



**Bispebjerg og Frederiksberg
Hospital**

UNIVERSITY OF COPENHAGEN



The Left Atrial Appendage Closure by Surgery study (LAACS)

Jesper Park-Hansen, MD
Bispebjerg-Frederiksberg University Hospital
Copenhagen, Denmark
Department of Cardiology.

Declaration of interest

- I have nothing to declare

Background

- Atrial fibrillation (AFIB) occurs in 30-67 % heart surgery

Rader. Am Heart J. 2010

Lahtinen. Ann Thorac Surg, 2004

Almassi. Ann Surg, 1997

- Stroke occurs in 1-3% of all CABG during the 1st year

Crystal Circulation. 2002

Mack MJ JACC 2013

- Risk of stroke is at least 4% per year for most heart-operated patients with AFIB (*according to their CHADS-score*)

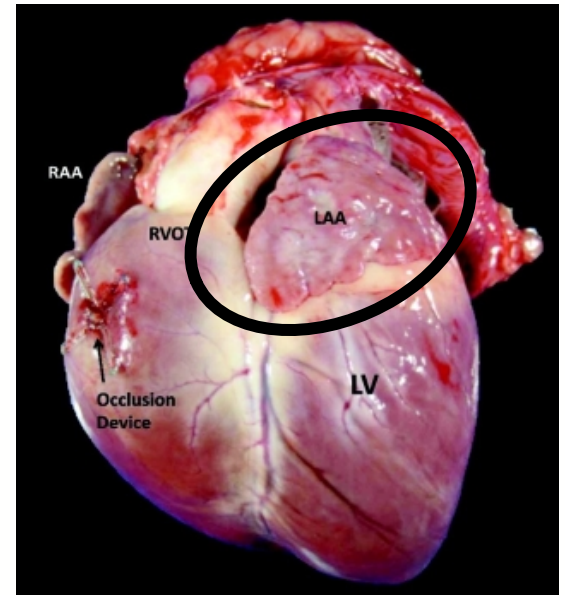
Bianchari. Scan Cardiovasc. J 2011

Background

- 15-20% of patients with AFIB have clots in the left atrium

→90% of those are evident in the left atrial appendage

Manning Ann Intern Med. 1995
Pearson JACC 1991



Background

Evidence behind Left Atrial Appendage Closure with device

PROTECT-AF – non-inferiority to warfarin.

Reddy, Circulation 2013

PREVAIL-AF – non-inferiority to warfarin >7 days

Holmes, JACC 2014

What about surgical closure?

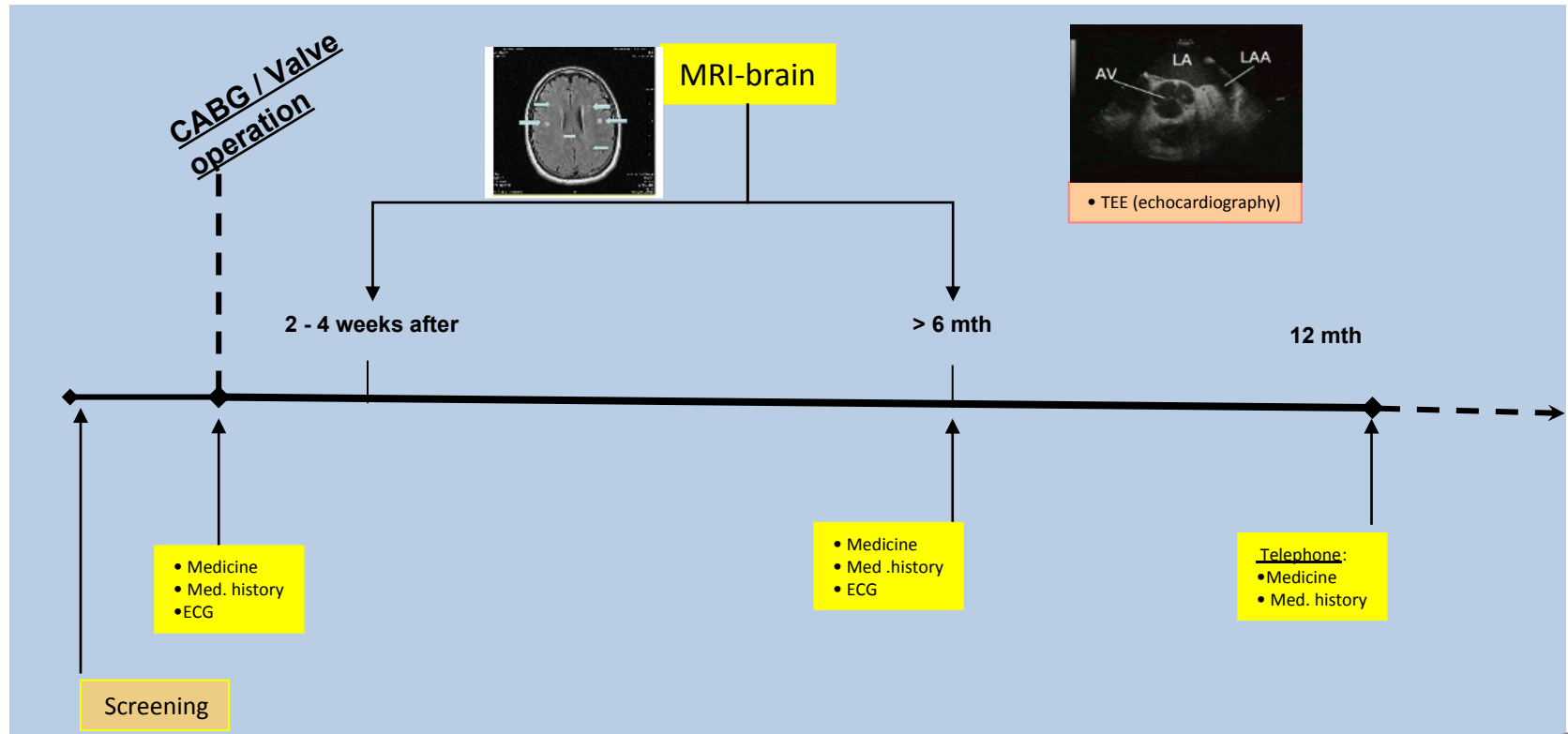
Hypothesis

Left Atrial Appendage Closure at the time of **Surgery** may **protect** from post-operative **cerebral ischemia**, **regardless of AF** status at time of surgery

Methods

- Screening all patients referred for first time heart surgery 2010-2015
- Block-randomization 1:1 LAACS vs Control
- Stratified by expected anticoagulation 3 first months post-op
- Recommended double closure – purse-string + single running suture

Methods



Endpoint definition

- Post-operative cerebral ischemic events - Composite endpoint of first ischemic stroke/TIA or silent cerebral infarcts (SCI) after surgery
 - Increase in the numbers of SCI between MRI-1 to MRI-2 or post-operative findings of fresh SCI by clinical brain imaging unrelated to study enrollment.
 - SCI as a precursor for larger stroke
 - All stroke/TIA were diagnosed by neurologists in clinical setting.
 - Radiologists were blinded to randomization.

Results

Invited 914

Enrolled 205

Randomized 187

Per protocol 141

Results

Table 1. Baseline characteristics according to randomized left atrial appendage closure

Variable	Not closed (n=86)	Closed (n=101)	P-value
Age – years	69.3±8.8	67.6±9.6	0.21
Men - n (%)	75 (87.2)	84 (83.2)	0.44
Atrial fibrillation - n (%)	12 (12.8)	18 (16.8)	0.43
Clinical characteristics			
Congestive heart failure - n (%)	15 (17.9)	16 (15.8)	0.76
Atrial fibrillation - n (%)	12 (12.8)	18 (16.8)	0.43
Diabetes - n (%)	19 (22.1)	31 (30.7)	0.21
Hypertension - n (%)	60 (69.8)	75 (74.3)	0.42
CHADS-VASc – unit	2.9±1.4	2.9±1.5	1.00
Prior stroke - n (%)	15 (17.4)	11 (10.9)	0.19
Chronic kidney disease* - n (%)	14 (16.3)	15 (14.9)	0.78
Verapamil - n (%)	4 (4.5)	2 (2.0)	0.42
Surgery type			
AVR only - n (%)	17 (19.1)	17 (16.8)	0.60
AVR with CABG - n (%)	20 (22.5)	22 (21.8)	0.81
AVR with aortic surgery - n (%)	1 (1.1)	1 (1.0)	1.00
AVR with MVR - n (%)	0 (0)	2 (2.0)	0.50
Aortic surgery only - n (%)	1 (1.1)	0 (0)	0.46
CABG only - n (%)	40 (46.5)	50 (49.5)	0.68
CABG with MVR - n (%)	2 (2.3)	2 (2.0)	1.00
MVR only - n (%)	4 (4.5)	7 (6.9)	0.55
Tricuspid surgery only - n (%)	1 (1.2)	0 (0)	0.46
Tricuspid surgery only - n (%)	1 (1.2)	0 (0)	0.46
Perioperative atrial fibrillation - n (%)	52 (60.5)	50 (50.0)	0.15

Abbreviations: CHADS-VASc: Congestive heart failure, hypertension, age [≥75 years], diabetes, stroke/peripheral vascular disease, age [≥65 years], sex-category, OAC: Oral anticoagulation, VKA: Vitamin K-antagonist, NOAC: Novel oral anticoagulation, IQR: interquartile range.

*eGFR<30ml/min

Results

Screened > 6000 patients

Invited 914

Enrolled 205

Randomized 187

86

Control

101

LAACS

Per protocol 141

77

Control

64

LAACS

Composite
endpoint

14

p=0,02

5

14

p=0,04

4

8

p=0,07

3

8

p=0,09

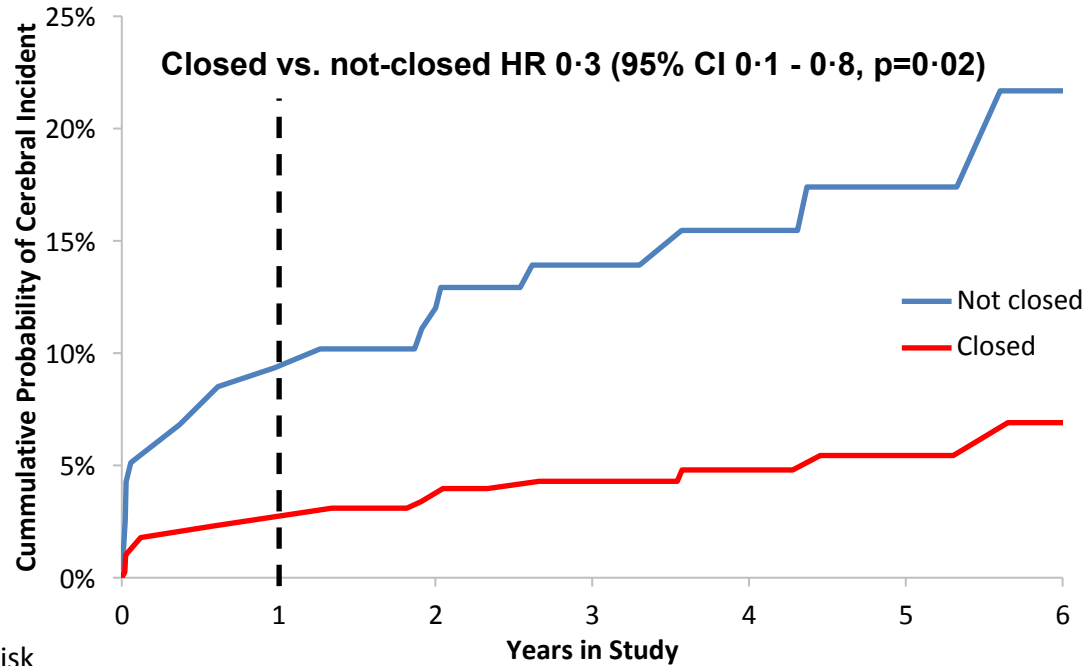
2

Stroke only

Breakdown of events

Type of Event	Open LAA (n= 86)	Closed LAA (n=101)
Ischemic Stroke	N=6 (7%)	N=2 (2%)
TIA	N=2 (2.3%)	N=1 (1%)
Clinical SCI	N=4 (4.7%)	N=1 (1%)
SCI study-MRI	N=2 (2.3%)	N=1 (1%)
Death	N=12 (14%)	N=12 (12%)

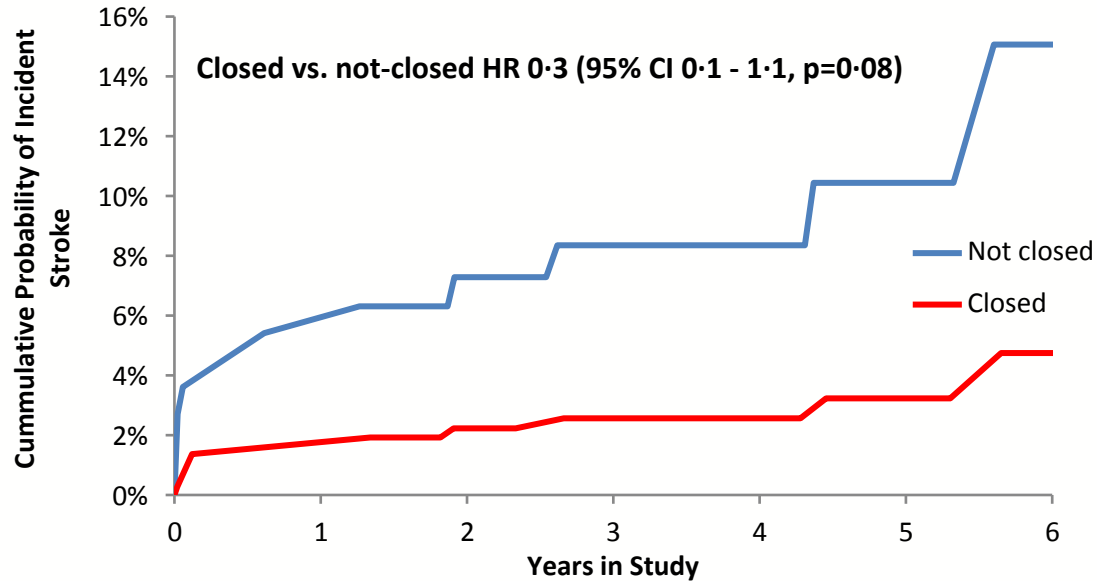
Cumulative incidence



N at risk

Closed	86	77	66	44	30	16	6
Not Closed	101	91	84	59	39	21	6

Stroke/TIA only



No. at risk							
Not closed	80	74	63	43	30	16	6
Closed	99	91	84	59	39	21	6

Conclusion

Left atrial appendage closure on occasion to open heart surgery seems to protect against cerebral ischemic events in the years following surgery.

Acknowledgements – The LAACS team

My supervisor:

Helena Domínguez



Imaging Team:

Gina Al-Farra

Jakob Møller

Robert Riis

Bodil Damgaard

Egill Rostrup

Cardiologists:

Brian Nilsson

Anders M. Greve

Jesper Hastrup Svendsen

Ulrik Dixen

Nadia Lander Landex

Heart Surgeons:

Susanne Holme

Akhmadjon Irmukhamedov

Christian Carranza

Anesthesia:

Christian Hagdrup

Neurologists:

Christina Rostrup Kruuse

Thomas Truelsen

Medicine students:

Anne Nørskov

Johan Clausen

Lubna Sabah

Qing Ling

Anne Sofie Madsen

Mads Svane Liljequist

Mie Jonsson

Supplementary slides

LAACS study - Denmark

Cross-over

We were concerned with potential cross-over.

Either too many randomized to LAA closure that did not undergo the procedure or the opposite. This could be due to communication of randomization or deliberate protocol violation (not wishing to perform LAACS procedure or convincement of LAACS benefit)

Therefore:

Closure of the LAA was continuously monitored.

If there was a difference between actually performed and allocation of 4, the next block (n 16) was randomized 3:1 to compensate for inequality.

This occurred once in the course of the study
(with an overweight of patients randomized to
LAACS who did not undergo closure)

Medicine

Medicine	Not Closed	Closed	P-Value
ASA - n (%)	69 (80.2)	75 (74.3)	0.32
Clopidogrel - n (%)	14 (16.3)	19 (18.8)	0.63
OAC			
VKA - n (%)	26 (30.2)	36 (35.6)	0.44
NOAC - n (%)	2 (2.2)	2 (2.0)	1.00
Beta-blocker - n (%)	47 (54.7)	61 (60.4)	0.47
Verapamil - n (%)	4 (4.5)	2 (2.0)	0.42
Calcium-blocker - n (%)	19 (21.3)	34 (33.7)	0.08
Digoxin - n (%)	5 (5.6)	3 (3.0)	0.47
Renin-angiotensin system blocker - n (%)	40 (46.5)	54 (53.5)	0.37
Amiodarone - n (%)	23 (26.7)	18 (17.8)	0.17
Statin - n (%)	74 (86.0)	81 (80.2)	0.38

Supplemental results

- There were no adverse events associated with the procedure.
- In the group with open LAACS according to the protocol, 9 (64%) of the 14 primary events occurred beyond the first year of follow-up
- Tests of interaction revealed no dependency of the preventative effect of LAACS on baseline AF status, CHA₂DS₂-VASc score or use of OAC (p=0.55, p=0.56 and p=0.49 for interaction, respectively).

Study limitations

-It was only possible to perform full sets of MRI scans in 75 patients – Possible selection bias. However the signal from MRI was weak. 2 vs 1.

-The TEE sample size of 10 patients was relatively small, since many patients turned down an additional TEE. However; 10/10 was complete. (mean 524 days)