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Comparative Effectiveness of Left Atrial Appendage Occlusion Among Patients with Atrial Fibrillation Undergoing Concomitant Cardiac Surgery: A Report from the Society of Thoracic Surgeons Adult Cardiac Surgery Database

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Background

- The left atrial appendage (LAA) is implicated as the site of thrombus formation in 90% of thromboembolic events among patients with non-rheumatic atrial fibrillation (AF)
- Although systemic oral anticoagulation with either warfarin or a direct oral anticoagulant is effective at significantly reducing the risk of thromboembolic stroke, as few as half of all eligible patients take these medications
- The LAA can be surgically occluded at the time of cardiac surgery (S-LAAO) although there are limited data supporting effectiveness of this approach

Blackshear and Odell *Ann Thorac Surg*. 1996;61(2):755–759 Hsu JC *et al JAMA Cardiol*. 2016;1(1):55–62

Objective

- To perform a large comparative effectiveness analysis of S-LAAO vs. no S-LAAO in a contemporary, nationally representative cohort of Medicare beneficiaries with AF who underwent cardiac surgery in the United States
- Primary outcome
  - Re-hospitalization for thromboembolism at 1 year
- Secondary outcomes
  - hemorrhagic stroke, all-cause mortality, and a composite endpoint consisting of all-cause mortality, thromboembolism, and hemorrhagic stroke

Methods – Data Sources

- Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database from 2011-2012
  - >1,000 participating institutions reflecting ~90% of CT surgical programs in the US
- A validated deterministic linkage process allowed for ascertainment of longitudinal data on morbidity and mortality for those with fee-for-service Medicare

Jacobs JP *et al Ann Thorac Surg*. 2016;101(1):33–41 Jacobs JP *et al Ann Thorac Surg*. 2010;90(4):1150–1156

Methods

- Inclusion
  - ≥65 years
  - First time cardiac surgery
  - AF or atrial flutter
  - Operations
    - CABG
    - Mitral surgery ± CABG
    - Aortic surgery ± CABG
  - ≥6 months of follow-up after discharge
- Exclusions
  - Off pump operations
  - Operations for endocarditis, combined aortic and mitral disease, congenital heart disease, transplant, ventricular assist device implants
  - Cardiogenic shock
  - Missing data on S-LAAO, primary surgical procedure, or discharge anticoagulation
  - Inability to link to Medicare claims

Statistical Methods

- Inverse probability weighted (IPW) Cox proportional hazards models or Fine-Gray models were used to estimate the risk-adjusted association between S-LAAO and no S-LAAO and outcomes
- The IPW model was tested with Cramer Phi statistics and falsification endpoints
- Exploratory secondary analyses with stratification by discharge anticoagulation status were performed

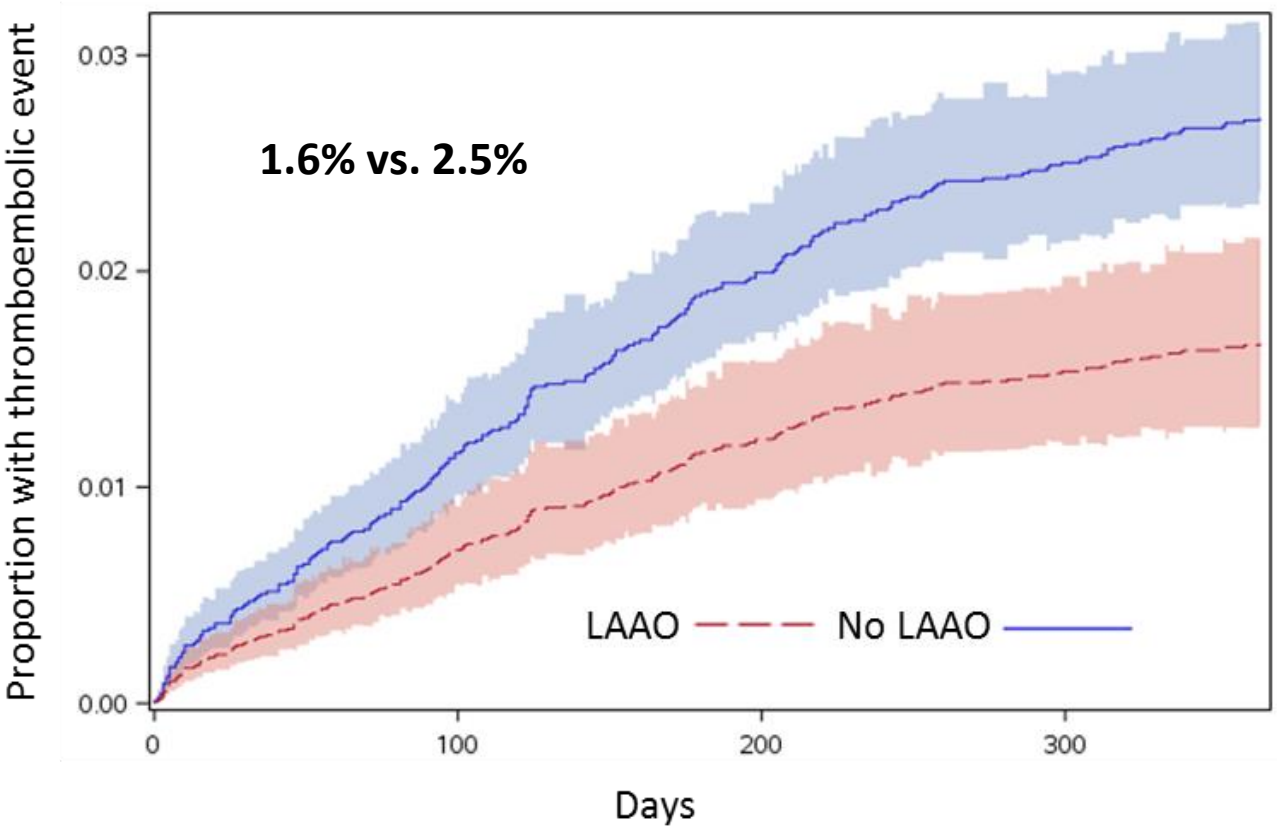
Results

- 10,524 patients met study criteria
- Median age 76, interquartile range (IQR) 71-81
- 39% female
- Median CHA_2DS_2-VASc 4, IQR 3-5
- Primary operation
  - 30% mitral procedure ± CABG (n=3,162)
  - 35% aortic procedure ± CABG (n=3,635)
  - 35% isolated CABG (n=3,726)
- **37% underwent S-LAAO (n=3,892)**

Results

- S-LAAO was associated with:
  - Non-paroxysmal AF
  - Higher ejection fraction
  - Lower STS PROM score
  - Fewer stroke risk factors (diabetes, hypertension, and history of stroke)
  - Mitral operations and surgical ablation
  - Academic medical centers

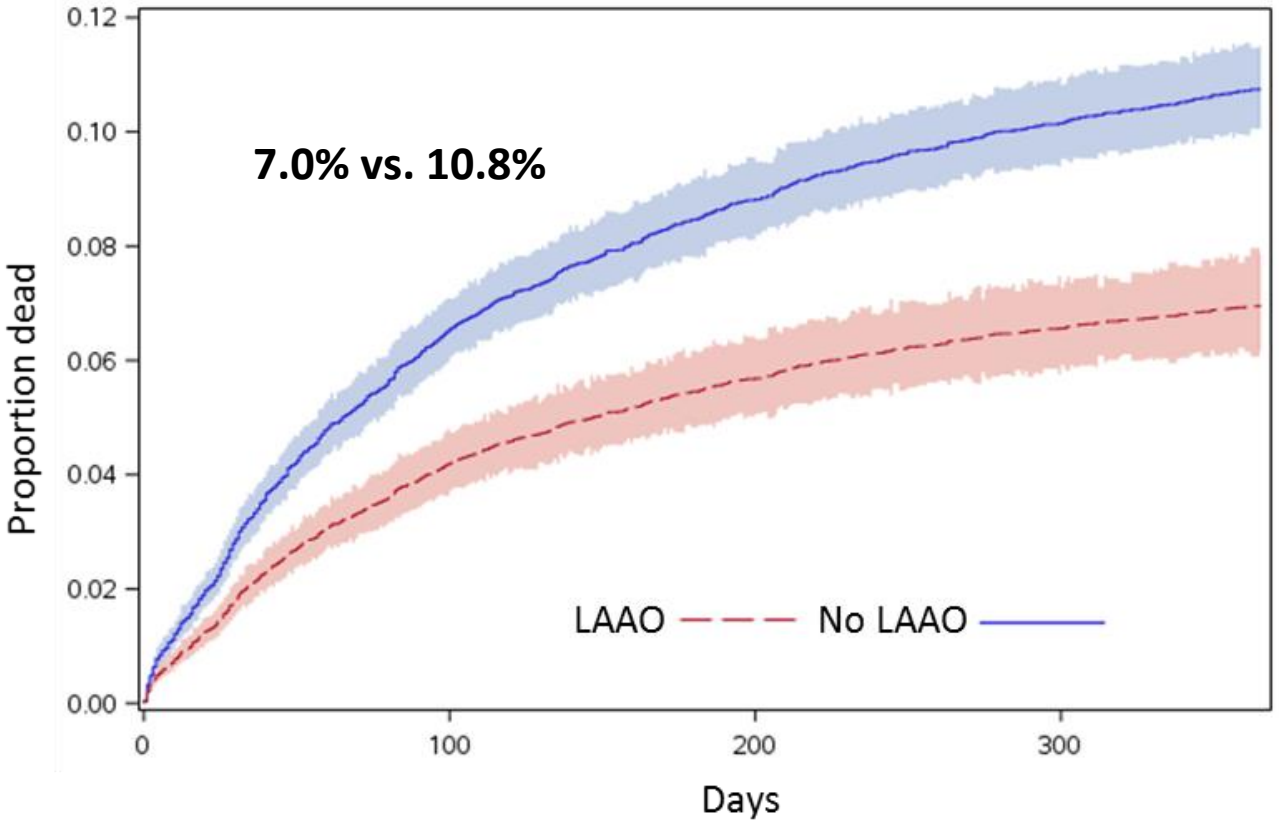
Thromboembolism



Unadjusted
HR 0.63, CI 0.47-0.84, p=0.0016

Adjusted
HR 0.62, CI 0.46-0.83, p = 0.001

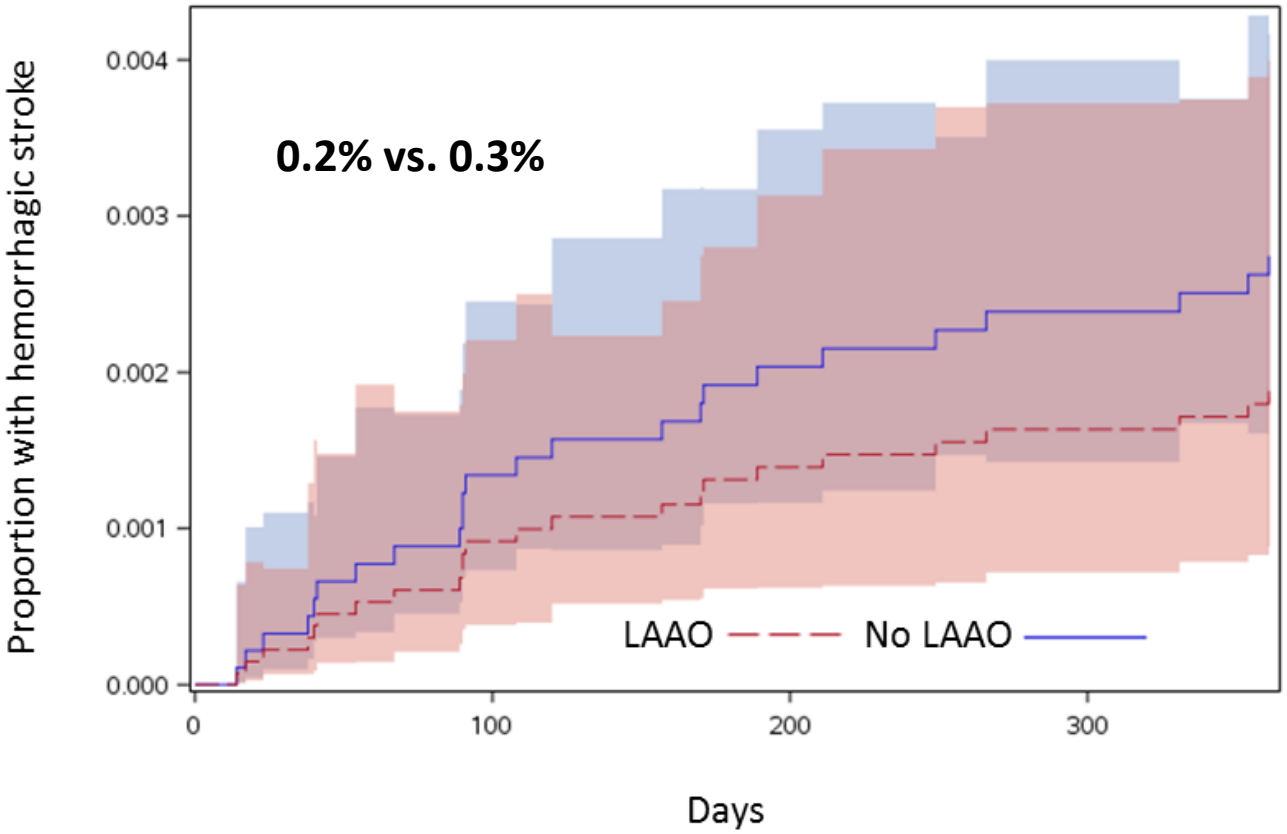
All-cause mortality



Unadjusted
HR 0.63, CI 0.55-0.73, p<0.0001

Adjusted
HR 0.85, CI 0.74-0.97, p = 0.015

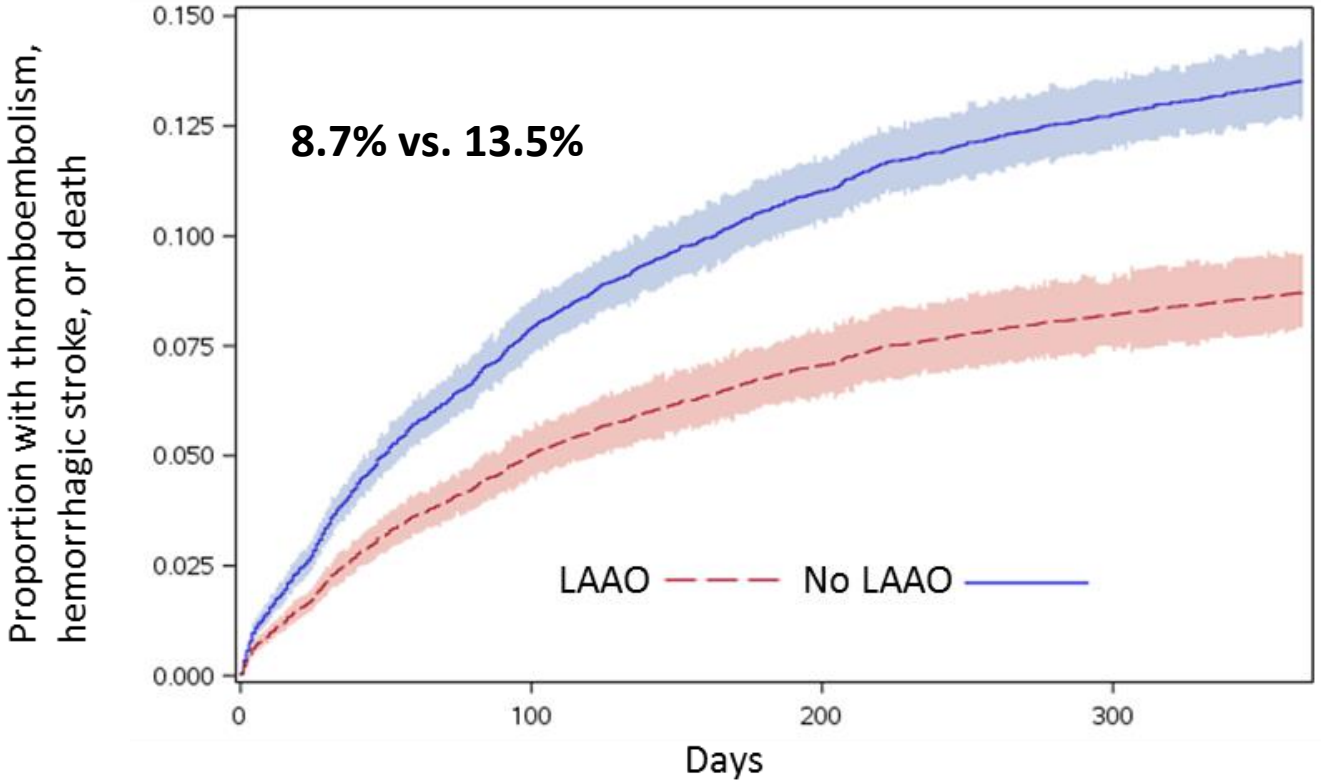
Hemorrhagic Stroke



Unadjusted
HR 0.70, CI 0.29-1.69, p=0.43

Adjusted
HR 0.64, CI 0.26-1.56, p = 0.33

Composite



Unadjusted
HR 0.63, CI 0.55-0.71, p<0.0001

Adjusted
HR 0.70, CI 0.70-0.90, p=0.0002

Discharge anticoagulation

	No Anticoagulation (n=3,848)		Anticoagulation (n=6,676)	
Outcome	Adjusted HR/sHR (CI)	P-value	Adjusted HR/sHR (CI)	P-value
Thromboembolism	0.29 (0.14-0.60)	0.0009	1.04 (0.76-1.42)	0.80
Hemorrhagic stroke	0.13 (0.01-3.36)	0.22	0.32 (0.09-1.17)	0.08
Death	1.06 (0.87-1.30)	0.55	0.88 (0.74-1.05)	0.15
Composite	0.91 (0.75-1.10)	0.33	0.89 (0.77-1.04)	0.15

Results Summary

- S-LAAO was associated with a ~40% reduction in thromboembolism and 15% reduction in all-cause mortality
- Exploratory analyses suggest that the association between S-LAAO and a reduction in thromboembolism is strongest among those discharged without oral anticoagulation

Limitations

- Retrospective, non-randomized study design
- Endpoints determined by claims data
- No data on method or completeness of S-LAAO
- Discharge anticoagulation status may not be predictive of long term anticoagulation strategy

Conclusions

- In a nationally representative cohort of older patients with AF undergoing cardiac surgery, S-LAAO was associated with a reduction in thromboembolism and all-cause mortality
- Although randomized trial data are needed, this study suggests it is reasonable to routinely consider use of S-LAAO in patients with AF undergoing cardiac surgery

Back-Up Slides

Baseline Characteristics

Patient Characteristic	No S-LAAO (n=6,632)	S-LAAO (n=3,892)	p-value
Age (years)	76.4 (6.4)	75.0 (5.9)	<0.0001
Female sex, %	2491 (37.56%)	1566 (40.24%)	0.0065
Race			0.3350
White, %	6122 (92.31%)	3628 (93.22%)	
Black, %	194 (2.93%)	103 (2.65%)	
Hispanic, %	107 (1.61%)	50 (1.28%)	
Other, %	209 (3.15%)	111 (2.85%)	
Paroxysmal AF, %	3347 (50.47%)	1688 (43.37%)	<0.0001
Current smoking, %	471 (7.10%)	213 (5.47%)	0.0011
BMI, kg/m^2			0.7718
<18.5	82 (1.24%)	50 (1.28%)	
18.5–24.99	1741 (26.25%)	989 (25.41%)	
25–29.99	2397 (36.14%)	1437 (36.92%)	
30+	2412 (36.37%)	1416 (36.38%)	
EF, %			<0.0001
<30	483 (7.28%)	197 (5.06%)	
30–49	1754 (26.45%)	970 (24.92%)	
50+	4395 (66.27%)	2725 (70.02%)	
CHF, %	2945 (44.41%)	1784 (45.84%)	0.1540

Patient Characteristic	No S-LAAO	S-LAAO	p-value
Prior stroke, %	995 (15.00%)	533 (13.69%)	0.0659
Hypertension, %	843 (12.71%)	566 (14.54%)	0.0077
Hyperlipidemia, %	5179 (78.09%)	2929 (75.26%)	0.0008
Diabetes			<0.0001
No diabetes	4218 (63.60%)	2720 (69.89%)	
Non-insulin, %	1695 (25.56%)	896 (23.02%)	
Insulin, %	719 (10.84%)	276 (7.09%)	
Coronary artery disease, %	5117 (77.16%)	2568 (65.98%)	<0.0001
Acute coronary syndrome prior to operation, %	2425 (36.57%)	868 (22.30%)	<0.0001
GFR, mL/min/1.73 m^2			<0.0001
>60, %	4014 (60.52%)	2513 (64.57%)	
30–59, %	2264 (34.14%)	1275 (32.76%)	
15–29, %	225 (3.39%)	74 (1.90%)	
<15 including dialysis, %	129 (1.95%)	30 (0.77%)	
Lung disease, %	2105 (31.74%)	1082 (27.80%)	<0.0001
Obstructive sleep apnea, %	5911 (89.13%)	3423 (87.95%)	0.0653
CHA_2DS_2-VASc Score	4.1 (1.4)	3.9 (1.4)	<0.0001
STS risk score			<0.0001

Falsification Endpoints

		Unadjusted		IPW Adjusted	
Outcome	**Rate[a]**	**sHR (CI)**	**p-value**	**sHR (CI)**	**p-value**
Lower extremity fracture	0.7 vs. 0.7	0.90 (0.56- 1.45)	0.68	1.06 (0.67-1.70)	0.80
Pneumonia	2.3 vs. 2.6	0.86 (0.66-1.10)	0.23	0.95 (0.73-1.23)	0.68

Abbreviations: CI, confidence interval; IPW, inverse probability-weighted; sHR, subdistribution hazard ratio; All other abbreviations can be found in Table 1.

[a]Raw rate (%) of outcome for S-LAAO vs. no S-LAAO groups, respectively

Outcomes

- Primary
  - Re-hospitalization for thromboembolism (International Classification of Diseases, Ninth Revision [ICD-9] codes 434.x or 444.x [thromboembolic stroke or systemic embolism] or 435.x [transient ischemic attack]) to 1 year
- Secondary
  - Hemorrhagic stroke (ICD-9 codes 430–432), death, and a composite endpoint comprised of thromboembolism, hemorrhagic stroke, or death to 1 year.