LEFT ATRIAL APPENDAGE OCCLUSION IN RESEARCH AND IN REAL-WORLD PRACTICE

Reply to the Editor:

We read with interest Dr Gupta's letter¹ regarding our report² and are grateful for the opportunity to further discuss our findings. We believe that many of his concerns might be assuaged by clarification of our statistical methods. First, the Hosmer–Lemeshow test, which has been historically used in clinical research, has fallen out of favor among biostatisticians because of its arbitrary selection of bin numbers.^{3,4} Recent recommendations advocate for tailored threshold criteria on the basis of the field of application and visual assessment of calibration plots, which allows in-depth examinations of the model's predictive power.³ As shown in Figure 1 in our report, our propensity score model has produced an appropriately skewed distribution toward 0 in the control group and 1 in the intervention group.

Second, we used propensity scores for weighting rather than matching. This was done to comply with reporting standards mandated by the National Inpatient Sample, which dictate that survey-specific analyses be used to account for clustering and stratification.⁵ We assigned propensity scores to each hospitalization using a multilevel multivariate logistic regression model. Subsequently, normalized inverse probabilities generated by the propensity score model were multiplied by National Inpatient Sample discharge weights to be used as weights for each data element in the univariate logistic regression that estimates the odds for stroke. Congestive Heart Failure, Hypertension, Age (≥ 75 years), Diabetes, Stroke/Transient Ischemic Attack, Vascular Disease, Age (65–74 years), Sex (Female) scores were not used for weighting of regression analyses because of the similar distribution between the 2 comparison groups.

Retrospective studies such as ours allow researchers to answer questions of a different nature from those targeted by randomized controlled trials (RCTs). In our study we sought to evaluate whether left atrial appendage (LAA) ligation, as currently practiced by surgeons across the United States, is associated with lower stroke risk. Whether the observed lack of association was because of incomplete occlusion using existing methods or true futility of the procedure remains unclear. As Dr Gupta noted, we are unable to delineate the technique of ligation and thus cannot account for technical variations that might contribute to our results. However, RCTs such as the Left Atrial Appendage Occlusion Study (LAAOS) III,⁶ seek to explore whether LAA occlusion, when successfully completed, reduces

FIGURE 1. Histogram of propensity score distribution among patients who received left atrial appendage (LAA) ligation and control participants. The propensity score model was designed to predict probability of receiving LAA ligation for each patient. The resulting propensity scores were significantly skewed toward 1 among patients who eventually underwent LAA ligation and toward 0 among control participants. CABG, Coronary artery bypass grafting.

stroke incidence. Despite a potential discrepancy between findings of the RCT and our study, the validity of our finding would not be negated. Instead, it would imply that nationally prevalent LAA ligation practices must be improved and future efforts at optimizing patient selection, developing novel occlusion devices, or implementation of routine intraoperative practices, such as transesophageal echocardiogram, might be of value.

In conclusion, evidence-based evaluation of surgical procedures has recently become a sophisticated science requiring cross-disciplinary efforts from biostatisticians, clinicians, and government/industry funding entities. The best answer to any research question is frequently a thoughtful “it depends...” rather than a simple yes/no because of the complexities inherent in all real-world practices that have been deliberately suppressed in research settings. Surgeons should endeavor to interpret conclusions of each study in the context of its methodology and limitations to optimally modify their practice.

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Unfortunately, the LAA literature is akin to the maze data, with incredible heterogeneity making data analysis extremely challenging. Although signals exist that surgical treatment may benefit select populations, this remains speculative. Naturally, a prospective, randomized trial that uses a standard technique may ultimately answer the question. Until then, and for the time being, debates will continue online, at meetings, and in the literature.

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WE MUST AMPUTATE!?

Reply to the Editor:

Controversy remains regarding the fate of the left atrial appendage (LAA). Multiple forms of open and closed ligation exist, apparently with low morbidity and mortality.

Unfortunately, the jury is still out. Proponents of a “no-touch technique” cite high failure rates and equivalent outcomes. Surgical studies, on the other hand, have generally been underpowered and nonprospective.

In their recent article in the *Journal*, Juo and colleagues¹ made a valiant effort to resolve the LAA dilemma. In 2 separate responses, one by us and the other by Gupta and colleagues,² several design flaws and statistical limitations were highlighted. Nevertheless, their message resonated with us. The Left Atrial Appendage Occlusion Study II (LAAOS II), a randomized, controlled trial, evaluated LAA occlusion in patients undergoing cardiac surgery.³ No difference in stroke rate was seen. Similarly, the PREVAIL (Watchman LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy) trial also failed to demonstrate superiority of mechanical closure of the LAA for stroke prevention.⁴ Furthermore, surveillance echocardiograms have found unexpectedly high failure rates (40%-60%) for surgical occlusion of the LAA.^{5,6} On the other hand, a well-designed retrospective study by Caliskan and colleagues⁷ looking at a surgical closure device in patients undergoing cardiac surgery showed a significant neurologic benefit in patients who discontinued oral anticoagulation.

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“APPENDING” ONTO LEFT-SIDED THORACOSCOPIC OPERATIONS: AN OBVIOUS TWO-FOR-ONE BARGAIN?

Reply to the Editor:

Since the left atrial appendage (LAA) was identified as the thromboembolic source in at least 90% of nonvalvular atrial fibrillation-related strokes,¹ excluding this appendage has been the subject of a seemingly endless number of clinical trials, surgical techniques, and occlusive devices.