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Clinical Research

Impact of Estimated Glomerular Filtration Rate on Vascular Disease Extent and Adverse Cardiovascular Events in Patients Without Chronic Kidney Disease

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See editorial by Ahmed et al., pages 1371-1373 of this issue.

ABSTRACT

Background: Estimated glomerular filtration rate (eGFR) predicts major adverse cardiovascular events (MACE) in patients with chronic kidney disease (CKD), though the effect of eGFR on MACE and vascular disease extent among individuals with normal or mildly impaired renal function requires definition. Our aim was to examine the prognostic implications of eGFR and its effect on atherosclerosis burden in individuals without CKD undergoing vascular imaging studies.

Methods: The study enrolled 2746 consecutive patients undergoing clinically-driven coronary angiography who had an eGFR $>$ 60 mL/min/1.73 m^2 and no history of CKD. Same-day carotid duplex results were available for 317 patients. Patients were followed for up to 3 years for the occurrence of all-cause mortality, myocardial infarction, and stroke.

Results: After adjustment for potential clinical and biochemical confounders, eGFR was found to be independently associated with coronary artery disease extent in the entire study population and among patients with normal renal function (n = 1170; eGFR $>$ 90 mL/min/1.73 m^2): odds ratio (OR) = 1.16 (95% confidence interval [CI], 1.09-1.24) and OR = 1.25 (95% CI, 1.11-1.4) per 10 mL/min decrements in eGFR, respectively. Similarly, eGFR was independently associated with carotid artery stenosis in the entire cohort (OR, 1.86 [95% CI, 1.12-3.1]). By Cox regression analysis, eGFR was an independent predictor of the composite MACE end point (hazard ratio, 1.16

RÉSUMÉ

Introduction : Le taux de filtration glomérulaire estimé (TFGe) prédit les événements cardiovasculaires indésirables majeurs (ÉCIM) chez les patients ayant une néphropathie chronique (NPC), bien que l'effet du TFGe sur l'étendue des ÉCIM et de la maladie vasculaire chez les individus ayant un fonctionnement rénal normal ou légèrement altéré doive être précisé. Notre but était d'examiner les implications pronostiques du TFGe et son effet sur le fardeau de l'athérosclérose chez les individus sans NPC subissant des études en imagerie vasculaire.

Méthodes : 2746 patients consécutifs ayant subi une coronarographie en clinique qui avaient un TFGe $>$ 60 ml/min/1,73 m^2 et n'avaient pas d'antécédents de NPC ont été inscrits à l'étude. Les résultats au duplex carotidien ont été disponibles le même jour pour 317 patients. Les patients ont été suivis jusqu'à 3 ans en ce qui a trait à l'occurrence de la mortalité toutes causes confondues, à l'infarctus du myocarde et à l'accident vasculaire cérébral.

Résultats : Après l'ajustement des facteurs parasites cliniques et biochimiques potentiels, le TFGe s'est révélé comme étant indépendamment associé à l'étendue de la coronaropathie dans l'ensemble de la population étudiée et chez les patients ayant un fonctionnement rénal normal (n = 1170; TFGe $>$ 90 ml/min/1,73 m^2) : ratio d'incidence approché (RIA) = 1,16 (intervalle de confiance [IC] à 95 %, 1,09-1,24) et RIA = 1,25 (IC à 95 %, 1,11-1,4) par décréments de 10 ml/min dans le TFGe, respectivement. De manière similaire, le

Cardiovascular disease is a major cause of mortality and morbidity in patients with chronic kidney disease (CKD).[1] In this population, the effect of CKD on the risk of coronary artery disease (CAD) is reflected by an inverse graded relationship between renal function and major adverse cardiovascular events (MACE) when the estimated glomerular filtration rate (eGFR) is $<$ 60 mL/min/1.73 m^2.[2] The overall prevalence of moderate to severe reductions in eGFR ($<$60 mL/min/1.73 m^2) in the general population is approximately 5%[3] (though it rises markedly with age, approximating 33% in octogenarians[4]). However, mildly reduced or normal eGFRs are far more prevalent in the general population (31% and 64%, respectively).[3] Therefore, the association between renal function within the normal or mildly impaired range and cardiovascular disease has important potential consequences from the public health perspective. Whether eGFR

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[95% CI, 1.04-1.28]), and all-cause mortality (hazard ratio, 1.38 [95% CI, 1.19-1.60]).
Conclusions: eGFR is an independent predictor of atherosclerotic vascular disease extent and MACE rates in patients with normal or mildly impaired renal function.

TFGe a été indépendamment associé à la sténose carotidienne dans l'ensemble de la cohorte (RIA, 1,86 [IC à 95 %, 1,12-3,1]). Par l'analyse de régression de Cox, le TFGe a été un prédicteur indépendant du critère de jugement combiné des ÉCIM (rapport de risque, 1,16 [IC à 95 %, 1,04-1,28]) et de la mortalité toutes causes confondues (rapport de risque, 1,38 [IC à 95 %, 1,19-1,60]).
Conclusions : Le TFGe est un prédicteur indépendant de l'étendue de la maladie vasculaire athérosclérotique et des taux d'ÉCIM chez les patients ayant un fonctionnement rénal normal ou légèrement altéré.

within the normal or mildly impaired range is associated with the extent of atherosclerotic vascular lesions and independently predicts the risk of MACE in patients without CKD is unclear.

We sought to examine the relation between eGFR within the normal or mildly reduced range (>60 mL/min/1.73 m^2) and the extent and severity of carotid and coronary artery atherosclerotic disease. To this end, we analyzed the association between eGFR, coronary artery angiography and carotid duplex findings, and MACE rates, in a large, prospective registry of patients without CKD, undergoing clinically-driven coronary angiography.

Methods

Patient selection

The Tel Aviv Prospective Angiographic Survey (TAPAS) is a single centre registry which prospectively enrolls all patients undergoing cardiac catheterization at the Tel Aviv Medical Center.[5-7] The current study consisted of 2746 consecutive patients without CKD referred for coronary angiographic evaluation. Patients with a previous history of renal disease (n = 1643) were excluded. Per protocol, a subset of patients (n = 317) underwent a carotid ultrasound and Doppler study within 24 hours of the coronary procedure. All participants provided written informed consent for participation in the study, which was approved by the institutional ethics committee.

Definitions of renal function

Definitions of CKD and normal vs impaired eGFR were based on the US National Kidney Foundation classification (normal eGFR > 90 mL/min/1.73 m^2; mildly reduced eGFR 60-89 mL/min/1.73 m^2; moderately reduced eGFR > 30-59 mL/min/1.73 m^2; severely reduced eGFR > 15-29 mL/min/1.73 m^2; and end stage renal failure eGFR < 15 mL/min/1.73 m^2).[3] eGFR was calculated using both the Modification of Diet in Renal Disease (MDRD)[8] and the Cockcroft-Gault[9] formula and the results per both methods were well correlated ($r = 0.78$; $P < 0.0001$). Because the MDRD formula systematically underestimates glomerular filtration rate (GFR) in healthy individuals, the Cockcroft-Gault formula was used in the present study of patients without CKD.[10,11]

Definitions of carotid artery disease

Atherosclerosis of both the left and right internal carotid arteries (ICAs) was assessed by a sonography technician who was blinded to clinical and coronary angiographic data. The ICAs were scanned with carotid duplex equipment (HD11 XE; Philips Healthcare, Andover, MA) with a 3-12 MHz linear array transducer, using a previously described protocol.[12] ICA atherosclerosis was evaluated by the maximum percentage of diameter reduction recorded by B-mode ultrasound, and by the peak diastolic and peak systolic velocity (PSV) per Doppler. Lesion severity was defined as the greatest ICA stenosis (CAS) observed either on the right or left ICA. Ultrasound and Doppler findings were classified into 1 of the following 5 categories:[13] normal (PSV < 125 cm/sec with no signs of atherosclerotic lesions); mild CAS (PSV < 125 cm/sec in the presence of an atherosclerotic lesion); moderate CAS (PSV 125-230 cm/sec, corresponding to 50%-70% diameter stenosis); severe CAS (PSV > 230 cm/sec, >70% diameter stenosis); and total or near occlusion (defined as 0 PSV and no visible flow). For the present analysis total or near occlusion,

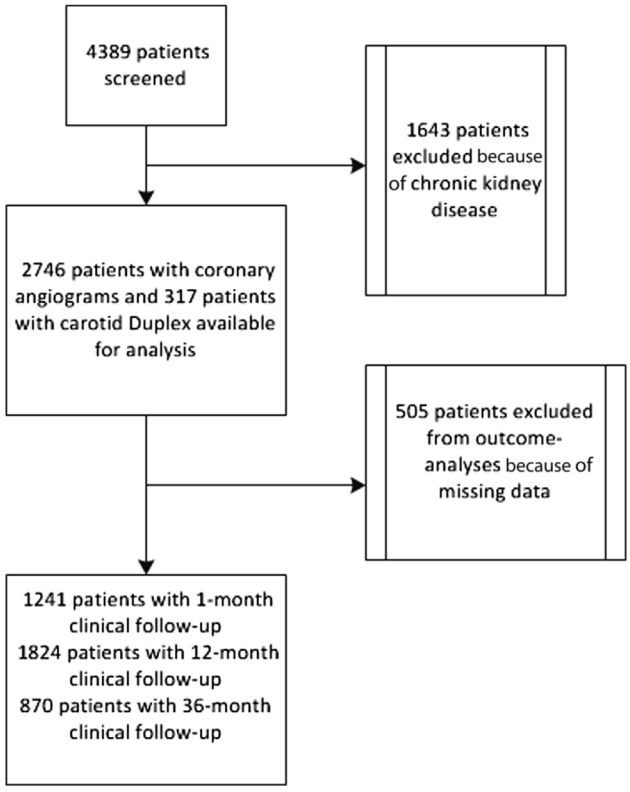

Figure 1. Screened population, exclusions, enrollment, and loss to follow-up throughout the study period.