



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

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Cardioneurologia: stroke e dintorni

**Ecocardiografia nella valutazione e nel trattamento del
forame ovale pervio e dei DIA. Quali indicazioni alla
chiusura**

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EACVI recommendations on cardiovascular imaging for the detection of embolic sources:

Several clinical and imaging findings suggest an embolic stroke:

- a. abrupt onset of stroke symptoms;
- b. previous infarctions in various arterial distributions;
- c. multiplicity in space (infarct in both the anterior and posterior circulation, or bilateral);
- d. multiplicity in time (infarcts of different ages);
- e. other signs of systemic thromboembolism (e.g. edge-shaped infarcts of kidney or spleen; Osler splits; blue toe syndrome); and
- f. territorial distribution of the infarcts involving the cortex, or subcortical ‘large lenticulostriate infarct’.

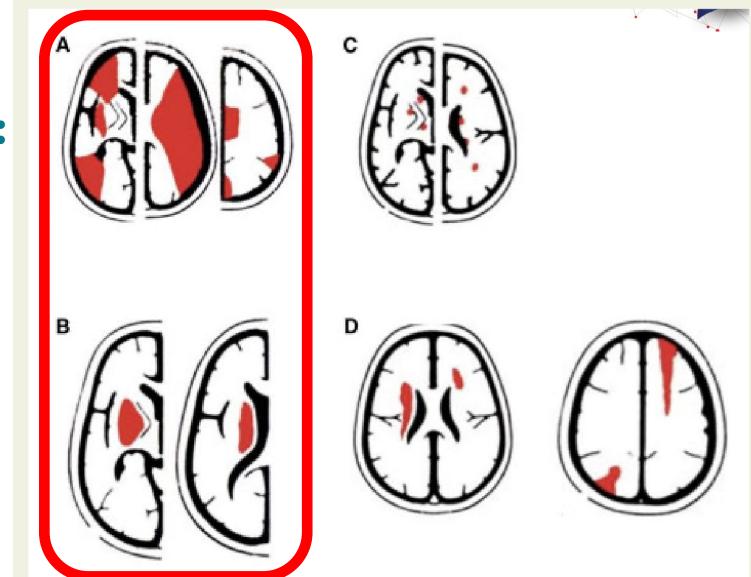


Figure 1 Schematic drawings of patterns of brain infarctions signalling different stroke mechanisms.¹⁶ (A) Cardioembolic stroke is probable in cortical infarcts with territorial distribution; (B) the same holds true for large striatocapsular infarcts; (C) but not for lacunar infarcts, by definition located subcortically; and (D) low-flow infarct can be located subcortical (left panel) or cortical (right panel), but their distribution is interterritorial not territorial.



EACVI recommendations on cardiovascular imaging for the detection of embolic sources:

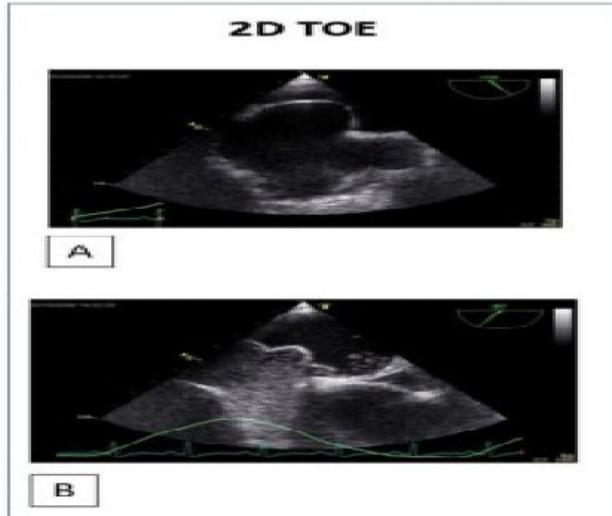
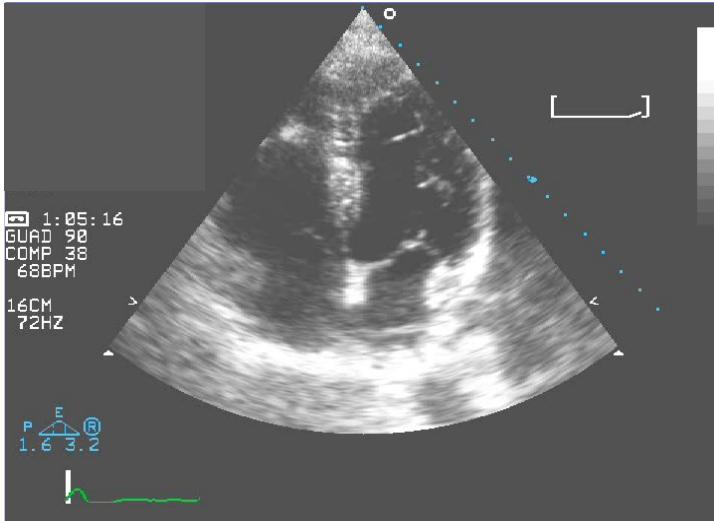


Table 4 Major and minor/unclear sources of ischaemic stroke

Major sources of stroke risk	Minor or unclear sources of stroke risk
Atrial fibrillation	Mitral valve prolapse
Recent myocardial infarction	Mitral annulus calcification
Previous myocardial infarction (LV aneurysm)	Spontaneous echo contrast
All cardiomyopathies including non-compaction and takotsubo cardiomyopathies	Calcified aortic stenosis
Cardiac masses (except calcifications)	Valvular strands
Intracardiac thrombus	Atrial septal aneurysm without PFO
Intracardiac tumours	PFO
Fibroelastoma	Atrial septal pouch
Marantic vegetations	Giant Lambi's excrescences
Rheumatic valve disease (mitral stenosis)	
Aortic arch atheromatous plaques	
Endocarditis	
Prosthetic valve (mechanical especially)	



EACVI recommendations on cardiovascular imaging for the detection of embolic sources:



Recommendations for evaluation of atrial septal anomalies (ASA, PFO)

In patients with cryptogenic stroke or TIA, PFO should be ruled out by contrast TTE and, if contrast TTE is negative, on contrast TOE.

ASA is defined as a >10 mm excursion from the plane of the atrial septum or a combined total excursion right and left ≥ 15 mm.

Contrast TOE is the reference method for defining a PFO. Contrast TTE has a lower sensitivity than other techniques, including transcranial Doppler. However, if contrast TOE is negative in the case of cryptogenic stroke, a second method should be performed (i.e. contrast TTE or transcranial Doppler).

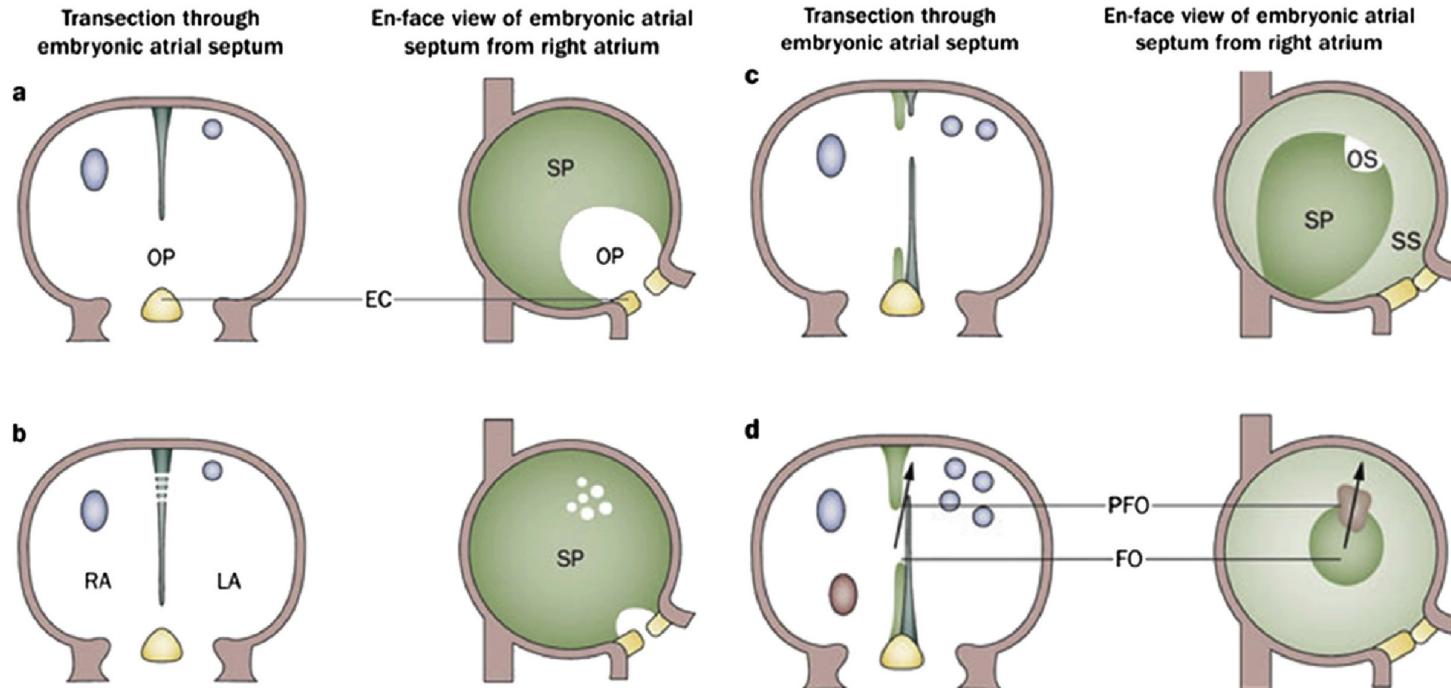
At-risk PFO should be defined, based on the following: presence of an ASA, PFO size, length of the tunnel, number of bubbles crossing the interatrial septum (≥ 30 bubbles) (presence of Chiari network or Eustachian valve can be linked to a causal role of PFO).

3D contrast TOE may provide additional information in assessing interatrial septal anatomy and localization of the right-to-left shunt.

Contrast TOE should be systematically performed before the indication of a PFO closure and interpreted by the heart-brain team before any decision.



Embryology of atrial septum and PFO

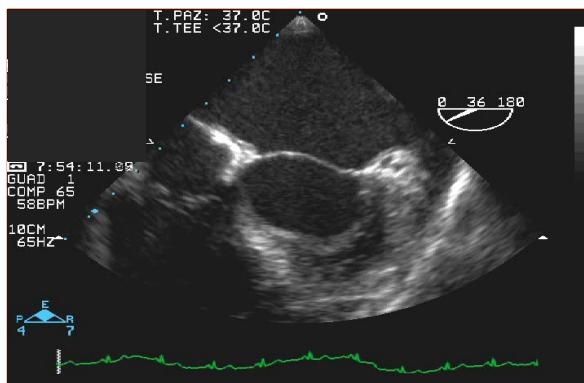
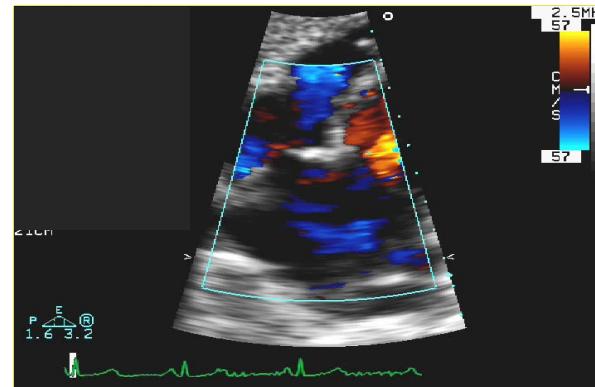
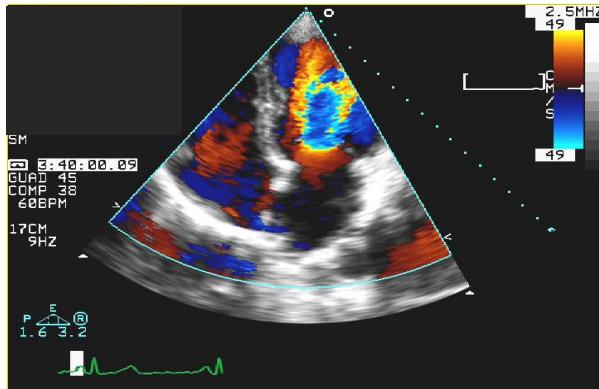




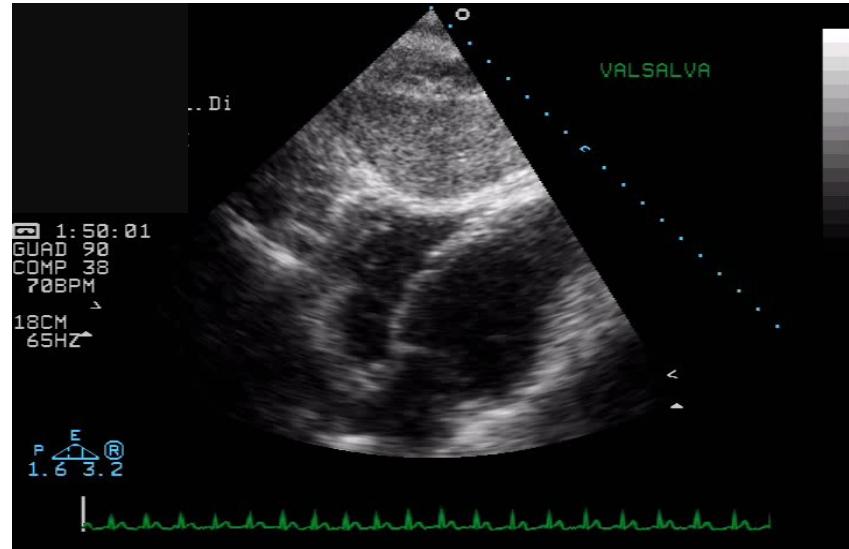
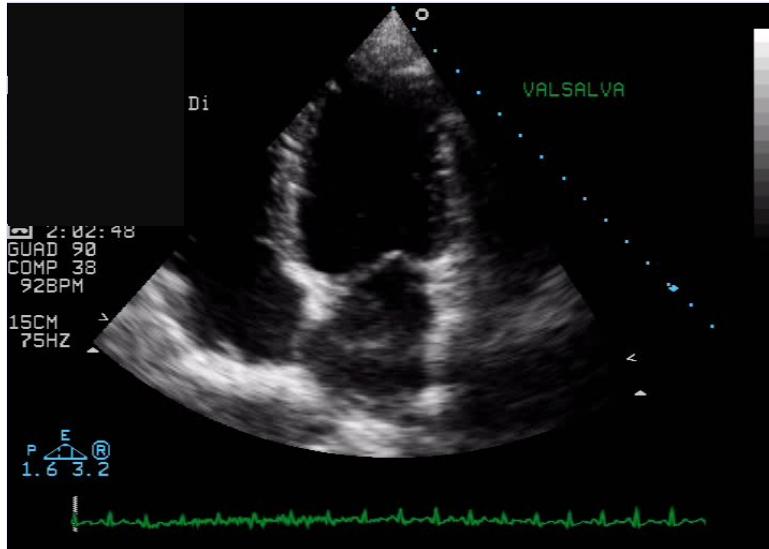
Patent Foramen Ovale Closure: State of the Art

	Patent Foramen Ovale	Atrial Septal Defect
Anatomy	Fusion of primum and secundum atrial septa does not occur as an infant leading to flap valve opening	Congenital failure of overlap of the atrial septa leads to a hole in atrial septum)
Shunt	Right to left shunt occurs when right atrial pressure exceeds left atrial pressure (usually transient after rapid rise and fall in thoracic pressure)	Continuous left-to-right (usually) shunting
Epidemiology	20–34% of adult population ¹	1.6/1,000 live births ⁴⁸
Consequences	In most cases there is no clinical consequence and the defect remains undetected May permit paradoxical embolus	Continuous left-to-right shunt may cause volume loading of right heart, which may reduce long-term survival if not corrected May increase pulmonary artery pressure, reduce exercise tolerance and promote arrhythmia Can also allow paradoxical embolus (indication for closure)

TTE or TOE?

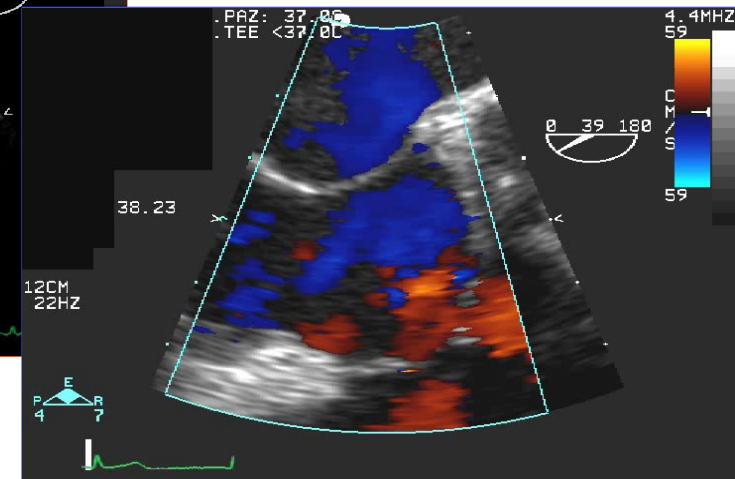
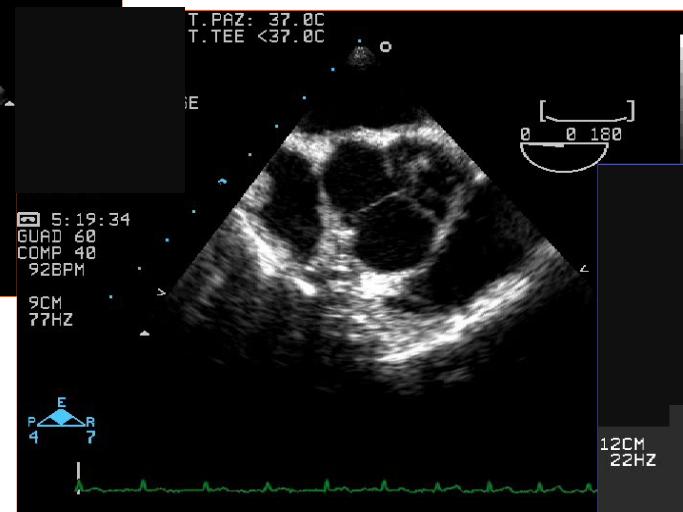
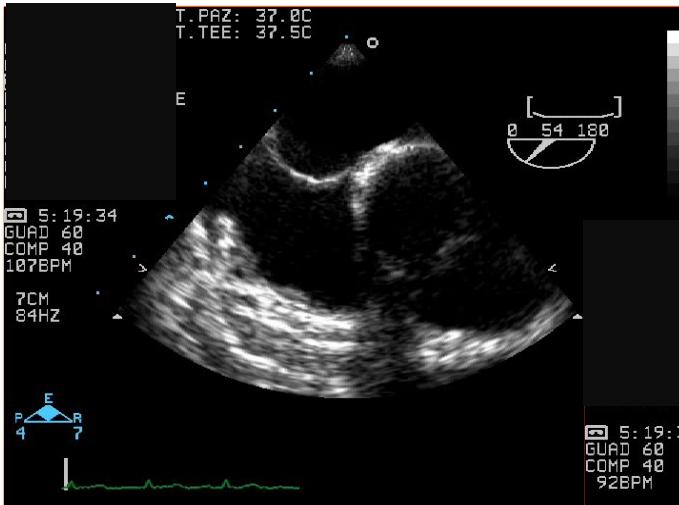


TTE windows



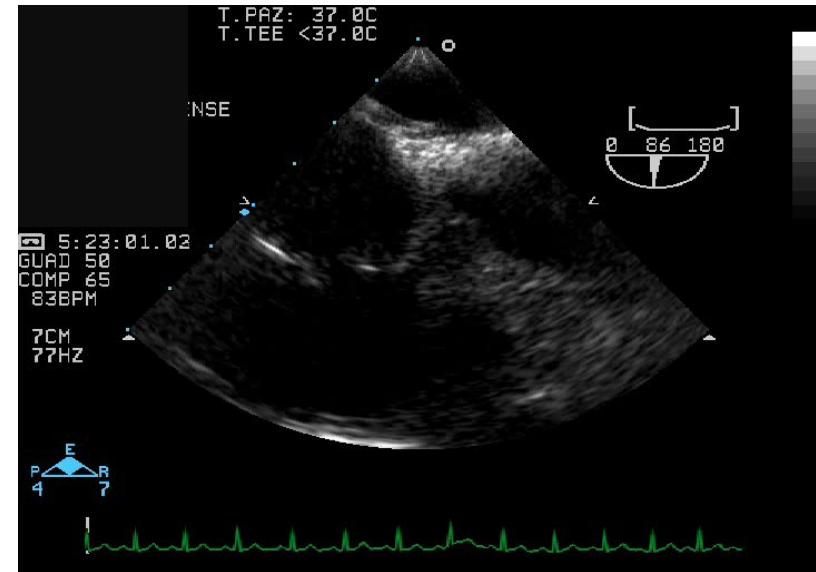
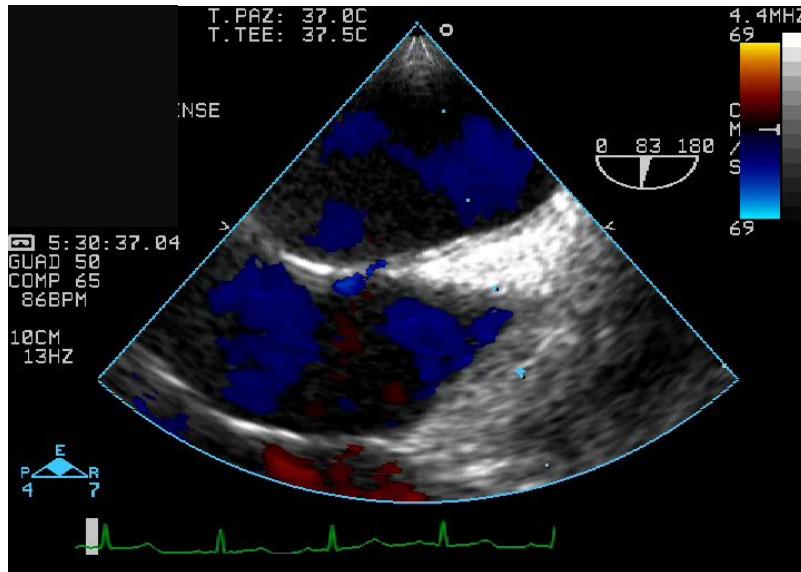


TOE





TOE



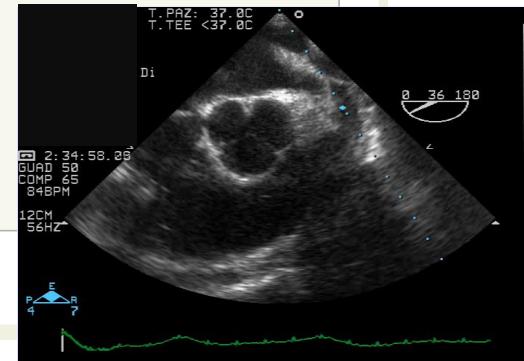
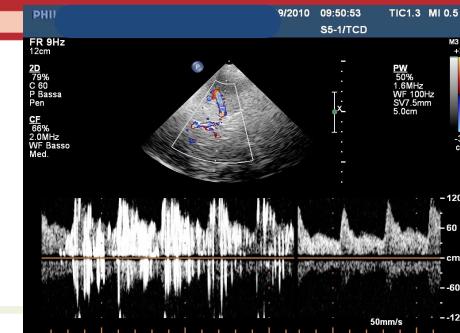
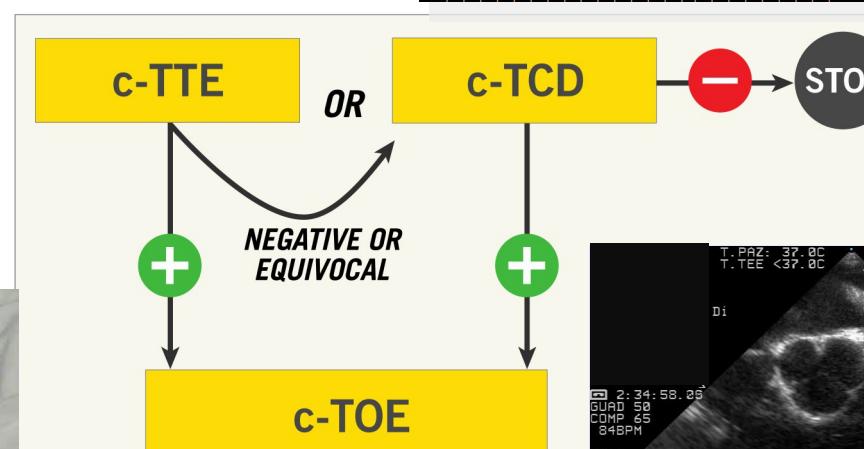
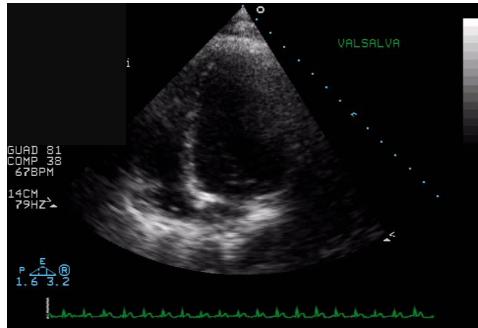


European position paper on the management of patients with patent foramen ovale. General approach and left circulation thromboembolism



Table 2 PFO variables to be assessed for decision making and interventional treatment.

- PFO morphology: size, location, length of the tunnel
- Spatial relationship and distances between the PFO and the aortic root, vena cava, valves and the free walls of the atrium
- Comprehensive evaluation of the atrial septum, including inspection for atrial septal aneurysms, movement, and other atrial septal defects
- Presence/absence of a Eustachian valve and/or Chiari network
- Thickness of the septum primum and secundum
- Colour Doppler evaluation of the shunt at rest and after a Valsalva manoeuvre



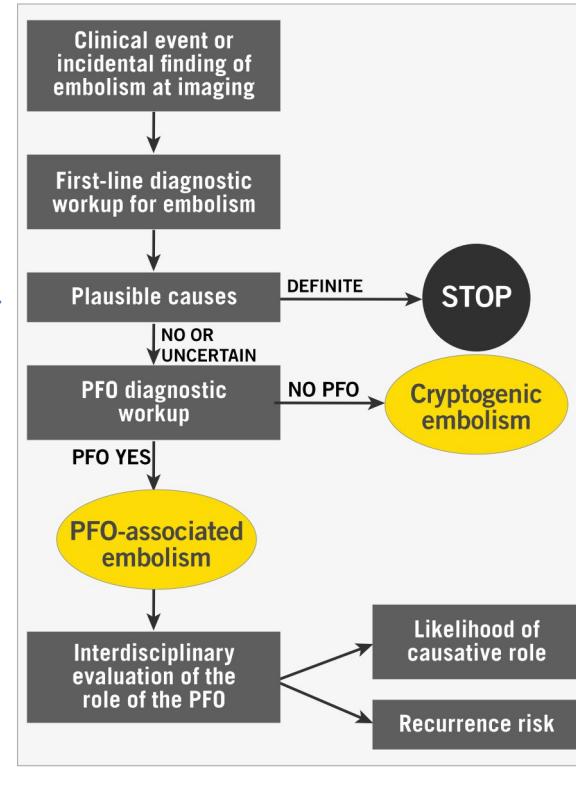
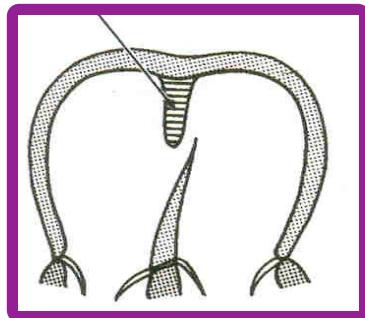


Figure 2 Algorithm for the diagnostic workup of cryptogenic left circulation thromboembolism.



AF

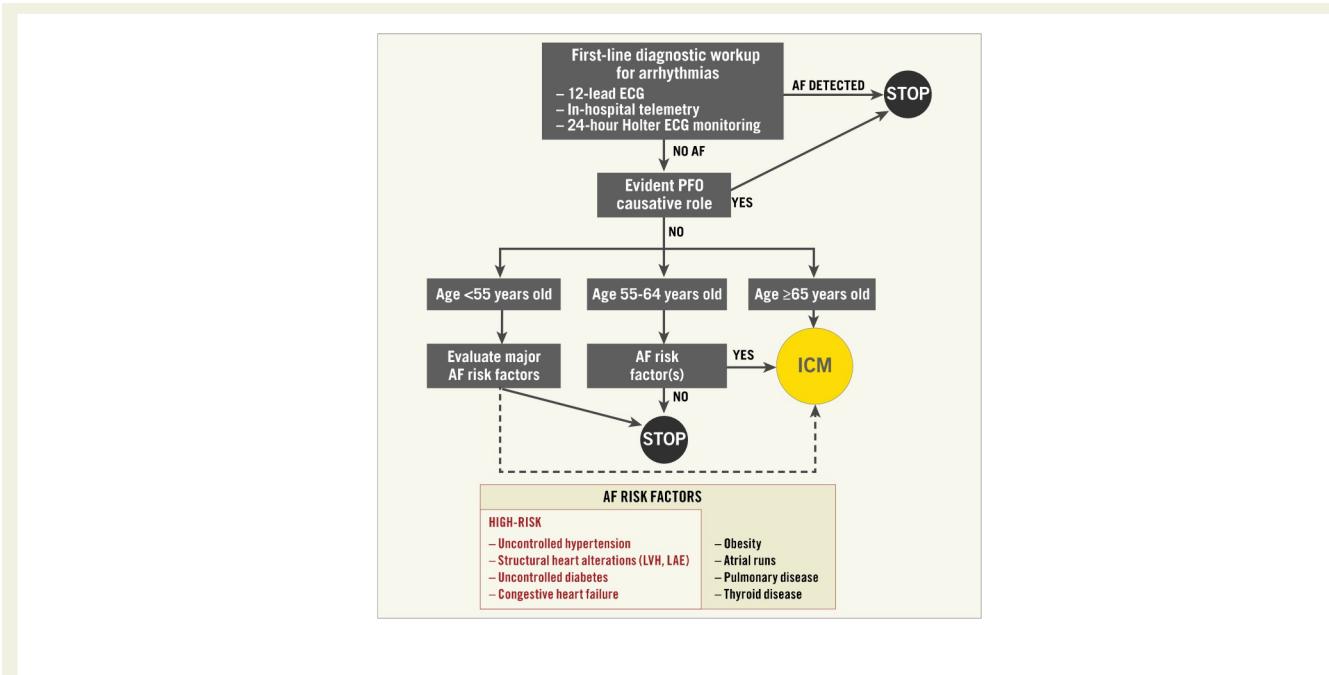


Figure 3 Flow chart for the screening of overt atrial fibrillation in cryptogenic left circulation thromboembolism. The cut-off ages of 55 and 65 years old have been chosen according to data from large epidemiological studies.^{166,173} Patients <55 years may be considered for ICM when they have high clinical suspicion of AF (i.e., ≥2 high-risk factors for AF). ECG: electrocardiography; LAE: left atrium enlargement; LVH: left ventricle hypertrophy.



Table 5 PICO question. Should percutaneous closure of PFO vs. medical therapy be used for secondary prevention of stroke or other left circulation thromboembolism in patients with high-risk PFO features?

Population	Secondary prevention of stroke, TIA, or other left circulation thromboembolism
Intervention	Percutaneous closure of PFO
Comparison	Medical therapy
Main outcomes	Stroke, TIA, death, bleedings, atrial arrhythmias

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 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.

STATEMENTS

The interventional procedure must be proposed to each patient evaluating the individual probability of benefit based on an assessment of both the role of the PFO in the thromboembolic event (Table 4) and the expected results and risks of a lifelong medical therapy. The role of the patient should be proactive, keeping in highest regard his/her values and preferences regarding outcomes and therapy trade-offs, and informing him/her about the uncertainties of their condition.

European position paper on the management of patients with patent foramen ovale. Part II - Decompression sickness, migraine, arterial deoxygenation syndromes and select high-risk clinical conditions

Decompression sickness

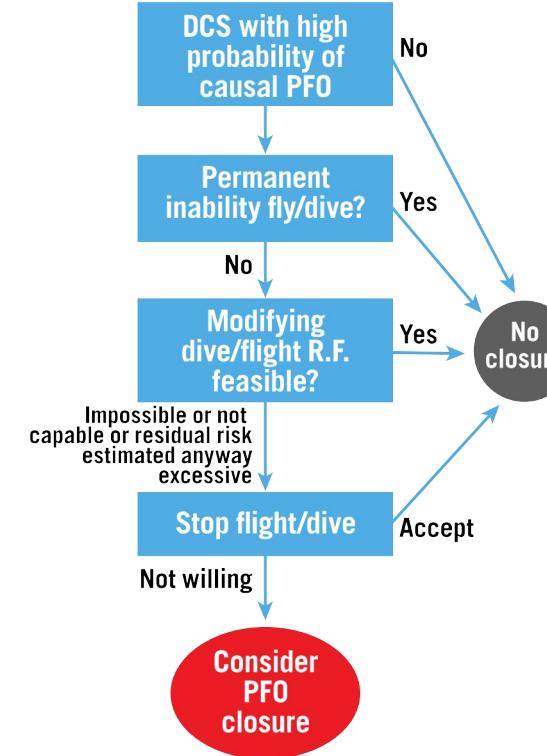


Figure 2 Flow chart for therapeutic decision making for DCS.
 R.F.: risk factors.





Migraine

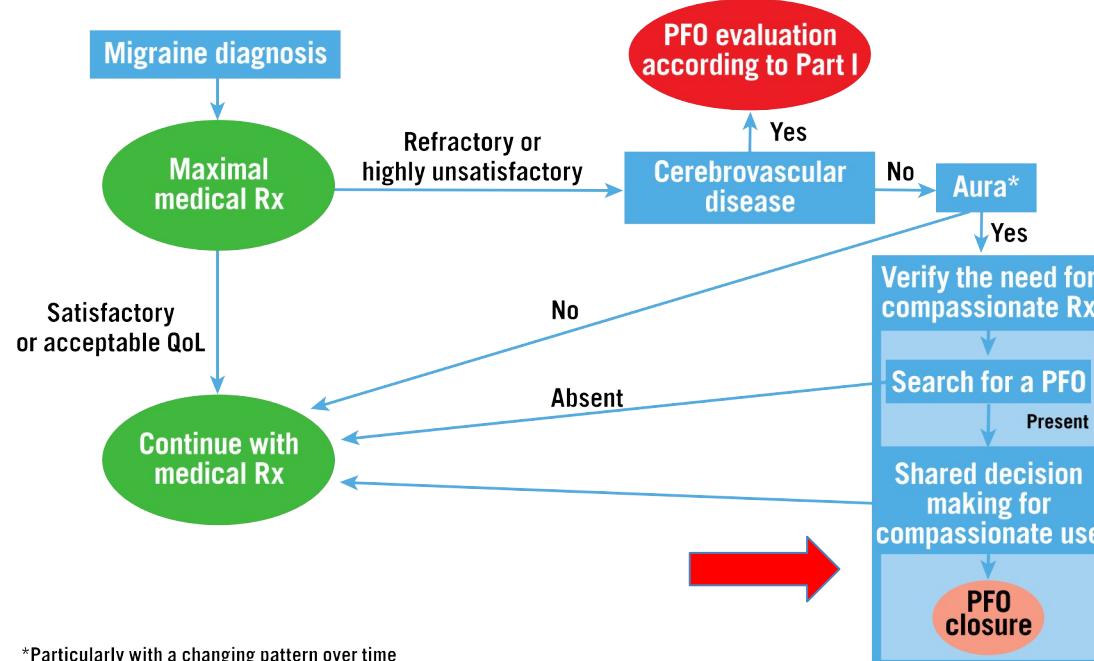


Figure 3 Algorithm for the management of PFO-associated migraine. Rx: therapy.



PRACTICAL SUMMARY 3: ARTERIAL DEOXYGENATION SYNDROMES

WHAT TO DO

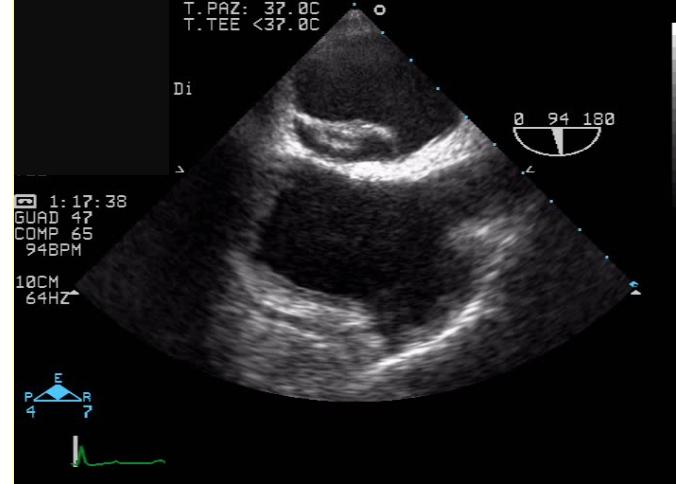
- Individually assess and weigh the role of all factors involved in the desaturation syndrome
- Whenever possible obtain invasive evidence of the PFO role
- Where appropriate, propose PFO closure with shared decision making underscoring the lack of evidence

WHAT NOT TO DO

- Routinely close PFO
 - Close a PFO in the presence of severe chronic pulmonary hypertension
 - Close a PFO without clear evidence of a crucial role in desaturation
-

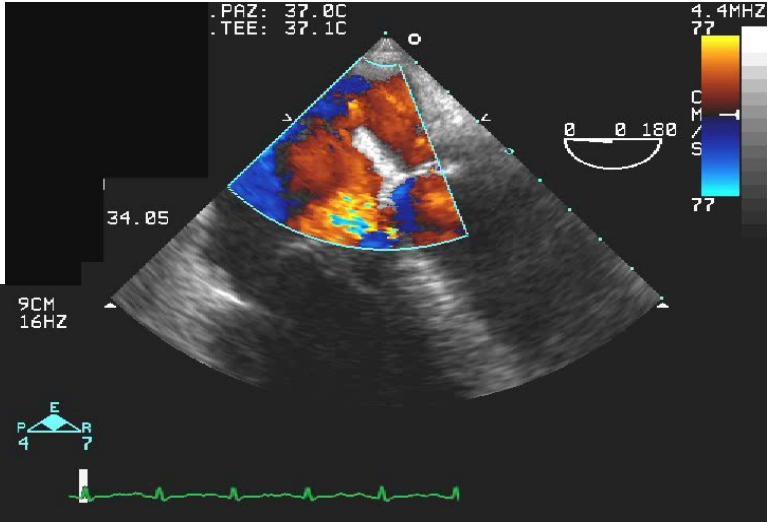
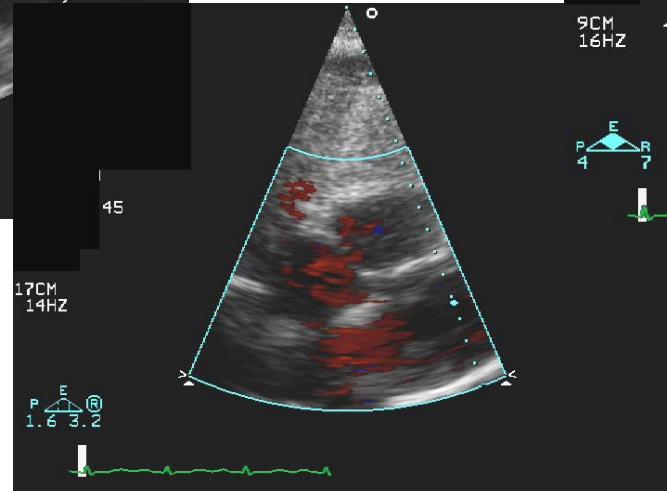
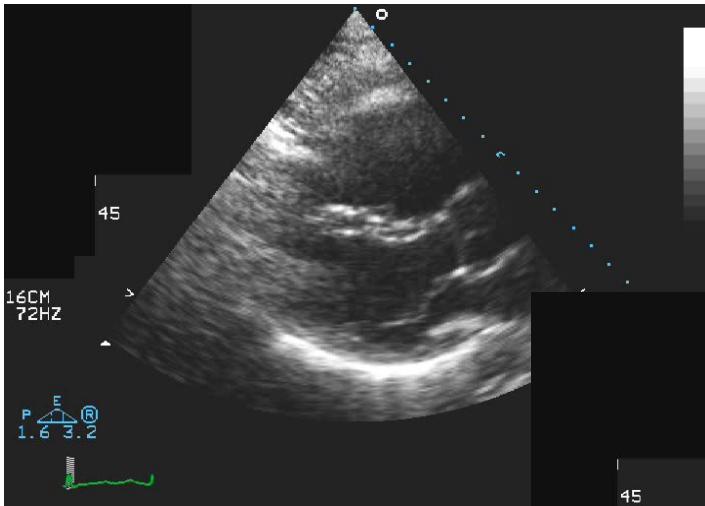


Atrial septal pouch



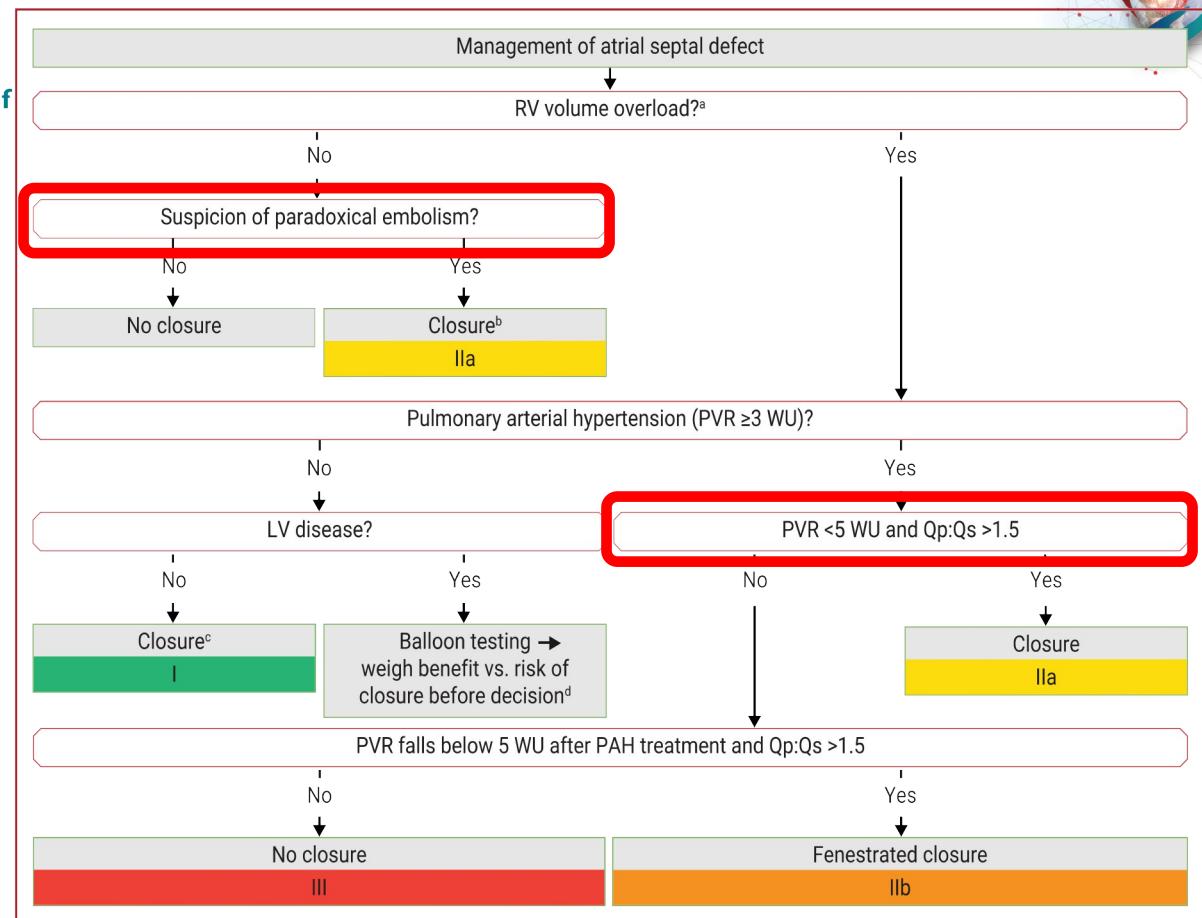


Atrial septal defect



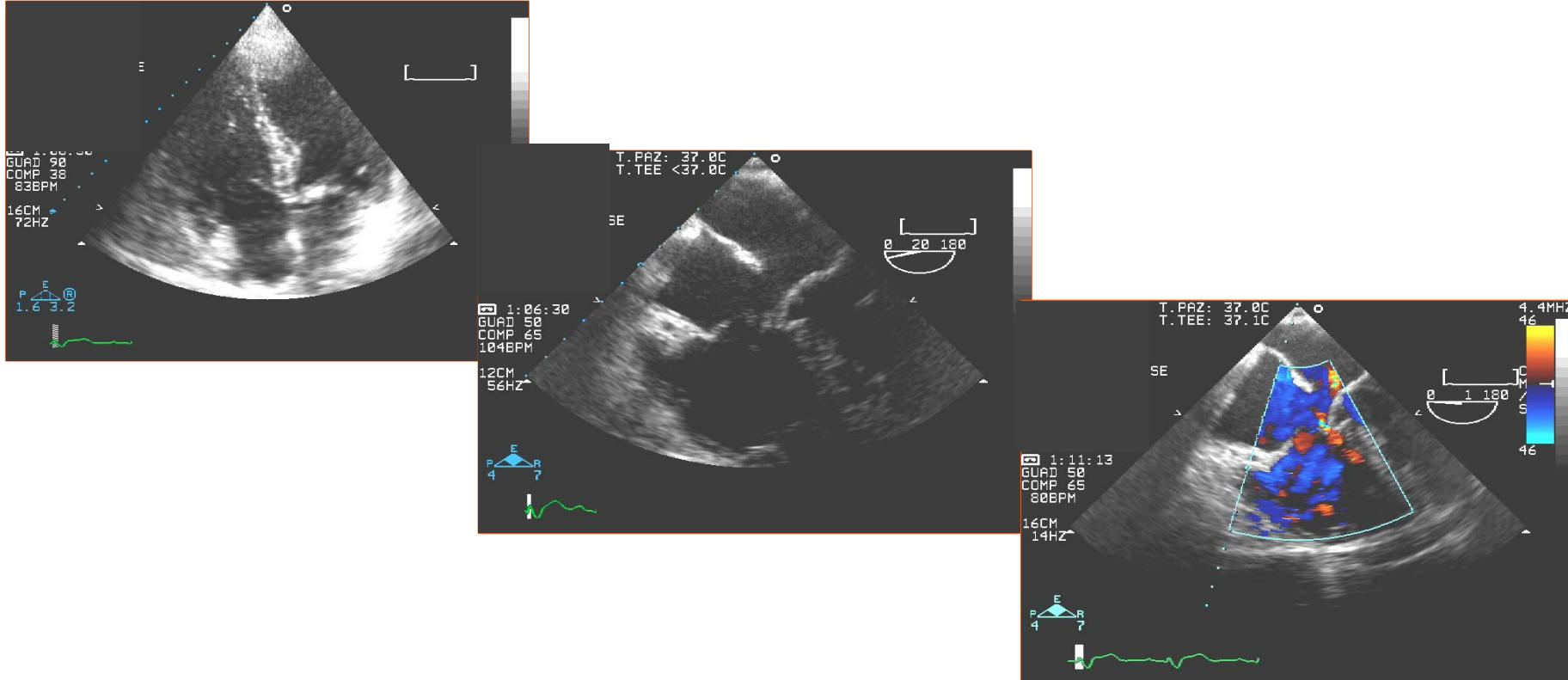


2020 ESC Guidelines for the management of adult congenital heart disease





Atrial septal defect





Study	Year	Device	n	Endpoints	Results	Comments
CLOSURE ¹¹²	2012	STARFlex Septal Closure System	909	Composite of death (0–30 days), neurological death (≥ 31 days), stroke or TIA at 2-year follow-up	Non-significant reduction in primary endpoint (HR 0.78; 95% CI [0.45–1.35]; p=0.37)	Left atrial thrombus formation in closure group Inadequate closure at 2 years
PC Trial ¹³	2013	Amplatzer PFO Occluder	414	Composite of death, stroke, TIA or peripheral embolism at 4.5 years	Non-significant reduction in primary endpoint (HR 0.63; 95% CI [0.24–1.62]; p=0.34)	Underpowered trial High volume of crossover to PFO closure during follow-up
RESPECT ^{18,19} Long-term data published in 2017	2013 Long-term data published in 2017	Amplatzer PFO Occluder	980	Composite of early death, stroke or TIA	Non-significant reduction in primary endpoint at median follow-up 2.1 years (HR 0.49; 95% CI [0.22–1.11]; p=0.08) Long-term follow-up (median 5.9 years) showed significant reduction with closure (HR 0.55; 95% CI [0.31–0.99]; p=0.046)	As treated analysis shows a benefit in favour of closure even at the early timepoint.
CLOSE ²²	2017	11 approved devices (Amplatzer PFO Occluder >50%)	663	Fatal or non-fatal stroke	Significant reduction in stroke with occlusion compared with antiplatelet therapy only (HR 0.03, 95% CI [0-0.26]; p<0.001)	1:1:1 randomisation PFO closure versus antiplatelets versus anti-coagulation
Gore REDUCE ²⁰	2017	Helex Septal Occluder or Cardioform Septal Occluder	664	Co-primary endpoints of clinical stroke and incidence of new brain infarction	Significant reduction in clinical stroke at median follow-up 3.2 years (HR 0.23; 95% CI [0.09–0.62]; p=0.002) Significant reduction in new brain infarction (RR 0.51; 95% CI [0.29–0.91]; p=0.04)	2:1 randomisation to PFO closure
DEFENSE PFO ²¹	2018	Amplatzer PFO Occluder	120	Stroke, vascular death or Major bleeding at 2-year follow-up	Significant reduction in primary endpoint with PFO closure. No events in PFO closure arm versus 12.9% 2-year event rate in medication only arm (p=0.013)	



Tips and tricks: come orientarsi tra i vari dispositivi per la chiusura del forame ovale pervio

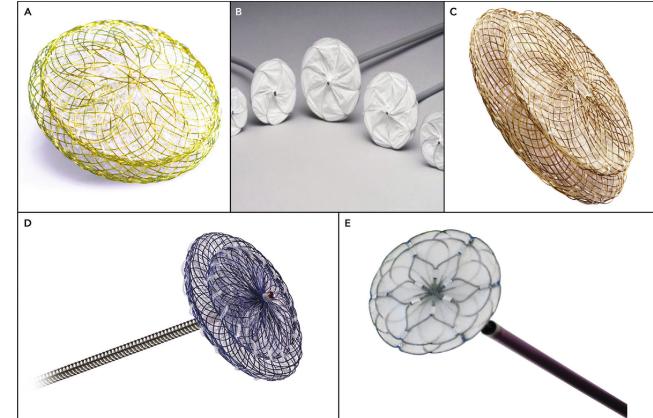
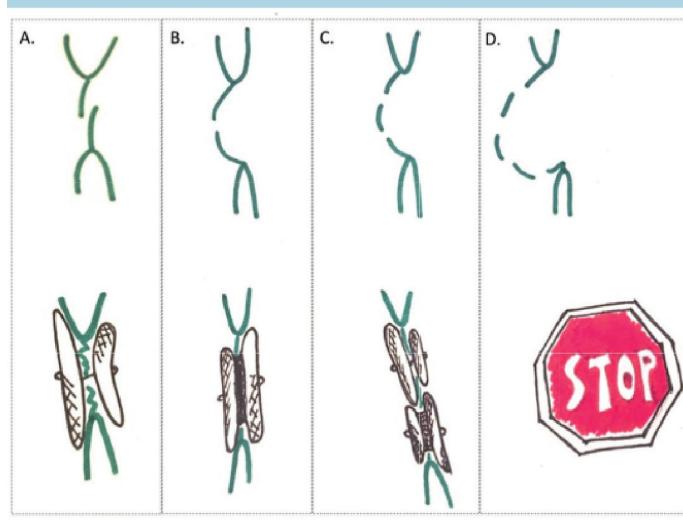
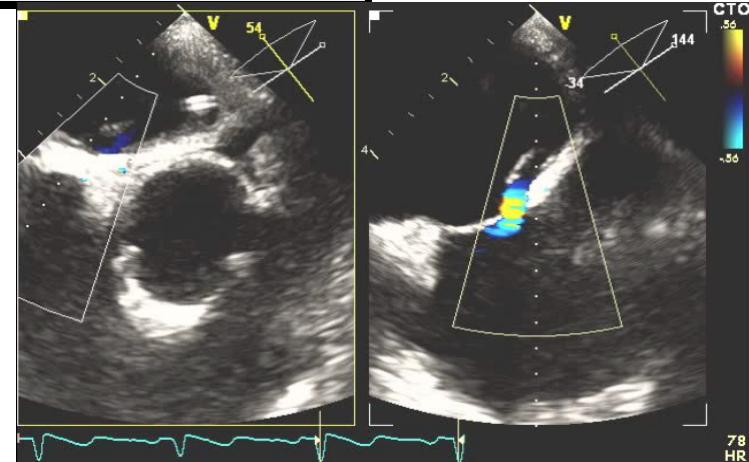
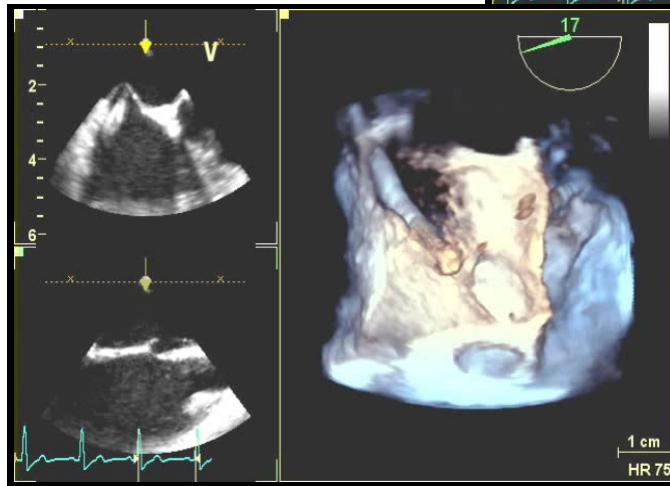
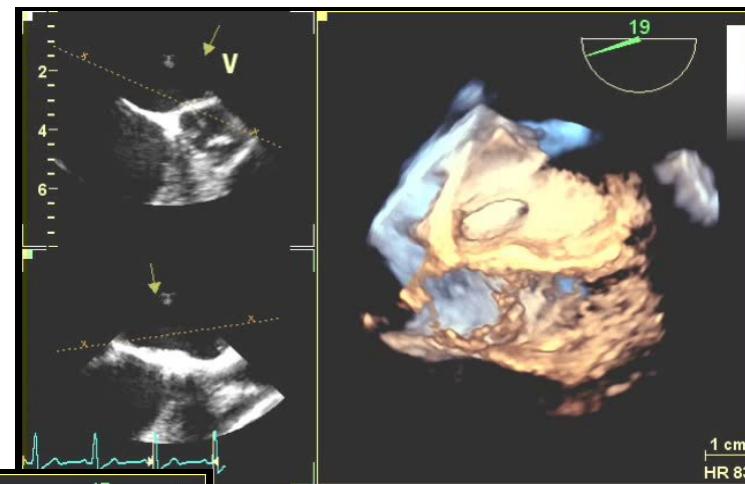
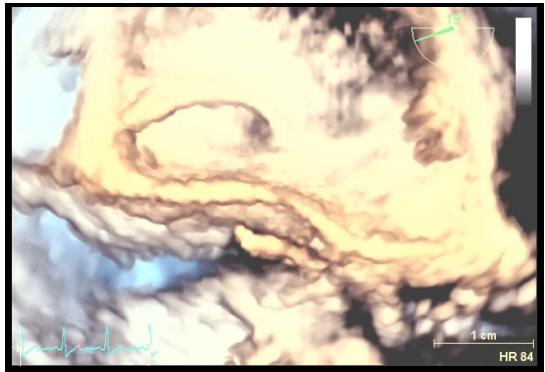
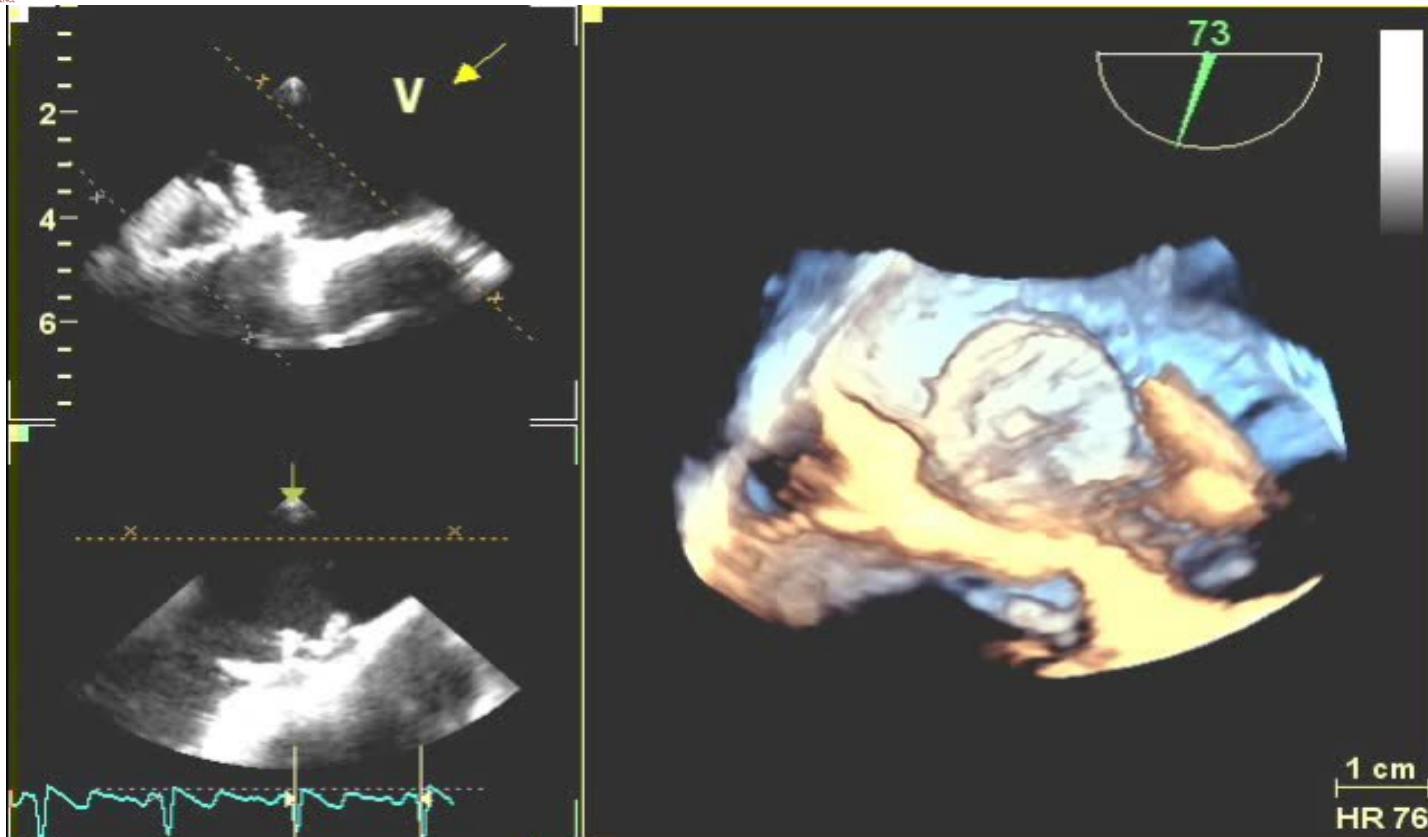
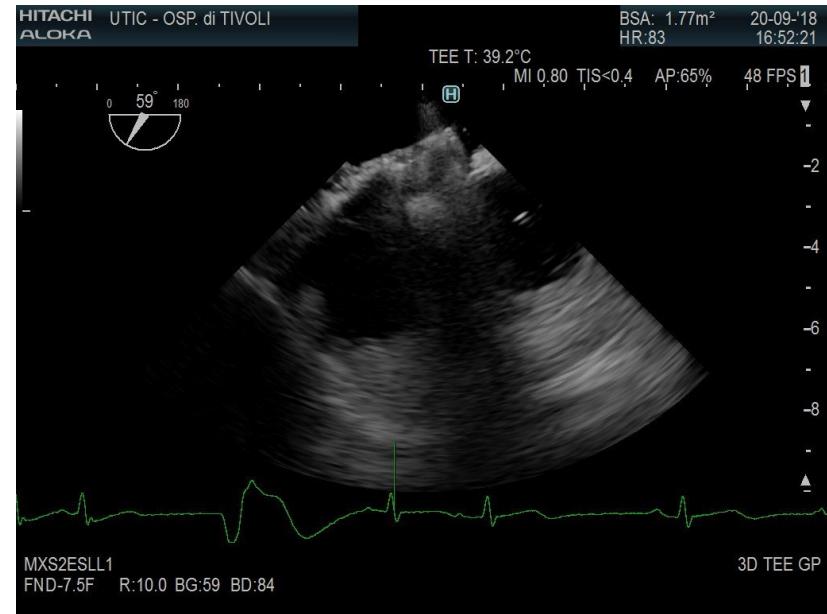
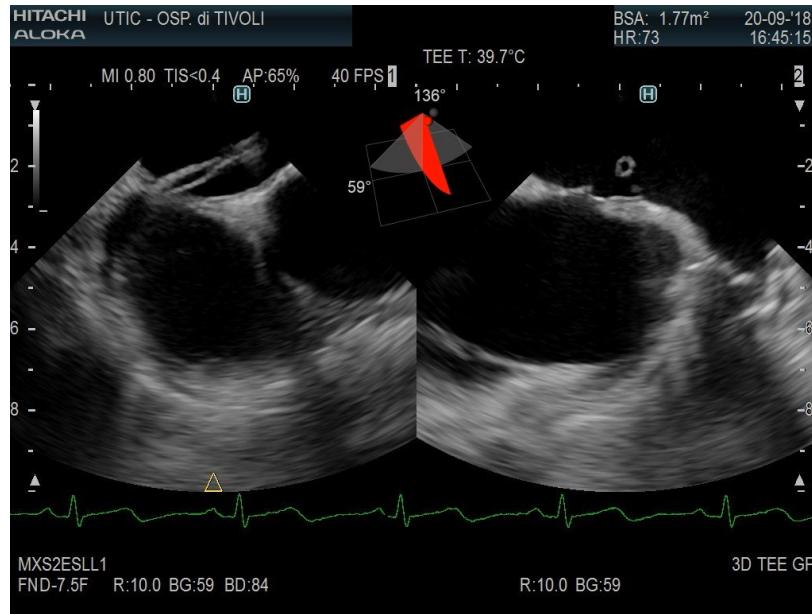
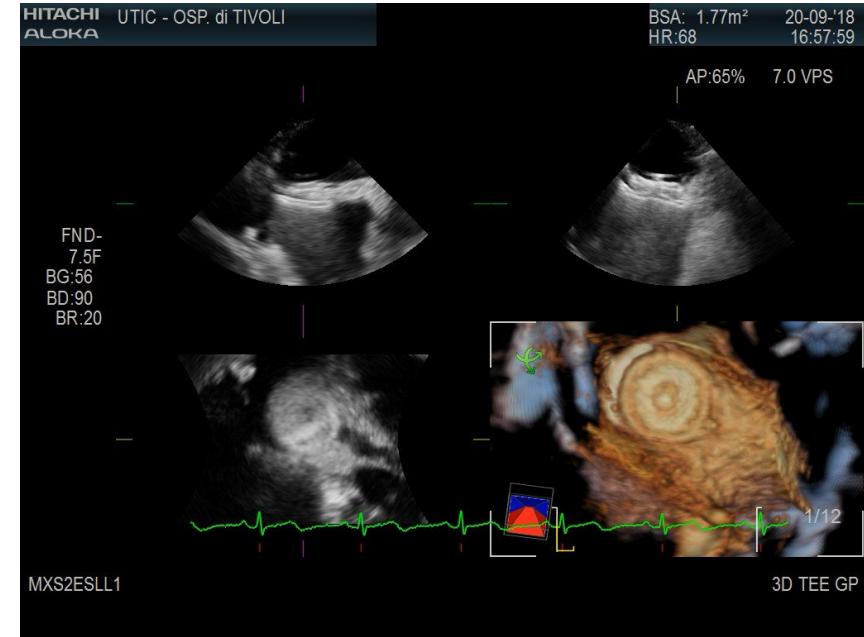
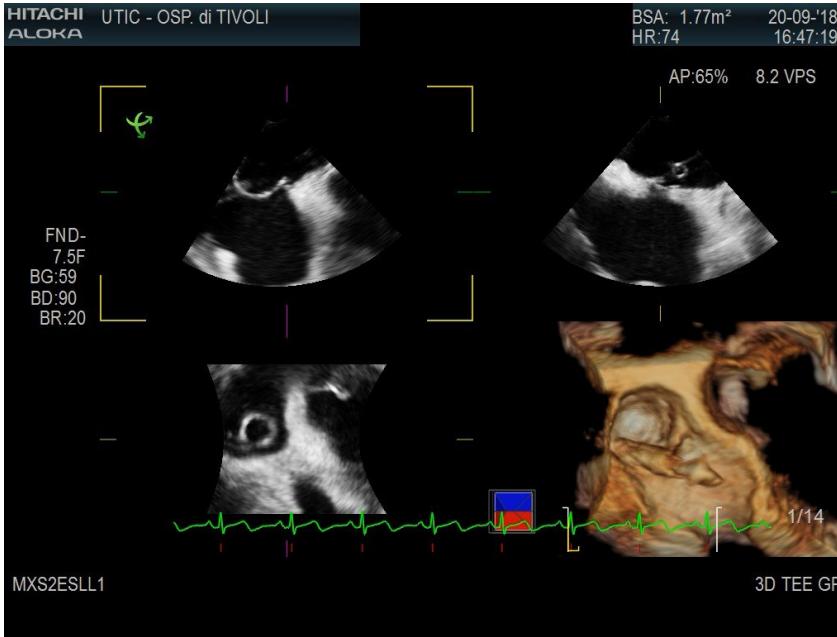


Figura 2. Scelta del dispositivo occlusore in base ad anatomia delle fenestrazioni del setto interatriale. (A) Forame ovale pervio: dispositivo non autocentrante. (B) Unica fenestrazione (difetto interatriale tipo ostium secundum): dispositivo autocentrante tipo Amplatzer Septal Occluder. (C) Due o più fenestrazioni in due sedi separate non chiudibili da un unico dispositivo trattate con dispositivo non autocentrante e dispositivo autocentrante tipo Amplatzer Septal Occluder. (D) Multiple fenestrazioni in multiple sedi dell'aneurisma: chiusura percutanea non raccomandata. Adattata da Ewert et al.⁶.











Novel percutaneous suture-mediated patent foramen ovale closure technique: early results of the NobleStitch EL Italian Registry

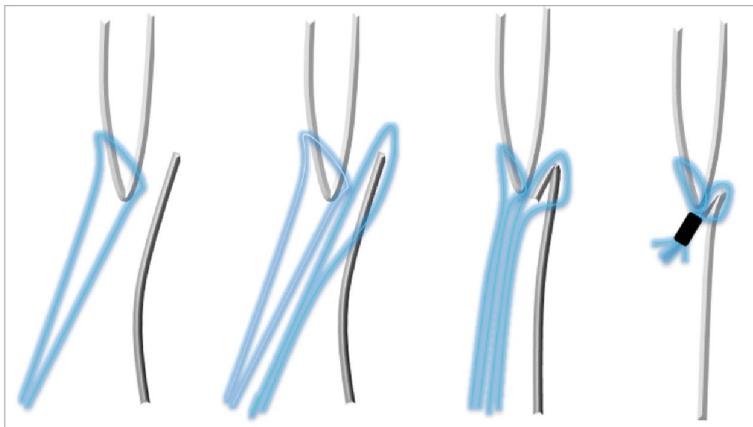


Figure 2. Schematic drawing showing the basic concept of the NobleStitch EL technique. A suture is sequentially pierced through the septum secundum and primum and then the two sutures are bound together.

