## CRP Predicts Safe Patient Discharge after Colorectal Surgery: Reply

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We would like to thank Aurelién Duprè, Johan Gagniér, Heloïse Samba, Michel Rivoire, and Karem Slim for their comments about our article "Procalcitonin Reveals Early Dehiscence in Colorectal Surgery: The PREDICS Study."[1] It is very rewarding to realize that this paper is stimulating so many observations, this means that we are talking about an interesting topic.[2]

Thank you for underlining that PREDICS is a large prospective observational study, involving 3 high-volume colorectal centers in Italy. It is to note that we described study methods in our first preliminary paper[3]; anyway, we are glad to share with you that sample size was calculated for a difference of at least 10% between the area under the receiver operating characteristics (ROC) curves (AUCs) of C-reactive protein (CRP) and procalcitonin (PCT). In the pilot study,[3] an AUC of 0.884 was observed for PCT at third postoperative day and used for the calculation. The prevalence of anastomotic leakage was assumed to be 14% according to the preliminary study, but was much lower in the PREDICS study data (5.6%). Total number of patients to include was estimated to be 441. The study was designed to have 80% power with an alpha error of 0.05.

Regarding strengthening the reporting of observational studies in epidemiology checklist,[4] we decided not to publish it because we consider it a useful tool only during study design; anyway, in the "Materials and methods" section, we carefully described all study characteristics (inclusion and exclusion criteria, variables reported in the database, and statistical analysis).

Positive and negative likelihood ratio (PLR and NLR) for PCT in third and fifth postoperative days (PODs) are, respectively: 7.14 and 0.44, and 9.9 and 0.33. For CRP, PLR and NLR in third POD are 3.26 and 0.50, and in fifth POD are 5.28 and 0.30, respectively. According to these results, usefulness of procalcitonin both in third and fifth POD is greater than CRP, confirming the results previously shown in our article with ROC curves. Therefore, according to PREDICS outcomes, together with this LR analysis, we keep stating that PCT and CRP could be usefully added as a diagnostic tool in early diagnosis of anastomotic leak (AL) in patients undergoing colorectal surgery for cancer. It should not absolutely be a fight between the 2 biomarkers, but a fight for better patient care. So, because adding PCT to CRP in fifth POD enhances AL diagnosis in a statistically significant way, we are proud to keep stating that this advantage is worth for patients' life. In fact, if the patient is discharged earlier and will do well at home, we save money; on the contrary, if AL is diagnosed early, it is possible to avoid sepsis and late reoperation, and try to pursue medical therapy saving money again, and—most important—avoiding longer hospital stay and worsening oncological outcomes. We are all currently using tremendously expensive technologies in the operating room for laparoscopy and robotic surgery, and nobody is questioning this huge amount of money because it improves patient outcomes. Why should we then discuss about 20 Euros more or less (10 Euro for each PCT measurement) when patients' quality of life can be significantly improved?

The authors are stating, citing their own work, that AL diagnosis is difficult, and we absolutely agree to this conclusion. For this reason, further research in this field is more than welcome to give additional help to the clinician and guide further diagnostic and therapeutic steps when biomarker levels are high.

Using biomarkers will never replace the surgeon for anastomotic leak diagnosis, but is a good help we should definitely accept to use.

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### REFERENCES

1. Giaccaglia V, Salvi PF, Antonelli MS, et al. Procalcitonin reveals early dehiscence in colorectal surgery: the PREDICS study. *Ann Surg*. 2016; 263:967–972.
2. Giaccaglia V, Antonelli MS, Salvi PF, et al. Reply to letter: a different approach to the use of C-reactive protein and procalcitonin in postoperative infectious complications. Ann Surg 2016 [Epub ahead of print].
3. Giaccaglia V, Salvi PF, Cunsolo GV, et al. Procalcitonin, as an early biomarker of anastomotic leak, facilitates enhanced recovery after surgery. *Crit Care*. 2014;29:528–532.
4. [No authors listed]. STROBE statement: checklist of items that should be included in reports of observational studies (STROBE initiative). *Int J Public Health*. 2008;53:3–4.