Patent Foramen Ovale: The Missing Link between Deep Venous Thrombotic Disease and Embolic Stroke

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In 1877, Kohnhern, a German anatomist, performed an autopsy on a young woman with a patent foramen ovale (PFO) who had died from a nonhemorrhagic stroke. He hypothesized that a clot passing through the PFO must have caused the patient's demise and thus provided the first description in the medical literature of a paradoxical embolism.[1] In the 128 years since Kohnhern's original description of paradoxical embolism, there has been a great deal of study of the potential association between PFO and stroke. Clinical diagnostic techniques have been developed to permit the antemortum diagnosis of PFO and multiple therapeutic options have been developed and explored. However, despite much scholarly activity, an evidence-based consensus regarding the optimal treatment of patients with PFO and cryptogenic stroke has yet to be developed.

The foramen ovale represents a central location in the intratrial septum where the septum primum and the septum secundum overlap (Fig 1). In utero, these tissues grow to overlap but remain unfused allowing ongoing communication between the right atrium and left atrium. This allows venous blood to return from the placenta to reenter the systemic circulation without traversing the pulmonary circulation. Shortly after birth, the septum primum and septum secumdum fuse and the communication between right and left atrium closes in the majority of cases.[2] Failure of the septum primum and the secundum to fuse results in a PFO.

In a large autopsy study preformed at the Mayo Clinic involving 965 hearts, the incidence of PFO was found to be 27%.[3] Pooled autopsy studies have demonstrated a similar incidence of PFO of 26% with a range of 17 to 35%.[4] Clinically, the antemortum diagnosis of PFO is best made using echocardiography. Transthoracic echocardiography (TTE)

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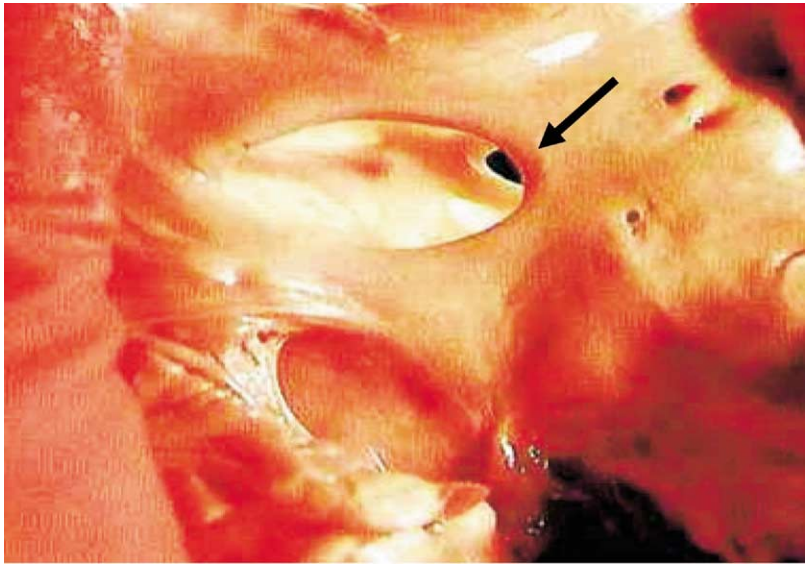

FIG 1. Autopsy specimen demonstrating patent foramen ovale (single arrow) as viewed from the right atrial side. Left-sided septum primum is seen within the foreman ovale and right-sided septum secundum (underlying the arrow) is seen. Photo courtesy of NMT Medical.

has limited ability to detect PFO and the incidence of PFO detected by TTE in large active laboratories has been 10 to 18%. Properly performed, transesophageal echocardiography (TEE) in large active laboratories has detected PFO in 18 to 33% of patients studied. The incidence of PFO by TEE very closely approximates the incidence of PFO in pooled autopsy data and has lead to the position that a properly preformed TEE is the clinical gold standard for antemortum detection of PFO. To be properly preformed, the TEE study should include Doppler flow interrogation and imaging with intravenous injection of agitated saline or echo imaging contrast agent during a Valsalva maneuver or with external abdominal compression to demonstrate right-to-left flow across the intraatrial septum.[5] TEE also provides potentially import information regarding atrial septal morphology, the presence of an atrial septal aneurysm, and the presence or absence of intraatrial thrombus or masses. The absence of the demonstration of a PFO on transthoracic imaging (TTE) does not exclude the potential of a PFO.

More recently, intracardiac echo has been used as both a diagnostic imaging modality as well as a direct transcatheter therapeutic maneuver. Less invasive screening has been recently advocated using IV contrast and either transcranial Doppler (TCD) imaging or carotid duplex scan-