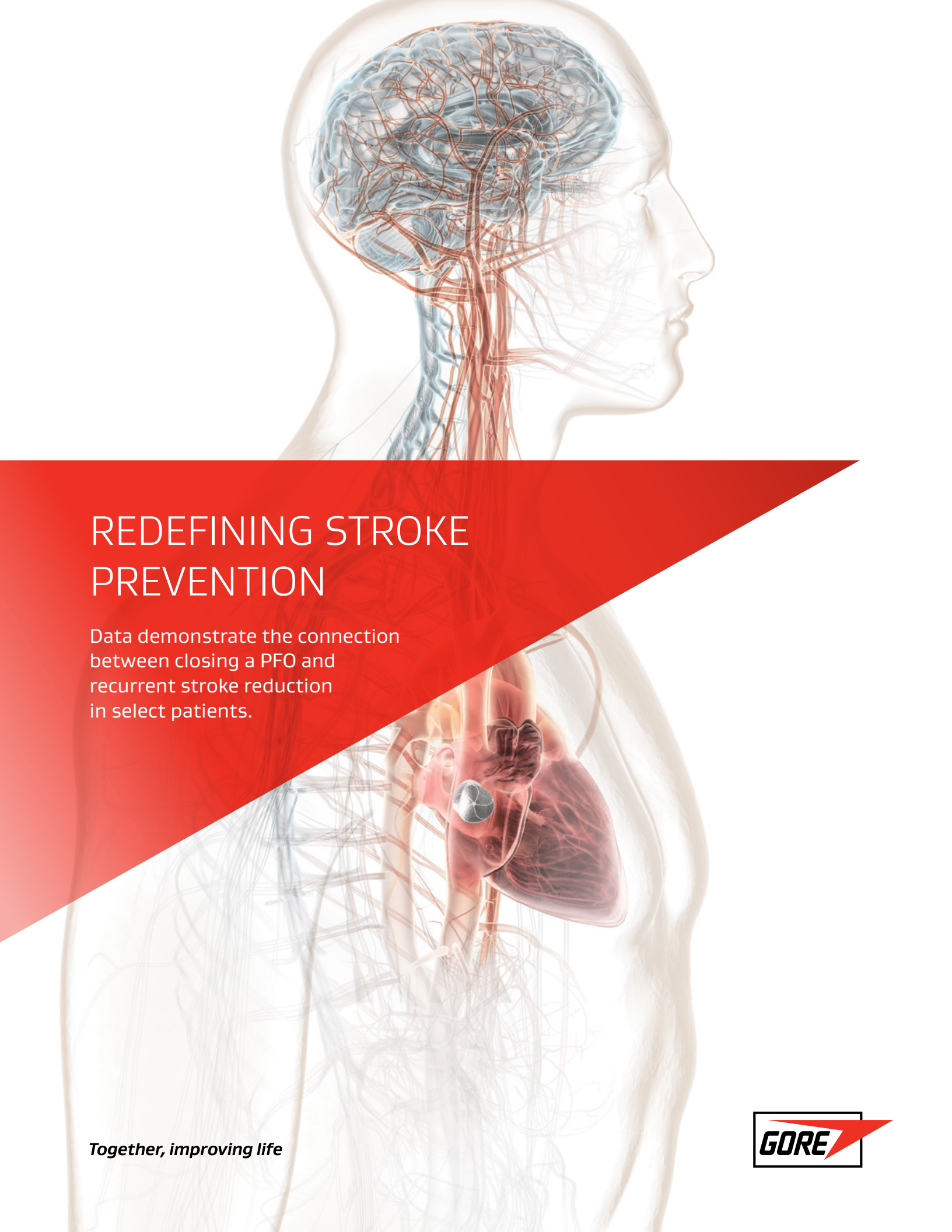


REDEFINING STROKE PREVENTION

Data demonstrate the connection between closing a PFO and recurrent stroke reduction in select patients.

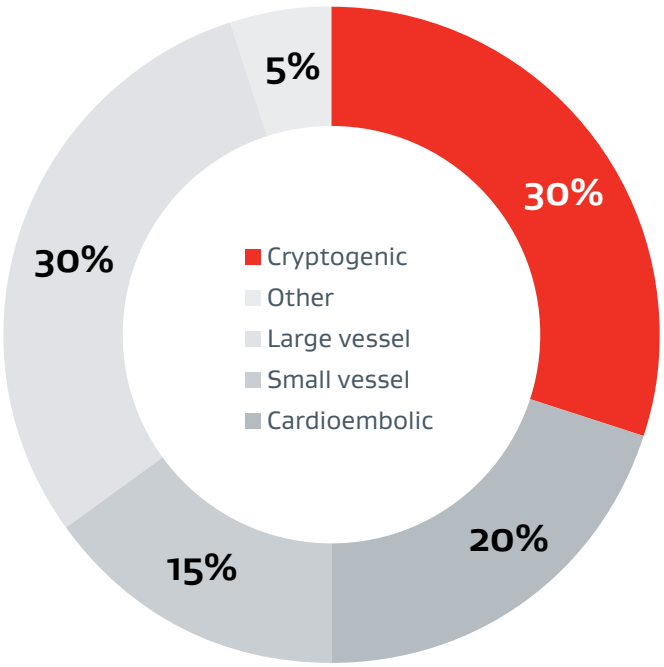
Together, improving life

GORE

Cryptogenic Stroke

A stroke without consistently transparent causes

How many ischemic strokes are cryptogenic?



~1/3
of ischemic strokes are cryptogenic[1]

~200K
cryptogenic strokes occur annually in the U.S.[1]

~4.5M
cryptogenic strokes occur annually worldwide[1,2]

Cryptogenic Stroke

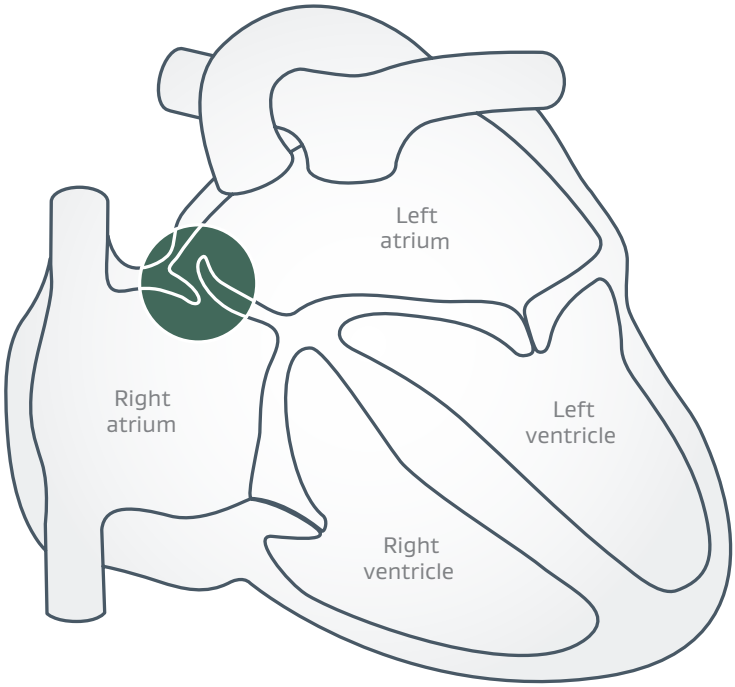
The connection to patent foramen ovale (PFO)

The American Heart Association states that certain conditions should be considered if standard poststroke workup has not determined probable causation for the cryptogenic stroke, including but not limited to[1]:

- Occult paroxysmal atrial fibrillation
- PFO
- Inherited thrombophilia
- Aortic arch atheroma

40–50%

of patients who have had a cryptogenic stroke have a PFO[3]



A PFO may permit emboli to travel from the right to the left atria, possibly leading to a stroke.

Glossary of terms: Atrial fibrillation (AFIB); Computed tomography (CT); Computed tomography angiography (CTA); Deep vein thrombosis (DVT); Fluid-attenuated inversion recovery (FLAIR); Magnetic resonance angiography (MRA); Magnetic resonance imaging (MRI); Pulmonary embolism (PE); Reversible cerebral vasoconstriction syndrome (RCVS); Transcranial doppler (TCD); Transesophageal echocardiography (TEE); Transthoracic echocardiogram (TTE).

Gore REDUCE Clinical Study

Original Follow-Up (Median 3.2 years)

Prospective, randomized, multicenter, multinational and open-label trial

664

PATIENTS ENROLLED

cryptogenic stroke and PFO*/ages 18–59

441

CLOSURE GROUP

GORE Device[†,‡] plus antiplatelet therapy

223

MEDICAL THERAPY GROUP

Antiplatelet therapy

Endpoints

- Freedom from recurrent clinical ischemic stroke through at least 24 months
- Incidence of new brain infarct (defined as clinical ischemic stroke or silent brain infarct) through 24 months

Patient selection

- Cryptogenic ischemic stroke within 180 days
  - Ischemic stroke = clinical symptoms ≥ 24 hours or with MRI evidence of infarction
  - Cryptogenic:
    - No stenosis > 50% or ulcerated plaque in relevant intra- or extra-cranial vessels
    - No atrial fibrillation or high-risk source of cardioembolism
    - Non-lacunar (based on syndrome and/or size)
    - No evidence of hypercoagulable disorder
    - No other known cause of stroke
- PFO*
- No indication for anticoagulation
- No uncontrolled diabetes mellitus, hypertension, autoimmune disease, alcohol or drug abuse

Image confirmation

- MRI at baseline and at 2 years or at time of event

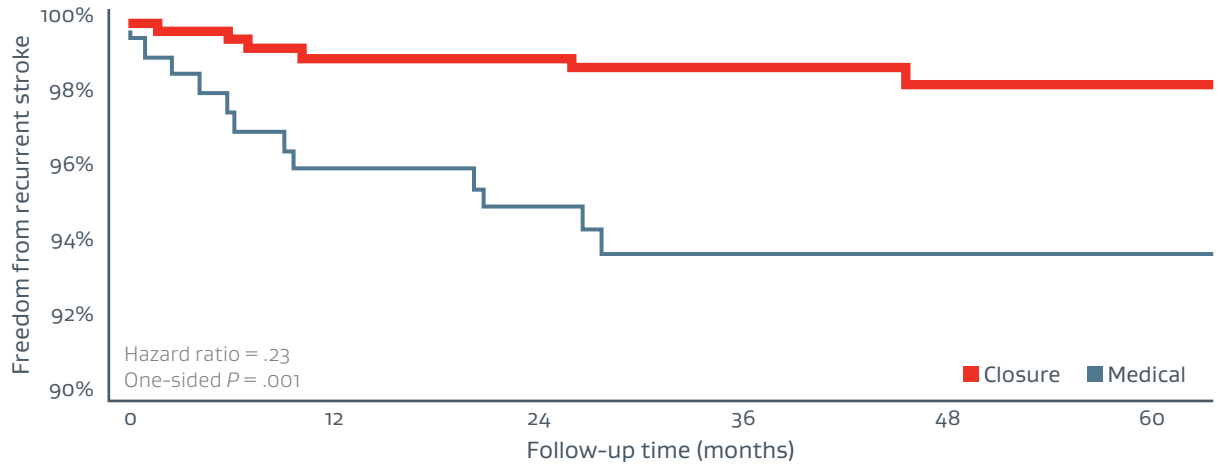
PFO Closure Through Original Follow-Up (Median 3.2 years)

Proven to reduce recurrent stroke risk

REDUCE Study: as published in *The New England Journal of Medicine*[4]

77% RELATIVE STROKE REDUCTION

with PFO CLOSURE + medical therapy versus medical therapy alone[†,4]



4X THE PROTECTION against recurrent stroke than medical therapy alone[†,4]

Stroke risk[†,4]

Closure group	Medical therapy group	Absolute stroke reduction[§]
1.4% (6/441)	5.4% (12/223)	4%

REDUCE Study sub-analysis

- As effective for patients 18–45 as patients 46–59 years[†,4]
- All PFO shunt sizes and anatomies benefited from PFO closure[†,4]

* PFO confirmed by transesophageal echocardiography (TEE) with bubble study demonstrating right-to-left shunt at rest or during Valsalva maneuver. Patients with PFO eligible regardless of shunt size within sizing parameters of the IFU or presence of atrial septal aneurysm.

† The REDUCE Study determined safety and efficacy of patent foramen ovale (PFO) closure with the GORE® CARDIOFORM Septal Occluder or GORE® HELEX® Septal Occluder plus antiplatelet medical management compared to antiplatelet medical management alone in patients with a PFO and history of cryptogenic stroke. All PFO anatomies were incorporated into this study within indicated sizing parameters of the *Instructions for Use*.

‡ GORE® CARDIOFORM Septal Occluder and GORE® HELEX family of devices.

§ The 4% represents the difference between 5.4% and 1.4% respectively.

REDUCE Clinical Study

Original Follow-Up Safety Profile

PFO closure plus medical therapy. Proven to be as safe as medical management alone.*,4

There was no significant difference in the overall serious adverse event (SAE) rate between the PFO closure and medical management group in the REDUCE Study*,4

REDUCE Study: any SAE

Closure (N = 441)	Medical (N = 223)	*P*-value†
102 (23.1%)	62 (27.8%)	.22

No statistical difference in risk of serious atrial fibrillation, bleeding, deep vein thrombosis or pulmonary embolism with PFO closure.*,4

REDUCE Study: SAEs of interest

	Closure (N = 441)	Medical (N = 223)	*P*-value†
Any serious adverse event	102 (23.1%)	62 (27.8%)	.22
Atrial fibrillation	10 (2.3%)	1 (0.4%)	.11
Bleeding	8 (1.6%)	6 (2.7%)	.57
Deep vein thrombosis	0	2 (0.9%)	.11
Pulmonary embolism	2 (0.5%)	1 (0.4%)	1.00
Migraine	2 (0.5%)	1 (0.4%)	1.00

Low risk of serious device or procedure-related SAEs.*,4

REDUCE Study: SAEs related to the procedure or device‡

6 (1.4%)
device-related

11 (2.5%)
procedure-related

Understanding the risk of atrial fibrillation following PFO closure

REDUCE Study: atrial fibrillation or flutter events*,[4]

	Closure (N = 441)	Medical (N = 223)	*P*-value†
Any atrial fibrillation or flutter	29 (6.6%)	1 (0.4%)	< .001
Serious atrial fibrillation or flutter	10 (2.3%)	1 (0.4%)	.11
Serious device-related atrial fibrillation or flutter	2 (0.5%)	-	-
Serious procedure-related atrial fibrillation or flutter	0	-	-

The REDUCE Study found post-implant atrial fibrillation generally does not result in long-term arrhythmia complications or require lifetime use of anticoagulation.*,[4,5]

66%
AFIB or flutter cases considered non-serious (19/29)

AFIB detected within 45 days post procedure[4]	24/29 (83%)
Cases that resolved within 2 weeks of onset[4]	17/29 (59%)

- The majority of atrial fibrillation and flutter events were non-serious.[4]
- Most of the atrial fibrillation and flutter events were resolved in 2 weeks.[4]

1.4% of all closure subjects in the REDUCE Study had ongoing non-serious atrial fibrillation or atrial flutter at the time of data analysis*,[4]

* The REDUCE Study determined safety and efficacy of patent foramen ovale (PFO) closure with the GORE® CARDIOFORM Septal Occluder or GORE® HELEX® Septal Occluder plus antiplatelet medical management compared to antiplatelet medical management alone in patients with a PFO and history of cryptogenic stroke. All PFO anatomies were incorporated into this study within indicated sizing parameters of the *Instructions for Use*.

† *P*-value were calculated with the use of Fisher's exact test.

‡ Subjects may have experienced both device- and procedure-related SAEs.

REDUCE Clinical Study

Long-Term Outcomes

Groundbreaking stroke risk reduction

The REDUCE Study continues to show the largest reduction in recurrent ischemic stroke in all PFO shunt sizes over medical management alone.*[4,6]

69%

relative stroke risk reduction with PFO closure plus medical management versus medical management alone at extended follow-up*[6]

25

number needed to treat (NNT) to prevent one stroke at 5 years[6]

Closure (N = 441) Medical (N = 223)	Original follow-up (Median 3.2 years)[4]	Extended follow-up (Median 5.0 years)[6]
Ischemic stroke reduction relative to medical management alone	77% (*P* = .002)	69% (*P* = .007)
Closure group ischemic strokes	6 (1.4%)	8 (1.8%)
Medical therapy group ischemic strokes	12 (5.4%)	12 (5.4%)
NNT	28	25

High closure performance

Enduring effective closure across anatomies.*[4,6]

	12-month assessment[7]	24-month assessment
GORE® CARDIOFORM Septal Occulder effective closure rate†	98%	99%

Data on file 2020; W. L. Gore & Associates, Inc.; Flagstaff, AZ.

Continued legacy of patient safety

Long-term results continue to demonstrate a legacy of patient safety with 2,069 patient years of data.[4,6]

Device and procedure serious adverse events (SAEs)

0

new device- or procedure-related SAEs at 5 years[6]

Closure (N = 441)	Original follow-up (Median 3.2 years)[4]	Extended follow-up (Median 5.0 years)[6]
Device SAE	6 (1.4%)	No change
Procedure SAE	11 (2.5%)	No change

Atrial fibrillation[4,6]

1

additional non-serious atrial fibrillation case after device implant found during extended follow-up and it resolved[6]

Closure (N = 441)	Original follow-up (Median 3.2 years)[4]	Extended follow-up (Median 5.0 years)[6]
Any atrial fibrillation	29 (6.6%)	30 (6.8%)
Serious atrial fibrillation	10 (2.3%)	No change
Serious device-related or procedure-related atrial fibrillation	2 (0.5%)	No change

Other safety information[4,6]

Consistently demonstrating no significant difference in risk of bleeding, deep vein thrombosis or pulmonary embolism in 5-year follow-up versus medical management alone.[4,6]

0

clinical sequelae associated with wire frame fractures at original follow-up or during extended follow-up[6]

0

reported erosions at original follow-up or during extended follow-up[4,6]

Closure (N = 441)	Original follow-up (Median 3.2 years)[4]	Extended follow-up (Median 5.0 years)[6]
Clinical sequelae associated with wire frame fractures	0 (0%)	No change
Any deep vein thrombosis/ pulmonary embolism	3 (0.7%)	5 (1.1%)
Serious bleeding	8 (1.8%)	12 (2.7%)
Cardiac erosion	0 (0%)	No change

* The REDUCE Study determined safety and efficacy of PFO closure with the GORE® CARDIOFORM Septal Occluder or GORE® HELEX® Septal Occluder plus antiplatelet medical management compared to antiplatelet medical management alone in patients with a PFO and history of cryptogenic stroke. All PFO anatomies were incorporated into this study within indicated sizing parameters of the *Instructions for Use*.

† Effective closure defined as freedom from large shunt > 25 bubbles as detected by transthoracic echocardiography adjudicated by Echo Core Lab.

Patient Selection Algorithm

The following algorithm may help identify patients most likely to benefit from PFO closure:

STEP 1: Tissue diagnosis

Stroke-like symptoms in patients

Is the MRI positive for acute ischemic stroke?[8]

YES

NO

Acute ischemic stroke

Are there signs of advanced atherosclerosis on FLAIR Imaging?[8]

Manage in accordance with current guidelines and/or hospital protocols

NO

YES

STEP 2: Vessel imaging

STEP 2: Vessel imaging

Vessel imaging (CTA, MRA, carotid ultrasound)[9]

Is there large vessel atherosclerosis?[8]

YES

NO

Manage in accordance with current guidelines and/or hospital protocols

Is there other vessel disease?[8]

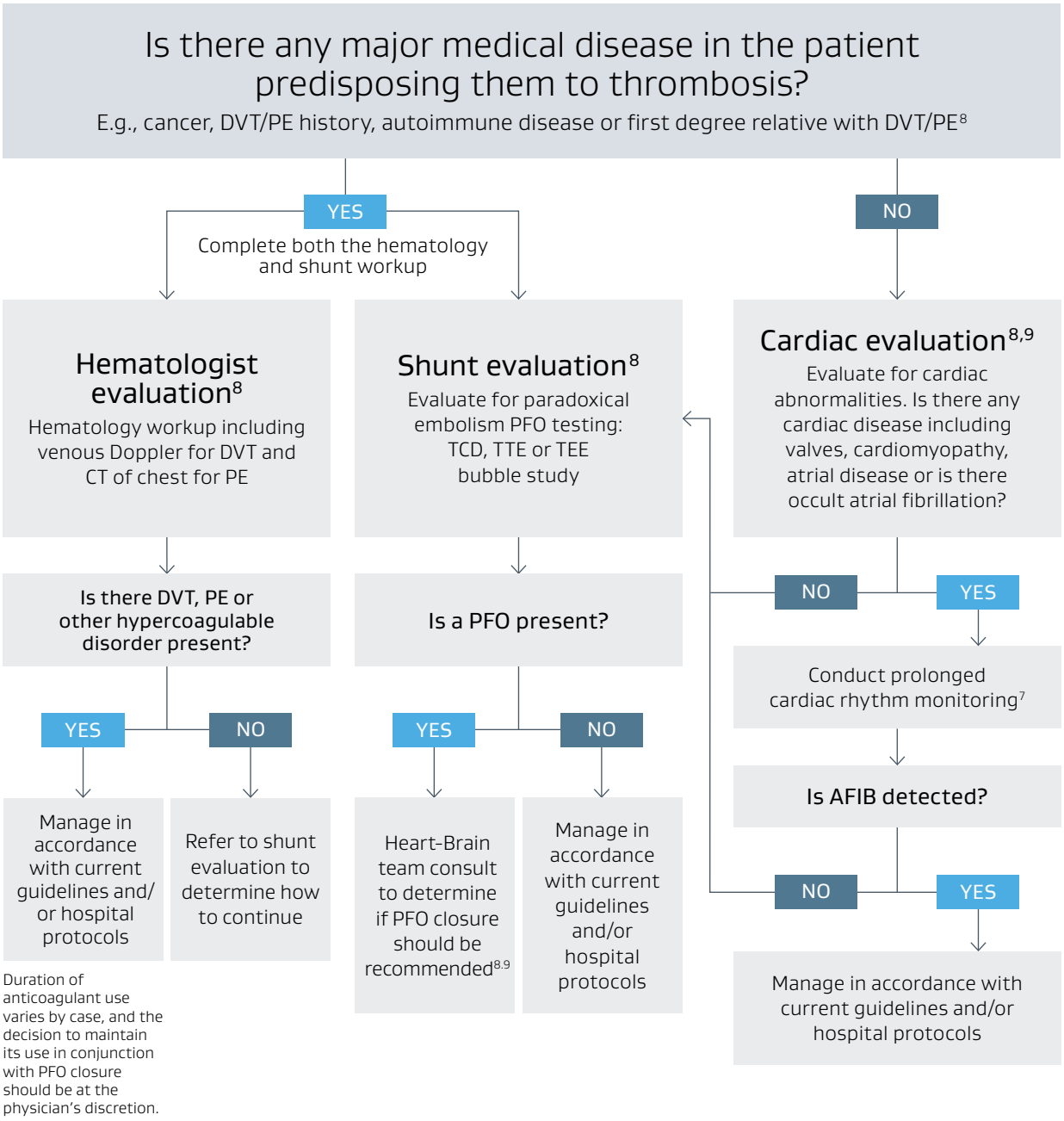
Dissection, RCVS, Moyamoya, Vasculitis, Microangiopathic disease

YES

NO

STEP 3: Emboli workup

STEP 3: Emboli workup



Used with permission from John J. Volpi, M.D., BA Neurology Houston, Texas. This algorithm represents John J. Volpi, M.D.'s general clinical practice.

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PFO Closure Procedure

Procedure basics

PFO closure is a minimally invasive transcatheter procedure, usually performed under general anesthesia or conscious sedation in a catheterization laboratory.

Expected procedural timelines*

1-2 hours†
Total length of procedure

2 days†
Time from admit to discharge

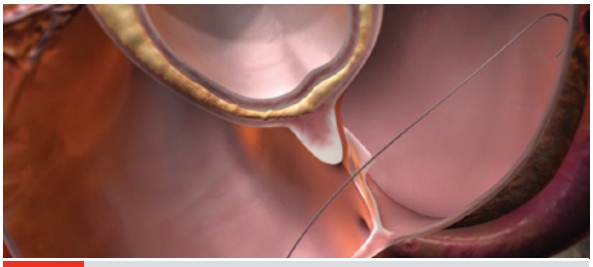
Permanent implant for PFO closure

The GORE® CARDIOFORM Septal Occluder is a permanent implant designed to prevent emboli from traveling from the right to the left atria.

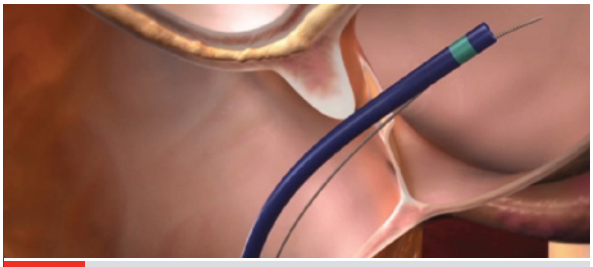
The implant conforms to the anatomy of the heart and creates a framework on which the patient's own tissue will eventually grow over and through, thus closing the PFO.

99%
Effective closure across PFO anatomies
at 24 months‡,§

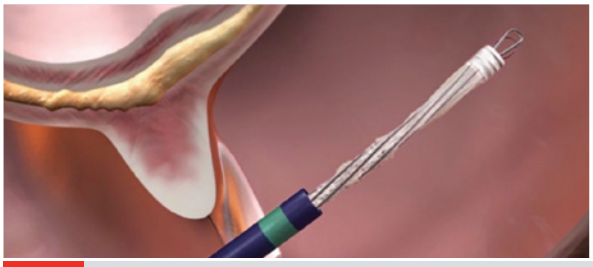
The procedure, step by step[II]

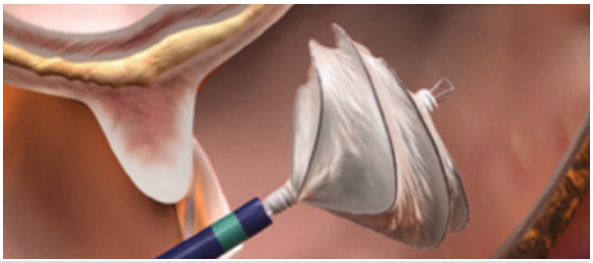


1 A small incision is made in the right groin. A catheter is threaded via guidewire through the vein and up to the heart. The guidewire is threaded through the PFO from the right to left atrium.



2 The device is navigated over the guidewire via the catheter and through the PFO.

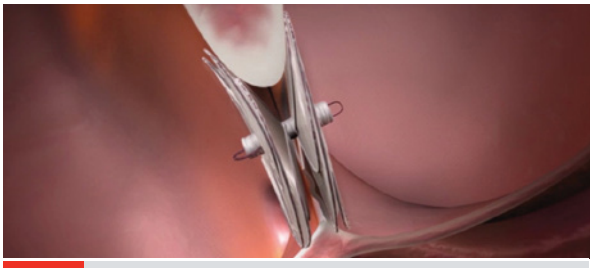




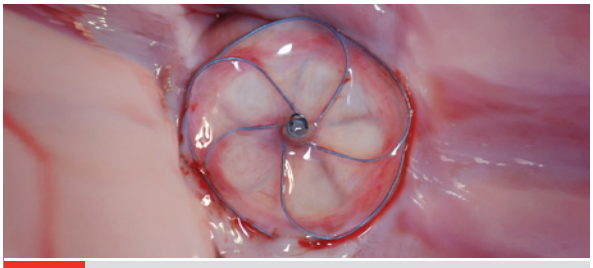
3 The physician deploys the first disc of the PFO closure device inside the left atrium.

4 The first disc is positioned to appose the left side of the septum.

5 The device's second disc is deployed and positioned to appose the right side of the septum, closing the PFO.



6 The two discs are locked together in their final position, and the device is released from the catheter.



7 The device serves as a scaffold onto which the patient's own cells grow into new tissue.

* Individual outcomes may vary. Individual patients present a range of variables that may impact procedural timeframes. Licensed health care professionals (HCP) are responsible for making decisions about patient care.

† Data on file 2020; W.L. Gore & Associates, Inc.; Flagstaff, AZ.

‡ Effective closure defined as freedom from large shunt > 25 bubbles as detected by transthoracic echocardiography adjudicated by Echo Core Lab.

§ Data on file 2020; W.L. Gore & Associates, Inc.; Flagstaff, AZ.

II Refer to *Instructions for Use*.

Post-Procedure Therapy and Care*†

Post-procedural follow-up visit protocol

DISCHARGE

Physical exam, TTE

1 MONTH

Physical exam, TTE

6 MONTHS

Physical exam, TTE

12 MONTHS

Physical exam, TTE‡

Post-procedural medical therapy protocol

- One of the following antiplatelet options:
  - ASPIRIN Acetylsalicylic Acid (81-325 mg daily)
  - Combination: ASPIRIN Acetylsalicylic Acid (50-100 mg daily)/dipyridamole (225-400 mg daily)
  - Clopidogrel (alone) (75 mg daily)
- Antiplatelet therapy should be used indefinitely

Physicians should evaluate patient need for antibiotic therapy following device implantation.

Following implant, most patients can return to their prior lifestyle after 2 weeks.

Post-procedural patient activity level

Day 1

Hospital rest for up to 1 day

Day 14+

Strenuous physical routine

* The information provided is intended to be general guidance based on current medical practices in the field. The steps described here may not be complete, and are not intended to be a replacement for the *Instructions for Use* (IFU) or the education, training and professional judgment of health care providers (HCP). Licensed HCP remain responsible for making decisions about patient care and the use of medical technologies. Refer to the IFU for complete safety information.

† Recovery and follow-up based on REDUCE Study protocols.

‡ In instances where device stability is in question, fluoroscopic examination without contrast is recommended.

PFO Closure Health Economics

PFO closure demonstrates economic and quality of life benefits

In select patients, PFO closure plus medical therapy reduces stroke burden costs and improves quality of life compared to medical management alone.[5,10]

Cost-effective

After 2.3 years, closing a PFO is more cost-effective than medical management alone.[5]

Improves quality of life

Patients who underwent PFO closure reported significantly higher physical vitality, general health, mental health and social functioning than non-closure patients.[10]

Access additional PFO Closure Health Economics and Additional Resources provided by Gore at

pfoeducation.com

PRACTICE ADVISORY UPDATE:

PFO and Secondary Stroke Prevention

Current guidance from the American Academy of Neurology (AAN), the American Heart Association/ American Stroke Association (AHA/ASA), and the Society for Cardiovascular Angiography & Interventions (SCAI) concludes that closure of a PFO may be recommended for some people that have had a PFO-associated stroke.[8,9,11]

2020 AAN Practice Advisory[8]:	2021 AHA/ASA Guidelines[9]:	2022 SCAI Guidelines[11]:
▪ In patients younger than 60 years with a PFO and embolic-appearing infarct and no other mechanism of stroke identified, clinicians may recommend closure following a discussion of potential benefits and risks.	▪ In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO with high-risk anatomic features,* it is reasonable to choose closure with a transcatheter device and long-term antiplatelet therapy over antiplatelet therapy alone for preventing recurrent stroke.	▪ In patients between the ages of 18 and 60 with a prior PFO-associated stroke, the SCAI guideline panel recommends PFO closure rather than antiplatelet therapy alone (strong recommendation, moderate certainty of evidence).
▪ In patients who opt to receive medical therapy alone without PFO closure, clinicians may recommend an antiplatelet medication such as aspirin or anticoagulation.		▪ In patients 60 years or older with a prior PFO-associated stroke, the SCAI guideline panel suggests PFO closure rather than long-term antiplatelet therapy alone (conditional recommendation, very low certainty of evidence).

Access additional PFO guideline information at

pfoguidelines.com

* In the evidence, each study defines high-risk anatomic features in a different way.

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Consult Instructions for Use
eifu.goremedical.com

INDICATIONS FOR USE IN THE U.S.: The GORE® CARDIOFORM Septal Occluder is a permanently implanted device indicated for the percutaneous, transcatheter closure of the following defects of the atrial septum: Ostium secundum atrial septal defects (ASDs); patent foramen ovale (PFO) to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18 and 60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke. CONTRAINDICATIONS: The GORE® CARDIOFORM Septal Occluder is contraindicated for use in patients: Unable to take antiplatelet or anticoagulant medications such as aspirin, heparin or warfarin; with anatomy where the GORE® CARDIOFORM Septal Occluder size or position would interfere with other intracardiac or intravascular structures, such as cardiac valves or pulmonary veins; with active endocarditis, or other infections producing bacteremia, or patients with known sepsis within one month of planned implantation, or any other infection that cannot be treated successfully prior to device placement; with known intracardiac thrombi. Refer to *Instructions for Use* at eifu.goremedical.com for a complete description of all applicable indications, warnings, precautions and contraindications for the markets where this product is available. ℞ Only

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