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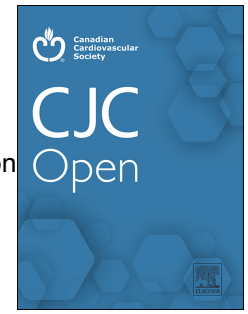

Stroke Prevention with Left Atrial Appendage Closure in Patients with Atrial Fibrillation and Prior Intracranial Haemorrhage

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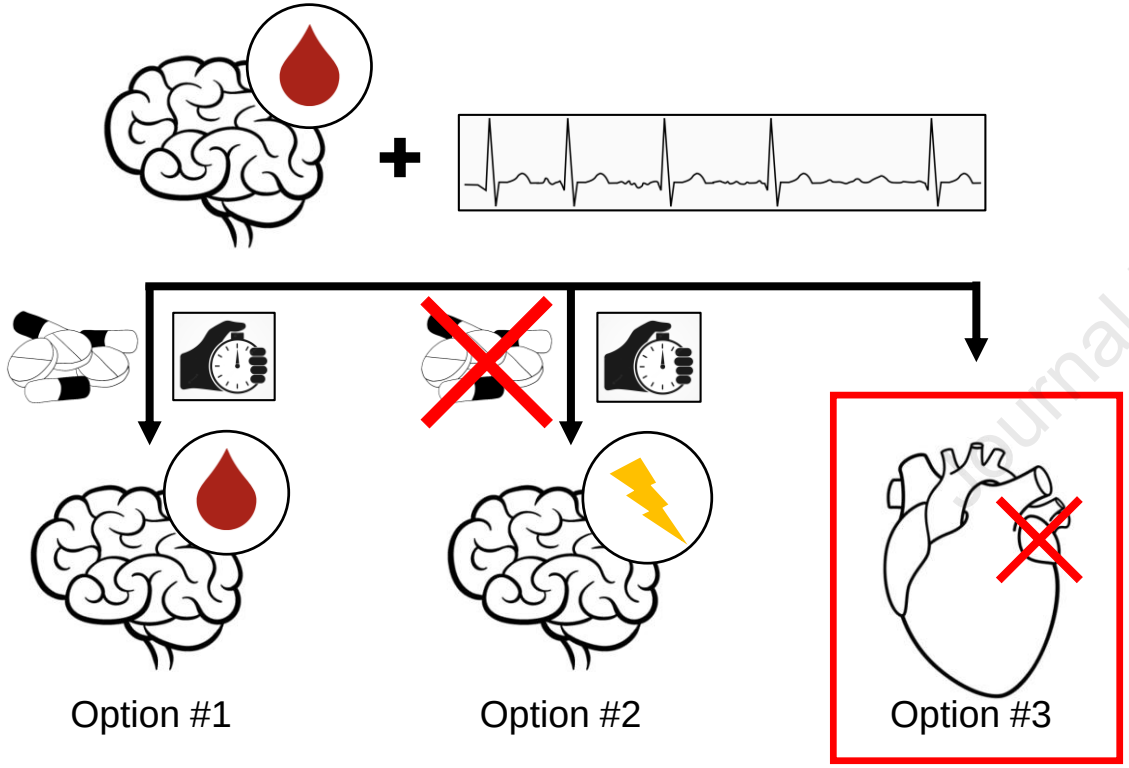
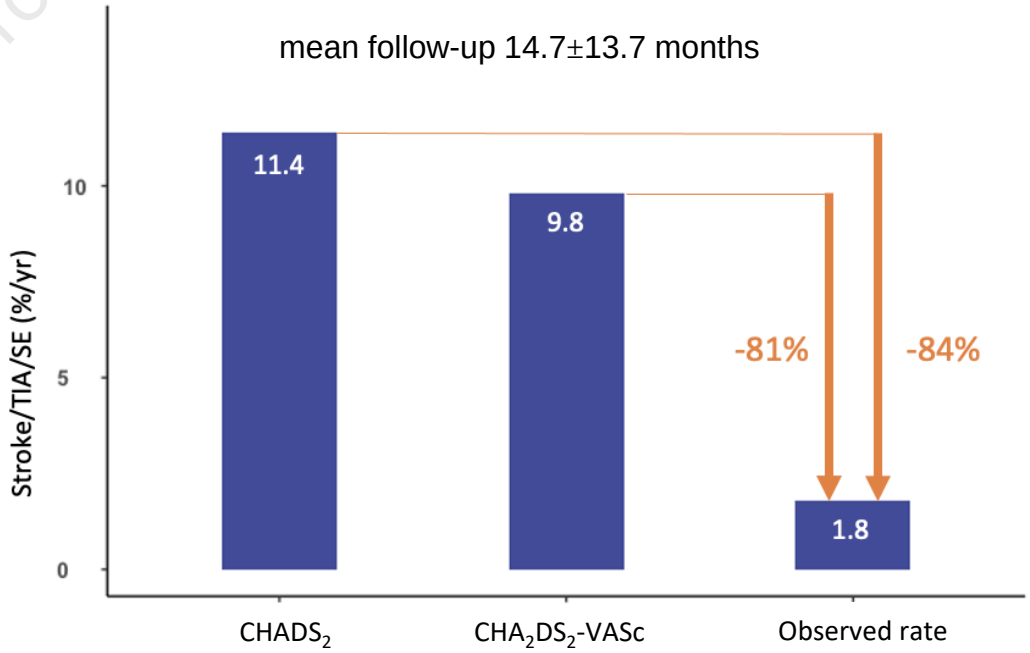
Left atrial Appendage Closure after Intracranial Haemorrhage

Oral anticoagulation is deemed a contraindication after intracranial haemorrhage (ICH) if the cause cannot be eliminated and risk of recurrence is high. That leaves atrial fibrillation (AF) patients at high risk of thromboembolic events.



Methods: Retrospective analysis of ICH patients with non-valvular AF and high stroke-risk undergoing left atrial appendage closure (LAAC) at Vancouver General Hospital. Comparison of observed follow-up stroke/TIA/systemic embolization rate with predicted event-rate based on $CHADS_2$ and CHA_2DS_2-VASc scores.

Results: Between 2010 and 2022 138 ICH patients underwent endovascular LAAC (Age 76.1±8.5 years; CHA_2DS_2-VASc 4.4±1.5; HASBLED 3.7±0.9). Short term DAPT (1-6 months) post-LAAC followed by aspirin alone for minimum 6 months was reported in 86.2% of patients.



Endovascular LAAC is a feasible alternative to OAC for stroke prevention in patients with non-valvular AF and prior ICH.

Gilhofer et al. 2022

Stroke Prevention with Left Atrial Appendage Closure in Patients with Atrial Fibrillation and Prior Intracranial Haemorrhage

Short title: LAA-closure after Intracranial Haemorrhage

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Structured Abstract

Background: Oral anticoagulation (OAC) is deemed a relative contraindication after intracranial haemorrhage (ICH) if the cause cannot be eliminated and risk of recurrence is high. That leaves atrial fibrillation (AF) patients at high risk of thromboembolic events. Endovascular left atrial appendage closure (LAAC) can be an alternative to OAC for patients requiring stroke prevention.

Methods: We performed a retrospective single-centre analysis of 138 consecutive ICH patients with non-valvular AF and high stroke-risk undergoing LAAC between 2010 and 2022 who underwent LAAC at Vancouver General Hospital. We report the baseline characteristics, procedural results and follow-up data comparing the observed stroke/TIA rate with the predicted event-rate based on their CHA_2DS_2-VASc scores.

Results: Average age was 76.1±8.5 years, mean CHA_2DS_2-VASc score 4.4±1.5, and mean HASBLED score 3.7±0.9. Procedural success rate was 98.6%, complication rate was 3.6% with no peri-procedural death, stroke or TIA. Antithrombotic regimen post-LAAC consisted of short term DAPT (1-6 months) followed by aspirin alone for minimum 6 months in 86.2%. At mean follow-up of 14.7±13.7 months there were 9 deaths (6.5%, 7 cardiovascular, 2 non-cardiovascular), 2 strokes (1.4%) and 1 TIA (0.7%). The annualized observed stroke/TIA rate was 1.8%, which was lower than the adjusted predicted stroke rate of 7.0% (95% CI 4.8-9.2%). Two (1.5%) patients suffered another ICH (both on aspirin monotherapy). One device-related thrombus (0.7%) was confirmed and treated with OAC without sequelae.

Conclusion: Endovascular LAAC is a feasible alternative to OAC for stroke prevention in patients with non-valvular AF and prior ICH.

Keywords

Intracranial haemorrhage; Stroke prevention; Atrial fibrillation; high bleeding risk; left atrial appendage closure

Abbreviations

ACP	AMPLATZER Cardiac Plug
AF	Atrial fibrillation
AICD	Automated implantable cardioverter defibrillator
ASA	Acetylsalicylic acid
BMI	Body mass index
CAA	Cerebral amyloid angiopathy
CABG	Coronary artery bypass grafting
CHF	Congestive heart failure
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CT	Computer tomography
CCTA	Cardiac Computer tomographic angiogram
CV	Cardiovascular
DAPT	Dual antiplatelet therapy
DOAC	Direct oral anticoagulant
eGFR	Estimated glomerular filtration rate
HR	Hazard ratio
ICE	Intracardiac echocardiography
ICH	Intracranial haemorrhage
LAA	Left atrial appendage
LAAC	Left atrial appendage closure
LMWH	Low molecular weight heparin
LVEF	Left ventricular ejection fraction
MI	Myocardial infarction
OAC	Oral anticoagulation

SAPT	Single antiplatelet therapy
TIA	Transient ischaemic attack
TOE	Transoesophageal echocardiography
TTE	Transthoracic echocardiography
VKA	Vitamin K antagonist

Introduction

Atrial fibrillation (AF) affects 1-2% of the general population, and the prevalence increases up to 18% in patients >85 years-old.[1] AF increases the risk of stroke by fivefold, and lifelong oral anticoagulation (OAC) is recommended for patients at high stroke risk according to the $CHADS_2$ and CHA_2DS_2-VASc scores. However, OAC increases bleeding risk, with rates of fatal (0.6%/year) and major (3.0%/year) bleeding approximately five times higher with warfarin than without.[2] The most feared bleeding complication is intracranial haemorrhage (ICH), accounting for 58% of all bleeding-associated deaths in anticoagulated patients.[3] Even with the use of direct OAC (DOAC), there is still significant risk of ICH (apixaban 0.3%/year, dabigatran 0.2%–0.3%/year, edoxaban 0.2%–0.3%/year, rivaroxaban 0.4%/year) compared with warfarin (0.3%–1.8%/year).[4] Furthermore, ICH in patients on OAC is associated with a significantly poorer prognosis compared to ICH in patients not on OAC (52% vs. 26% 3-month mortality, respectively[5]), independent of the type of OAC.[4, 6, 7] This is most likely due to more rapid hematoma expansion as a result of the coagulopathy.[5]

The risk of recurrent bleeding after ICH can vary based on the pathophysiology, reported at 4.4% per patient-year in patients with cerebral amyloid angiopathy (CAA) versus 2.1% per patient-year after hypertensive ICH. Even without further OAC use, the rate of recurrent ICH is high, 2.3%/year with CAA and 2.1%/year with hypertensive ICH.[5] Patients with prior lobar ICH and the detection of microbleeds in cerebral imaging are reported to have a risk of recurrent lobar ICH of 10%/year.[5] In CAA-associated ICH the recurrence rate increases to ~27% in patients with extensive cortical superficial siderosis.[5] OAC after the index ICH can triple the risk of recurrence [hazard ratio (HR) 3.0].[8] Nevertheless, non-valvular AF patients who suffered an ICH can be at significant risk of ischaemic stroke and may benefit from restarting OAC in reducing ischaemic stroke and mortality, despite risk of recurrent ICH.[9] The American College of Chest Physicians guidelines as well as the American Heart Association/American Stroke Association secondary stroke prevention guidelines indicate that

the decision on resuming antithrombotic therapy in patients after ICH should be individualized according to their risk of subsequent arterial or venous thromboembolism and the risk of recurrent ICH, respectively.[9]

Endovascular left atrial appendage closure (LAAC) is increasingly performed as an alternative to OAC in patients with non-valvular AF who are considered poor candidates for long-term OAC. In particular, a few series had shown that LAAC may be safe and feasible in ICH patients, with the use of (single or dual) antiplatelet therapy or short-term OAC (45 days) post-LAAC.[10, 11] In the randomized RESTART study, the continued use of antiplatelet therapy for secondary prevention after cardiac procedures did not lead to an increased rate of recurrent ICH compared to patients, in whom the antiplatelet medication was stopped after ICH.[12] While the 2016 AF guidelines by the European Society of Cardiology provided a list of factors supporting withholding or reinitiating OAC after ICH independent of the option of LAAC, the updated version of 2020 highlights the consideration that AF acts as a risk marker and withholding OAC after LAAC could result in undertreating the overall risk of stroke related to atrial cardiomyopathy.[1] Nonetheless, a recent ICH is still considered an absolute contraindication against OAC and non-valvular AF patients with a high bleeding risk need to be carefully evaluated, modifiable risk factors must be addressed, and the decision of an adequate stroke prevention strategy based on an individual assessment.[1]

In our institution, we have been performing LAAC for ICH patients for stroke prevention for over a decade, and we hereby report our single-centre consecutive case series.

Materials and Methods

We performed a retrospective analysis of consecutive ICH patients with non-valvular AF and high stroke-risk ($CHADS_2 \geq 1$ or CHA_2DS_2-VASc≥ 2) who underwent endovascular LAAC at Vancouver General Hospital. We included ICH from any aetiology. While either cranial computer tomography or cranial MRI was sufficient for the diagnosis of ICH, the diagnosis of

CAA was based on cranial MRI. Indication for LAAC was confirmed in regular interdisciplinary meetings with colleagues from neurology, neuroradiology and neurosurgery for all patients. Minimum of 4 weeks was recommended between the neurologic event and LAAC. However, timing of LAAC was primarily depending on the timing of referral.

Baseline characteristics, bleeding risk, baseline and discharge antithrombotic therapy, procedural results, peri-procedural complications, and follow-up events were collected. Device surveillance imaging post-LAAC was performed at 3 months with transoesophageal echocardiography (TOE) and/or cardiac computer tomography angiography (CCTA). Clinical in-person or telephone follow-ups were performed at 3 and 12 months post-LAAC, and annually thereafter. Institutional research ethics board approval was obtained for our retrospective study.

LAAC procedure: LAAC was performed with AMPLATZER Cardiac Plug (ACP) (St. Jude Medical, St Paul, MN), Amulet (second generation ACP), WATCHMAN (Boston Scientific, Natick, MA) or WATCHMAN FLX devices. Patients were given loading doses of aspirin and clopidogrel prior to entering the procedure room. LAAC was performed under general anaesthesia with TOE guidance, or under conscious sedation using intracardiac echocardiography (ICE). Detailed implantation steps were previously described.[13] Heparin was administered to achieve activated clotting time >250s. Every patient was loaded with aspirin 325mg and clopidogrel 300mg if not already on one of these medications. Standard antithrombotic therapy on discharge included aspirin 81mg/d for at least 6 months and clopidogrel 75mg/d for 1 to 3 months.

Statistical Analysis: Descriptive statistics were used to describe the baseline characteristics of patients. Continuous variables were reported as mean ± standard deviation, or median and interquartile range. Categorical variables were reported as absolute frequency and percentage. The efficacy of LAAC in preventing thromboembolic events was tested by comparing the predicted event-rate by the $CHADS_2$ and CHA_2DS_2-VASc scores with the

observed event-rate at follow-up. The average annual risk for the whole study population was calculated from the predicted individual patient annual risk. The observed annualized thromboembolic event-rate (stroke, TIA and systemic embolism) was subtracted from the predicted event-rate and divided by the predicted event-rate x 100, to obtain the % relative risk reduction. For comparison of the predicted and the observed event rates we demonstrated the 95% confidence interval (CI) of the predicted rate. Statistical significance was achieved if the observed event rate was outside of the 95% CI of the predicted rate. Statistical analysis was performed with SPSS 21 (IBM, New York).

Results

We included 138 consecutive ICH patients who underwent LAAC between September 2010 and February 2022. Baseline demographics and the types of ICH are described in Table 1. The average age was 76.1±8.5 years, 69.6% were men, mean CHA_2DS_2-VASc score was 4.4±1.5, and mean HASBLED score was 3.7±0.9. The types of ICH included subdural hematoma (41.3%), intracerebral haemorrhage (46.4%), subarachnoid haemorrhage (11.6%), and CAA (12.3%), although cranial MRI was not performed in all patients. Therefore, CAA could be underestimated. In 108 patients (78.3%), the ICH occurred while on OAC. The average time between ICH and LAAC was 27.2±49.7 months. Prior to the procedure, 24 patients (17.4%) were on OAC, 1 (1.4%) was on low-molecular weight heparin (due to presence of LAA thrombus on pre-procedural TOE), 4 had aspirin plus OAC, 6 patients (4.3%) were on DAPT, and 58 (41.5%) were on single antiplatelet therapy (SAPT) (56 on aspirin, 2 on clopidogrel); 45 (32.6%) were not on any antithrombotic therapy (Table 2). LAAC devices implanted were ACP in 10.9% of cases, Amulet 38.4%, WATCHMAN 36.2% or WATCHMAN FLX in 14.5% (Table 3). Procedural success was 136/138 (98.6%), with 2 cases of device embolization (1.4%) in our early experience with the ACP device that were both percutaneously retrieved without sequelae. The majority of procedures (90.6%) were performed under general anaesthesia with

TOE-guidance. Few LAAC procedures were performed under conscious sedation using ICE guidance mainly because of the presence of oesophageal strictures. Additional gastrointestinal bleeding or neurological sequelae post ICH were not a reason for decision to use conscious sedation instead of general anesthesia. Combined invasive procedures were performed in 3.6% of cases (1 coronary angiogram, 1 percutaneous coronary intervention, 1 AV-nodal ablation, 1 cardioversion and 1 AF-ablation). After device release, peri-device leaks were observed in 13 patients (9.4%) on TOE with mean leak size of 1.8mm (range 1-4mm), but no leak ≥5mm. Procedural complications included one pericardial tamponade (0.7%; occurred several hours post-procedure; successfully drained percutaneously), and one mild pericardial effusion (0.7%) not requiring intervention. There was no peri-procedural death, stroke, transient ischaemic attack (TIA) or myocardial infarction (MI). There was one (0.7%) peri-procedural major (gastrointestinal bleed from oesophageal ulcers due to the TOE probe) and one (0.7%) minor (gastrointestinal bleed followed by polypectomy during hospitalization) bleeding events.

Post-procedure, the majority of patients (92.5%) was discharged on DAPT (70.9% for 1 month, 14.9% for 3 months, 3.0% for 6 months, and 3.7% for longer than 6 months), with median duration of 1 month (IQR 1 to 1; min. 6 days, max. 24 months). Five patients (3.7%) received single antiplatelet therapy for at least six months, but one stopped aspirin after 42 days for unclear reasons. One patient (0.7%) received a DOAC and aspirin for one year post-LAAC after a left ventricular thrombus was diagnosed. The two patients with device embolization that were successfully retrieved and not deemed candidates for another closure attempt were continued on warfarin, which they were on prior to the procedure. One patient who initially received DAPT for one month was switched to warfarin by the family physician in the first year after LAAC for unclear reasons.

Patients were followed for a mean duration of 14.7±13.7 months post-LAAC (Table 4). Three patients were lost to follow-up. There were nine deaths (6.5%): seven were (5.1%) presumed cardiovascular, two (1.4%) were non-cardiovascular. None of the deaths was related

to the LAAC procedure. There were two strokes (1.4%) and one TIA (0.7%), and device imaging of these patients did not reveal any device-related thrombus (DRT) or other complication related to the LAAC. No change in antithrombotic therapy was undertaken in any of the three patients after the neurologic event, all three remained on single antiplatelet therapy. The annualized observed stroke/TIA rate was 1.8%, which was lower than the adjusted predicted stroke rate based on their $CHADS_2$ score (8.3%, 95% CI: 5.8% - 10.8%) as well as their CHA_2DS_2-VASc score (7.0%, 95% CI: 4.8% - 9.2%) (figure 1). There was no systemic embolization following LAAC. The annualized observed rate of stroke, TIA and systemic embolization was lower than the adjusted predicted rate for stroke, TIA and systemic embolization according to the $CHADS_2$ (11.4%, 95% CI: 8.2% - 14.6%) and the CHA_2DS_2 VASc scores (9.8%, 95% CI: 6.8% - 12.8%) (figure 2). This resulted in a relative risk reduction (RRR) in stroke of 78.3% and a number needed to treat (NNT) of 13 and a RRR in stroke, TIA and systemic embolization of 84.2% and a NNT of 10 based on the $CHADS_2$ score, as well as a RRR in stroke of 74.3% and a NNT of 19, and a RRR in stroke, TIA and systemic embolization of 81.6% and a NNT of 13 based on the CHA_2DS_2 VASc score. Seven patients (5.1%) had minor bleeding (mostly gastrointestinal bleeding, one scleral bleed). Major bleeding events occurred in six (4.0%) cases. While four patients had GI bleeding, two (1.4%) had another ICH (both occurred on aspirin monotherapy, one was fatal). Supplemental figures S1 and S2 illustrate cumulative event curves.

Device surveillance post-procedure was performed using TOE in 65 patients (47.1%) and/or with CCTA in 93 patients (67.4%). There was only one confirmed case of DRT (0.7%) on top of a well-seated Amulet device while on aspirin that was initially treated with a two-month regimen of full-dose apixaban additionally to aspirin but reappeared after stopping the DOAC and therefore had another three-month regimen with full-dose apixaban with complete resolution of the non-mobile thrombus. So far, the patient had no ischemic or bleeding events

since LAAC. In 5 patients with follow-up TOE after median 3 months a moderate peri-device leak (3-5mm) and in 1 patient a major peri-device leak (>5mm) was detected.

Discussion

In our retrospective real-world case series, we report high procedural success and safety in 138 patients with ICH who underwent percutaneous LAAC. The annualized stroke/TIA event-rate at follow-up was 1.8%, which was lower than the expected rate based on their baseline CHA_2DS_2-VASc score (RRR 74.3%). Patients were predominantly discharged on DAPT post-procedure, with no recurrent ICH while on this regimen post-LAAC, and low incidence of DRT post-LAAC.

The optimal stroke preventative therapy for patients with prior ICH is not established. AF trials with DOAC reported lower rates of ICH compared with warfarin.[6, 14, 15] However, patients with a history of ICH were excluded from these trials. Thus, administering DOAC in this high-risk population remains an unstudied strategy and the recurrent bleeding risk is unknown. Without OAC the incidence of recurrent ICH varied between 2.3 and 14.0% in several neuropathologic studies and the reported mortality rate after recurrent ICH was 23.5 - 32.0%.[18-20] It is unclear what the risk of recurrent ICH will be if anticoagulation is resumed, and registry-based observational studies had reported rates of 4.3% during a mean of 43 months, 7.5% during a median 16.5 months and 8.2% during median 9.9 months follow-up.[21, 22]

Although OAC cessation exposes patients to a significantly higher risk of thromboembolism, a history of ICH is considered a contraindication for resumption of OAC if the cause for the bleed could not be identified.[1] Aneurysmal bleeds that can be clipped or coiled or ICH that occur in the setting of an overdose of vitamin K antagonists should be viewed differently from ICH while on adequately dosed DOACs, or multiple microbleeds in patients with CAA. However, many physicians as well as patients are reluctant to resume OAC after such a dramatic event, irrespective of the cause of the ICH.

Endovascular LAAC has become an established alternative to OAC in patients with non-valvular AF at high bleeding risk. However, published randomized controlled trials only included patients eligible to warfarin.[16] Ongoing randomized trials that are including patients contraindicated to OAC are slow in patient-enrolment, in fact, the ASAP-TOO study was stopped prematurely because of very slow enrolment.[17] The STROKE-CLOSE study randomizing ICH patients to LAAC versus medical therapy is also facing enrolment issues. Thus, data on ICH patients with LAAC is unlikely to be derived from adequately powered randomized trials. Our study adds to the current literature containing few small case series that showed LAAC to be safe and effective in ICH patients.[11]

Pouru et al. reported a series of 104 AF patients with a prior ICH who were treated with LAAC, which resulted in a 69% relative reduction of the risk of thromboembolic events compared to their predicted risk without any stroke prophylaxis according to CHA_2DS_2-VASc.[10] In our study, we confirmed a similar relative risk reduction of 74% with an annualized rate of stroke or TIA of 1.8%.

The ideal antithrombotic therapy post-LAAC in the ICH population is currently undefined. One observational study found that antiplatelet use after ICH did not appear to be associated with an increased risk of ICH recurrence in 127 survivors of lobar haemorrhage (HR 0.8; 95% CI, 0.3–2.3; p=0.73) and 80 survivors of deep haemorrhage (HR 1.2; 95% CI, 0.1–14.3; p=0.88).[25] In a Spanish observational LAAC registry including 160 patients with a history of ICH, the recurrent rate of ICH was 0.8% at a mean follow-up of 22.9 months.[26] Their patients received aspirin for at least 6-12 months and clopidogrel for 3-6 months.[26] In our series the majority of patients was treated with DAPT for one (70.9%) to three months (14.9%) and subsequently with aspirin for at least six months post-LAAC. We did not observe significant bleeding or DRT related to this regimen. Despite reporting our safe strategy with short term DAPT after LAAC, further studies are necessary to evaluate the optimal postprocedural antithrombotic strategy.

A systematic review on 407 LAAC patients with a history of ICH was published by Garg et al. reporting a periprocedural bleeding risk of almost 0% and a minimal rate of recurrent ICH of 0.05%, as well as a very low rate of ischaemic stroke of 0.54% after a mean follow-up period of 14 months.[27] With a similar follow-up time frame, we saw two recurrent ICH in our cohort resulting in a recurrence rate of 1.7% which was higher than reported by Garg. One patient had a fatal ICH 17 months post-LAAC while she was on aspirin alone. She had CAA and high risk of stroke with CHA_2DS_2-VASc score of 4. She tolerated DAPT with aspirin and clopidogrel for one month without any side-effects post-LAAC. The second patient with recurrent ICH had CHA_2DS_2-VASc of 5 with recurrent strokes and TIAs. He suffered an ICH while on OAC 8 months before LAAC. Post-LAAC he was treated with DAPT with aspirin and clopidogrel for one month, before switching to aspirin alone. Unfortunately, two months after LAAC he suffered a recurrent non-fatal ICH while on aspirin, which was then stopped. He recovered from this event, and had no further event at 3 years post-LAAC.

The optimal timing of LAAC after an ICH is also not established. The American Heart Association guidelines acknowledge that the optimal time to resume OAC in patients after an ICH is uncertain but that for most patients, it might be reasonable to wait for one week (class IIb, level of evidence B).[8] Based on currently available data Da Silva et al. suggest that OAC can be safely restarted in select groups of patients within four weeks after ICH after careful assessment of risks for ICH recurrence and thromboembolism in case the cause of the bleeding could be eliminated.[28] The European Society of Cardiology guidelines also recommend to either restart OAC or plan LAAC after at least four weeks following the index bleeding event.[1] In our cohort, 111 out of 138 patients with AF and previous ICH did not have adequate stroke prevention prior to LAAC. As many patients from our cohort were referred from physicians outside our institution or other centers in the province, we had limited influence in the timing of referrals and LAAC. We typically wait at least a month after ICH before performing LAAC, in keeping with the above recommendations. The long average time between ICH and LAAC

in our cohort is mostly due to delayed referrals. However, we are convinced that adequate stroke prevention either with OAC or LAAC is essential, even if delayed.

Limitations: Given the relatively small sample size and non-randomized design of our single-centre retrospective series, there can be potential bias in patient selection and outcomes. Patients referred for LAAC may represent a more healthy and robust group, which may explain the low long-term bleeding and cardiovascular complications in our cohort. Conversely, patients who were severely disabled post-ICH may not be referred for LAAC. In terms of antithrombotic regimen post-LAAC, we preferentially used DAPT post-LAAC in our ICH cohort; we were not able to compare the safety of other antithrombotic strategies.

Conclusion

Endovascular LAAC is a feasible alternative to OAC for stroke prevention in patients with non-valvular AF and prior ICH. Further studies are necessary to assess the long-term outcomes and the optimal antithrombotic therapy post-LAAC in this challenging patient cohort.

Conflict of interest statement:

This study was not funded. Dr. Saw has received unrestricted research grant supports (from the Canadian Institutes of Health Research, Heart & Stroke Foundation of Canada, National Institutes of Health, University of British Columbia Division of Cardiology, AstraZeneca, Abbott Vascular, St Jude Medical, Boston Scientific, and Servier), salary support (Michael Smith Foundation of Health Research), speaker honoraria (AstraZeneca, Abbott Vascular, Boston Scientific, and Sunovion), consultancy and advisory board honoraria (AstraZeneca, St Jude Medical, Abbott Vascular, Boston Scientific, Baylis, Gore, FEops), and proctorship honoraria (Abbott Vascular, St Jude Medical and Boston Scientific). No disclosures for other authors.

Table 1: Baseline demographics of ICH patients

N (%), mean ± SD	ICH Patients (n=138)
Age (years)	76.1 ± 8.5
Men	96 (69.6%)
BMI (kg/m2)	26.2 ± 5.0
Hypertension	113 (81.9%)
Dyslipidaemia	89 (64.5%)
Diabetes mellitus	34 (24.6%)
Smoking history (active or remote)	67 (49.0%)
COPD	14 (10.1%)
Coronary artery disease	41 (29.7%)
Previous myocardial infarction	26 (18.8%)
Previous percutaneous coronary intervention	27 (19.6%)
CABG	11 (8.0%)
Heart failure	30 (21.7%)
LVEF <40%	18 (13.0%)
History of valve surgery	8 (5.8%)
Previous stroke/TIA	78 (56.5%)
Systemic embolization	6 (4.3%)
Permanent/persistent AF	84 (60.9%)
Paroxysmal AF	54 (39.1%)
Pacemaker/AICD	26 (18.8%)
Creatinine (µmol/l)	109.3 ± 64.7
eGFR (ml/kg/1.73m2)	63.3 ± 22.1
Haemoglobin at baseline	134.3 ± 16.6
Platelet count at baseline	201.8 ± 66.8
$CHADS_2$ score	2.9 ± 1.3
CHA_2DS_2-VASc score	4.4 ± 1.5
HASBLED score	3.7 ± 0.9
Previous major bleeding	138 (100%)
Previous major bleeding while on OAC	108 (78.3%)
Intracranial bleeding	138 (100%)
Epidural bleeding	0 (0%)
Subdural bleeding	57 (41.3%)
Subarachnoid bleeding	16 (11.6%)
Intracerebral bleeding	64 (46.4%)
Cerebral amyloid angiopathy	17 (12.3%)
Additional major bleeding	13 (9.4%)

AF = atrial fibrillation; AICD = automated implantable cardioverter defibrillator; BMI = body mass index; eGFR = estimated glomerular filtration rate; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; ICH = intracranial haemorrhage; TIA = transient ischaemic attack

Table 2: Medications at baseline

	ICH Patients (n=138)
Aspirin	56 (40.1%)
Clopidogrel	2 (1.4%)
DAPT	6 (4.3%)
OAC (DOAC/VKA)	24 (17.4%)
DOAC	14 (10.1%)
Aspirin + AC (DOAC/VKA/LMWH)	4 (2.9%)
None	45 (32.6%)

DAPT = dual antiplatelet therapy; DOAC = direct oral anticoagulation; ICH = intracranial haemorrhage; LMWH = low molecular weight heparin; OAC = oral anticoagulation; VKA = Vitamin K antagonist

Table 3: LAAC procedural characteristics

	ICH Patients (n=138)
WATCHMAN	50 (36.2%)
Mean device size	29.0 ± 3.3
WATCHMAN FLX	20 (14.5%)
Mean device size	30.0 ± 3.7
ACP	15 (10.9%)
Mean device size	26.1 ± 3.7
Amulet	53 (38.4%)
Mean device size	27.3 ± 4.7
Overall mean device size (mm)	28.2 ± 4.2
Procedural success	136 (98.6%)
First device implanted	105 (76.1%)
General anesthesia	125 (90.6%)
Combined intervention	5 (3.6%)
Total procedural time (min)	83.7 ± 37.7
Fluoroscopy time (min)	17.5 ± 12.1
Contrast dye used (ml)	110.2 ± 80.6
Successful transseptal puncture	138 (100%)
Procedural TOE	125 (90.6%)
Procedural ICE	13 (9.4%)

ACP = Amplatzer cardiac plug; ICE = intracardial echocardiography; ICH = intracranial haemorrhage; LAAC = left atrial appendage closure; TOE = transoesophageal echocardiography

Table 4: Follow-Up events

	ICH Patients with Clinical Follow-Up (n=134)
Mean duration of follow-up	14.7 ± 13.7
Stroke	2 (1.4%)
TIA	1 (0.7%)
Deaths	9 (6.5%)
CV Death	7 (5.1%)
Non-CV Death	2 (1.4%)
Bleeding major	6 (4.0%)
Bleeding minor	7 (5.1%)

CV = cardiovascular; ICH = intracranial haemorrhage; TIA = transient ischaemic attack

Figure 1. The predicted annual rate of stroke and TIA in our study cohort, based on $CHADS_2$ and CHA_2DS_2-VASc scores, compared with the cumulative observed rate of stroke/TIA during the study period. The observed annual event rate was 78% and 74%, respectively, lower than predicted. (TIA = transient ischaemic event; yr = year; CHADS2 = congestive heart failure, hypertension, age≥75, diabetes mellitus, stroke or TIA symptoms previously; CHA2DS2-VASc = congestive heart failure, hypertension, age≥75, diabetes mellitus, stroke or TIA symptoms previously, vascular disease history, age≥65)

Figure 2. The predicted annual rate of stroke, TIA and systemic embolization in our study cohort, based on $CHADS_2$ and CHA_2DS_2-VASc scores, compared with the cumulative observed rate of stroke, TIA and systemic embolization during the study period. The observed annual event rate was 84% and 81%, respectively, lower than predicted. (TIA = transient ischaemic event; yr = year; CHADS2 = congestive heart failure, hypertension, age≥75, diabetes mellitus, stroke or TIA symptoms previously; CHA2DS2-VASc = congestive heart failure, hypertension, age≥75, diabetes mellitus, stroke or TIA symptoms previously, vascular disease history, age≥65)

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Figure 1

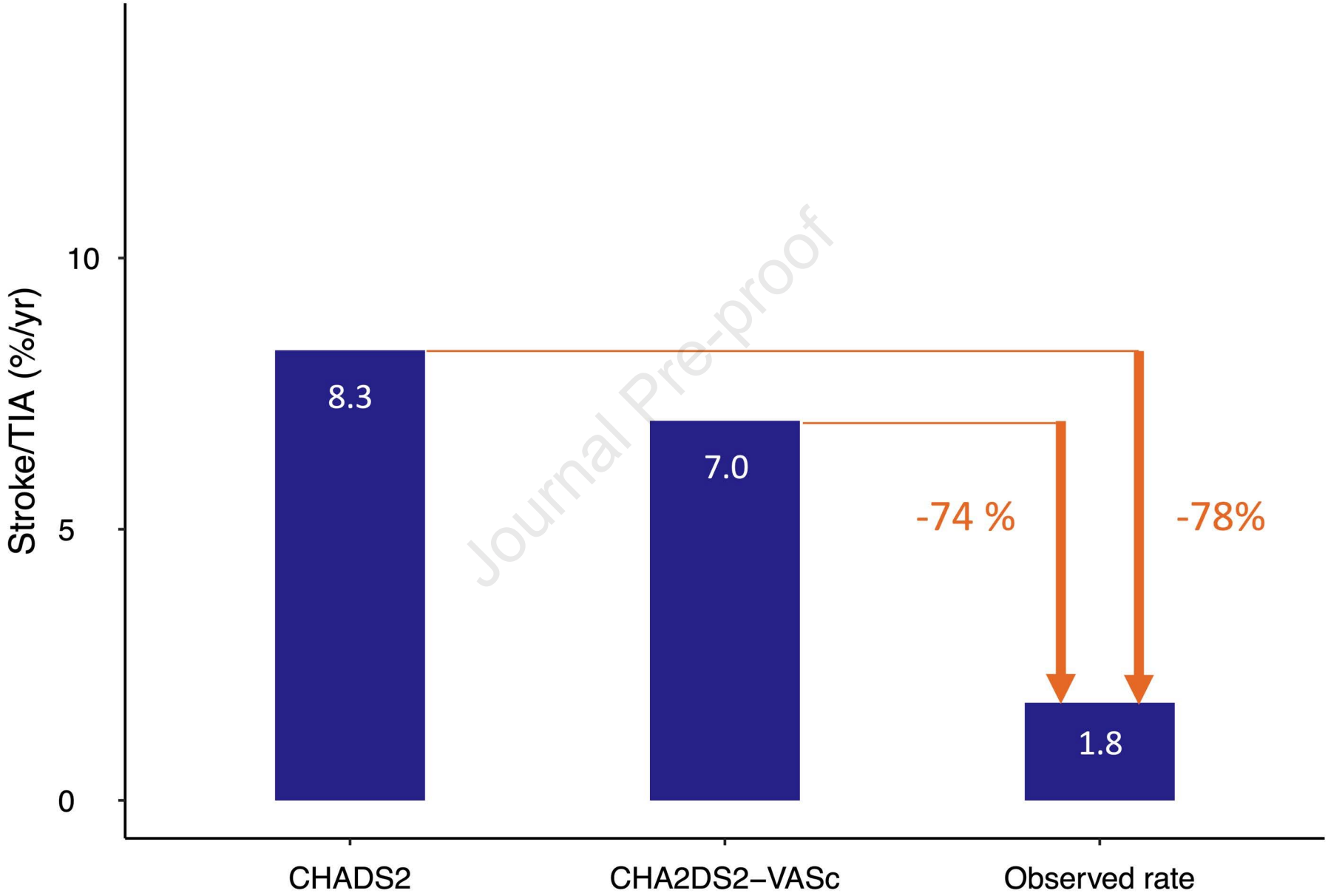

Figure 2