Patent foramen ovale and atrial fibrillation: can neuroimaging help to distinguish the etiology?

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Aims and objectives

The causes of stroke may be classified by etiology in known and undetermined etiology (cryptogenic). Cardio-embolism and macro- and micro-angiopathy are the most frequent etiologies of ischemic strokes, more than 40% of which are cryptogenic, mainly in subjects aged <55 years. The causes of cryptogenetic stroke comprehend paradoxical AF, arterial dissection, vasospasm, migraine-induced stroke and PFO.

A PFO is a residual inter-atrial element of fetal anatomy and circulation that persists after birth in approximately 25% of adults. It is a potential route for embolic transit from the systemic venous circulation to the brain, and its prevalence is higher in young patients with cryptogenic stroke than in those with a known stroke etiology. It is considered small if it has a diameter of 2-5 mm, and large if its diameter 6-10 mm, but it is also possible to quantify its size by measuring right-to-left shunt (RLS).

The most frequent mechanism explaining an increased risk of recurrent stroke is paradoxical embolism due to the systemic passage of venous thrombi through an inter-atrial conduit. Microaggregates and small blood clots may cross the PFO, avoiding intrapulmonary lysis and leading to an increased risk of brain injury.

A stroke may also be secondary to AF, the most frequent cardiac arrhythmia (population prevalence about 0.4%), which alters mechanical cardiac synchronism and has hemodynamic consequences that can lead to thrombus formation and systemic embolization.

The authors found a different vascular distribution of lesions for each cryptogenetic stroke.

The aim of this study was to map of the specific ischemic lesion patterns of distribution of PFO-stroke and AF-stroke in our study population.
Methods and materials

We retrospectively reviewed the medical records of 750 patients admitted to our hospital with a clinical suspicion of acute ischemic stroke between January 2008 and February 2016.

All patients underwent CT Scan of the brain in the Emergency Department and 534 patients underwent magnetic resonance (MR) Brain Scan during the admission in Neurology Department.

By diagnostic test, including both laboratoristic and instrumental, the patient subtypes were classified using the five categories of the TOAST classification system. Patients with atherosclerotic disease of carotid artery (335), small-artery occlusion (212), other vasculopathies (13) and hematologic disorders (19) were excluded (Fig.1).

Only the 171 patients who had a cryptogenic stroke were included in the study, all of whom had undergone a complete clinical neurological examination, transcranial colour Doppler ultrasonography with contrast (c-TCD), transthoracic echocardiography (TEE) with saline solution, cerebral computed tomography (CT) with or without an angiographic phase (CT-Philips, Brilliance 16 slice) and a standard MR (Fig. 1).

Particularly MR brain Scans were acquired with Two different MR Units: Philips, Achieva Intera Achieva 1.5 T before 2010 and Philips, Achieva D-Stream 1.5 T after. Sequences of protocol included fluid-attenuated inversion-recovery (FLAIR), DWI sequences and angiographic sequences.

Finally, analysis of the background data of all of the patients identified two groups with different pre-existing diseases: 128 with PFO and 43 with AF. In few patients in PFO-group (18) imaging was not available and it was considered only radiologic reports.

The DWI and FLAIR sequences were used to confirm the ischemic lesions, which were classified in cortical, subcortical and cortical/sub-cortical. Only 153 patients were enrolled for this analysis because imaging for 18 was not available.

As in other studies, the affected vascular territories were divided into the Anterior Cerebral Artery (ACA), MCA, VB including PCA (Posterior Cerebral Artery), brainstem and cerebellar. If more than one territory was involved, we used the definition "multisite (MS) stroke". All 171 patients were considered for this analysis, because also the reports of 18 patients with imaging not available described the sites of ischemia of the brain.

Two neuroradiologists, with respectively 6 and 20 years of experience, made these analyses.
This type of work does not require approval by Ethics Committee, because of the retrospective nature of the study, but before all diagnostic exams patients received and signed informed consent.

The differences in the frequency of lesion patterns and the corresponding vascular territory of the lesion between the patients with PFO- and AF-stroke were compared using Pearson’s #2 test. The statistical analyses were made using XLSTATS (©Rodney Carr 1997-2004) and Graph Pad InStat software (©1992-2009 by GraphPad Software).
Results

Of 171 patients n= 74 were males and n= 97 were females. Of these patients, 43 (male n= 16; female n= 27) had AF and 128 (male n= 58; female n= 70) had PFO. The mean age was respectively of 50,51 (± 18,38 SD) for patients with PFO and of 74 with AF (± 26,62 SD).

VB and MS territories were equally frequently involved in the PFO-stroke group (32.8%), and this frequency was significantly different from that observed in the AF-stroke group (VB: 9.3%, p=0.002; MS: 16.3%, p=0.03) (Tab.1).

MCA was the third territory in the PFO-stroke group to be involved (33/128; 25.8%) with a lower frequency respect to the AF-stroke group (32/43; 74.4%) and fourth territory in PFO-stroke group was ACA (11/128; 8.6%), which showed significant differences respect to other group (0/43; 0%).

The AF-stroke resulted most frequently localized in MCA territories (74%), but without any statistical difference between the two group (p=1.31).

In our study we did not find lesions in ACA territories for AF-stroke.

The analysis of radiological characteristics showed frequencies of localization of PFO-stroke lesions were: 34.3% cortical, 31.2% subcortical and 20.3% cortical-subcortical. While AF-stroke lesions were: cortical-subcortical 60.6%, cortical 32.5% and subcortical 6.9% (Fig. 2). The difference of cortical involvement between PFO- and AF-stroke was statistically significant (p=0.007).

We found a greater frequency of MS stroke in patients with more severe RLS (37,5%).

For c-TCD and TTE evaluation after Valsalva manoeuvre, we have found the presence of a severe degree of shunt in 47 patients with a good correlation level between the two methods (K-Choen = 0.640). Of these patients n=18 presented a MS involvement and n=16 patients presented a VB involvement.
Fig. 2: Summary graphic representation of all vascular territories involved stroke in PFO- and AF-stroke.

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Conclusion

As demonstrated by our statistical analysis, in clinical practice PFO may be considered a cause of stroke on the basis of radiological findings, when VB vascular territory or MS brain involvement are present in younger patients (<50 age).
References
