# Closure of Patent Foramen Ovale to Prevent Cryptogenic Stroke

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## Medical treatment of paradoxical embolism in the presence of patent foramen ovale (PFO)

The presence of a PFO or atrial septal aneurysm has no therapeutic consequence in otherwise healthy adults. In contrast, patients suffering a cerebrovascular accident (CVA), a transient ischemic attack (TIA), or other systemic embolism in the presence of a PFO and without any other cause of ischemic accidents are considered for prophylactic medical therapy to reduce the risk of a recurrent embolic event. There is evidence that patients with a PFO and paradoxical embolism are at increased risk for recurrent cerebrovascular events. A retrospective French multicenter study reported a yearly risk of 1.2% to sustain a recurrent CVA and of 3.4% to suffer a recurrent CVA or TIA despite oral anticoagulants or antiplatelet drugs in patients with PFO and cryptogenic stroke. Similarly, in the Lausanne Stroke Registry the CVA recurrence rate among 140 patients with PFO and stroke amounted to 1.9% per year, whereas the combined CVA and TIA recurrence rate was 3.8% per year. To date there is no consensus about type of treatment (oral anticoagulation versus antiplatelet therapy versus device closure versus surgical repair) or duration of medical therapy after an index event. The Lausanne Stroke Registry found no differences in risk reduction for recurrent CVA and TIA between different modes of anticoagulant therapy.

## Percutaneous PFO Closure

Nonsurgical closure of PFOs has become possible with the advent of umbrella devices, initially developed for percutaneous closure of atrial septal defects (ASD). The first percutaneous closure of an ASD with a Dacron double-umbrella was performed in 1974. In the meantime various percutaneous closure devices have been developed and used clinically. The devices currently available for clinical use in Europe include the Sideris Buttoned Device, the Guardian Angel device (successor of the AngelWing device), the Starflex device (successor of the Rashkind, Clamshell, and Cardioseal device), the PFO-Star, the Amplatzer PFO Occluder (modification of the Amplatzer ASD Occluder), and the Helex device. Percutaneous closure of PFO has been demonstrated to be feasible and safe and therefore represents a valuable alternative to medical treatment or surgery in patients with PFO and paradoxical embolism.

Percutaneous closure of PFO after presumed paradoxical embolism has been reported in 36 patients using the Clamshell device. The acute implantation procedure was successful in all 36 patients and there were no serious complications. By echocardiography, complete closure of the defect was achieved in 28 patients (82%), 5 patients had a very small residual defect of <1mm and 1 patient had a residual defect measuring 3mm. During a mean follow-up of 3 years, 97% of patients were free of recurrent embolism (1 recurrence in 1 patient).

The experience at the University Hospital Bern since April 1994 consists of percutaneous PFO closure with various devices in 211 patients with presumed paradoxical embolism. PFO closure was successful in

206 patients. One attempt failed because of need for surgical revision of an accidental femoral artery laceration at the beginning of the procedure. The PFO was incidentally closed intraoperatively. The other failures occurred in a patient with a marked atrial septal aneurysm who had device embolization into the pulmonary artery the day after the procedure with catheter extraction to the femoral vein and removal with cut-down and in 3 patients (1 after previous surgical repair) with failure to canulate the PFO demonstrated by echocardiography. At the last available echocardiographic bubble test, complete closure was documented in 80% of patients (96% of those treated with an Amplatzer PFO Occluder) and trivial or significant shunts (>25 bubbles in left atrium) in 10% each. During follow-up with 3-6 months of therapy with aspirin following PFO closure, a recurrent embolic event was observed in 1.6% of patients per year. Overall, the incidence of recurrences and events appears favorable compared with the projected natural course. Recurrences after catheter closure occur predominantly early and a significant advantage for the interventional therapy may materialize with time.

The presence of an atrial septal aneurysm did not negatively influence follow-up events which points to the fact that the mobility of the septum is no longer important once the PFO is closed.

Randomized multi-center trials (PC trial, PEPSI trial) comparing catheter closure with conservative therapy with at least 6 months of anticoagulation (aspirin or coumadin) are ongoing.

The calculated occurrence of cryptogenic strokes associated with a PFO in the US amounts to somewhere between 30,000 and 100,000 per year. This corresponds to more than 10% of yearly coronary angioplasty cases, for reference. The recently published associations between PFO and decompression illness in divers or migraine open other vast fields of potential indications for catheter closure.