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Heart & Vascular Center

2024 Northern California Structural Heart Summit

Current FDA approved and upcoming expanding indications for LAAO. What does the data show us?

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Learning Objectives:

- Current selection criteria for left atrial appendage occlusion (LAAO) device implantation
- Future indications
  - Patients with absolute contraindications to the anti-coagulants
  - DOAC eligible patients
  - Concomitant LAAO and other procedures
  - LAAO in specific group of patients

Current Selection Criteria:

Current indications for percutaneous LAAO in the United States

LAAO is indicated to reduce the risk of thromboembolism from the LAA in patients with NVAF who

1 Are at increased risk for stroke and systemic embolization based on $CHADS_2$ or $CHADS_2$-VASc score ≥ 2.
2 Are deemed suitable for at least short-term antithrombotic therapy post-LAAO.
3 Have an appropriate rationale to seek a nonpharmacologic alternative to OAC.
5 No other indication for OAC than AF (e.g., prior VTE, mechanical valve, presence or predisposition to left atrial or left ventricular thrombus).
6 Anatomy appropriate for LAAO.

ACC/AHA/HRS 2023 Guidelines:

Recommendations for Percutaneous Approaches to Occlude the LAA
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	Recommendations
2a	B-NR	1. In patients with AF, a moderate to high risk of stroke (CHA_2DS_2-VASc score ≥2), and a contraindication (Table 14) to long-term oral anticoagulation due to a nonreversible cause, percutaneous LAAO (pLAAO) is reasonable.[1–4]
2b	B-R	2. In patients with AF and a moderate to high risk of stroke and a high risk of major bleeding on oral anticoagulation, pLAAO may be a reasonable alternative to oral anticoagulation based on patient preference, with careful consideration of procedural risk and with the understanding that the evidence for oral anticoagulation is more extensive.[1–3,5,6]

Circulation. 2024;149. e1413

Expanding Indications:

- Patients with absolute contraindications to anti-coagulants: Where the current data stands?

Expanding Indications:

- ASAP TOO trial

The Assessment of the Watchman Device in Patients Unsuitable for Oral Anticoagulation (ASAP-TOO) trial

David R. Holmes, MD,[a] Vivek Y. Reddy, MD,[b] Maurice Buchbinder, MD,[c] Kenneth Stein, MD,[d] Myriah Elletson[d] Martin W. Bergmann, MD,[e] Boris Schmidt, MD,[f] and Jacqueline Saw, MD, FRCPC[g] *Rochester, Minneapolis, MN; New York, NY; Stanford, CA; Hamburg, Frankfurt, Germany; and British Columbia, Canada*

Background Oral anticoagulants (OACs) reduce stroke risks with nonvalvular atrial fibrillation (AF); however, they are underused because of absolute or relative contraindications due to real or perceived risk of bleeding. Although left atrial appendage closure is increasingly performed in OAC-ineligible patients, this has not been studied in a randomized controlled trial.

Study objectives The ASAP-TOO study is designed to establish the safety and effectiveness of the Watchman left atrial appendage closure device in patients with nonvalvular AF who are deemed ineligible for OAC. The primary effectiveness end point is the time to first occurrence of ischemic stroke or systemic embolism. The primary safety end point includes all-cause death, ischemic stroke, systemic embolism, or device- or procedural-related event requiring open cardiac surgery or major endovascular intervention.

Study design This is a multinational, multicenter prospective randomized trial. Patients meeting the inclusion criteria with CHA_2DS_2-VASc score ≥ 2 and who are deemed by 2 study physicians to be unsuitable for OAC will be randomized in a 2:1 allocation ratio to Watchman versus control. Control patients will be prescribed single antiplatelet therapy or no therapy at the discretion of the study physician. Up to 888 randomized subjects will be enrolled from up to 100 global investigational sites. Both device group and control patients will have follow-up visits at 3, 6, and 12 months and then every 6 months through 60 months.

Summary This trial will assess the safety and efficacy of Watchman in this challenging population of high–stroke risk AF patients. (Am Heart J 2017;189:68-74.)

ASAP TOO:

- Not recruiting at this time, about 481 patients enrolled as opposed to planned 888
- Results of the recruited patients are not published as of yet

STROKE CLOSE trial:

ACTIVE, NOT RECRUITING

Prevention of Stroke by Left Atrial Appendage Closure in Atrial Fibrillation Patients After Intracerebral Hemorrhage

ClinicalTrials.gov ID NCT02830152

Sponsor Karolinska Institutet

Information provided by Per Wester, Karolinska Institutet (Responsible Party)

Last Update Posted 2024-06-12

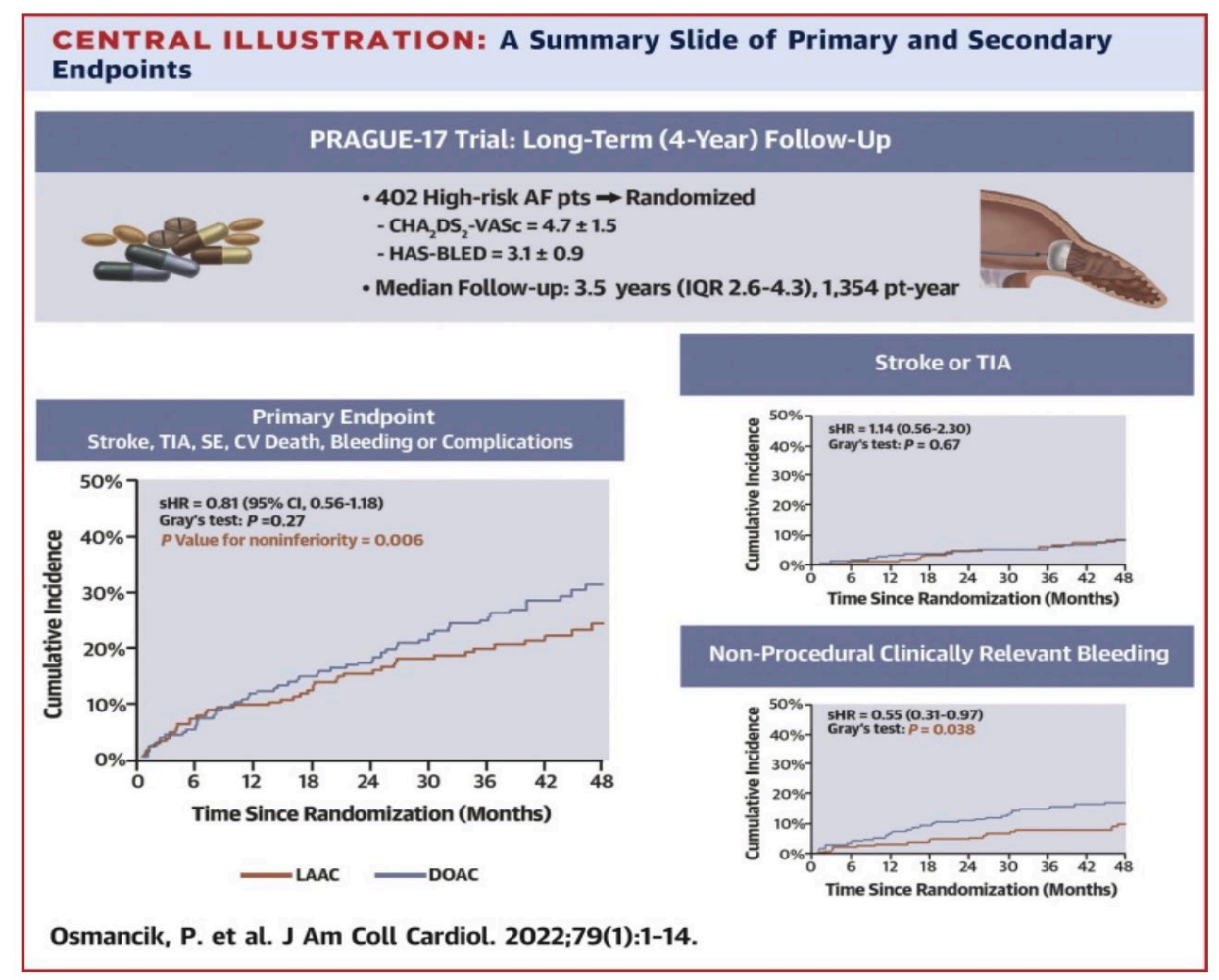
- Two arms, one arm LAAO with an amulet device with no initiation of oral anti-coagulants and other arm on medical therapy
- All patients enrolled must have a history of intracranial hemorrhage
- This study is also not recruiting currently

LAAO and DOACs:

- PRAGUE-17 trial
- Randomized trial comparing LAAO with DOACs in patients with clinically relevant bleeding and prior cardioembolic events or at risk of stroke
- Primary end-point was a composite of safety and efficacy events (cardioembolic events, cardiovascular death, clinically relevant bleeding or procedure/device related complications)

J Am Coll Cardiol. 2020;75:3122

PRAGUE-17 trial:



Risk of procedure-related complication was 5%

LAAO and DOACs:

CHAMPION-AF Clinical Trial (CHAMPION-AF)

ClinicalTrials.gov ID NCT04394546
Sponsor Boston Scientific Corporation
Information provided by Boston Scientific Corporation (Responsible Party)
Last Update Posted 2024-09-23

+ Expand all content — Collapse all content

Study Details | Researcher View | No Results Posted | Record History

On this page
- Study Overview
- Contacts and Locations
- Participation Criteria
- Study Plan

Study Overview

Brief Summary
The primary objective of this study is to determine if left atrial appendage closure (LAAC) with the WATCHMAN FLX device is a reasonable alternative to non-vitamin K oral anticoagulants in patients with non-valvular atrial fibrillation.

Study Start (Actual) 2020-10-15
Primary Completion (Estimated)

Amplatzer Amulet LAAO vs. NOAC (CATALYST)

ClinicalTrials.gov ID NCT04226547
Sponsor Abbott Medical Devices
Information provided by Abbott Medical Devices (Responsible Party)
Last Update Posted 2024-08-28

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Study Details | Researcher View | No Results Posted | Record History

On this page
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Study Overview

Brief Summary
The objective of this trial is to evaluate the safety and effectiveness of the Amulet LAA occluder compared to NOAC therapy in patients with non-valvular AF at increased risk for ischemic stroke and who are recommended for long-term NOAC therapy.

Study Start (Actual) 2020-07-07
Primary Completion (Estimated)

LAAO and DOACs:

- Both of these trials will compare safety and efficacy of LAAO with DOACs in **patients with no apparent contraindications to the DOACs (patients are enrolled based on stroke risk and not by long-term DOAC ineligibility)**
- These trials have distinct safety and efficacy end-points (unlike the PRAGUE-17 trial)
- Additionally, the safety outcomes will be adjudicated with a superiority design framework and not by non-inferiority
- The results of these trials and earlier trials (ASAP TOO and STROKE CLOSE) will inform the applicability of LAAO devices to a wider population with atrial fibrillation

Concomitant Procedures:

ESC European Society of Cardiology

Europace (2023) **25**, 390–399
https://doi.org/10.1093/europace/euac181

CLINICAL RESEARCH

Combined atrial fibrillation ablation and left atrial appendage occlusion procedure in the United States: a propensity score matched analysis from 2016–2019 national readmission database

Deepak Kumar Pasupula [1]*, Sudeep K. Siddappa Malleshappa [2], Muhammad B. Munir [3], Anusha Ganapati Bhat [4], Antony Anandaraj [1], Avaneesh Jakkoju [5], Michael Spooner [1], Ketan Koranne[1], Jonathan C. Hsu [6], Brian Olshansky [7], and A. John Camm [8]

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Europace. 2023;25:390-399

LAAO and AF ablation:

In this retrospective study from NRD data, we identified patients undergoing combined LAAO and CA procedures on the same day in the USA from 2016 to 2019. A 1:1 propensity score match was performed to identify patients undergoing LAAO-only and CA-only procedures. The number of LAAO + CA procedures increased from 28 (2016) to 119 (2019). LAAO + CA patients (n = 375, mean age 74 ± 9.2 years, 53.4% were males) had non-significant higher MACE (8.1%) when compared with LAAO-only (n = 407, 5.3%) or CA-only patients (n = 406, 7.4%), which was primarily driven by higher rate of pericardial effusion (4.3%). All-cause 30-day readmission rates among LAAO + CA patients (10.7%) were similar when compared with LAAO-only (12.7%) or CA-only (17.5%) patients. The most frequent primary reason for readmissions among LAAO + CA and LAAO-only cohorts was heart failure (24.6 and 31.5%, respectively), while among the CA-only cohort, it was paroxysmal atrial fibrillation (25.7%).

Conclusion We report an 63% annual growth (from 28 procedures) in combined LAAO and CA procedures in the USA. There were no significant difference in MACE and all-cause 30-day readmission rates among LAAO + CA patients compared with matched LAAO-only or CA-only patients.

Option trial:

OPTION is a multinational, multicenter, prospective randomized clinical trial. Patients with a CHA_2DS_2-VASc of ≥2 in men or ≥3 in women and who underwent a AF catheter ablation procedure between 90 and 180 days prior to randomization (sequential) or are planning to have catheter ablation within 10 days of randomization (concomitant) will be randomized in a 1:1 allocation of WATCHMAN FLX vs control. Control patients will start or continue market-approved oral anticoagulation for the duration of the trial. A total of 1600 patients were randomized from 130 global investigational sites. Follow-up for both device and control patients will occur at 3, 12, 24, and 36 months.

The primary effectiveness noninferiority endpoint is stroke (ischemic or hemorrhagic), all-cause death, or systemic embolism at 36 months. The primary safety superiority endpoint is nonprocedural bleeding through 36 months (International Society on Thrombosis and Haemostasis [ISTH] major bleeding or clinically relevant nonmajor bleeding). The secondary noninferiority endpoint is ISTH major bleeding through 36 months (including procedural bleeding).

Am Heart J. 2022:35-42

LAAO and TAVR (WATCH TAVR trial):

Circulation

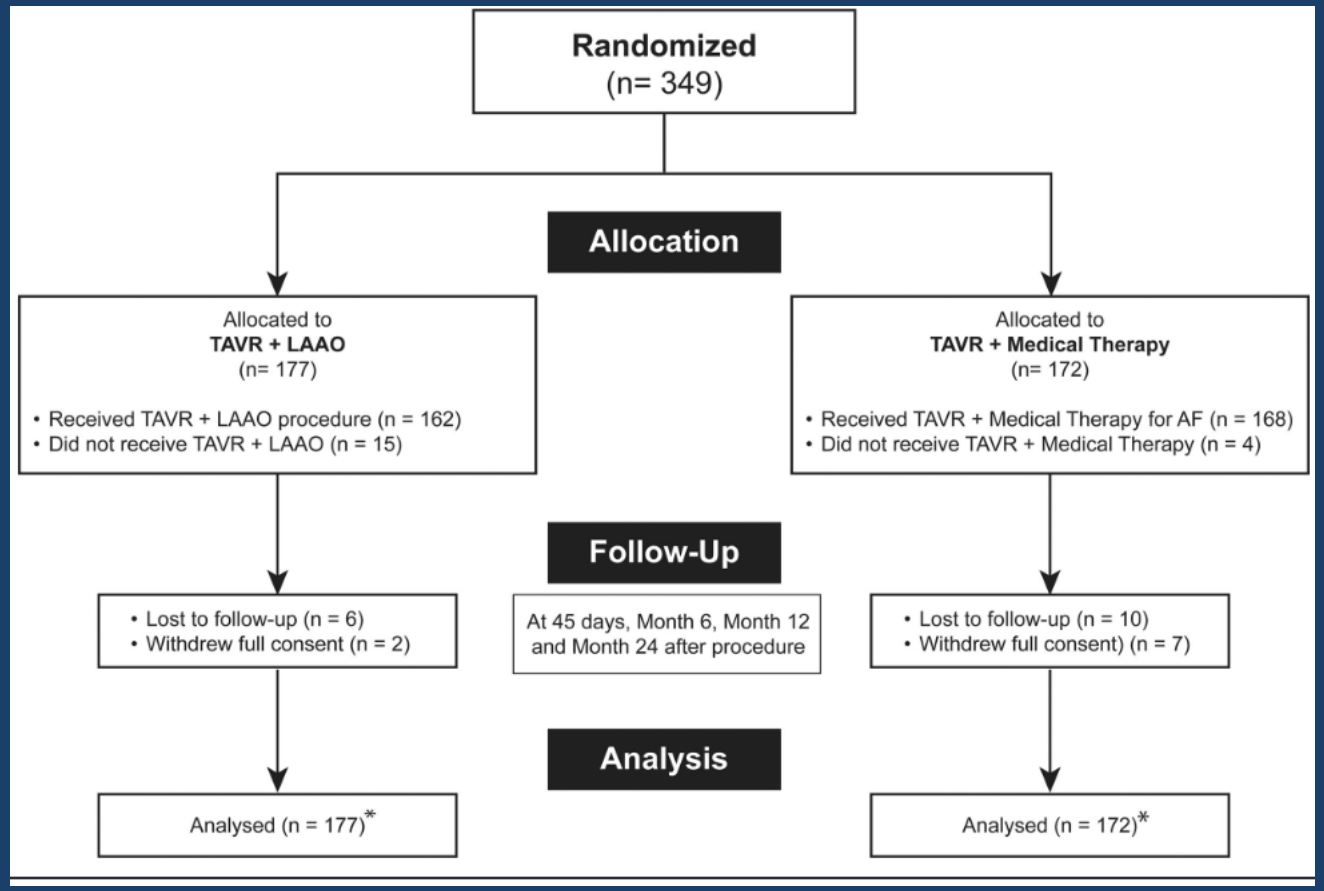
ORIGINAL RESEARCH ARTICLE

Concomitant Left Atrial Appendage Occlusion and Transcatheter Aortic Valve Replacement Among Patients With Atrial Fibrillation

Samir R. Kapadia, MD; Amar Krishnaswamy, MD; Brian Whisenant, MD; Srinivasa Potluri, MD; Vijay Iyer, MD; Joseph Aragon, MD; Philip Gideon, MD; Justin Strote, MD; Robert Leonardi, MD; Himanshu Agarwal, MD; German Larrain, MD; Carlos Sanchez, MD; Sidakpal S. Panaich, MD; James Harvey, MD; Torsten Vahl, MD; Venu Menon, MD; Kathy Wolski, MS; Qiuqing Wang, MS; Martin B. Leon, MD

Circulation. 2024;149:734-743

LAAO and TAVR (WATCH TAVR trial):

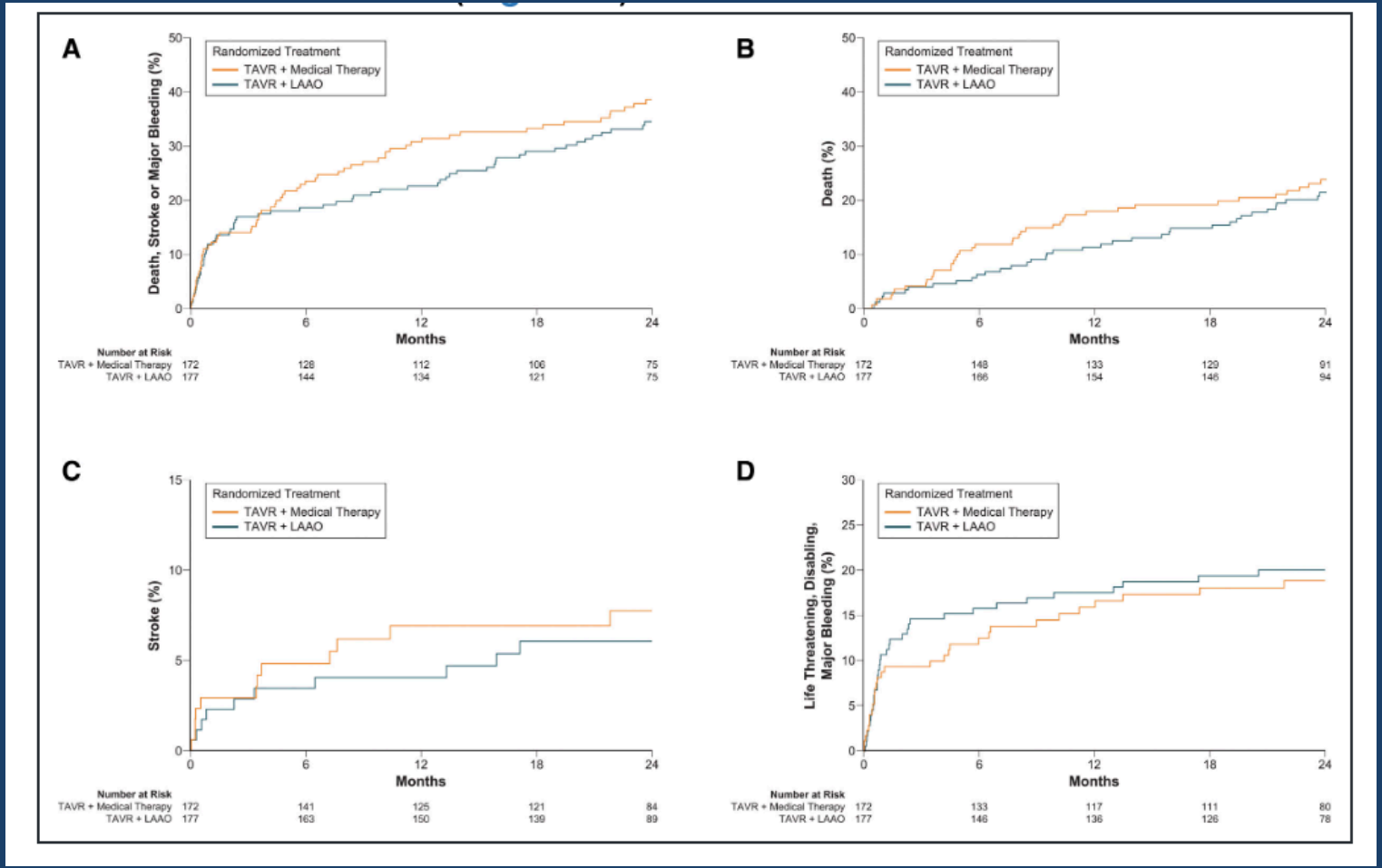


LAAO and TAVR:

Primary End Point and Additional Clinical Outcomes

The composite primary end point (all-cause mortality, stroke or major/life-threatening bleeding event within 2 years after randomization) was observed in 60 (33.9%) of patients randomized to TAVR + LAAO compared with 64 (37.2%) patients randomized to TAVR + medical therapy (Figure 2). For the ITT analysis of composite primary end point, TAVR + LAAO was noninferior to TAVR + medical therapy (22.67 versus 27.33 events per 100 patient-years with TAVR alone; HR, 0.86 [95% CI, 0.60–1.22]; $P_{noninferiority}<0.001$). However, TAVR + LAAO strategy was not superior to TAVR + medical management ($P=0.40$). The event rates were comparable for the primary

LAAO and TAVR:



LAAO and mitral valve interventions:

- Limited data on safety and effectiveness

ELSEVIER

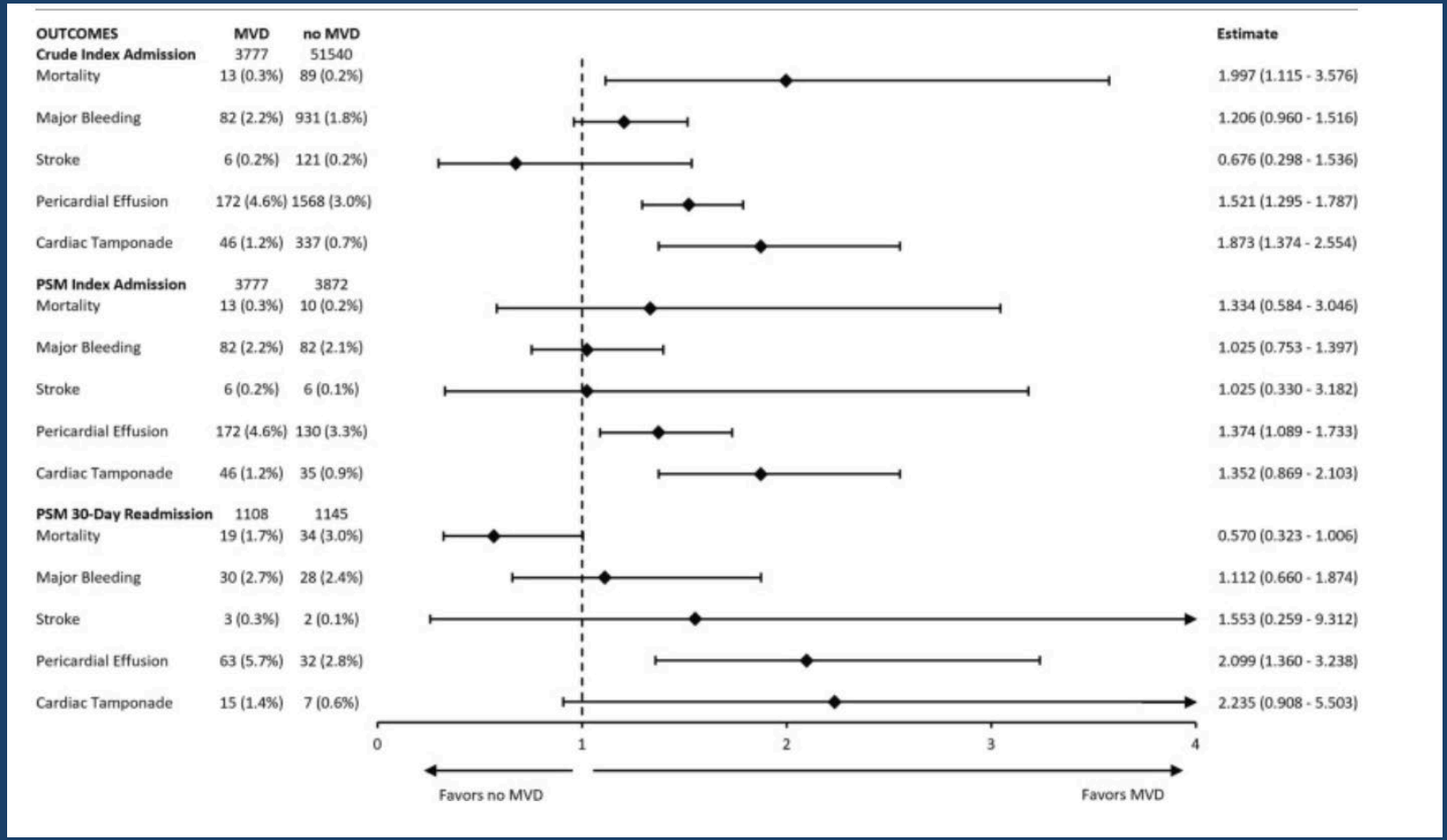
Cardiovascular Revascularization Medicine

Volume 63, June 2024, Pages 23-30

Percutaneous left atrial appendage occlusion in mitral valve disease: A Nationwide Readmission Database analysis

Rafey Feroze [a 1], Waqas Ullah [b 1], Puneet Kang [c], Tabitha Lobo [c], Nawaf Alhabdan [c], Mohammed Alghammass [a], Sung-Han Yoon [a d], Luis Augusto Palma Dallan [a], Steven J. Filby [a]

LAAO and mitral valve interventions:

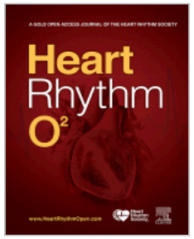


LAAO in special patient populations:

CLINICAL | ATRIAL FIBRILLATION · Volume 4, Issue 7, P433-439, July 2023 · *Open Access* Download Full Issue

Intracranial bleeding and associated outcomes in atrial fibrillation patients undergoing percutaneous left atrial appendage occlusion: Insights from National Inpatient Sample 2016–2020

Muhammad Zia Khan, MD, MS [*,1] · Islam Shatla, MD [†,1] · Douglas Darden, MD [‡] · ... · Gagan D. Singh, MD, MS [§] · Uma Srivatsa, MD, MS [§] · Muhammad Bilal Munir, MD [§] ... Show more



Affiliations & Notes · Article Info

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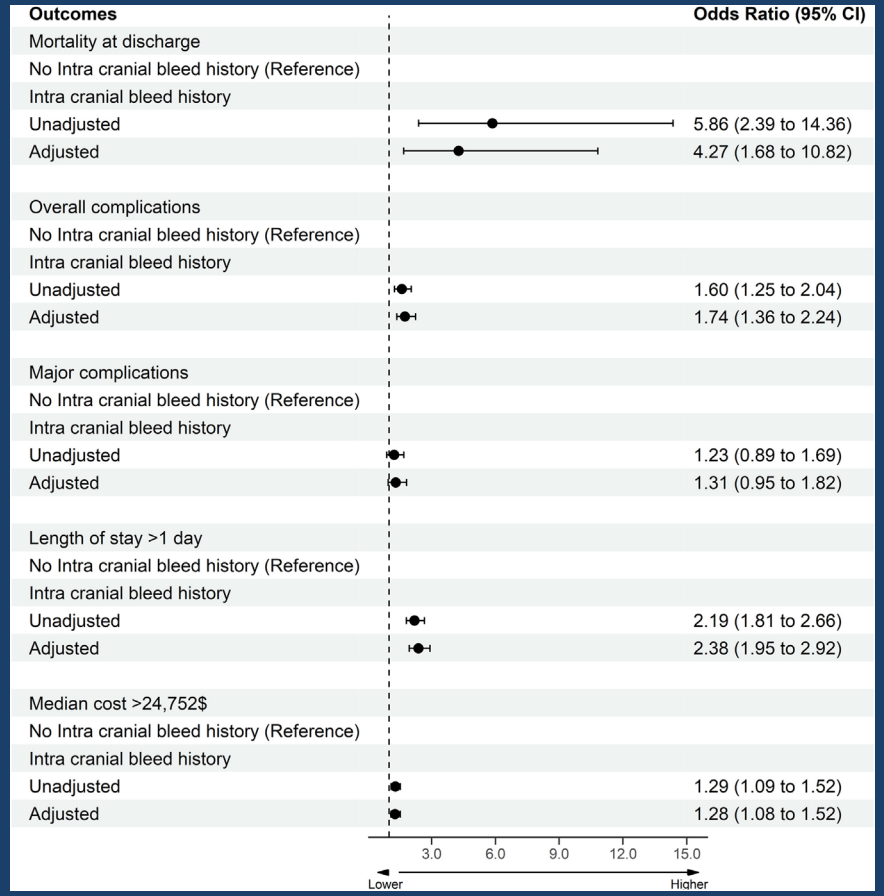
- 89,300 LAAO implantations from year 2016-2020
- Only 565 (0.6%) of implantations occurred in patients with a history of intracranial bleeding and contraindications to anti-thrombotics

Heart Rhythm O2. 2023 Jun 8;4(7):433-439

LAAO and ICH:


Outcomes
Odds Ratio (95% CI)
Mortality at discharge
No Intra cranial bleed history (Reference)
Intra cranial bleed history
Unadjusted
5.86 (2.39 to 14.36)
Adjusted
4.27 (1.68 to 10.82)
Overall complications
No Intra cranial bleed history (Reference)
Intra cranial bleed history
Unadjusted
1.60 (1.25 to 2.04)
Adjusted
1.74 (1.36 to 2.24)
Major complications
No Intra cranial bleed history (Reference)
Intra cranial bleed history
Unadjusted
1.23 (0.89 to 1.69)
Adjusted
1.31 (0.95 to 1.82)
Length of stay >1 day
No Intra cranial bleed history (Reference)
Intra cranial bleed history
Unadjusted
2.19 (1.81 to 2.66)
Adjusted
2.38 (1.95 to 2.92)
Median cost >24,752$
No Intra cranial bleed history (Reference)
Intra cranial bleed history
Unadjusted
1.29 (1.09 to 1.52)
Adjusted
1.28 (1.08 to 1.52)
3.0
6.0
9.0
12.0
15.0
Lower
Higher

LAAO in special patient populations:

- Patients with chronic kidney disease and end-stage renal disease on dialysis

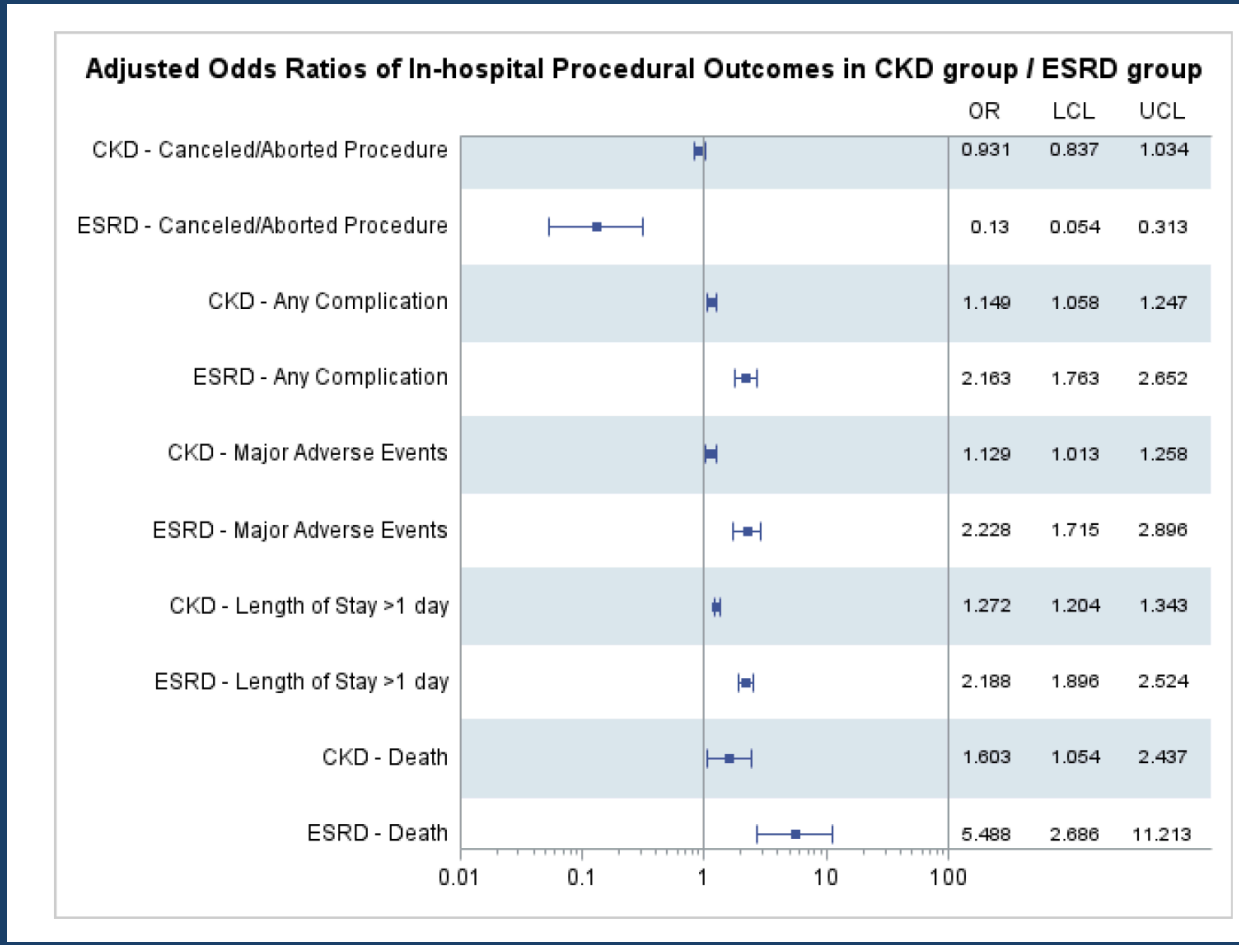
HeartRhythm Heart Rhythm Society

Association of Chronic Kidney Disease and End-Stage Renal Disease with Procedural and Long-Term Outcomes after First Generation Watchman Device: Insights from the NCDR LAAO Registry

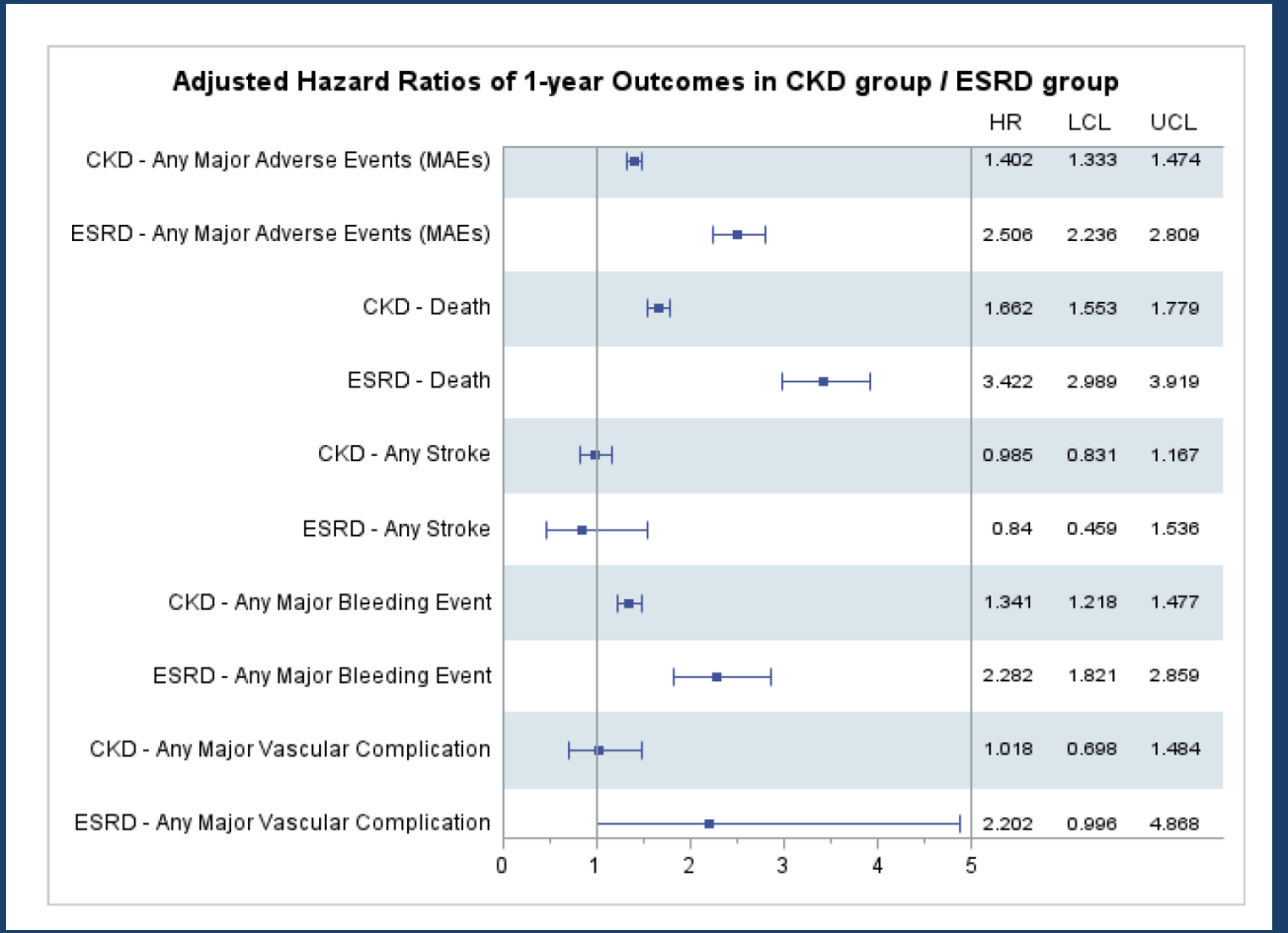
Muhammad Bilal Munir, MD[1], Zhen Tan, MS[2], Patrick H. Pun, MD[3], Yongfei Wang, MS[2], Anwar Tandar, MD[4], Douglas Darden, MD[5], Jonathan C. Hsu, MD[6], Daniel J. Friedman, MD[7], Jeptha Curtis, MD[8], James V. Freeman, MD, MPH, MS[8]

Data were extracted from the National Cardiovascular Data Registry LAAO Registry from January 2017 to December 2019 and linked to Centers for Medicare & Medicaid Services billing claims. Patients were stratified into three groups: no CKD, CKD, and ESRD on dialysis. Multivariate analyses were utilized to assess the associations of CKD and ESRD with procedural and long-term outcomes, respectively.

Short-term outcomes:



Long-term outcomes:



THANK YOU