

PFOs – Are There Holes in the Argument? To Close or Not

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Presenter Disclosure Information

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Topic

PFO Closure

Conflict of Interest

None

Unlabeled Use

None

Five Considerations In The Decision to Close or Not

1. The evidence on the closure procedure
 - ❖ Efficacy
 - ❖ Safety
2. Alternative therapies
3. The patient's values and preferences

Given the evidence, some patients will choose closure, others will not. How we present this evidence will influence their decisions.

Three Open-label Trials of PFO Closure In patients ~16-60 with cryptogenic IS*

Study	N	Mean F/U (years)	Stroke Rate			
			Closure	Anti-Platelet	RD†	HR (95% CI)
REDUCE	664	3.2	1.4%	5.4%	4.0%	0.23 (0.09-0.62)
RESPECT	980	5.9	3.4%	6.3%	2.9%	0.55 (0.31-0.99)
CLOSE	473	5.3	0.0%	5.0%	5.0%	0.03 (0.00-0.26)*

*closure vs. antiplatelet only group
†estimated at the mean follow-up

Adverse Events

Patients with Adverse event Closure Group/Medical Group

Study	N	Patients with procedure or device-related complication†	Afib Requiring Rx	DVT/PE
REDUCE	664	3.8%/NA	NS	1%/1%
RESPECT	980	4.2%/NA	13%/10%	3%/1%
CLOSE	473	5.9%/NA	5%/1%	0%/0%

†Includes cardiac perforation, cardiac thrombus, stroke, pericardial tamponade, PE, bleeding, infective endocarditis. Gore did not list arrhythmias as a procedure complication, but RESPECT and CLOSE did.

How Reliable is the Evidence for PFO Closure?

B+

1. All three trials were open label
2. 2/3 trials reported substantial losses
3. None required prolonged rhythm monitoring
4. None report f/u beyond median 5 years

Primary Outcomes

Primary Outcomes by Group

Trial	Total N	Closure	Antiplatelet
Reduce	664	6	12
Respect	980	18	28
Close	473	0	14
TOTAL		24	54

REDUCE

Evidence for Surveillance Bias

End Point	PFO Closure Group	AP-Only Group	Effect Size	P- Value
	No. of patients/total no. (%)			
Clinical Ischemic Stroke	6/441 (1.4)	12/223 (5.4)	0.23 (0.09-0.62)	0.002
New Brain Infarction	22/383 (5.7)	20/177 (11.3)	0.51 (0.29-0.91)	0.04
Clinically apparent	5/383 (1.3)	12/177 (6.8)	0.19 (0.07-0.54)	0.005
Silent	17/383 (4.4)	8/177 (4.5)	0.98 (0.43-2.23)	0.97

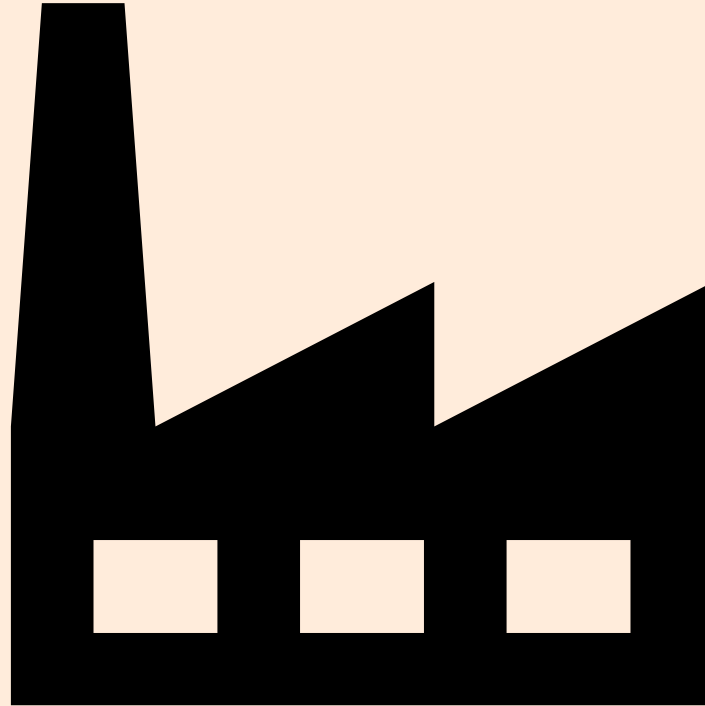
Losses in 2017 PFO trials

Trial	Total N	Losses	
		Closure	Antiplatelet
REDUCE	664	9%	15%
RESPECT	980	21%	33%
CLOSE	473*	0%	<1%

*PFO closure vs antiplatelet arm only

Europeans stay connected.

Did The 2017 Trials Ask The Correct Question?



(This symbolizes industry.)

CLOSE Results

Oral Anticoagulation vs. Antiplatelet Therapy

Outcome	# Outcomes		HR	95% CI
	OAC N=187	AP N=174		
Any Stroke	3	7	0.44	0.11-1.48
Disabling	1	1	0.96	0.08-11.85
Death	1	0	2.84	0.15-414.86

Informed Consent to Promote Patient-Centered Care*

Background

You have a hole in your heart . . .

Potential Risks

Procedure

PFO closure involves . . .

Other Treatments

Potential Benefits

Experience of Your Team

*HM Krumholz. JAMA 2010;303:1190

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Potential Benefits

“What we know about PFO closure is based on five studies that included about 2000 patients who had the closure procedure. The studies followed patients for up to 8 years. Based on the results of these studies, PFO closure is likely to reduce your risk of stroke: Among 100 patients who have their PFO closed, 2 will have another stroke within 5 years. Among 100 patients who take aspirin instead, 6 will have a stroke within 5 years.”

*HM Krumholz. JAMA 2010;303:1190

Communicating PFO Closure Benefit At 5 Years



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Potential Risks

If you choose to have your PFO closed, there are risks related to the procedure and the device. These include:

- ❖ An irregular heart beat called atrial fibrillation. During the closure procedure, some patients will develop atrial fibrillation. For most patients, this will resolve within a month and will not require further treatment. However, for every 1000 patients who have their PFO closed, about 40 will develop atrial fibrillation that will last for more than a month. By comparison, about 10 patients who receive medical therapy will develop atrial fibrillation lasting more than a month. Atrial fibrillation is important because it can cause recurrent stroke and often requires use of a blood thinning medication.

*HM Krumholz. JAMA 2010;303:1190

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Potential Risks (continued)

- ❖ A Serious Complication During the Procedure.
During closure of the PFO, serious problems can occur. These include atrial fibrillation, bleeding from the skin puncture side, bleeding around the heart, stroke, heart perforation, and blood clots in the heart or lung. These complications can usually be treated without long-term consequences. Among 1000 patients who have a PFO closed, about 40 will have one of these or other complications.

*HM Krumholz. JAMA 2010;303:1190

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Summary

In circumstances of:

- ❖ Imperfect evidence
- ❖ A small absolute risk reduction
- ❖ Uncertain long-term effects
- ❖ Unexamined alternative therapy

High quality shared making is critically important

END

Thank You