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# Cystatin C, Renal Function, and Cardiovascular Risk

Pierre Delanaye, MD ; Etienne Cavalier, MD ; Jean-Marie Krzesinski, MD, PhD

*University of Liège, CHU Sart Tilman B-9000 Liège, Belgium*

## TO THE EDITOR

We read with interest the article by Menon and colleagues (1) concerning cystatin C as a cardiovascular risk factor. We believe their paper considerably increases the quality of articles published on this topic, especially because glomerular filtration rate (GFR) was measured with a reference method.

We have some comments. First, it is important to keep in mind that this study analyzes cystatin C as a cardiovascular risk factor.

Because all the patients had chronic kidney disease (CKD) (GFR <55 mL/min per 1.73 $m^2$), this study cannot be used to assert that cystatin C is definitively better than creatinine for detecting stage 3 kidney disease (GFR <60 mL/min per 1.73 $m^2$). Regarding the study methods, the authors do not mention when cystatin C was measured in the frozen samples. Were the samples measured retrospectively? If so, are the authors sure of the stability of the cystatin C in samples frozen, for example, for more than 10 years? The authors found that cystatin C is associated with body mass index. This interesting result should be discussed in light of the recent literature (2). The authors compared cystatin C with estimated GFR to predict cardiovascular risk. Why have they not studied an equation based on cystatin C, such as the one published by Rule and colleagues (3)?

In their interesting discussion, Menon and colleagues speculate as to why cystatin C may be a better predictor of cardiovascular risk than actual GFR by iothalamate clearance. We suggest another hypothesis. Of course, cystatin C is strongly related to GFR. Nevertheless, cystatin C concentration seems also to be influenced by other factors, such as muscle mass (2), dysthyroidism (hyperthyroidism increases cystatin C concentration, although it also increases GFR), and corticotherapy (which increases cystatin C concentration) (3). From comparative physiology, we know that GFR is strongly related to basal metabolic rate (4). Moreover, corticotherapy and hyperthyroidism also increase basal metabolic rate. Basal metabolic rate is also influenced by muscular mass, which is the greatest reserve of nucleated cells in the body and produces cystatin C (2). All the factors influencing cystatin C concentration could thus be related to a common "superior" factor: basal metabolic rate. This working hypothesis is further reinforced by data from the comparative physiology that suggest basal metabolic rate (like cystatin C) could be an important predictor of life span (5).

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### Potential Financial Conflicts of Interest

None disclosed

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