Take me to your bleeder: Recombinant factor VIIa—finding its way in cardiac surgery

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In this issue of the Journal, Dr Zindovic and colleagues examined whether data from the Nordic Consortium for Acute Type A Aortic Dissection database indicated that use of recombinant factor VIIa (rFVIIa) was associated with mortality, stroke, or renal replacement therapy after acute type A aortic dissection (ATAAD) surgical repair. Bleeding in ATAAD repair is a concern to all surgeons performing such operations. Any adjunct to attenuate bleeding is appreciated, and in ATAAD, rFVIIa has been suggested to do so. When looking at the use of rFVIIa elsewhere, however, there are concerns that although beneficial with respect to bleeding, this agent may be associated with a higher occurrence of untoward events. Zindovic and colleagues found no difference in mortality rates perioperatively or up to 5 years. Nor did they find a difference in perioperative stroke or renal replacement therapy.

Among the strengths of the article were the multicenter nature of the study, the relatively large sample size (120 matched pairs of patients), and the thoughtful analysis performed to examine results in comparable patients from the larger unmatched cohort. Previous studies of rFVIIa in ATAAD have been limited to fewer patients. In one study, 23 patients received rFVIIa, and 25 patients received rFVIIa in another. This larger sample size allows for a more robust examination of the relationship between rFVIIa and outcomes. The propensity score using matching relying on discordant pairs was thoughtfully done.

Zindovic and colleagues also did well to identify the weaknesses of their own work. They highlighted the retrospective design, problems with missing data, lack of granularity with respect to some aspects of the study (eg, timing of drug administration), selection bias, and missing unmeasured confounders, both known and unknown. Indeed, there were sufficiently missing data for some variables (creatinine kinase MB and lactate) that they were not included for fear of limiting the matching to unacceptable levels. Even so, 44 of the 171 patients (25%) receiving rFVIIa were excluded because of missing data.

Central to decision making with respect to rFVIIa use is knowledge of the magnitude of benefit, the safety of use, and the indication(s) for use. No strong evidence regarding the magnitude of benefit is available because studies are hampered by no prospective design and inherent limitations of low numbers and retrospective analyses. The work of Zindovic and colleagues gives us a fairly good, albeit retrospective, analysis of the safety of using rFVIIa in ATAAD surgery. However, in non-ATAAD cardiac surgery, some have found a less-compelling safety profile, whereas some have similarly found rFVIIa use safe. In pediatric cardiac surgery, an odds ratio of 3.9 for thrombotic complications was found using rFVIIa. In a study of adult complex cardiac surgery, the odds ratios of 2.8 for in-hospital mortality and 2.1 for renal complications were found. Chapman and colleagues found no difference in 30-day mortality, stroke, or renal failure using rFVIIa in high-risk cardiac surgery.

Thus, guidance for appropriate use of this product remains obscure. Although some of us fumble around in this darkness, champions will undoubtedly illuminate the path.

References

