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iVIEW

EDITOR'S PAGE

LA Septal Pouch as a Source of Thromboembolism: Innocent Until Proven Guilty?

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Every 40 s someone in the U.S. has a stroke, and every 4 min a patient dies from a stroke. Of the 800,000 strokes a year, close to 200,000 are recurrent attacks (1). Strokes have a profound impact which is even greater in women and minorities (2). National statistics from death certificate data demonstrate an increase in deaths attributed to stroke for blacks (3). The BASIC (Brain Attack Surveillance in Corpus Christi) study demonstrated an increased incidence of stroke among Mexican Americans compared with non-Hispanic whites (4). Given the substantial morbidity, the estimated direct and indirect cost of stroke for 2010 is $73.7 billion (1). Large-scale preventive efforts, while ideal, are difficult to implement and even more difficult to adhere to, and our ability to minimize the incidence of strokes has been modest at best. Not surprisingly, there is a great amount of enthusiasm to identify treatable causes to prevent first and recurrent strokes.

Determining the etiology of a stroke may influence prognosis, therapy and, very importantly, the likelihood of stroke recurrences. Of all strokes, approximately 87% are ischemic, and 10% are due to intracerebral hemorrhage; about 20% of strokes arise from the heart and are thought to be, albeit often with a bit more optimism than based on high-quality data, best suited for prevention with interventional technologies (5). Such cardioembolic strokes are generally large and prone to early recurrence with higher mortality—all of which make prevention a more pressing issue. It is generally understood that the exact source of the embolism must be identified to prevent recurrences and thus provide effective therapy. In 10% to 30% of instances, the etiology of the stroke is not obvious despite a detailed work up; this group, termed cryptogenic stroke, represents an unfortunate gap in our knowledge (6).

In patients without valvular disease, the left atrium (LA) is thought to be involved in a thromboembolic process in 2 ways: either as a source when the clot arises from the LA appendage, or less frequently, as a passageway for venous thrombi through a patent foramen ovale (PFO). With respect to cardioembolic strokes, the disease process that has justifiably received the most attention is atrial fibrillation (AF) and the structure that has received the most attention is the LA appendage. In nonvalvular AF, LA thrombi almost exclusively tend to arise in the LA appendage and preventing their access to the systemic circulation, as with an LA appendage occlusive device, can be beneficial. The PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) trial demonstrated that in the setting of nonvalvular AF, excluding the LA appendage from the systemic circulation with a device was noninferior to anticoagulation therapy with warfarin (7). In rheumatic heart disease, the risk of embolic stroke is much higher, but curiously, an LA thrombus is identified in the appendage in only one-half the patients. In the remaining patients, it is often located elsewhere in the LA (8). This raises the intriguing question—where else can a thrombus arise in the LA (that might allow us to whittle away the cryptogenic stroke group) and why does that structure host a thromboembolic source?

The possible importance of a pouch-like structure on the LA side of the interatrial septum was described recently in an autopsy study (9). Termed a left atrium septal pouch (LASP), this structure was proposed to represent an incomplete fusion of the septum primum

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and septum secundum, during closure of foramen ovale. When a foramen ovale closed spontaneously, in a significant number the septum primum and septum secundum fused only at the caudal limit of the zone of overlap. This incomplete fusion resulted in a pouch that, in the majority of instances, communicated with the LA. This kangaroo pouch–like structure was seen in about one-third of hearts with a depth of 8 ± 4 mm. Data from the angiographic computed tomography scans has also indicated that the prevalence and depth of the structure in live patients is similar to that observed in autopsy studies (10). It is conceivable that incomplete fusion at cranial limit of the zone of overlap would result in a right atrial septal pouch with an inferiorly facing mouth.

Two papers in this issue of *iJACC* provide some further data on this entity (11,12). A pictorial essay by Gurudevan et al. (11) proposes the feasibility of imaging an atrial pouch with clarity. It has been tacitly believed that the LA, except for the appendage, is a smooth structure. The aforementioned autopsy study suggested that in about one-third of subjects the LA pouch could contribute to stasis, thus fulfilling some elements of the 1850s concept of the Virchow triad necessary for a thrombus formation. Whether this theoretical possibility in the LASP was actually associated with thrombus in the living human being was still an unclear element. In the current presentation, authors provide 3 examples where the answer may be affirmative. Two of 3 examples appear to have developed a thrombus probably due to stasis within the LA. Although stasis within the pouch may have played a role, 1 of the 3 patients seemed to have developed a thrombus due to endothelial denudation. The chronic inflammation seen at the site of attachment of the thrombus to the atrial septum supported this contention; history of deep venous thrombosis was also present in this patient.

Granted that LASP can play host to a thrombus, how often does it lead to a stroke? Like a lot of literature about PFO, there is much to be learned before one can place such a discovery in perspective. A possibility cannot be denied that the LASP could turn out to be a big player in the story of cardioembolic strokes arising from the LA. In this issue of *iJACC*, Tugcu et al. (12), provide the first prospective look at stroke due to LASP and show that the incidence of stroke is not significantly influenced by LASP. While the paper does have a number of limitations, it included a sizable population and had used reasonable imaging technology. This suggests that even if LASP can cause strokes, it seems from early data and the clinical experience of rarely seeing a clot in the LASP compared to the frequency in the LA appendage, that it is not likely to have a materially large population attributable risk of cryptogenic strokes.

However, before dismissing this entity into the footnotes of medicine or before elevating it into a full member of the treatable stroke foci pantheon, we believe that this area still needs more robust evaluation. Future investigations will need to focus on 1) the population attributable risk of stroke and embolism due to the LASP; and 2) factors affecting the thrombogenicity of the pouch. We presented these 2 very different reports to show the usual ferment of science that occurs when a relatively new entity is implicated. Our discerning readers will surely ponder about what shapes one's thinking about literature—the excitement of an observational hypothesis (how pulmonary vein flows could influence thrombus formation in a LASP) in the Gurudevan report (11) with the reality of hard data, despite its limitations, from the Tugcu (12) report. Such exchanges will finally resolve the role of the LASP as a possible culprit in embolic strokes and whether it has the potential to be a viable target for therapy in cardioembolic strokes, especially those that may carry a cryptogenic label. To quote Thomas Jefferson, it is laudable to encourage investigation but should we not hold back conclusion (13)?

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