Commentary: To OAC or not to OAC? That is the question

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Biologic surgical aortic valve replacement (B-SAVR) has increased during the last 2 decades and now exceed the number of mechanical prostheses implanted across a wide range of age groups. With the advent of transcatheter aortic valve replacement, options for valve-in-valve repair have made (correctly or not) structural valve degeneration of biological valves less of a concern. The main advantage of biological valves, of course, is the avoidance of long-term anticoagulation and the inherent bleeding risks associated with the use of warfarin.

The initial impetus to consider oral anticoagulation with warfarin (Coumadin [OAC]) after B-SAVR came from observations of the increase risk of thromboembolic events in the early period after surgery. The observations identified 90 days as the period of increased risk, and that period was suggested for OAC. The concept was to use OAC while the sutures and sewing ring healed, because these were thought to be the source for potential clot formation. There are little randomized data in this area. One randomized trial suggested that the use of antiplatelet therapy was beneficial; whereas another suggested that OAC had no benefit. A large meta-analysis has also suggested that OAC carries no benefit. The use of no OAC after B-SAVR has been called into question after a large Danish study suggested that lack of early OAC was associated with an increased mortality, and findings of leaflet thickening and immobility have been identified on 4-dimensional computed tomographic scans for both B-SAVR and transcatheter aortic valve replacement valves.

A more recent meta-analysis by Papak and colleagues examined the evidence of varying antiplatelet and anticoagulation strategies for both B-SAVR and transcatheter aortic valve replacement. Papak and colleagues found moderately strong evidence that mortality, thromboembolic events, and bleeding rates were similar between those given aspirin and warfarin after B-SAVR. Observational data suggested lower mortality and thromboembolic events with aspirin combined with warfarin than with aspirin alone, but the effect size was small, and the combination was offset by a substantial increase in bleeding risk. The recommendation from this meta-analysis was for aspirin rather than warfarin therapy for the first 3 months after surgery for patients for whom there is no other indication for anticoagulation, such as atrial fibrillation or history of thromboembolism.

Studies involving warfarin anticoagulation are difficult to interpret, because most studies do not report the duration that the international normalized ratio (INR) is within therapeutic range. In studies that do report this variable, the INR is typically outside the therapeutic range for most of the time. Clearly, this has major implication for the effectiveness of treatment. The lack of superiority of warfarin in studies could be a result of this issue, and a more stringent management of anticoagulation thus might demonstrate a benefit.

With this background, what do our current society guidelines say? The American College of Cardiology and American Heart Association guidelines suggest for B-SAVR lifetime aspirin therapy and OAC for 3 months (INR 2.5), with a level of evidence IIb B. The European Society of Cardiology and European Association for Cardio-Thoracic Surgery guidelines suggest low-dose aspirin (IIa C) or OAC (IIb C) for 3 months after B-SAVR. The American College of Chest Physicians guidelines suggest aspirin rather than OAC in the first 3 months after B-SAVR (2C). With such differing societal recommendations, the question of anticoagulation of surgical biologic valves (B-SAVR) remains unanswered.

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In this issue of the Journal, Chang and colleagues\(^2\) have attempted to add knowledge in this area. Chang and colleagues\(^2\) identified 2537 patients from Taiwan’s National Health Insurance Database who received a first-time B-AVR between 2001 and 2010. They excluded a number of patients (1451) for previous use of warfarin, warfarin use for longer than 3 months, double-valve procedures, previous valve surgeries, or concomitant surgeries. Of note, they also excluded any patient who died within the first 3 months. This left them with a study group of 1086 patients. They divided these into patients who had no OAC (n = 286) and those who received OAC within 3 months of the procedure (n = 718). They then used propensity matching to generate 282 pairs. Their primary end point was major adverse cardiac and cerebrovascular event (MACCE; acute coronary syndrome, heart failure, ischemic stroke, and death), and their secondary end point was bleeding that changed clinical practice. The results suggest a decrease in MACCE rate driven mainly by a decrease in mortality for OAC use in the first 3 months that occurred mainly within the first month. There was no increased bleeding or reoperation in the OAC group. Chang and colleagues\(^1\) concluded that they “provide preliminary evidence that short-term use of postoperative warfarin (<3 months) following bioprosthetic AVR may be associated with a reduction in MACCE compared to nonuse. The benefit appears to be most significant with short term use (<30 days).”

We found this an interesting study, but with a number of limitations that make interpretation of the data difficult. The major limitation is the fact that the difference in MACCE is driven mainly by mortality in the no-OAC group. Unfortunately, the database cannot give us the cause of death. If this increased mortality can be related to thromboembolic events or valve thrombosis, then the data might make sense. There is no way to tell which patients might be critically ill after the procedure and whether the treating physician avoided OAC because of this illness. This would clearly seed the no-OAC group with patients at greater risk of mortality unrelated to OAC use. It is also difficult to fully accept the propensity matching of Chang and colleagues.\(^2\) Propensity matching is meant to remove preprocedural differences and will not take into account postprocedural differences on which the decision for OAC use may have been made. In addition, Chang and colleagues\(^2\) found that the use of OAC for less than 14 days also conveyed a MACCE benefit. This very short use of OAC is difficult to understand without the MACCE events being thrombotic in nature, and we do not get this information. We applaud Chang and colleagues\(^2\) for this attempt to understand the potential need for OAC after B-SAVR, but the answer to the question remains murky.

The evidence supporting antiplatelet and anticoagulation strategies after B-SAVR is moderate at best and needs to be answered further in a prospective, randomized fashion. Such trials must include INR therapeutic level reporting as well as radiologic evidence of valve leaflet thrombosis. A more rigorous evaluation of direct oral anticoagulants (DOACS) is also warranted in this study population. To OAC or not OAC? That is the question—and to us it remains unanswered.

References