Patent Foramen Ovale (PFO) and Cryptogenic Stroke or Transient Ischemic Attack: a Follow-up Study

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This thesis is based on the following studies, referred to in the text by their roman numerals.


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UNIVERSITY OF GOTHENBURG
PATENT FORAMEN OVALE (PFO) AND CRYPTOGENIC STROKE OR TRANSIENT ISCHEMIC ATTACK: A FOLLOW-UP STUDY

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Abstract

Aims: The overall aim of this thesis was to study the long-term clinical outcomes in terms of survival, complications, recurrent stroke or transient ischemic attack (TIA), and quality of life in a group of patients with patent foramen ovale (PFO) and cryptogenic stroke. Patients who had undergone PFO closure were compared with patients who had not. The first aim was to provide a long-term clinical follow-up of patients who had undergone PFO closure. The second aim was to study whether a multidisciplinary PFO conference could maintain stringent criteria for PFO closure to identify patients at high risk of paradoxical embolization. The third aim was to compare long-term outcomes of PFO closure versus non-closure in patients who had been carefully selected by a multidisciplinary PFO conference. The fourth aim was to assess health-related quality of life after PFO closure compared to a normal population and compared to patients with a PFO and ischemic stroke who had not undergone PFO closure.

Methods: Paper I was a retrospective long-term follow-up study that included all patients who between 1997 and 2006 underwent PFO closure in the GUCH center in Gothenburg. Paper II is a descriptive study of the PFO conferences and includes all patients with a PFO who were referred to our GUCH center for PFO closure between 2006 and 2009. Paper III is a prospective clinical follow-up study and includes all the patients discussed at PFO conferences in 2006–2009. Paper IV is a prospective study in which quality of life was assessed using the SF-36 Health Survey in all patients included in Paper I and III, compared with an age- and gender-matched reference group from the Swedish SF-36 normative database.

Results: In Paper I, percutaneous PFO closure was successfully performed in 85 of 86 patients. The follow-up rate was 100%. No cardiovascular or cerebrovascular deaths occurred. Two patients (both women) died of lung cancer during follow-up. The mean follow-up time was 7.3 years (5 to 12.4 years). Mean age at PFO closure was 49 years. Two patients suffered from recurrent stroke or TIA, a recurrence rate of 0.3% per year. No long-term device-related complications were observed. In Paper II, 311 patients were evaluated at the PFO conferences. The acceptance rate for closure was similar throughout these years, with an average of 46%. Patients accepted for closure were younger (mean age 50 years vs. 58 years, p<0.001). In Paper III, all patients in Paper II were followed up almost five years later. Of 314 patients, 151 (48%) were accepted for closure and 163 (52%) were not accepted. PFO closure did not provide significant benefit compared with the non-closure group for the primary endpoint (a composite of all-cause mortality, stroke and TIA) or for the secondary endpoints (stroke, TIA or all-cause mortality in isolation), either in the intention-to-treat analysis or in the as-treated analysis. Finally, Paper IV demonstrated that device closure of a PFO provides significantly better health-related quality of life at long-term follow-up, in comparison to the non-closure group; closure patients reported similar quality of life compared to an age- and gender-matched normative population (p<0.05). The non-closure group showed poorer quality of life compared to both the closure group and to an age- and gender-matched normative population (p<0.05).

Conclusions: Percutaneous PFO closure is associated with very low risk of recurrent stroke and is feasible in most patients. No mortality and no long-term device-related complications related to PFO closure were observed. The acceptance rate of less than 50% at the PFO conference underscores the complex relationship between cryptogenic stroke and PFO and the importance of a multidisciplinary approach. PFO closure does not provide any improved clinical outcomes regarding the composite of all-cause mortality, stroke and TIA compared to the non-closure group. Neither could any significant differences be demonstrated regarding recurrent stroke or TIA or regarding all-cause mortality. However, percutaneous PFO closure appears to have a favorable impact on quality of life. Larger prospective observational studies and randomized studies are necessary to assess the real benefit of PFO closure and its influence on quality of life.

Keywords: Patent foramen ovale (PFO), cryptogenic stroke, PFO closure.