PFO What's New?

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Stroke Unit

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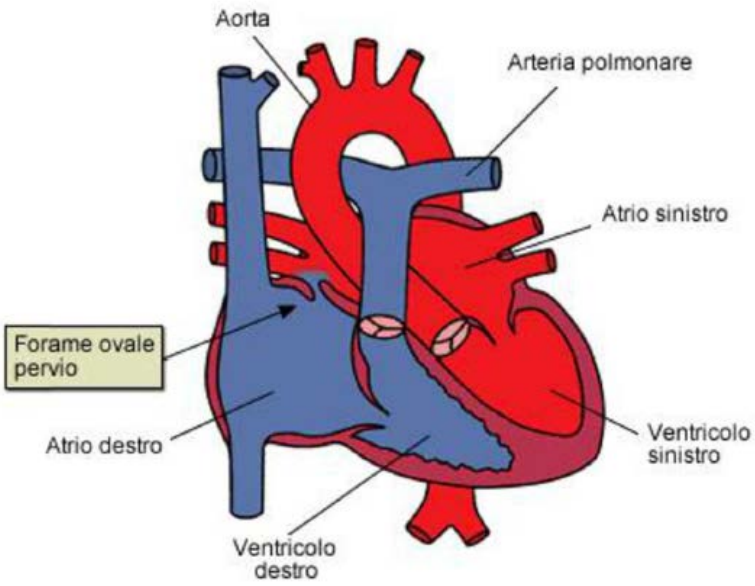
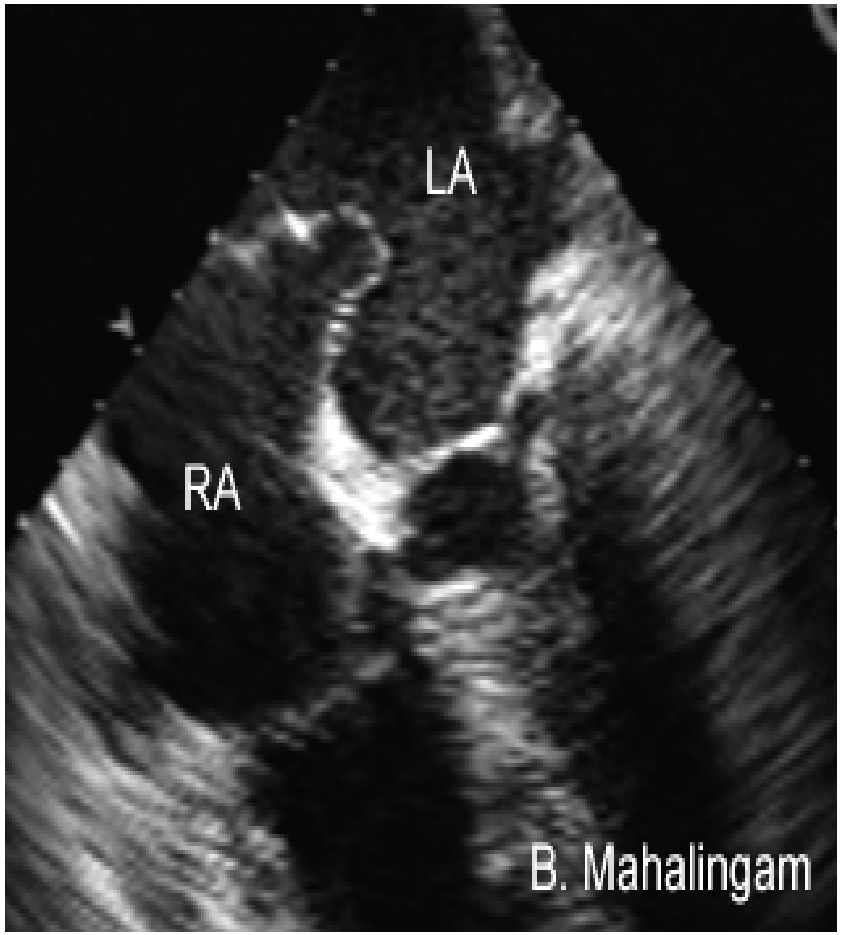
Arcispedale S. Anna Ferrara

Patent foramen ovale (PFO)



- In fetus oxygenated blood returning to the right atrium via the umbilical vein, needs to be delivered to brain and vital organs before further loss of oxygen occurs. To facilitate this rapid transit, an interatrial communication evolved in all mammals, known as the **foramen Ovale**.
- After birth, the foramen ovale flap (the **septum primum**) physiologically closes against the septum secundum when pulmonary vascular resistance and right atrial pressure decrease.
- During the first 2 years of life, closure of the interatrial communication occurs in most cases.
- In 20–25% population this foramen remains patent. A **PFO** is like a trap door between the atria with a spectrum of possible states of flow.
- At rest there may be no flow between the atria, or if the flap is partially open, there may be a left-to-right shunt.
- A transient **right-to-left shunt (RLS)** may occur during certain maneuvers that reverse the inter-atrial pressure gradient by increasing venous return to the right atrium, such as coughing, sneezing, deep breathing and the Valsalva maneuver .

Atrial Septal Aneurism (ASA)



- An ASA is a saccular deformity of the atrial septum defined by base width of 1.5 cm or greater, with at least 1.1 cm excursion into either the left or the right atrium

- An ASA is associated with 15% of PFOs and is often seen with the largest size PFO

Argomento complesso e insidioso… Ma grande opportunità di crescita!

- **Offre prospettiva storica**
- **Insegna a decidere in assenza di certezze**
- **Argomento "ponte" :**
    1. Stroke criptogenico, concetto ESUS e metodi classificativi (TOAST, ASCO, CCSS, …)
    2. Altre condizioni non stroke: embolia periferica, emicrania c/s aura, SCUBA divers, platipnea-ortodeoxia
    3. con cardiologi
- **Principale metodica strumentale di screening: sensibilità 94%, specificità 92%**

Diagnostica ecografica

- Scopo: accertare eventuale shunt dx-sx (RLS), senza definirne la sede: per lo piu' in fossa ovale, talora polmonare
- Decubito supino (*vs* sitting position)
- Insonazione ACM o casco (o finestra occipitale in mancanza di finestra)
- Mdc: 9 cc fisiologica +1 cc aria agitati (o 0.5 sangue+ 9 cc fisiologica + 1 cc aria)
- Esame in 2 tempi: basale poi Valsalva (salvo basale già ampiamente significativo)
- Esame in Valsalva previo training pz: durata 5-10" con riduzione di almeno 25% PSV in ACM
- Corretta sequenza: bolo mdc ☞ latenza di 5" ☞ Valsalva 5-10"

Ricerca shunt cardiopolmonare dx-sx

ELSEVIER

CrossMark

Ultrasound in Med. & Biol., Vol. 40, No. 11, pp. 2637–2641, 2014

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2014.06.017

● *Original Contribution*

ADDING BLOOD TO AGITATED SALINE SIGNIFICANTLY IMPROVES DETECTION OF RIGHT-TO-LEFT SHUNT BY CONTRAST-TRANSCRANIAL COLOR-CODED DUPLEX SONOGRAPHY

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- EX LABORE FRUCTUS -

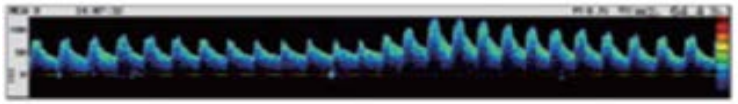
Ricerca shunt cardiopolmonare dx-sx

Metodo di refertazione

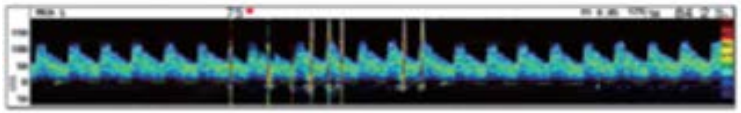
- n.b. definizione di MES o HITS (ampiezza e verso rispetto linea base; durata e suono tipici)
- Venice International Consensus 1999 (Jauss Zanette et al.2000)
- Basale e Valsalva distinti (RLS “permanente” o “latente”)
- Intervallo di tempo prima di insorgenza MES (misurato in cicli ♥)
- Grading RLS (right-to left-shunt): 0 // 1-10 // > 10 // doccia o tendina

Right to left shunt (RLS)

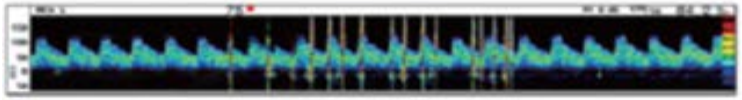
Normal TCD, 0 signals



Right-to-Left Shunt, <10 signals

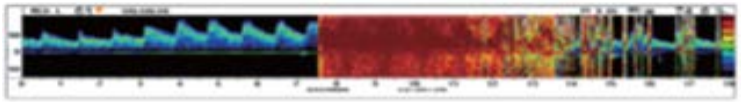


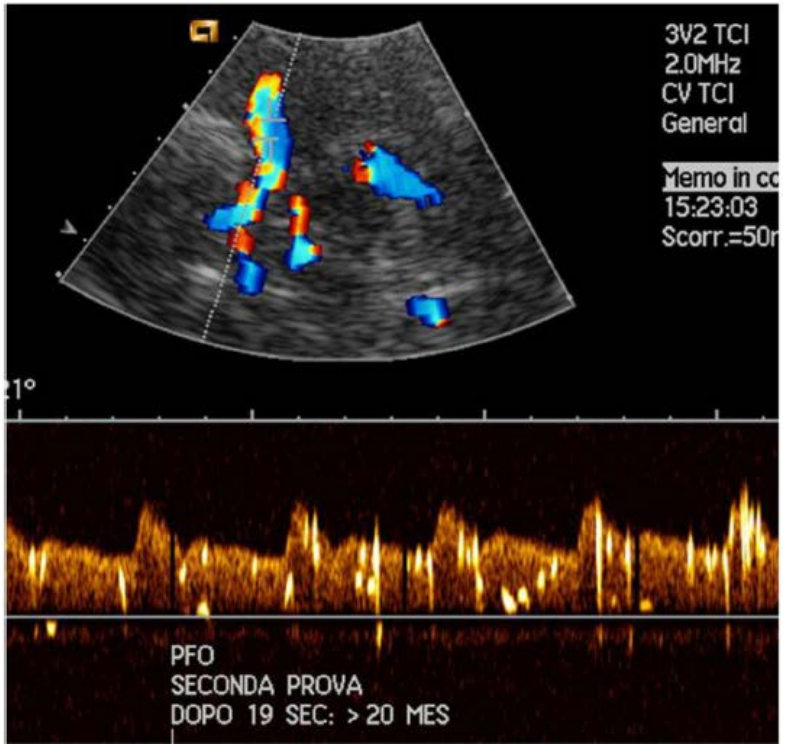
Right-to-Left Shunt, 10-25 signals



Shower pattern (>25 signals)

Curtain pattern





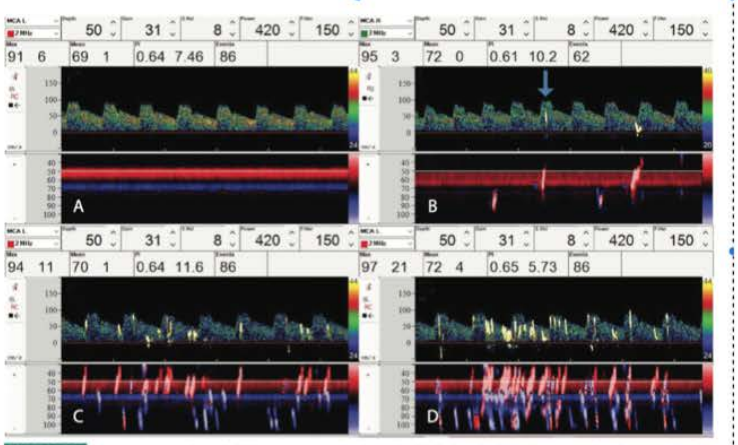


FIGURA 7.3. Monitoraggio unilaterale TCD su arteria cerebrale media (Multi-Dop T*, DWL Compumedics Germany GmbH). A) assenza di MES, categoria 1 shunt assente; B) comparsa di <10 MES, categoria 2 shunt lieve; C) comparsa di >10 MES, categoria 3 shunt moderato; D) effetto doccia, categoria 4 shunt severo. La freccia azzurra indica la comparsa di un MES.

Grading RLS secondo Venice ICC

Diagnosi e ruolo dell'imaging nella valutazione del PFO: doppler transcranico

Claudio Baracchini, Alessio Pieroni, Federica Viaro

TABELLA 7.I. Graduazione dello shunt destro-sinistro con monitoraggio TCD monolaterale o bilaterale.

	Monitoraggio TCD monolaterale	Monitoraggio TCD bilaterale
Categoria 1 Shunt assente	0 MES	0 MES
Categoria 2 Shunt lieve	1-10 MES	1-20 MES
Categoria 3 Shunt moderato	>10 MES	>20 MES
Categoria 4 Shunt severo	Effetto doccia* o Effetto tendina°	Effetto doccia* o Effetto tendina°

*Effetto doccia: quando i MES sono ancora distinguibili tra loro.
°Effetto tendina: quando i MES non si possono più contare e coprono la traccia Doppler.

Spencer Logarithmic Scale Criteria

Tecnologia Power Motion-Mode

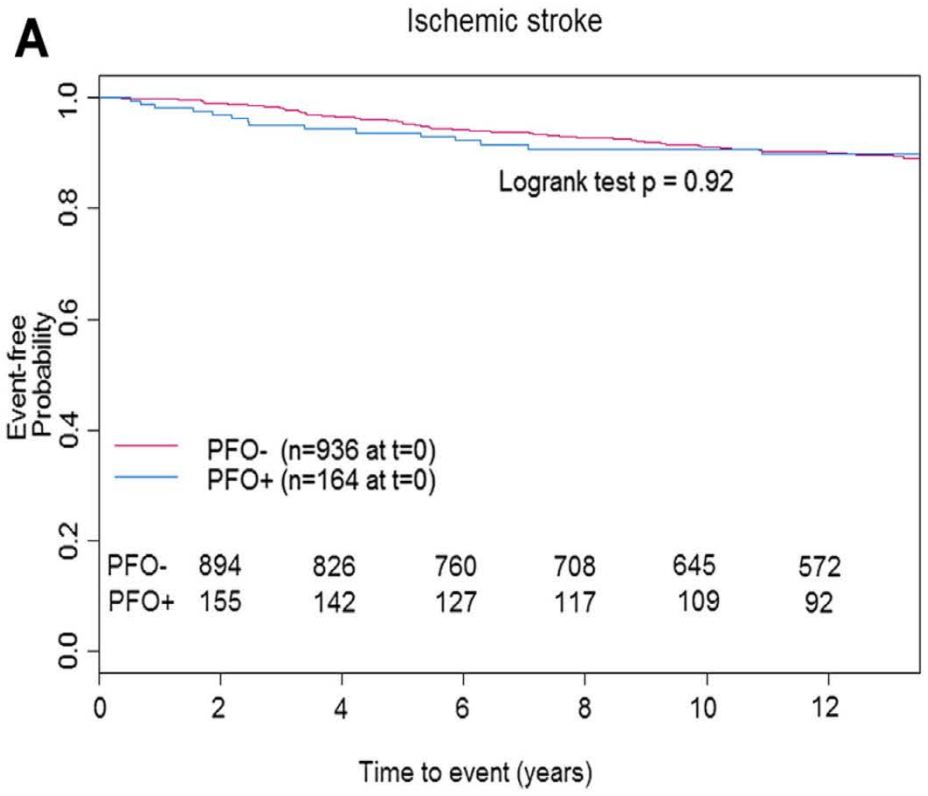
Rileva segnali da piu' volumi campione a diverse profondità

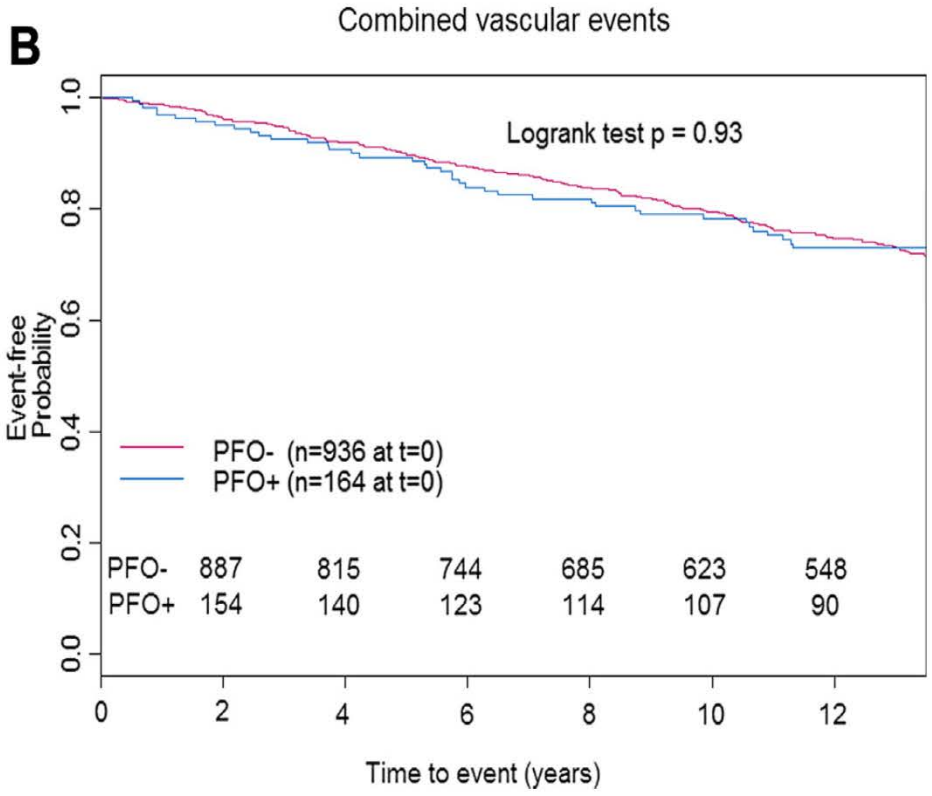
Piu' classi di RLS, ma metodo meno "immediato"

TABELLA 7.II. Graduazione dello shunt destro-sinistro con monitoraggio power M-mode bilaterale.

	Monitoraggio power M-mode bilaterale
Grado 0	0 MES
Grado I	1-10 MES
Grado II	11-30 MES
Grado III	31-100 MES
Grado IV	101-300 MES
Grado V	>300 MES

PFO not associated with increased stroke risk in the NOMAS population





Di Tullio MR et al. *J Am Coll Cardiol* 2013;62:35-41

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Early conceptual understanding of PFO pathogenicity

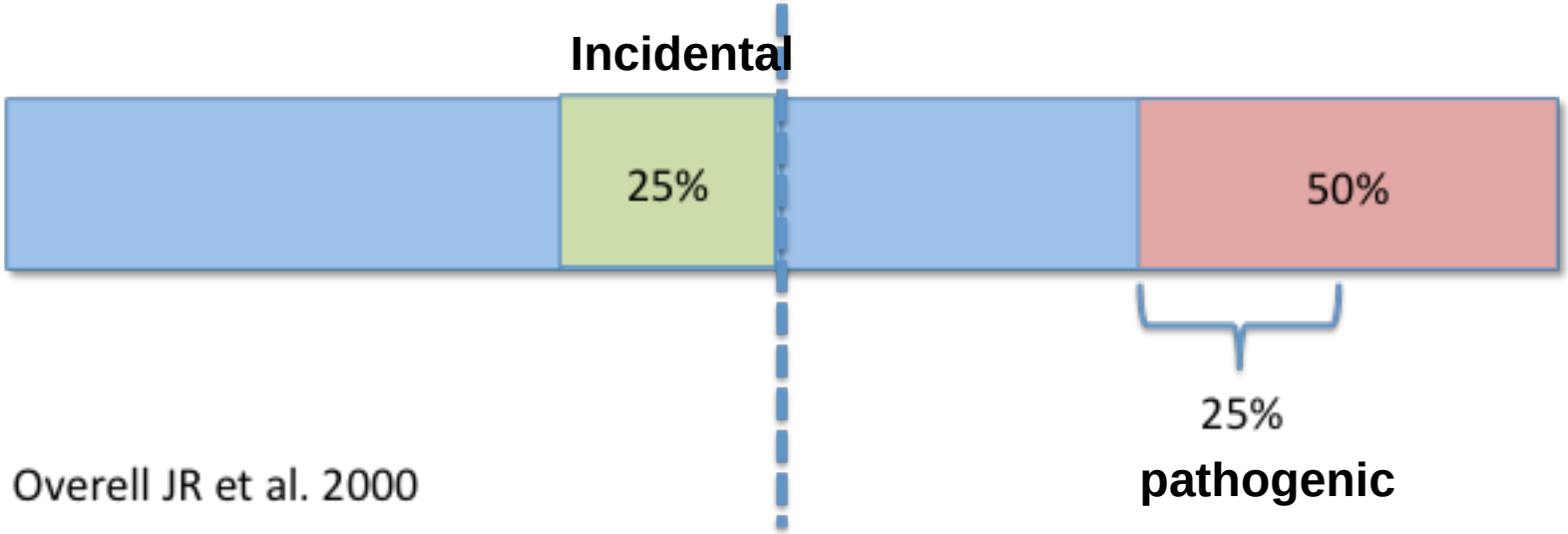
…in younger patients with cryptogenic stroke*,

all PFOs are pathogenic

Prevalence of PFO

- General population
- Cryptogenic stroke

(Same age distribution as the general population)



Overell JR et al. 2000

Risk of Paradoxical Embolism (RoPE) score

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

Kent DM et al for the RoPE Investigators. *Neurology* 2013;81:619-625

An index to identify the likelihood that a PFO is causal for the index stroke

	Cryptogenic stroke (n = 3,023)			CS patients with PFO (n = 1,324)	
RoPE score	No. of patients	Prevalence of patients with a PFO, % (95% CI)[a]	PFO-attributable fraction, % (95% CI)[a]	No. of CS patients with PFO[a]	Estimated 2-y stroke/TIA recurrence rate (Kaplan-Meier), % (95% CI)
0-3	613	23 (19-26)	0 (0-4)	108	20 (12-28)
4	511	35 (31-39)	38 (25-48)	148	12 (6-18)
5	516	34 (30-38)	34 (21-45)	186	7 (3-11)
6	482	47 (42-51)	62 (54-68)	236	8 (4-12)
7	434	54 (49-59)	72 (66-76)	263	6 (2-10)
8	287	67 (62-73)	84 (79-87)	233	6 (2-10)
9-10	180	73 (66-79)	88 (83-91)	150	2 (0-4)

Kent DM et al for the RoPE Investigators. *Neurology* 2013;81:619-625

Prevalence of PFO

- General population

- Cryptogenic stroke

Age > 70y with hypertension, diabetes, prior stroke, current smoker, no cortical infarcts
i.e. **RoPE score = 0**

Kent DM et al. Neurology 2013

Prevalence of PFO

- General population

- Cryptogenic stroke

Age < 30y with no hypertension, no diabetes, no history of stroke, nonsmoker, cortical infarcts
i.e. **RoPE score = 10**

Kent DM et al. Neurology 2013

PFO e LES

Lupus (2015) 0, 1–6
http://lup.sagepub.com

CONCISE REPORT

Brain unidentified bright objects ("UBO") in systemic lupus erythematosus: sometimes they come back. A study of microembolism by cMRI and Transcranial Doppler ultrasound

A Bortoluzzi[1], M Padovan[1], C Azzini[2], A De Vito[2], F Trotta[1] and M Govoni[1]
[1]Department of Medical Science, Section of Rheumatology, University of Ferrara and Azienda Ospedaliero Universitaria Sant'Anna di Cona, Ferrara, Italy; and [2]Department of Neuroscience, Section of Neurology, Azienda Ospedaliero Universitaria Sant'Anna di Cona, Ferrara, Italy

PFO e LES

Table 1 List of comorbidities and thrombophilic state of our NPSLE and SLE patients

	NPSLE (no. of patients)	*SLE (no. of patients)*
	16	7
Comorbidities		
Hypertension	2	2
Dyslipidemia	1	1
Carotid atherosclerosis	1	–
Valvular heart disease[a]	1	–
Smoking	1	1
Thrombophilic antibodies		
aPL	4	–
LA	1	–
aPL and LA	2	2

[a]Including mitral valve prolapse.
NPSLE: systemic lupus erythematosus with neuropsychiatric involvement; SLE: systemic lupus erythematosus; aPL: antiphospholipid antibodies; LA: Lupus anticoagulant.

cMRI and Transcranial Doppler ultrasound in SLE
A Bortoluzzi *et al.*

Table 2 Correlation between the presence of MES, PFO and WMHL in NPSLE and SLE patients

Type first NP event	*NPSLE[a] no. of pts (%) 16*	*SLE no of pts (%) 7*	p *value*
TCD evaluation			
MES +	11/16 (68.7)	1/7 (14.2)	0.027
TTE evaluation			
PFO +	11/16 (68.7)	1/7 (14.2)	0.027
cMRI			
WMHL +	[illegible]	2/7 (28.5)	
WMHL + MES +	9/16 (56.2)	1/7 (14.2)	Ns
WMHL + MES −	4/16 (25)	1/7 (14.2)	Ns
WMHL − MES +	1/16 (6.25)	0 (0)	Ns
WMHL − MES −	2/16 (12.5)	5/7 (71.4)	Ns

[a]Fifteen diffuse, one focal.
TCD: transcranic Doppler ultrasound; MES: microembolic signals; PFO: patent foramen ovale; cMRI: conventional magnetic resonance imaging; WMHL: white matter T2-hyperintense small punctuate lesions; NPSLE: systemic lupus erythematosus with neuropsychiatric involvement; SLE: systemic lupus erythematosus.


WHAT'S
NEW

2013

two and a half *negative* RCT on closure *vs* medical therapy

CLOSURE 1 Furlan AJ et al. *New Engl J Med*. 2012:366:

PC Trial Meier B et al. *New Engl J Med*. 2013;368:1083-91

RESPECT Carroll JD et al. *New Engl J Med*. 2013;368:1092-110

…closing a PFO after a cryptogenic ischemic stroke is not advisable

2013

two and a half *negative* RCT on closure *vs* medical therapy

CLOSURE 1 Furlan AJ et al. *New Engl J Med*. 2012:366:

PC Trial Meier B et al. *Ne*

RESPECT Carroll JD e

…closing a PFO after a cryptogenic ischemic stroke is not advisable

2017

two and a half *positive* RCT on closure *vs* medical therapy

RESPECT long-term Saver Jl et al. *New Engl J Med.* 2017;377:1022-1032

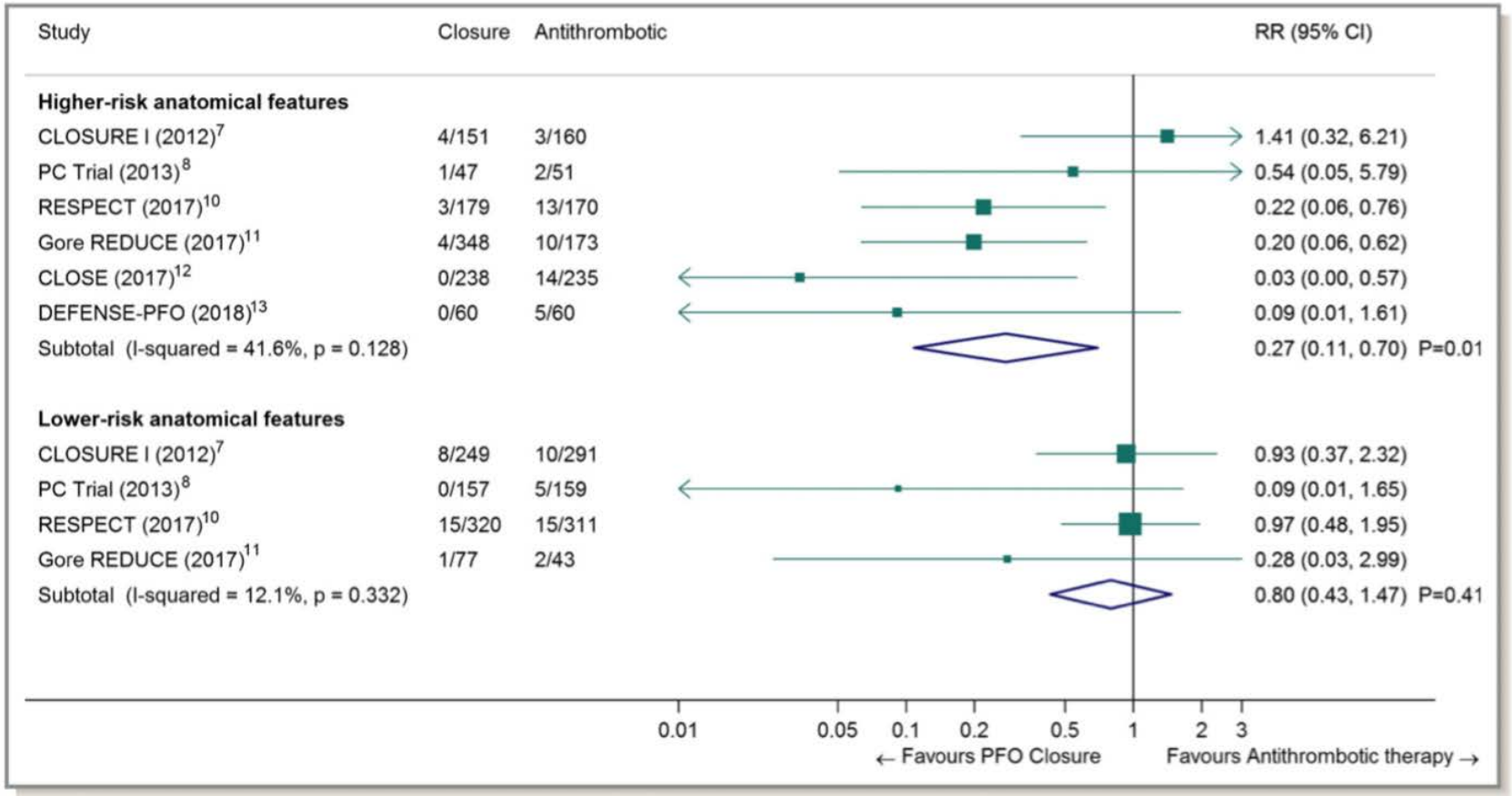
GORE REDUCE Søndergaard L et al. *New Engl J Med.* 2017;377:1033-1042

CLOSE Mas JL et al. *New Engl J Med.* 2017;377:1011-1021

DEFENSE PFO Lee PH et al. *J Am Coll Cardiol* 2018;71:2335-2342

…PFO closure, a "mechanical vaccination" against stroke

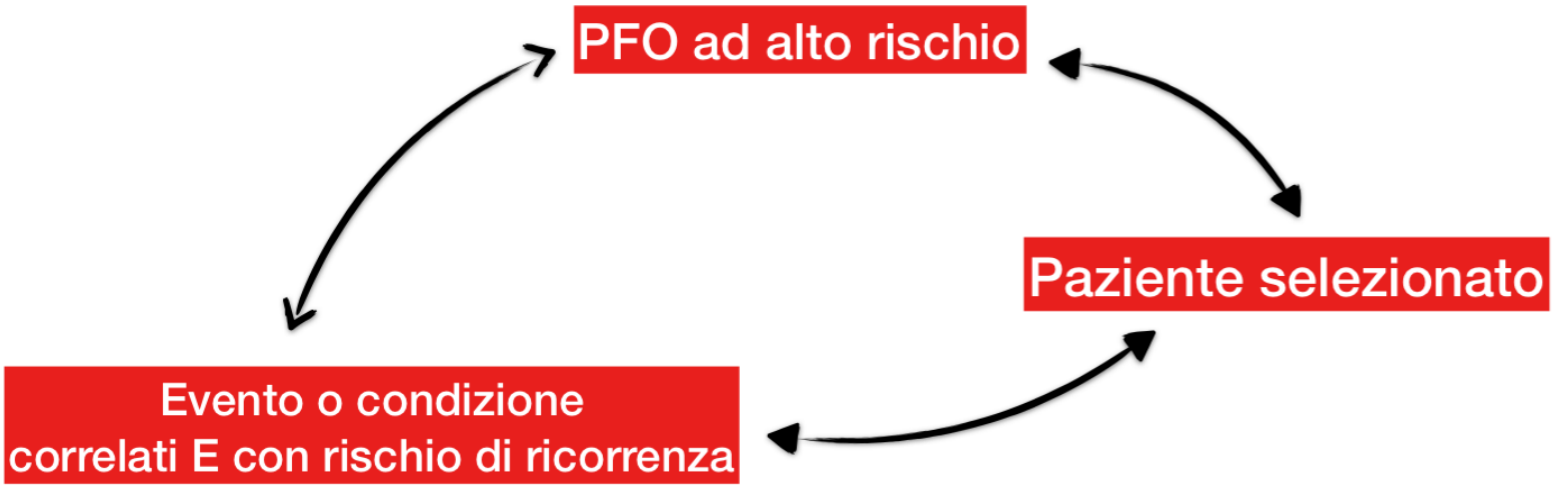
Importanza di un corretto grading:
1.Chiusura di PFO in pz 60 anni o meno con ictus criptogenico previene piu' ictus rispetto a tp medica
2. Il vantaggio e' maggiore se PFO e' ampio



Caratteristiche anatomiche correlate a maggior rischio di ricorrenza di ictus

- Oltre al **grado** di shunt (cioè **ampiezza** PFO): aspetti funzionali come shunt dx-sx in respirazione libera (al **basale** in TCD)
- Associazione con Aneurisma Setto Interatriale (ASA)
- Altre persistenze embrionali (rete di Chiari, valvola Eustachio prominente)
- Variabili di fossa ovale: fusione irregolare dei septa ▶più' orifizi; grado overlapping dei setti▶lunghezza tunnel, ecc.
- Sono aspetti definiti da eco TE (che ha anche compito di confermare sede dello shunt)

Per la prevenzione dell'ictus,
il maggior vantaggio dalla chiusura di un PFO si ottiene combinando una serie di selezioni



Altre condizioni cliniche con rischio di ricorrenza poste in relazione a PFO

- Embolia periferica
- Malattia da decompressione in SCUBA divers
- Emicrania/emicrania con aura
- TVP/TEP in trombofilia
- Sindrome Platipnea ortodeoxia
- Come orientarsi sul ruolo del PFO secondo letteratura?
- Strumenti a disposizione: linee guida aggiornate, consensus, Rope score

Take home message

- **Giovane**
- **Evento Neurologico documentato**
- **Caratteristiche anatomiche di maggiore rischio**

LE EVIDENZE DISPONIBILI CON FOLLOW-UP A LUNGO TERMINE SUPPORTANO IN MODO SOLIDO L'EFFICIACIA E SICUREZZA DELLA PROCEDURA DI CHIUSURA PERCUTANEA DEL FORAME OVALE PERVIO


THIS IS NOT THE END.
We are moving toward a grand and glorious finish.

A quale pazienti proporre la chiusura del PFO?

European Position Paper (2018)

ESC European Society of Cardiology

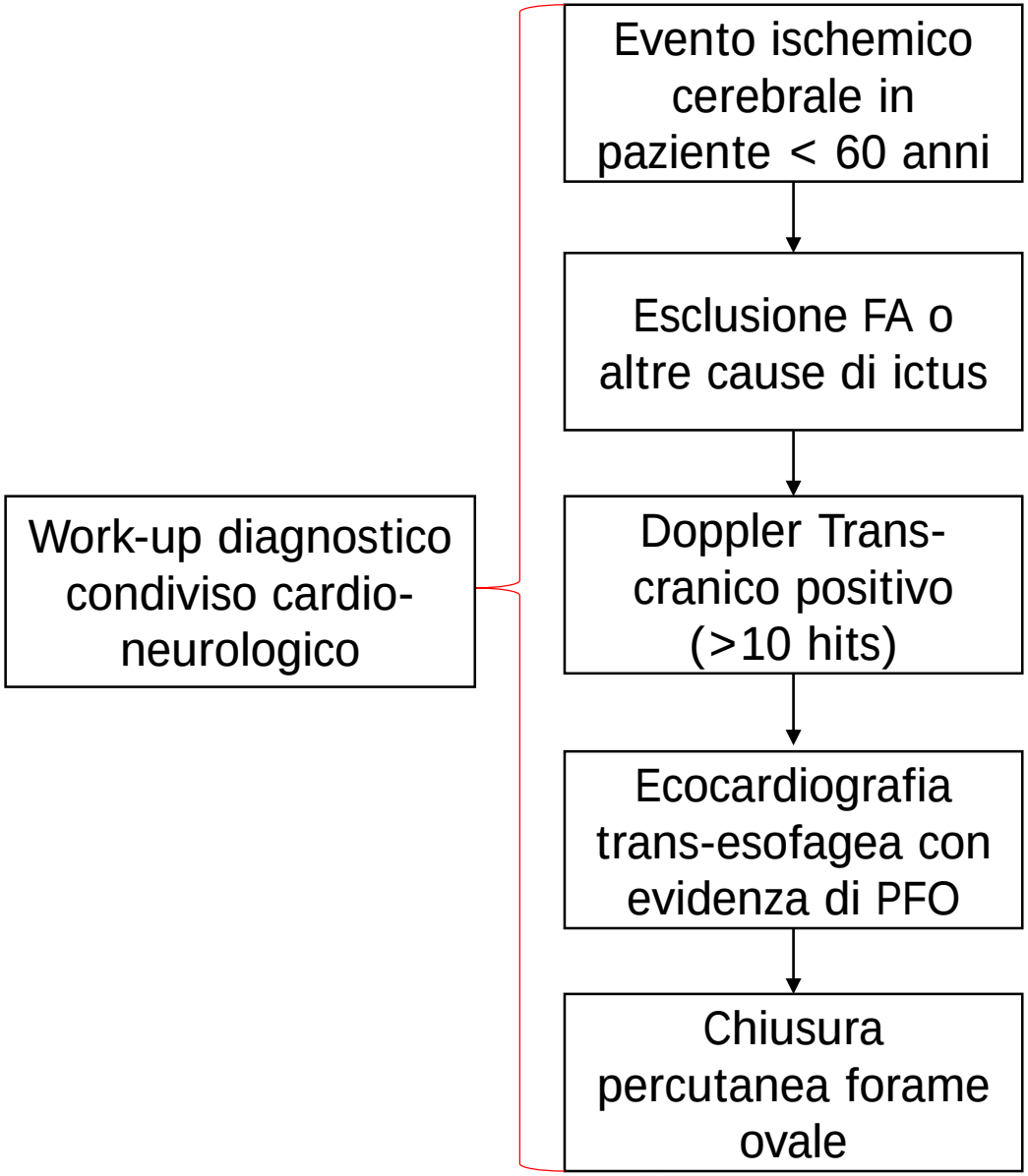
European Heart Journal (2018) 00, 1–14
doi:10.1093/eurheartj/ehy649

EXPERT REVIEW

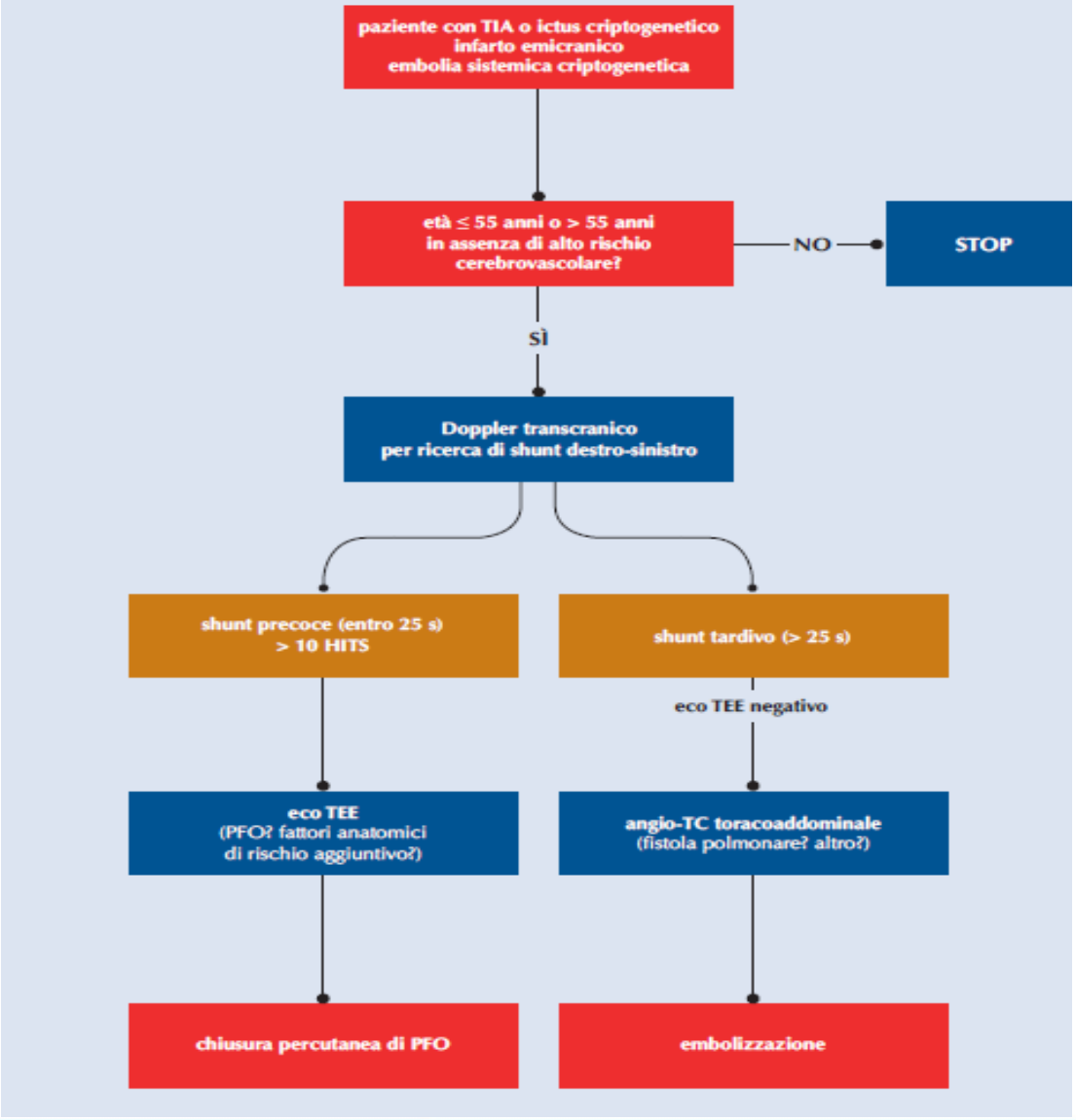
European position paper on the management of patients with patent foramen ovale. General approach and left circulation thromboembolism

Christian Pristipino[1]*, Horst Sievert[2,3], Fabrizio D'Ascenzo[4], Jean Louis Mas[5], Bernhard Meier[6], Paolo Scacciatella[4], David Hildick-Smith[7], Fiorenzo Gaita[4], Danilo Toni[8], Paul Kyrle[9], John Thomson[10], Genevieve Derumeaux[11], Eustaquio Onorato[12], Dirk Sibbing[13], Peter Germonpré[14], Sergio Berti[15], Massimo Chessa[16], Francesco Bedogni[16], Dariusz Dudek[17], Marius Hornung[2], and Jose Zamorano[18], 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)

PDTA FOP Emilia Romagna



FLOWCHART DI AVVIO DELL'ITER DIAGNOSTICO-TERAPEUTICO PER PFO



Prevalence of patent foramen ovale in cryptogenic transient ischaemic attack and non-disabling stroke at older ages: a population-based study, systematic review, and meta-analysis

Sara Mazzucco, Linxin Li, Lucy Binney, Peter M Rothwell, on behalf of the Oxford Vascular Study Phenotyped Cohort

Trials clinici su ictus criptogenico in PFO finora hanno escluso età > 60 anni

Altre patogenesi di ictus competono con ictus da PFO, che sono teoricamente comunque possibili

D'altronde TVP, immobilità, TEP, ipercoagulabilità sono piu' frequenti all'avanzare dell'età

↓

TCD per PFO si dimostra fattibile e sicuro in ultra-60enni con TIA e minor stroke

Anche in anziani la prevalenza di PFO è superiore se ictus criptogenico

Attuale gap di conoscenza riguardo indicazioni a chiusura in ultra-60y: valutazione caso per caso

PFO e prevenzione secondaria

Practice advisory update summary: Patent foramen ovale and secondary stroke prevention

Report of the Guideline Subcommittee of the American Academy of Neurology

Steven R. Messé, MD, Gary S. Gronseth, MD, David M. Kent, MD, MSc, Jorge R. Kizer, MD, MSc, Shunichi Homma, MD, Lee Rosterman, DO, John D. Carroll, MD, Koto Ishida, MD, Navdeep Sangha, MD, and Scott E. Kasner, MD, MSCE

Neurology® 2020;94:1-10. doi:10.1212/WNL.0000000000009443

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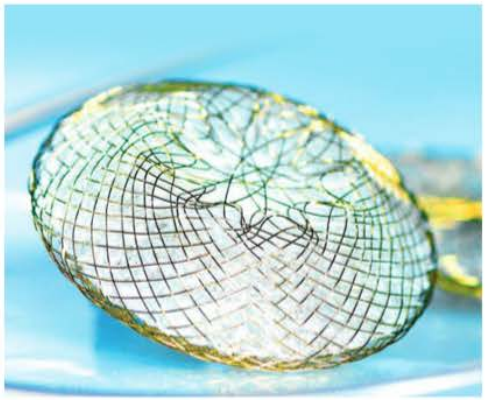
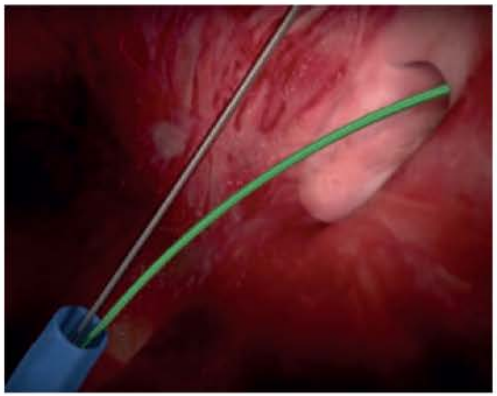
Anatomia setto (TEE) e scelta device



Figulla Occlutech

Amplatzer Septal Occluder

Gore Cardioform



Noble Stitch EI system

PFO device suture-like

Senza dispositivo metallico

Non necessita di terapia antitrombotica post impianto

Non rischio di erosione

Possibilità di puntura transettale successiva

Cosa significa "possibilità puntura trans-settale successiva"?

- La presenza di un device in fossa ovale puo' rendere piu' tecnicamente difficile eseguire un intervento di ablazione, qualora necessario in caso di diagnosi di aritmia

- La riconversione in RS migliora in effetti la prognosi sul compenso cardiaco ed è metodica perseguibile, ove indicata

Terapia anti-trombotica post chiusura PFO

Coagulazione e' fondamentale per la ri-epitelizzazione di un device metallico, tale processo impiega circa 6 mesi

Razionale terapia antitrombotica nel breve termine: prevenzione della complicanza trombotica in situ (2%). Essa puo' avvenire generalmente entro 2 mesi da impianto.

Nei trials strategie diverse: piu' spesso DAPT per 6 mesi.

Razionale terapia antitrombotica nel lungo termine: in relazione a prevenzione di ictus in pz con precedente ictus; consigliata a lungo termine se basso rischio emorragico

GRAZIE DELL'ATTENZIONE