

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

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av

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

- I Mirzada N, Ladenvall P, Hansson P-O, Johansson MC, Furenäs E, Eriksson P, Dellborg M. Seven-year follow-up of percutaneous closure of patent foramen ovale. *IJC Heart & Vessels*. 2013; 1: 32-6
- II Mirzada N, Ladenvall P, Hansson PO, Eriksson P, Dellborg M. Multidisciplinary management of patent foramen ovale (PFO) and cryptogenic stroke/TIA. *Journal of multidisciplinary healthcare*. 2013; 6: 357-63
- III Mirzada N, Ladenvall P, Hansson PO, Eriksson P, Dellborg M. Recurrent stroke in patients with patent foramen ovale: An observational prospective study of percutaneous closure of PFO versus non-closure. *Submitted*
- IV Mirzada N, Ladenvall P, Hansson PO, Eriksson P, Charles Taft, Dellborg M. Quality of life after percutaneous closure of patent foramen ovale in patients after cryptogenic stroke. *Submitted*

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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.