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Original Article

Long-term Clinical Outcomes in Contemporary Patients Undergoing Left Atrial Appendage Occlusion Procedures in Ontario, Canada

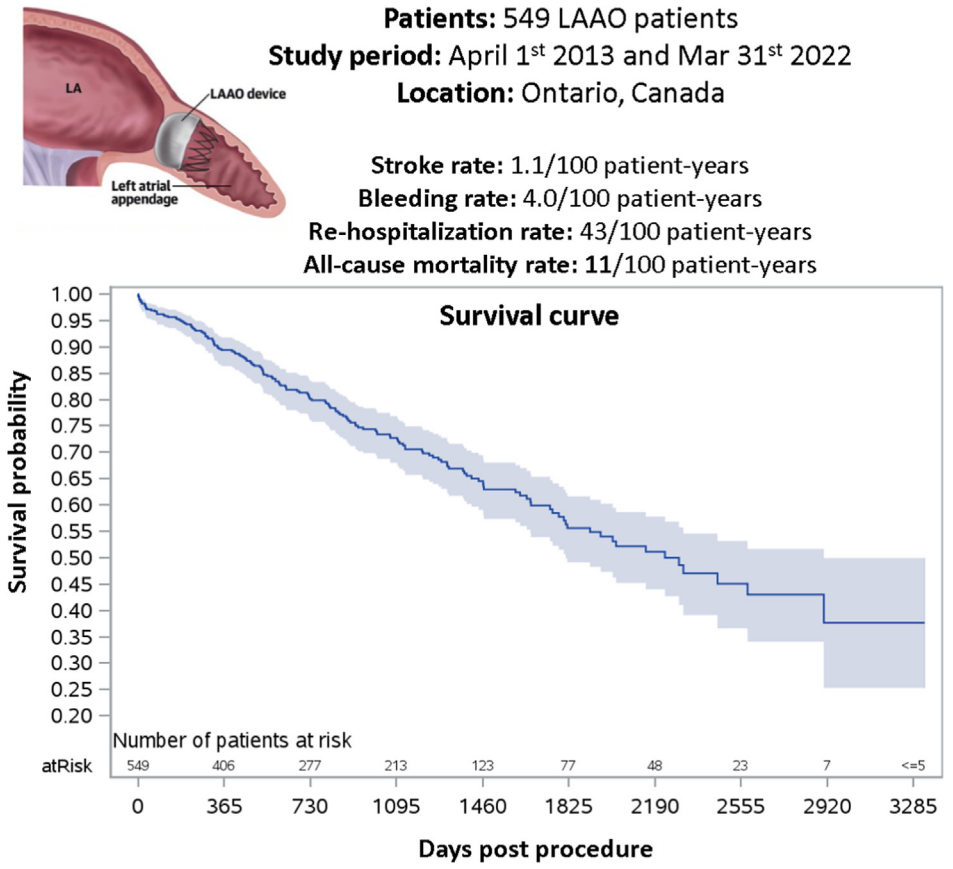
Sheldon M. Singh, MD,[a,b] Feng Qui, MSc,[c] and Harindra C. Wijeysundera, MD[a,b,c,d]

[a] *Schulich Heart Centre, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada*

[b] *Department of Medicine, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada*

[c] *ICES, Toronto, Ontario, Canada*

[d] *Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada*



ABSTRACT

Background: Percutaneous left atrial appendage occlusion (LAAO) is an alternative for stroke prevention in patients with atrial fibrillation with contraindications to oral anticoagulation. Population-level real-world

RÉSUMÉ

Contexte : La fermeture percutanée de l'appendice auriculaire gauche (FPAAG) est une intervention possible pour prévenir les accidents vasculaires cérébraux (AVC) chez les patients atteints de fibrillation auriculaire chez qui

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data describing the use and outcomes of LAAO procedures are evolving, with a paucity of longer-term follow-up data. We report on the patient characteristics, procedure complications, and longer-term clinical outcomes in all patients undergoing LAAO procedures in Ontario, Canada.

Methods: **All patients undergoing LAAO procedure between April 1, 2013 and March 31, 2022 were identified. Linked administrative databases were utilized to determine patient clinical and procedural characteristics. Outcomes of interest included procedural complications at 7 and 30 days, and longer-term rates of stroke, bleeding, all-cause rehospitalization, and mortality.**

Results: **A total of 549 individuals were included in the study cohort. The average age was 75 ± 8 years, with 66% being of male sex, with a mean CHA_2DS_2VASc score of 4.4 ± 1.6, and with 68% not receiving oral anticoagulation. Follow-up for 2.6 ± 2.0 patient-years was available. Stroke occurred in 2.8% during the follow-up period (1.1 per 100 patient-years), bleeding in 10% (4.0 per 100 patient-years), and any hospital readmission in 63% (43 per 100 patient-years). A total of 29% of the cohort died during the follow-up period (11 per 100 patient-years), with 1.8% of the cohort dying during the procedural hospitalization. The mortality rate was unchanged during the study period (*P* for trend = 0.72).**

Conclusions: **Long-term stroke and bleeding rates are low in patients undergoing LAAO procedures in Ontario, Canada. All-cause mortality in this population is high and remained unchanged during the study period.**

les anticoagulants oraux sont contre-indiqués. Les données populationnelles en contexte réel décrivant l'utilisation de la FPAAG et les résultats cliniques qui y sont associés sont de plus en plus nombreuses, mais il y a toujours peu de données sur le suivi à long terme. Nous présentons ici les caractéristiques des patients, les complications liées à l'intervention et les résultats cliniques à long terme pour l'ensemble des patients ayant subi une FPAAG en Ontario (Canada).

Méthodologie : **Tous les patients ayant subi une FPAAG entre le 1er avril 2013 et le 31 mars 2022 ont été recensés. Des bases de données administratives liées ont été utilisées pour relever les caractéristiques des patients et des interventions. Les résultats cliniques d'intérêt incluaient les complications liées à l'intervention à 7 et à 30 jours ainsi que les taux de divers événements à long terme : AVC, hémorragie, réadmission à l'hôpital toutes causes confondues et mortalité.**

Résultats : **Au total, 549 personnes faisaient partie de la cohorte à l'étude. L'âge moyen des patients était de 75 ± 8 ans, et 66 % étaient des hommes. La moyenne du score CHA_2DS_2VASc s'élevait à 4,4 ± 1,6, et 68 % des patients ne prenaient pas d'anticoagulants par voie orale. En moyenne, les données de suivi portaient sur 2,6 ± 2,0 patients-années. Un AVC est survenu chez 2,8 % des patients au cours du suivi (1,1 pour 100 patients-années), une hémorragie est survenue chez 10 % des patients (4,0 pour 100 patients-années) et le taux de réadmission hospitalière toutes causes confondues s'élevait à 63 % (43 pour 100 patients-années). Au total, 29 % des patients de la cohorte sont morts au cours de la période de suivi (11 pour 100 patients-années), et 1,8 % des patients de la cohorte sont morts au cours de l'hospitalisation liée à l'intervention. Le taux de mortalité est demeuré le même au cours de la période à l'étude (valeur *p* de 0,72 pour la tendance).**

Conclusions : **Les taux de survenue d'AVC et d'hémorragie à long terme sont faibles chez les patients ayant subi une FPAAG en Ontario (Canada), mais leur taux de mortalité toutes causes confondues est élevé et est demeuré le même au cours de la période à l'étude.**

Percutaneous left atrial appendage occlusion (LAAO) is emerging as an alternative for stroke prevention in patients with nonvalvular atrial fibrillation (AF). Published randomized controlled trials have demonstrated noninferiority in rates of stroke and improved survival associated with LAAO, compared to warfarin in patients without contraindications to oral anticoagulation (OAC).[1] Despite this, current clinical guidelines across multiple jurisdictions currently recommend LAAO for patients with contraindications to OAC, with these recommendations being of a lower tier or class and based on weak evidence.[2-4]

As the goal of LAAO is to prevent future stroke and bleeding events, further information is needed regarding the safety and efficacy of this therapy. Follow-up data for up to 4 and 5 yearsfor patients without contraindications to OAC undergoing LAAO in clinical trials are available.[1,5]But long-term follow-up data on the effectiveness of LAAO in patients with contraindications to OAC—the population currently indicated to receive this therapy—are limited, with even less population-level data available. Specifically, currently published data from the US National Cardiovascular Data Registry (NCDR) LAAO Registry[6] and Medicare[7] are limited to 1 year of follow-up. Two-year outcome data are available from Europe with the Early Real-World Clinical Outcomes in AF Patients Receiving the Watchman Left Atrial Appendage Closure Technology (EWOLUTION) trial).[8] Ten-year follow-up data have been provided in a multicentre registry, but this was limited to 66 patients undergoing LAAO procedures more than a decade ago.[9] Thus, a paucity of contemporary population data in a multiethnic jurisdiction with long-term follow-up exists in patients currently undergoing these procedures.

In this study, we report the patient characteristics, adverse events, and long-term clinical outcomes in all patients undergoing LAAO procedures in Ontario, Canada between April 1, 2013 and March 31, 2022, thereby providing additional population-level data on the real-world safety and long-term effectiveness of LAAO procedures.

Methods

Study design and setting

This population-level study was conducted using administrative datasets located and analyzed at ICES (previously the Institute for Clinical and Evaluative Sciences) and linked

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Corresponding author: Dr Sheldon M. Singh, Room A222, 2075 Bayview Ave, Toronto, Ontario M3N 3M5, Canada. Tel.: +1-416-480-6100 x83659; fax: +1-416-480-5707.
E-mail: sheldon.singh@sunnybrook.ca
See page 777 for disclosure information.

using unique encoded patient identifiers. ICES is an independent, nonprofit research institute, and its legal status under Ontario's health information privacy law allows it to collect and analyze healthcare and demographic data, without consent, for health system evaluation and improvement. ICES is a prescribed entity under Ontario's Personal Health Information Protection Act, allowing researchers to link deidentified population-based data with clinical registries to conduct approved research studies under regulated privacy and security policies and procedures (see link to Data and Privacy at www.ices.on.ca). The use of ICES data in this project was authorized under Section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a research ethics board, and the need for individual patient consent was waived. Therefore, institutional review board approval was waived. We adhered to the **S**trengthening **t**he **R**eporting of **Ob**servational Studies in **E**pidemiology (STROBE) statement for reporting of observational studies.

Context

In Canada, regulatory approval for percutaneous LAAO was first provided by Health Canada in January 2016. Prior to this date, the use of an LAAO device was permitted under Health Canada's Medical Device Special Access Program—a program that, on a case-by-case basis, permits the use of unlicensed devices by physicians on a compassionate basis when this approach is perceived to be superior to alternatives or when other therapeutic options are unavailable.

Ontario is Canada's most populous province, with 14.6 million individuals who have access to universal healthcare through a single-payer healthcare system. Consistent with previously published cardiovascular society guidelines, a provincial guidance document was published in January 2019 reiterating the patient eligibility criteria for LAAO procedures and highlighting the need for interdisciplinary decision-making prior to patients undergoing LAAO procedures.[10] In the spring of 2020, limited government funding of LAAO procedures became available in Ontario.

Data sources

The CorHealth Ontario Cardiac Registry is mandated to collect data on all invasive cardiac procedures in Ontario. This database was utilized to identify all patients undergoing LAAO procedures. The Canadian Institute for Health Information Discharge Abstract Database provided data on hospitalizations and patient comorbidities. The National Ambulatory Care Reporting System (NACRS) database provided data on hospital-based ambulatory care including emergency department visits. The Ontario Health Insurance Plan database was used to ascertain physician claims. The Ontario Registered Persons Database reported sex, and birth and death dates. Statistics Canada postal code data were used to ascertain rurality. The Ontario Drug Benefit prescription database was used to determine prescription drug use for patients aged $\geq$ 66 years. These data sources were linked using unique encoded identifiers and analyzed at ICES.

Study cohort

Ontario residents between 18 and 105 years of age possessing a valid Ontario Health Insurance Plan number and undergoing a percutaneous LAAO procedure with any commercially available or investigational LAAO device between April 1, 2013 and March 31, 2022 were identified. When a patient was entered more than once within the CorHealth Ontario database (n = 6), only the first patient entry was considered.

Baseline clinical characteristics of the cohort were defined using a 10-year look-back period within the available administrative databases. A hospital frailty index was calculated using administrative comorbidity codes as previously described.[11] The administrative databases were used to identify risk factors for stroke, permitting calculation of the CHA_2DS_2VASc [**C**ongestive Heart Failure, **H**ypertension, **A**ge > 75 years, **D**iabetes, Stroke, **V**ascular disease, **A**ge > 65 Years, **S**ex **C**ategory (Female)] score. Oral anticoagulation use within 90 days prior and subsequent to the procedure was obtained for the subset of the cohort aged $\geq$ 66 years.

Social deprivation

Neighborhood-level data (from the 20,160 dissemination areas in Ontario) on social deprivation were gathered from the 2016 version of the Ontario Marginalization Index (ON-Marg).[12] The ON-Marg is a geographic index derived from census data that can be used to measure health inequities in Ontario across the following 4 dimensions: dependency (concentrations of individuals having no income, including seniors, children, and adults whose work is not compensated); material deprivation (income, quality of housing, educational attainment, and family structure characteristics); ethnic concentration (recent immigrants, and/or belonging to a visible minority group as defined by Statistics Canada); and residential instability (types and density of residential accommodations, and family structure characteristics reflective of neighborhood quality, cohesiveness, and supports). Quintiles describe marginalization for each dimension on a scale of 1 to 5 for each geographic unit, with 1 indicating the least marginalized and 5 indicating the most marginalized.

Procedure characteristics

Characteristics, including length and location of hospital stay, associated with the LAAO procedure were determined. As transesophageal echocardiography (TEE) is recommended during follow-up to assess for adequacy of LAAO, physician billing codes were utilized to ascertain the use of TEE within 1 year post-procedure.

Outcomes

Patents were followed until death or June 30, 2022, which was the end of available follow-up. Procedural complications, including death, and hospitalization for ischemic stroke and/or transient ischemia attack (TIA) or bleeding at 7 and 30 days, were determined. Consistent with prior work, validated approaches utilizing hospital discharge diagnoses were employed to identify these clinical endpoints.[13,14] Pericardial effusion requiring drainage was determined utilizing physician billing codes for percutaneous and surgical drainage of an effusion. All-cause hospital readmission rates and mortality during this time period were determined also.

Using all available follow-up data until June 30, 2022, the long-term rate of ischemic stroke and/or TIA, bleeding,

all-cause hospital readmission, and all-cause mortality for the cohort were determined.

Statistical analysis

Summary statistics were provided for the overall cohort. Cells with fewer than 6 individuals were censored per ICES contractual obligations with data providers. Continuous variables were reported as mean ± standardized deviation (SD), and categorical variables were reported as frequencies and percentages. Incident rates were calculated as the number of events per 100 patient-years of follow-up. The Kaplan-Meier method was used for survival estimates and to demonstrate the time-dependence of death. Cumulative incidence functions, accounting for the competing risk of death, were calculated to determine the estimated rates of stroke and/or TIA, bleeding, and all-cause rehospitalization. Statistical analysis was performed using SAS software, version 9.4 (SAS Institute, Cary, NC).

Results

Study cohort

A total of 549 individuals underwent an LAAO procedure in Ontario between April 1, 2013 (fiscal year 2013) and March 31, 2022 (fiscal year 2021). Baseline characteristics are summarized in Table 1. The average patient was aged 75 ± 8 years, was male (66%), was frail (57% frailty index score ≥ 5), had a prior history of bleeding (56%), and was not currently receiving oral anticoagulation (68%). The mean CHA_2DS_2-VASc score was 4.4 ± 1.6.

Social deprivation

Figure 1 describes the variability in social deprivation markers of LAAO patients. A larger proportion of patients lived in neighborhoods with a higher dependency score, with 36% classified in the quintile corresponding to the highest dependency level, likely a reflection of the fact that this cohort was elderly. Additionally, 27% of LAAO patients lived in a neighborhood with a high neighborhood instability score, a maker of neighborhood cohesiveness and support. Representation of patients from neighborhoods of varying ethnic diversity and material deprivation was nearly equal.

Procedural characteristics and complications

The average hospital length of stay associated with LAAO procedures was 2.6 ± 8.3 days, with 36% of patients utilizing an intensive care unit bed on the day of the procedure. A total of 74% of the cohort was not prescribed OAC post-procedure. A total of 53% of the cohort had a TEE within 1 year post-procedure.

Peri-procedural stroke or TIA was rare (Table 2). Pericardial effusion requiring drainage occurred in 1.4% of the cohort. A total of 11% of the cohort was rehospitalized within 30 days of the procedure. Death during the index hospitalization occurred in 10 individuals (1.8%).

Long-term clinical outcomes

Patients dying during the index hospital admission (n = 10) were excluded from longer-term follow-up. On average, patient follow-up was available for 2.6 ± 2.0 patient-years.

Table 1. Baseline characteristics of the cohort

Variable	Value
Demographics	
Age, y	75 ± 8
Male sex	66
Rural location	11
Stroke risk factors	
Congestive heart failure	52
Hypertension	92
Diabetes	45
Coronary artery disease	44
Prior myocardial infarction	15
Peripheral vascular disease	5.1
Prior stroke	18
Prior arterial embolism	2.0
CHA_2DS_2VASc score	4.4 ± 1.6
Noncardiac comorbidities	
Chronic obstructive lung disease	34
Prior cancer	14
Dementia	4.6
Renal failure	15
Dialysis	11
Liver disease	8.9
Prior upper gastrointestinal tract bleed	25
Prior lower gastrointestinal tract bleed	33
Prior intracranial bleed	15
Prior bleeding from any site	56
Alcohol use	6.4
Frailty	7.8 ± 7.6
Frailty, intermediate to high risk (≥ 5)	57
Frailty, low risk (< 5)	42
Drug use	
Any oral anticoagulant use within 90 d pre-procedure	32

Values are %, or mean ± standard deviation.

CHA_2DS_2VASc, (**C**ongestive Heart Failure, **H**ypertension, **A**ge > 75 years, **D**iabetes, Stroke, **V**ascular disease, **A**ge > 65 years, female).

Stroke and/or TIA was rare and occurred in 2.8% of the population (1.1 per 100 patient-years). The stroke rate was similar regardless of the year of the LAAO procedure (*P* for trend = 0.32; Table 3).

Hospitalization for bleeding during the follow-up period occurred in 10% of the cohort (4 per 100 patient-years). A statistically significant increase in the rate of bleeding was noted during later years of the study period (*P* for trend = 0.01; Table 3).

A total of 63% of individuals within the cohort were rehospitalized during the follow-up period (43 per 100 patients-years). The rate of rehospitalization was similar regardless of the year the LAAO procedure was performed (*P* for trend = 0.06; Table 3).

Figure 2 demonstrates the time course of stroke and/or TIA, bleeding, and rehospitalization relative to the LAAO procedure.

Survival was estimated with the Kaplan-Meier method (Fig. 3). Death occurred in 160 individuals (29%) within the cohort (11 per 100 patient-years), and it also was similar in earlier and later years of the study period (*P* for trend = 0.72; Table 3).

Discussion

This report describes the initial adoption and provides longer-term follow-up of patients undergoing LAAO procedures in Ontario, Canada. It highlights the low rate of stroke and/or TIA and bleeding post-LAAO, and it draws

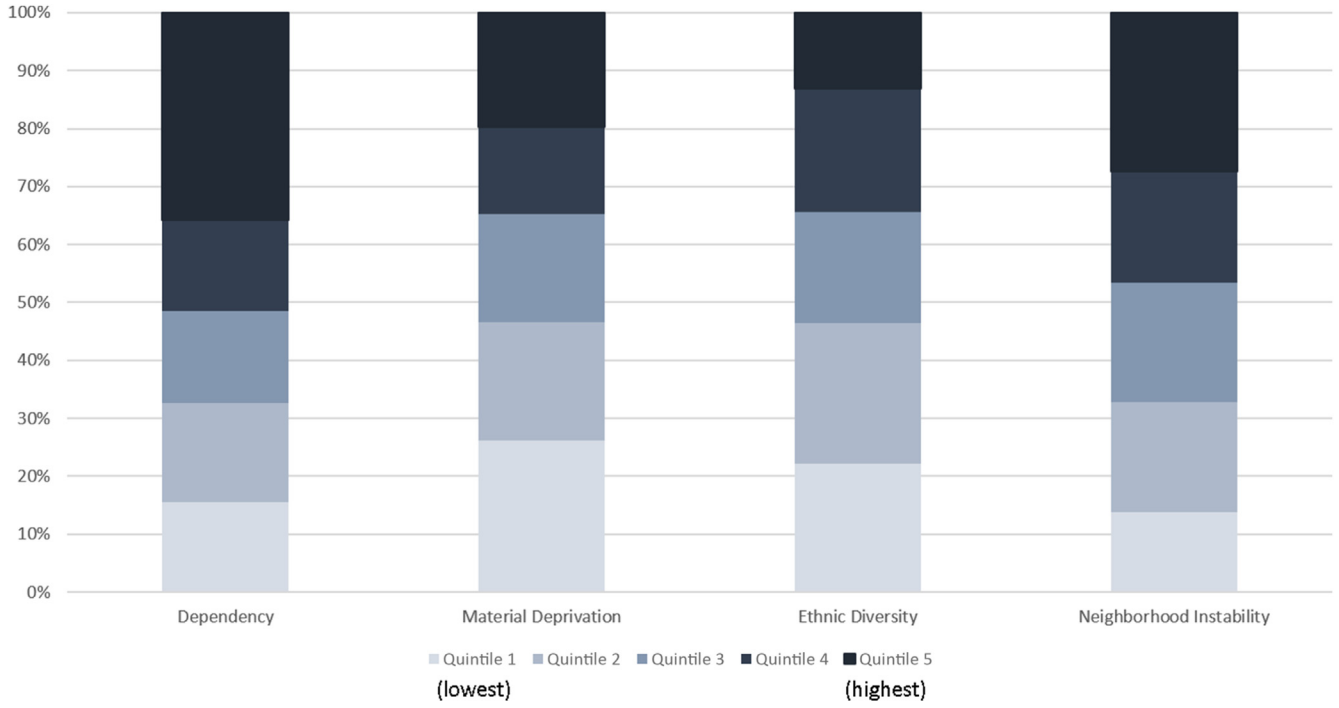

Figure 1. Social deprivation indicators of the left atrial appendage occlusion cohort.

attention to the high mortality incidence in this patient population. These data provide longer-term surveillance on the use of this technology in a multiethnic and diverse population and provides clinicians with insight on patient selection for LAAO procedures.

Conceptually, exclusion of the left atrial appendage from the systemic circulation prevents thrombus formation within the left atrial appendage, thereby reducing the risk of AF-related stroke and systemic embolization without the need for ongoing anticoagulation. Noninferior rates of stroke and systemic embolism with LAAO relative to OAC were noted in a meta-analysis of LAAO vs warfarin (> 7 days post-procedure stroke rate: LAAO, 1.3 per 100 patient-years vs warfarin, 0.95 per 100 patient-years),[1] as well as a recent randomized clinical trial of LAAO vs direct OAC (annualized stroke rate: LAAO, 2.08% vs direct OAC, 1.77%).[5] Large-scale registries in patients with contraindications to OAC consistently have highlighted the low stroke rate, compared to the predicted and/or historical stroke rate in untreated patients. For example, in Europe, 2-year outcome data from the EWOLUTION trial reported a 1.3% per 100 patient-year stroke rate in a population with a mean CHA_2DS_2VASc score of 4.5 $\pm$ 1.6, which was noted to be 83% of the historical stroke rate (estimated at 7.2% per year).[8] Data from the US NCDR including patients with a mean CHA_2DS_2VASc score of 4.8 $\pm$ 1.5 reported a stroke rate of 1.4 per 100 patient-years.[6] The findings in this cohort of patients from Ontario, Canada are consistent with the reports from other jurisdictions and confirm the low (1.1 per 100 patient-years), and more importantly, sustained reduction in stroke during long-term follow-up after LAAO.

The goal of LAAO procedures is to eliminate the need for long-term OAC, thereby eliminating bleeding associated with OAC use. Bleeding was noted in 10% of the cohort during longer-term post-procedure follow-up, which is an important reduction, as 56% of this cohort had hospitalizations for bleeding prior to the LAAO procedure. All bleeding may not be eliminated in this population, most of whom have a tendency toward bleeding. However, the frequency and severity of bleeding may be decreased with the elimination of OAC. The rate of post-procedure bleeding (4 per 100 patient-years) is similar to that reported in other registries evaluating LAAO therapy.[6,8] This low rate of any bleeding post-procedure highlights both an additional benefit of LAAO in AF patients and the fact that this treatment option is indeed viable for AF patients at risk for stroke who are not able to tolerate OAC.

A noteworthy point is that bleeding rates increased with procedures performed during later years of the study period. As the rate of bleeding is highest immediately post-procedure (Fig. 1), one may speculate that the temporal increase in bleeding may be related to post-procedure antithrombotic and/or anticoagulation use. A possible result of the increased use of LAAO in later years at new centres adopting this technology is that new operators were less familiar with the nuances of post-procedure antithrombotic and/or anticoagulant use and provided a post-procedure regimen associated with increased bleeding. Alternatively, increasing procedure volumes in later years may have resulted in the selection of patients at higher risk of bleeding. Further work to understand the factors contributing to this trend toward increased bleeding rates is suggested.

Patients in this cohort were on average elderly, frail, had multiple comorbidities, were from regions with high markers of dependency on others, and had contraindications to OAC—characteristics common to patients undergoing LAAO

Table 2. Complications

Variable	Within 7 d	Within 30 d
Death	6 (1.15)	12 (2.2)
Stroke and/or TIA	< 6	< 6
Any bleeding	7 (1.3)	18 (3.3)
Pericardial effusion requiring drainage	8 (1.4)	8 (1.4)
Any rehospitalization	18 (3.3)	58 (11)

Values are n (%), or n.
TIA, transient ischemic attack.

procedures in other jurisdictions.[6-8,15] We did not observe a substantial gradient in terms of access across neighborhood social-deprivation or ethnic factors. These patient characteristics likely contributed to the longer length of stay and intensive unit admission observed during the index LAAO procedure, and further, to the high rate of any hospitalization (43 per 100 patient-years) during longer-term follow up. Additionally, the overall mortality rate was high (11 per 100 patient-years) but was consistent with the experience in other jurisdictions. For example, 1-year mortality reported in the US NCDR was 8.52%,[8] and 2-year mortality was 16.4% in the European EWOLUTION trial,[6] with the majority of deaths being noncardiac in nature. A more contemporary study of 300 patients receiving the WATCHMAN FLX device (Boston Scientific, Marlborough, MA) reported a 10.8% 1-year mortality rate, with again, the majority of deaths being noncardiac in nature.[15] Thus, despite a low rate of stroke, the mortality rate is high in patients currently undergoing LAAO procedures.

The high mortality rate reported in real-world LAAO procedures is counter to that observed in clinical trials comparing LAAO to warfarin (3.1 per 100 patient-years).[1] This discrepancy is likely due to selection bias in enrollment of patients in clinical trials, magnified by current guidelines recommendations for LAAO use in patients with contraindications to OAC, and further exaggerated by restrictive reimbursement patterns that increase selection of the sickest patients, who clinicians may deem to be most deserving of this technology. This high mortality rate is important, as it may erode the cost-effectiveness of LAAO procedures in clinical practice. A recent consensus document from the Society for Cardiovascular Angiography & Interventions (SCAI) and the Heart Rhythm Society (HRS) suggests a minimum life expectancy of > 1 year when selecting patients to undergo LAAO.[16] This recommendation is less constrictive than that provided by the National Health Service (NHS) in England, which has stated that patients with an anticipated survival of < 3 years should not receive LAAO.[17] Strategies to identify LAAO candidates at high risk of short-term death, including frailty assessments, and physician-patient discussions and shared decision making are recommended.

The restricted use of LAAO procedures in clinical practice is supported by regulatory bodies, society guidelines, and health technology assessment agencies. Current cardiovascular society guideline recommendations provide less favourable recommendations on the use of LAAO due to the limited effectiveness data and the perception that OAC should remain the preferred therapy due to a low bleeding risk and survival data with OAC in AF patients without contraindications to OAC.[3,4] Regulatory agencies also have echoed these sentiments.[18] Furthermore, health technology assessment agencies have demonstrated that LAAO is cost-effective, compared to aspirin, in patients with contraindications to OAC, but it has questionable cost-effectiveness in patients without contraindications to OAC.[19] The provision of additional real-world data on the effectiveness of LAAO procedures should encourage policymakers to reevaluate restrictions placed on LAAO procedures. This approach, coupled with increased reimbursement for these procedures, may facilitate the use of LAAO in patients with fewer comorbidities, thereby allowing for uptake in a population with improved survival. Indeed, a similar phenomenon has been observed with other cardiovascular procedures, such as transcatheter aortic valve replacement procedures.[20] Furthermore, given the results of the Left Atrial Appendage Closure vs Novel Anticoagulation Agents in Atrial Fibrillation (PRAGUE-17)[5] and **L**eft **A**trial **A**ppendage **O**cclusion **S**tudy **III** (LAAOS II) studies,[21] as well as the several ongoing studies evaluating LAAO therapy compared to direct OAC (NCT03795298 and NCT04226547), a possible outcome is that LAAO therapy in the future may be provided to patients earlier in the course of this disease and prior to the development of life-limiting comorbidities.

Limitations

Important limitations of this study must be acknowledged. First, administrative databases may be limited in their ability to identify all procedural complications and may not identify

Table 3. Stroke, bleeding, all-cause rehospitalization and mortality rates per fiscal year

Fiscal y	Stroke and/or TIA (per 100 p-y)	*P* for trend	Bleeding (per 100 p-y)	*P* for trend	All-cause rehospitalization (per 100 p-y)	*P* for trend	Death (per 100 p-y)	*P* for trend
2013	2.3	0.32	2.4	0.01	37	0.06	11	0.72
2014	0.66		1.3		31		9.2	
2015	1.1		5.2		38		14	
2016	0.4		3.0		50		11	
2017	1.3		3.4		38		10	
2018	0.84		3.5		44		8.7	
2019	0		4.7		34		9.7	
2020	2.0		5.7		48		15	
2021	4.4		9.0		80		11	
Overall	1.1		4.0		43		11	

p-y, patient-years; TIA, transient ischemic attack.

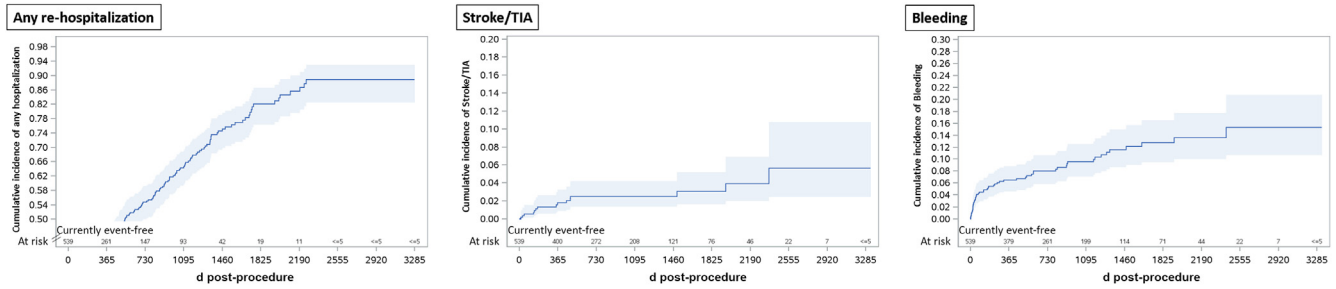

Figure 2. Cumulative incidence of any rehospitalization, stroke and/or transient ischemic attack (TIA), and bleeding.

strokes and/or TIAs diagnosed solely in an outpatient setting, thereby underestimating rates of stroke. Additionally, administrative databases do not allow identification of the etiology of stroke, such as a cardioembolic event related to AF vs an atheroembolic or other stroke related to vascular disease. Our approach employed validated approaches to identify bleeding and strokes to improve overall stroke estimates.[7,8] Furthermore the current strategy allows for identification of important clinical events that require an emergency department visit or hospitalization. Furthermore, reporting all-cause hospitalizations will provide additional insight into overall healthcare use in this population. Second, post-procedure antithrombotic use was not reported, as unlike with registry data, with the administrative databases employed, precise ascertainment of the use of aspirin, or compliance with and/or actual ingestion of oral anticoagulants or other antithrombotic agents reported to be prescribed, is not possible. Third, over half the cohort was enrolled within the latter 3 years of the study period, thereby limiting the number of individuals with $>$ 2 years of follow-up. Finally, we are unable to report on the specific LAAO device deployed in each patient. This point is noteworthy because, although long-term clinical outcomes are similar with the 2 commercially available devices during the study period, procedural complications may differ.[22] Finally, our work reports on solely patients undergoing an LAAO procedure. We are not able to provide insight into patient selection criteria or why anticoagulation was not prescribed prior or subsequent to the LAAO procedure. The strengths of this work include the longitudinal population-based design of consecutive patients undergoing LAAO, with nearly complete follow-up facilitating reporting on hospitalizations and survival. Furthermore, unlike prior work, the current data provide longer-term population-level follow-up not available in previous reports.

Conclusion

In conclusion, LAAO is associated with a low rate of stroke, and bleeding. High mortality persists in this patient population. Efforts to improve patient selection and reduce procedure complications may be beneficial to minimize mortality associated with these procedures. Consideration of upstream use of this nonpharmacologic approach to stroke reduction should be given, to provide this therapy to a population without life-limiting comorbidities.

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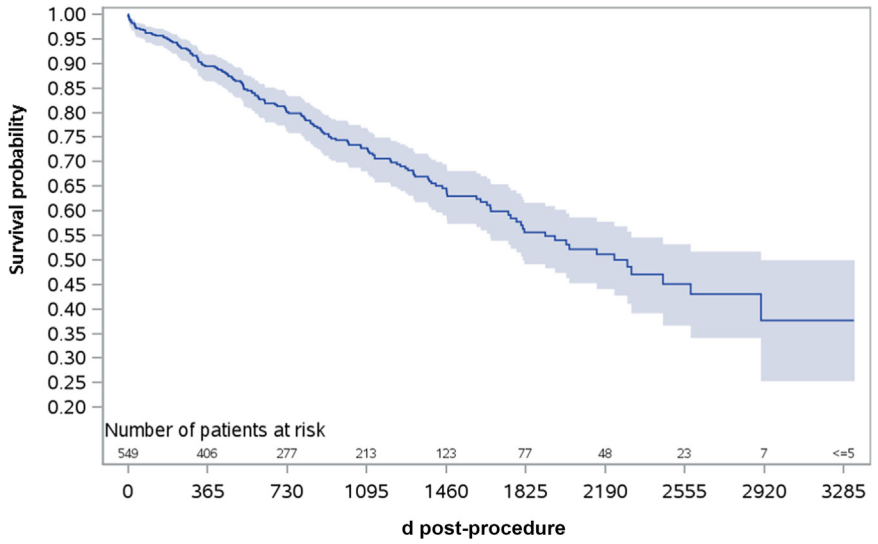

Figure 3. Overall survival.

document used data adapted from the Statistics Canada Postal Code Conversion File, which is based on data licensed from Canada Post Corporation, and/or data adapted from the Ontario MOH Postal Code Conversion File, which contains data copied under license from Canada Post Corporation and Statistics Canada. Parts of this material are based on data and/or information compiled and provided by Canadian Institute for Health Information (CIHI) and the Ontario MOH. The authors thank IQVIA Solutions Canada Inc. for use of their Drug Information File. Parts of this material are based on data and information compiled and provided by the Ontario MOH. Parts of this report are based on Ontario Registrar General (ORG) information on deaths, the original source of which is ServiceOntario. The views expressed therein are those of the author and do not necessarily reflect those of ORG or the Ministry of Public and Business Service Delivery. The analyses, conclusions, opinions, and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

Ethics Statement

The research reported has adhered to the relevant ethical guidelines.

Patient Consent

The use of ICES data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a research ethics board, and the need for individual patient consent was waived.

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Disclosure

The authors have no conflicts of interest to disclose.

References

1. Reddy VY, Doshi SK, Kar S, et al. 5-year outcomes after left atrial appendage closure: from the PREVAIL and PROTECT AF trials. J Am Coll Cardiol 2017;70:2964-75.

2. Task Force for the Diagnosis and Management of Atrial Fibrillation of the European Society of Cardiology (ESC). 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2020;42:373-498.

3. Andrade JG, Aguilar M, Atzema C, et al. The 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society comprehensive guidelines for the management of atrial fibrillation. Can J Cardiol 2020;36:1847-948.

4. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2104 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. J Am Coll Cardiol 2019;74:104-32.

5. Osmancik P, Herman D, Neuzil P, et al. 4-year outcomes after left atrial appendage closure versus nonwarfarin oral anticoagulation for atrial fibrillation. J Am Coll Cardiol 2022;79:1-14.

6. Price MJ, Slotwiner D, Du C, et al. Clinical outcomes at 1 year following transcatheter left atrial appendage occlusion in the United States. JACC Cardiovasc Interv 2022;15:741-50.

7. Kabra R, Girotra S, Sarrazin MV. Clinical outcomes of mortality, readmissions, and ischemic stroke among Medicare patients undergoing left atrial appendage closure via implanted device. JAMA Network Open 2019;2:e1914268.

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

9. Mesnier J, Cruz-Gonzlaes I, Peral V, et al. Ten-year outcomes following percutaneous left atrial appendage closure in patients with atrial fibrillation and absolute or relative contraindications to chronic anticoagulation. Circ Cardiovasc Interv 2021;14:e010821.

10. CorHealth Ontario. Ontario percutaneous left atrial appendage closure patient eligibility criteria guidelines and facility quality criteria. Available at: https://www.corhealthontario.ca/Ontario-Percutaneous-LAAC-Patient-Eligibility-Criteria-Guidelines-and-Facility-Quality-Criteria.pdf. Accessed April 1, 2023.

11. Gilbert T, Neuburger J, Kraindler J, et al. Development and validation of a hospital frailty risk score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet 2018;391:1775-82.

12. Matheson F, Moloney G, van Ingen T. 2016 Ontario marginalization index: user guide. 1st revision. Toronto: joint publication Ontario Agency for Health Protection and Promotion/Public Health Ontario, 2022.

13. Tu K, Wang M, Young J, et al. Validity of administrative data for identifying patients who have had a stroke or transient ischemic attack using EMRALD as a reference standard. Can J Cardiol 2013;29:1388-94.

14. Arnason T, Wells PS, van Walraven C, Forster AJ. Accuracy of coding for possible warfarin complications in hospital discharge abstracts. Thromb Res 2006;118:253-62.

15. Betts TR, Gygier M, JEN Kudsk, et al. Real-world clinical outcomes with a next-generation left atrial appendage closure device: the FLXibility post-approval study. Europace 2023;25:914-21.

16. Saw J, Holmes D, Cavalcante JL, et al. SCAI/HRS expert consensus statement on transcatheter left atrial appendage closure. JACC Cardiovasc Interv 2023;16:1384-400.

17. NHS England Specialised Services Clinical Reference Group for Cardiac Services. Clinical commissioning policy: left atrial appendage occlusion for patients with atrial fibrillation and relative or absolute contraindications to anticoagulation (adults). Available at: https://www.england.nhs.uk/wp-content/uploads/2018/07/1692-left-atrial-appendage-occlusion.pdf. Accessed April 1, 2023.

18. Masoudi F, Calkins H, Kavinsky C, et al. 2015 ACC/HRS/SCAI left atrial appendage occlusion device societal overview. J Am Coll Cardiol 2015;66:1497-513.

19. Health Quality Ontario. Left atrial appendage closure device with delivery system: OHTAC recommendation. Available at: http://www.hqontario.ca/Portals/0/Documents/evidence/reports/ohtac-recommendation-watchman-03-08-2017.pdf. Accessed April 22, 2023.

20. Mauri V, Abdel-Wahab M, Bleiziffer S, et al. Temporal trends of TAVI treatment characteristics in high volume centers in German y 2013-2020. ClinRes Cardiol 2022;111:881-8.

21. Whitlock RP, Belley-Cote EP, Paparella D, et al. Left atrial appendage occlusion during cardiac surgery to prevent stroke. N Engl J Med 2021;384:2081-91.

22. Qiao J, Zhang B, Wang J, et al. Comparison between Amplatzer and Watchman left atrial appendage closure devices for stroke prevention in atrial fibrillation: a systematic review and meta-analysis. Cardiology 2022;147:290-7.