Epidemiology of Posttransplantation Chronic Kidney Disease Can Be Altered by Choice of Formula Estimating Glomerular Filtration Rate

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ABSTRACT

Background. Epidemiology of posttransplantation chronic kidney disease (CKDPT) has different characteristics than in the general population. Precise determination of glomerular filtration rate (GFR) is essential in the clinical decision making process as well as in management of a population that is based on epidemiological data. The aim of our study was to analyze the impact of an applied GFR estimation method on the epidemiology of CKDPT during the first year after transplantation.

Methods. We estimated GFR (eGFR) using the 4-variable Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula in 215 renal transplant recipients. We also measured and estimated creatinine clearance using the Cockroft-Gault (C-G) formula. Based on these data, we analyzed the influence of these formulas on the epidemiology of CKDPT.

Results. The largest fraction of patients is in stage 3 of CKDPT (40% to 62%). Application of the CKD-EPI formula instead of MDRD results in a decrease of prevalence of stage 3 by 3.9% at the early period (weeks 2 to 8) and by 13.8% at the late period (weeks 9 to 52) after transplantation. This is coexistent with reclassification from stage 3B to 3A and 3A to stage 2. Use of a measured or C-G–based creatinine clearance instead of the MDRD formula results in decrease of prevalace of stage 3 by 16.5% and 13%, respectively, in the early period and by 32.5% or 27%, respectively, in the late period.

Conclusions. Epidemiology of CKDPT depends on the method of calculation of eGFR. Application of creatinine clearance or the C-G formula results in an increase of prevalence of patients with better graft function.

TRANSPLANTED kidney function depends on multiple factors that are not observed in the general population. Therefore, epidemiology of posttransplantation chronic kidney disease (CKDPT) in this group of patients has different characteristics. Results of estimation of glomerular filtration rate (eGFR) may be different in the population of kidney transplant recipients due to their comorbidities, altered nutritional status, and donor-related factors, which are not included in formulas calculating eGFR. Correct estimation of graft function is critical for a proper decision-making process in daily clinical practice as well as for epidemiological analyses, which are the background for planning of medical care. Data from a population of patients with chronic kidney disease (CKD) indicate that change of formula estimating GFR results in reclassification of a significant number of patients to another stage of CKD. Matsushita et al. conclude that application of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) in comparison to the Modification of Diet in Renal Disease (MDRD) results in reclassification of 34.7% of patients from stage 3A to stage 2. This study also confirmed that CKD-EPI performs better in terms of prognosis because patients who were reclassified to stage 2 had a lower incidence of all-cause mortality and

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0041-1345/14
http://dx.doi.org/10.1016/j.transproceed.2014.09.008

cardiovascular mortality [1]. This observation needs confirmation in a population of renal transplant recipients because results of studies performed on this population are inconsistent [2–4]. The aim of our study was to analyze the influence of method of calculation of eGFR on epidemiology of CKDPT during the first year after surgery.

METHODS

We calculated eGFR using the 4-variable MDRD formula and CKD-EPI equation in 215 consecutive renal graft recipients (85 female, 130 male) with mean age of 45.6 ± 14.6 (median 48; range: 18 to 77) years, who underwent transplantation at Medical University of Gdansk. Creatinine clearance (CrCl) also was measured based on 24-hour urine collection and was estimated using the Cockroft-Gault (C-G) formula. The prevalence of the 5 stages CKDPT was then calculated for each applied formula. The calculations were performed for 2 periods after the kidney transplantation procedure: early period, 2 to 8 weeks, and late period, 9 to 52 weeks. Patients with unstable creatinine concentration were excluded from the study. Laboratory tests were performed at the Clinical Laboratory of the Medical University of Gdansk. Statistical calculations were performed with use of Statistica software for Windows (Statsoft version 10.1). Data were expressed as median and range or mean with standard deviation (SD). The limit of significance was set at .05. Statistical analysis was conducted with use of paired *t* test.

RESULTS

The results of the assessment of kidney graft function in the study population are described in Table 1. These results represent mean values based on analysis of our population of 215 kidney graft recipients. Mean values of calculated GFR allow comparison of the performance of the applied assessment formulas.

We have noticed significant differences in values of GFR depending on the method of calculation. Application of the C-G formula or measurement of CrCl overestimates GFR in comparison to MDRD or CKD-EPI. These differences are statistically significant ($P < .05$) for comparison of CKD-EPI vs CrCl, MDRD vs CrCl, and MDRD vs C-G clearance at a period of 2 to 8 weeks and for MDRD vs CG and MDRD vs CrCl at a period of 9 to 52 weeks. We also have noticed that MDRD may underestimate GFR in comparison with CKD-EPI; however, the difference was not statistically significant.

Based on these data, we have calculated changes in the prevalence of the CKDPT stages as the result of applying different formulas for estimating GFR. The results of our analysis are shown in Table 2 and Table 3. Analysis performed this way allows one to notice more clearly the causes of differences in epidemiological data.

The results from Tables 2 and 3 show that distribution of the prevalence of posttransplantation CKD is dependent on the method of assessment of GFR. Results of our study show that depending on the GFR prediction method used, 40% to 61.9% of patients are at CKDPT stage 3. Within stage 3, there is an advantage of patients at stage 3A over 3B that is further increased when calculation of GFR is performed by relatively overestimating methods (C-G, measured clearance method).

We have noticed that in contrast to MDRD, application of the CKD-EPI formula results in a decrease of prevalence at stage 3 of CKDPT by 3.9% at the early period (weeks 2 to 8) and by 13.8% at the late period (weeks 9 to 52) after transplantation. These patients are reclassified to stage 2 of CKDPT. Use of the C-G formula or measurement of CrCl results in reclassification of a significant number of patients from CKDPT stage 3B to 3A and 3A to stage 2. When applying measured CrCl instead of the MDRD equation, the prevalance of CKDPT at stage 3 decreases by 16.5% and 32.5 % at the early period (weeks 2 to 8) and late period (weeks 9 to 52), respectively. This is accompanied by a decrease in prevalance of stage 3B reaching up to 66.8% at the early period. Use of C-G–based CrCl instead of the MDRD equation results in a decrease of the prevalace of stage 3 by 13% at the early period and by 27% at the late period. This is obviously a reflection of overestimation of glomerular filtration by methods based on CrCl attributable to the nature of CrCl (glomerular filtration and tubular secretion) [5,6]. However, other factors specific to the pathophysiology of the renal transplantation procedure should be taken into account. All these observations show

Table 1. Mean eGFR and Creatinine Clearance in Kidney Transplant Recipients Calculated With Use of Four Formulas: MDRD, CKD-EPI, Cockroft-Gault (C-G) Creatinine Clearance and Measured Creatinine Clearance

Time After Kidney Transplantation	Formula of Calculation of GFR			
	e-GFR MDRD	e-GFR CKD-EPI	C-G Creatinine Clearance	Measured CrCl
Weeks 2 to 8	49.68*,†	51.45*	58.96	57.30
Weeks 9 to 52	53.59*,†	56.08	61.94	59.35

Abbreviations: eGFR, estimated glomerular filtration rate; MDRD, 4-variable Modification of Diet in Renal Disease formula [mL/min/1.73 m^2]; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration formula [mL/min/1.73 m^2]; C-G, Cockroft-Gault formula [mL/min]; CrCl, creatinine clearance based on 24-h urine collection [mL/min].

*$P < .05$ for comparison against C-G clearance.

†$P < .05$ for comparison against CrCl.

Table 2. Prevalence of CKD Stages in Kidney Transplant Recipients 2 to 8 Weeks After Renal Transplantation, Based on Different Methods of Assessing GFR

CKDPT Stage, eGFR Range [mL/min]	Formula for Calculation of GFR			
	MDRD [%]	CKD-EPI [%]	C-G [%]	CrCl [%]
Stage 1, ≥90	2.7	5.6	5.6	6.9
Stage 2, 60 to 89.9	21.4	21.9	35	34.5
Stage 3, 30 to 59.9	61.9	59.5	53.7	51.7
Stage 3A, 45 to 59.9	35.1	34.3	38.2	42.8
Stage 3B, 30 to 44.9	26.8	25.2	15.5	8.9
Stage 4, 15 to 29.9	8.4	7.9	3.7	5.2
Stage 5, <15	5.6	5.1	1.8	1.7

Abbreviations: CKD, chronic kidney disease; PT, posttransplantation; eGFR, estimated glomerular filtration rate; MDRD, 4-variable Modification of Diet in Renal Disease formula; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration formula; C-G, Cockroft-Gault formula; CrCl, creatinine clearance based on 24-h urine collection.