

ESC Heart & Brain Workshop

Stroke prevention:

Patent foramen ovale closure

Prof. Markus Schwerzmann, University Hospital Inselspital, Bern, CH

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Further Together

Declaration of Interest

Nothing to disclose

Cryptogenic stroke¹

- Ca. 25% (10-40%) of patients with ischemic stroke have no probable cause found after standard workup (TTE, 24-hour Holter monitoring, MRI or CT of the infarct in the brain / neck and brain arteries, blood work).
- Embolic strokes of undetermined source (nonlacunar brain infarcts without substantial proximal arterial stenosis or major cardioembolic sources) represent 80 to 90% of all cryptogenic ischemic strokes.
- Occult, low-burden, paroxysmal atrial fibrillation is increasingly recognized as a source of cryptogenic stroke, especially in older patients (>60 y. of age).
- Low risk of recurrence with aspirine: 1-2% per year.

1. Saver JL. Cryptogenic Stroke. *N Engl J Med*. 2016;374:2065-74.

Cryptogenic stroke (CS) is a diagnosis of exclusion

Conventional classification:

Atherosclerotic
Small arterial occlusion
Cardioembolic
Other causes
Cryptogenic

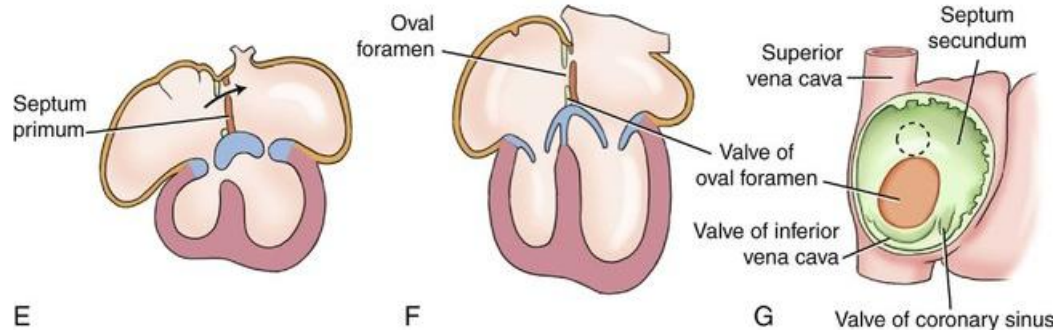
Potential etiologies of CS:

Paroxysmal atrial fibrillation
Aortic arch atheromas
Inherited thrombophilias
Patent foramen ovale



Patent foramen ovale (PFO)

- Persistent opening between the atrial septum primum and secundum at the level of the fossa ovalis
- Prevalence: 27.3%¹
- Mean size ca. 5 mm
- Larger shunt size:
 - atrial septal aneurysm
 - prominent valvula Eustachii

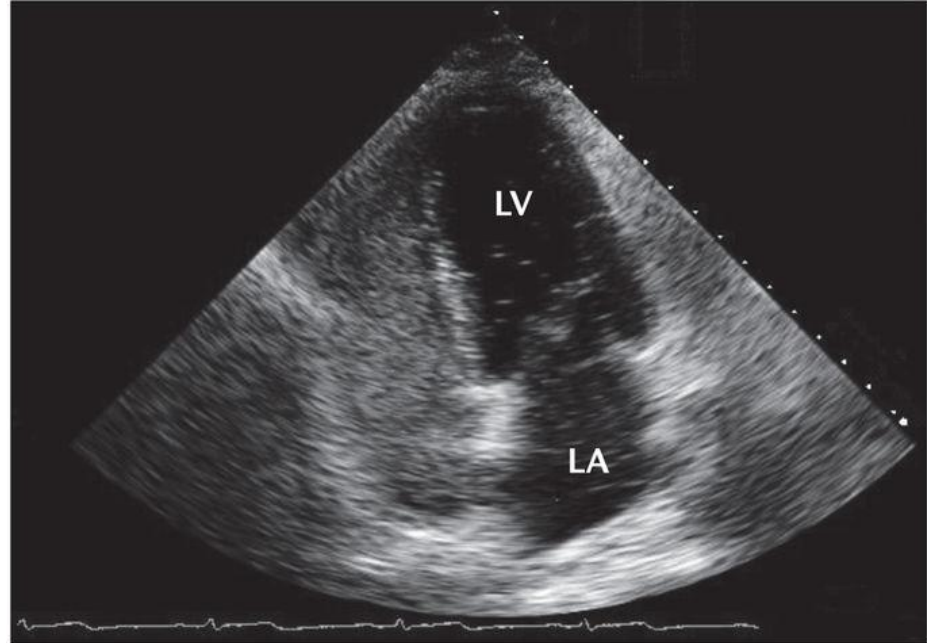


1. Hagen PT, et al. Incidence and Size of Patent Foramen Ovale During the First 10 Decades of Life: An Autopsy Study of 965 Normal Hearts. *Mayo Clinic Proceedings*. 1984;59:17-20.

PFO and stroke

NEJM 1988¹

- 60 adults < 55 years with ischemic stroke and normal cardiac exam
- PFO prevalence
 - controls: 10%
 - stroke with identif. cause: 21%
 - stroke with risk factor: 40%
 - stroke without identif. cause: 54%



1. Lechat P, et al. Prevalence of patent foramen ovale in patients with stroke. *N Engl J Med.* 1988;318:1148-52.

PFO closure and stroke: 1992-2016

Circulation 1992¹

- Case series of 36 patients with presumed paradoxical embolism (strokes, TIAs, systemic arterial emboli, brain abscesses)
- Transcatheter closure can be accomplished with little morbidity

Clinical trials

- **CLOSURE:** N Engl J Med. 2012;366:991-9
- **PC:** N Engl J Med. 2013;368:1083-91
- **RESPECT:** N Engl J Med. 2013;368:1092-10

None of the trials showed superiority of PFO closure vs. medical therapy in the prevention of recurrent vascular events.

1. Bridges ND, et al. Transcatheter closure of patent foramen ovale after presumed paradoxical embolism. *Circulation*. 1992;86:1902-1908.

PFO and stroke

RoPE score 2013¹

- Age, cortical infarct, nonsmoker, first event, no diabetes nor hypertension
- Score 10: 29 y. old with cortical infarction and no CV risk factor
- Score 0: 70 y. old smoker with hypertension, diabetes, prior stroke and no cortical infraction

ROPE Score	PFO %	Attrib. Risk	Recurr. Rate @2y
0-3	23	0	20 (12-28)
4	35	38	12 (6-18)
6	47	62	8 (4-12)
8	67	84	6 (2-10)
9-10	73	88	2 (0-4)

1. Kent DM, et al. An index to identify stroke-related vs incidental patent foramen ovale in cryptogenic stroke. *Neurology*. 2013;81:619-25

PFO and stroke – what have learned so far

- Paradoxical embolism can lead to stroke but is usually a diagnosis of presumption
- There are „incidental“ PFOs and there are „dangerous“ PFOs
- 2014 AHA stroke prevention guidelines: For patients with a cryptogenic ischemic stroke or TIA and a PFO without evidence for DVT, available data do not support a benefit for PFO closure (Class III; Level of Evidence A).
- Study design matters: identification of „dangerous“ PFOs, length of f/u, not all devices are performing equally well

PFO closure and stroke – a new era begins (2017)

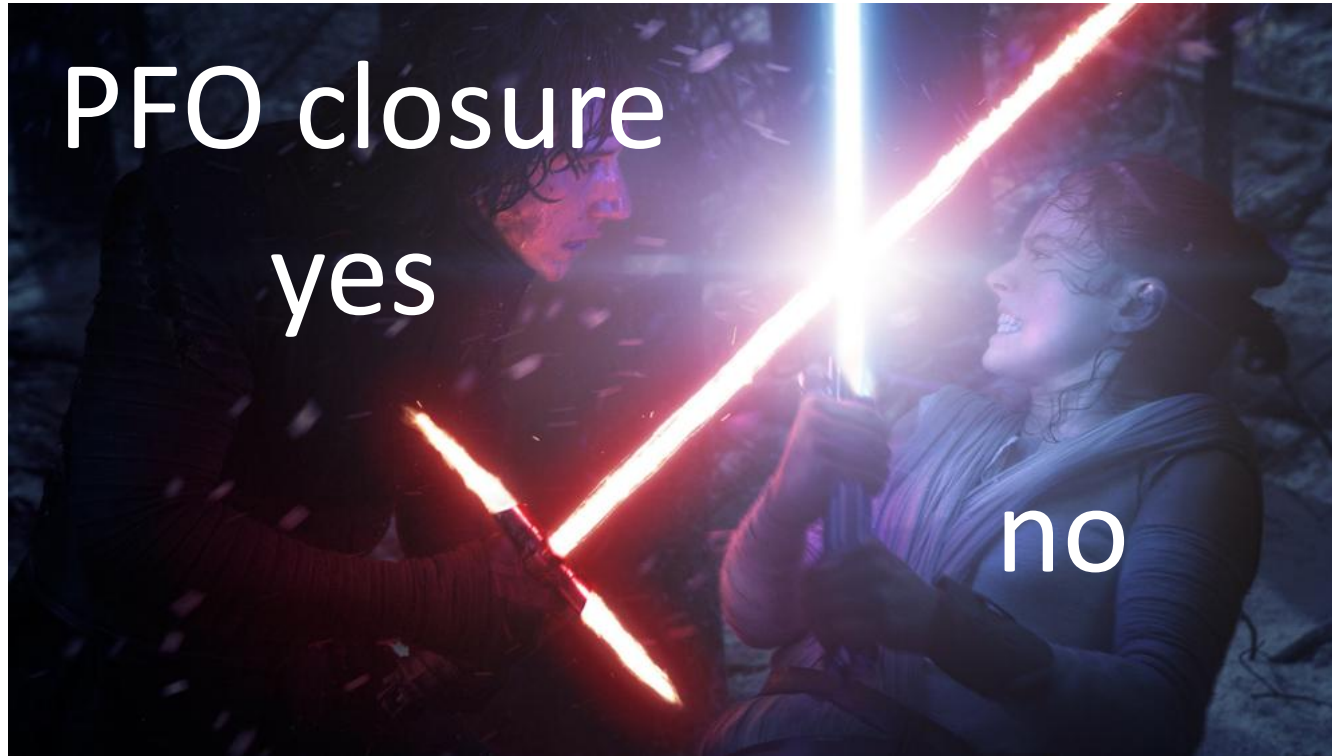


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	RESPECT ext. f/u (n=980; 46 y.)	CLOSE (n=664; 43y.)	REDUCE (n=664; 45 y.)
Design	<ul style="list-style-type: none"> • Event driven • 1:1 rand. • Device vs. medical therapy 	<ul style="list-style-type: none"> • 900 pts. • 1:1:1 • Antiplatelet vs. OAC vs. device 	<ul style="list-style-type: none"> • N=664 • 2:1 • Device + ASA vs. antiplatelet
Follow-up	<ul style="list-style-type: none"> • 5.9 y (IQR 4.2-8y) 	<ul style="list-style-type: none"> • 5 +/- 2 y. 	<ul style="list-style-type: none"> • 3.2 y (IQR 2.2-4.8)
Primary endpoint	<ul style="list-style-type: none"> • Stroke • All-cause mortality 	<ul style="list-style-type: none"> • Stroke 	<ul style="list-style-type: none"> • Stroke • Brain infraction
Device	<ul style="list-style-type: none"> • Amplatzer • ASA for 6 mo. 	<ul style="list-style-type: none"> • 11 diff. devices 	<ul style="list-style-type: none"> • HELEX or GSO • Plus antiplat. tx.
Inclusion criteria	<ul style="list-style-type: none"> • 18-60 y. of age • CS* (270 days prior) 	<ul style="list-style-type: none"> • 16-60 y. of age • CS* (6 months prior) 	<ul style="list-style-type: none"> • 18-59 • CS* (180 days prior)
Outcome	<ul style="list-style-type: none"> • Closure superior • HR 0.55 (0.31-0.999) 	<ul style="list-style-type: none"> • Closure superior to antiplatelet • HR 0.04 (0-0.27) 	<ul style="list-style-type: none"> • Closure superior (stroke prevention) • HR 0.23 (0.09-0.62)

CS* cryptogenic stroke

PFO and stroke – Assessing the evidence for closure

- „A PFO and a sizable interatrial shunt should no longer result in the categorization of a stroke as cryptogenic.“¹
- PFO closure patients < 60 y. of age and “cryptogenic stroke” are 30-50% less likely to have a stroke recurrence than patients with antiplatelet therapies (NNT ca. 20-40 for 1 stroke over 5 years).²
- Device-related complications: 2-3%;
Atrial fibrillation after device implantation: 6%

1. Ropper AH. Tipping Point for Patent Foramen Ovale Closure. *N Engl J Med*. 2017;377:1093-1095.

2. Farb A, et al. Patent Foramen Ovale after Cryptogenic Stroke - Assessing the Evidence for Closure. *N Engl J Med*. 2017;377:1006-1009

Suggested algorithm for CS and PFO

