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PATENT FORAMEN OVALE CLOSURE FOR STROKE, MYOCARDIAL INFARCTION, PERIPHERAL EMBOLISM, MIGRAINE, AND HYPOXEMIA Preface

### Permalink

<https://escholarship.org/uc/item/26r7q683>

### ISBN

978-0-12-816966-7

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### Publication Date

2020

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Peer reviewed

# Preface

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A patent foramen ovale (PFO) is a congenital vestige of the fetal circulation that persists in one-fourth of adults. Once considered benign, the presence of PFO-mediated right-to-left shunt has been associated with a multitude of pathological conditions including ischemic stroke, migraine headache, myocardial infarction, peripheral embolism, hypoxemia, decompression sickness, Raynaud syndrome, and coronary spasm. A unifying pathophysiologic hypothesis is that a chemical substance, particulate matter, or deoxygenated blood from the venous circulation crosses the PFO canal from the right to the left atrium to produce these clinical conditions.

The failure to significantly prove an advantage of PFO closure in three randomized cryptogenic stroke trials (CLOSURE I, PC, early RESPECT) and three migraine trials (MIST, PRIMA, PREMIUM), with relatively wide enrollment criteria and short follow-up duration, temporarily put transcatheter PFO closure out of the limelight, with dwindling interest from the neurology and cardiology communities. After release of the long-term follow-up data from the RESPECT trial, and meta-analyses of the early three cryptogenic stroke trials, that showed superiority of PFO closure over medical therapy for secondary prevention of stroke, the United States Food and Drug Administration approved the Amplatzer PFO Occluder (Abbott; Chicago, IL) in October 2017 for percutaneous PFO closure to reduce risk of recurrent stroke from paradoxical embolism. Prior to this, percutaneous PFO closures were performed off-label with the use of similar atrial septal defect closure devices. The off-label availability of PFO closure devices in the United States and free availability in most other countries proved to be a dilemma for researchers recruiting patients for clinical trials, resulting in slow patient enrollment and, likely, clinician-biased preference for off-label PFO closure for the higher-risk patients, as opposed to a 50% chance of their randomization to a medical therapy arm. More recent results retrospectively condone this attitude based on intuition.

Between late 2017 and early 2018, four positive cryptogenic stroke trials (long-term RESPECT, CLOSE, Gore REDUCE, and DEFENSE-PFO) placed PFO closure back into the spotlight with renewed interest among clinicians. These studies showed that with good patient selection and longer follow-up, it can be demonstrated that PFO closure significantly reduces the risk of recurrent stroke compared to standard of care medical therapy in patients with imaging-confirmed ischemic stroke of no other apparent etiology.

In addition to closure of PFO for cryptogenic stroke (more accurately termed a “PFO-associated stroke”), this book also advocates for consideration of PFO closure in other symptomatic, and often debilitating, conditions. Unlike the situation for PFO-associated stroke, there are no current randomized clinical trials that document the benefit of PFO closure over medical therapy for any of these other pathologies. It is probable that a new randomized clinical trial for PFO and migraine will be carried out over the next few years. The other conditions, however, are relatively infrequent and will likely never be subjected to the rigors of a randomized trial. The data presented in these chapters will aid in the guidance of physicians who care for these patients.

When treating patients with a PFO-mediated pathology, clinicians will encounter a multitude of questions, including appropriate imaging assessment of the PFO anatomy and shunt physiology, ischemic stroke risk assessment and workup, suitable patient selection, device choice and implantation technique, and consideration of percutaneous closure for a variety of pathologies mentioned above. This book will serve cardiologists, neurologists, pulmonologists, internists, general practitioners, and researchers with an interest in PFO-related conditions; it embodies the most current and comprehensive review of the clinical manifestations, diagnosis, and management of PFO pathologies as described by some of the leading experts in the field. What was once considered an innocent bystander remnant of the fetal circulation has now been shown to be a potential pathway of death, stroke, migraine, and unexplained hypoxemia, all preventable by transcatheter closure on an outpatient basis. Since it is present in 25% of the world’s population, a PFO should be classified as the most common congenital heart defect and should be treated with concern for the problems that it can generate.

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