



Mid-regional pro-adrenomedulin as a marker of perioperative mortality in non-cardiac surgery

Mid-regionalni pro-adrenomedulin kao marker perioperativnog mortaliteta u nekardijalnoj hirurgiji

To the Editor:

Recently published study revealed that out of a total number of patients undergoing a major non-cardiac surgery, 5% of them could have myocardial infarction¹. After 30 days from the major non-cardiac surgery, over 11% of patients would probably die, most likely due to cardiovascular (CV) causes.

There are several widely used methods for estimating preoperative cardiac risk based on risk scores and risk stratification scales, e.g., the Revised Cardiac Risk Index (RCRI)^{2,3}.

It is known that patients suffering from different diseases (not only cardiovascular ones) with increased mid-regional fragment of the pro-adrenomedullin molecule (MR-proADM) levels (different mechanisms of secretion involved) are at high risk of mortality⁴⁻⁶. In a large number of trials, the predictive role of MR-proADM as a biomarker for clinical outcome was investigated in non-surgical patients^{7,8}. Results of the GISSI and LAMP studies, conducted in patients with chronic heart failure and myocardial infarction, demonstrated that MR-proADM concentrations higher than 0.75 nmol/L and 0.73 nmol/L, respectively, were predictors of poor outcome^{5,9}.

Because of that, we performed a prospective observational study with an aim to evaluate MR-proADM as a risk marker for CV mortality in non-cardiac surgical patients older than 55 years who had at least one CV risk factor, which is usually the case in the real-life. MR-proADM was determined before surgery by using a sandwich immunoluminometric assay (MR-proADM, BRAHMS AG, Hennigsdorf/Berlin, Germany). Mean MR-proADM in 264 healthy individuals in previous investigations was 0.33 ± 0.07 nmol/L (range 0.10–0.64 nmol/L) and the assay had a measuring range from 0 to 100 nmol/L⁴.

We enrolled 81 patients undergoing major abdominal ($n = 56$), thoracic ($n = 4$), orthopedic ($n = 20$) and vascular ($n = 1$) surgery under general anesthesia with at least one of the following CV risk factors: diabetes mellitus, hypertension, hyperlipidemia, active smoking, or a family history of cardiac disease. Exclusion criteria were emergent surgery and the inability to understand or sign the informed consent. We

routinely calculated the Revised Cardiac Risk Index (Lee score)³. The clinical endpoint of the study was mortality within 30 days after the surgery.

The study included 42 women (51.9%) and 39 men (48.1%), aged 71.29 ± 6.62 years (range: 55–87 years). Within 30 days after the surgery 14 (17.3%) patients died, all due to cardiac causes and all being subjected to the abdominal surgery. This high and early postoperative mortality rate in our study could be explained by the fact that study included relatively small number of elderly patients with different co-morbidities who underwent an extensive surgery carrying a particularly high risk for poor outcome. Patients who died were older than 65 years (75.7 ± 6.7) and all of them underwent the abdominal resection (mostly radical) due to malignant abdominal tumors. Our results are in line with those obtained in other studies with elderly patients. Heriot et al.¹⁰ reported that postoperative mortality in elderly patients with colorectal cancer was as high as 15.6%. A mortality rate of 16% was found in patients over 70 years of age undergoing major elective orthopedic surgery¹¹.

The concentration of MR-proADM was statistically significantly higher in the deceased patients when comparing to survivors ($p < 0.001$). On the other hand, the values of Lee were not significantly different with respect to fatal outcome ($p = 0.283$).

The patients with MR-proADM in the upper quartile had statistically significant shorter survival, comparing to other patients ($p = 0.007$). The survival time of patients with MR-proADM in the upper quartile was 15 (95% CI 6.46–23.54) days and in other patients it was 28 (95% CI 20.7–28.66) days. The group of deceased patients included 9 (45%) patients with MR-proADM above 0.86 (the upper quartile) and 5 (8.2%) with MR-proADM below 0.86. Our patients with higher NYHA class and Lee score above 6.60 had MR-proADM in the upper quartile. They also had the worst 30-day prognosis. In a number of studies on patients with heart failure, good correlation between NYHA class, natriuretic peptides and MR-proADM was shown¹².

In our study, MR-proADM compared to the Lee score was a better predictor of postoperative mortality in the pa-

tients (with at least one CV risk factor) subjected to extensive non-cardiac surgery. Therefore, measuring MR-proADM concentrations might help in identifying a high-risk patients before performing non-cardiac surgery. These patients could have benefit from a risk reduction measurements.

We need more studies regarding the prognostic role of MR-proADM in perioperative risk stratification keeping in mind that our study had several limitations (small number of patients, elderly population with different comorbidities who underwent an extensive non-cardiac surgery). Nevertheless, we believe that MR-proADM is a promising prognostic biomarker for the preoperative risk assessment, either alone or together with other risk factors. This biomarker is involved in many (patho)physiological processes and might be not only a marker of CV risk, but general perioperative risk.

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