Cystatin C and contrast-induced nephropathy

Sir,

The paper by Kimmel et al. [1] concludes that cystatin C blood level variations are a more reliable parameter than serum creatinine increments for the diagnosis of contrast-induced nephropathy (CIN).

However, this conclusion does not seem sufficiently supported by the data to us. Since the definition of CIN is based on serum creatinine variations, it is not clear what the meaning is of the cystatin C increase when the former does not occur. Does it reflect a true GFR reduction or some other condition, i.e. the release of cystatin C from atherosclerotic vascular lesions during arterial catheterization [2] or the biological variability of the parameter [3]?

We are also puzzled with the variability of cystatin C in the period d-1/d0. Looking at Figure 1, our feeling is that it is quite large. As a matter of fact, it was reported that the critical difference for sequential values is 37% for serum cystatin C—a value that includes the cystatin C levels plotted in Figure 1—and only 14% for serum creatinine [3].

The authors state that the temporary increase in GFR possibly due to the peri-procedural hydration does not translate into a cystatin C decrement because of its slower kinetics vis-à-vis serum creatinine. However, what is the evidence for such a statement? Is it just speculation to explain the dichotomic trends between serum cystatin C and creatinine levels? The issue is very important, since if cystatin C really has a delayed progression with respect to serum creatinine, we might suspect that the interval d0/d2, 48 h, is too long to grasp mild, transient serum creatinine variations occurring in-between.

We think that, although cystatin C is an attractive biomarker of GFR, before concluding that it should be the preferred biomarker for the development of CIN, an experimental design with a more strict timing in sampling and a much larger case population is necessary.

Conflict of interest statement. None declared.

Reply

Sir,

We thank Gambaro et al. for the discussion of some aspects of our paper [1] focussing on the value of cystatin C as a biomarker in contrast-induced nephropathy (CIN).

There is an international consensus for the need of new biomarkers in acute kidney injury (AKI), and CIN is one of the most frequent reasons of AKI. Up to now, all biomarkers in AKI have limitations, but a whole panel of markers will be tested in ongoing studies. The definition of AKI is revised by the RIFLE criteria, with the intention to include changes in the glomerular filtration rate (GFR) and urine output [2].

In AKI and CIN, renal function is commonly monitored by following the variations in serum creatinine, but this variable has limitations as a marker of GFR in these patients. The serum creatinine concentration depends not only on the urinary clearance of creatinine but also on the rate of production and the volume of distribution [2]. Furthermore, acetylcysteine seems to affect the tubular handling of creatinine directly, so a decrease in serum creatinine concentration with this drug does not necessarily lead to a protective effect on the GFR [3].

Small molecular weight proteins, like cystatin C, have long been proposed as markers of GFR as they are normally freely filtered through the glomerular membrane. Cystatin C is produced at a constant rate by all nucleated cells and is freely filtered through the glomerular membrane. Cystatin C is associated with an increased coronary atherosclerotic burden and a stable plaque phenotype in patients with ischemic heart disease and normal glomerular filtration rate. Atherosclerosis 2008; 198: 373–380


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Small molecular weight proteins, like cystatin C, have long been proposed as markers of GFR as they are normally freely filtered through the glomerular membrane. Cystatin C is produced at a constant rate by all nucleated cells and is catabolized by the tubulus [4]. Dharnidharka et al. reported in a meta-analysis that cystatin C is a superior marker of GFR [5]. One of the major problems in AKI and CIN trials is a lot of different definitions and a missing gold standard for GFR changes in AKI.

Finally, we will briefly address the comments in detail:

1. The value of the two discussed biomarkers of GFR can be summarized: cystatin C is promising, but has to be better validated in special clinical situations and creatinine has its well-known limitations, especially in CIN. Our study does not prove the superiority of cystatin C over creatinine in CIN, but we detected changes in cystatin C not observed by creatinine. Today we indeed do not yet know the clinical benefit of a cystatin C-based CIN definition and we need larger trials (with hopefully