



VENERDI' 1 MARZO

ICTUS CRIPTOGENETICO OLTRE I 60 ANNI. IL FORAME OVALE VA CHIUSO?

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Clinical Challenge



71 year old male (MD) MTbiker

No HTN, No DM, No Carotid disease, No hypercoagulable state, No Family history, No smoking, No CAD, No Hyperlipemia, No symptomatic palpitations, No drugs

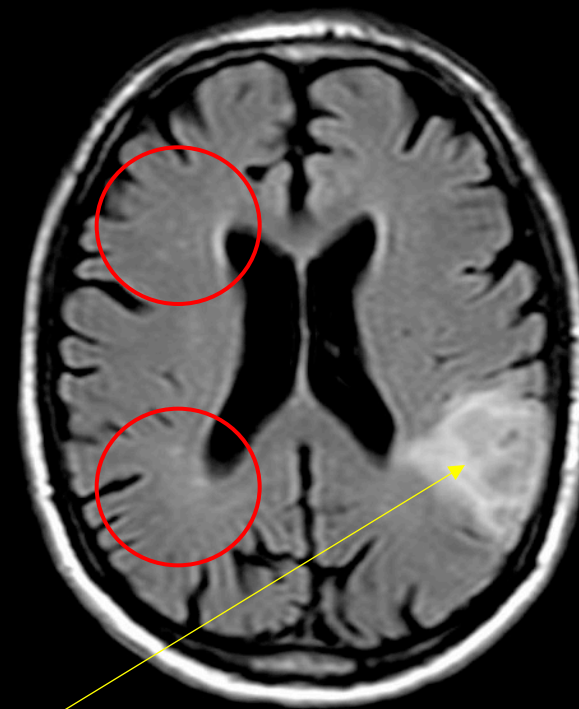
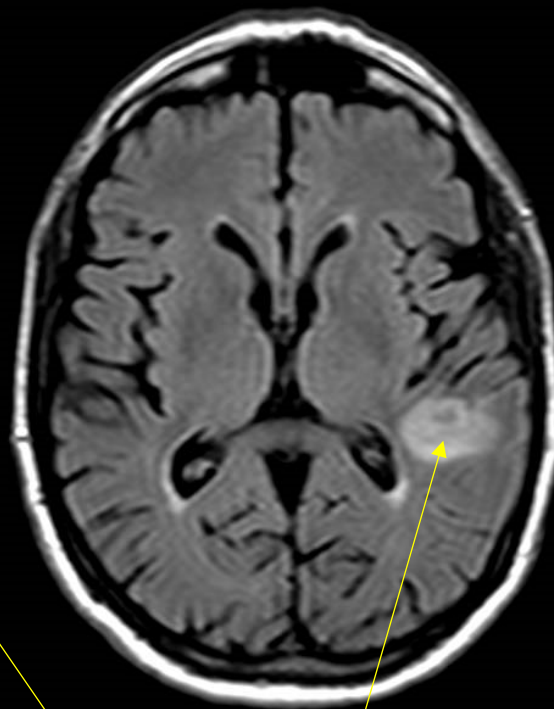
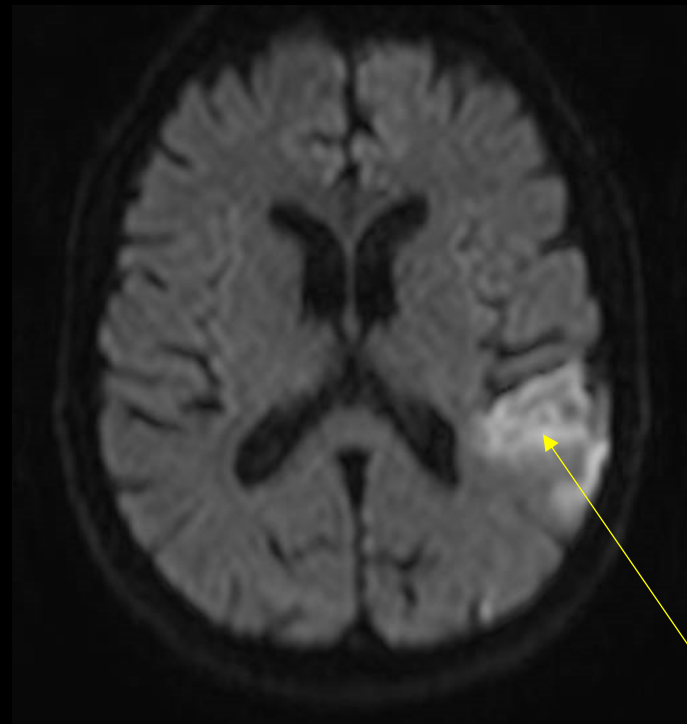
September 2018: Stroke upon awakening

..2 days after the acute event MRI

DW

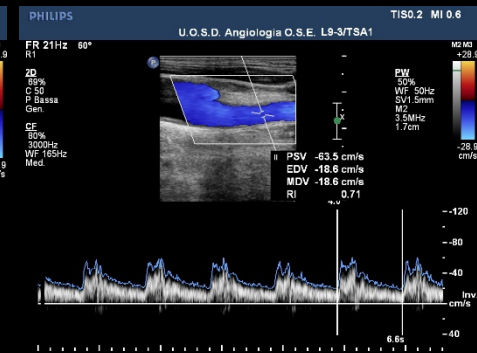
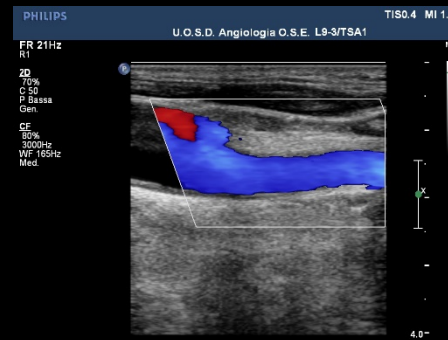
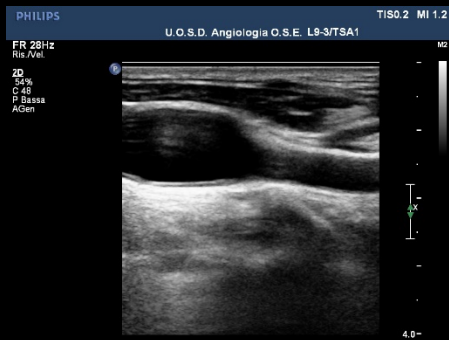
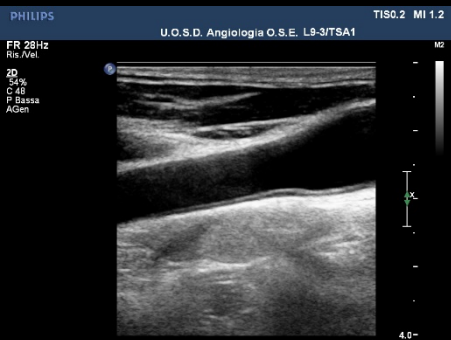
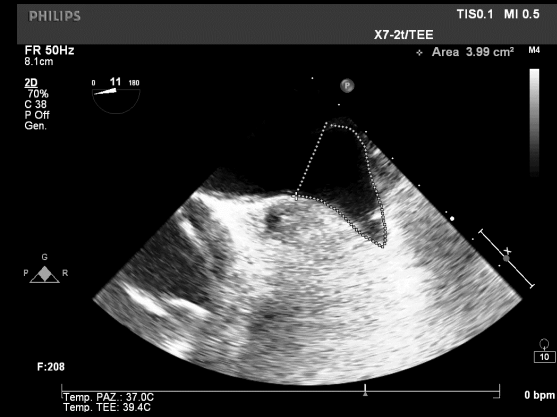
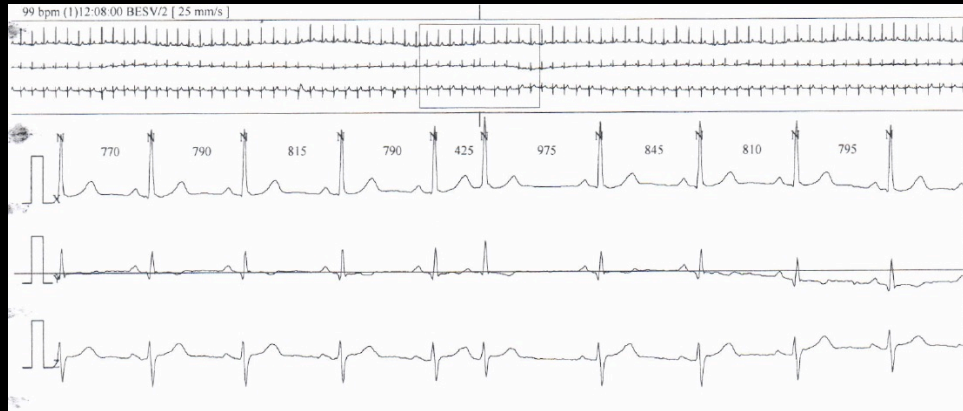
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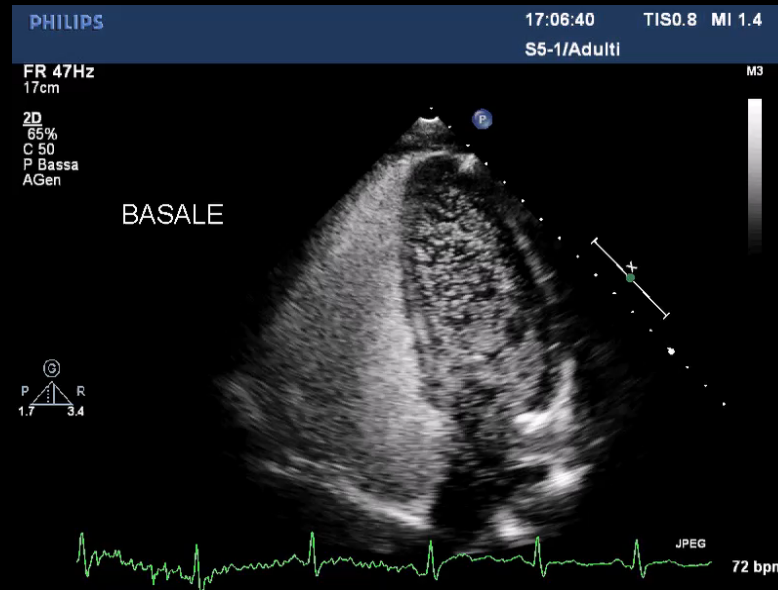


Acute lesion

Diagnostic Workup

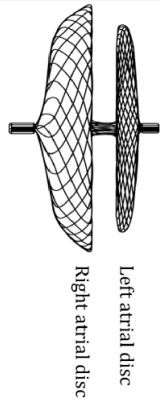


Found to have a PFO with spontaneous R-L shunt



FDA Labeling

«....indicated for percutaneous transcatheter closure of a patent foramen ovale (PFO) to reduce the risk of recurrent ischemic stroke in patients, *predominantly* between **the age of 18 and 60 years**....»

Table 1. FDA Approval of PMA Application for AMPLATZER™ PFO Occluder on October 28, 2016	
Indications and Usage	
<p>“The AMPLATZER™ PFO Occluder is indicated for percutaneous transcatheter closure of a patent foramen ovale (PFO) to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18 and 60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke.”</p>	 <p>Right atrial disc Left atrial disc</p>
<p style="text-align: center;"><u>FDA Documents</u></p> <p>Approval letter: http://www.accessdata.fda.gov/cdrh_docs/pdf12/P120021a.pdf</p> <p>Approval announcement: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm527096.htm</p> <p>Summary of safety and effectiveness data: http://www.accessdata.fda.gov/cdrh_docs/pdf12/P120021b.pdf</p>	

28 Oct 2016



The screenshot shows the FDA website's 'Medical Devices' section. The main heading is 'GORE® CARDIOFORM Septal Occluder - P050006/S060'. Below the heading are social media sharing options for Facebook, Twitter, LinkedIn, Pinterest, Email, and Print. A photograph of the device is shown below the text. The device is a white, circular, mesh-like structure with a central handle and two discs.

30 March 2018

Recommendations derived from the patient age range studied in the RESPECT and REDUCE trials



European position paper on the management of patients with patent foramen ovale. General approach and left circulation thromboembolism

Cardiovascular Interventions (EAPCI), European Stroke Organisation (ESO), European Heart Rhythm Association (EHRA), European Association for Cardiovascular Imaging (EACVI), Association for European Paediatric and Congenital Cardiology (AEPC), ESC Working group on GUCH, ESC Working group on Thrombosis, European Haematological Society (EHA), European Underwater and Baromedical Society (EUBS)

TYPE OF STATEMENT

Strong statement for the intervention

POSITION

The position of our societies is to perform percutaneous closure of a PFO in carefully selected patients aged from 18 to

STATEMENTS

65 years with a confirmed cryptogenic stroke, TIA, or systemic embolism and an estimated high probability of a causal role of the PFO as assessed by clinical, anatomical and imaging features.

An index to identify stroke-related vs incidental patent foramen ovale in cryptogenic stroke

Characteristic	Points	RoPE score
No history of hypertension	1	
No history of diabetes	1	
No history of stroke or TIA	1	
Nonsmoker	1	
Cortical infarct on imaging	1	
Age, y		
18-29	5	
30-39	4	
40-49	3	
50-59	2	
60-69	1	
≥70	0	
Total score (sum of individual points)		
Maximum score (a patient <30 y with no hypertension, no diabetes, no history of stroke or TIA, nonsmoker, and cortical infarct)		10
Minimum score (a patient ≥70 y with hypertension, diabetes, prior stroke, current smoker, and no cortical infarct)		0

The RoPE Score: 5
34% likelihood that PFO was the source of embolism

Our patient falls outside the age range of the RoPE score

Virtually no patients in this age group (>70) in the meta-analysis so validity is questionable

PFO Prevalence in Elderly

Patent Foramen Ovale and Cryptogenic Stroke in Older Patients

Michael Handke, M.D., Andreas Harloff, M.D., Manfred Olschewski, M.Sc.,
Andreas Hetzel, M.D., and Annette Geibel, M.D.

503 consecutive stroke patients (18-85 years old)
131 < 55 years old & 372 > 55 years old
227 cryptogenic stroke & 276 with identified source

PFO present	Cryptogenic	Known cause	Odds	p
<55 younger	43.9%	14.3%	4.7	<0.001
>55 older	28.3%	11.9%	2.9	<0.001

Paradoxical embolism is a cause of cryptogenic stroke in both age groups

PFO closure outside the recommended age range > 60 years old

Identifiable known embolic stroke sources exclusion

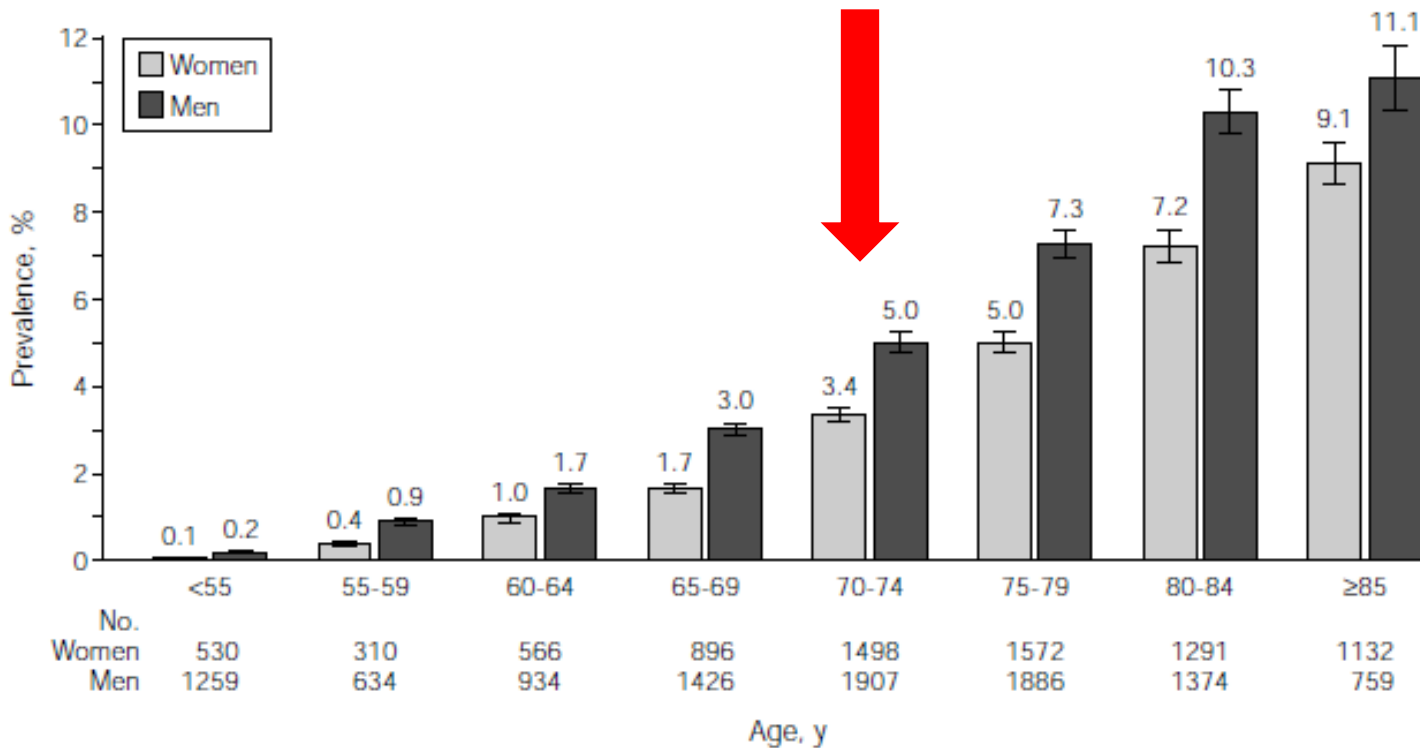
Sources	Tool(s)	Rule Out
Carotid disease	Ultrasound/CT/Angio	easy
Aortic arch atheroma	TEE ultrasound	easy
Acquired/inherited hypercoagulable state*	Blood test/History	easy
Atrial fibrillation	Holter ECG/ICM	difficult
LAA/LV thrombus	TEE/TTE ultrasound	easy
Endocarditis/Left valves disease	TEE/TTE ultrasound	easy

* Stroke patients > 60 years old have an increased prevalence of circulation prothrombotic antibodies. Anti-phospholipid antibodies, MTHRF disease, Factor V, Protein C and S, SLE, undiagnosed cancer, cancer survivors

Atrial Fibrillation

Leading stroke risk > 60

The single most important embolic source to evaluate in the older population



Atrial Fibrillation

There is uncertainty regarding the duration of arrhythmic episodes which increase the risk of embolism

According to the HRS/EHRA/ECAS

1. Episodes > 30 sec constitute clinically significant AF
2. During prolonged monitoring episodes of AF > 5 minutes have a predictive value for embolism

Our work up for Atrial Fibrillation

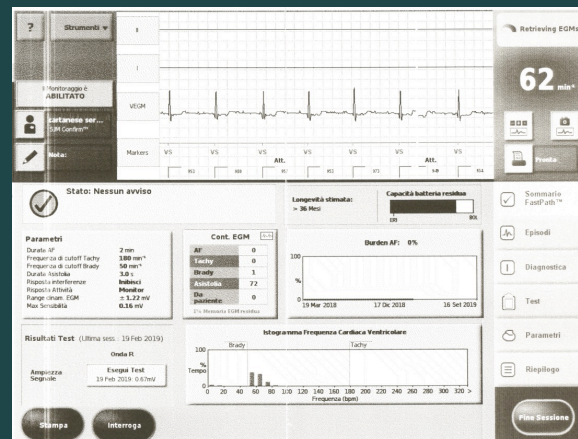
- In older patients monitoring for atrial fibrillation becomes increasingly important as patient age
- No current consensus on duration of monitoring

Age at Stroke	Type/Duration of Monitoring*
<50	24-48 Holter ECG monitoring
50-60	2 weeks external monitoring
60-70	4 weeks external monitoring or more
>70	Insertable cardiac monitoring > 3 months or more

* Depends on index suspicion: thyroid disease, dilated LA, ultrasound smoking imaging, HTN, MV disease, low LAA ejection velocities, LV dysfunction.

Priority: Rule Out Atrial Fibrillation

Insertable Cardiac Monitoring



(3 months monitoring)

So what should we do?

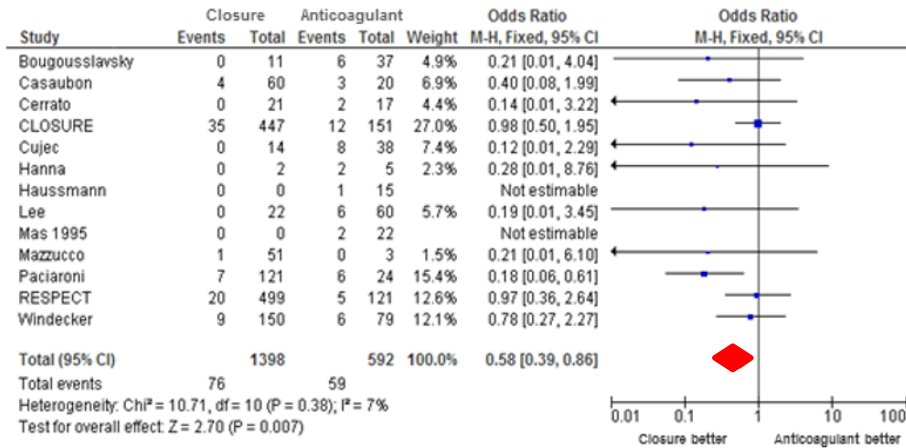


Medical therapy?

No conclusive evidence that in patients with PFO, OAC or antiplatelet/DAPT works better than PFO closure and net clinical benefit questionable

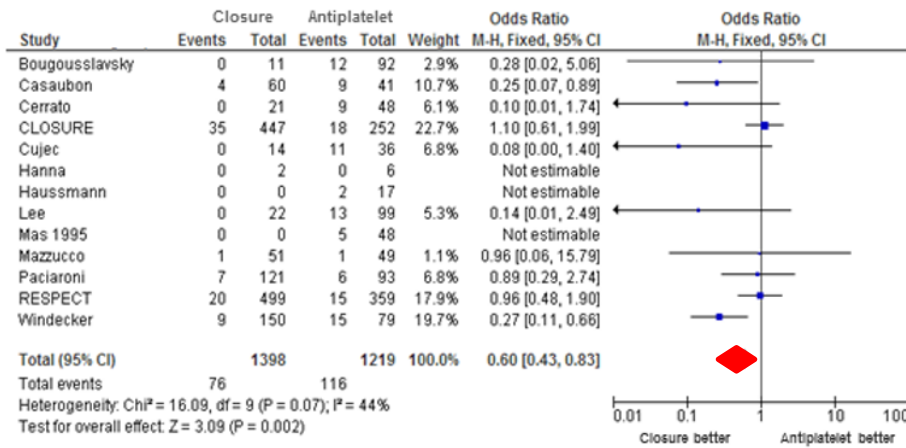
PFO closure vs anticoagulant/antiplatelet therapy in patients with cryptogenic stroke: **Net Clinical Benefit**

ANTICOAGULANT
OR for net clinical benefit (recurrent stroke/TIA and **bleeding**)



-42%

ANTIPLATELET
OR for net clinical benefit (recurrent stroke/TIA and **bleeding**)



-40%

PFO Closure Efficacy and Safety

Comparison of outcome after patent foramen ovale closure in older versus younger patients

Justin G. Luermans¹, MD, PhD; Werner Budts², MD, PhD; Jurriën M. Ten Berg¹, MD, PhD; Herbert W. Plokker¹, MD, PhD; Maarten J. Suttorp¹, MD, PhD; Martijn C. Post^{1*}, MD, PhD

Patients (335)	Closure Rate*	All Complications
<55 (215)	92.3%	14%
>55 (120)	87.9%	18%
p	0.22	0.12

Closure rate and complications are similar in both younger and older patients

How to close PFO?

Suture

Umbrella device

Safety Outcomes After Percutaneous Transcatheter Closure of Patent Foramen Ovale

Alexander E. Merkler, MD*; Gino Gialdini, MD*; Shadi Yaghi, MD; Peter M. Okin, MD; Costantino Iadecola, MD; Babak B. Navi, MD, MS; Hooman Kamel, MD

Background and Purpose—We sought to evaluate the real-world rate of safety outcomes after patent foramen ovale (PFO) closure in patients with ischemic stroke or transient ischemic attack (TIA).

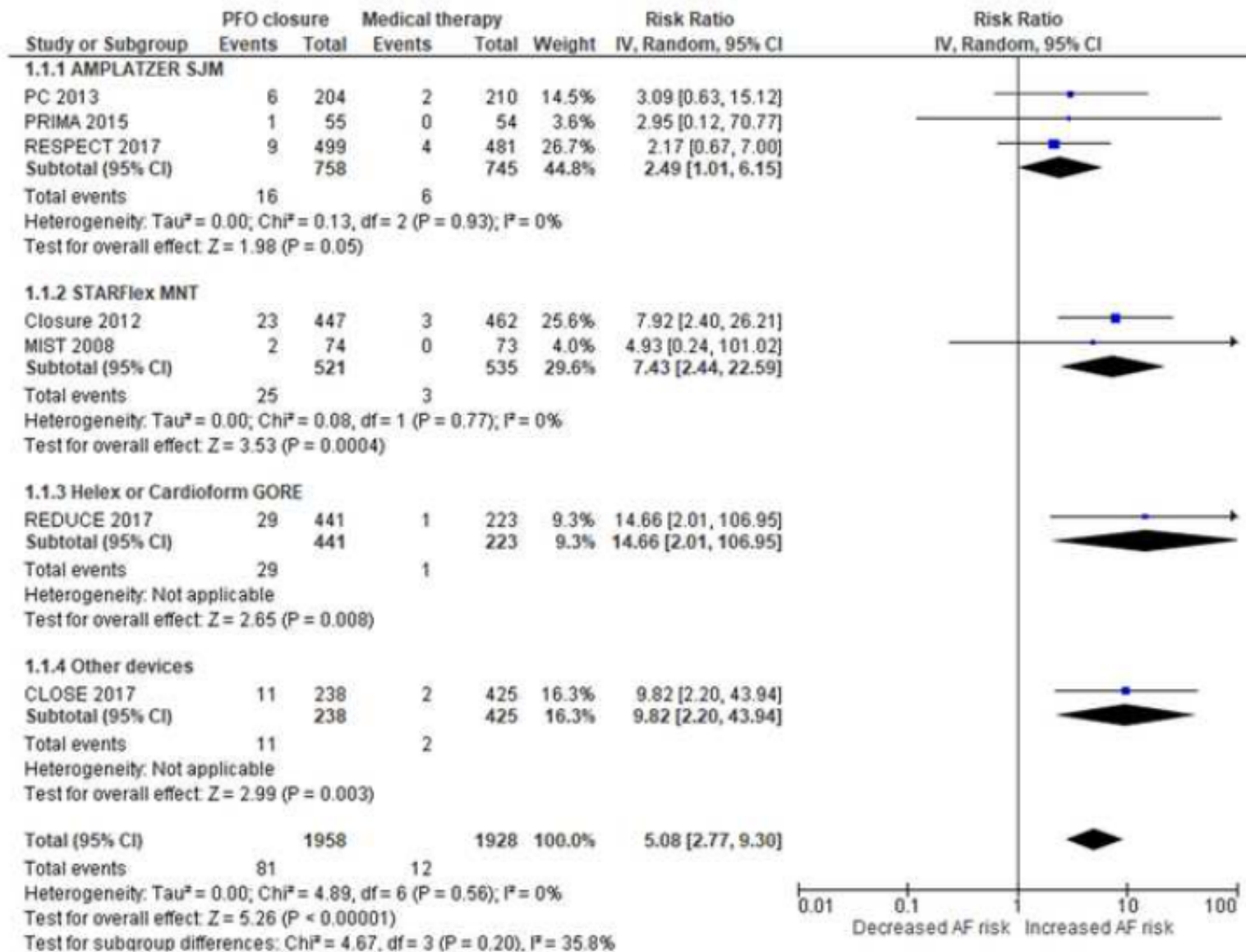
Methods—We performed a retrospective cohort study using administrative claims data on all hospitalizations from 2005 to 2013 in New York, California, and Florida. Using *International Classification of Diseases, Ninth Revision, Clinical Modification* codes, we identified patients who underwent percutaneous transcatheter PFO closure within 1 year of ischemic stroke or TIA. Our outcome was an adverse event occurring during the hospitalization for PFO closure, defined as in prior studies as atrial fibrillation or flutter, cardiac tamponade, pneumothorax, hemothorax, a vascular access complication, or death. Crude rates were reported with exact confidence intervals.

Results—We identified 1887 patients who underwent PFO closure after ischemic stroke or TIA. The rate of any adverse outcome during the hospitalization for PFO closure was 7.0% (95% confidence interval [CI], 5.9%–8.2%). Rates of adverse outcomes varied by age and type of preceding cerebrovascular event. In patients >60 years of age, the rate of adverse outcomes was 10.9% (95% CI, 8.6%–13.6%) versus 4.9% (95% CI, 3.8%–6.3%) in patients ≤60 years of age. The rate of adverse outcomes was 9.9% (95% CI, 7.3%–12.5%) in patients with preceding ischemic stroke versus 5.9% (95% CI, 4.7%–7.1%) after TIA.

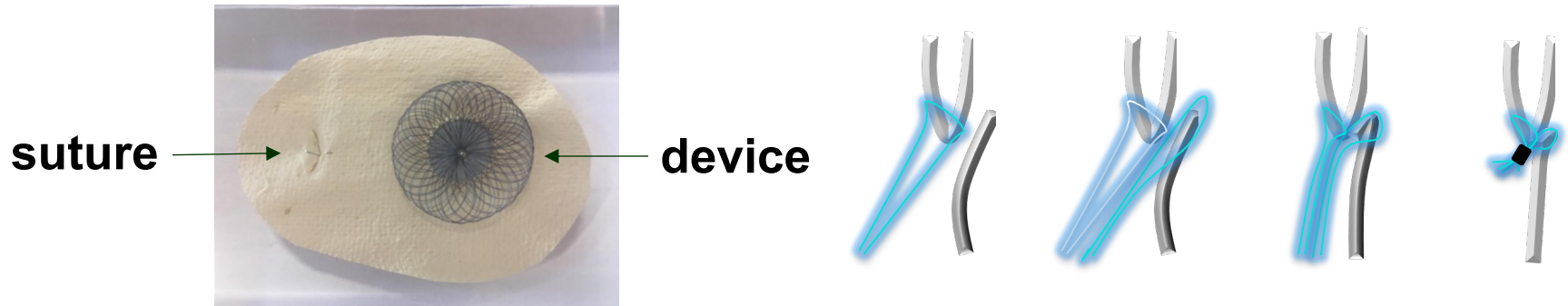
Conclusions—Approximately 1 in 14 patients who underwent percutaneous transcatheter PFO closure after ischemic stroke or TIA experienced a serious periprocedural adverse outcome or death. The risk of adverse outcomes was highest in older patients and in those with preceding ischemic stroke. (*Stroke*. 2017;48:00-00. DOI: 10.1161/STROKEAHA.117.018501.)

7.1% serious periprocedural adverse outcome or death

Atrial Fibrillation/Flutter After PFO Closure

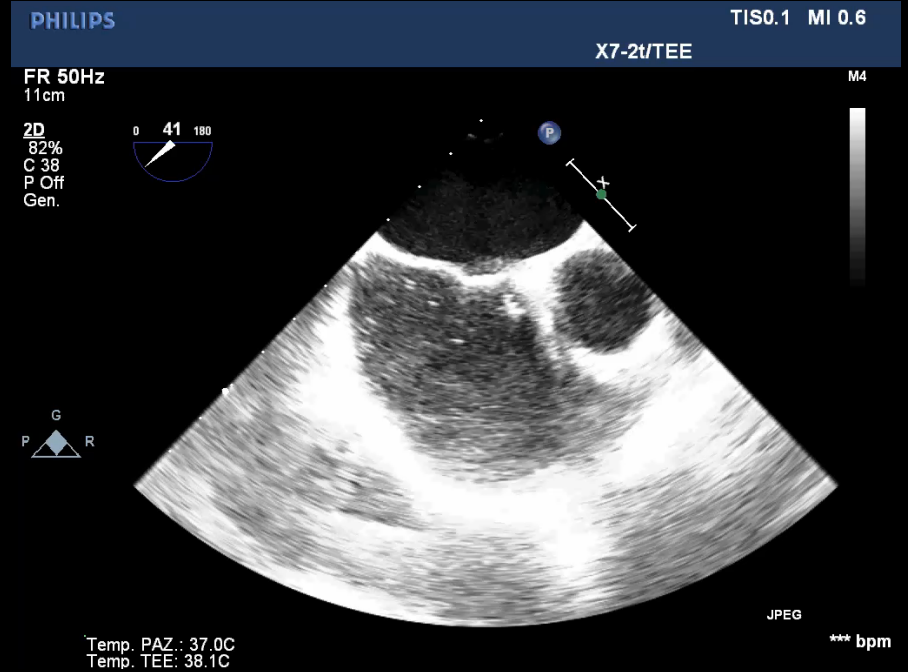
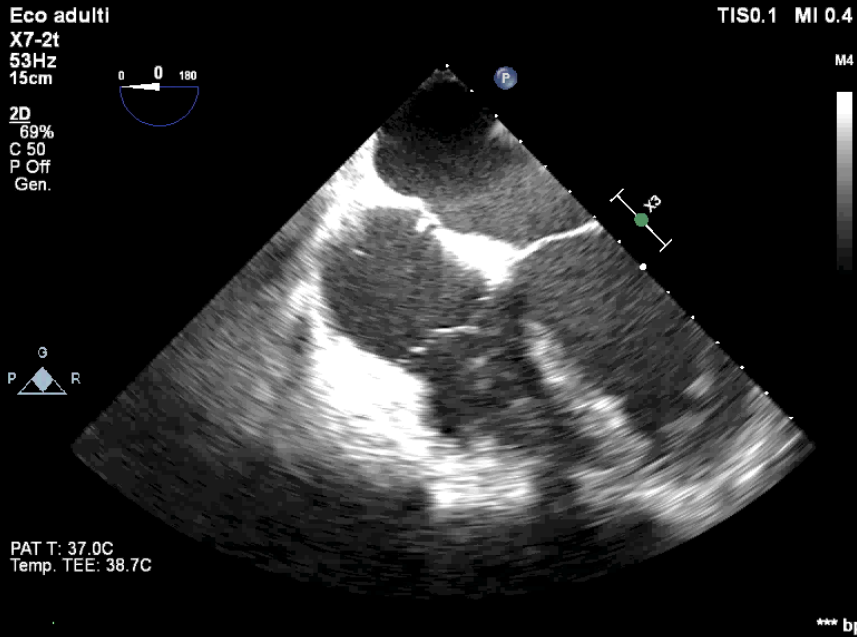


Suture vs Device PFO Closure

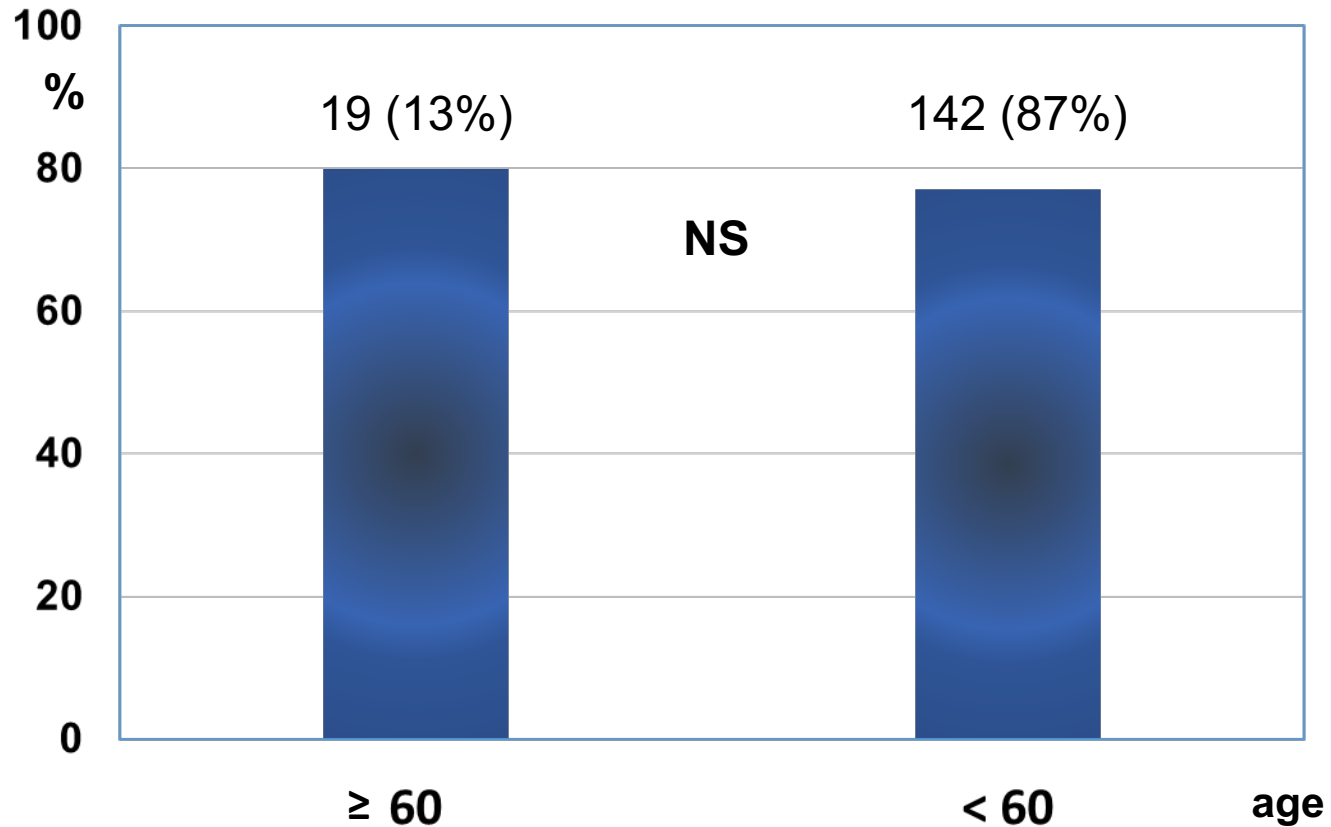


- No need of a permanent DEVICE (“deviceless” procedure)
- No obstruction/encumbrance of the atrial chambers
- No risk of migration/embolization/erosion/perforation
- No allergenic risk (no metallic alloy)
- No need of long term anti-coagulation/antiplatelet rx
- No risk of left side air embolism during the procedure
- No need of intra-procedural TE or IC echo monitoring
- No need of anesthesiological support (local anesthesia)
- No effect on atrial geometry and functionality
- No limitations for future left heart procedures (MVP, AFA, LAAC)
- No induction of supraventricular arrhythmias (atrial fibrillation)
- Repeatable if initial attempt is unsuccessful
- Safer than traditional devices and long-term effective closure

Suture Closure of PFO



Noblestitch Closure Rate*



(161 patients undergoing PFO closure by suture technique (2016-2018); mean FU 10.3 months; no complications and no recurrency at FU - data on files submitted for publication; Cardiologia – San Eugenio)

* 0 shunt at max follow up

PFO closure after 60 years

Summary & Conclusions

- Older age **DOES NOT** preclude paradoxical embolism. Prevalence of PFO in older cryptogenic stroke/TIA patients is similar to younger patients;
- Similar efficacy and safety of PFO closure;
- In old patients, sources of embolism should be more deeply searched particularly regarding atrial fibrillation (ICM);
- Suture-mediated PFO closure might reduce complications with similar efficacy in older patients;
- **After accurate screening, PFO closure in old patients may be absolutely appropriate**