The Optimal Intensity of Vitamin K Antagonists in Patients With Mechanical Heart Valves: A Meta-analysis

I enjoyed the article by Vink et al. (1), which again revisits an old and most important clinical chestnut, but I have serious misgivings about their conclusions. Some years ago, we did a detailed and comprehensive analysis of 1,134 patients who had received St. Jude prosthetic valve(s) over a 13-year period (2). The follow up was 100% complete—4,936 patient years—and the study had a 60% post-mortem examination rate for early deaths.

The recommendation we made as the result of our analysis, namely that the INR should be kept between 2.5 and 3.0, is at complete variance with that of the authors. I believe that the problem arises from the fact that the target international normalized ratio (INR) range on which the authors focused may have no bearing whatsoever on the international normalized ratio (INR) range on which the investigators concerned to read the paper of Vink et al. (1) Their recommendation that all patients should be managed with an international normalized ratio (INR) of 3.0 to 4.5 reverses current trends to individualize antithrombotic management for each patient based on an assessment of their particular thromboembolic risk (2-4). Although having a “one size fits all” approach to anticoagulation management may have advantages for anticoagulation clinics, this approach will not benefit individual patients who may be exposed to the risks of unnecessarily high anticoagulation.

Their meta-analysis raises several concerns. First, meta-analysis is a technique for amalgamating data from randomized controlled trials (RCT) that have used the same methodology, not observational studies with different methodology. Second, reported thromboembolic rates are heavily influenced by definitions, data collection methods (prospective vs. retrospective), size and length of study, patient risk factors, concomitant surgery, and type of prosthesis (5,6). Other than the prosthetic type, these factors are not mentioned. Valve thrombosis rates are influenced by the number of patients who experienced anticoagulation interruption, to which most cases are related (7). Third, we question the use of target INRs rather than achieved INRs. Many events occur when the INR is outside the target range.

Fourth, retrospective conversion of prothrombin time ratios to INR has the potential to introduce huge errors. In American studies, it is highly unlikely that a single thromboplastin reagent would have been used for all patients in the study (8). Finally, there is a lack of acknowledgment of the five published RCTs comparing different anticoagulation intensity (9-13). Although most of these RCTs have limited applicability because of their methodologies, all reached the conclusion that a higher intensity of anticoagulation did not reduce the incidence of thromboembolism. Four RCTs showed a higher incidence of bleeding with higher intensity anticoagulation. The only RCT not to show this effect used overlapping INR ranges and did not record events in the first three months (13).

Although Vink et al. (1) acknowledge that high-intensity anticoagulation results in a higher incidence of bleeding, they appear to minimize this danger. Use of a higher range of INR, 3.0 to 4.5, for all patients imposes an imperative for extremely tight INR control. High variability of INR, with >30% of INRs outside the range 2.0 to 4.0, is the strongest

REFERENCES


Anticoagulation Management of Patients With Prosthetic Valves

As authors of previous European guidelines on anticoagulation of patients after valve surgery and as members of a committee currently revising those guidelines, we are concerned to read the paper of Vink et al. (1) Their recommendation that all patients should be managed with an international normalized ratio (INR) of 3.0 to 4.5 reverses current trends to individualize antithrombotic management for each patient based on an assessment of their particular thromboembolic risk (2-4). Although having a “one size fits all” approach to anticoagulation management may have advantages for anticoagulation clinics, this approach will not benefit individual patients who may be exposed to the risks of unnecessarily high anticoagulation.