

## Statement from the Regional HTA Centre of Region Västra Götaland, Sweden

### Percutaneous Transcatheter Closure of Patent Foramen Ovale

#### Question at issue:

Is percutaneous transcatheter closure of patent foramen ovale (PFO) a better method for prevention of a new ischemic stroke/TIA than long-term anticoagulant therapy, for adult patients with PFO that have had a cryptogenic ischemic stroke/TIA?

#### PICO (Patient, Intervention, Comparison, Outcome)

- P= Adult patients with PFO that have had a cryptogenic ischemic stroke/TIA.
- I= Percutaneous transcatheter closure of PFO, with or without continued medication.
- C= Medication.
- O= Primary: New stroke/TIA  
Secondary: Mortality, bleeding, procedure-related or device-related complications, and health-related quality of life, measured with a validated scale.

#### **Summary of the health technology assessment:**

##### Method and target group:

Venous thrombosis may under certain circumstances embolize from the right side (venous side) to the left side (arterial side) and cause a stroke. Cryptogenic stroke/TIA refers to an embolic stroke/TIA (brain attack/transient ischemic attack) without a clear source of the embolus, and where a PFO (open connection between the right and the left atria) is found. About 25% of all strokes are considered to be cryptogenic, and these patients are examined and handled primarily as others with ischemic stroke. Conventional medical treatment consists of thrombocyte aggregation inhibitors, ASA, or anticoagulant therapy, warfarin. Some patients are referred to GUCH, SU/Östra for consideration to transcatheter closure, and the decision is taken in a multi-disciplinary conference. If the patient is accepted, the procedure is initiated by puncture, and insertion of a 'device' into the femoral vein. The 'device' resembles a double-umbrella. The 'device' is endovascularly advanced into the correct location in the heart, where the device is deployed and expanded over the defect. The patient is followed-up for 6 months after the procedure, and if an ultrasonic examination then shows that the PFO has been eliminated, the warfarin treatment is discontinued, but the ASA medication is continued.

##### Level of evidence and studied patient benefit

Systematic literature search located two systematic reviews (one NICE-report, one other), six controlled studies with >50 patients, and five case series with >500 patients. The NICE-report and the systematic review were of high quality according to the AMSTAR criteria, but included only publications of low quality, and with a somewhat different PICO than the current one. All original papers assessed during the current HTA process were of low quality.

Primary outcome: 1,148 patients with cryptogenic stroke and a detected shunt were reported in controlled studies: 516 were treated with transcatheter closure, whereas the remaining patients were medically treated and followed-up for 24-52 months. 2.9% had a new stroke after transcatheter closure, compared to 13.1% after medical treatment.

The scientific support is insufficient for reduced frequency of a new stroke/TIA after transcatheter closure of PFO compared to medical treatment (very low level of evidence, GRADE ⊕).

Secondary outcome: The scientific basis is insufficient for evaluation of possibly reduced mortality by transcatheter closure (very low level of evidence, GRADE ⊕).

### **Risks**

The risk of atrial fibrillation, as complication to the intervention, ranged from 4.9% to 10%, occurring mostly during the first month. Thrombus formation on the device was reported in 0-3.3%, after six to 26 months. Procedure related complications were described in 0.8-11%, and the largest series indicated a complication risk of 0.8-1.8%. The most common complication was bleeding at the insertion site.

### **Ethical aspects**

There are ethical aspects to consider in implementing a costly, invasive procedure, related to certain risks, without assured efficiency.

### **Economic aspects**

Health economic studies and analyses are absent. The cost of transcatheter closure is approximately 110 000 SEK/patient, and about 35 patients/year are treated with this method. The cost of medical treatment (ASA) remains unaltered, whether the transcatheter closure is performed or not. Thus, the additive cost of the procedure is barely 4 MSEK/year. If further research would show that recurrence of stroke/TIA is reduced, can perhaps the cost reduction of stroke treatment compensate the additive cost of the procedure, or contribute to savings.

### **Summary and conclusion**

Cryptogenic strokes are relatively common and may lead to death and considerable morbidity. Present studies with/without control group shows that transcatheter closure of PFO may be conducted with relatively low risk, in the short-term, and suggests that the method reduces the frequency of new stroke/TIA. However, the scientific support is insufficient, as also for assessment of reduced mortality.

On behalf of the Regional HTA Centre of Region Västra Götaland, Sweden  
Göteborg, Sweden, 2011-05-25

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