PFO Closure for Stroke Prevention and Migraine Treatment

Bernhard Meier, MD

Conflicts of interest: Research grants and speaker fees from AGA Swiss Cardiovascular Center Bern University Hospital Bern, Switzerland Within the past 12 months, Bernhard Meier has had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship
Grant/Research Support

Company AGA

Disclosure Statement of Financial Interest

History of Interventional Cardiology 1953 Rubio-Alvarez Pulmonary wire valvuloplasty 1966 Rashkind Atrial septostomy PDA closure 1966 Porstmann 1974 King/Mills ASD closure 1975 Gianturco Coil occlusion of shunt 1977 Grüntzig PTCA (coronary angioplasty) Pulmonary balloon valvuloplasty (newborns) 1979 Semb Re-coarctation angioplasty 1981 Singer Pulmonary balloon valvuloplasty 1982 Kan 1982 Gallagher His bundle ablation 1983 Lababidi Aortic balloon valvuloplasty Mitral balloon valvuloplasty 1984 Inoue Ablation of WPW pathway 1984 Fisher

1986 Puel

1987 Simpson

1990 Palacios

1994 Sigwart

1996 Condado

1997 Oesterle

1998 Waxman

2001 Sievert

2002 Cribier

2003 Feldman

2000 Bonhoeffer

Coronary stent implantation

Coronary atherectomy (debulking)

Transluminal ablation of septal hypertrophy

PTMR (percutaneous transmyocardial laser revascularization)

Obliteration of left atrial appendage in atrial fibrillation

Brachytherapy against coronary restenosis

Percutaneous pulmonary valve replacement

Percutaneous aortic valve replacement

Percutaneous mitral valve repair

Pericardial balloon fenestration

Transatrial pericardial access

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Nurse, 39 Years, Mother of 2 Teenage-Boys



Nurse, 39 Years, Mother of 2 Teenage-Boys permanently aphasic after stroke



MIST Serious Adverse Events

74 patients
implant group
tamponade

pericardial effusion

retroperitoneal bleed

atrial fibrillation

chest pain

73 patients sham group

incision site bleed

anemia

nose bleed

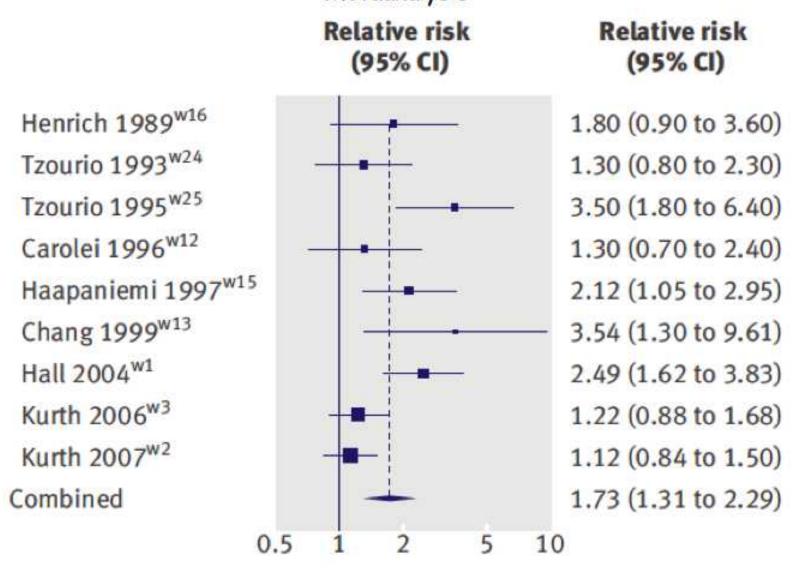
brainstem stroke

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Migraine and Stroke Metaanalysis

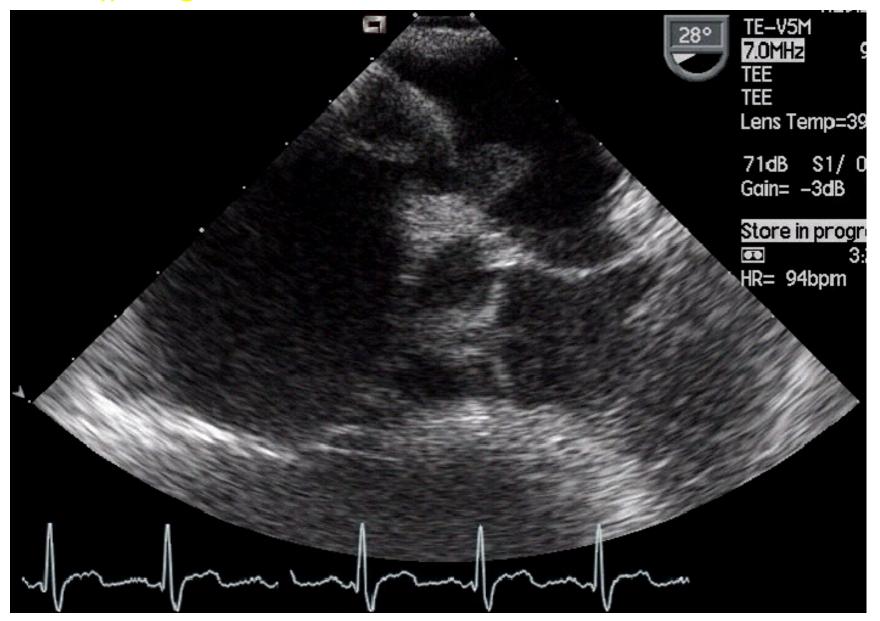


Heterogeneity: Q=22.9, df=8, P=0.004, $I^2=65\%$

Migraine and Stroke Metaanalysis Relative risk Relative risk (95% CI) (95% CI) 1.80 (0.90 to 3.60) 1.30 (0.80 to 2.30) Tzourio 1995w25 3 50 (1.80 to 6.40) Carolei 1996W12 1.30 (0.70 to 2.40) Haapaniemi 1 Chang 199 Hall 2004w1 Kurth 2006w3 .22 (0.88 to 1.68) Kurth 2007^{w2} 1.12 (0.84 to 1.50) .73 (1.31 to 2.29) Combined 5 10 0.5

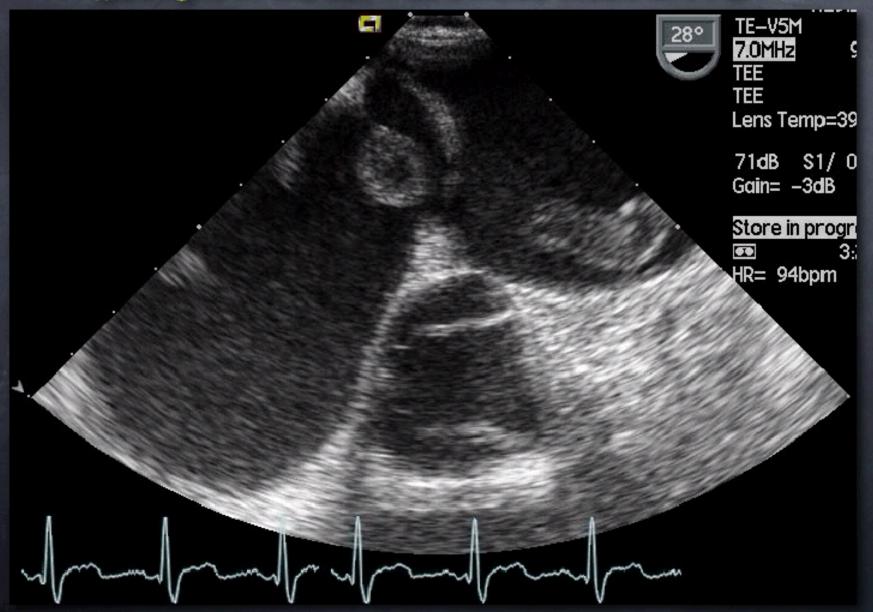
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"Caught in the act": thrombus stuck in PFO



Paradoxical Embolism (45-year-old man)

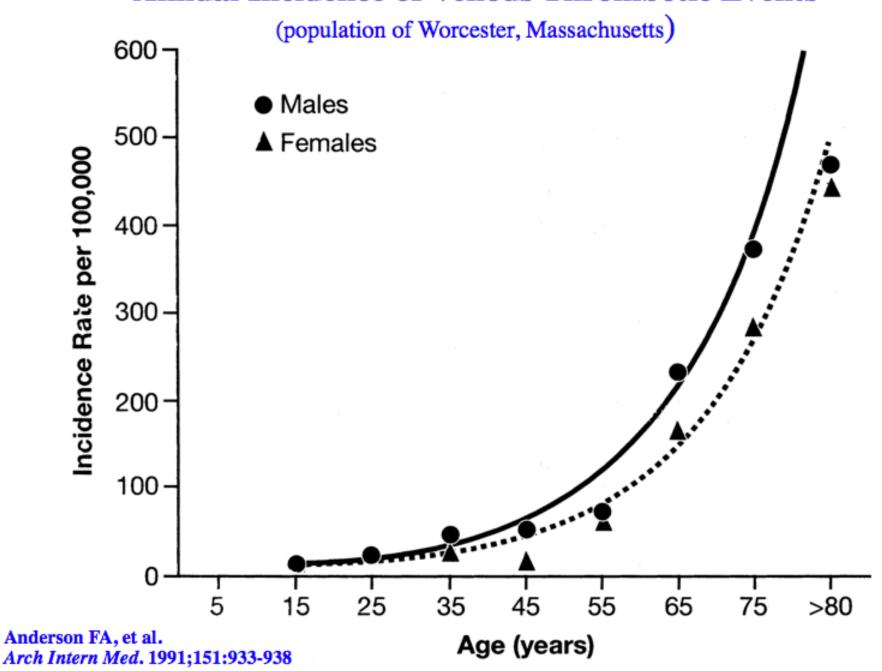
"Caught in the act": thrombus stuck in PFO



Paradoxical Embolism (45-year-old man) "Caught in the act": thrombus stuck in PFO

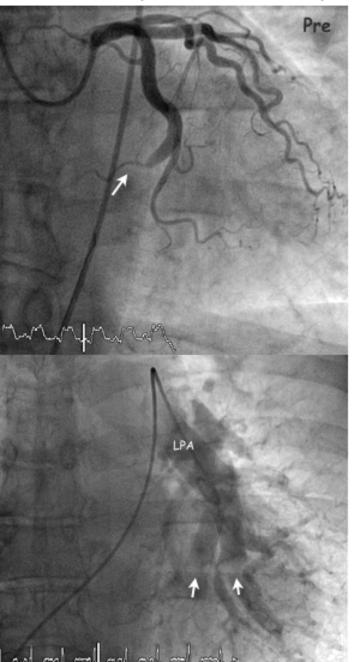


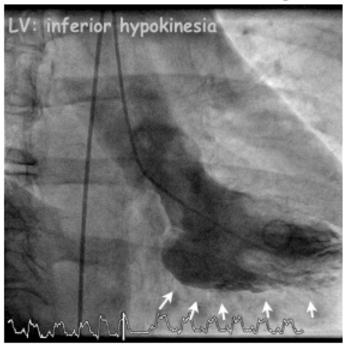
Annual Incidence of Venous Thrombotic Events



Pulmonary Embolism and Simultaneous Paradoxical Embolism to Dominant LCX with Inferior MI

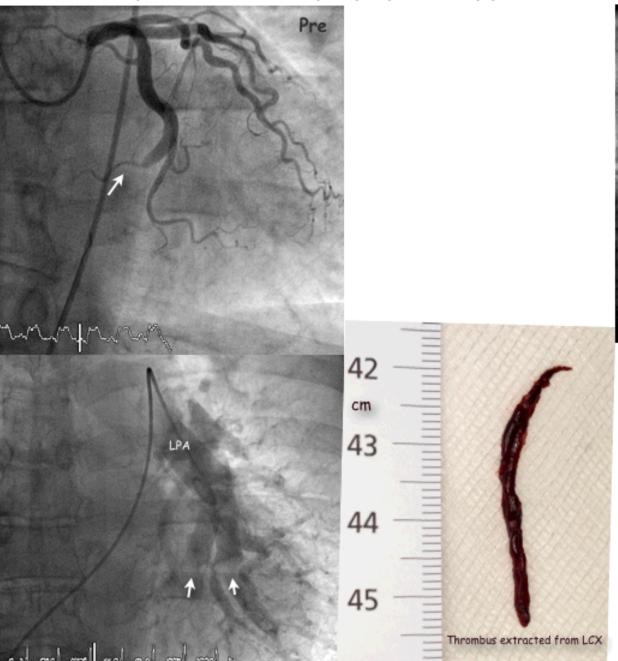
(Woman, 69 y, 8-hour train ride with pre-syncope, severe dyspnea at rest, and inferior ST-elevation the next morning)

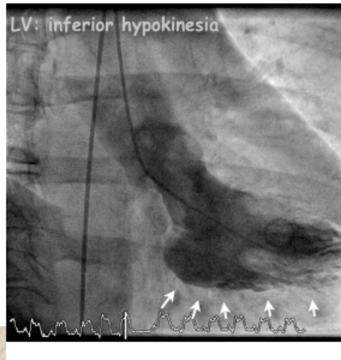




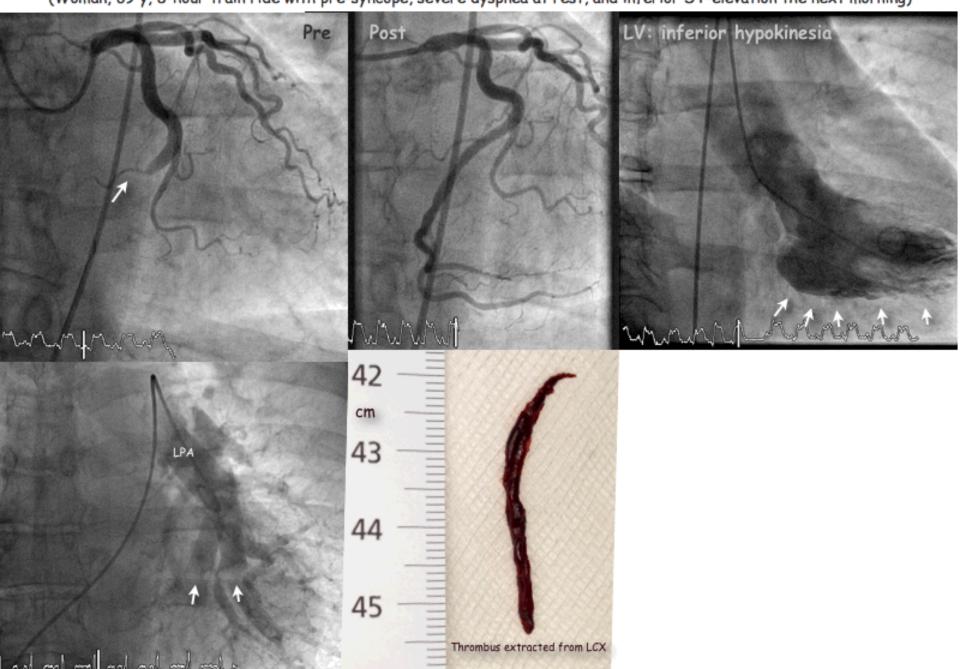
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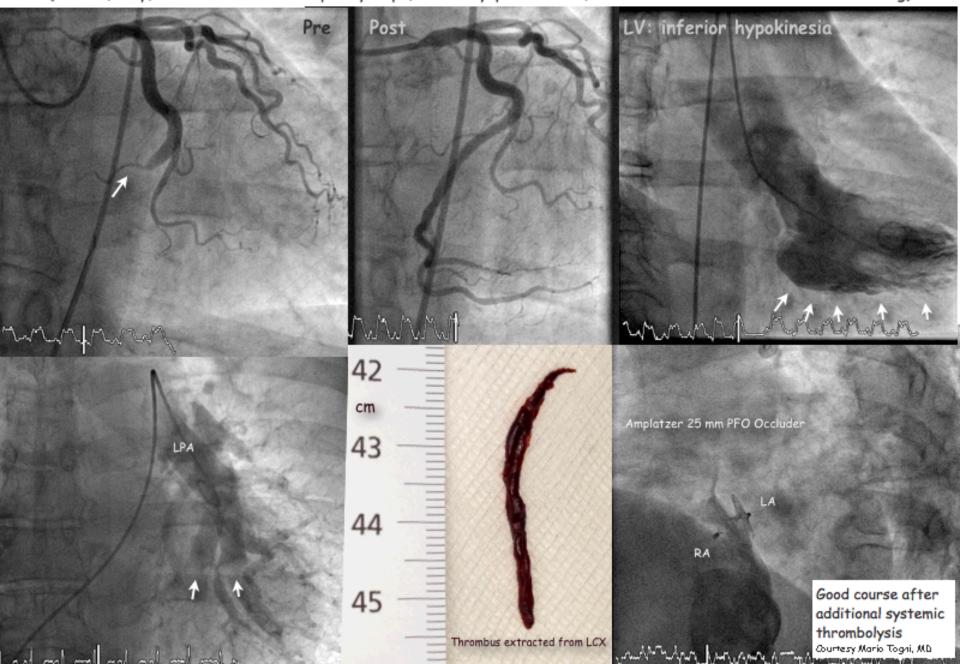
(Woman, 69 y, 8-hour train ride with pre-syncope, severe dyspnea at rest, and inferior ST-elevation the next morning) Post LV: inferior hypokinesia Pre twww42 cm Amplatzer 25 mm PFO Occluder 43 LPA 44 RA 45

Thrombus extracted from LCX

when here have a marine our promptions of

Pulmonary Embolism and Simultaneous Paradoxical Embolism to Dominant LCX with Inferior MI

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Venous

Thromboembolism (VTE)

and

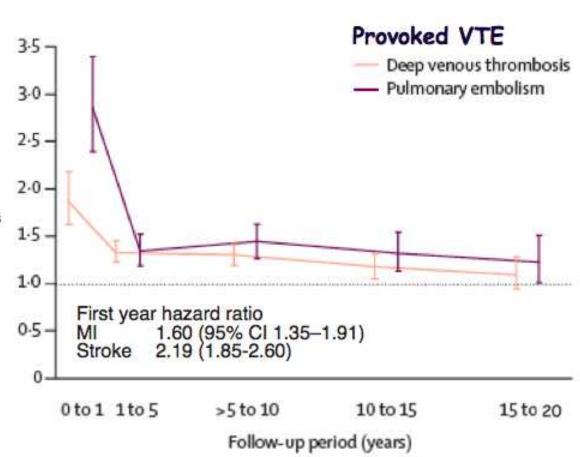
Stroke/MI

- 20-year population-based cohort study
- · Danish medical databases
- · No known cardiovascular disease
- 25 199 patients with deep venous thrombosis
- 16 925 patients with pulmonary embolism
- 163 566 population controls

Paper Sørensen HT, Lancet 2007; 370: 1773-9 (Denmark, Italy, US)

Editorial
O Lowe GD, Lancet 2007; 370: 1743-4
(Glasgow)

Relative Risk of MI or Stroke



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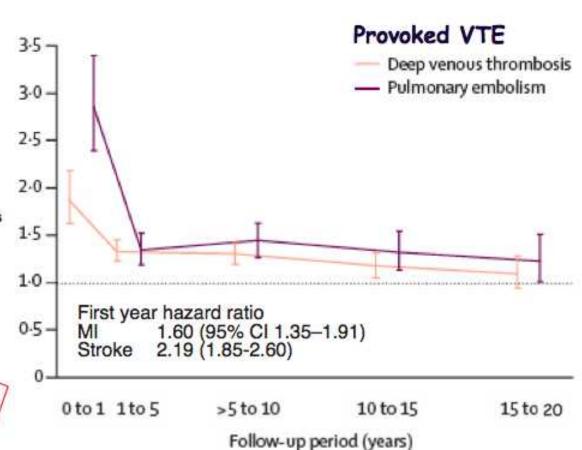
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- . 163 566 population controls

No consideration of PFO !

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Relative Risk of MI or Stroke



PFO as Predictor of Adverse Outcome in Patients With Major Pulmonary Embolism

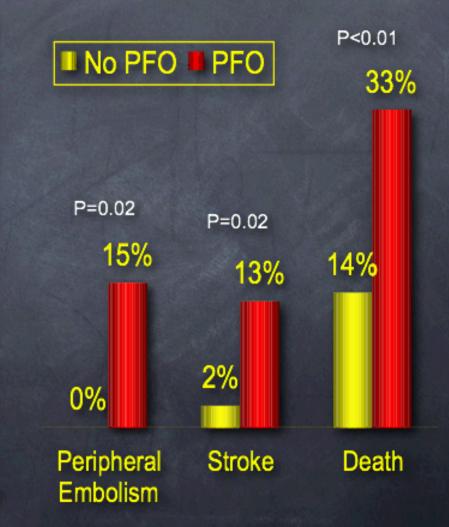
Konstantinides S et al. Circulation 1998;97:1946

- 139 patients with major pulmonary embolism undergoing TEE
 - 35% with PFO
 - 59±17 (17 89) years
- Clinical endpoints
 - death
 - cerebral embolism
 - arterial thrombo-embolism
 - major bleeding
- PFO independent predictor of mortality
- Suggested mechanism: paradoxical embolism

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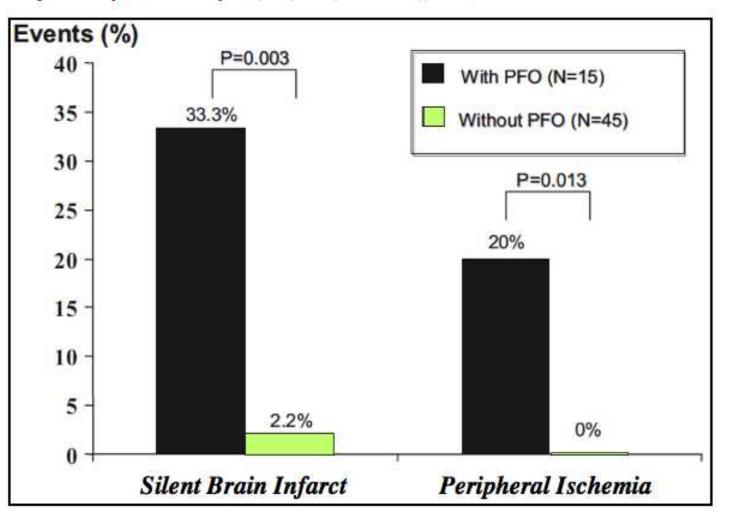


PFO: Pulmonary Embolism and Stroke

· MRI, diffusion-weighted

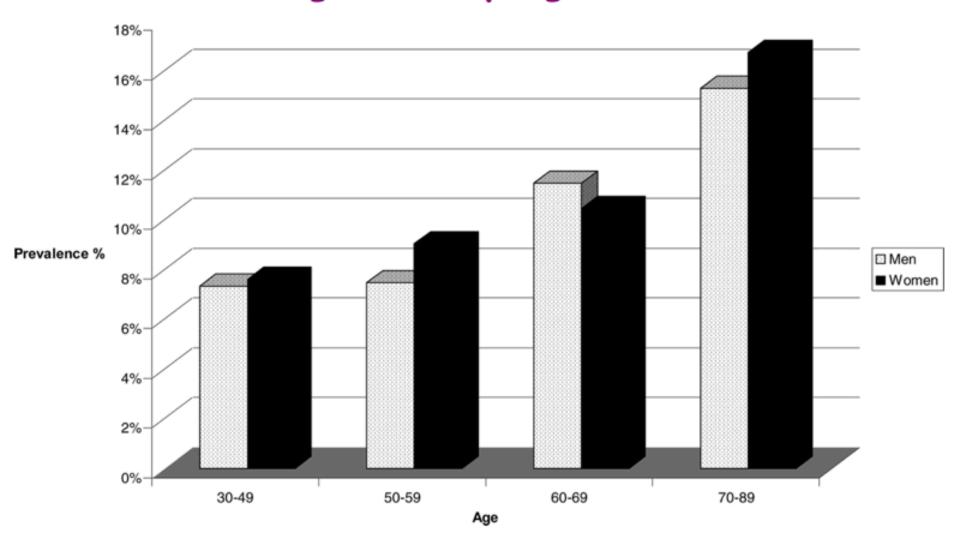
Clergeau MR, Stroke. 2009;40:3758-3762

- · 60 consecutive patients with pulmonary embolism
- · 6 with MR brain embolism
- · I with clinical signs
- PFO in 15 patients (25%)
- Silent brain infarcts 33.3% with PFO and 2.2% without PFO, P=0.003
- PFO independent predictor of silent brain infarcts, OR, 34.9 [3.1 to 394.3], P=0.004



Silent Cerebral Infarctions (by MR)

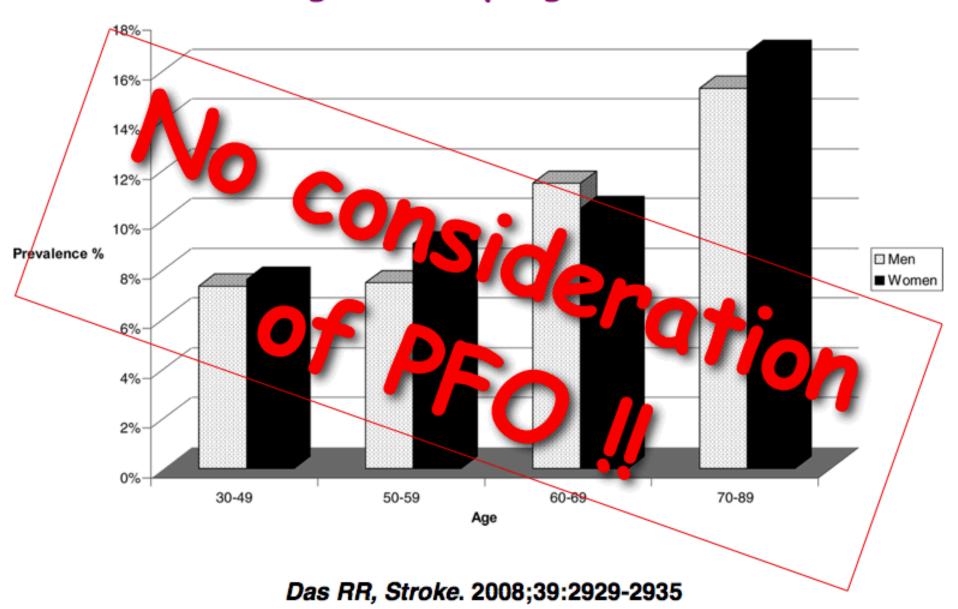
2,040 Framingham Offsprings (53% female; mean age, 62±9 years)



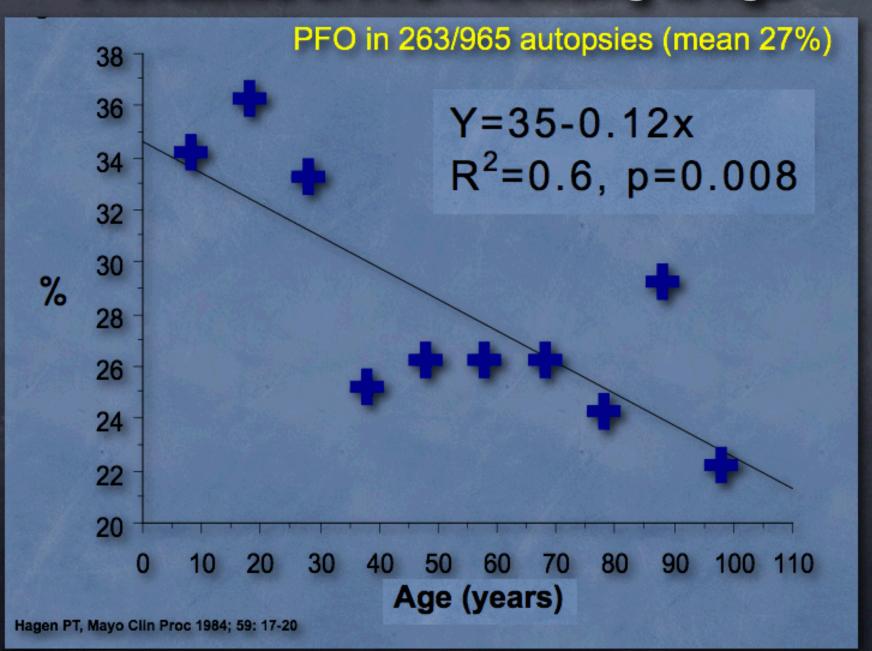
Das RR, Stroke. 2008;39:2929-2935

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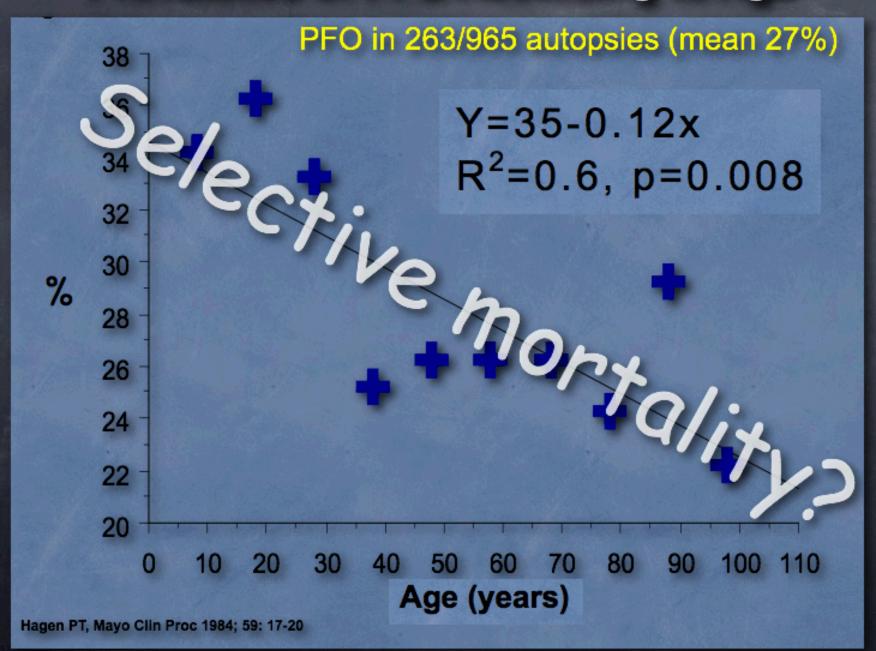
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Prevalence of PFO According to Age

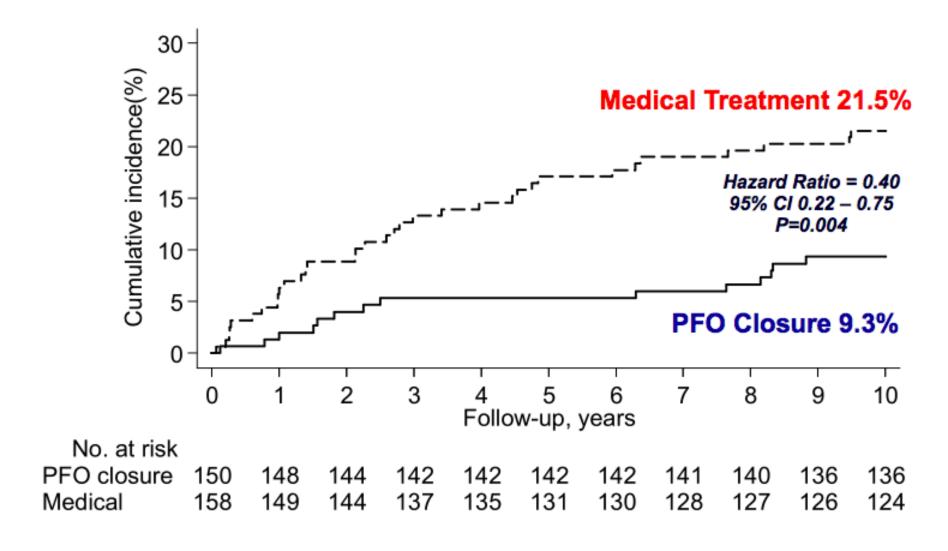


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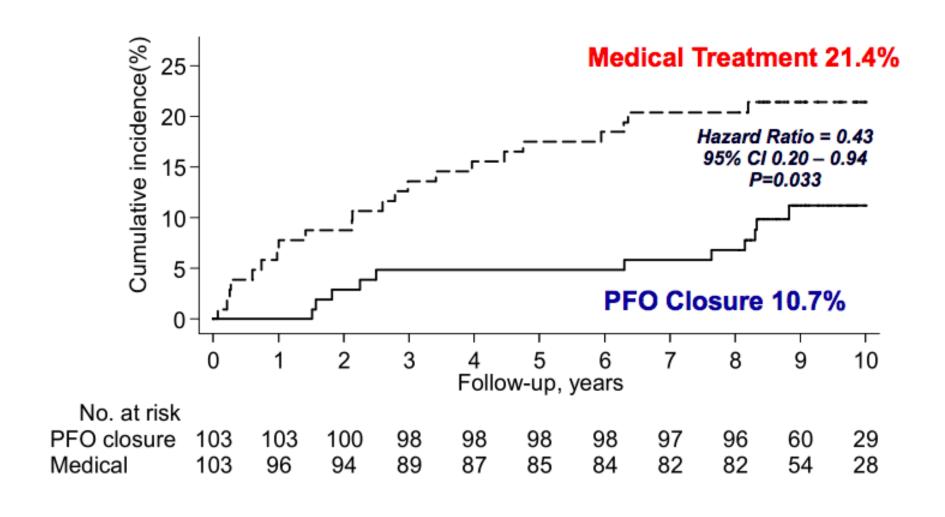
Primary Endpoint – Intention to Treat Population

Ischemic Stroke, TIA, or Peripheral Embolism at 10 Years



Primary Endpoint – Propensity Score Matched Cohort

Stroke, TIA, or Peripheral Embolism at 10 Years



(After first event with a PFO, 308 patients, 10-year follow-up)



Stroke

Death

TIA Periph. Embol. Stroke/TIA/PE Death/Stroke/TIA/PE

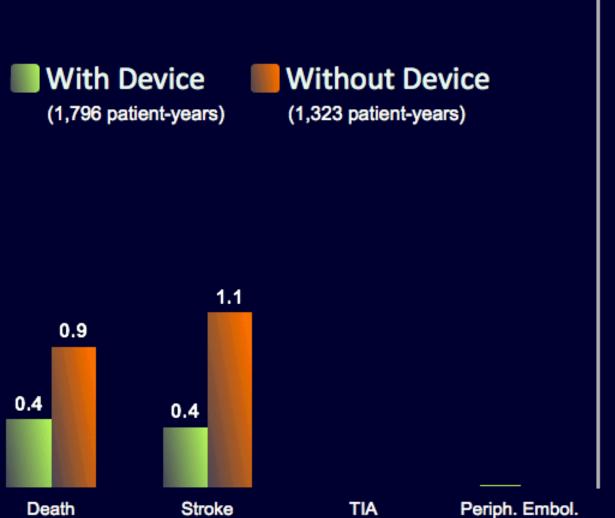
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Stroke/TIA/PE Death/Stroke/TIA/PE



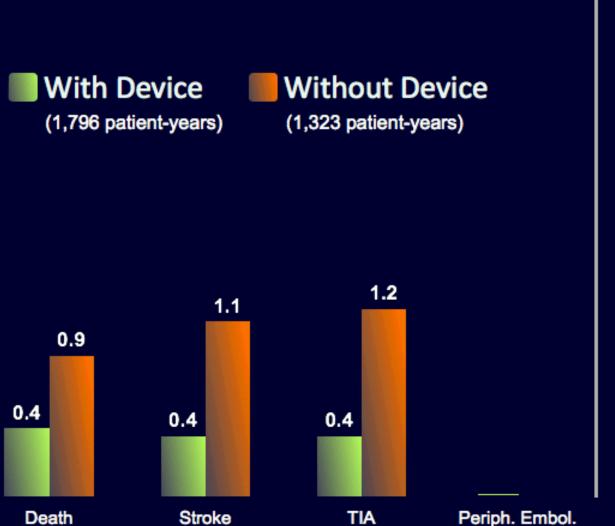


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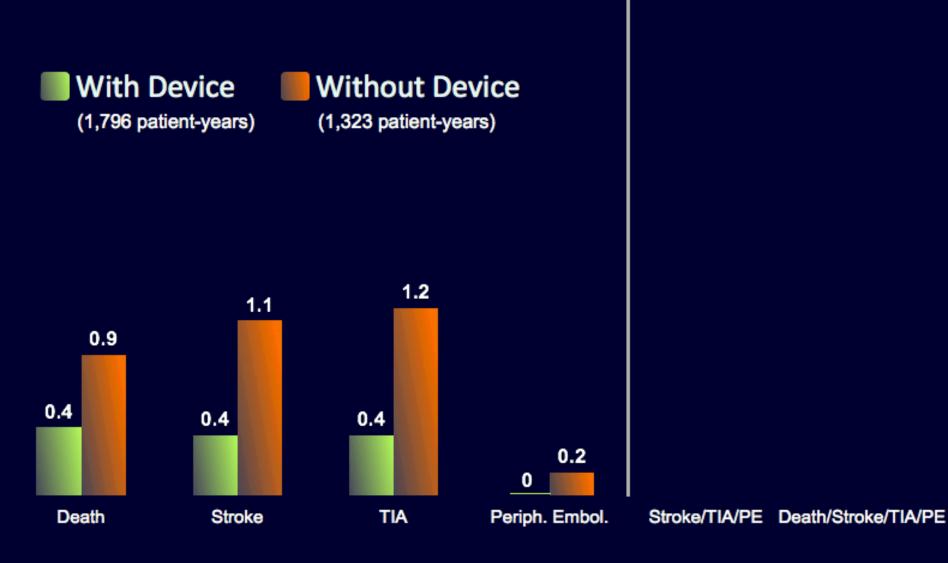
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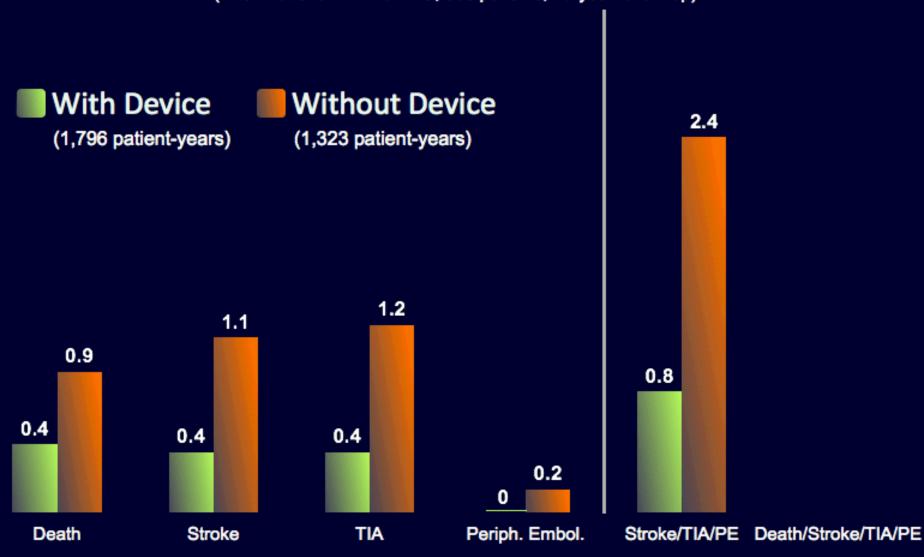


Stroke/TIA/PE Death/Stroke/TIA/PE

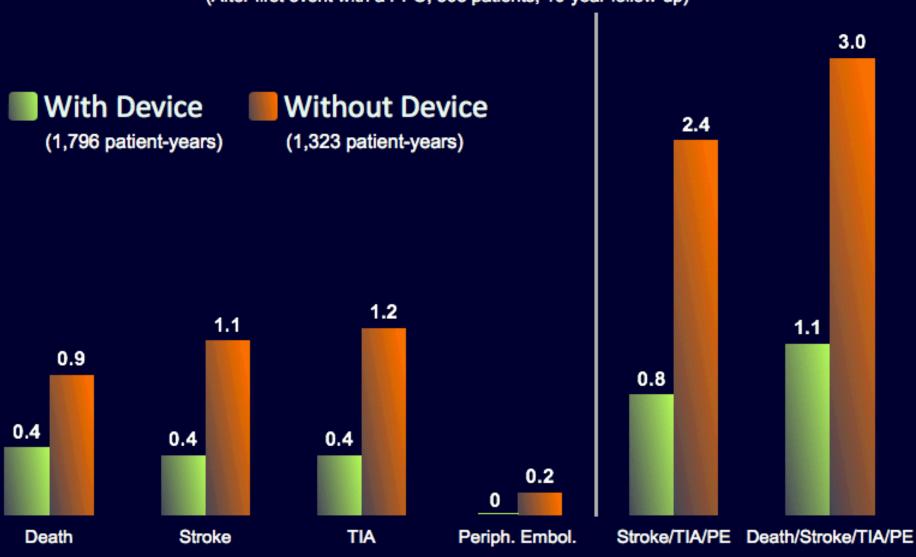
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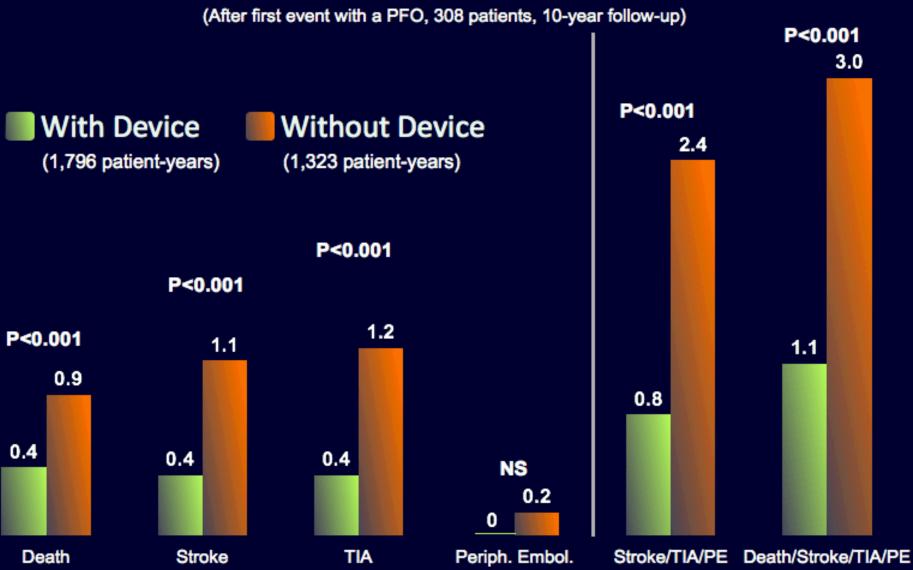


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Randomized Trials

Acronym

Place

Device

Patients

Status

*Endpoint driven; **Aspirin chronically in both groups

Randomized Trials

Acronym Place Device Patients Status

• PC global Amplatzer 410/425 FU phase

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Randomized Trials

Acronym	Place	Device	Patients	Status
• PC	global	Amplatzer	410/425	FU phase disclosed part.
• CLOSURE I	US	CardioSEAL	900/1500 (900)	

^{*}Endpoint driven; **Aspirin chronically in both groups

Randomized Trials

Acronym	Place	Device	Patients	Status
• PC	global	Amplatzer	410/425	FU phase
• CLOSURE I	US	CardioSEAL	900/1500 (900)	disclosed part.
• RESPECT	US	Amplatzer	~620/900*	recruiting

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Randomized Trials

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	US	CardioSEAL	900/1500 (900)	disclosed part.
	US	Amplatzer	~620/900*	recruiting
	global	HELEX	?/664	recruiting

^{*}Endpoint driven; **Aspirin chronically in both groups

PFO, never leave home with it!

Arterial occlusion

- lacunar
- intracerebral
- vertebral
- internal carotid
- common carotid
- brachiocephalic

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Cardiac embolus from

- left ventricle
- left atrium
 - left atrial appendage
 - left atrial foramen pouch
- myxoma or other tumor
- vegetation (septic embolus)

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- atrial septal defect
- pulmonary fistula

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Paradoxical embolus

- patent foramen ovale
- atrial septal defect
- pulmonary fistula
- Pulmonary venous bed embolus

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- Cryptogenic