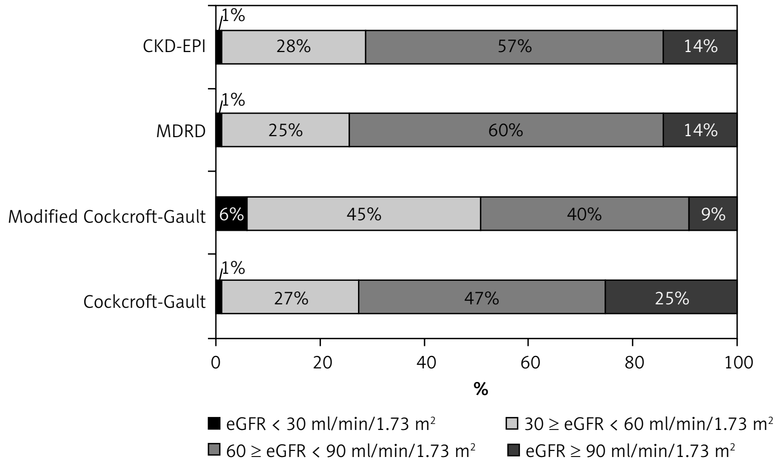

Figure 1. Distribution of eGFR/creatinine clearance values according to four different formulae used for calculations (n = 163 patients)

needed a valve operation more often than the other group.

The patients with eGFR < 60 ml/min/1.73 m^2 had significantly more complications with wound healing on 30-day follow-up (p = 0.004). There were no significant differences in 7-day or 30-day mortality and complications such as reoperation due to bleeding or low cardiac output (Table III).

On multivariate analysis, complications after bypass surgery were significantly more frequent in women (OR = 0.34; 95% CI: 0.05–1.68; p = 0.035), patients with diabetes (OR = 5.02; 95% CI: 0.47–2.75, p = 0.005), with high BMI (OR = 1.14; 95% CI: 0.03–0.22; p = 0.007), low concentrations of HDL cholesterol (OR = 0.93; 95% CI: 0.12–0.018; p = 0.009) and low eGFR (OR = 0.95; 95% CI: 0.07–0.005; p = 0.026).

In multivariate logistic regression, the following parameters correlated with death on the 30-day follow-up: age (OR = 1.21; 95% CI: 0.008–0.38, p = 0.04), high glycaemia on admission (OR = 1.02; 95% CI: 0.003–0.038; p = 0.018) and low left ventricular ejection fraction (OR = 1.10; 95% CI: 0.03–0.16; p = 0.003).

Impairment of kidney function with eGFR < 60 ml/min/1.73 m^2 is a well-established risk factor of worse prognosis in patients treated with CABG and PCI.

Patients with LMD have poor prognosis. They usually need urgent revascularization. The treatment of choice is CABG [21, 22]. As the procedure is either urgent or accelerated, there is a need for quick assessment of cardiosurgical risk. Reliable risk evaluation may increase the chances of survival.

In our study we investigated the degree of renal impairment in patients with LMD treated with CABG. Kidney function was assessed using eGFR/creatinine clearance according to three different formulae.

Distribution of eGFR evaluated by MDRD and CKD-EPI was very similar. We observed only a 3% difference between the number of patients in stage II and III of chronic kidney disease in favour of stage II according to the MDRD equation, and in favour of stage III according to the CKD-EPI equation. Similar distribution of eGFR according to MDRD was found by Cooper *et al.* [23] among patients treated with CABG. The distribution was as follows: 26% of patients with eGFR < 60 ml/min/1.73 m^2, 51% in stage II of chronic kidney disease, 22% with eGFR ≥ 60 ml/min/1.73 m^2 and 1% on dialysis.

We achieved slightly different percentage values in the distribution of creatinine clearance according to the Cockcroft-Gault formula. Although the number of patients in stage III of chronic kidney disease was comparable to the number of patients classified according to MDRD and CKD-EPI, fewer patients were found in stage II. The highest percentage (25%) of patients with eGFR > 90 ml/min/1.73 m^2 was observed when calculations were made using the Cockcroft-Gault formula.

Results achieved by the Cockcroft-Gault formula were overestimated due to excessive body weight of the patients. That is why we did our calculations once more according to the Cockcroft-Gault formula, using lean body mass. Then eGFR < 60 ml/min/1.73 m^2 was found in 51% of the patients, including 6% in stage IV.

According to Szummer *et al.* [24], the largest difference between the Cockcroft-Gault and MDRD estimations was seen when patients were divided according to gender, age, and weight, as the C-G formula estimated a lower GFR in women, the elderly, and those with low body weight. In the Szummer *et al.* study [24], C-G had a stronger association with 1-year mortality than did the MDRD equation, especially once a receiver operating characteristic analysis was performed.

Corsonello *et al.* [25] found that GFR adds to predictors of mortality in an elderly population

Table I. Clinical, laboratory and angiographic characteristics of patients (*n* = 163)

Parameter	Patients with eGFR < 60 ml/min/1.73 m^2 *N* = 42 % or mean (95% CI)	Patients with eGFR ≥ 60 ml/min/1.73 m^2 *N* = 121 % or mean (95% CI)	Value of *p*
Age [years]	71.64 (69.5–73.7)	63.69 (61.8–65.6)	< 0.001
Male sex	45.2	81.0	< 0.001
Body mass index (BMI) [kg/m^2]	30.1 (28.6–31.7)	27.4 (26.7–28.0)	0.0015
Stable coronary artery disease	28.6	49.6	0.02
Acute coronary syndrome	71.4	50.4	0.02
Left ventricular ejection fraction (%)	47.98 (44.3–51.6)	52.5 (50.6–54.3)	0.025
Diabetes	50.0	16.5	< 0.001
History of hypertension	76.2	77.7	0.842
Hyperlipidaemia	54.8	70.2	0.067
Smoking	26.8	65.8	< 0.001
Family history of CAD	43.9	34.2	0.267
Previous myocardial infarction	52.4	38.0	0.104
Left main coronary artery disease (LMD) (%)	71.3 (65.9–76.7)	70.1 (67.5–72.8)	0.689
Location of stenosis:			
Proximal segment	14.3	17.4	0.642
Middle segment	2.4	1.7	0.773
Distal segment	64.3	62.8	0.862
Whole length of main stem	19.0	18.2	0.908
Medium number of coronary arteries with significant stenosis	3.67 (3.46–3.87)	3.31 (3.15–3.48)	0.02
Number of coronary arteries with significant stenosis apart from LMS:			
0	2.4	5.0	0.476
1	2.4	15.7	0.023
2	21.4	22.3	0.904
≥ 3	73.8	57.0	0.054
Parsonnet's scale	7.81 (6.55–9.06)	4.49 (3.85–5.12)	< 0.001
Cleveland scale	3.0 (2.18–3.82)	1.72 (1.34–2.10)	0.004
Polish Operation Risk Scale	8.86 (7.97–9.75)	5.57 (4.94–6.20)	< 0.001
EuroSCORE numeric	6.69 (5.70–7.68)	3.9 (3.38–4.42)	< 0.001
EuroSCORE logistic	9.65 (6.29–13.02)	4.09 (3.31–4.88)	0.001
Haemoglobin [mg/dl]	13.4 (12.9–13.8)	14.1 (13.9–14.3)	0.003
Erythrocytes [m/μl]	4.36 (4.23–4.49)	4.60 (4.52–4.68)	0.002
Haematocrit (%)	39.1 (37.9–40.3)	41.4 (40.8–42.1)	< 0.001
Leukocytes [thousands/μl]	7.72 (7.09–8.35)	7.94 (7.53–8.36)	0.559
Platelets [thousands/μl]	236 (211–262)	223 (210–235)	0.348
Fibrinogen [mg/dl]	421 (385–456)	385 (367–404)	0.064
Creatinine [mg/dl]	1.35 (1.28–1.43)	0.98 (0.95–1.00)	< 0.001
Total cholesterol [mg/dl]	168.8 (154.3–183.4)	171.7 (164.1–179.3)	0.691
LDL (low-density lipoprotein) cholesterol [mg/dl]	93.9 (80.9–106.9)	102.3 (96.0–108.5)	0.202
HDL (high-density lipoprotein) cholesterol [mg/dl]	45.2 (40.6–49.8)	44.1 (42.0–46.1)	0.622
Triglycerides [mg/dl]	148.6 (123.5–173.7)	125.9 (113.4–138.5)	0.07
Glycaemia on admission [mg%]	124.6 (105.5–143.7)	108.6 (103.5–113.7)	0.153

Table II. Data on cardiac surgery (*n* = 161)

Parameter	Patients with eGFR < 60 ml/min/1.73 m^2 *N* = 42 % or mean (95% CI)	Patients with eGFR ≥ 60 ml/min/1.73 m^2 *N* = 119 % or mean (95% CI)	Value of *p*
Coronary artery bypass graft surgery (CABG)	90.5	69.7	0.007
Off-pump cardiopulmonary bypass (OPCAB)	9.5	30.3	0.007
Number of bypass grafts without jump grafts	2.71 (2.50–2.92)	2.57 (2.45–2.69)	0.244
Number of bypass grafts with jump grafts	3.52 (3.17–3.88)	3.19 (3.03–3.36)	0.086
Number of venous bypass grafts	2.0 (1.77–2.23)	1.76 (1.64–1.89)	0.062
Bypass graft LIMA-LAD	73.8	86.5	0.058
Bypass graft Ao-LAD	28.6	16.8	0.099
Bypass graft Ao-Cx/MB	93	83.2	0.118
Bypass graft to RCA	76.2	58	0.035
Arterial bypass graft Cx/MB	2.4	8.4	0.185
Arterial bypass graft to RCA	2.4	1.7	0.774
CABG and valve operation	14.3	4.2	0.026
Left ventricular operations	7.1	2.5	0.174

LIMA – left internal mammary artery, LAD – left anterior descending coronary artery, Ao – aorta, Cx – circumflex coronary artery, MB – marginal branch, RCA – right coronary artery.

Table III. Complications and mortality after CABG (*n* = 161)

Parameter	Patients with eGFR < 60 ml/min/1.73 m^2 *N* = 42	Patients with eGFR ≥ 60 ml/min/1.73 m^2 *N* = 119	Value of *p*
Mortality:	11.9	4.2	0.075
7-day mortality (0–7 days)	7.1	3.4	0.313
30-day mortality (8–30 days)	4.8	1.7	0.269
Complications with wound healing	35.7	15.1	0.004
Sternum dehiscence	16.7	6.7	0.055
Atrial fibrillation	0	3.4	0.314
Pneumonia and pleuritis	4.8	10.1	0.295
Reoperation due to bleeding	4.8	10.1	0.295
Reoperation due to low cardiac output	0	1.7	0.567
Cardiac tamponade	4.8	0	0.058
Stroke	0	1.7	0.567

discharged from an acute care medical ward, and that the GFR < 30 ml/min/1.73 m^2 cut-off marks the highest risk when computed by the C-G formula. This may be attributed to the fact that the C-G formula, as it is based on the GFR, decreases noticeably for extremely low weight, and to some extent accounts for the effects of malnutrition. The fact that the C-G formula tends to give lower creatinine clearance estimations in those with low body weight largely explains why it is also better at predicting mortality.

Similar discrepancies in estimating kidney function using the Cockcroft-Gault equation in comparison to MDRD and CKD-EPI formulae were observed Malyszko *et al*. [26].

In our further analysis we divided our study population with LMD treated with CABG into 2 groups, those with eGFR < 60 ml/min/1.73 m^2 (26%) and those with GFR ≥ 60 ml/min/1.73 m^2 (74%), to assess the influence of kidney function on early prognosis.

Similar to the results from other publications, patients with eGFR < ml/min/1.73 m^2 were older, had lower left ventricular ejection fraction and more often suffered from diabetes [23, 27, 28].

In our study we observed higher 30-day mortality in the group with chronic kidney disease with eGFR ≥ 60 ml/min/1.73 m^2 (11.9% vs. 4.2%). Statistical significance was not achieved, probably due to the small study group. Similarly, higher perioperative and 30-day mortality in patients with eGFR below 60 ml/min undergoing CABG was reported in other studied and cardiac surgery registries [23, 29, 30].

Serum creatinine concentration is considered as one of the main risk factors in cardiosurgical scores (in EuroSCORE > 2.0 mg/dl, in Cleveland score > 1.8 mg/dl and in the Polish Score of Surgical Risk > 1.2 mg/dl). Parsonnet's score incorporates regular dialysis as a risk factor. Nevertheless, serum concentration of creatinine may not reflect actual kidney function. That is why nowadays eGFR is crucial in precise assessment of kidney filtration [23, 28, 31].

In October 2011 a new logistic model of EuroSCORE II was presented during European Association for Cardio-Thoracis Surgery (EACTS) in Lisbon. A special calculator for this score is available on-line. In EuroSCORE II chronic kidney disease is included as a surgical risk factor, but the ranges of eGFR values are not concordant with National Kidney Foundation recommendations. The Cockcroft-Gault formula was recommended as a convenient equation to assess kidney function [32].

In our study we evaluated perioperative mortality risk according to five different cardiac surgical scores. The risk in patients with chronic kidney disease was increased according to all scores although serum creatinine concentration, not eGFR values, was taken into account.

Chronic kidney disease is frequent in patients with LMD treated with CABG, and it is associated with more frequent complications with wound healing in 30-day follow-up. Although we observed higher 30-day mortality in the group with chronic kidney disease, statistical significance was not achieved, probably due to the small study group. Diagnosis of LMD in patients with lower eGFR is more often established during hospitalizations due to acute coronary syndromes than in patients with stable angina. Patients with chronic kidney disease are more frequently operated on with off-pump cardiopulmonary bypass. However, despite the limitations, we shed new light on the importance of estimating GFR as more precise than creatinine, and stressed its possible role as a new predictive factor for complications in this particular population.

The novelty of this study is that it concerns 'real life' patients undergoing CABG. In addition, we analysed perioperative mortality, mortality after the procedure and the most common complications and assessed the prognosis using 5 different scores. Moreover, we paid particular attention to kidney function expressed as either eGFR by MDRD or CKD-EPI or creatinine clearance by the Cockcroft-Gault formula with correction for lean body mass. We stressed the role of estimating kidney function and using various scores for prognosis in predicting outcomes in this very vulnerable population of patients studied.

Our study is a retrospective analysis. We included consecutive patients with few exclusion criteria, resulting in a heterogeneous population. Our group consisted of both patients with LMD and stable angina and patients with LMD and acute coronary syndromes. We studied only Caucasians; therefore we could generalize our data to the European population.

Conflict of interest

The authors declare no conflict of interest.

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