CLOSURE-AF
DZHK TRIAL 16

Studie CLOSURE AF

Petr Peichl, Klinika kardiologie IKEM

INSTITUT KLINICKÉ A EXPERIMENTÁLNÍ MEDICÍNY
KLINIKA KARDIOLOGIE
IKEM

STUDY HYPOTHESIS: CLOSURE-AF

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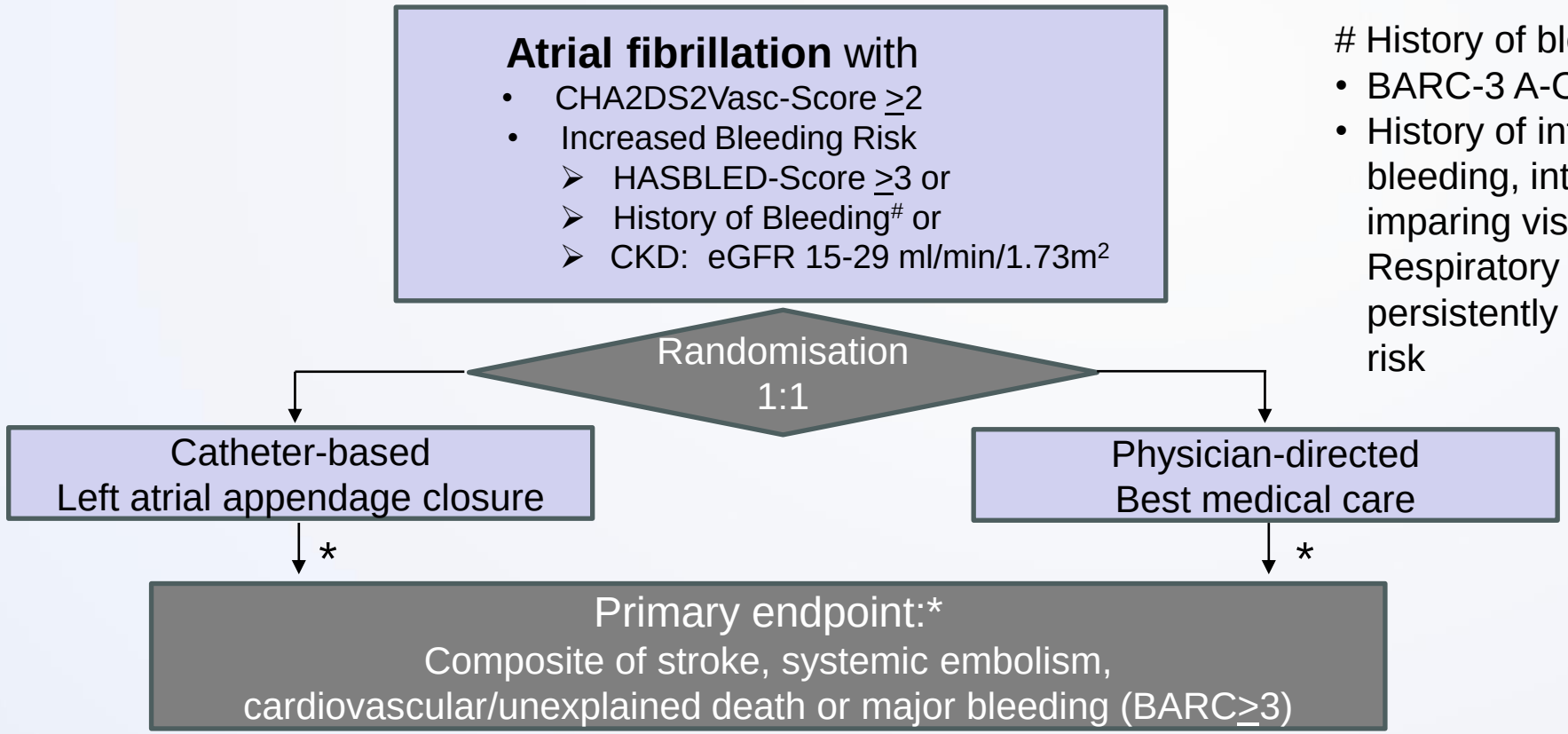
- **Catheter-based left atrial appendage closure is a potential alternative to oral anticoagulation for stroke prevention in patients with atrial fibrillation.**
- **Current guideline recommendations in patients with atrial fibrillation and high risk of stroke and high risk of major bleeding on OAK from AHA/ACC/ACCP/HRS are 2b B and from ESC IIb C.**
- **CLOSURE-AF was designed to compare catheter-based left atrial appendage closure and physician-directed best medical care (including DOAC treatment when eligible) in patients with atrial fibrillation with high risk of stroke and bleeding for a primary endpoint (tested for non-inferiority) of time to a composite of:**
  - **Stroke (ischemic or hemorrhagic)**
  - **Systemic embolism**
  - **Cardiovascular/unexplained death**
  - **Major bleeding (BARC ≥ 3)**

Study design: CLOSURE –AF 888pts



History of bleeding:
- BARC-3 A-C or
- History of intracranial/intraspinal bleeding, intraocular bleeding imparing vision, or GI, GU or Respiratory Tract bleeding with persistently increased bleeding risk

*At least 18 months and 6 months follow up after 1th and 2nd interim analysis, respectively.

Landmesser U et al.; *Am Heart J* 2025

Patient characteristics: CLOSURE-AF

Characteristic	Left atrial appendage closure (N=446)	Physician-directed Best medical care (N=442)	Total (N=888)
Age (IQR)– yr	**79.5** (74.6, 83.0)	**78.4** (72.8, 82.6)	**79.1** (73.9, 82.8)
Female – no./total no. (%)	**172**/446 (38.6)	**171**/442 (38.7)	**343**/888 (38.6)
Race/ethnic group – no./total no. (%)			
Caucasian	415/446 (93.0)	416/442 (94.1)	831/888 (93.6)
Black	2/446 (0.4)	1/442 (0.2)	3/888 (0.3)
Not disclosed	29/446 (6.5)	25/442 (5.7)	54/888 (6.1)
CHA2DS2-VASc-Score	**5.2 ± 1.5**	**5.1 ± 1.6**	**5.2 ± 1.5**
HAS-BLED score	**3.1 ± 0.9**	**3.0 ± 0.9**	**3.0 ± 0.9**
Diabetes – no./total no. (%)	**175**/446 (39.2)	**186**/442 (42.1)	**361**/888 (40.7)
Hypertension – no./total no. (%)	**417**/446 (93.5)	**417**/442 (94.3)	**834**/888 (93.9)
Dyslipidemia – no./total no. (%)	**269**/433 (62.1)	**241**/422 (57.1)	**510**/855 (59.6)
Smoking – no./total no. (%)	**30**/415 (7.2)	**50**/411 (12.2)	**80**/826 (9.7)
Stage IV chronic kidney disease	**114** (25.6)	**100** (22.6)	**214** (24.1)

Landmesser U et al.; *Am Heart J* 2025

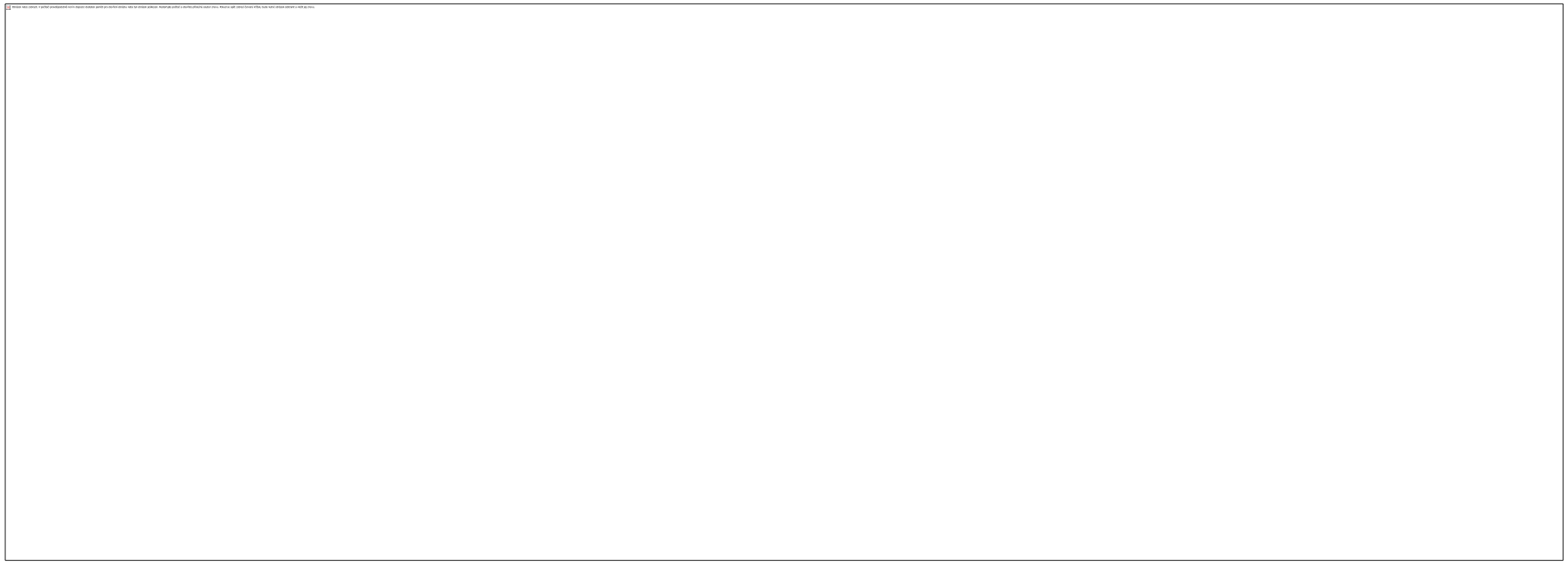
STUDY DESIGN: CLOSURE-AF

- **Recommendations for antithrombotic treatment in both study groups**

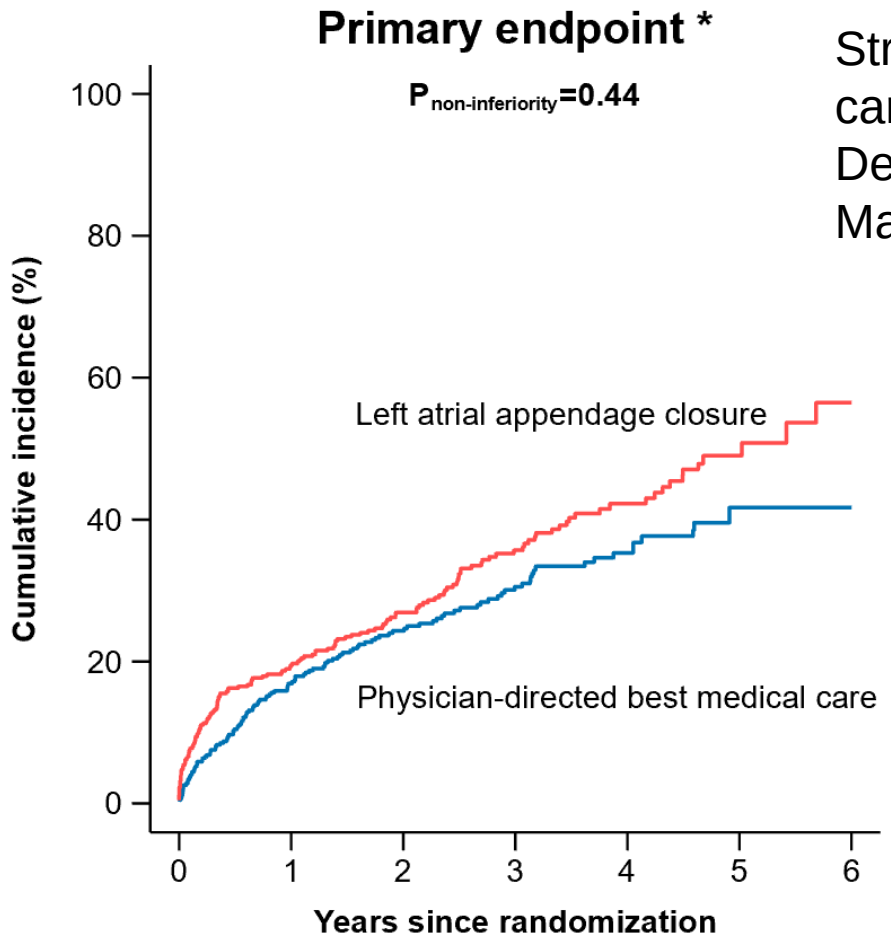
Catheter-based Left atrial appendage closure	Physician-directed Best medical care
Patient with high bleeding risk ➢ **Consider 3 months DAPT, then Aspirin only to be continued > 6 month when there is another clear indication** **Patients with excessive bleeding risk** ➢ **Consider minimum of 6 weeks DAPT or Aspirin monotherapy up to 3 months**	**Anticoagulation by DOAC should be considered if patient is eligible.**

Landmesser U et al.; *Am Heart J* 2025

Antithrombotic treatment in the study groups

Left atrial appendage closure	Physician-directed Best medical care
	

Primary outcome (ITT): CLOSURE AF



Stroke, Systemic Embolism, cardiovascular/unexplained Death, Or
Major bleeding (BARC≥3)

Patients at risk

Physician-directed best medical care	442	306	203	136	77	40	7
Left atrial appendage closure	446	304	202	117	71	33	9

*Noninferiority margin of 1.3

SECONDARY OUTCOMES: CLOSURE-AF

Outcome	Left Atrial Appendage Closure (N=446) Events/patient-years (Incidence per 100 patient-years)	Physician-directed Best Medical Care (N=442) Events/patient-years (Incidence per 100 patient-years)	Adjusted hazard ratio (95% CI)
Systemic embolism	**3**/1042.7 (0.29)	**1**/1045.4 (0.10)	2.99 (0.31, 28.79)
Stroke including ischemic or hemorrhagic stroke	**27**/1019.0 (2.65)	**27**/1015.1 (2.66)	1.02 (0.59, 1.74)
Major bleeding	**70**/941.5 (7.43)	**61**/978.7 (6.23)	1.21 (0.86, 1.71)
Cardiovascular or unexplained death	**99**/1045.2 (9.47)	**81**/1045.4 (7.75)	1.25 (0.93, 1.68)
All-cause death	**155**/1045.2 (14.83)	**141**/1045.4 (13.49)	1.12 (0.89, 1.40)

Periprocedural complications: CLOSURE AF

Peri-procedural complications at 7 days or discharge	
Pericardial tamponade	5
Major bleeding requiring transfusion (BARC 3-5)	18
Device embolization (removed surgically)	1
Procedure-related TIA	1
Peripheral embolism	1
Death within 7 days after implantation	2

STUDY SUMMARY AND CONCLUSIONS: CLOSURE-AF

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In this multicenter randomized trial, a strategy of LAAO did not achieve non-inferiority compared to physician-directed Best medical care in older patients with atrial fibrillation at high risk of stroke and bleeding.

LAAO was associated with a higher risk of the combined primary outcome of stroke, systemic embolism, major bleeding, and cardiovascular/unexplained death over a median follow-up time of 3 years in these elderly high-risk patients.

Jak interpretovat CLOSURE AF?

Parametr	CHAMPION-AF	CLOSURE-AF
Použitý okluder	Výhradně Watchman FLX	Různé typy (vč. Watchman a Amulet)
Typ populace	Mladší, vhodní pro dlouhodobou antikoagulaci	Vysoce rizikoví pacienti (vysoké riziko mrtvice i krvácení)
Hlavní výsledek	Non-inferiorní v porovnání s NOAK	Neprokázal non-inferioritu; okluze byla v této studii horší
Krvácení	Signifikantně nižší u okluderu (o 45 % méně neprocedurálního krvácení)	Bez jasné výhody oproti farmakoterapii
Mrtvice (ischemická)	Mírně vyšší počet u okluderu (3,2 % vs. 2,0 %)	Podobná jako ve skupině s BMC
Financování	Industry (výrobce Boston Scientific)	Nezávislé (vládou financovaný projekt v Německu)