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Editorial

Challenges in Assessing the Incidence of Atrial Fibrillation Hospitalizations

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See article by Meyre et al., pages 1332–1343 of this issue.

Atrial fibrillation (AF) is the most common sustained cardiac rhythm disorder, affecting 1%-4% of the global population.[1] The lifetime risk of developing AF is approximately 25%, which increases with age and other risk factors.[2] It is currently estimated that 33.5 million people worldwide[3] and more than 350,000 Canadians[4] have AF and the prevalence is expected to increase threefold over the next 3 decades with experts categorizing the disease as a future epidemic.[5] The increasing prevalence has important public health implications because AF is responsible for more disability than any other cardiac arrhythmia.[6] In a study that assessed the total costs of AF care in Canada, more than 50% of the costs of AF represent the direct and indirect costs associated with hospitalizations.[6,7] Further, using administrative data from across Canada, the Canadian Cardiovascular Outcomes Research Team reported that AF hospitalizations were rapidly increasing.[8]

Strong associations exist between AF and increased risk of stroke, development of heart failure, and increased mortality.[9] Stroke, in particular, is a leading cause of chronic disability and is associated with subsequent hospitalizations because of long-term cognitive decline and increased risk of recurrent stroke and mortality.[10] Further, approximately 25%-30% of strokes are attributable to the presence of AF.[11] Cognitive decline in AF patients, independent of previous stroke, has also raised concern about the downstream effects of heightened AF burden on health care systems.[12,13] Studies showed that in patients without a previous stroke, AF was an independent risk factor to accelerated cognitive decline and new-onset dementia, both of which might lead to increased long-term institutionalization and care.[12,14] In addition to the development of disease, AF further aggravates prevalent diseases, such as heart failure, chronic kidney disease, and chronic obstructive pulmonary disorder.[9] Therefore, although an evaluation of the true hospitalization burden due to AF is of extreme importance, it a difficult and complex task.

In this issue of the *Canadian Journal of Cardiology*, Meyre et al. report their comprehensive systematic review and meta-analysis to provide a more clear, accurate, and thorough understanding of the increased risk of hospitalizations in patients with AF.[15] The authors included 35 studies that assessed the incidence of all-cause hospitalizations in a total of 311,314 AF patients. Their study showed that the pooled incidence of all-cause hospitalizations was high (43.7 [95% confidence interval, 38.5-48.9] per 100 person-years), which translates to almost half of all AF patients requiring a hospitalization per year. Readers need to be cautious, however, because there was a tenfold heterogeneity between studies, with incidence rates ranging from 8.9 to 88.0 all-cause hospitalizations per 100 person-years. Among the 24 studies that reported the incidence of cardiovascular hospitalizations, AF-related admissions were the most frequent, followed by heart failure, bleeding, stroke, and myocardial infarctions. In a meta-regression analysis, only advancing age and presence of chronic pulmonary disease were identified as positive predictors for all-cause hospitalizations. The high incidence of hospitalizations, all-cause and cardiovascular, led the authors to conclude that effective strategies to reduce hospitalizations and adverse events due to AF are warranted to improve patients' lives and reduce the hospitalization burden of AF patients on health care systems.

Hospitalizations because of AF is a key patient-oriented outcome, in addition to a major effectiveness and health care outcome measure.[7,16] As research evolves to include the patient perspective, studies assessing outcomes important to patients are essential. Reductions in hospitalizations and strokes were identified as the most important outcomes among surveyed AF patients,[7,16] which makes the findings reported by Meyre et al. more relevant and important.[15]

As evidenced by the vast heterogeneity in all-cause hospitalization incidence between studies, the precision of the

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estimate for the association between AF presence and all-cause hospitalization is difficult to quantify. Consequently, the systematic approach to study identification and appraisal combined with the most rigourous meta-analytical techniques, including a random effects model that appropriately accounts not only for within study, but also between study, as used by the authors is necessary to attain this goal.[17] The authors further attempted to explain the residual hospital admission rate variations by applying the common techniques of regression and stratification to the combined results.

It is challenging to differentiate hospitalizations that were attributable to the presence of AF, aggravated by AF, or unrelated to AF. Therefore, the authors also provide evaluation of all-cause hospitalizations in addition to cardiovascular and noncardiovascular hospitalizations separately, which are assumed to reflect AF-related and non-AF-related events. However, ambiguity arises when the authors categorized hospitalization as AF-related, because this is not precisely defined.[15] Although it might be assumed that the primary admission diagnosis was AF, it can be argued that stroke, heart failure, and bleeding events were also AF-related hospitalizations, further emphasizing the challenge of determining the effect of AF.

Although the authors should be applauded for presenting a comprehensive and well written systematic review, which leads to an improve understanding of the burden of hospitalizations due to AF, important pieces of the puzzle concerning the entire disease burden on our health care systems are missing. First, the authors capture the number of hospitalizations, however, the length of stay in these studies was not reported. To understand the AF disease burden on our health care systems, it is important to understand the effect of AF on hospital duration, a surrogate marker for disease severity and resource utilization. Among the studies included in the meta-analysis of Meyre et al., the mean length of stay ranged from 4 to 9 days.[18-23] Future research could investigate these variations in the length of stay using the same techniques of meta-regression and stratification.[10] For example, length of stay might differ according to age or reason for admission. This was indicated in an Australian study, which showed the average length of stay for an AF patient 65 years or older was 12.8 ± 9.0 days,[24] which is greater than that of the overall AF populations included in the present meta-analysis.[15]

Most studies included in the review had a short follow-up time of 1-3 years,[15] and therefore the lifetime burden of AF on hospital admissions is not captured. In randomized trials or studies following patients from the date of new-onset AF or postintervention, AF patients might have more hospitalizations because of therapy changes necessary to effectively manage AF. Hospitalizations might decrease after patients are medically stabilized, therefore the lifetime incidence per 100 person-years might also be less than estimated in Meyre et al.[15]

However, the most difficult aspect of attributing hospitalizations to AF is the potential under-reporting of silent AF, a condition estimated to occur in approximately 10%-30% of AF patients.[11] Because these patients and their physicians are often completely unaware of paroxysmal AF, this untreated condition might unknowingly contribute to ischemic stroke and heart failure hospitalizations.[11] Thus, the estimate in Meyre et al. is on the basis of studies of patients with detected and known AF,[15] which might be an underestimate of the true AF disease burden.

Meyre and colleagues are to be congratulated for focusing our attention on the costly, life-threatening, and adverse quality of life outcomes associated with AF hospitalizations. The authors' conclusions that effective strategies are required to treat AF and reduce hospitalizations is certainly valid. Strategies including better anticoagulation management and newer technologies such as the left atrial appendage closure devices and catheter ablation have been investigated. The use of catheter ablation in particular has shown promise with observational studies indicating that there is a reduction in health care resource utilization, including hospitalizations, after ablation compared with before the procedure.[25,26] However, more data are warranted to investigate potential long-term reductions in stroke risk with left atrial appendage closure devices.[27,28] More methodologically rigourous studies on meaningful patient-centred outcomes, including hospitalizations, due to differing management strategies are certainly warranted.

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References

1. Rahman F, Kwan GF, Benjamin EJ. Global epidemiology of atrial fibrillation. Nat Rev Cardiol 2014;11:639-54.
2. Wang TJ, Larson MG, Levy D, et al. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study. Circulation 2003;107:2920-5.
3. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation 2014;129:837-47.
4. Heart & Stroke: Atrial Fibrillation. Available at: http://www.heartandstroke.ca/heart/conditions/atrial-fibrillation. Accessed August 7, 2019.
5. Morin DP, Bernard ML, Madias C, et al. The state of the art: atrial fibrillation epidemiology, prevention, and treatment. Mayo Clin Proc 2016;91:1778-810.
6. Coyne KS, Paramore C, Grandy S, et al. Assessing the direct costs of treating nonvalvular atrial fibrillation in the United States. Value Health 2006;9:348-56.
7. Xian Y, Wu J, O'Brien EC, et al. Real world effectiveness of warfarin among ischemic stroke patients with atrial fibrillation: observational analysis from Patient-Centered Research into Outcomes Stroke Patients Prefer and Effectiveness Research (PROSPER) study. BMJ 2015;351:h3786.
8. Kotowycz MA, Filion KB, Joza J, et al. In-hospital management of atrial fibrillation: the CHADS(2) score predicts increased cost. Can J Cardiol 2011;27:506-13.
9. Andrade JG, Verma A, Mitchell LB, et al. 2018 Focused update of the Canadian Cardiovascular Society guidelines for the management of atrial fibrillation. Can J Cardiol 2018;34:1371-92.

10. Li X, Tse VC, Au-Doung LW, Wong ICK, Chan EW. The impact of ischaemic stroke on atrial fibrillation-related healthcare cost: a systematic review. Europace 2017;19:937-47.

11. Dilaveris PE, Kennedy HL. Silent atrial fibrillation: epidemiology, diagnosis, and clinical impact. Clin Cardiol 2017;40:413-8.

12. Diener HC, Hart RG, Koudstaal PJ, Lane DA, Lip GYH. Atrial fibrillation and cognitive function: JACC review topic of the week. J Am Coll Cardiol 2019;73:612-9.

13. Ding M, Qiu C. Atrial fibrillation, cognitive decline, and dementia: an epidemiologic review. Curr Epidemiol Rep 2018;5:252-61.

14. Liu DS, Chen J, Jian WM, Zhang GR, Liu ZR. The association of atrial fibrillation and dementia incidence: a meta-analysis of prospective cohort studies. J Geriatr Cardiol 2019;16:298-306.

15. Meyre P, Blum S, Berger S, et al. Risk of hospital admission in patients with atrial fibrillation: a systematic review and meta-analysis. Can J Cardiol 2019;35:1332-43.

16. Perino AC, Shrader P, Turakhia MP, et al. Comparison of patient-reported care satisfaction, quality of warfarin therapy, and outcomes of atrial fibrillation: findings from the ORBIT - AF Registry. J Am Heart Assoc 2019;8:e011205.

17. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008-12.

18. Torp-Pedersen C, Crijns HJ, Gaudin C, et al. Impact of dronedarone on hospitalization burden in patients with atrial fibrillation: results from the ATHENA study. Europace 2011;13:1118-26.

19. Amin AN, Jhaveri M, Lin J. Temporal pattern and costs of rehospitalization in atrial fibrillation/atrial flutter patients with one or more additional risk factors. J Med Econ 2012;15:548-55.

20. Naccarelli GV, Johnston SS, Dalal M, Lin J, Patel PP. Rates and implications for hospitalization of patients >/=65 years of age with atrial fibrillation/flutter. Am J Cardiol 2012;109:543-9.

21. LaPointe NM, Lokhnygina Y, Rimmler J, et al. Use of rate and rhythm control drugs in patients younger than 65 years with atrial fibrillation. J Atr Fibrillation 2014;7:1062.

22. Bengtson LG, Lutsey PL, Loehr LR, et al. Impact of atrial fibrillation on healthcare utilization in the community: the Atherosclerosis Risk in Communities study. J Am Heart Assoc 2014;3:e001006.

23. DeVore AD, Hellkamp AS, Becker RC, et al. Hospitalizations in patients with atrial fibrillation: an analysis from ROCKET AF. Europace 2016;18:1135-42.

24. Nguyen TN, Cumming RG, Hilmer SN. The impact of frailty on mortality, length of stay and re-hospitalisation in older patients with atrial fibrillation. Heart Lung Circ 2016;25:551-7.

25. Samuel M, Avgil Tsadok M, Joza J, et al. Catheter ablation for the treatment of atrial fibrillation is associated with a reduction in health care resource utilization. J Cardiovasc Electrophysiol 2017;28:733-41.

26. Ladapo JA, David G, Gunnarsson CL, et al. Healthcare utilization and expenditures in patients with atrial fibrillation treated with catheter ablation. J Cardiovasc Electrophysiol 2012;23:1-8.

27. Boersma LV, Ince H, Kische S, et al. Evaluating real-world clinical outcomes in atrial fibrillation patients receiving the WATCHMAN left atrial appendage closure technology. Circ Arrhythm Electrophysiol 2019;12:e006841.

28. Piccini JP, Sievert H, Patel MR. Left atrial appendage occlusion: rationale, evidence, devices, and patient selection. Eur Heart J 2017;38:869-76.