

Left Atrial Appendage Occlusion Study (LAAOS) III

Richard Whitlock MD PhD

On Behalf of the LAAOS III Investigators

Professor of Surgery

Twitter: @RichardWhitloc2

AMERICAN COLLEGE of CARDIOLOGY

Background and Hypothesis

- Left atrial appendage occlusion (LAAO) is hypothesized to prevent ischemic stroke in AF
- Performed easily during cardiac surgery for other indications
- We tested if LAAO at the time of other cardiac surgery reduces ischemic stroke or systemic embolism



LAAOS III Intervention

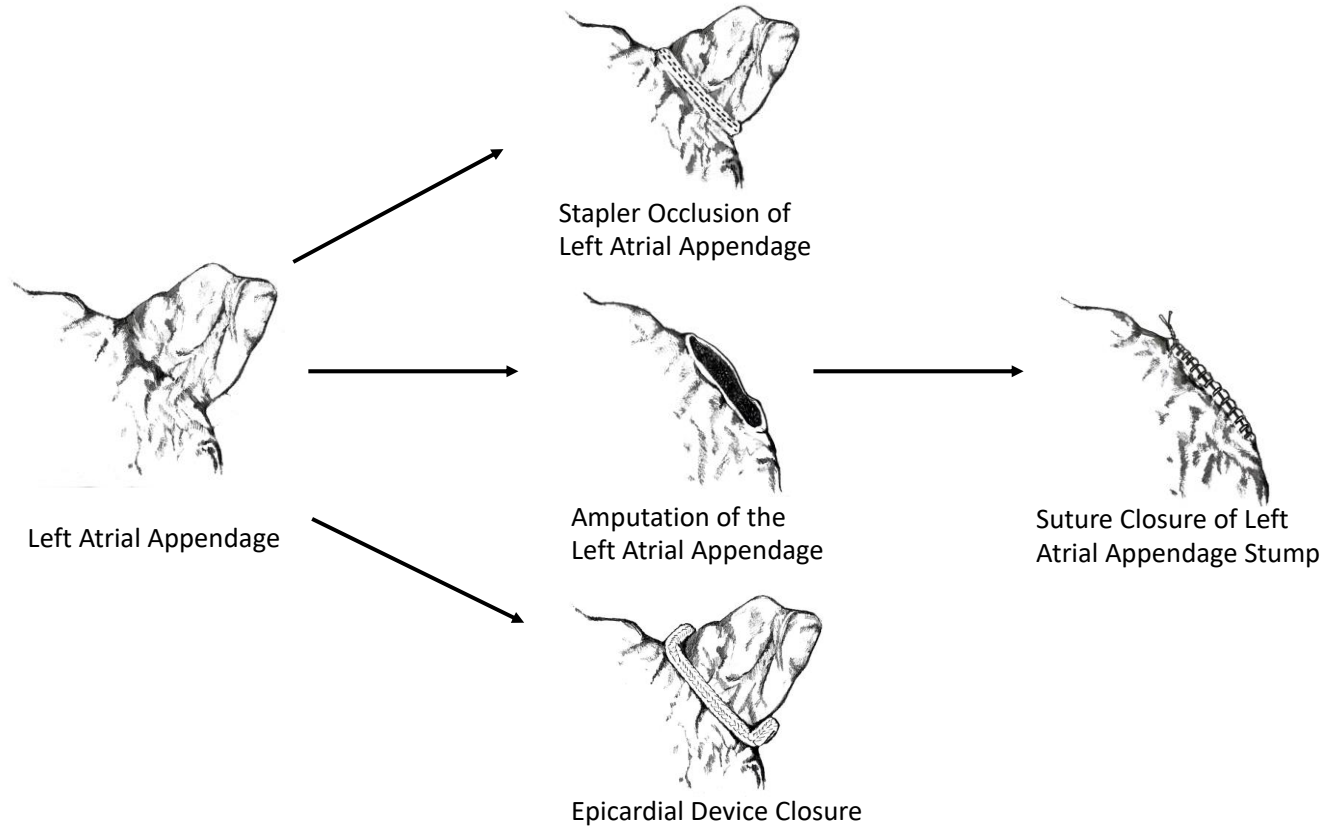
CHA_2DS_2-VASc ≥ 2

- LAA occlusion (R)
- No occlusion

Blinding of:

- Patient
- Research team
- Treating team

Epicardial Occlusion Techniques



LAAOS III Methods

- Primary outcome is ischemic stroke or systemic embolism
- Intention-to-treat analysis of all patients who had surgery
- Secondary landmark analysis, starting 30 days post-op
- Primary safety outcome was hospitalization for heart failure



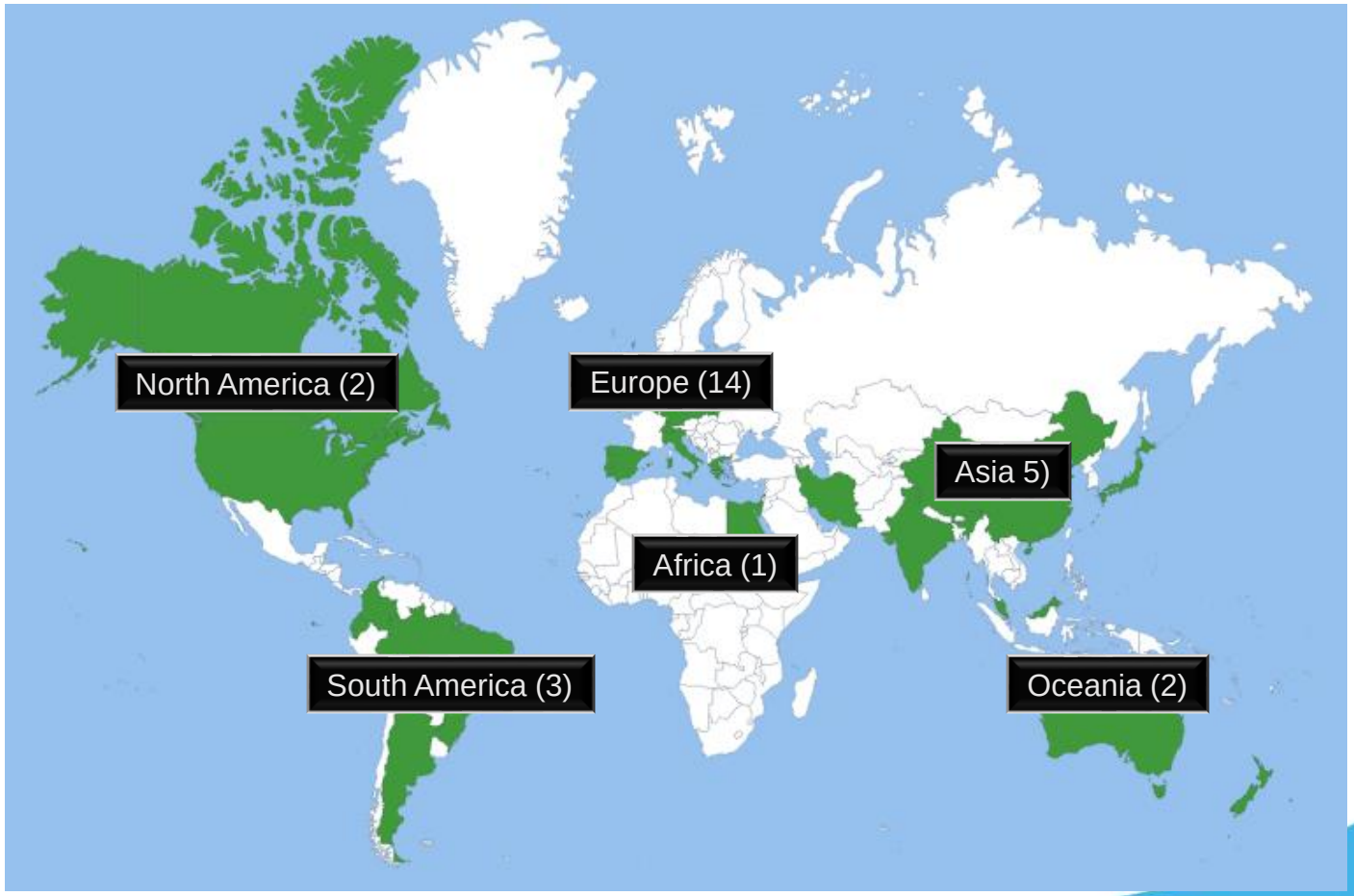
LAAOS III Follow-up

- Follow-up every 6 months with validated stroke questionnaire
- All patients received usual care, including anticoagulation, during follow-up
- DSMB recommended termination at planned interim analysis
- Mean follow-up 3.8 years



LAAOS III Network

- 4811 patients
- 105 centres
- 27 countries



Patient Characteristics

	LAAO (n=2379)	No LAAO (n=2391)
Age, mean (SD)	71.3 (8.4)	71.1 (8.3)
CHA_2DS_2-VASc, mean (SD)	4.2 (1.5)	4.2 (1.5)
Permanent atrial fibrillation (%)	692 (29.1%)	707 (29.6%)
Male (%)	1617 (68.0%)	1601 (67.0%)
Myocardial infarction (%)	567 (23.8%)	583 (24.4%)
History of stroke (%)	214 (9.0%)	219 (9.2%)
History of heart failure (%)	1348 (56.7%)	1372 (57.4%)
Peripheral arterial disease (%)	236 (9.9%)	256 (10.7%)
Diabetes mellitus (%)	770 (32.4%)	765 (32.0%)
Hypertension (%)	1960 (82.4%)	1941 (81.2%)

Surgical Characteristics

	LAAO (n=2379)	No LAAO (n=2391)
Procedure (%)		
Isolated CABG	482 (20.3%)	522 (21.8%)
Isolated Valve	552 (23.2%)	572 (23.9%)
Valve Procedure	1565 (65.8%)	1614 (67.5%)
Mitral	856 (36.0%)	880 (36.8%)
Aortic	837 (35.2%)	858 (35.9%)
Tricuspid	397 (16.7%)	427 (17.9%)
Aorta	146 (6.1%)	134 (5.6%)
Atrial fibrillation ablation	809 (34.0%)	753 (31.5%)

Operative Safety Outcomes

	LAAO n=2379	No LAAO n=2391	p-value*
Bypass time, mean (SD)	119 min (48)	113 min (47)	<0.001
Cross clamp time, mean (SD)	86 min (37)	82 min (37)	<0.001
Chest tube output, median (IQR)	520 ml (350-790)	500 ml (340-760)	0.06
Re-operation for bleeding	94 (4.0%)	95 (4.0%)	0.97
Prolongation of hospitalization due to heart failure	5 (0.2%)	14 (0.6%)	0.04
30-day mortality	89 (3.7%)	95 (4.0%)	0.68

*Not adjusted for multiplicity



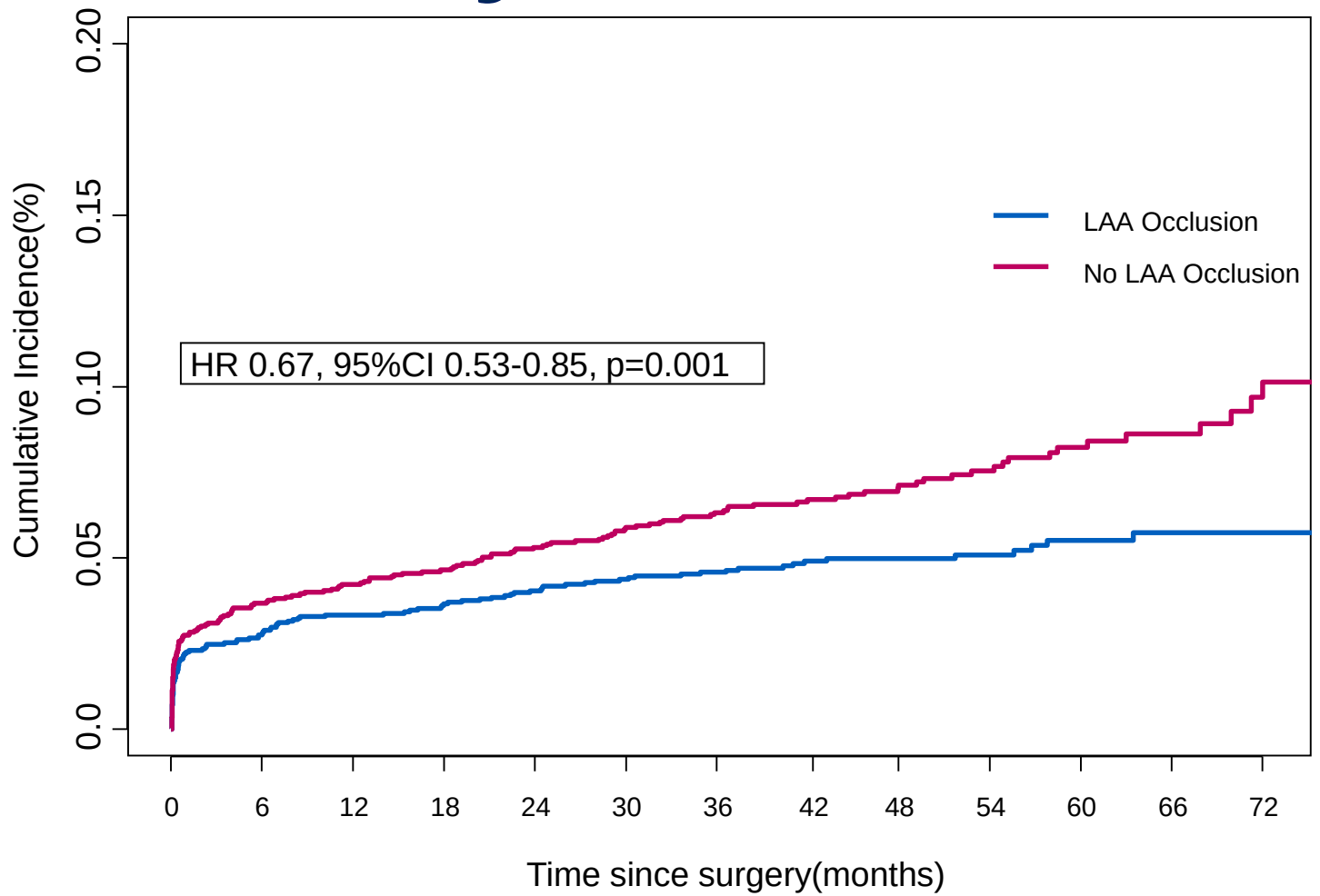
Oral Anticoagulation Use During Follow-up

	LAAO	No LAAO
Discharge	83%	81%
1 year	80%	79%
2 years	77%	78%
3 years	75%	78%

Primary Outcome at 3.8 Years

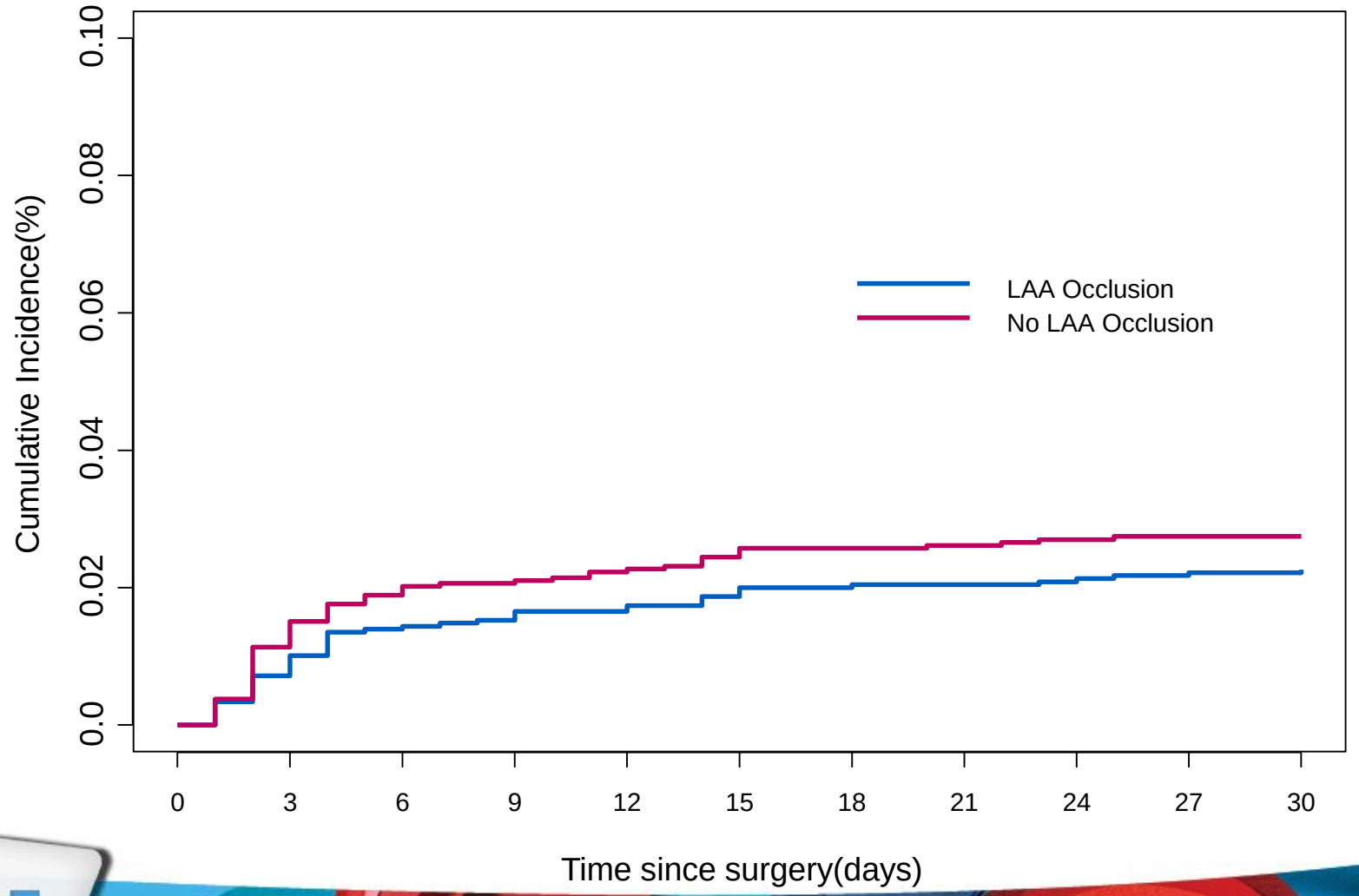
	LAAO (%)	No LAAO (%)	HR (95% CI)	p-value
Ischemic stroke or systemic embolism	4.8	7.0	0.67 (0.53-0.85)	0.001
Landmark analysis				
Before 30 days	2.2	2.7	0.82 (0.57-1.18)	
After 30 days	2.7	4.6	0.58 (0.42-0.80)	

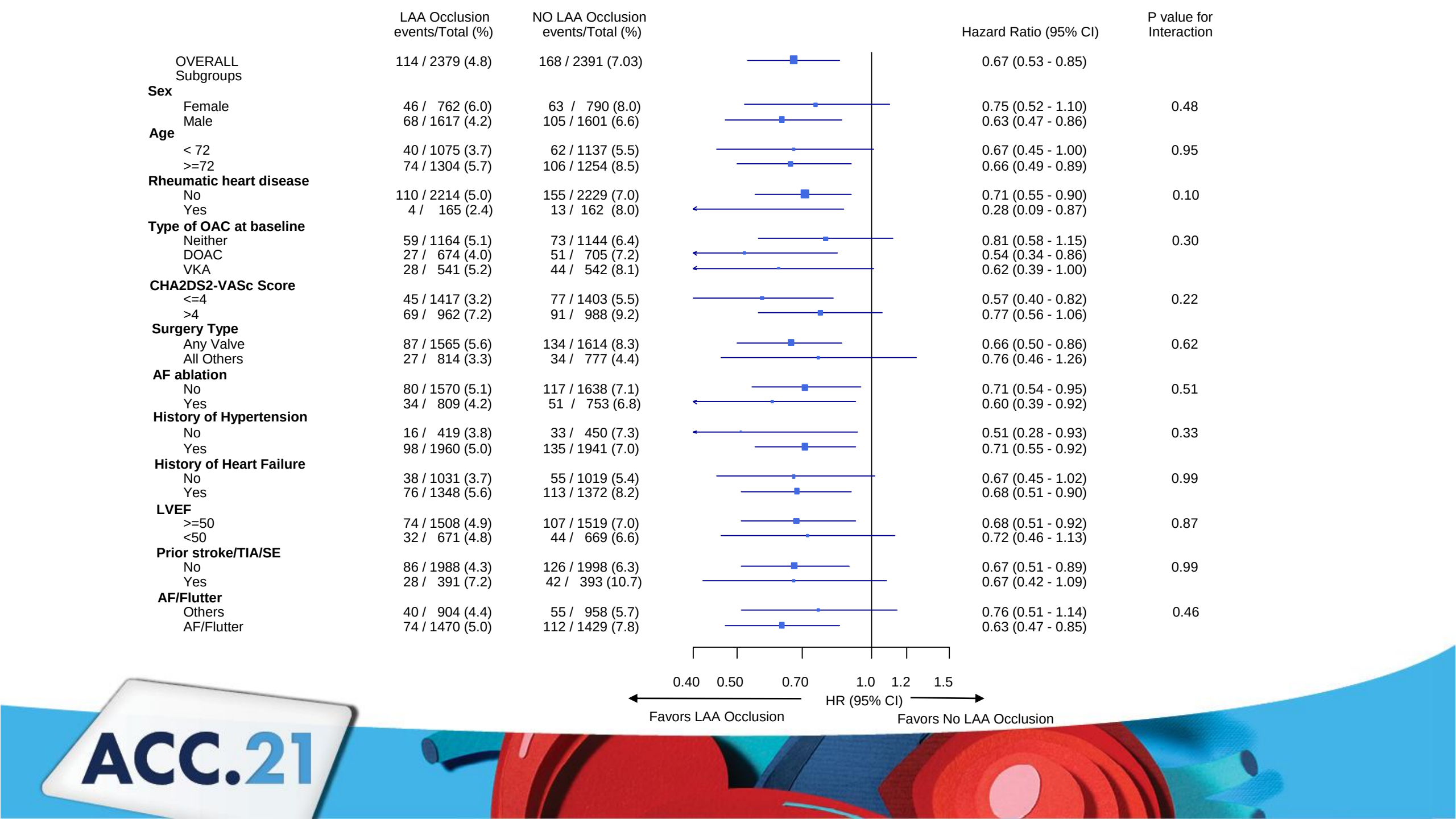
Stroke or Systemic Embolism



# at Risk													
LAA Occlusion	2379	2163	2105	2059	2020	1948	1642	1322	1046	781	550	349	199
No LAA Occlusion	2391	2134	2081	2030	1981	1897	1607	1291	1016	751	540	348	205

Stroke or Systemic Embolism < 30 Days




LAA Occlusion events/Total (%)
NO LAA Occlusion events/Total (%)
Hazard Ratio (95% CI)
P value for Interaction
OVERALL 114 / 2379 (4.8) 168 / 2391 (7.03) 0.67 (0.53 - 0.85)
Subgroups
Sex
Female 46 / 762 (6.0) 63 / 790 (8.0) 0.75 (0.52 - 1.10) 0.48
Male 68 / 1617 (4.2) 105 / 1601 (6.6) 0.63 (0.47 - 0.86)
Age
< 72 40 / 1075 (3.7) 62 / 1137 (5.5) 0.67 (0.45 - 1.00) 0.95
>=72 74 / 1304 (5.7) 106 / 1254 (8.5) 0.66 (0.49 - 0.89)
Rheumatic heart disease
No 110 / 2214 (5.0) 155 / 2229 (7.0) 0.71 (0.55 - 0.90) 0.10
Yes 4 / 165 (2.4) 13 / 162 (8.0) 0.28 (0.09 - 0.87)
Type of OAC at baseline
Neither 59 / 1164 (5.1) 73 / 1144 (6.4) 0.81 (0.58 - 1.15) 0.30
DOAC 27 / 674 (4.0) 51 / 705 (7.2) 0.54 (0.34 - 0.86)
VKA 28 / 541 (5.2) 44 / 542 (8.1) 0.62 (0.39 - 1.00)
CHA2DS2-VASc Score
<=4 45 / 1417 (3.2) 77 / 1403 (5.5) 0.57 (0.40 - 0.82) 0.22
>4 69 / 962 (7.2) 91 / 988 (9.2) 0.77 (0.56 - 1.06)
Surgery Type
Any Valve 87 / 1565 (5.6) 134 / 1614 (8.3) 0.66 (0.50 - 0.86) 0.62
All Others 27 / 814 (3.3) 34 / 777 (4.4) 0.76 (0.46 - 1.26)
AF ablation
No 80 / 1570 (5.1) 117 / 1638 (7.1) 0.71 (0.54 - 0.95) 0.51
Yes 34 / 809 (4.2) 51 / 753 (6.8) 0.60 (0.39 - 0.92)
History of Hypertension
No 16 / 419 (3.8) 33 / 450 (7.3) 0.51 (0.28 - 0.93) 0.33
Yes 98 / 1960 (5.0) 135 / 1941 (7.0) 0.71 (0.55 - 0.92)
History of Heart Failure
No 38 / 1031 (3.7) 55 / 1019 (5.4) 0.67 (0.45 - 1.02) 0.99
Yes 76 / 1348 (5.6) 113 / 1372 (8.2) 0.68 (0.51 - 0.90)
LVEF
>=50 74 / 1508 (4.9) 107 / 1519 (7.0) 0.68 (0.51 - 0.92) 0.87
<50 32 / 671 (4.8) 44 / 669 (6.6) 0.72 (0.46 - 1.13)
Prior stroke/TIA/SE
No 86 / 1988 (4.3) 126 / 1998 (6.3) 0.67 (0.51 - 0.89) 0.99
Yes 28 / 391 (7.2) 42 / 393 (10.7) 0.67 (0.42 - 1.09)
AF/Flutter
Others 40 / 904 (4.4) 55 / 958 (5.7) 0.76 (0.51 - 1.14) 0.46
AF/Flutter 74 / 1470 (5.0) 112 / 1429 (7.8) 0.63 (0.47 - 0.85)
0.40 0.50 0.70 1.0 1.2 1.5
HR (95% CI)
Favors LAA Occlusion
Favors No LAA Occlusion

Secondary Outcomes at 3.8 years

	LAAO (%)	No LAAO (%)	HR (95% CI)
Ischemic stroke	4.2	6.6	0.62 (0.48-0.80)
Systemic embolism	0.3	0.3	0.86 (0.29-2.55)
Death	22.6	22.5	1.00 (0.89-1.13)
Hospitalization for heart failure	7.7	6.8	1.13 (0.92-1.40)

Conclusions

- Surgical LAA occlusion reduces ischemic stroke by 33%
  - After first 30 perioperative days, by 42%
- No evidence of adverse effects
- Benefit additive to oral anticoagulation

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