

## Prognostic Value of Increased Preoperative C-Reactive Protein Levels. A Step towards the End of the Controversy?

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C-reactive protein (CRP) is a sensitive inflammation and infection marker which is accepted as a new risk marker in cardiovascular events. Several clinical studies have shown the usefulness of elevated levels of CRP to predict instability in patients with acute coronary syndrome or worst results in those undergoing percutaneous revascularization (higher mortality, infarction or restenosis), which are also associated with a higher number of readmissions in patients with heart failure. (1, 2)

In cardiac surgery, preoperative evaluation of CRP elevated levels has shown controversial results over the past 25 years.

In 1986, Boralessa et al. considered an association between the preoperative CRP elevated values and the development of postoperative higher complications. The following year, such results were refuted by Kress et al., who did not determine the predictive value for preoperative elevated CRP in a group of 80 patients and started the so mentioned controversy. (3, 4)

Since that, several authors argued and argue for (Boecken et al., Perry et al.) and against (Gaudino et al.) regarding the predictive value of a preoperative elevation of CRP. (5-7)

In this issue of the Journal, the study of Waldman et al. joins those who support the predictive value of an elevated level of preoperative CRP.

In this work, made on 169 patients undergoing different types of elective cardiac surgery, the authors concluded that a CRP value equal or higher than 2mg/dl was predictive for the development of systemic inflammatory response syndrome (SIRIS), as well as SIRIS with renal failure, atrial fibrillation, shock and postoperative death. The study has some interesting points and several aspects that may need a deep analysis.

Among the first, besides the choice of the topic, the intention to predict preoperative evolution and especially the development of complications and/or a bad result using a preoperative biomarker would be of great interest and obvious benefits. The study includes an important number of consecutive patients and represents the largest review published about the predictive value of preoperative elevated CRP levels in cardiac surgery. The idea to use a CRP of intermediate sensitivity by a greater number of institutions would be very important.

Regarding the points to analyze, although authors make clear that they are elective surgeries, preoperative

clinical manifestations are not specified, so among those coronary patients (50% of the population among coronary and combined) may have been included patients with acute coronary syndrome, probably with more active inflammatory processes compared to patients with no acute manifestations or with longer preoperative stabilization. Although previous angioplasty antecedent is mentioned, it would be important to establish how many of them underwent the surgery recently (for example, primary) and how many of them underwent it time ago. The presence or absence of decompensated heart failure and differences in preoperative stabilization time, as well as the use of drugs which may alter CRP values (aspirin is mentioned but no its dose or the use of other antiplatelet or anti-inflammatory drugs such as steroids) would also be points to consider.

The fact that less of 42% of a population of patients undergoing scheduled cardiac surgery have been treated with statins, with the consequent loss of perioperative benefits (among others, due to its probably anti-inflammatory effect) is a surprising aspect.

It is also seen a non significant tendency to have a higher EUROscore among those with elevated CRP, which should represent a choice of patients with higher preoperative risk, as well as a greater number of patients with preoperative renal failure, smokers, and carriers of chronic obstructive pulmonary disease, data that in a greater population would acquire significant value. As the authors state, the number of patients is not enough for other determinations (mortality), besides this study has been made in a unique institution.

Beyond those points, the discussion about the preoperative CRP predictive value is very interesting and contradictory. The reason of the conclusions seen in the literature and, perhaps, the solution may be found in the following points:

1. CRP is not only an inflammatory response marker, but also represents a mediator of such process.
2. Different moments in the evaluation of preoperative CRP and especially its relation with postoperative values (delta CRP). A unique CRP value may not show the inflammatory process over the time.
3. Different section values apart from the method of CRP measurement (qualitative in some studies, quantitative in others, to use or not to use high sensitivity CRP)
4. Inclusion of different patient populations of higher or

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lower risk (scheduled or emergency surgery, inclusion or not of high risk patients, different preoperative stability time).

5. The different and in some cases contradictory effects given to CRP, maybe due to the fact of presenting different ways (at least three). Some of them were linked to protective effects. Kew et al. report that patients with respiratory distress (an inflammatory pathology in its genesis) and elevated levels of CRP show better prognosis compared to patients with ARDS with lower CRP values. (9)

A very important point would be to know the consequences that may have the corroboration of the predictive value of an elevated preoperative CRP. A risk stratification (of any type) is important if it helps redirecting the treatment and the use of resources to those groups of patients who will obtain greater benefits (or greater reduction of risk). From this point of view, the practical clinical value of a preoperative elevated CRP would be linked to the development of any kind of strategy of prevention or treatment, which would depend on the fact that the inflammation is a factor of risk potentially modifiable. Meanwhile, the addition of biomarkers to the systems of perioperative risk calculations in cardiac surgery is an interesting suggestion, whose exact value would be determined in large prospective multicenter studies.

In this sense, Waldman et al. study presents a very important observation, whose practical importance would be appreciated in the near future.

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