Editorial

Editorial on the article entitled "Surgical ablation of atrial fibrillation during mitral-valve surgery"

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Atrial fibrillation (AF) is very commonly accompanied by mitral valve (MV) diseases. As hemodynamic overload on the left atrium (LA) either by regurgitant blood volume or by increased hydrostatic pressure secondary to mitral stenosis persists, atrial tissue undergoes pathologic changes such as enlargement of LA chamber, thinning of atrial wall and reduction in number of atrial myocytes, which are replaced by interstitial fibrosis. In addition to these arrhythmogenic environments in the atria, increased electrical autonomicity in the junction between pulmonary veins and LA leads to abnormal pacemaker activities, this now is regarded as the key culprit of AF. As many as 20-60% of patients undergoing MV surgeries are reported to have AF, and this coexisting AF has long been regarded as poor prognostic marker in patients undergoing MV surgeries (1). Thanks to longstanding dedicated efforts in cardiac surgical society initially propelled by Dr. James Cox, we now have a great solution to treat this disease—the Maze procedure (2).

Technical evolutions of AF surgery have replaced the initial cut-and-sew Maze procedure to ablation lesions using sophisticated devices such as cryo- and radio-frequency ablation systems. Greater understanding on the pathophysiologic mechanism of AF and recognition of drawbacks of initial Cox-Maze procedures has triggered a number of modifications of the ablation techniques to increase the procedural efficiency and to reduce the risks of troublesome bradyarrhythmias. These advancements have let surgeons undertake the AF ablation surgeries more easily and comfortably. There have been numerous researches that proved the efficacy of the Maze procedure in the elimination of AF including randomized trials (3-10). Nevertheless, there are still ongoing debates over routine performance of the Maze procedure in combination of MV surgeries. For instance, data from Society of Thoracic Surgeons database reveals that only around 40% of patients receive concomitant Maze procedure during major cardiac surgeries when patients present with AF (11): this findings indicate that a significant proportion of surgeons in North America are not fully convinced with the benefit of AF ablation procedure to offset the potential risks added by the procedure.

This time, Cardiothoracic Surgical Trials Network (CTSN) Investigators revealed results of a randomized trial on surgical ablation of AF during MV surgery (12). They randomized 260 patients with persistent or long-standing persistent AF who required MV surgery to undergo either surgical ablation of AF or no ablation to see whether there is a significant difference in freedom from AF at 6 and 12 months postoperatively. The addition of AF ablation procedure did not increase early procedural mortality or morbidity, and the only differences in the perioperative period is that CPB time was average 15 minutes longer in the ablation group that the control group, which was statistically significant.

As might be expected, patients in the ablation group showed significantly superior freedom from AF compared to the control group patients (63.2% *vs.* 29.4%, P<0.001). Some of expert surgeons in the field of AF surgery might have been disappointed by the relatively poor AF-free rate in the ablation group, however, this may be attributable to a rigorous manner of rhythm monitoring in this trial—patients underwent 3-day Holter monitoring, which will capture more AF burden than other monitoring tools such as snap electrocardiogram (EKG) shots or continuous monitoring with shorter duration that are used in most of

clinical researches on Maze procedures.

Superior freedom from AF by AF ablation procedure indeed is not a new finding as prior randomized trials had consistently proved superior rhythm outcomes of the AF ablation group compared with no-ablation group (3,7-10). Distinctive features of the trial by CTSN this time include enrollment of the largest cohort ever, multi-center involvement as well as further randomization of the ablation group patients into two subgroups—bi-atrial *vs.* left atrial ablation. Despite an overall superior success rate of AF elimination in the ablation group, the benefit was paid by a higher rate of permanent pacemaker (PPM) implantation (21.5% *vs.* 8.1%). Procedural drawbacks of initial Cox-Maze procedures include postoperative bradyarrhythmias such as sick sinus syndrome and conduction blocks necessitating permanent pacing. AF ablation procedures in the current era, however, has shown very low risk (<5%) of permanent pacing, and this is also supported by previous randomized trials and a recent meta-analysis (3). The authors of the CTSN trial explain this high rate of PPM implantation in the ablation group by high baseline risk profiles of subject patients (multi-valve surgeries, old age), however, not many expert AF ablation surgeons would agree on that—rather, the high rate of PPM perhaps is better explained by multi-center involvement, which will be more likely to demonstrate real world practices.

Another important finding in the paper is that there were no significant differences in the outcomes between biatrial maze procedure and pulmonary vein isolation (PVI) including freedom from AF and adverse events: freedom from AF was 66% in the biatrial maze group and 61% in the PVI group (P=0.60). Taking a more detailed look at the procedural characteristics, biatrial maze procedures involved PVI plus two additional linear ablations in addition to right atrial ablation. On the other hand, PVI group did not involve any of LA linear ablations as well as right side procedure. Negative results from this study may be a happy news to cardiac surgeons because we may not need more complex biatrial procedure to treat AF, however, the study results seem counterintuitive based on recent observational studies as well as a meta-analysis in support of significant superior rhythm outcomes in the biatrial AF ablation procedures (13,14). Of note, sample sizes for the study were not determined to compare the two AF ablation methods, and therefore they were significantly underpowered to distinguish the outcomes as the authors admit. For clearer answer for this question, trials on larger cohorts are required.

Finally, there were no significant differences in late adverse outcomes between the ablation and no-ablation group. Main purpose of the Maze procedure perhaps is to reduce risks of adverse outcomes such as stroke, heart failure and death by restoring normal sinus rhythm. In this regard, the study findings of similar clinical outcomes between the ablation and no-ablation groups seem quite disappointing. Moreover, recent observational studies including our prior researches have consistently shown that concomitant Maze procedure during valve surgeries may reduce risks of stroke and death (4-6,15,16). Of note, these clinical benefits are usually revealed throughout late period (>1 year) during follow-up. In this regard, 1-year follow-up in the CTSN trial is too short to see the overall clinical benefits of concomitant AF ablation procedure. In addition, again the study is quite underpowered to compared hard clinical endpoints (stroke, death) as this was not the primary purpose that the trial wanted to see. Based on prior observational studies, follow-up of at least 3 years is required to see the meaningful differences in net clinical outcomes.

Conducting randomized trials in the field of cardiac surgery has long been regarded challenging because of ethical and financial constrains as we deal with high risk procedures, and this recent CTSN trial led by Dr. Gillinov is among only few prospective randomized trials in our field. This trial not only revealed a clear view on the effects of AF ablation procedure during MV surgeries but also calls for further trials to answer important questions on the best way to ablate AF as well as on the long-term impacts of the Maze procedure in terms of prevention of serious adverse outcomes.

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Footnote

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