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Viewpoint

Atrial septal aneurysm and cryptogenic stroke: an arrhythmic approach to pathophysiology

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"In patients with cryptogenic strokes, more attention should be paid to the possible existence of paroxysmal atrial fibrillation, especially in those with atrial septal aneurysm with or without patent foramen ovale."

Keywords

Atrial septal aneurysm, patent foramen ovale, cryptogenic stroke, arrhythmia, atrial fibrillation, stroke.

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Dear Editor,

The connection between cryptogenic stroke and atrial septal aneurysm (ASA) with or without patent foramen ovale (PFO) has been a debated topic for decades with regard to pathophysiological mechanisms and clinical consequences. This debate has been raised by the unknown etiology of stroke and the concern associated with the cryptogenic stroke with an otherwise innocent cardiac pathology called ASA and PFO. Cryptogenic stroke accounts for up to 40% of ischemic strokes in children, adolescents and adults [1-5]. While there is an anatomical pathology in the interatrial septum, namely PFO and ASA, the embolic source of strokes has not been clearly defined. Hypothetically, the occurrence of thrombus has been attributed to the site of aneurismal recess tissue itself or, less likely, the PFO tunnel itself [1, 5, 6]. Another mechanistic theory is that thrombus occurs in the left or right atrial cavities, including the appendages, as in the cases of pulmonary embolism and stroke due to atrial fibrillation (AF) [7, 8]. Although the literature lacks definite evidences, arrhythmic associates of ASA are likely to be involved in the pathogenesis of cryptogenic strokes. This issue has been mentioned in the critical review of Leonard et al. [5]. Indeed, indirect evidences to support the association between cryptogenic stroke and ASA through AF have been reported sparsely in the literature. Patients with ASA have been shown to display significantly higher P-wave dispersion [9], and atrial electromechanical delay [10]. These electromechanical and electrophysiologic changes observed in ASA may potentially play a substrate role in inducing supraventricular arrhythmia or AF. Moreover, an increased prevalence of AF and paroxysmal supraventricular tachycardia has been reported in patients with ASA. Janion and Kurzawski have documented paroxysmal AF attacks in 17% of patients with ASA [9].

Beyond the structural abnormalities like valvular regurgitation and ascending aortic dilatation in ASA, premature atrial and ventricular contractions, supraventricular tachycardia and AF have shown an independent association with the presence of ASA [11-13]. Therefore, rather than the *in-situ* thrombus formation in aneurysmatic atrial septal tissue and paradoxical embolization through the PFO, paroxysmal AF-induced development of thrombus in the left or right atrial chamber and subsequent embolization is more

likely to be the scenario to explain the cryptogenic stroke in patients with ASA. In accordance with this scenario, closure of PFO with a device has not resulted in any benefit compared to medical therapy alone for the prevention of recurrent stroke or transient ischemic attack [14-16]. Non superiority of PFO closure to medical treatment supports the idea that the presence of PFO itself is not the main contributing factor for cerebral thromboembolic events or cryptogenic strokes. A recent analysis has revealed that the presence of an ASA is the main contributing factor for recurrent stroke in patients with PFO rather than shunt size [17]. Within this context, ASA should come forward in the discussion about the pathophysiological mechanism of cryptogenic strokes due to its association with AF. Therefore, in patients with cryptogenic strokes, more attention should be paid to the possible existence of paroxysmal AF, especially in those with ASA with or without PFO.

Declaration of interest

The Authors declare that there is no conflict of interest. Financial support: none.

References

- Kuriki A, Ueno Y, Kamiya Y, Shimizu T, Doijiri R, Tateishi Y, Kikuno M, Shimada Y, Takekawa H, Yamaguchi E, Koga M, Ihara M, Ono K, Tsujino A, Hirata K, Toyoda K, Hasegawa Y, Hattori N, Urabe T. Atrial Septal Aneurysm may Cause In-Hospital Recurrence of Cryptogenic Stroke. J Atheroscler Thromb. 2021;28(5):514-523.
- Hart RG, Catanese L, Perera KS, Ntaios G, Connolly SJ. Embolic Stroke of Undetermined Source: A Systematic Review and Clinical Update. Stroke. 2017;48(4):867-72.
- Hart RG, Diener HC, Coutts SB, Easton JD, Granger CB, O'Donnell MJ, Sacco RL, Connolly SJ; Cryptogenic Stroke/ESUS International Working Group. Embolic strokes of undetermined source: the case for a new clinical construct. Lancet Neurol. 2014;13(4):429-38.
- 4. Sacco RL, Diener HC, Yusuf S, Cotton D, Ounpuu S, Lawton WA, Palesch Y, Martin RH, Albers GW, Bath P, Bornstein N, Chan BP, Chen ST, Cunha L, Dahlöf B, De Keyser J, Donnan GA, Estol C, Gorelick P, Gu V, Hermansson K, Hilbrich L, Kaste M, Lu C, Machnig T, Pais P, Roberts R, Skvortsova V, Teal P, Toni D, Vandermaelen C, Voigt T, Weber M, Yoon BW; PRoFESS Study Group. Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. N Engl J Med. 2008;359(12):1238-51.
- Leonard Y, Marras M, Calcaterra G, Bassareo PP. Association between atrial septal abnormalities (patent foramen ovale, atrial septal defect, interatrial septal aneurysm) and cryptogenic stroke in children. J Pediatr Neonat Individual Med. 2021;10(1): e100154.

- Ghosh S, Ghosh AK, Ghosh SK. Patent foramen ovale and atrial septal aneurysm in cryptogenic stroke. Postgrad Med J. 2007;83(977):173-7.
- Essa H, Hill AM, Lip GYH. Atrial Fibrillation and Stroke. Card Electrophysiol Clin. 2021;13(1):243-55.
- Yetkin E, Cuglan B, Turhan H, Ozturk S, Yetkin O. Ignored Identity of Age-Dependent Increase in Pulmonary Embolism: Atrial Fibrillation. Chest. 2019;156(6):1271-2.
- Janion M, Kurzawski J. Atrial fibrillation in patients with atrial septal aneurysm. Cardiol J. 2007;14(6):580-4.
- Russo V, Rago A, Di Meo F, Papa AA, Ciardiello C, Cristiano A, Calabrò R, Russo MG, Nigro G. Atrial Septal Aneurysms and Supraventricular Arrhythmias: The Role of Atrial Electromechanical Delay. Echocardiography. 2015;32(10): 1504-14.
- Yetkin E, Ileri M, Korkmaz A, Ozturk S. Association between atrial septal aneurysm and arrhythmias. Scand Cardiovasc J. 2020;54(3):169-73.
- Atak R, Ileri M, Ozturk S, Korkmaz A, Yetkin E. Echocardiographic Findings in Patients with Atrial Septal Aneurysm: A Prospective Case-Control Study. Cardiol Res Pract. 2019;2019:3215765.
- Yetkin E, Atalay H, Ileri M. Atrial septal aneurysm: Prevalence and covariates in adults. Int J Cardiol. 2016;223:656-9.

- Furlan AJ, Reisman M, Massaro J, Mauri L, Adams H, Albers GW, Felberg R, Herrmann H, Kar S, Landzberg M, Raizner A, Wechsler L; CLOSURE I Investigators. Closure or medical therapy for cryptogenic stroke with patent foramen ovale. N Engl J Med. 2012;366(11):991-9.
- Meier B, Kalesan B, Mattle HP, Khattab AA, Hildick-Smith D, Dudek D, Andersen G, Ibrahim R, Schuler G, Walton AS, Wahl A, Windecker S, Jüni P; PC Trial Investigators. Percutaneous closure of patent foramen ovale in cryptogenic embolism. N Engl J Med. 2013;368(12):1083-91.
- 16. Dowson A, Mullen MJ, Peatfield R, Muir K, Khan AA, Wells C, Lipscombe SL, Rees T, De Giovanni JV, Morrison WL, Hildick-Smith D, Elrington G, Hillis WS, Malik IS, Rickards A. Migraine Intervention With STARFlex Technology (MIST) trial: a prospective, multicenter, double-blind, sham-controlled trial to evaluate the effectiveness of patent foramen ovale closure with STARFlex septal repair implant to resolve refractory migraine headache. Circulation. 2008;117(11): 1397-404.
- Turc G, Lee JY, Brochet E, Kim JS, Song JK, Mas JL; CLOSE and DEFENSE-PFO Trial Investigators. Atrial Septal Aneurysm, Shunt Size, and Recurrent Stroke Risk in Patients With Patent Foramen Ovale. J Am Coll Cardiol. 2020;75(18):2312-20.