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EDITORIAL COMMENT

Pericardial Invasion

Lessons Learned From Surgical and Transcatheter Aortic Valve Replacement*

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Atrial fibrillation is the most common arrhythmic complication observed after cardiac surgery. The reported incidence of post-operative atrial fibrillation (POAF) after cardiac surgery ranges from 10% to 65% (1). The wide range of incidence is driven by myriad factors, including differences in surgical procedure, patient demographic characteristics, POAF surveillance method, duration of surveillance, and criteria for diagnosis. POAF typically occurs 2 to 4 days after surgery and often resolves spontaneously or with modest medical treatment. Despite its rather predictable course, multiple published studies have demonstrated that POAF has been associated with longer hospital length of stay, longer rehabilitation length of stay, significantly higher overall costs associated with the procedure, and most importantly, more frequent and severe patient morbidities (1,2).

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The established mechanisms that contribute to POAF have been recently summarized in the literature (3). Facilitating factors in the mechanism of POAF can be classified into acute factors (related to the surgical intervention) and chronic factors (related to underlying atrial pathology and age). The delayed onset and transient nature of POAF suggest that components of the pro-arrhythmic effect of cardiac surgery take some time to develop and have reversible mechanisms. Inherently, some of this effect is due to the disruption of normal cardiac and thoracic physiology, as evidenced by decreasing rates of POAF from cardiac surgery (10% to 65%) (1) to noncardiac, thoracic surgery (9% to 29%) (4) to noncardiac, nonthoracic surgery (1% to 13%) (5). Pericardial inflammation is thought to strongly contribute to this spectrum of incidence, although there is a paucity of data comparing rates of POAF for similar procedures that can be performed with and without a pericardiotomy.

Transcatheter aortic valve replacement (TAVR) is a newly established treatment option for patients with symptomatic aortic stenosis who are high risk for open surgery. Because a similar procedural result is achieved with TAVR and surgical aortic valve replacement, and because only one procedure involves a pericardiotomy, this population provides a direct way to evaluate the relative contribution of pericardial invasion to the development of POAF. Moreover, because TAVR can be delivered in different ways (transfemoral, transapical, and transaortic), there are unique risks for each procedure. Understanding the incidence of POAF for each procedure could be important for clinicians to appropriately council patients and consider pre-operative prevention measures.

In this issue of the *Journal*, Tanawuttiwat et al. (6) extend our understanding of POAF into the rapidly developing world of TAVR. Their study is a single-center, retrospective analysis of consecutive patients who underwent aortic valve replacement from March 2010 to September 2012. Major exclusions included a history of AF, bicuspid aortic valve, and death within 48 h after surgery. A total of 123 subjects were included in the analysis, with POAF as the main outcome of interest. Procedural and hospital telemetry data were used to characterize the incidence of POAF during the entire hospitalization and at a standard 30-day follow-up clinic visit. Demographic, clinical, and echocardiographic data were used to adjust for effects of confounding variables. Patients were classified by procedural method of AVR: surgical (SAVR), transfemoral (TF-TAVR), transapical (TA-TAVR), or transaortic (TAo-TAVR).

The mean age of this cohort was approximately 85 years, and the group was almost entirely of Caucasian ethnicity. The pre-operative mean Society of Thoracic Surgeons (STS) risk score was 7.67 ± 3.45. No oral antiarrhythmic agents were used to prevent AF, although surgical patients received post-operative atrial pacing for at least 24 h and had other important differences in post-operative care. Overall, POAF was identified in 42.3% of this cohort. Not surprisingly, POAF was associated with lung disease, left atrial enlargement, left ventricular hypertrophy, and prolonged intubation.

The main finding of the study was that POAF incidence varied according to procedural type, with the highest incidence in SAVR (60%) and TA-TAVR (53%), and then TAo-TAVR (33%) followed by TF-TAVR (14%). The investigators used multivariate regression modeling to compare surgical versus nonsurgical techniques, procedures with and without pericardiotomy, and procedures with and without a chest wall incision. After multivariate analysis, the development of POAF was most closely associated with procedures that involved a pericardiotomy (SAVR and TA-TAVR) versus without pericardiotomy (odds ratio: 0.18;

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95% confidence interval: 0.05 to 0.59). Compared with SAVR, only the TF-TAVR procedure had a statistically supported lower incidence in POAF, although there were strong trends in the same direction for the other TAVR procedures as well.

Despite the inherent limitations of a retrospective single-center study, the investigators are to be commended for conducting a rigorous collection and evaluation of the data. Although there were relatively small numbers of patients in each treatment group, the high rates of observed POAF allowed for an adequate assessment of the outcome. The main drawback to this study was the inherent biases of nonrandomized treatment arms, specifically patient selection of SAVR and TAVR. The criteria for choosing patients for TAVR (deemed inoperable or with an estimated surgical mortality >15%) clearly chose a less healthy and older group of patients. Nevertheless, the highest POAF incidence occurred in the group that was self-selected to be younger and healthier, which seemed to strengthen the validity of the investigators' observations. Among the TAVR choices, the transfemoral approach was the preferred method, and other methods were only chosen in cases of small iliofemoral arterial diameter. This likely introduced bias of patient size or other vascular disease among the different groups of TAVR. Other clear differences existed in post-operative treatment strategies involving atrial pacing, more aggressive blood transfusions, and presumably, longer duration of mechanical ventilation in the surgical arm. Remaining unanswered is the relative contribution of the surgery itself or the actual post-operative care that led to the higher rates of POAF in the SAVR group. Clinically, this might not mean much because the 2 will remain linked (cardiac surgery requires rigorous post-operative care).

Although POAF is strongly linked to longer hospital stays and higher cost of care, the more immediate and tangible concern for patients is thromboembolic complications, especially cerebrovascular accidents (CVA). In the current study, the investigators made additional observations about the timing and duration of the POAF, the variable anticoagulation strategies, and the incidence of CVA. There were too few CVA events to draw sustainable conclusions. However, of the 5 CVAs, 4 occurred in the TF-TAVR group. Three of these occurred in the early in the post-operative course, independently of the development of AF, and presumably were related to manipulation of the delivery system within the aorta. In this cohort of 123 patients, only 2 CVAs could have been related to POAF. When choosing the type of TAVR, minimizing the stroke rate seems to be more related to patient factors and procedural type than to the presence of POAF. This was supported by published observations from the PARTNER 1A (Placement of AoRtic TraNscathetER Valves) trial, in which the risk of early neurologic events was greater in the TAVR group (5.5%) than the SAVR group (2.4%; $p = 0.04$), although over time, this difference was no longer demonstrated (7). This risk is likely to diminish with less traumatic delivery systems, improved technique, and inclusion of lower-risk patients.

In our increasingly cost-conscious world of medical care, minimizing risks of complications and safely reducing the length of a hospitalization are desirable goals. The results from the study by Tanawuttiwat et al. (6) add to our overall understanding of the contribution of pericardiotomy to the incidence of POAF. Decisions about the relative merits of SAVR versus TAVR and between types of TAVR should include data from this study. Extended further, the unique comparisons of procedures with and without pericardiotomy may provide a way to study specific mechanisms related to the pericardium and help develop targeted, cost-effective AF prevention strategies.

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