

EDITORIAL COMMENT

Atrial Fibrillation and Transcatheter Aortic Valve Replacement



The Burden of Advanced Cardiovascular Disease in Aortic Stenosis*

Jonathon M. White, MD, Susheel K. Kodali, MD

Atrial fibrillation (AF) is well established as an important predictor of risk across a broad spectrum of cardiac disease. An association with increased mortality has been demonstrated in ischemic heart disease, heart failure, and valvular disease (1-5). In addition, AF is a common problem following surgical aortic valve replacement (SAVR) where it has been associated with increased adverse events, including mortality (6). What remains unknown is whether this association between AF and adverse events reflects a direct causal role or rather a marker for more advanced cardiac disease.

Transcatheter aortic valve replacement (TAVR) is currently accepted as an alternative to SAVR for patients with aortic stenosis at high surgical risk, with emerging data now suggesting improved outcomes with TAVR in this population (7). Recently, studies in intermediate-risk patients have demonstrated excellent early outcomes (8). Ongoing randomized clinical trials will answer whether TAVR will become the preferred therapy in lower-risk patients. Randomized trials have demonstrated that AF rates are higher after SAVR compared with TAVR (30.5% vs. 11.7% at 30 days in CoreValve US Pivotal Trial and 16.0% vs. 8.6% in PARTNER A [Placement of Aortic Transcatheter Valve Trial]), and it is possible that reduced AF burden

is playing a role in the improved late outcomes with TAVR (7,9). However, there is still a paucity of data examining the role that AF might play following TAVR, limited to a few small studies with conflicting results (10-12). As such, the ability to tease out the importance of AF in this clinical setting has been limited.

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In this issue of *JACC: Cardiovascular Interventions*, the study by Chopard et al. (13) represents the largest study to date documenting the relationship between AF and clinical outcomes following TAVR. The investigators' retrospective analysis comes from the FRANCE 2 (French Transcatheter Aortic Valve Intervention Registry), using the data of almost 4,000 inoperable patients treated in 33 centers. The study used 12-lead electrocardiograms obtained during in-hospital follow-up to define patients as having pre-existing AF, new-onset AF, or no AF. Pre-existing AF was shown to be extremely common in inoperable patients undergoing TAVR—25.8% in this study. In those without established AF, the finding of newly documented AF was less common—6% of the remaining patients. The investigators analyzed the impact of pre-existing and new-onset AF independently.

Patients with pre-existing AF were older, had more comorbidities, worse left ventricular function, and more paravalvular leak after TAVR. When compared with patients without documented AF, no difference in adverse events at 30-day follow-up was seen. However, at 1 year, a significant increase in all-cause mortality was noted in those with AF (26.5% vs. 16.6%), as well as worse heart failure symptoms and a higher rate of rehospitalization. Importantly, no differences in stroke or major bleeding were observed; however, an important limitation of this study is that

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From the New York Presbyterian/Columbia University Structural Heart and Valve Center, New York, New York. Dr. Kodali receives research support and is a consultant for Edwards Lifesciences and Medtronic; and serves on the Scientific Advisory Board for Thubrikar Aortic Valve, Inc. Dr. White has reported that he has no relationships relevant to the contents of this paper to disclose.

data regarding antiplatelet and anticoagulation regimens are not reported.

Patients with new-onset AF were older but not obviously more comorbid than those in whom AF was not observed. However, they were treated more frequently by nontransfemoral access routes and were more likely to suffer procedure-related adverse events, suggesting that underlying comorbidity is likely. At both 30-day and 1-year follow-up, those with new AF had an increase in adverse events, including all-cause mortality at 1 year (20.7% vs. 11.1%).

On multivariate analysis, both pre-existing AF (odds ratio [OR]: 1.72) and newly documented AF after TAVR (OR: 1.79) were shown to be among the strongest independent predictors of all-cause 1-year mortality with odds similar to paravalvular leak and chronic kidney disease. This observation was consistent across almost all subgroups on further analysis.

The present study is important and has many strengths as it is the first, large registry-based analysis to describe the scope of the AF problem and its potential role in modifying risk in inoperable TAVR patients. Many questions remain however. Although AF appears to be an important independent predictor of risk, whether AF truly modifies risk in these patients or merely reflects other comorbidity and worse heart failure is impossible to know. Indeed, the investigators surmise that worse heart failure might drive the worse outcomes observed in AF patients. In this study, patients with pre-existing AF were sicker, had more incidences of heart failure, and worse paravalvular leak. Patients with new AF were more likely to have undergone a nontransfemoral approach, an intuitive cause of AF as well as a reflection of a more comorbid population with more extensive vascular disease. Although multivariate models can suggest that AF is problematic in and of itself, knowing this for sure is not possible and requires further study. Data supporting improved outcomes from the restoration or maintenance of sinus rhythm in the general population are lacking and whether such strategies might benefit TAVR patients is not known.

Two major limitations of this study warrant mention. Although no differences in stroke or bleeding outcomes were noted, the interaction among stroke,

bleeding, and antithrombotic therapy is complex and data on the use of these medications might further inform the reported results. New-onset AF was defined by analysis of a single 12-lead electrocardiogram, without the use of continuous telemetry. A recent study by Urena et al. (14) found asymptomatic arrhythmias to be common immediately before TAVR (6.4% had asymptomatic new AF) and found that the discovery of new arrhythmias was highly likely to alter patient management. Asymptomatic AF is a common problem, so it seems likely that the burden of new AF is underestimated in the present study, although whether short, asymptomatic episodes of AF are prognostically important remains unclear. Furthermore, no data are available regarding patient rhythm at discharge. Not only does sustained AF at discharge have important implications for patient management, it might also portend a clinical course that is different to patients with short, paroxysmal episodes of AF following a procedure. The impact of the exclusion of 251 patients who died in-hospital before follow-up is not known but the lack of electrocardiogram data on these patients could have affected the overall results.

Finally, whether treatment directed specifically at AF might improve clinical outcomes remains unclear. The relationship between AF, heart failure, and procedural outcomes including stroke and bleeding is a complex one. What is clear, however, is that inoperable patients with AF carry a large burden of cardiovascular disease and should be considered for comprehensive heart failure and antithrombotic treatment, all directed at reducing the long-term consequences of heart failure even after relief of valvular obstruction from aortic stenosis. The study by Chopard et al. (13) highlights the importance of AF and heart failure both before and after TAVR and the need for further studies concerning the AF and heart failure-specific management of this patient population.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Susheel K. Kodali, New York Presbyterian/Columbia Structural Heart and Valve Center, 177 Fort Washington Avenue, 5th Floor, Room 5C-501, New York, New York 10032. E-mail: sk2427@cumc.columbia.edu.

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