Canadian Journal of Cardiology 32 (2016) 281–282

Editorial

Left Atrial Appendage Closure for Atrial Fibrillation: A Story Still Being Written

Iqbal H. Jaffer, MBBS,[a,c] and Richard P. Whitlock, MD, PhD, FRCSC[b,c]

[a] *Thrombosis and Atherosclerosis Research Institute, McMaster University, Hamilton, Ontario, Canada*

[b] *Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada*

[c] *Division of Cardiac Surgery, McMaster University, Hamilton, Ontario, Canada*

See article by Fahmy et al., pages 349-354 of this issue.

Clot formation within the left atrial appendage (LAA) has been implicated in up to 80% of strokes in patients with atrial fibrillation (AF).[1] It is for this reason that closure or ligation of this structure has been aggressively pursued in the past few years. The development of several devices and strategies to occlude the LAA internally (Amplatzer Amulet, St. Jude Medical, St. Paul, MN; WATCHMAN, Boston Scientific, Boston, MA) and externally (Atriclip Atricure, West Chester, Ohio; TigerPaw System II, Maquet Medical Systems, Rastatt, Germany; Lariat, SentreHeart, Redwood City, CA) is a testimony to the strong interest within the medical community to manage patients who are at high risk of bleeding complications who are intolerant of or unable to receive long-term anticoagulation. Although the development of the non–vitamin K antagonist oral anticoagulants (NOACs) can be seen as a success for the management of patients with AF, there continues to be a subset of patients for whom oral anticoagulation is not feasible in the long term. The **Protect**ion in Patients with **A**trial **F**ibrillation (PROTECT-AF) trial sought to evaluate the efficacy of the WATCHMAN LAA occluder compared with warfarin by randomizing patients with atrial fibrillation and $CHADS_2$ (**C**ongestive Heart Failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke/Transient Ischemic Attack) $\geq$ 1 in a 2:1 fashion.[2] The trial suggested noninferiority of the WATCHMAN device and, more importantly, added another option to the armamentarium of clinicians who manage these patients.[2] Currently, the trend in clinical practice is to use devices such as the WATCHMAN in patients who are at high risk of long-term anticoagulation because of previous bleeding issues or for older patients who are viewed to be at a high risk of falls.

In this issue of the *Canadian Journal of Cardiology*, Fahmy et al.[3] describe their experience in a series of 26 consecutive patients with either intracranial hemorrhage (ICH) or intraocular hemorrhage (IOH) who underwent percutaneous closure of the LAA with a variety of devices because of their increased risk of complications with oral anticoagulation. Among the 26 patients, there was 1 transient ischemic attack at 20.6 months and 1 death at 13 months.[3] The authors conclude that this strategy of LAA occlusion/closure is safe and effective in this patient population with AF who are at high risk because of previous major bleeding issues. These patients were managed after the procedure with dual-antiplatelet therapy (clopidogrel and aspirin) for 1-3 months followed by aspirin alone for at least 6 months.

This small series adds to the existing data demonstrating successful use of LAA occlusion in patients at increased risk for OAC-related complications. Helsen et al.[4] and Horstmann et al.[5] have both described similar cohorts who had an ICH while receiving OAC and subsequently underwent LAA occlusion for stroke prevention successfully. However, the generation of evidence supporting these approaches must not stop here. There are also reports that restarting OAC is relatively safe, with the rebleeding rates being lower than the thrombotic rates if the drug is not restarted.[6] The authors of the **C**erebral **H**aemorrhage **i**n Patients **R**estarting **O**ral A**n**ticoagulant Th**e**rapy (CHIRONE) study, which was an observational study that looked at the rate of recurrence of ICH in patients taking a vitamin K antagonist (VKA), showed a low rate of recurrent ICH among 267 patients who resumed VKA therapy and were followed for a median of 16.5 months. Unfortunately, this study did not report the rate of thromboembolic complications in patients who did not restart OAC.[6] Claassen et al.[7] showed that in patients who had a warfarin-associated ICH, the risk of thromboembolism is higher than the risk of recurrent ICH,[7] an observation reproduced in the registry of the Canadian Stroke Network.[8] With the limitations of observational data, however, trials of restarting OAC (with both VKA and NOACs) have been initiated.[9] The evidence supporting LAA occlusion for stroke prevention in patients with AF is still

Received for publication September 10, 2015. Accepted September 16, 2015.

Corresponding author: Dr Richard P. Whitlock, Population Health Research Institute, DBCVSRI, Rm 1C1-5B, 237 Barton St E, Hamilton, Ontario L8L 2X2, Canada. Tel.: +1-905-527-4322 ×44091; fax: +1-905-577-8017.

E-mail: richard.whitlock@phri.ca

See page 282 for disclosure information.

http://dx.doi.org/10.1016/j.cjca.2015.09.008

developing. This report highlights the need for a trial of LAA occlusion vs restarting OAC in patients with a history of ICH while receiving OAC. Other trials that should be considered include evaluating external LAA closure in patients at high risk of bleeding and thrombotic complications, because the percutaneous devices still require a degree of anticoagulation that may be worrisome in an already high-risk population. Additionally, most trials of NOACs and percutaneous closure devices have addressed the question of what to do for patients with nonvalvular AF, but the utility of LAA occlusion in patients with valvular AF is a question that is currently being evaluated in the **L**eft **A**trial **A**ppendage **O**cclusion **S**tudy (LAAOS) III.[10] This trial is currently randomizing patients with AF undergoing cardiac surgery to occlusion or non-occlusion of the LAA in addition to a routine strategy of anticoagulation. The report of Fahmy et al.[3] represents an important step in evidence generation but should be interpreted as hypothesis generating, the hypothesis being that the procedure of LAA occlusion is safe and efficacious for stroke prevention in patients with a history of ICH or IOH; however, this needs to be tested formally in a trial. There is an abundance of work ongoing within this realm of LAA occlusion. The next 5 years will greatly enhance our understanding of the contribution of the LAA to stroke in patients with AF and will allow clinicians to risk stratify their patients with AF even further in an attempt to minimize stroke risk as well as bleeding risk.

Disclosures

I.H.J. has no relevant disclosures. R.P.W. discloses financial honoraria from Atricure.

References

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. Circulation 2015;131:e29-322.

2. Fountain RB, Holmes DR, Chandrasekaran K, et al. The PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic PROTECTion in Patients with Atrial Fibrillation) trial. Am Heart J 2006;151:956-61.

3. Fahmy P, Spencer R, Tsang M, Gooderham P, Saw J. Left atrial appendage closure for atrial fibrillation is safe and effective after intracranial or intraocular hemorrhage. Can J Cardiol 2016;32:349-54.

4. Helsen F, Nuyens D, De Meester P, Rega F, Budts W. Left atrial appendage occlusion: single center experience with PLAATO LAA Occlusion System(®) and AMPLATZER Cardiac Plug. J Cardiol 2013;62:44-9.

5. Horstmann S, Zugck C, Krumsdorf U, et al. Left atrial appendage occlusion in atrial fibrillation after intracranial hemorrhage. Neurology 2014;82:135-8.

6. Poli D, Antonucci E, Dentali F, et al. Recurrence of ICH after resumption of anticoagulation with VK antagonists: CHIRONE study. Neurology 2014;82:1020-6.

7. Claassen DO, Kazemi N, Zubkov AY, Wijdicks EF, Rabinstein AA. Restarting anticoagulation therapy after warfarin-associated intracerebral hemorrhage. Arch Neurol 2008;65:1313-8.

8. Yung D, Kapral MK, Asllani E, Fang J, Lee DS. Reinitiation of anticoagulation after warfarin-associated intracranial hemorrhage and mortality risk: the Best Practice for Reinitiating Anticoagulation Therapy After Intracranial Bleeding (BRAIN) study. Can J Cardiol 2012;28:33-9.

9. RESTART. Restart or Stop Antithrombotics Randomised Trial Eudra CT # 2012-003190-26. Available at: http://www.controlled-trials.com/ISRCTN71907627. Accessed November 2, 2015.

10. Whitlock R, Healey J, Vincent J, et al. Rationale and design of the Left Atrial Appendage Occlusion Study (LAAOS) III. Ann Cardiothorac Surg 2014;3:45-54.