

# Chiusura dell'auricola sinistra in corso di intervento cardiocirurgico per la prevenzione dell'ictus ischemico

LAAOS III trial

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# Background

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- Atrial fibrillation is responsible for approximately a quarter of ischemic strokes, many of which are cardioembolic and originate from the left atrial appendage.
- Oral anticoagulation most likely reduces thrombus formation in the left atrial appendage and has proven efficacy and safety in preventing ischemic stroke in patients with atrial fibrillation.
- Oral anticoagulation is limited by non-adherence to prescribed medications, drug discontinuation, underdosing, and, for patients treated with vitamin K antagonists, poor control of the INR.
- Left atrial appendage occlusion is hypothesized to reduce the risk of stroke among patients with atrial fibrillation, but this has not been proved in a randomized trial.
- When patients with atrial fibrillation undergo cardiac surgery, concomitant occlusion of the left atrial appendage may be performed as an adjunctive procedure.

# Rationale of the trial

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- Concomitant occlusion performed at the time of cardiac surgery would reduce the risk of ischemic stroke among patients with a history of atrial fibrillation receiving usual care, including anticoagulation.
- If effective, concomitant occlusion would provide protection against ischemic stroke in addition to the protection provided by anticoagulant therapy.
- Once performed, the effects of the procedure are permanent.

Original Article

# Left Atrial Appendage Occlusion during Cardiac Surgery to Prevent Stroke

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# Aim of the study

- To evaluate the efficacy and safety of concomitant left atrial appendage occlusion in participants with a history of atrial fibrillation undergoing cardiac surgery for another indication.
- To determine whether concomitant occlusion would prevent ischemic stroke or systemic embolism in participants who continued to receive usual care, including anticoagulation.

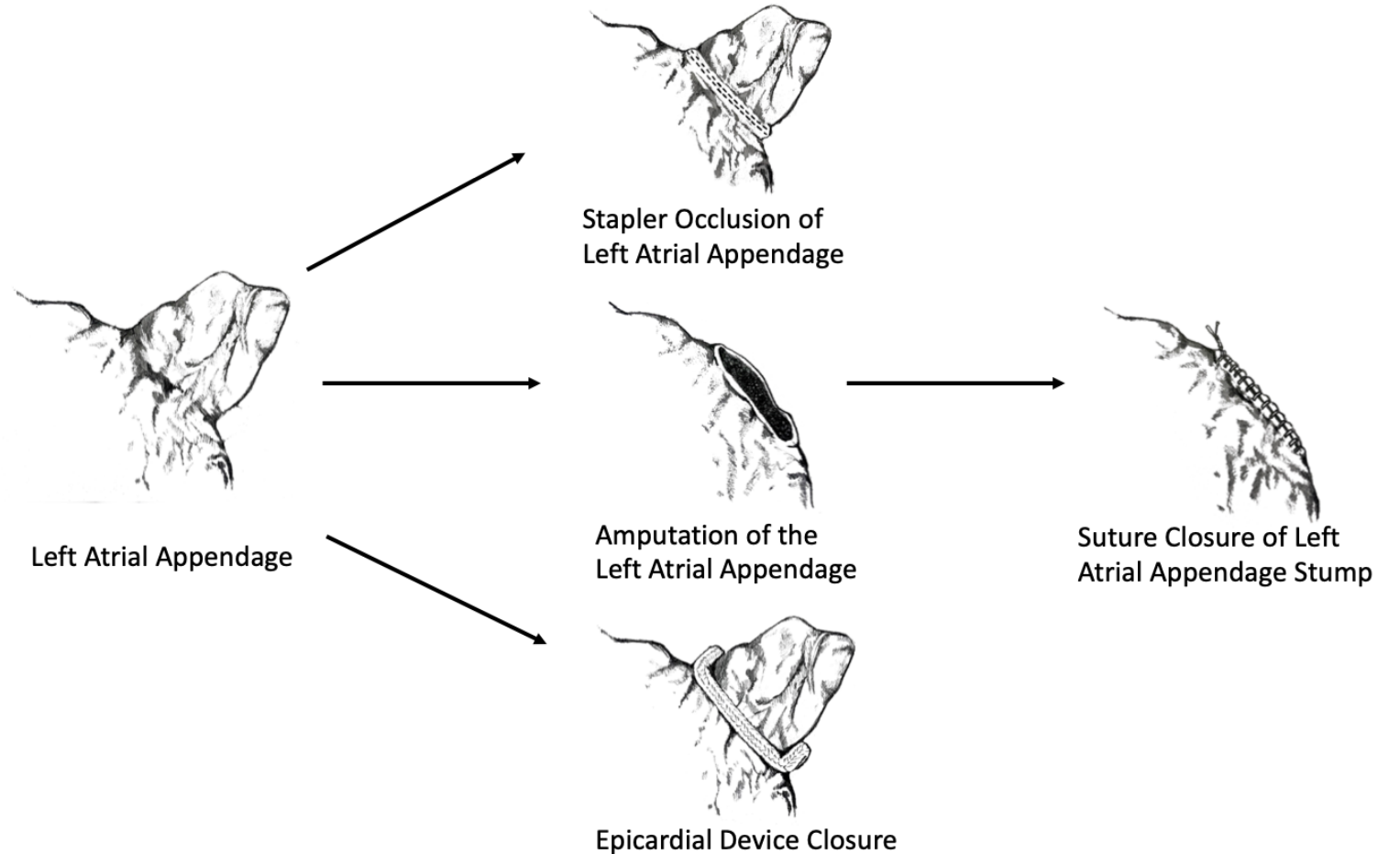
# Methods

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- Multicenter, randomized trial involving participants with atrial fibrillation and a CHA2DS2-VASc score of at least 2 who were scheduled to undergo cardiac surgery for another indication.
- The participants were randomly assigned to undergo or not undergo occlusion of the left atrial appendage during surgery; all the participants were expected to receive usual care, including oral anticoagulation, during follow-up.
- The primary outcome was the occurrence of ischemic stroke (including transient ischemic attack with positive neuroimaging) or systemic embolism.
- The participants, research personnel, and primary care physicians (other than the surgeons) were unaware of the trial-group assignments.

# Epicardial occlusion techniques permitted within LAAOS III

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# Baseline Characteristics

Variable	Occlusion (N = 2379)	No Occlusion (N = 2391)
<b>Participants</b>		
Age — yr	71.3±8.4	71.1±8.3
Male sex — no. (%)	1617 (68.0)	1601 (67.0)
Type of atrial fibrillation — no. (%)		
Permanent	692 (29.1)	707 (29.6)
Persistent	577 (24.3)	508 (21.3)
Paroxysmal	1110 (46.7)	1176 (49.2)
Medical history — no. (%)		
Previous myocardial infarction	567 (23.8)	583 (24.4)
Previous stroke	214 (9.0)	219 (9.2)
Rheumatic heart disease	165 (6.9)	162 (6.8)
Peripheral arterial disease	236 (9.9)	256 (10.7)
History of heart failure	1348 (56.7)	1372 (57.4)
Diabetes mellitus	770 (32.4)	765 (32.0)
Aortic plaque	240 (10.1)	231 (9.7)
Smoking, former or current	1127 (47.4)	1173 (49.1)
Hypertension	1960 (82.4)	1941 (81.2)
CHA <sub>2</sub> DS <sub>2</sub> -VASc score†		
Mean	4.2±1.5	4.2±1.5
Median (interquartile range)	4 (3–5)	4 (3–5)
Atrial fibrillation on baseline ECG — no. (%)	1392 (58.5)	1338 (56.0)
Left ventricular ejection fraction <50% — no./total no. (%)	671/2179 (30.8)	669/2188 (30.6)

Variable	Occlusion (N = 2379)	No Occlusion (N = 2391)
<b>Anticoagulant therapy within 7 days before surgery</b>		
Vitamin K antagonist — no. (%)	541 (22.7)	542 (22.7)
Direct oral anticoagulant — no. (%)	674 (28.3)	705 (29.5)
Neither direct oral anticoagulant nor vitamin K antagonist — no. (%)	1164 (48.9)	1144 (47.8)
<b>Cardiac surgery</b>		
Surgical procedure performed — no. (%)		
Isolated CABG	482 (20.3)	522 (21.8)
Isolated valve replacement	552 (23.2)	572 (23.9)
Other	1344 (56.5)	1296 (54.2)
Any 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)
Pulmonic	2 (0.1)	4 (0.2)
Any aortic procedure	146 (6.1)	134 (5.6)
Concomitant surgical ablation of atrial fibrillation — no. (%)	809 (34.0)	753 (31.5)
Received assigned procedure — no. (%)	2131 (89.6)	2262 (94.6)
<b>Left atrial appendage occlusion‡</b>		
Occlusion attempted — no. (%)	2131 (89.6)	NA
Occlusion method — no./total no. (%)§		
Cut and sew	939/1685 (55.7)	NA
Stapler	189/1685 (11.2)	NA
Closure device	255/1685 (15.1)	NA
Closure from within	233/1685 (13.8)	NA
Other approved techniques	69/1685 (4.1)	NA



# Baseline characteristics

- The mean age of the participants was 71 years, and 67.5% were men.
- The mean CHA2DS2-VASc score was 4.2, and approximately half the participants were receiving oral anticoagulation at baseline.

# Anticoagulation during follow-up

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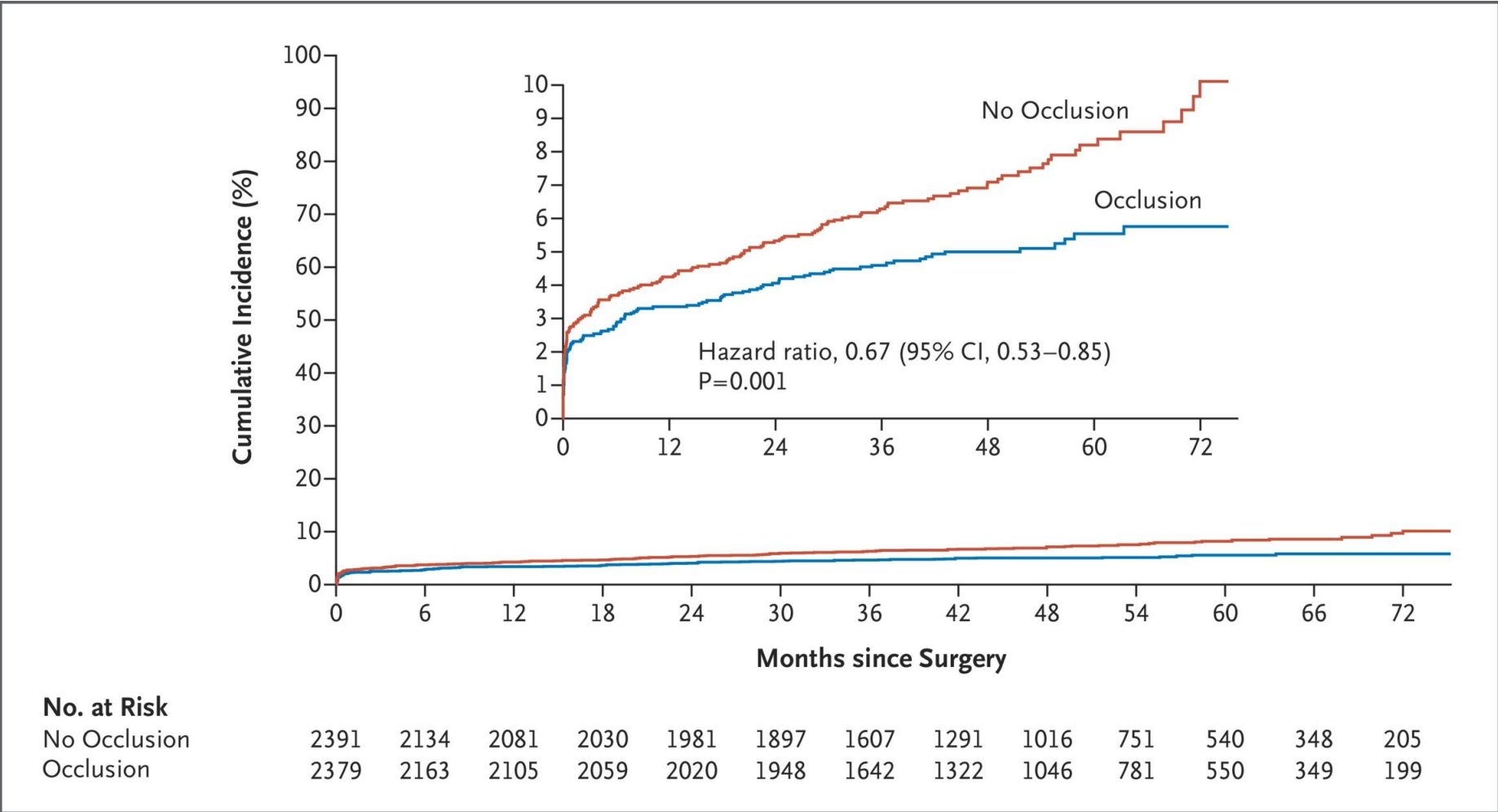
	Left Atrial Appendage Occlusion			No Left Atrial Appendage Occlusion		
	Any anticoagulation	Vitamin K antagonist	Direct oral anticoagulant	Any anticoagulation	Vitamin K antagonist	Direct oral anticoagulant
<b>Discharge</b>	83.4%	64.8%	18.6%	81.0%	62.6%	18.4%
<b>One Year</b>	79.6%	44.6%	35.0%	78.9%	43.2%	35.6%
<b>Two Years</b>	77.1%	39.2%	37.9%	77.7%	39.7%	38.0%
<b>Three Years</b>	75.3%	38.3%	37.0%	78.2%	39.4%	38.8%

# Trial outcomes

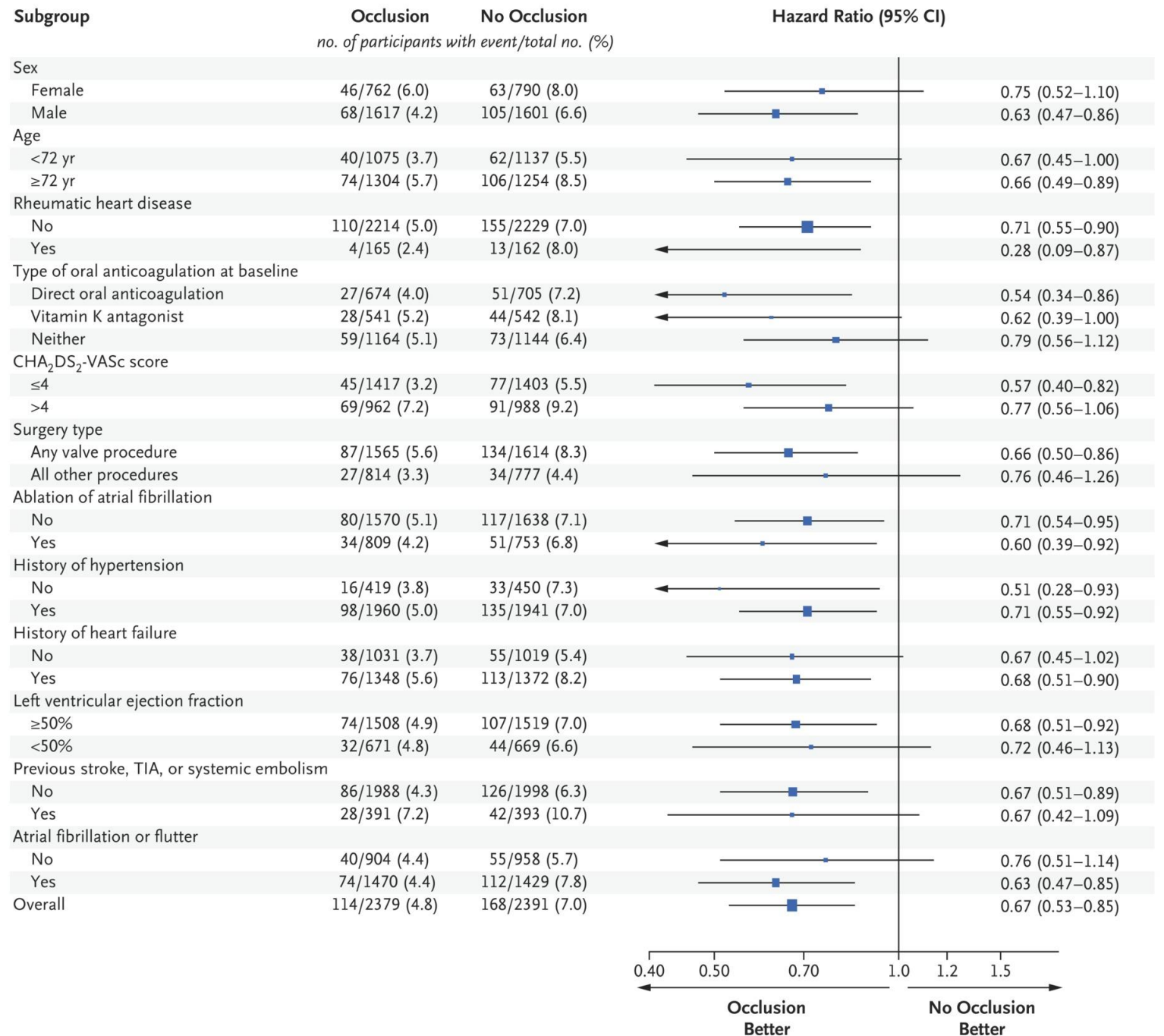
Outcome	Occlusion (N=2379)	No Occlusion (N=2391)	Comparison†
	<i>no. of participants (%)</i>		
<b>Primary</b>			
Ischemic stroke or systemic embolism	114 (4.8)	168 (7.0)	0.67 (0.53 to 0.85)‡
Ischemic stroke	109 (4.6)	164 (6.9)	0.66 (0.52 to 0.84)
Systemic embolism	6 (0.3)	7 (0.3)	0.86 (0.29 to 2.55)
<b>Secondary</b>			
Any stroke or systemic embolism	127 (5.3)	187 (7.8)	0.67 (0.54 to 0.84)
Any stroke	113 (4.7)	176 (7.4)	0.63 (0.50 to 0.80)
Ischemic stroke, systemic embolism, or death from any cause	601 (25.3)	639 (26.7)	0.93 (0.83 to 1.04)
Death from any cause	538 (22.6)	537 (22.5)	1.00 (0.89 to 1.13)
Hospitalization for heart failure§	183 (7.7)	162 (6.8)	1.13 (0.92 to 1.40)
Major bleeding event	248 (10.4)	267 (11.2)	0.93 (0.78 to 1.11)
Myocardial infarction	49 (2.1)	56 (2.3)	0.87 (0.59 to 1.28)
Ischemic stroke or systemic embolism within the first 30 days after surgery	53 (2.2)	65 (2.7)	0.82 (0.57 to 1.18)
Ischemic stroke or systemic embolism beyond 30 days after surgery¶	61 (2.7)	103 (4.6)	0.58 (0.42 to 0.80)
<b>Operative</b>			
Bypass time — min	119±48	113±47	5 (3 to 8)
Cross-clamp time — min	86±37	82±37	4 (1 to 6)
Median chest-tube output (IQR) — ml	520 (350 to 790)	500 (340 to 760)	20 (-2 to 42)**
Reoperation for bleeding within 48 hours after surgery — no. (%)	94 (4.0)	95 (4.0)	0.99 (0.75 to 1.32) ††
Prolongation of index hospitalization due to heart failure — no. (%)	5 (0.2)	14 (0.6)	0.36 (0.13 to 0.99) ††
Death within 30 days — no. (%)	89 (3.7)	95 (4.0)	0.94 (0.71 to 1.25) ††

# Cumulative Incidence of Stroke or Systemic Arterial Embolism

Whitlock RP et al. N Engl J Med 2021;384:2081-2091



# Subgroup Analysis



# Study limitations

- Lack of information about the relative efficacy of left atrial appendage occlusion as compared with oral anticoagulation.
- The findings from LAAOS III apply primarily to surgical occlusion of the appendage performed as a concomitant procedure and not to stand-alone surgical or endovascular occlusion → cannot discern whether all surgical closure methods are comparable
- Not examine whether occlusion was sustained over follow-up.

# Conclusions

- Among participants with atrial fibrillation who had undergone cardiac surgery, most of whom continued to receive ongoing antithrombotic therapy, the risk of ischemic stroke or systemic embolism was lower with concomitant left atrial appendage occlusion performed during the surgery than without it.