EDITORIAL

Cystatin C: More than a renal function marker

Cistatina C: más que un marcador de la función renal

The work by Dr. Francisco Ortuño-Andériz et al.,\(^1\) is an important contribution to delineate the use of cystatin C in intensive care. Cystatin C was described as a marker of glomerular filtration rate, GFR, about 30 years ago,\(^2,3\) but it was not until 1994, when it was stated to be a more accurate marker for GFR than creatinine,\(^4\) that substantial efforts were initiated to define its role as a marker of GFR. Today, when the search string "cystatin C, AND (renal OR glomerular)" is used in the PubMed Search system, about 2400 articles are obtained. However, only a few of them concern the use of cystatin C in intensive care. Most of them try to determine the use of cystatin C and creatinine as markers of GFR in various clinical situations. Presently, there seems to be an emerging consensus that cystatin C- and creatinine-based GFR-estimating equations, producing eGFR\(_{\text{cystatin C}}\) and eGFR\(_{\text{creatinine}}\)-values, display similar diagnostic performances, if race, sex and age terms supplement creatinine in the creatinine-based equations. But the best estimation of GFR is obtained, when the mean of eGFR\(_{\text{cystatin C}}\) and eGFR\(_{\text{creatinine}}\) is used, which also allows a quality check of the GFR-estimate, by comparing the two estimates.\(^5-8\)

A tool to perform this quality check can be found at www.eGFR.se.

There is also a consensus concerning another inference, namely that cystatin C is a much better risk factor than creatinine for early death, myocardial infarction, hospitalization and end-stage renal disease. This seems to be independent of whether only the concentration values of cystatin C and creatinine or eGFR\(_{\text{cystatin C}}\) and eGFR\(_{\text{creatinine}}\)-values are used.\(^9,10\) The observation by Dr. Francisco Ortuño-Andériz et al.\(^1\) that a higher concentration value of cystatin C is significantly correlated to a higher mortality in the studied patient population agrees with the above-mentioned observations on cystatin C and mortality. It has been speculated that the superior capacity of cystatin C as a risk factor for mortality is due to the fact that inflammation raises the cystatin C level. These speculations were based upon the observations that there is a significant statistical correlation between the CRP and cystatin C levels in large patient populations.\(^11\)

However, it has been proven that there is no causal relationship between the presence of inflammation and an increased level of cystatin C by studies in which severe inflammation was induced in non-inflamed patients by elective surgery without any post-surgical rise in the cystatin C level.\(^12\) It has also been shown that the presence of sepsis, and thus of inflammation, in patients in intensive care units does not increase the level of cystatin C.\(^13\) The statistical correlation between the levels of CRP and cystatin C, in the large patient populations studied, is therefore probably caused by unrecognized factors producing raised levels of both CRP and cystatin C. One such factor might be that chronic inflammation causes both a raised level of CRP and progression of the atherosclerotic process, *inter alia*, narrowing of the renal arteries and thus a decrease in GFR and an increase in the cystatin C level. If now inflammation *per se* does not cause a raised level of cystatin C and thus not contributes to the capacity of cystatin C as a marker of mortality, other such factors have to be looked for. Few, if any, such suggestions have been proposed. But one suggestion is that cystatin C, due to its much larger size than creatinine, might be a superior marker of changes in the pore size of certain human membranes, e.g., the renal glomerular membranes.\(^14\) One pertinent observation is that the glomerular pore size decreases during the last trimester of pregnancy and at an accelerated rate at eclampsia/pre-eclampsia.\(^15\) More studies of critically ill patients, like those of Dr. Francisco Ortuño-Andériz et al., might reveal other, and perhaps more important factors, contributing to the understanding of why a raised level of cystatin C indicates an increase in mortality.

References


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