Pre-Operative Cardiac Risk Assessment in Noncardiac Surgery

Are Natriuretic Peptides the Magic Bullet?*

Daniel Bolliger, MD, Manfred D. Seeberger, MD, Miodrag Filipovic, MD
Basel, Switzerland

Natriuretic peptides (NPs) are well-established risk markers in a broad range of acute (1,2) and chronic (3–5) cardiac diseases. In addition, they are the basis of important diagnostic and therapeutic decisions (6–8). In nonsurgical patients, NPs fulfill all the recently published criteria for clinically useful risk markers (9): prospective validation of an incremental prognostic value, evidence for changes in clinical management, improvement in outcome on the basis of the changes made, and cost-effectiveness of the analysis. Conversely, in surgical patients, the role of NPs as clinical risk markers is far less well established. Independent assessment of their value in surgical patients is mandatory because the perioperative period is complicated by specific problems, for example, rapid hemodynamic changes, exaggerated stress response and hypercoagulability causing myocardial ischemia, heart failure, arrhythmias and renal failure.

In this issue of the Journal, Karthikeyan et al. (10) present their meta-analysis of the predictive value of NPs (brain natriuretic peptide [BNP] and N-terminal pro-brain natriuretic peptide [NT-proBNP]) on adverse cardiovascular outcomes in patients undergoing noncardiac surgery. The authors analyzed 9 studies including >3,200 patients to determine the association of pre-operatively elevated NP levels with major adverse cardiac events (MACE) within 30 days after noncardiac surgery. One-quarter of the patients had elevated levels of the NPs, and 9.6% of the included patients experienced at least 1 perioperative MACE. After adjustment for other known risk factors, the pooled data showed an adjusted odds ratio of 19.3 (95% confidence interval: 8.5 to 43.7) for MACE in case of elevated NP levels. These results agree with another recent meta-analysis that reported an unadjusted odds ratio of 17.37 (95% confidence interval: 3.31 to 91.15) for MACE within 30 days among patients undergoing vascular surgery (11). Despite many well-acknowledged shortcomings and heterogeneities of the studies included in the meta-analysis, Karthikeyan et al. (10) found clear evidence for the association between pre-operatively elevated levels of NPs and post-operative occurrence of MACE.

From a clinical point of view, it is equally important to be aware of the negative predictive value of the NPs, in other words, the association between nonelevated levels of the NPs and favorable post-operative outcome. For patients undergoing major vascular surgery, we have found that the negative predictive value of BNP levels <50 pg/ml is as high as 0.965 (95% confidence interval: 0.879 to 0.996) (12). This finding is in agreement with a previous study of patients undergoing nonvascular surgery (13) and with the meta-analysis by Rodseth et al. (11) of patients undergoing vascular surgery suggesting that patients with normal levels of NPs may proceed directly to surgery with no additional pre-operative cardiac testing. One may speculate that this approach is very likely to be cost effective, but this hypothesis needs to be proved in a future prospective study.

Evidence for changes in clinical management and improvement in outcome on the basis of the test results are further criteria for the usefulness of risk makers. Improved outcome for BNP-guided management of patients with heart failure has been demonstrated in nonsurgical settings (6,8), but data for surgical patients are missing. Based on the available data, the importance and meaning of pre-operatively elevated levels of NPs remain unclear: Should the patients undergo further cardiac testing? Should cardiac medication be adjusted? Should perioperative monitoring be more invasive or should the post-operative stay in an intensive care unit be prolonged?

Another unsolved issue is the optimal time for pre-operative NP testing. Initiation of a new therapy on the day before surgery does not seem to be a promising approach. There is strong evidence for both statins (14,15) and beta-blockers (16,17) that perioperative treatment is beneficial only if initiated at least several days to weeks before surgery. Based on the time requirements and the positive and negative predictive values of NP testing, the following approach seems reasonable: Analysis of BNP or NT-proBNP should be performed 4 to 5 weeks before scheduled surgery in cases of intermediate- to high-risk surgery and presence of clinical risk factors and/or reduced physical capacity according to the current American College of Cardiology/American Heart Association guidelines (18). If
NP levels are below a discrimination threshold (that still has to be determined) and the patient is clinically stable, the patient can proceed with surgery without the need for further testing. If NP levels are above the threshold, further testing, optimization of medical therapy, and—in some cases—invasive therapy should be performed. For these patients, repeat testing shortly before surgery might allow for adjustment of perioperative treatment strategies (choice of surgical and anesthetic technique, fluid management, intensified intraoperative and post-operative monitoring). However, it has to be clearly pointed out that this NP-based approach is speculative and, accordingly, needs to be rigorously evaluated in well-designed prospective trials.

In conclusion, the study by Karthikeyan et al. (10) gives important and clear evidence for a high prognostic potential of NPs in patients scheduled for noncardiac surgery. However, studies to evaluate whether specific NP-based treatment modifications will result in improved outcome of surgical patients still need to be performed. Should future studies find outcome relevance of such a concept, NPs will be indeed the magic bullet of pre-operative risk optimization. So far, however, they are interesting and promising tools for risk stratification that require further evaluation.

Reprint requests and correspondence: Dr. Daniel Bolliger, Department of Anesthesia, University of Basel Hospital, CH-4031 Basel, Switzerland. E-mail: dabolliger@uhbs.ch.

REFERENCES


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