The rationale and sequencing of opening and closing structures has been well studied in mechanical sciences and disciplines. The report by Attinger-Toller et al. (1) in this issue of JACC: Cardiovascular Interventions extends this conversation to the specific medical field of aortic stenosis (AS) and atrial fibrillation (AF), about which there is burgeoning interest.

This interest relates to the overlapping Venn diagrams that demonstrate substantial intersection between these 2 diseases. AS increases with increasing age; although its morbidity and mortality have been documented since seminal work in the 1950s and 1960s (2), within the past 15 years, interest has grown exponentially. This growth is based on factors including, among others, the following: 1) up to approximately 30% of patients with severe AS did not receive guideline-based surgical aortic valve replacement; and 2) transcatheter aortic valve replacement (TAVR) has been developed, tested, applied in approximately 250,000 patients and procedures worldwide since its introduction in 2002 (3).

The dramatic growth in TAVR was based initially on its application in patients believed to be either high risk or inoperable for surgical aortic valve replacement. These high-risk features include advanced age and multiple comorbidities, the latter of which often make long-term anticoagulation (AC) problematic. The goals of TAVR in this population include documented survival benefit in some subsets, reduction in hospitalizations for congestive heart failure, and, perhaps most important, an improvement in quality of life.

Although TAVR demonstrated a survival benefit, there was a higher than expected incidence of disabling post-procedural and follow-up strokes, especially with the first-generation devices. Potential mechanisms include embolization from the aorta, the native valve, and/or the left atrial appendage, as well as periprocedural interruption of antithrombotic agents in patients with AF. Since those early studies, intense research has been directed at reducing the risk for stroke. Reduction in the size of delivery systems has helped. In addition, ongoing studies are evaluating the role of embolic protection carotid filters during the procedure.

AF has also generated great interest because it is the most common significant arrhythmia; it is associated with increasing age, and it plays a central role in the etiology of stroke in older patients (4,5). Specifically, nonvalvular AF has been believed to be the putative mechanism of stroke in at least 20% of older patients. Although AC has been studied intensively and has been found to decrease stroke rates, it is underused, often because of bleeding concerns (6). For these issues, local site-specific treatment strategies have been developed. Now tested in 2 well-designed randomized clinical trials and 2 registries in the United States resulting in U.S. Food and Drug Administration approval for a specific device for left atrial appendage closure (LAAC) (WATCHMAN, Boston Scientific, Natick, Massachusetts), as well as multiple registries outside the United States with different devices, local site-specific therapy has been found to be noninferior and even superior to at least conventional warfarin, with a dramatic reduction in hemorrhagic stroke, decreased bleeding from long-term AC, a survival advantage, and improved quality of life (7).

An important issue in this opening and closing space is the fact that up to 35% to 40% of patients
undergoing TAVR have AF, and many of these patients are at risk for stroke by virtue of the arrhythmia (8). Also, many have relative or even absolute contraindications to long-term AC. Transcatheter LAAC following successful TAVR could therefore be a reasonable option for stroke prevention, without the need for systemic AC with its bleeding complications. For these reasons, this study of 52 patients with severe AS at increased stroke risk and bleeding undergoing concomitant TAVR and LAAC is extremely important (1). Opening the stenotic valve with a new valve while closing the left atrial appendage merges the goals of TAVR—improving survival, decreasing congestive heart failure, improving quality of life—and LAAC—improving survival, decreasing stroke, decreasing the need for long-term AC, and improving quality of life.

Attinger-Toller et al. (1) evaluated a cohort of 52 patients (mean age 85 ± 5 years, mean CHADS2-VASc score 3.9 ± 1.1, mean HAS-BLED score 2.6 ± 0.9, mean Society of Thoracic Surgeons score 7.8 ± 5.5) undergoing combined LAAC and TAVR compared with 52 patients with similar baseline characteristics undergoing isolated TAVR. Median follow-up was 9.4 months (range: 0 to 40 months). As an observational study rather than a randomized trial, performance of concomitant LAAC was based on patient wishes and physician and surgeon preference, not random assignment. The primary 30-day safety endpoint was a composite (all-cause mortality, stroke, transient ischemic attack, bleeding, acute stage 2 or 3 kidney injury, major vascular complications, and a clinically significant pericardial effusion). A clinical efficacy endpoint included events from day 30 to the time of last clinical follow-up (mean 9.4 months). This endpoint included all-cause mortality and stroke as well as life-threatening or major bleeding. Finally, in this small series, post-procedural medications varied, which could have implications for interpretation of the results. For example, in the combined TAVR-LAAC patients, oral AC in general was discontinued, although in 5 patients (10%) it was continued for “some additional period.”

There are several extremely important items to consider in this small series. First, a total of 7 different TAVR devices were used, with variable designs, for example, self-expanding versus balloon expandable. It is thus not possible to assess interactions between TAVR designs and LAAC device.

Second, approximately 90% of TAVR procedures were transfemoral; determining whether there was or could be any interaction between specific access approaches, for example, transfemoral versus transapical, and LAAC is not possible.

Third, only an Amplatz Cardiac Plug device was used for all LAAC procedures. There are several different devices for this purpose used worldwide (7); accordingly, whether the application of these other devices would affect outcomes in concomitant procedures cannot be determined.

Fourth, LAAC was performed during the index procedure, usually after TAVR. This has important implications. From the patient standpoint, it eliminates the need for a second procedure. From the procedural performance standpoint, it makes intuitive sense to ascertain the stability of the primary procedure, TAVR, before initiating the second one, LAAC. Also, it is safer to perform LAAC after TAVR because if on rare occasions there is embolization of the left atrial appendage occluder, in the presence of uncorrected AS, the embolized device could get trapped in the left ventricular outflow tract, with catastrophic interruption of forward blood flow.

Finally, in this small series, post-procedural medications varied, which could have implications for interpretation of the results. For example, in the combined TAVR-LAAC patients, oral AC in general was discontinued, although in 5 patients (10%) it was continued for “some additional period.” Patients then received dual-antiplatelet therapy for 1 to 6 months; in contrast, patients undergoing isolated TAVR received continued AC in combination with either dual- or single-antiplatelet therapy. This variability makes attribution of any specific effect of drug versus device to outcomes at least difficult.

Taking these issues into consideration, evaluation of the procedural, clinical safety, and efficacy outcomes is extremely valuable. Although the numbers are very small, as documented, there was no difference in safety outcomes. Some events might be intuitively considered more common with LAAC, such as pericardial effusion, but there was only 1 versus 0 events. Acute kidney injury was also numerically more frequent with concomitant therapy, perhaps related to the administration of more contrast and adding LAAC to the TAVR procedure, but the numbers, 4 versus 1, are only anecdotal (1).

From a clinical standpoint, at 9.4-month follow-up, the clinical efficacy endpoint was achieved in 75% of the concomitant group compared with 82% in isolated TAVR patients (95% confidence interval: 0.49 to 2.92). Multivariate analysis did not reveal a significant difference between concomitant and isolated procedures for the composite clinical efficacy endpoint. Although mortality occurred in 20% of these older high-risk patients, no deaths were believed to be “directly associated with LAAC.”
CONCLUSIONS

This was a proof-of-concept pilot study, with the attendant limitations described in the report itself. Nevertheless, this novel concept of opening one—the valve with TAVR—and closing the other—the left atrial appendage with LAAC—appears to be safe but needs much larger, well-designed studies. As a potential strategy, however, the concept is strikingly attractive and would achieve the goals of TAVR—improving survival, alleviating congestive heart failure, and improving quality of life—as well as the goals of LAAC—reducing the burden of stroke from AF without the need for AC, decreasing long-term bleeding, and thereby also improving quality of life. After 10 years of well-scrutinized research, the first transcatheter LAAC device was approved in the United States in 2015; the time is right to test this extremely attractive “opening and closing” concept in a formal prospective study.

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REFERENCES


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