

The inadvertent compounding of misconceptions regarding the surgical treatment of atrial fibrillation in mitral valve patients

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We thank the editors of the *Journal of Thoracic Disease* for inviting us to provide editorial commentary on a paper by Blackstone et al. that was published earlier this year in the Journal of Thoracic and Cardiovascular Surgery (1). This article is a follow-up re-analysis of a portion of the data reported in a randomized controlled trial (RCT) conducted by the Cardiothoracic Surgical Trials Network (CTSN) investigators that was published in the New England Journal of Medicine (NE7M) in May 2015 (2). The CTSN RCT was designed to determine if patients with long-standing persistent atrial fibrillation (LSPAF) undergoing mitral valve surgery (MVS) benefit from the concomitant surgical ablation of the AF. It clearly documented that patients who have LSPAF and need MVS have less AF 1-year after surgery if their AF is surgically treated (63.9%) rather than not treated (29.4%) (P<0.001). This was an important finding confirmed by a multi-center, prospective RCT.

Unfortunately, the CTSN authors then compared the results of the two types of surgical procedures that were used in the surgical ablation arm of the RCT, pulmonary vein isolation (PVI) and another surgical approach that they called a "Biatrial maze procedure". Judging by the lesion patterns and surgical devices described in the Appendix of the original CTSN RCT, the authors were apparently attempting to perform a Maze-IV procedure (3). They acknowledged that their study was insufficiently powered to make such a comparison but nevertheless, it was made and reported in

the NE7M. The results of this under-powered subgroup analysis of the two AF surgical techniques suggested that PVI was essentially as effective as their so-called "Biatrial maze procedure" in treating LSPAF associated with mitral valve disease, with successful AF ablation rates of 61% and 66%, respectively (P=0.60). Unfortunately, this underpowered portion of the RCT comparing PVI to a "Biatrial maze procedure" quickly became the "take away" message of the CTSN RCT and undoubtedly led to the subsequent treatment of concomitant LSPAF with a clearly inadequate surgical procedure, PVI. The statistical similarity of the success rates of the two surgical procedures for LSPAF occurred not only because the comparison was underpowered, but also because of the inexplicably low 66% 1-year success rate for the "Biatrial maze procedure". That figure is far less than the reported 1-year success rates for properly performed Maze-III procedures (both cutand-sew and totally cryosurgical Maze-III) and Maze-IV procedures, which have consistently been $\ge 90\%$ at 1-year follow-up (4-10) and in fact, remain above 85% for up to 15 years (6). The reason the "Biatrial maze procedure" had such dismal results in the CTSN RCT was that it was not, in fact, a Maze procedure and some of the technology used was unreliable.

The 66% 1-year success rate for the "Biatrial maze procedure" in the CTSN RCT should have raised an immediate red flag for the reviewers and editors of the *NE7M* regarding whether or not the patients were actually receiving a properly performed Maze-IV procedure. In the case of the CTSN RCT, the lesions described in the appendix of the NE7M paper superficially resemble a Maze-IV procedure, leading the reader to believe that their "Biatrial maze procedure" was a properly performed Maze-IV procedure. It was not (3,11). The critical coronary sinus lesion of all Maze procedures (Maze-I, II, III, and IV) (3,11-15) appeared in none of the drawings of the surgical technique in the paper's appendix and it was not mentioned in the manuscript. Thus, one can logically assume that it was not performed as a part of the "Biatrial maze procedure" described in the CTSN RCT. The detrimental effect on outcomes of eliminating the coronary sinus lesion in a Maze procedure is roughly equivalent to using a saphenous vein rather than a LIMA to bypass the LAD coronary artery during a CABG procedure.

Bipolar radiofrequency clamps, which are highly reliable ablation devices (16), were used to isolate the pulmonary veins in both the PVI procedure and in the "Biatrial maze procedure". However, as noted in the Appendix to the CTSN RCT, 41% of the other linear lesions in the left atrium in the "Biatrial maze" group were created with unipolar pens, which are notoriously unreliable in creating contiguous, uniformly transmural linear lesions in the atria (16). Moreover, all of the right atrial lesions in the "Biatrial maze procedure" were created using those same unreliable unipolar pens. In addition, surgeons were allowed to combine the right atrial lesions of the "Biatrial maze procedure" with the socalled "flutter line" across the cavo-tricuspid isthmus in the right atrium, a combination that electrically isolates the lower one-half to one-third of the right atrium (15). This is the area of the atrial pacemaker complex (17) in the right atrium where sinus bradycardia impulses originate when the heart rate is below 60 beats per minute, e.g., during sleep. One of the right atrial lesions used in the "Biatrial maze procedure" described in the CTSN RCT actually bisects the atrial pacemaker complex in the right atrium, a certain way to cause more pacemakers to be needed postoperatively (18). Thus, the "Biatrial maze procedure" in the CTSN RCT was not a Maze-IV procedure at all but rather, a series of incomplete lines of conduction block placed in both atria, some of which were placed in the wrong locations, especially in the right atrium. These socalled "Biatrial maze procedures" were not actual Maze-IV procedures, so readers of the NE7M were provided with misleading and potentially dangerous information. The potential adverse effect on patient care demonstrates

why it is so critical that any cardiac surgical procedure be performed correctly, especially if it is to serve as one of the treatment arms of a RCT.

Patients who received the so-called "Biatrial maze procedures" as a part of the CTSN RCT also required more permanent pacemakers postoperatively than almost any other report, a finding that further enhanced the erroneous "take-away" message that patients who have LSPAF and need MVS should be treated with PVI rather than with a Maze procedure because the latter cause patients to need more permanent pacemakers. In fact, there was no statistical difference in postoperative SA node dysfunction in patients who had AF ablation (34.6%) and those who had no AF ablation (33.3%). The increased need for postoperative pacemakers in the AF ablation group was due to an increase in postoperative "heart block" being higher in the AFablation group (53.9%) than in the no AF ablation group (44.4%). Heart block can be created only by damaging the AV node-His bundle complex, which is located in the atrial septum with extension into the ventricular septum. Thus, it is anatomically impossible to create heart block with by surgical procedure without creating an atrial septal lesion (18). However, the Maze-IV procedure does not include an atrial septal incision (3,18) and neither did the "Biatrial maze procedure" described in the CTSN RCT (1). This means that the ablation surgical procedure itself could not possibly have been the cause of the increased incidence of heart block following surgery.

The CTSN RCT authors noted that patients in the surgical ablation arm were older, had more mitral valve replacements, and more multivalve replacements than the untreated arm, all of which are associated with an increased need for postoperative pacemakers due to heart block (1). Another major reason for the increased pacemaker requirements in the surgical group, not mentioned by the authors of the CTSN RCT, is that the AF surgical procedures employed (PVI or "Biatrial maze procedure"), despite their inadequacies, successfully ablated more of the LSPAF in the surgical ablation group than in the non-ablated group. It is well documented that successful ablation of atrial fibrillation, especially the LSPAF type, frequently "unmasks" an underlying sick sinus syndrome so that curing the problem (LSPAF) necessarily increases the need for more pacemakers for that reason (18). The adage that "successful AF surgery begets increased pacemaker requirements" is true, but it is not because the surgical procedure itself is damaging the SA node or the AV Node-His bundle complex.

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In summary, the CTSN RCT sub-analysis that was reported as a comparison (albeit an underpowered one) of PVI vs. an alleged Maze-IV procedure for the treatment of concomitant LSPAF was, in fact, a comparison between PVI and a so-called "Biatrial maze procedure" that did not adhere to the concept of creating a maze pattern of lesions in the atria. This error emphasizes the fallacy of using the word "maze" as a generic term for any type of surgery performed for atrial fibrillation (11,19), including untested and incomplete surgical procedures in either or both atria. The Maze procedure is one of two specific lesion patterns (Maze-III or Maze-IV) that strictly adhere to a specific set of lesions to accomplish a specific set of goals. In addition to the specific pattern, it is crucial that every single lesion be contiguous (no gaps) and uniformly transmural, whether performed using a knife, a pair of scissors, a cryoprobe, or bipolar and unipolar radiofrequency (RF) devices. Electrophysiologically, the Maze-III procedure (both the "cut-and-sew" Maze III and the totally cryosurgical Maze-III) and the Maze-IV procedure are identical, the only difference being in the devices used to create the lesions, the way the pulmonary veins are isolated, and the conduct of the two operations (11). Eliminating any one of the recommended lesions (e.g., the coronary sinus lesion) or using ablation devices that are known to create incomplete lesions (e.g., unipolar RF devices), immediately identifies that operation as being something other than a true Maze-III or Maze-IV procedure regardless of how much it might superficially resemble them.

We were asked to editorialize on Blackstone's improved follow-up statistical analysis of the original CTSN RCT data. Because that RCT was so egregiously flawed, a further analysis of its misleading data amounts to a compounding of misinformation and thus, cannot help but further confuse the readers of both articles. Nevertheless, Blackstone et al. have documented that even despite receiving an operation that only superficially resembled a Maze-IV procedure, the patients who received a so-called "Biatrial maze procedure" have statistically less AF on further follow-up than those patients who received PVI. In other words, their follow-up analysis shows that even poorly performed bi-atrial surgical procedures are superior to PVI for the ablation of LSPAF. Perhaps this will encourage more surgeons to learn the intricacies of the Maze-III and Maze-IV procedures and apply one of them in the future rather than using a PVI for LSPAF in mitral valve patients. Based on the surgical results of numerous experienced arrhythmia surgeons over the past three decades, the comparison of an accurately performed

Maze-III or Maze-IV procedure with PVI for the treatment of LSPAF, with or without concomitant MVS, should not require a very sophisticated statistical analysis to document the major difference in their respective outcomes.

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None.

Footnote

Conflicts of Interest: JL Cox, MD: Consultant and Stockholder in the following companies: Atricure, Inc., Mason, Ohio, USA; Adagio Medical Inc., Laguna Hills, California, USA. Also on Board of Directors in the following companies: SentreHEART Inc., Redwood City, California, USA; PAVmed, Inc., New York City, New York, USA; Lucid Diagnostics, Inc., Cleveland, Ohio, USA. PM McCarthy, MD: Consultant for Edwards Lifesciences, Inc., Irvine, California, USA; and he also receives royalties from Atricure, Inc., Mason, Ohio, USA; Medtronic, Inc., Minneapolis, MN, USA; Abbott Vascular, Inc., Minneapolis, MN, USA.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

- Blackstone EH, Chang HL, Rajeswaran J, et al. Biatrial maze procedure versus pulmonary vein isolation for atrial fibrillation during mitral valve surgery: New analytical approaches and end points. J Thorac Cardiovasc Surg 2019;157:234-43.e9.
- Gillinov AM, Gelijns AC, Parides MK, et al. Surgical ablation of atrial fibrillation during mitral-valve surgery. N Engl J Med 2015;372:1399-409.
- Ruaengsri C, Schill MR, Khiabani AJ, et al. The Cox-maze IV procedure in its second decade: still the gold standard?. Eur J Cardiothorac Surg 2018;53:i19-25.
- Cox JL, Boineau JP, Schuessler RB, et al. Five-year experience with the maze procedure for atrial fibrillation. Ann Thorac Surg 1993;56:814-23; discussion 823-4.
- Cox JL, Schuessler RB, Lappas DG, et al. An 8 1/2-year clinical experience with surgery for atrial fibrillation. Ann Surg 1996;224:267-73; discussion 273-5.

- Prasad SM, Maniar HS, Camillo CJ, et al. The Cox maze III procedure for atrial fibrillation: long-term efficacy in patients undergoing lone versus concomitant procedures. J Thorac Cardiovasc Surg 2003;126:1822-8.
- Weimar T, Schena S, Bailey MS, et al. The cox-maze procedure for lone atrial fibrillation: a single-center experience over 2 decades. Circ Arrhythm Electrophysiol 2012;5:8-14.
- 8. Ad N, Holmes SD, Massimiano PS, et al. Long-term outcome following concomitant mitral valve surgery and Cox maze procedure for atrial fibrillation. J Thorac Cardiovasc Surg 2018;155:983-94.
- Stulak JM, Sundt TM 3rd, Dearani JA, et al. Ten-year experience with the Cox-maze procedure for atrial fibrillation: how do we define success?. Ann Thorac Surg 2007;83:1319-24.
- Musharbash FN, Schill MR, Sinn LA, et al. Performance of the Cox-maze IV procedure is associated with improved long-term survival in patients with atrial fibrillation undergoing cardiac surgery. J Thorac Cardiovasc Surg 2018;155:159-70.
- Cox JL, Churyla A, Malaisrie SC, et al. When Is a Maze Procedure a Maze Procedure? Can J Cardiol 2018;34:1482-91.
- 12. Cox JL. The surgical treatment of atrial fibrillation. IV. Surgical technique. J Thorac Cardiovasc Surg

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1991;101:584-92.

- Cox JL. The Maze III procedure for treatment of atrial fibrillation. In: Sabiston DC Jr. editor. Atlas of Cardiothoracic Surgery. 1st editon. Philadelphia: W.B. Saunders Co., 1995:460-75.
- Cox JL. The cut-and-sew Maze-III procedure. In: Gardner TJ, Spray TL. editor. Operative Cardiac Surgery. 6th edition. London: Hodder Education Publishers, 2018.
- Cox JL, Malaisrie SC, Kislitsina ON, et al. The electrophysiologic basis for lesions of the contemporary Maze operation. J Thorac Cardiovasc Surg 2019;157:584-90.
- Bugge E, Nicholson IA, Thomas SP. Comparison of bipolar and unipolar radiofrequency ablation in an in vivo experimental model. Eur J Cardiothorac Surg 2005;28:76-80; discussion 80-2.
- Boineau JP, Schuessler RB, Canavan TE, et al. The human atrial pacemaker complex. J Electrocardiol 1989;22 Suppl:189-97.
- Cox JL, Ad N, Churyla A, et al. The Maze Procedure and Postoperative Pacemakers. Ann Thorac Surg 2018;106:1561-9.
- Ad N. How do we spell maze (2.0)? A dialogue concerning definition and outcome. J Thorac Cardiovasc Surg 2019;157:246-7.

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