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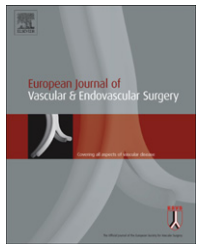

Estimated Glomerular Filtration Rate (eGFR) as a Predictor of Outcome after Infrainguinal Bypass in Patients with Critical Limb Ischemia

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Abstract *Objectives:* Renal insufficiency is a risk factor for poor outcome after infrainguinal bypass in patients with critical limb ischemia (CLI). Estimated glomerular filtration rate (eGFR) takes age, gender and body size into account and therefore represents actual renal function more accurately than serum creatinine level alone. The aim of this study was to determine the impact of different stages of renal insufficiency on outcome and to assess the prognostic significance of eGFR in patients with CLI.
Material and methods: 603 patients with CLI who underwent infrainguinal bypass between January 2002 and December 2005 at our institution were included in this retrospective study. We estimated GFR using the Modification of Diet in Renal Disease (MDRD) Study equation. Survival, leg salvage and amputation-free survival were calculated using Kaplan–Meier method. Cox regression analysis was performed to calculate hazard ratios for different outcome variables.
Results: Adjusted hazard ratio (HR) of mortality, limb loss and limb loss and/or death for eGFR <30 ml/min/1.73 m^2 versus serum creatinine >200 μmol/l was 4.0 (95% CI 2.22–7.39) vs 3.5 (95% CI 1.82–6.84), 6.5 (95% CI 2.71–15.59) vs 6.2 (95% CI 2.47–15.56) and 4.0 (95% CI 2.40–6.63) vs 3.6 (95% CI 2.03–6.25), respectively.
Conclusion: Estimated GFR is better predictor of survival, leg salvage and amputation-free survival than serum creatinine alone. eGFR <30 ml/min/1.73 m^2 is independent risk factor for all three outcome endpoints.

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Introduction

Cardiovascular mortality is higher among patients with end-stage renal disease (ESRD) compared to normal population.[1] Dialysis dependent patients have usually heavily calcified distal arteries and wound healing is poor due to anemia, malnutrition, impaired immunity and tendency to infection.[2–5] Thus, patients with ESRD and critical limb ischemia undergoing infrainguinal bypass have poorer post-operative survival and higher amputation rates.[4,6,7] The impact of mild to moderate renal insufficiency on outcome after arterial reconstructions is less well known. Diabetes mellitus and hypertension are most common underlying causes of renal insufficiency and may further worsen the outcome.[8–10] However, renal insufficiency per se seems to be independent risk factor for poor prognosis.[11,12] Chronic inflammatory activity and endothelial dysfunction are found in patients with albuminuria and elevated serum creatinine levels independently of other cardiovascular risk factors and this seems to be associated to progression of atherosclerosis.[8,13,14]

Measurement of serum creatinine is most commonly used method to assess renal function, but it is an inaccurate estimate of actual renal function, especially in early renal insufficiency.[15] Direct measurement of glomerular filtration rate is the gold standard, but neither inulin clearance nor isotopic methods are practical in clinical use. Glomerular filtration rate can, however, be estimated with serum creatinine based equations; either Modification of Diet in renal Disease (MDRD)[16] or Cockcroft-Gault (CG)[17] formula. These formulas take age, gender, and body size into consideration and are therefore much more accurate in estimating renal function than serum creatinine alone. For example, glomerular filtration rate can in some patients decline to half the normal level before creatinine level reaches the upper limit of normal.[18] There is evidence, that reduced estimated glomerular filtration rate (eGFR) is associated with increased postoperative mortality both after cardiac[19] and other vascular[20,21] procedures.

The aim of this study was to assess the usefulness of eGFR as a predictor of survival, leg salvage and amputation-free survival after infrainguinal revascularization in CLI patients and, specifically, find out the impact of moderate renal insufficiency on the outcome.

Material and Methods

We retrospectively reviewed our institution's vascular registry (Husvasc). Consecutive 603 patients who underwent infrainguinal bypass for chronic critical limb ischemia (Fontaine class III or IV) between January 1st 2002 and December 31st 2005 at our institution were included in the study. Registry includes patient demographics, comorbid conditions, indications for surgery, specific operative details, complications and outcome at discharge. Follow-up data includes graft patency and dates of any graft revision or graft occlusion and also dates of major amputation or death. Dates of death were retrieved from population registry center. Follow-up visits according to our surveillance programme were at 1, 6, 12 and 24 months. Registry data of all patients included in study were cross-checked against patient records and any missing data in the registry was retrieved from the patient's records.

Primary end point was major amputation or death. Only amputations above the ankle were considered as major amputations. Serum creatinine (Scr) was measured one day before surgery. Serum creatinine levels were measured using IDMS (isotope dilution-mass spectrometry) traceable enzymatic assay (Roche Diagnostics, Basel, Switzerland), which is one of the most accurate methods available at present.[22] Glomerular filtration rate was estimated using the 4-variable Modification of Diet in Renal Disease (MDRD) Study equation for creatinine results traceable to an IDMS method : eGFR (mL/min/1.73 m^2) = $175 \times (S_{cr}/88.4)^{-1.154} \times (Age)^{-0.203} \times (0.742$ if female) $\times$ (1.210 if African American) (SI units).[22–24] Chronic kidney disease (CKD) is divided into five stages according to The National Kidney Foundation - Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) guidelines[25] (Table 1). We summed up stages 1 and 2 as well as stages 4 and 5 to establish three categories : eGFR >60 ml/min/1.73 m^2 (no or mild renal insufficiency), eGFR 30–60 ml/min/1.73 m^2 (moderate renal insufficiency) and eGFR <30 ml/min/1.73 m^2 (severe renal insufficiency or renal failure) (Table 1). Comparisons between groups were made using Kruskal-Wallis test for continuous variables and Chi-squared test for categorial variables. Median and interquartile range was also calculated for continuous variables. Serum creatinine was analysed as categorical variable as well by establishing three categories for comparison with GFR, i.e. S-creatinine <120 μmol/L, S-creatinine 120–200 μmol/L, and S-creatinine >200 μmol/L. The lower cut-of value was selected, because it is generally considered the upper limit of normal creatinine value. The upper cut-of value of 200 μmol/L was selected, because values above it represent severe renal insufficiency. Values between these cut-off points represent therefore moderate renal insufficiency.

The median age of study population was 73 years (interquartile range 65–80). The median follow-up time was 5 months (interquartile range 0–46 months). Baseline characteristics and co-morbidities of study population are presented in details in Table 2. Indication was critical limb ischemia in all patients, 40% had rest pain and 60% had ulcer or gangrene. The proportions of femoro-popliteal, crural and pedal bypasses were 181(30%), 261(43%) and 81(13%),

Table 1 Staging of renal insufficiency according to National Kidney Foundation- Kidney Disease Outcomes Quality Initiative (NKF- K/DOQI) guidelines and our modification

Stage	GFR (ml/min/1.73 m^2)	Description	Our modification (GFR and description)
1	≥90	Normal renal function	> 60 no or mild renal insufficiency
2	60–89	Mild renal insufficiency	
3	30–59	Moderate renal insufficiency	30–60 moderate renal insufficiency
4	15–29	Severe renal insufficiency	< 30 severe renal insufficiency or renal failure
5	<15	End stage renal disease (uremia)	