



Cystatin C: A Novel Predictive Marker for Cardiovascular Disease Sistatin C: Kardiyovasküler Hastalıklar İçin Yeni Prediktif Bir Markör

Hamdi Puşuroğlu, Özgür Akgül

Mehmet Akif Ersoy Research and Training Hospital for Pulmonary and Cardiovascular Diseases, Department of Cardiology, İstanbul, Turkey

Dear Editor,

Chronic kidney disease (CKD) is associated with an increased risk of developing cardiovascular diseases and adverse cardiovascular events. In clinical practice, serum creatinine, the Cockcroft-Gault, and the Modification of Diet in Renal Disease (MDRD) are commonly used to assess renal function (RF).

Cystatin C (CysC) is a cysteine protease inhibitor that is produced at a constant rate in all nucleated cells and freely filtered by the glomeruli without secretion and subsequent tubular reabsorption (1). The CysC level is less affected by age, gender, diet, or body muscle mass; therefore, CysC is more reliable in determining renal function than serum creatinine levels and creatinine-based estimated glomerular filtration rate (GFR) formulas, especially in conditions of decreased mass and patients with creatinine levels within normal range.

In recent years, CysC has emerged as a potential marker for cardiovascular risks in different clinical scenarios. Parikh et al. have shown that increased CysC levels are independently associated with cardiovascular risk factors such as age, female sex, body mass index, low HDL cholesterol, and smoking (2). Shlipak et al. have shown that increased CysC levels are associated with all-cause mortality, death from cardiovascular diseases, risk of myocardial infarction, and risk of stroke in elderly (3). The predictive value of CysC levels for peripheral arterial disease, heart failure, and chronic kidney disease in elderly patients has been reported in various studies.

Over the last few years, studies have focused on the association of CysC with cardiovascular events and mortality in patients with coronary artery disease. Ix et al. have shown that increased CysC levels are associated with all-cause mortality, cardiovascular events, and incident heart failure in patients with stable coronary artery diseases. In this study, the risk association with higher cystatin C concentrations do not differ among patients with or without renal dysfunctions (4). Taglieri et al. have assessed 525 patients taking part in the Systemic Inflammation Evaluation in Patients with NSTEMI-ACS (SIESTA) study and shown that serum creatinine

and GFR are not predictors for the study end-point though increased levels of CysC are independent predictors of cardiac events at the one-year follow-up (5). In our study, we observed that admission creatinine ≥ 1.5 mg/dL and GFR < 60 mL/min per 1.73 m² are two of the strongest risk factors for one-month cardiovascular mortality in patients undergoing primary angioplasty for ST-elevation myocardial infarction (6). However, neither creatinine levels upon admission nor the GFR values were independent risk factors. Instead, CysC levels were independently distinguished the one-month cardiovascular mortality, and CysC was also found to be useful in identifying patients with a risk of cardiovascular mortality with an admission creatinine level of < 1.5 mg/dL. CysC is a sensitive early marker of preclinical kidney dysfunction which is associated with adverse cardiovascular events. To date, this effect was supposed to be due to the sensitive power of cystatin C for predicting progressive decrease of kidney function in many clinical studies.

It has been suggested that high cystatin C concentrations are directly related to both inflammation and atherosclerosis, and that inflammation may be one of the mechanisms associated with cystatin C and cardiovascular risk. Cathepsin S has elastolytic and collagenolytic properties and plays a role in extracellular matrix remodeling by the degradation of matrix proteins. CysC is an inhibitor of Cathepsin L and S and it has been speculated that inflammatory cytokines stimulate the production of cathepsins while that increased CysC levels, in turn, may reflect a counterbalance activity. The imbalance between proteases and inhibitors determines their clear effects on cardiovascular system.

In conclusion, CysC levels are prognostic markers that can be useful as risk assessment tools in cardiovascular diseases.

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Received/Başvuru: 09.04.2014, Accepted/Kabul: 23.09.2014

Correspondence/İletişim

Hamdi PUŞÜROĞLU
Mehmet Akif Ersoy Göğüs Kalp Damar Cerrahisi Eğitim ve
Araştırma Hastanesi, Kardiyoloji, İSTANBUL, TÜRKİYE
E-mail: hpusts@gmail.com

For citing/Atıf için

Pusuroglu H, Akgul O. Cystatin c: a novel predictive marker for cardiovascular disease. *J Turgut Ozal Med Cent* 2015;22:143-4 DOI: 10.7247/jtomc.2014.2022