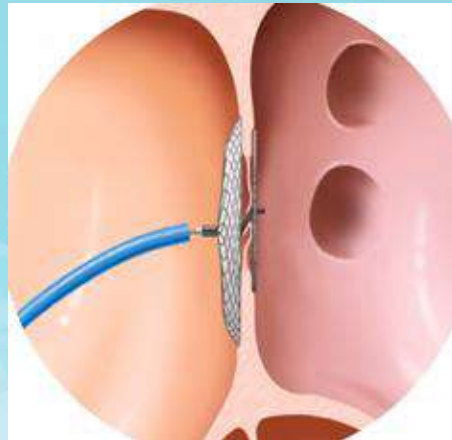


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Cuando Cerrar un PFO?



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Ex Presidente CACI; Presidente SOLACI



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Stroke en pacientes jóvenes

795,000 strokes annually

34% of all strokes occur in patients younger than 65 (270,300)

10% growth in numbers in last 10 years

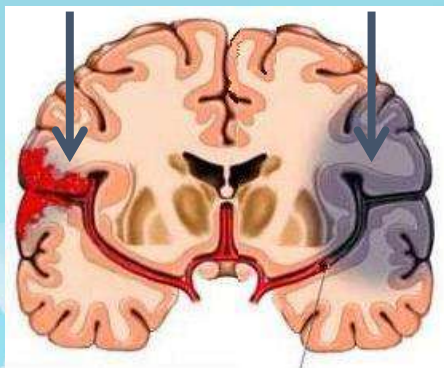
Treatments frequently unproven

Mozzafarian, D, et al. *Circulation* 2105: 131:e29-e33

Mecanismos del ACV o stroke

VESSEL RUPTURE
15%

ARTERY OCCLUSION
85%



25-30% Atherothrombotic
Stenotic artery feeding area of infarction

20% Cardioembolic
A thrombus or other material dislodges from the heart of aortic arch

15-20% Lacunar/Small Vessel

25-30% Cryptogenic
Unknown cause

5-10% "Other"

"Cryptogenic Stroke superficial brain convexity infarcts and lack of evidence of large vessel or cardiogenic causation"

– JP Mohr

Adams HP Jr, *Stroke*. Jan 1993;24:35-41

T5: ETIOLOGIA INDETERMINADA

Criptogénico

30% de ACV
Causa tromboembólica
Paciente joven
FOP (40%)

ESUS

ACV embólico de causa indeterminada (ESUS)

Criterios diagnósticos

1. ACV isquémico detectado por TAC o RM que no es lacunar
2. Ausencia de estenosis arterial aterosclerótica mayor de 50 % en arterias intra o extracraneanas relacionadas al área isquémica.
3. Ausencia de condiciones de riesgo mayor para cardioembolia. (FA, prótesis valvulares, disfunción VI severa, trombo ventricular)
4. Ausencia de otras causas específicas de ACV

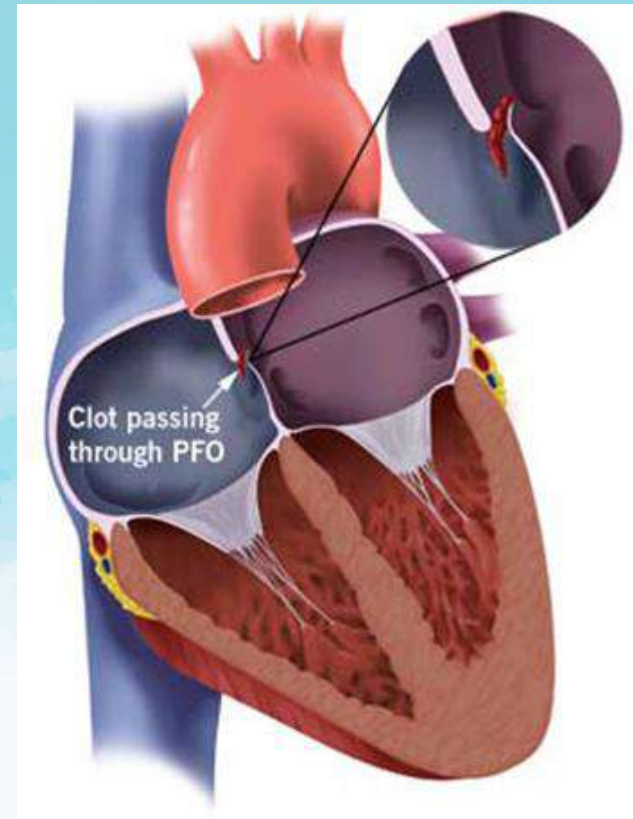
Estudios a realizar

- ✓ TAC o RM cerebral
- ✓ Imágenes de las arterias extra e intracraneanas (angiografía directa, o angio RM o TC, o ultrasonido vasos de cuello + Doppler transcraneano)
- ✓ Electrocardiograma
- ✓ Monitoreo del ritmo cardíaco no menor de 24 horas
- ✓ Ecocardiograma Doppler transtorácico

Figura 4. Criterios diagnósticos y estudios a realizar para ESUS. Según referencia 4.

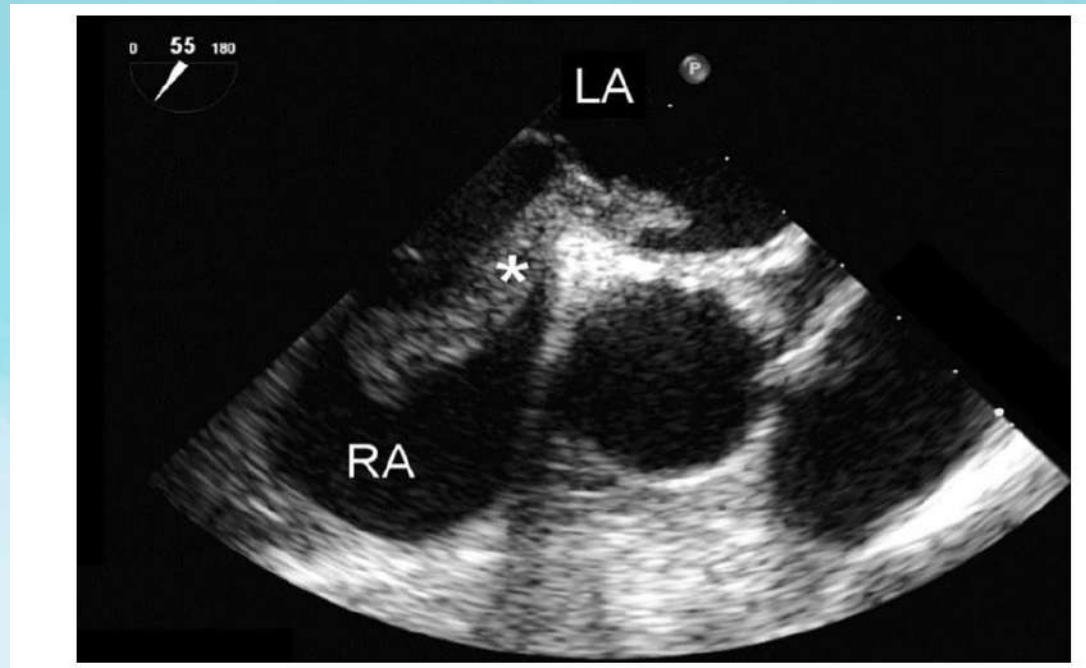
ESUS y Foramen oval permeable

- Some patients with PFO experience a stroke at a young age.
- PFO can allow clots to go from the right side of the heart to the left, travel to the brain and cause a stroke.
- Mechanism is **presumed to be** paradoxical embolism.
 - Venous thrombus crosses the PFO and then occludes a systemic artery.



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Embolia paradójala capturada en ETE



Transesophageal echocardiography in a 55° view.

Boutaina N, et al. *Circulation*. 2008;118:e154-e155

Recurrencia de stroke

	RECURRENCE RATE IN MEDICAL MANAGEMENT ARM	MEAN STUDY FOLLOW-UP
RESPECT Trial	5.8%	5.9 years
REDUCE Trial	5.4%	3.2 years
CLOSE Trial	6.2%	5.3 years
Mas et al. (Observational)		4 years
• Patients with PFO	2.3%	
• Patients with PFO and ASA	15.2%	

Punto de inflexión en el cierre de PFO

Three positive trials for PFO closure published simultaneously in the *New England Journal of Medicine*.

TRIAL NAME	NO. OF PATIENTS	MEAN OR MEDIAN NO. OF YEARS OF FOLLOW-UP	COMPARATOR	PRIMARY OUTCOME	HAZARD RATIO [†]	P VALUE [†]
RESPECT ¹	980	5.9	Antiplatelet therapy or warfarin	Composite of recurrent nonfatal ischemic stroke, fatal ischemic stroke, or early death after randomization	0.55	0.046
REDUCE ²	664	3.2	Antiplatelet therapy	Ischemic stroke and new brain infarction on imaging	0.23	0.002
CLOSE ³	663	5.3	Antiplatelet therapy or anticoagulation ^{††}	Stroke	0.03	< 0.001

[†] The hazard ratio and P value are for the expected probability of stroke or other primary outcome after closure of the PFO versus medical treatment in the intention-to-treat analysis.

^{††} Anticoagulation refers to any form of anticoagulation. Note: The hazard ratio of 0.03 includes antiplatelet therapy only as a comparator.

1. Saver JL, Carroll JD, Thaler DE, et al. Long-term outcomes of patent foramen ovale closure or medical therapy after stroke. *N Engl J Med*. 2017; 377: 1022-32.
2. Søndergaard L, Kasner SE, Rhodes JF, et al. Patent foramen ovale closure or antiplatelet therapy for cryptogenic stroke. *N Engl J Med*. 2017; 377: 1033-42.
3. Mas J-L, Derumeaux G, Guillon B, et al. Patent foramen ovale closure or anticoagulation vs. antiplatelets after stroke. *N Engl J Med*. 2017; 377: 1011-21.

Selección de pacientes – Criterios de inclusión

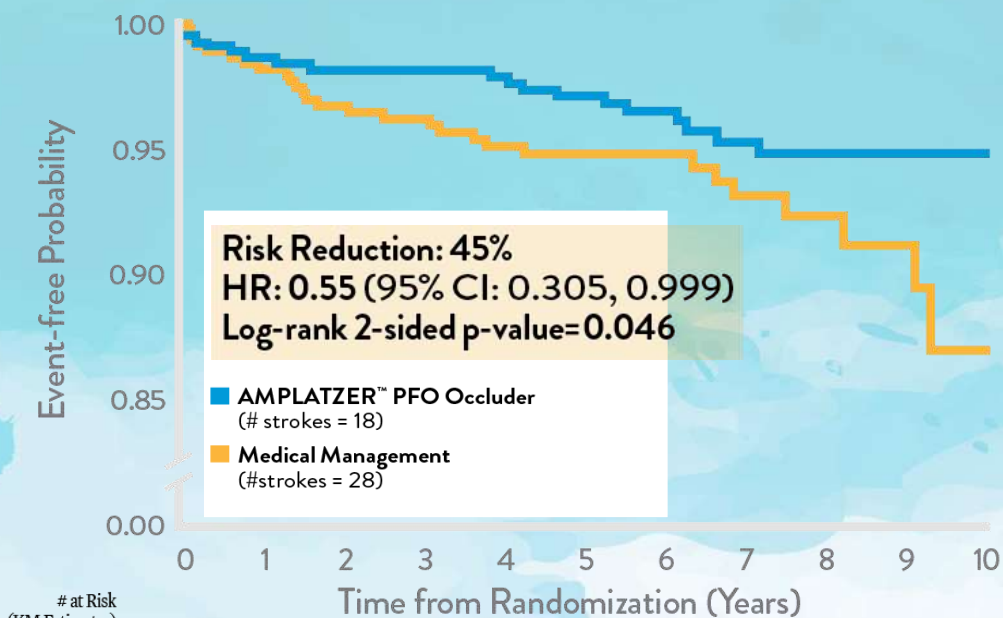
	RESPECT	REDUCE	CLOSE
AGE	18-60 years	18-60 years	16-60 years
STROKE DEFINITION	Acute focal neurological deficit, either <ul style="list-style-type: none"> • Symptoms \geq 24 hours or greater, or • Symptoms $<$ 24 hours infarct and infarct on imaging 	Ischemic stroke: symptoms persisting \geq 24 hours OR TIA: symptoms persisting $<$ 24 hours and has infarct on imaging	Ischemic stroke (or retinal ischemia), confirmed by imaging regardless of duration of symptoms (less than or greater than 24 hours)
IS IT CRYPTOGENIC?	Cryptogenic stroke is defined as a stroke from an unknown cause	<ul style="list-style-type: none"> • Vascular imaging rules out potential sources thromboembolism • No evidence of hypercoagulable state • Absence of an identifiable source of thromboembolism in systemic arterial circulation 	Absence of another identifiable cause of stroke (or retinal ischemia) on a thorough etiological work

Selección de pacientes – Criterios de inclusión

	RESPECT	REDUCE	CLOSE
TIME OF EVENT TO ENROLLMENT	Within the last 270 days	Within last 180 days	Within last 6 months
PFO CHARACTERISTICS	Visualization of microbubbles per TEE in the left atrium within three cardiac cycles from the right atrial opacification at rest and/or during Valsalva release	Transesophageal echocardiography (TEE) with bubble study demonstrating spontaneous right-to-left shunting or right-to-left shunting during Valsalva maneuver	<p>PFO with large shunt > 30 microbubbles on TTE or TEE detected spontaneously or exclusively during provocation maneuvers > 30 microbubbles on TTE or TOE</p> <p>PFO associated with atrial septal aneurysm on TEE: base of aneurysm \geq 15 mm and excursion > 10 mm</p>

RESPECT Trial Results: Efficacy

FREEDOM FROM RECURRENT ISCHEMIC STROKE (INTENTION TO TREAT)



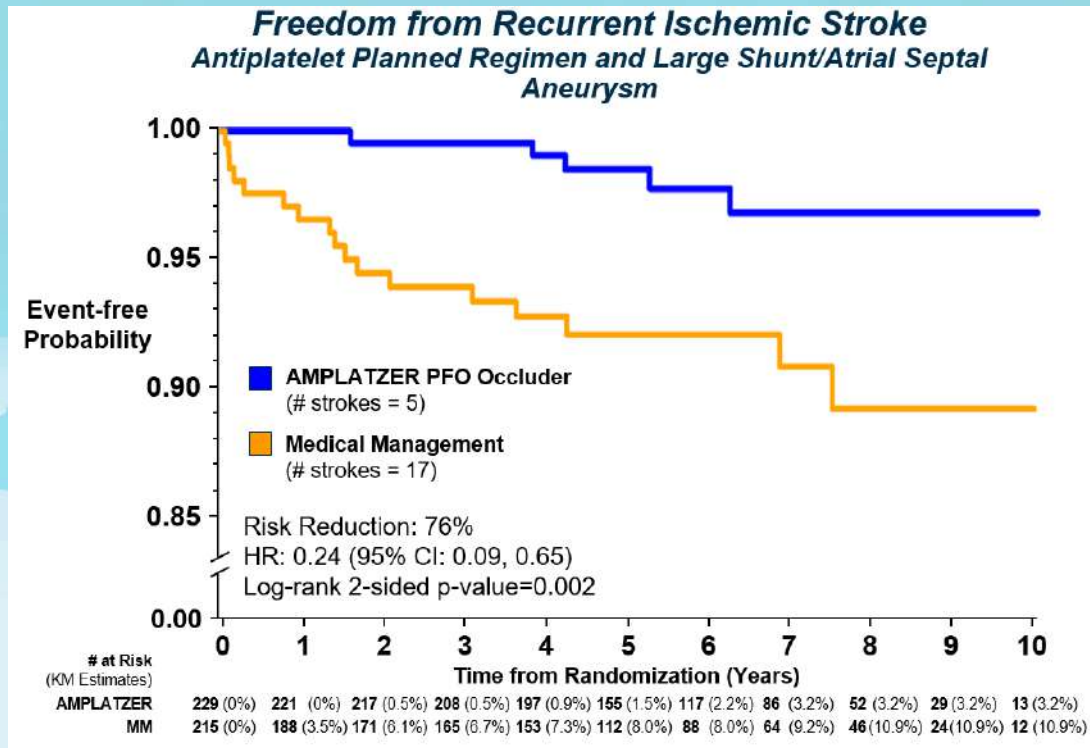
45% RELATIVE RISK REDUCTION IN FAVOR OF PFO CLOSURE FOR **ANY** RECURRENT ISCHEMIC STROKE OR EARLY DEATH **OVER 5.9 YEARS OF FOLLOW-UP.**

# at Risk (KM Estimates)	0	1	2	3	4	5	6	7	8	9	10
AMPLATZER	499 (0%)	476 (1.4%)	464 (1.6%)	447 (1.6%)	421 (1.9%)	352 (2.6%)	262 (3.3%)	197 (4.5%)	128 (5.0%)	77 (5.0%)	41 (5.0%)
MM	481 (0%)	433 (1.8%)	394 (3.2%)	380 (3.7%)	354 (4.7%)	282 (5.0%)	218 (5.0%)	150 (6.6%)	104 (7.3%)	59 (8.5%)	31 (12.5%)

Saver JL, Carroll JD, Thaler DE, et al. Long-term outcomes of patent foramen ovale closure or medical therapy after stroke. *N Engl J Med.* 2017; 377: 1022-32.

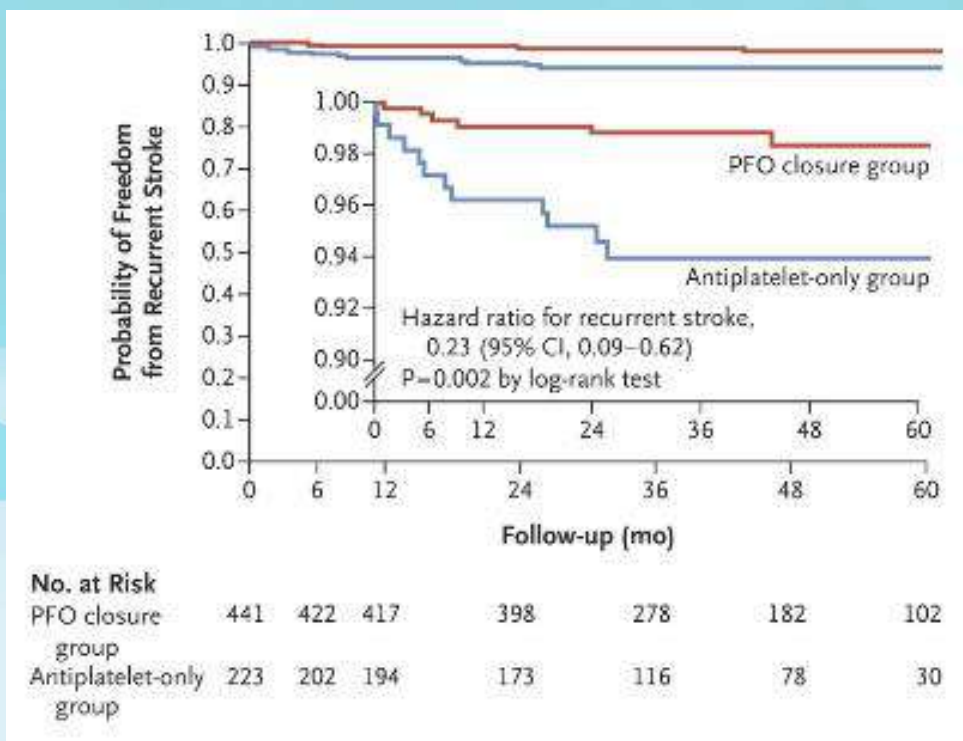
RESPECT Trial Results: Efficacy

GREATER BENEFIT IN SUBSTANTIAL SHUNT OR ASA GROUP



76% RELATIVE RISK REDUCTION IN FAVOR OF PFO CLOSURE

REDUCE Primary Efficacy (ITT)



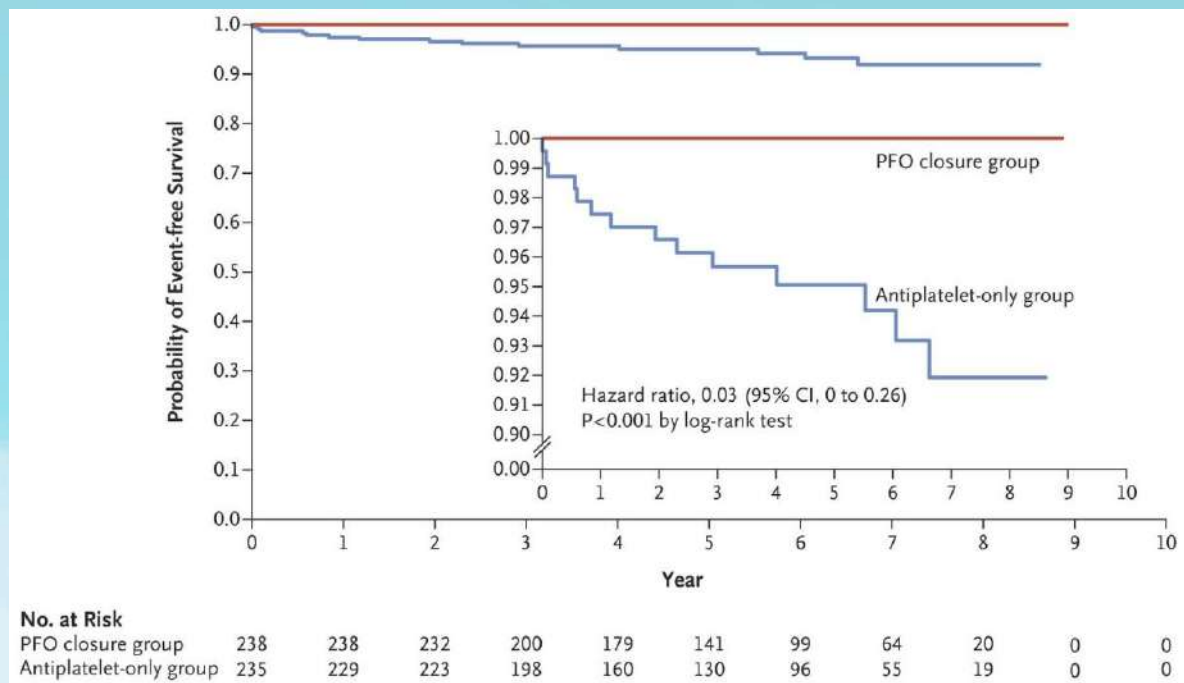
RECURRENT STROKE:

77% relative risk reduction in favor of PFO closure in reducing risk of recurrent stroke.

Søndergaard L, Kasner SE, Rhodes JF, et al. Patent foramen ovale closure or antiplatelet therapy for cryptogenic stroke. *N Engl J Med.* 2017; 377: 1033-42.

CLOSE Efficacy Outcomes

(Intention to Treat)



Significant benefit of PFO closure vs. antiplatelet therapy for preventing stroke recurrence.
One stroke avoided at 5 years for every 20 treated patients.

Mas J-L, Derumeaux G, Guillon B, et al. Patent foramen ovale closure or anticoagulation vs. antiplatelets after stroke. *N Engl J Med.* 2017; 377: 1011-21.

RESPECT Trial Results: Safety

EVENT TYPE	PFO CLOSURE GROUP (N = 499; 3141 PT-YRS)		MEDICAL MANAGEMENT GROUP (N = 481; 2669 PT-YRS)		P-VALUE**
	EVENTS	RATE*	EVENTS	RATE*	
Per Pt-Yr					
Atrial fibrillation/flutter	9	0.29	4	0.15	0.37
Major bleeding	18	0.57	15	0.56	0.96
Death from any cause	7	0.22	11	.41	0.21
DVT/PE	18	0.57	4	.15	0.006

	N (OVERALL %)
Device-related SAE	13 (2.6%)
• Device Embolization	0 (0.0%)
• Device Thrombus	0 (0.0%)
• Aortic Erosion/Dissection	0 (0.0%)
Procedure-related SAE	12 (2.4%)

REDUCE SAEs

Table 3. Adverse Events.

Adverse Event	PFO Closure Group (N=441)	Antiplatelet-Only Group (N=223)	P Value*
	<i>no. of patients (%)</i>		
Any serious adverse event	102 (23.1)	62 (27.8)	0.22
Device related	6 (1.4)	NA	NA
Procedure related	11 (2.5)	NA	NA
Death†	2 (0.5)	0	0.55
Serious bleeding adverse event	8 (1.8)	6 (2.7)	0.57
Procedure associated‡	4 (0.9)	NA	NA
Other§	4 (0.9)	6 (2.7)	0.09
Any atrial fibrillation or flutter	29 (6.6)	1 (0.4)	<0.001
Serious atrial fibrillation or flutter¶	10 (2.3)	1 (0.4)	0.11
Serious device-related adverse event	6 (1.4)	NA	NA
Device dislocation	3 (0.7)		
Device-related thrombosis	2 (0.5)		
Aortic dissection	1 (0.2)		
Any deep-vein thrombosis or pulmonary embolism	3 (0.7)	2 (0.9)	1.00

Need explanation for symbols

Søndergaard L, Kasner SE, Rhodes JF, et al. Patent foramen ovale closure or antiplatelet therapy for cryptogenic stroke. *N Engl J Med.* 2017; 377: 1033-42.

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- THREE MAJOR RANDOMIZED CLINICAL TRIALS SUPPORT PFO CLOSURE IN YOUNGER PATIENTS WITH CRYPTOGENIC STROKE:
 - RESPECT
 - REDUCE
 - CLOSE

Mi paciente cumple los criterios de los pacientes incluidos en estos estudios?

FOP

- Sospecha Clínica:
ACV luego de valsalva
Ejercicio intenso
Situación predisponente para TVP
TEP + ACV
Sin factores de riesgo vascular.

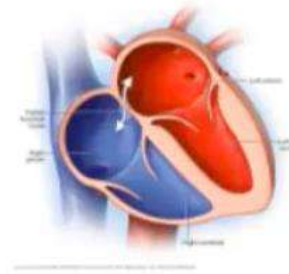




Table 4: RoPE Score Calculator

<i>Characteristic</i>	<i>Points</i>	RoPE SCORE
No history of hypertension	1	
No history of diabetes	1	
No history of stroke or TIA	1	
Non-smoker	1	
Cortical infarct on imaging	1	
Age		
18 to 29 years	5	
30 to 39 years	4	
40 to 49 years	3	
50 to 59 years	2	
60 to 69 years	1	
≥ 70 years	0	
Total Score (sum of individual points) =		
Maximum Score (A patient less than 30 years with no hypertension, no diabetes, no history of stroke or TIA, non-smoker, and cortical infarct)		10
Minimum Score (A patient ≥ 70 years with hypertension, diabetes, prior stroke, current smoker, and no cortical infarct)		0

- Paciente de sexo femenino de 37 años de edad que como factor de riesgo cardiovascular es ex tabaquista.

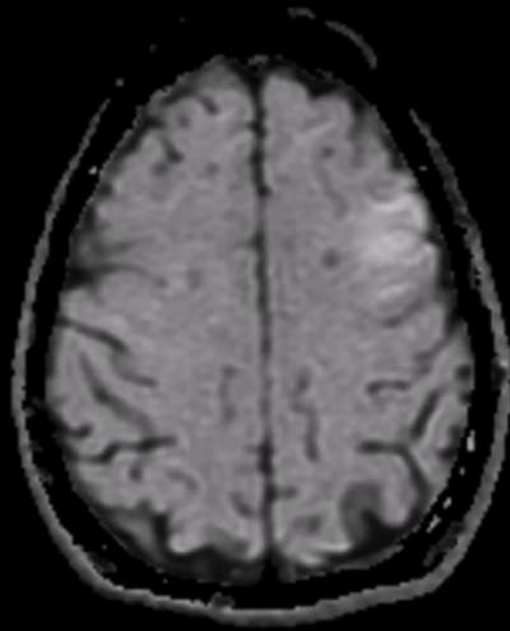
Antecedentes de enfermedad cardiovascular:

- 2 meses previos a su ingreso cursó internación en otra institución por accidente cerebrovascular isquémico cortical frontolateral izquierdo sintomático por disartria, sin secuelas.
- Doppler carotídeo sin estenosis ni disección.
- Monitoreo ECG sin arritmias

2022

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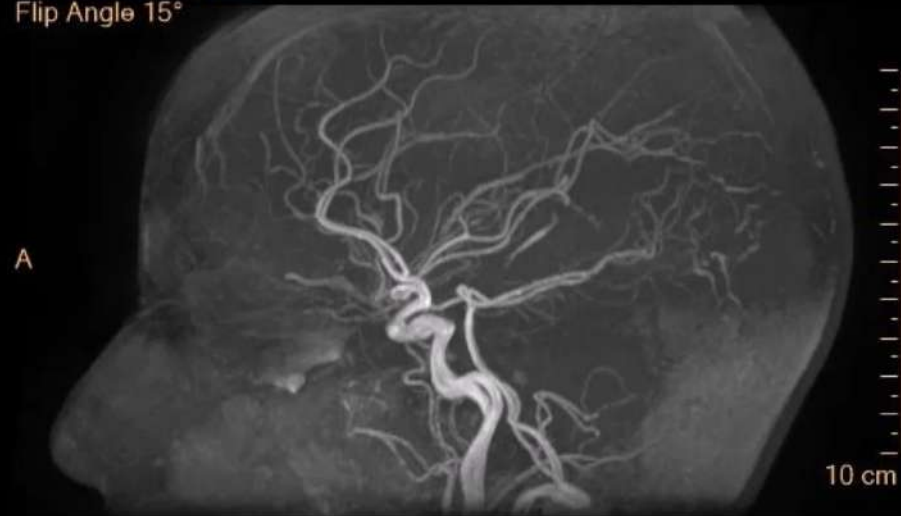
L 0.47
W 0.94



2022

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Zoom 1.00



WL 251
PHILIPS

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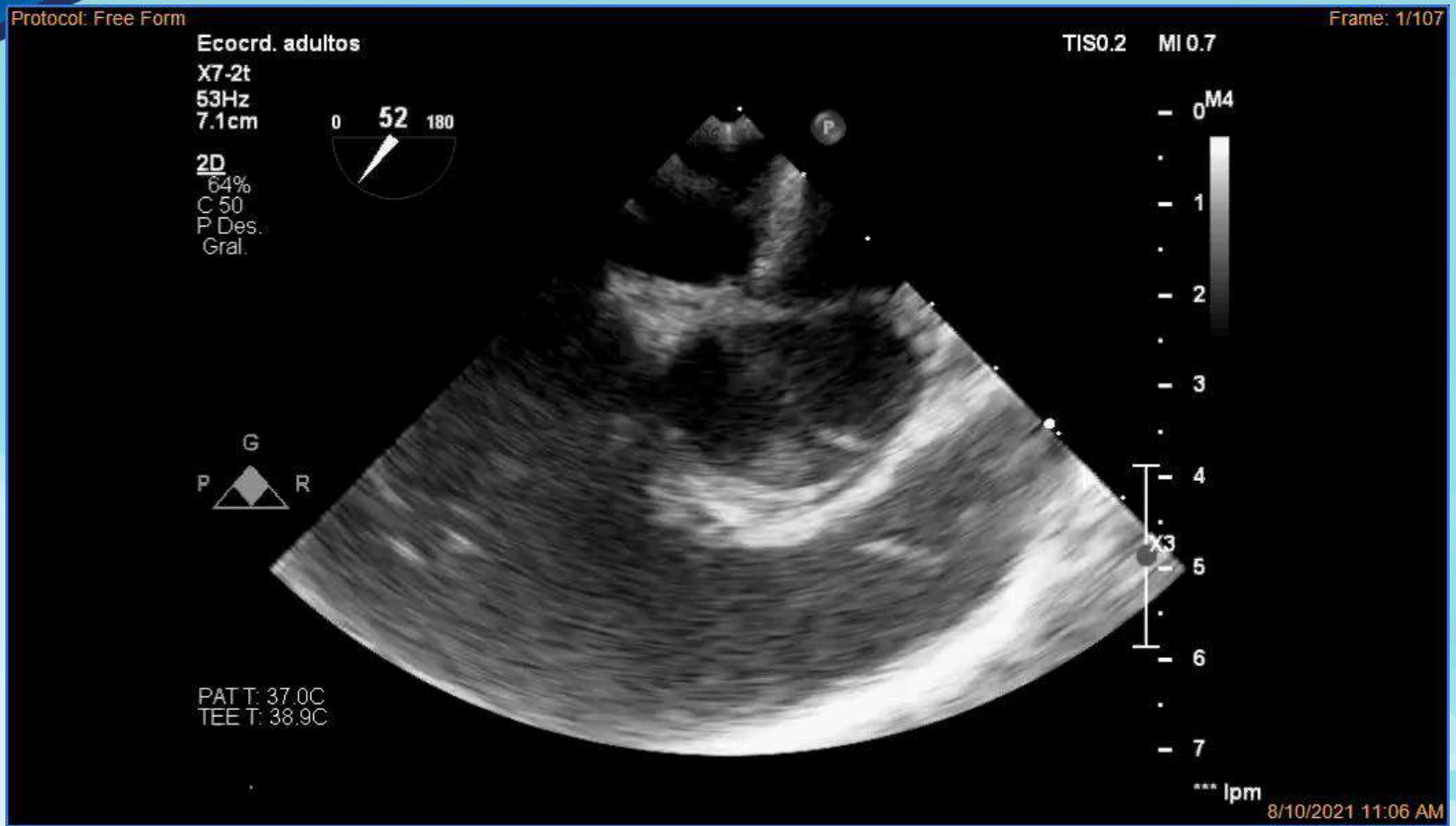
- Ecocardiograma transesofágico: AI y AD normal. Ambas orejuelas normales. Sin imágenes de trombos. FOP tuneliforme de 3 x 15 mm con pasaje de 15 burbujas. Cavidades ventriculares de tamaño normal. FSVI normal. Sin valvulopatías de jerarquía.

History of hypertension	<input checked="" type="radio"/> No +1	<input type="radio"/> Yes 0
History of diabetes	<input checked="" type="radio"/> No +1	<input type="radio"/> Yes 0
History of stroke or TIA	<input checked="" type="radio"/> No +1	<input type="radio"/> Yes 0
Smoker	<input checked="" type="radio"/> No +1	<input type="radio"/> Yes 0
Cortical infarct on imaging	<input type="radio"/> No 0	<input checked="" type="radio"/> Yes +1
Age	<input type="text" value="37"/>	years

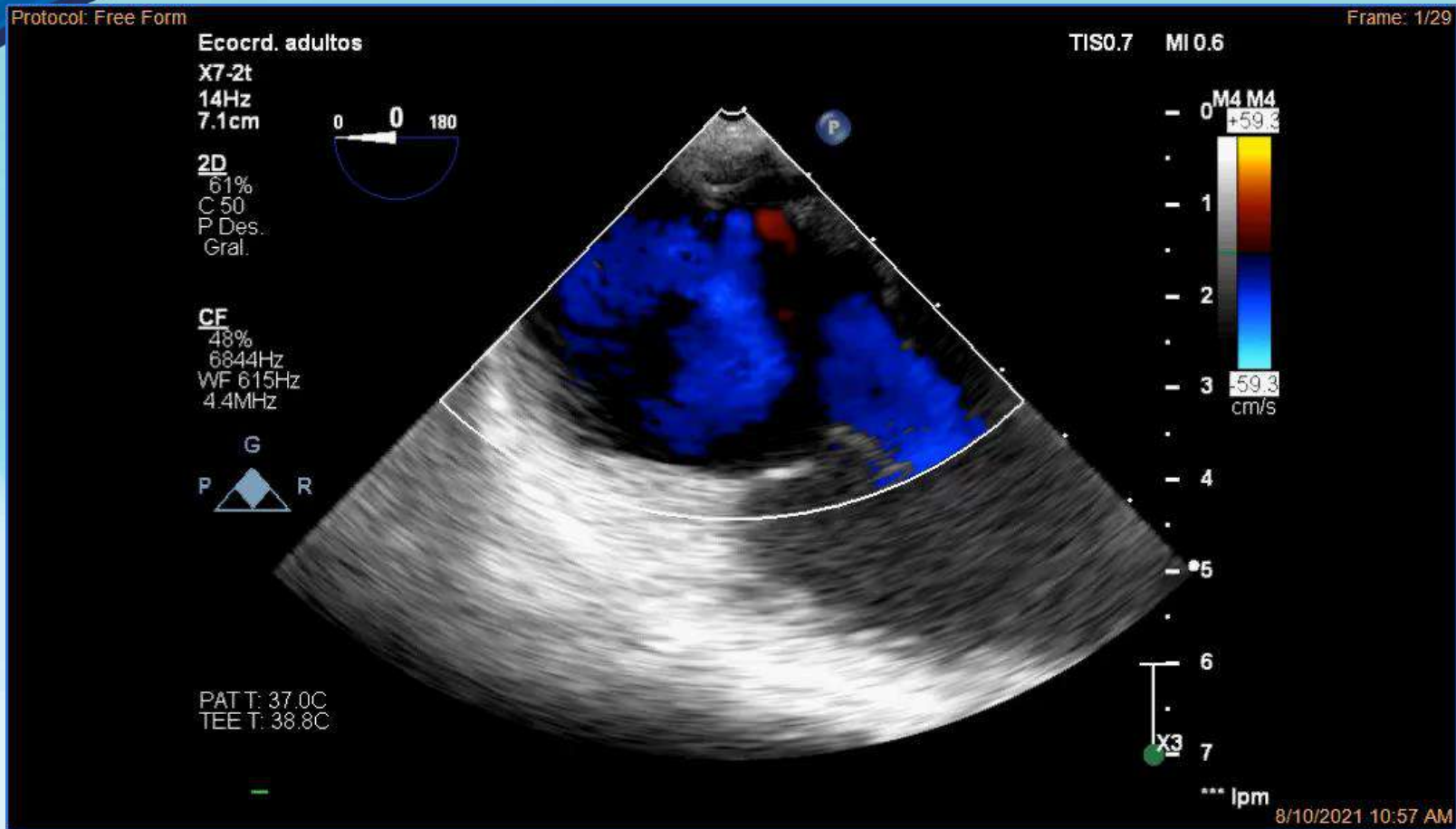
9 points

88% chance that stroke is due to PFO.

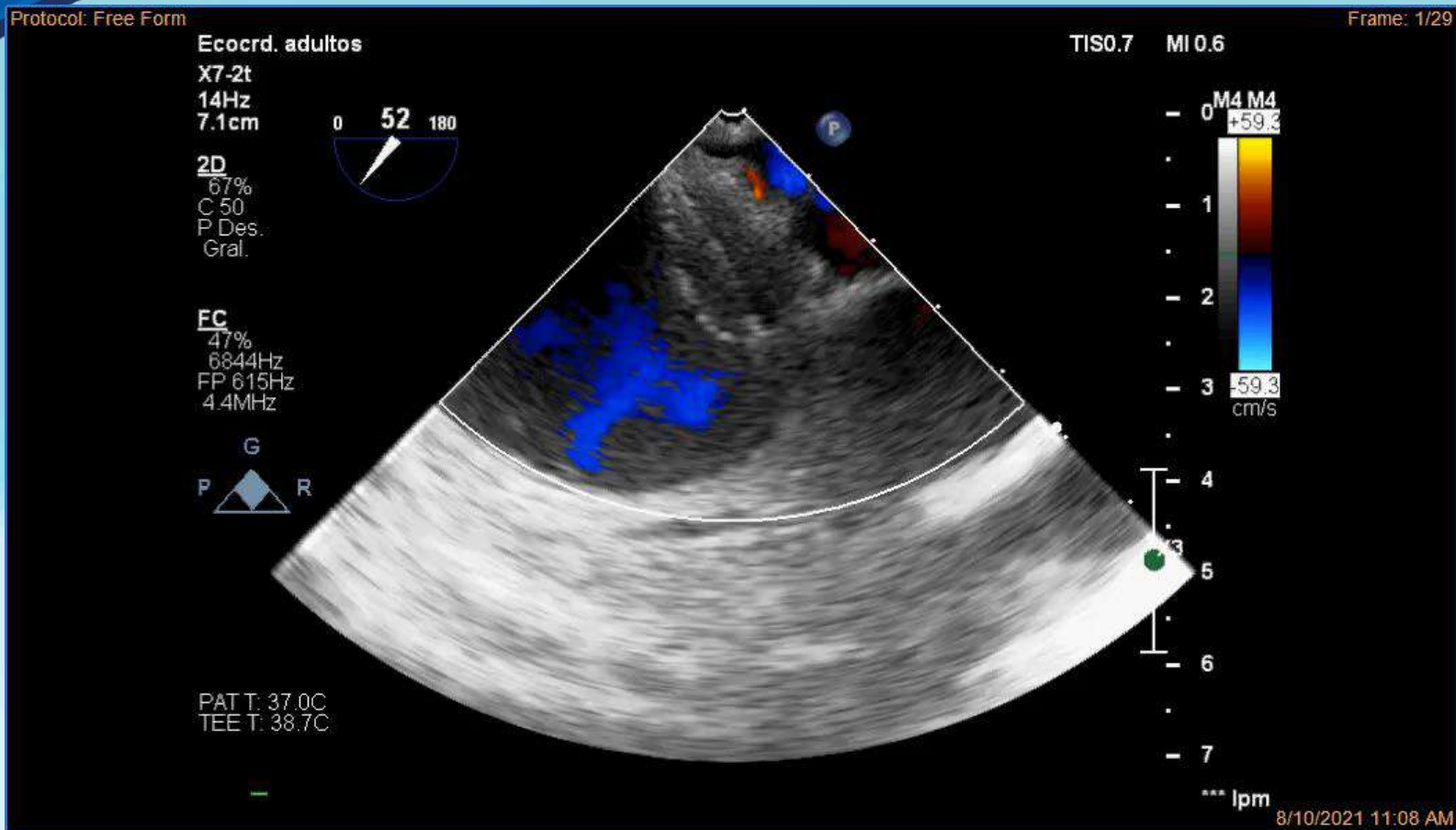
2% risk of 2 year recurrence of stroke/TIA.

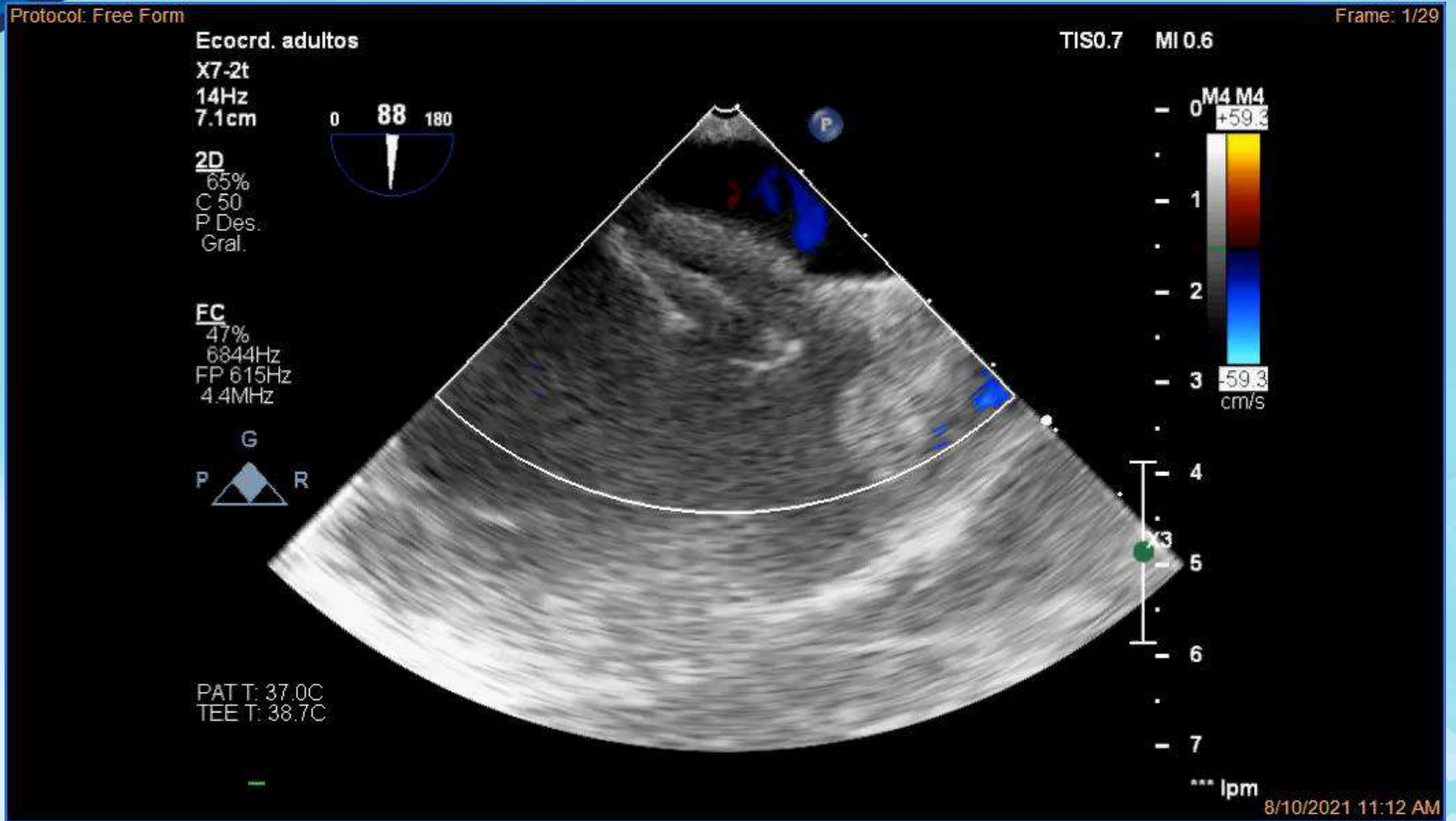


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European position paper on the management of patients with patent foramen ovale. General approach and left circulation thromboembolism



Christian Pristipino^{1*}, MD; Horst Sievert^{2,3}, MD; Fabrizio D'Ascenzo⁴, MD; Jean Louis Mas⁵, MD; Bernhard Meier⁶, MD; Paolo Scacciatella⁴, MD; David Hildick-Smith⁷, MD; Fiorenzo Gaita⁴, MD; Danilo Toni⁸, MD; Paul Kyrle⁹, MD; John Thomson¹⁰, MD; Genevieve Derumeaux¹¹, MD, PhD; Eustaquio Onorato¹², MD; Dirk Sibbing¹³, MD; Peter Germonpré¹⁴, MD; Sergio Berti¹⁵, MD; Massimo Chessa¹⁶, MD; Francesco Bedogni¹⁶, MD; Dariusz Dudek¹⁷, MD; Marius Hornung², MD; Jose Zamorano¹⁸, MD;

joint task force of European Association of Percutaneous 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).

Position statements	Strength of the statement	Level of evidence	Ref.
Drug therapy and follow up after percutaneous closure			
It is reasonable to propose dual antiplatelet therapy for 1 to 6 months after PFO closure	Conditional	A	27, 29, 51, 112, 132, Supplementary Figure 11
We suggest a single antiplatelet therapy be continued for at least 5 years	Conditional	C	27-29, 51, 112, 132, 128, 138-140
The extension of the therapy with single antiplatelet beyond 5 years should be based on the balance between patient's overall risk of stroke for other causes and haemorrhagic risk	Strong	C	–
The choice of the type of antiplatelet drug in the follow-up is currently empiric	Strong	A	27-29, 51, 112, 132

EuroIntervention 2018

Conclusiones

- El cierre de FOP en pacientes con ACV criptogénico/ESUS demostró en 3 ensayos clínicos con seguimiento a largo plazo, beneficios respecto al tratamiento farmacológico en la prevención de la recurrencia de ACV.
- **La identificación de los pacientes que se beneficiarán con estas terapéuticas requiere una meticulosa evaluación multidisciplinaria, en la cuál la colaboración entre el cardiólogo y el neurólogo es imprescindible.**

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