MC Medicor | International Center for Cardiovascular Diseases | Izola, Slovenia

Informed Consent Form

ClinicalTrials.gov Identifier: NCT05558774

Study Title: Long-term Echocardiographic and Clinical Outcomes After Percutaneous Closure of Patent Foramen Ovale

This submission includes the informed consent documents approved by the Slovenian National Ethics Committee and used for participants enrolled in this study. The documents consist of:

- Informed Consent for Percutaneous Closure of Patent Foramen Ovale (6 pages)
- Consent for Contrast Transthoracic Echocardiography Follow-up (2 pages)

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1 September 2022

Clinical team

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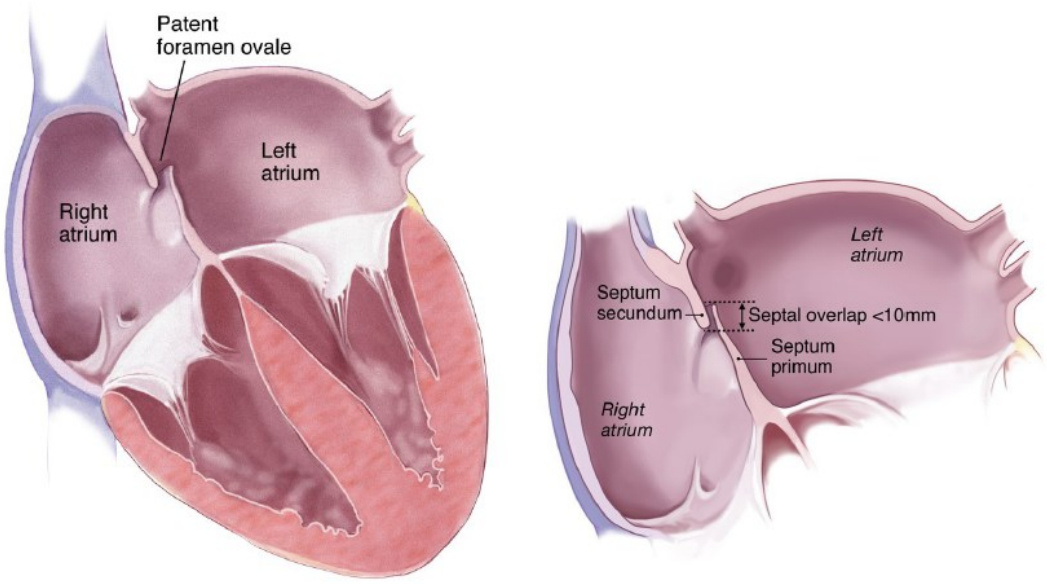
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WHAT IS A PATENT FORAMEN OVALE (PFO)?

A patent foramen ovale is an opening in the wall of the heart separating the two atria. The opening is covered by a flap resembling a small valve. In the fetus, the foramen ovale allows blood to flow from the right atrium to the left atrium. The fetus does not breathe through its own lungs; instead, it receives oxygen-rich blood from the mother's placenta through the right atrium and the foramen ovale. At birth, when the child begins breathing, resistance in the pulmonary circulation decreases and pressure in the left atrium exceeds that in the right atrium, pushing the flap of the foramen ovale closed. In most people, the foramen ovale also fuses during the first year of life, permanently closing the opening between the atria. In 25% of people, the foramen ovale does not fuse and can open when pressure in the right atrium rises. Such an increase in pressure occurs when straining during bowel movements, coughing, sneezing, or lifting heavy objects. The great majority of people with a PFO do not need further examinations or treatment, although there are some exceptions that require medical attention. In people who have blood clots in their veins and right atrium, an increase in right atrial pressure may allow the clots to pass through the opened flap of the foramen ovale into the left atrium and from there into the aorta and arteries throughout the body. If a clot reaches the arteries of the brain, it can interrupt blood flow and cause a transient ischemic attack or a stroke. Stroke caused by the passage of a blood clot through a PFO occurs primarily in younger people who have no other causes of stroke.



HOW CAN WE RECOGNIZE A STROKE?

The symptoms most commonly reported by patients during a stroke are:

• Paralysis, numbness, or tingling on one side of the face, one half of the body - an arm, or a leg.

• Impaired or lost vision in one or both eyes.

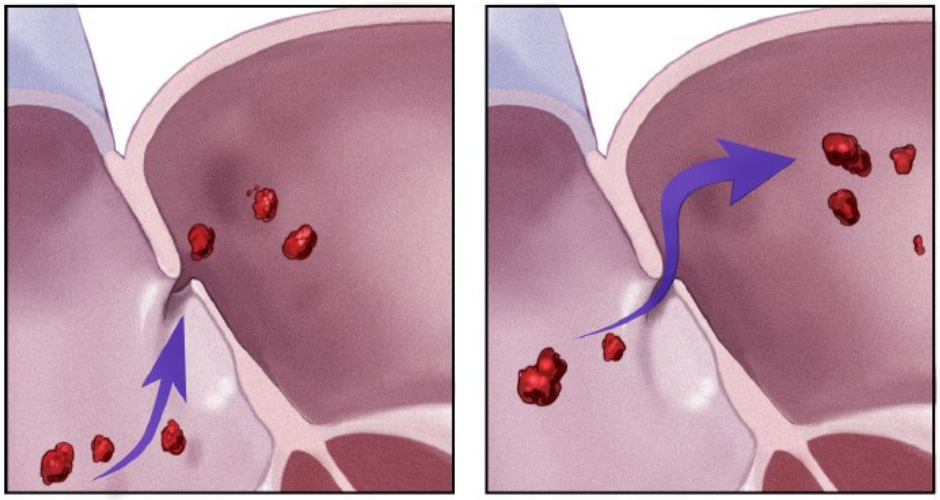
• Impaired or lost speech, or inability to understand the speech of others.

• Sudden severe headache without an obvious cause.

• Loss of balance or unsteady walking, usually in combination with another symptom.

HOW CAN WE PREVENT RECURRENCE OF A STROKE ASSOCIATED WITH A PFO?

When we determine that a stroke is likely to be causally associated with a PFO, recurrence can most effectively be prevented by closing the foramen ovale through a vein in the groin.



WHAT EXAMINATIONS ARE REQUIRED BEFORE CLOSURE OF THE FORAMEN OVALE?

In patients who have experienced a stroke, we perform the following additional examinations:

• CT (computed tomography) or MRI (magnetic resonance imaging) of the head to confirm the stroke;

• Doppler ultrasound of the carotid arteries to rule out significant atherosclerotic changes in the neck arteries that could have caused the stroke;

• Contrast transcranial Doppler ultrasound (TCD) to demonstrate passage of contrast from the venous to the arterial circulation during the Valsalva maneuver;

• Thrombophilia testing to identify an increased tendency to form blood clots;

• ECG/Holter monitoring to identify possible heart rhythm disorders that could cause a stroke;

• Transthoracic echocardiography to identify concomitant heart disease that could lead to clot formation in the heart;

• Transesophageal echocardiography (with a probe in the esophagus) to definitively confirm the PFO and characterize its morphology.

PERCUTANEOUS CLOSURE OF THE FORAMEN OVALE: PROCEDURE

The closure is performed in the cardiac catheterization laboratory under X-ray and transesophageal ultrasound guidance, which requires inserting a probe into the esophagus. To help you tolerate the procedure, you will be given sedative medication beforehand. You will remain conscious during the procedure, and your task will be to breathe calmly and remain still. We will access the heart through the femoral vein. Before inserting the catheter, we will administer local anesthesia at this site (a needle prick and a brief burning sensation). We will first reconfirm the presence of the PFO, during which you will feel pressure in the area of the liver. This will be followed by insertion of the closure device.

Immediately after the PFO is closed, you will again feel brief pressure in the area of the liver. Once the device is appropriately positioned and its effectiveness confirmed, we will remove the catheter and suture the puncture site in the groin. We will also remove the ultrasound probe from the esophagus. You will then be admitted to the ward, where you will remain on bed rest until the following morning.

The next morning, you will probably be transferred for short-term rehabilitation and will receive instructions regarding medication (aspirin, clopidogrel). After returning home, for 2–3 weeks you should perform only normal daily activities and avoid heavy lifting, contact sports, straining, and excessive physical exertion. You must pay attention to the puncture site in the groin, which should not get wet until it has healed (take care when showering). After 3–4 weeks, there are no further restrictions on physical activity, and you can resume the same lifestyle as before the procedure. In the event of any complications or uncertainties, call MC Medicor at 05 662 55 17 or 05 662 55 18.

Complications of PFO closure are very rare. Bleeding into the pericardial sac or displacement of the closure device into another part of the heart may occur. If a complication cannot be resolved in the catheterization laboratory, an experienced cardiac surgeon is on standby to resolve it by open-heart surgery.

RESULTS OF PERCUTANEOUS PFO CLOSURE AT MC MEDICOR

Percutaneous closure of a PFO is very effective and substantially less invasive than open-heart surgery. By April 2023, we had successfully performed 348 procedures at MC Medicor. Our results, which we regularly present at national and international professional meetings and publish in national and international scientific literature, are comparable with those of the best centers worldwide.

Rojko M, Suligoj NC, Zvan B, Zorc M, Kar S, Noc M. Long-term Echocardiographic Features After Percutaneous Closure of Patent Foramen Ovale. Interv Cardiol. 2026 Jan 19;21:e01. doi: 10.15420/icr.2025.30

The foramen ovale was closed in 94% of patients after 6 months, and the same closure rate was confirmed after 2 years. Two patients (0.6%) experienced a transient ischemic attack (TIA) in the years following closure, while none experienced a completed stroke with permanent neurological consequences (CVI). In one patient (0.3%), the closure device migrated to another part of the heart, requiring immediate open-heart surgery, which successfully resolved the complication; the patient had a normal postoperative course. One patient (0.3%) experienced significant bleeding at the groin puncture site, which was managed conservatively without surgery.

BY SIGNING, YOU CONFIRM THE FOLLOWING:

- You have understood the purpose and method of the procedure.
- We have explained the possible side effects and risks of the procedure to you.
- We have answered all your questions regarding the procedure.
- You have voluntarily decided to undergo the procedure, without pressure from us.
- You permit information about the procedure to be entered into the MC Medicor procedure registry.

Patient's name and Patient's signature

_____

Date and time _____

Name of person who discussed the procedure with the patient Signature of that person

_____

Date and time _____

CONSENT FOR CONTRAST TRANSTHORACIC ECHOCARDIOGRAPHY (TTE)

PATIENT _____

DATE OF BIRTH _____

EMAIL ADDRESS _____

PERSONAL TELEPHONE NUMBER

_____

Dr. Maja Rojko has informed me about the examination and the subsequent course of follow-up for study purposes.

I have understood the explanation and have had the opportunity to ask additional questions.

BY SIGNING, I CONFIRM THAT I AGREE TO UNDERGO THE EXAMINATION.

By signing, I also confirm that I permit data concerning my procedure to be entered into the Medicor registry of consecutive patients, which is used for ongoing analysis of procedural success, comparisons with international centers, and publications in the scientific literature, without disclosure of my name or personal data.

Date _____

Patient’s signature _____

FOLLOW-UP CONTRAST TTE AFTER PERCUTANEOUS PFO CLOSURE

INCLUSION CRITERIA

Blood pressure and heart rate _____

(ECG attached in the event of an irregular rhythm)

Height and weight _____

Associated chronic diseases _____

Regular medication _____

PROTOCOL / FLOWCHART

More than a functional shunt (>10 bubbles)

_____

Follow-up TEE _____

Pulmonary CT angiography (CTA) _____

RECURRENT ISCHEMIC EVENT

Neurological diagnostic investigations

_____

Comparison of imaging studies (CT/MRI)

_____