Antithrombotics After PFO Device Closure: What and How Long?

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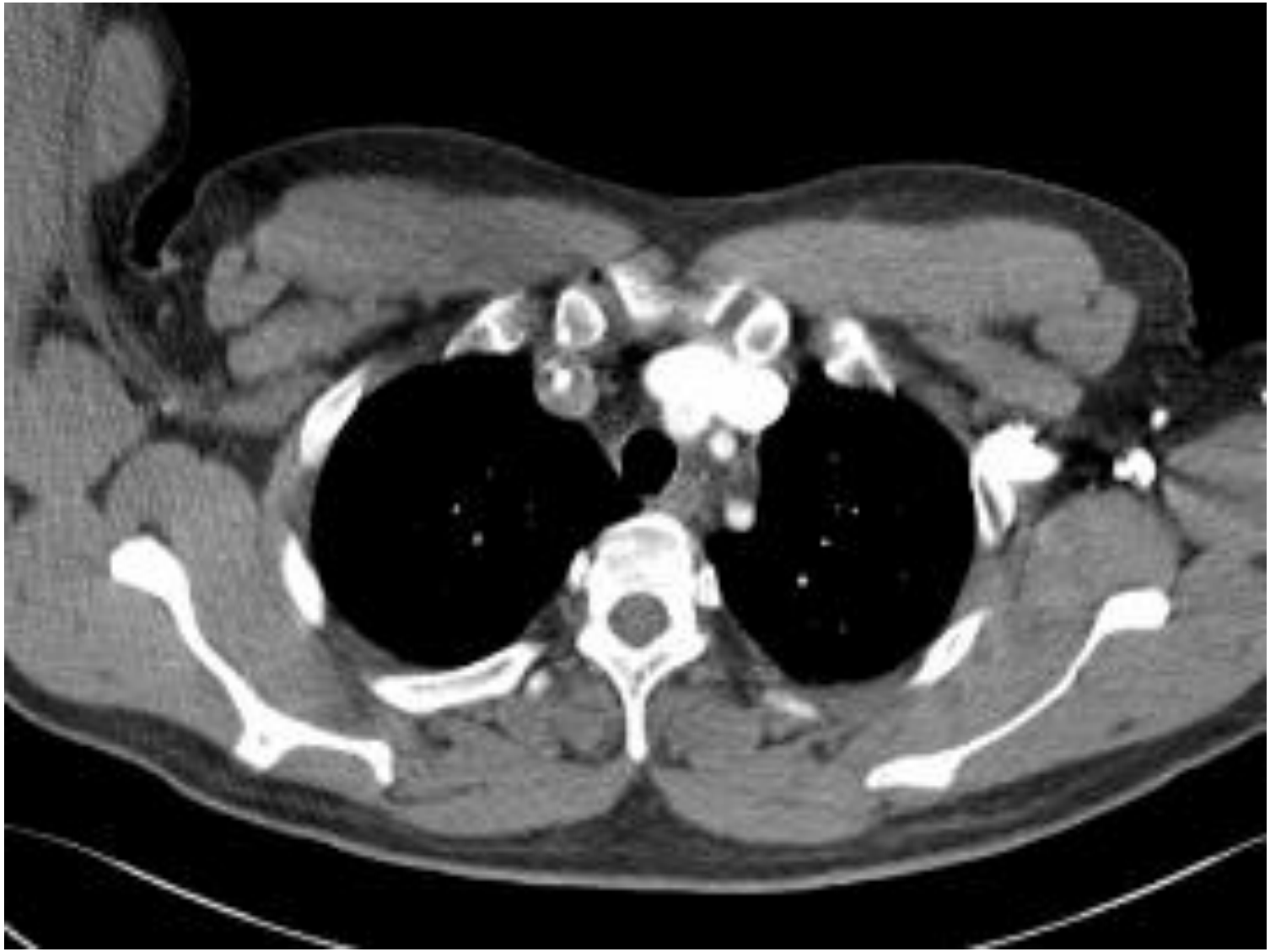
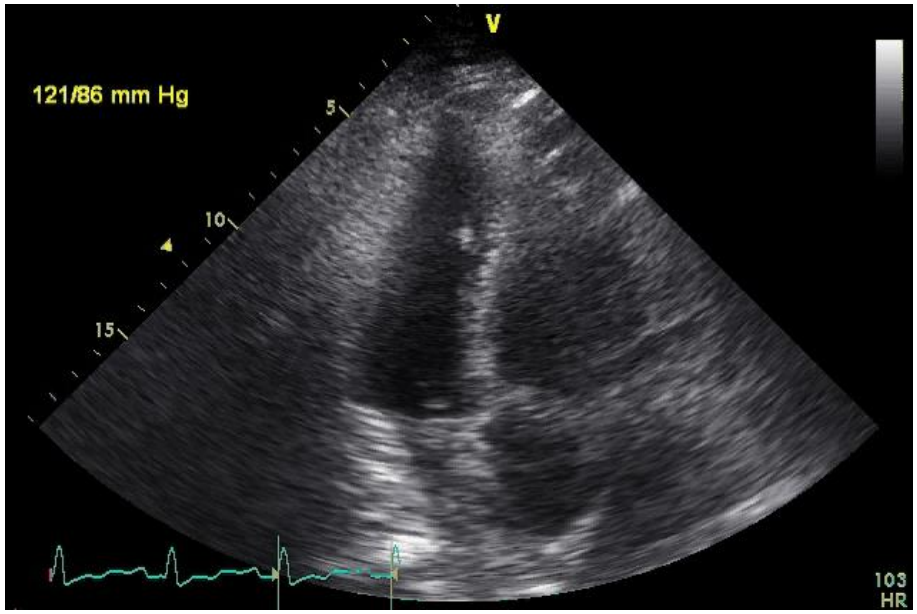
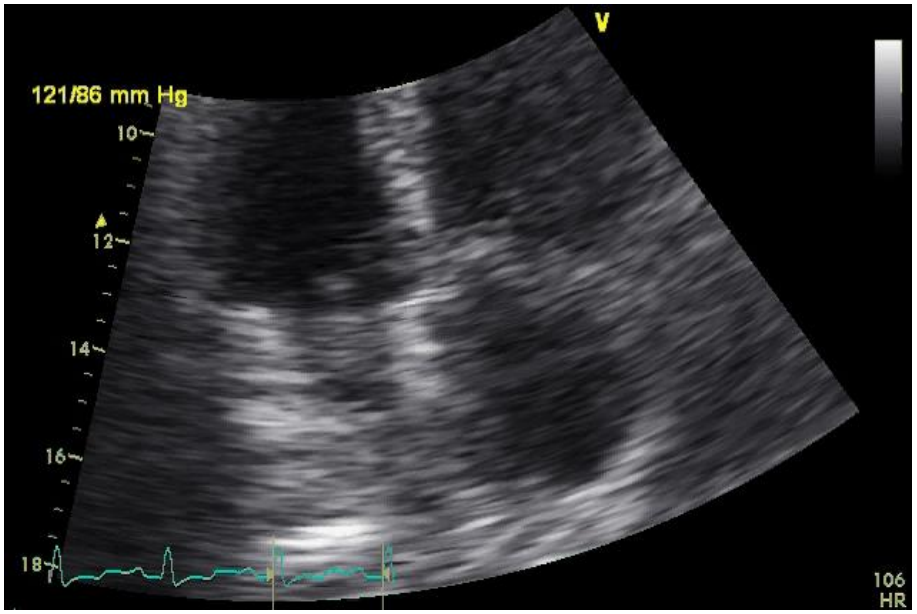
- C.C : Dyspnea (for 30 min)
- P.I : Open surgery for hip fracture (TA)
- Risk Fx : Hypertension (-), DM (-), non-smoker
- Initial VS : BP 60/40mmHg, HR 104 BPM

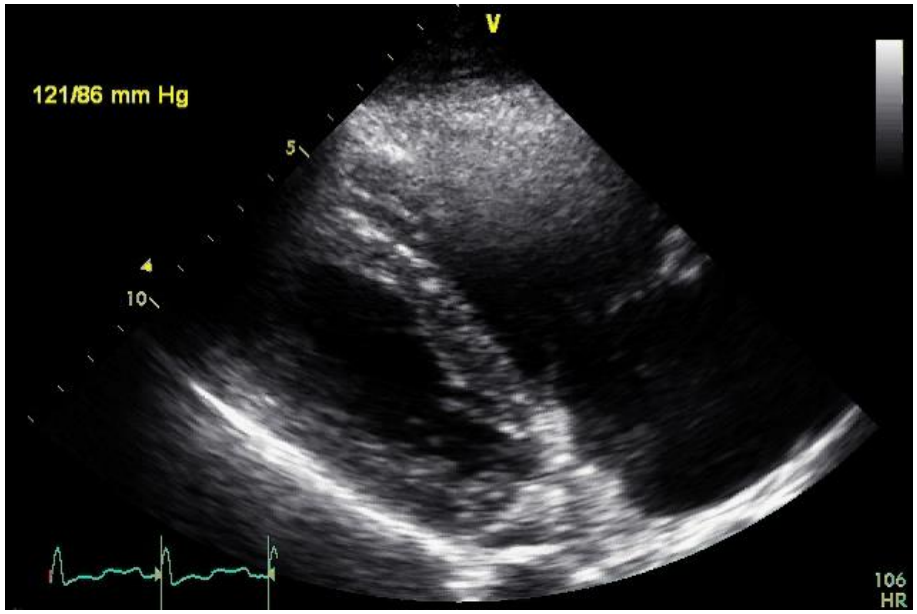
Pulmonary CT angiography



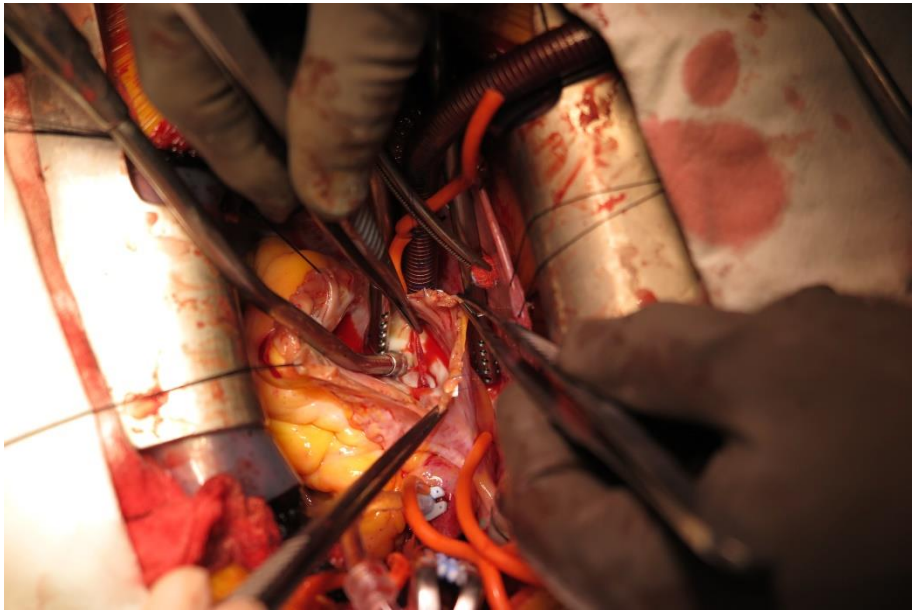
TTE

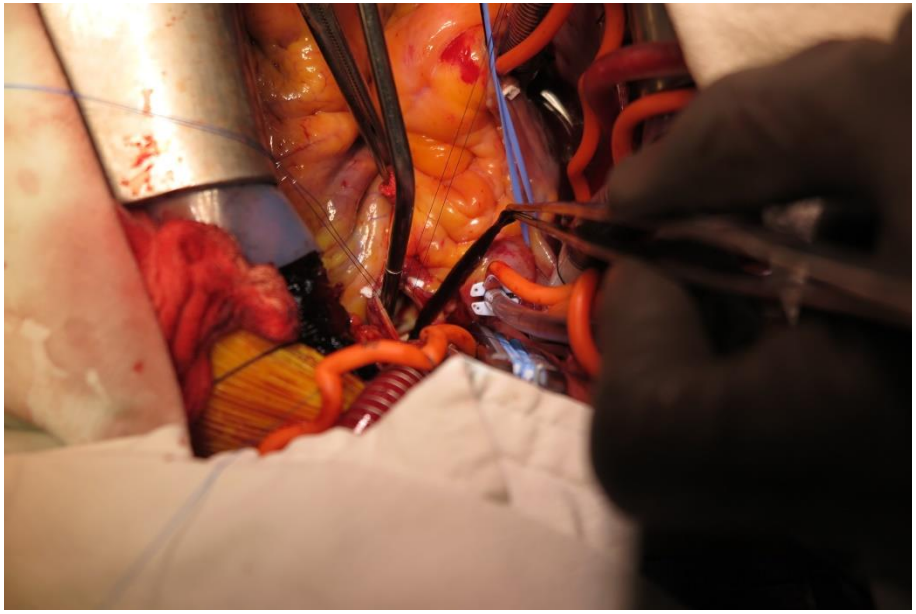

121/86 mm Hg
5
10
15
103
HR

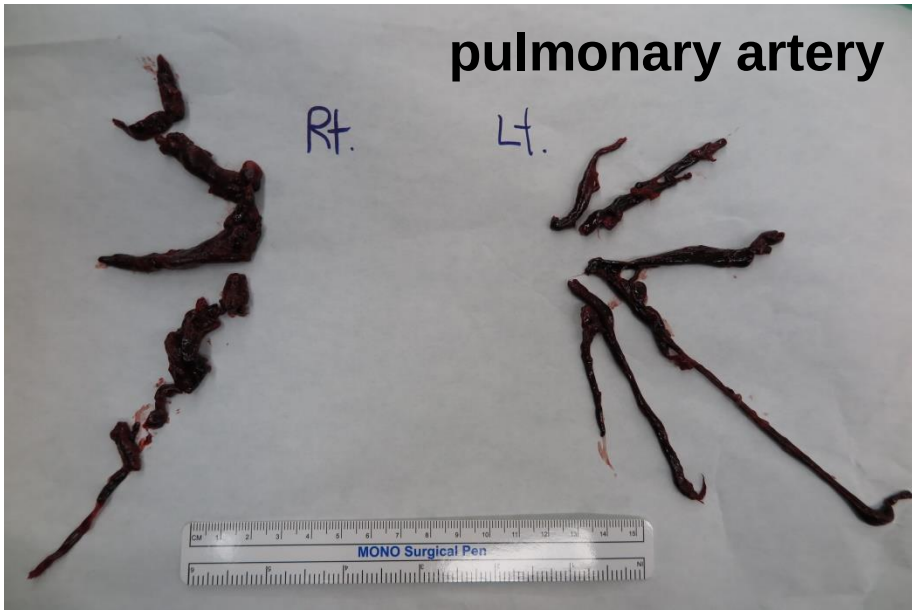

121/86 mm Hg
10
12
14
16
18
106
HR

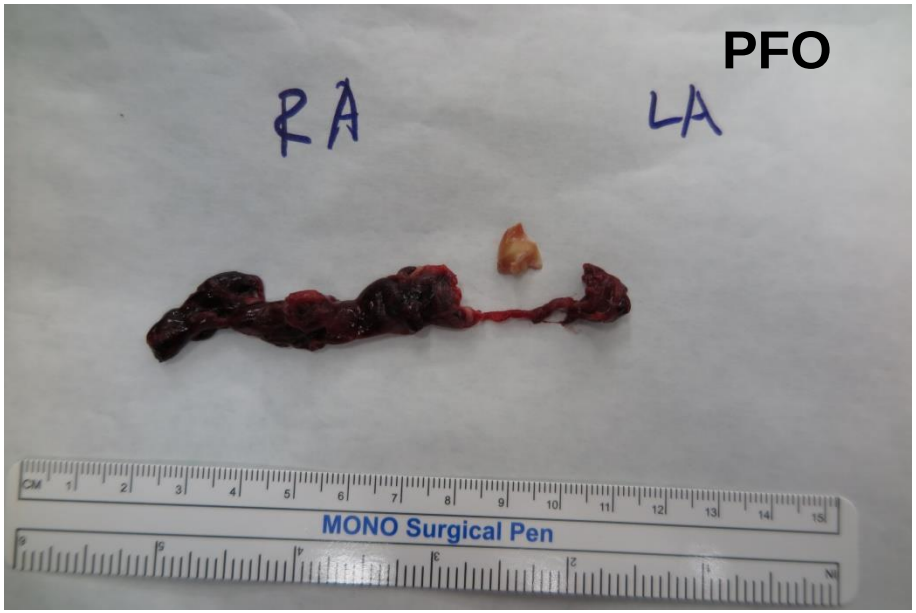

121/86 mm Hg
5
10
106
HR

Open Surgery

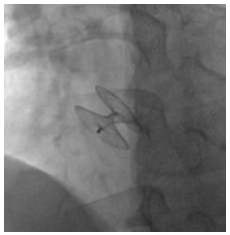






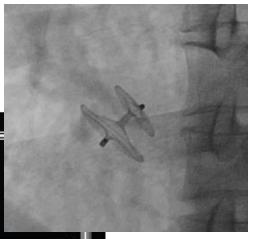


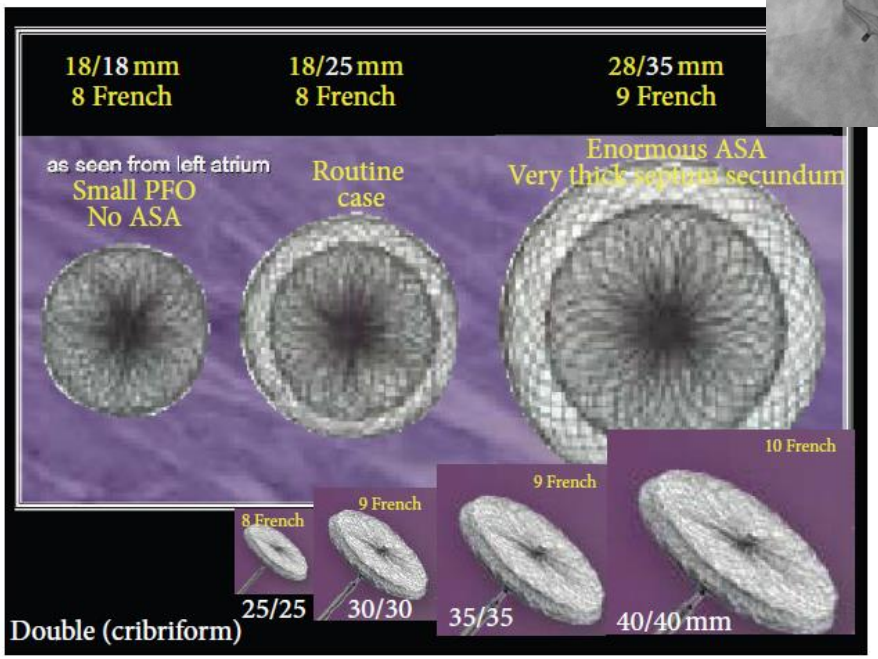
PFO Devices

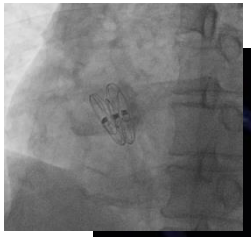


Occlutech PFO occluder

Amplatzer PFO occluder



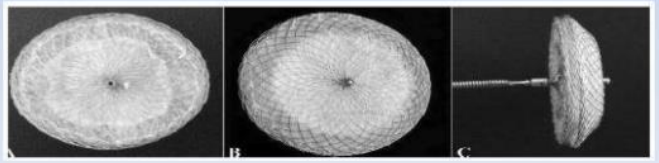




Gore cardioform septal occluder

Cocoon PFO occluder

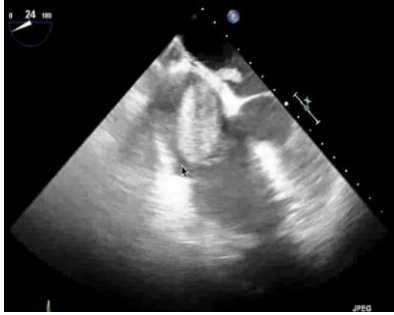
- Self-Expanding Platinum-Coated Nitinol Devices
- Coating helps to Prevent Nickel Release



Complications after PFO closure

- Arrhythmias (including Atrial fibrillation)
- Pericardial effusion/Cardiac tamponade
- Device embolization/erosion
- Device erosion
- Re-intervention for device removal
- Stroke/Peripheral embolism
- **Thrombus formation**

Thrombus after PFO closure

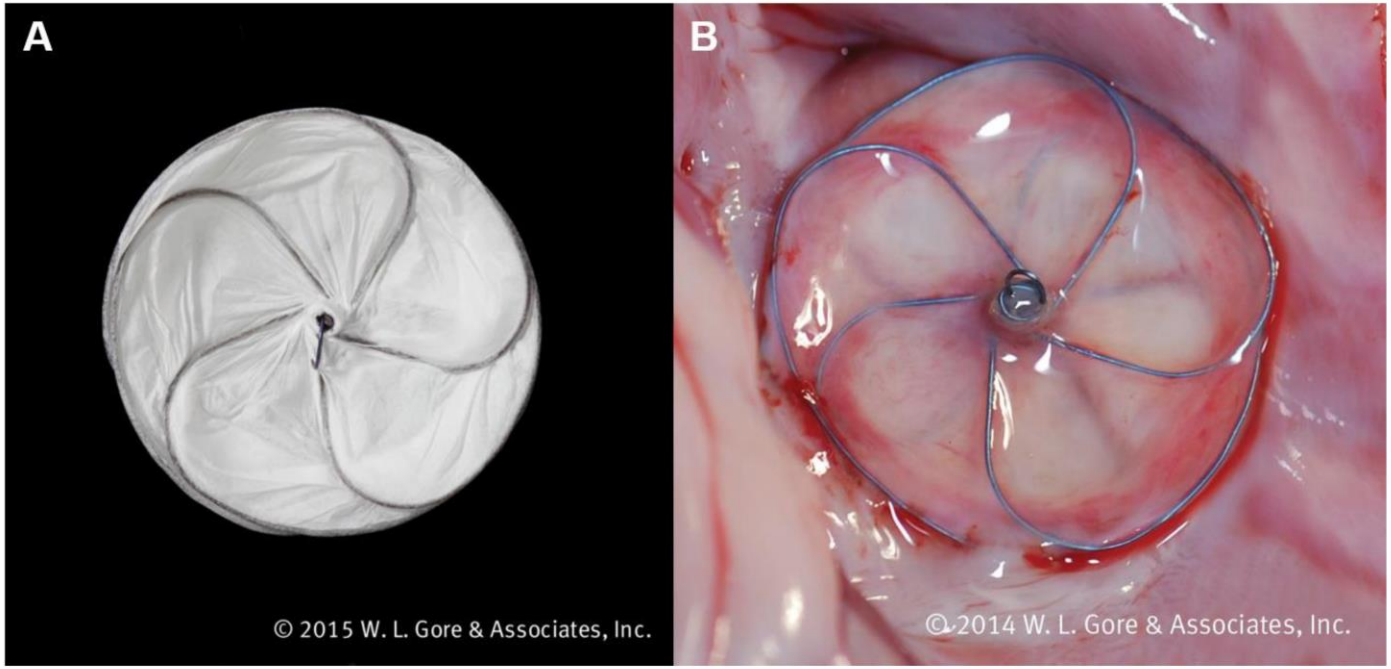


- Observed in **1–2 % of patients** in all types of devices.
- May result in serious complications, including **systemic embolism**, and **recurrent neurologic episodes**.
- May occur **during procedure** on either the delivery sheath or the device or **after the intervention.**
- Has been noted even up to **5 years after the procedure**.
- The incidence is **highest within the first 4 weeks** after procedure and is **extremely rare after 8–12 months.**

Natural Process after PFO closure

- The majority of PFO devices are composed of **metal** (usually nitinol) and a **polyester mesh**.
- **Coagulation** within the wire mesh facilitates **fibrous tissue growth** into the device which promotes a complete **endothelialization** and final occlusion of the shunt.
- **Endothelialization and scar tissue formation** on the device is necessary to obtain complete shunt closure and to prevent subsequent **thrombus formation**.

Animal study



- Pictures provided by the Gore company. (A) A commercially available PFO occluder. (B) **One month** after implantation of the device in canine model, full endothelialization and complete sealing of the PFO is observed.

However, it is unclear whether this phenomenon universally happens in human or not (even yes, we do not know when? and how?).

To decide on post-procedural antithrombotic therapy

- **Device thrombosis** is one of the most frequent complications after PFO closure.
- **Endothelialization** of the device can continue up to **five years post implantation.**
- **Premature discontinuation** of therapy may cause **minor cerebrovascular events** after PFO closure.

Antithrombotics after PFO Closure

- Post-procedural antithrombotic therapy **still remains controversial**.
- It is reasonable to decide on the post-procedural therapy **according to the strategies used in RCTs.**
- Most RCTs prescribed or recommended a **dual antiplatelet therapy in the first one to six months after closure**, continuing with a **single drug beyond 2 years.**
- In all positive trials, **an antiplatelet therapy was prolonged for the entire duration of the study** in the majority of patients (in 2/4 studies it was prescribed for five years).

Management after PFO closure

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
The value of residual shunt after percutaneous closure cannot be deduced from available studies	Strong	C	124, 141-47

Eurointervention. 2019;14:1389-1402

Predictor for thrombus formation

- A total of 1,000 consecutive pts were investigated after PFO (n= 593) or ASD (n= 407) closure.
- TEE was scheduled after four weeks and six months.

Table 2. Thrombus Formation at 4-Week TEE and 6-Month TEE After Closure

		TEE Due (n)	TEE Performed (%)		Thrombus (%, n)	
Occluder	n	6 Months	4 Weeks	6 Months	4 Weeks	6 Months
Rashkind	1	1	100%	100%	0%	0%
Buttoned Device	52	52	67%	69%	0%	0%
ASDOS	42	42	66%	83%	3.6% (n = 1)	0%
Angel Wings	30	30	0%	97%	0%	3.3% (n = 1)
CardioSEAL	27	27	52%	93%	7.1% (n = 1)*	0%
StarFLEX	142	111	74%	70%	5.7% (n = 6)*	0%
Amplatzer	418	375	78%	70%	0%*	0.3% (n = 1)
PFO-Star	127	127	60%	66%	6.6% (n = 5)*	1.5% (n = 1)
Helex	161	138	76%	80%	0.8% (n = 1)	0%

*The difference between the Amplatzer occluder against the CardioSEAL occluder, the StarFLEX occluder, and the PFO-Star occluder was significant ($p < 0.05$).

TEE = transesophageal echocardiography.

J Am Coll Cardiol 2004;43:302–9

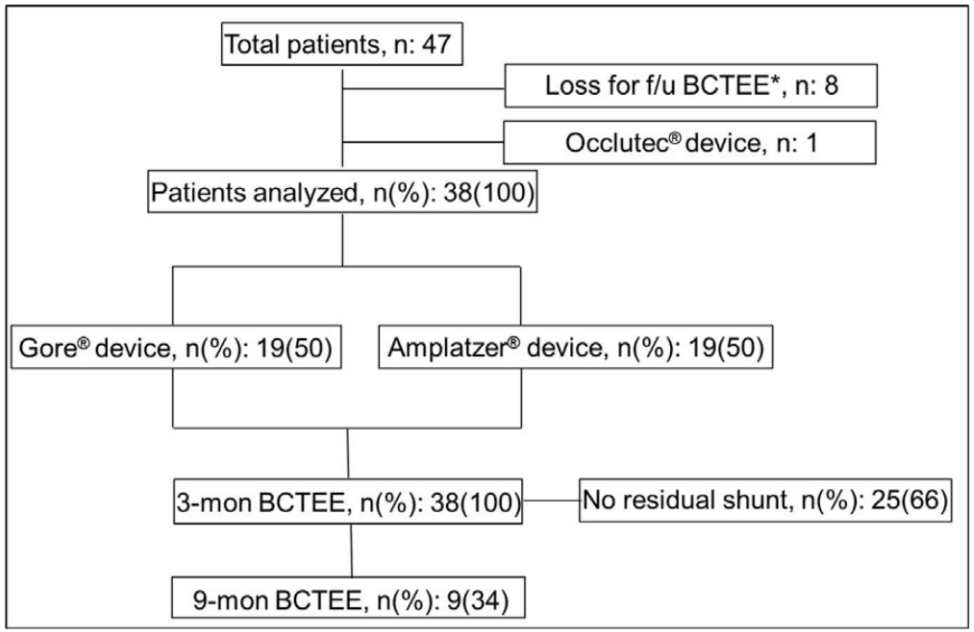
Predictor for thrombus formation

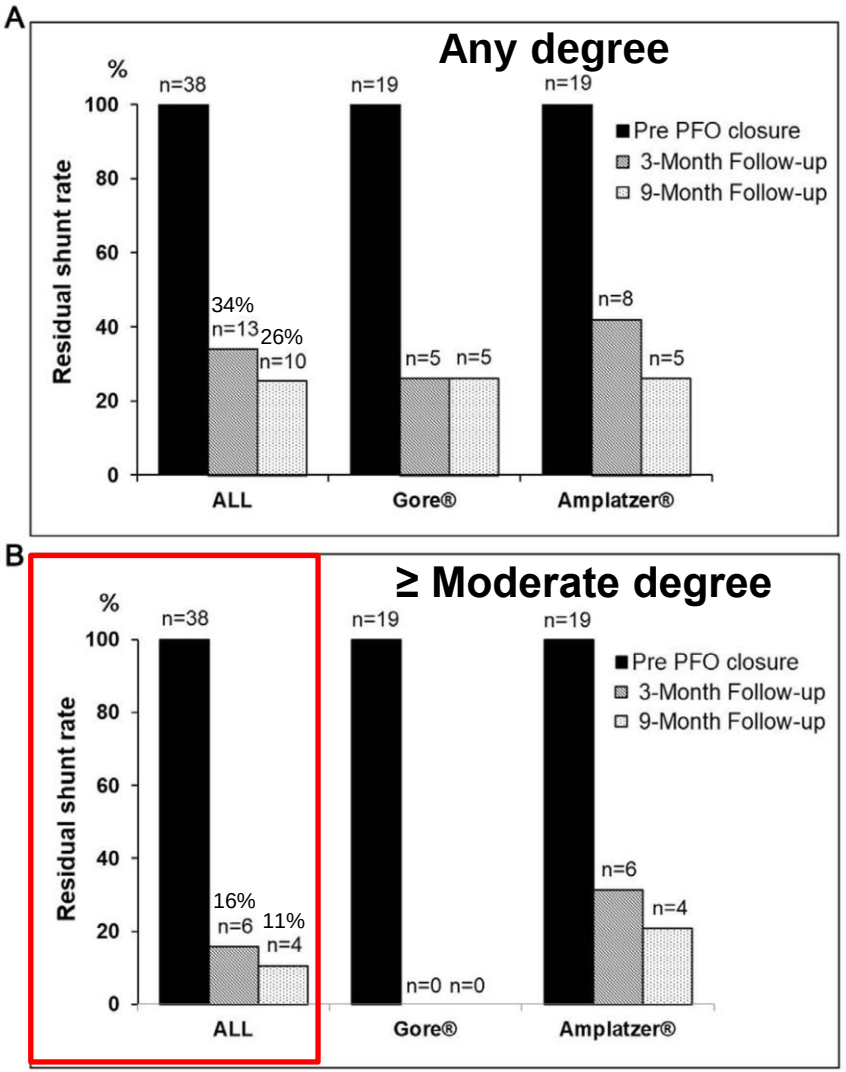
Table 3. Potential Risk Factors for Thrombus Formation

Risk Factors After Defect Closure	Patients Without Thrombi	Patients With Thrombi	p Value
Atrial fibrillation	66/980 (6.2%)	4/20 (20%)	< 0.05
Residual shunt immediately after closure	287/980 (29%)	3/20 (15%)	NS
Persistent atrial septal aneurysm	13/980 (1.3%)	4/20 (20%)	< 0.01
Wire fracture	47/980 (4.8%)	3/20 (15%)	NS
Protein S deficiency	8/456 (1.8%)	0/20 (0%)	NS
Protein C deficiency	9/456 (2%)	0/20 (0%)	NS
Resistance to activated protein C	25/456 (5.5%)	0/20 (0%)	NS
Mean age	47 yrs	48 yrs	NS
Gender			
Male	412/980 (42%)	9/20 (45%)	NS
Female	568/980 (58%)	11/20 (55%)	NS
Hypertension	228/980 (23%)	3/20 (15%)	NS
Coronary artery disease	51/980 (5%)	0/20 (0%)	NS
Diabetes	37/980 (4%)	0/20 (0%)	NS
Warfarin	95/980 (10%)	3/20 (15%)	NS
Aspirin	505/980 (52%)	6/20 (30%)	NS
Aspirin + clopidogrel	380/980 (39%)	11/20 (55%)	NS
Protamin	798/980 (81%)	19/20 (95%)	NS

J Am Coll Cardiol 2004;43:302–9

Residual Shunt after PFO Closure in Patients With Cryptogenic Stroke





DAPT (aspirin and clopidogrel): 6M

No thrombus
No ischemic events

J Stroke Cerebrovasc Dis 2019;28:347−353

Management of thrombus formation

- Due to **high risk of embolization,** an **aggressive management is required**.
- **Most (**over 80%**) patients were successfully treated with anticoagulation**.
- The majority of thrombi resolve **within 4 weeks to 6 months** after treatment with **anticoagulation**.
- A **TEE** should be performed following anticoagulation treatment to confirm resolution of the device related thrombus.
- **Thrombolysis or even surgical removal** of the device should be considered in patients who do not respond to medical therapy.

Conclusions

- **Thrombus formation** after PFO device closure is rare but can be associated with serious complications.
- **Optimal antithrombotic therapy** as well as careful **echocardiographic assessment** in follow up must be carried out.
- After PFO device closure, it is proposed **DAPT for 1–6 months** and **single antiplatelet therapy** be continued for at least **5 years**.
- When device related thrombosis detected, it should be treated with **anticoagulation** and followed with appropriate surveillance imaging.

תודה
Dankie
Gracias
Спасибо
شكراً
Merci
Takk
Köszönjük
Terima kasih
Grazie
Dziękujemy
Děkojame
Ďakujeme
Vielen Dank
Paldies
Kiitos
Täname teid
谢谢
Thank You
Tak
感謝您
Obrigado
Teşekkür Ederiz
감사합니다
Σας Ευχαριστούμ
ขอบคุณ
Bedankt
Děkujeme vám
ありがとうございます
Tack

Antithrombotics After PFO Device Closure

Impact of Discontinuation of Antithrombotic Therapy Following PFO closure in Patients With Cryptogenic Embolism

- A total of 453 consecutive patients (mean age: 48±13 years, men: 51%) who underwent PFO closure due to a cryptogenic ischemic event were included.
- All patients were on AT (antithrombotic theray) following PFO closure (antiplatelet therapy: 92.7%, anticoagulation: 7.3%).

✓ A propensity score matched analysis including **46 patients who discontinued the AT within 1-year** post-PFO closure and **120 patients with an ongoing AT** showed the **lack of differences in ischemic events** between groups (0 vs. 0.2 stroke/transient ischemic attack per 100 patient-years in the no-AT and AT groups, respectively).

✓ These results suggest that, **in patients without other co-morbidities increasing the risk of stroke**, **temporary AT following PFO closure may be a reasonable strategy.**

Am J Cardiol 2019;123:1538−1545

Management of thrombus formation

- Due to **high risk of embolization,** an **aggressive management is required**.
- **Most (**over 80%**) patients were successfully treated with only conservative medical therapy**.
- The majority of thrombi resolves **within 4 weeks to 6 months** after treatment with **anticoagulation**.
- A **TEE** should be performed following anticoagulation treatment to confirm resolution of the device related thrombus.
- **Thrombolysis or even surgical removal** of the device should be considered in patients who do not respond to medical therapy.

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