

# Assessment of Hypercoagulation State in Patients with Embolic Cerebrovascular or Transient Ischemic Attack and Patent Foramen Ovale

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**Background:** Patent foramen ovale (PFO) causes a right-to-left shunt in about a quarter of normal population. Hypercoagulation may be a risk factor for embolic cerebrovascular accidents (CVA) in these patients by paradoxical emboli. In this study, we checked hypercoagulation states in the embolic CVA patients with PFO.

**Methods:** In a cross-sectional study, 40 patients with CVA or transient ischemic attack (TIA) and PFO participated in the study. Serum level of Homocystein, lupus anticoagulant screening test, Factor V Leiden, Anti Cardiolipin Antibody (ACLA) (IgG, IgM), Anti-thrombin III, protein C, protein S, Anti B2 glycoprotein I and platelet count were checked in all patients. The data were analyzed using the statistical package for social science series (SPSS 15.0) and descriptive statistical method.

**Results:** The mean age was  $42.4 \pm 12.1$ . Seventeen (42.5%) patients were females. Twenty-two (55%) cases were diagnosed as having CVA and the others as TIA. Three (7.5%) of the patients were diabetic and 8 (20%) had a history of different stages of hypertension. Hyperlipidemia was detected in 6 (15%) patients and according to the laboratory data none had any signs of hypercoagulation.

**Conclusion:** According to the present study, hypercoagulation as a cofactor in CVA patients with PFO did not seem to be a direct risk factor for embolic CVA at least any higher than for normal population.

**Keywords:** CVA, PFO, Hypercoagulation

## Introduction

Patent foramen ovale (PFO) causes a right-to-left shunt in about a quarter of the normal population.<sup>1</sup> According to several studies the significant association between cryptogenic stroke and PFO in patients supports the hypothesis that the paradoxical embolism could be a relevant cause of stroke.<sup>2</sup> This association has been shown in several studies of patients less than 55 years of age. This relationship is especially detected in the presence of atrial septum aneurysm (ASA).<sup>3,4</sup> However, other researchers suggested that in the setting that ~25% of the population have a PFO, the simple association of PFO with stroke is not enough to establish the diagnosis of paradoxical embolism.<sup>5,6</sup> Thus, some other risk factors for embolic cerebrovascular

accidents (CVA) such as hypercoagulation states may be considered as a co-factor in embolic CVA patients with PFO.

In regard to detecting any stage of hypercoagulation in patients with a history of stroke or at high risk for stroke as evidenced by prospective data, it may be useful to perform some especial laboratory tests such as C-reactive protein, homocysteine, antiphospholipid antibodies, lupus anticoagulant screening test, Plasminogen, Clotting time and lipoprotein (a). However, factor V Leiden, prothrombin G20210A, protein C, protein S, and antithrombin are not recommended for routine testing but may be useful for research protocols.<sup>7</sup>

The present study attempted to establish the relationship between hypercoagulation state and embolic CVA in patients with PFO.

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## Patients and Methods

This cross-sectional study was performed on 40 patients with PFO detected in trans-esophageal

echo (TEE), and embolic CVA or TIA attacks, less than 2-month from their admission.

These patients were expected to have PFO with significant right to left shunt and ejection fraction more than 55%. Exclusion criteria included the patients with signs of atheromatic plaque in carotid artery, LV aneurysm, clot in left (Lt) cavity, mitral stenosis, supra ventricular arrhythmia, atrial fibrillation, atrial flutter, smoke pattern in left ventricular cavity or any other causes of embolic CVA.

Informed consent was obtained from all patients for inclusion in the study. The data were collected through completion of formal questionnaires by the patients. Demographic data obtained from the patients or their medical records included history of malignancy, rheumatologic disease, diabetic mellitus (DM), hypertension (HTN), hyperlipidemia, smoking and previous CVA. The serum level of homocystein, lupus anticoagulant screening test, Factor V leiden, ACLA (IgG, IgM), anti- thrombin III, protein C, protein S, Anti B2 glycoprotein1, platelet count were checked in all patients. The data were analyzed using the statistical package for social science series (SPSS 15.0) and descriptive statistical method.

## Results

The mean age was  $42.4 \pm 12.1$ . Seventeen (42.5%) patients were females. Twenty-two (55%) of the patients were diagnosed as having CVA and others had TIA. Thirty-four patients (85%) had no history of addiction or cigarette smoking. None of the patients had a history of previous CVA, TIA, malignancy or rheumatologic diseases. Three

(7.5%) cases were diabetic. Eight (20%) patients had a history of different stages of hypertension. Hyperlipidemia was detected in 6 (15%) patients. Thirteen (32.5%) patients were found to have large PFO by Echocardiography ( $\geq 4$ mm or 50 bobble passed after 5 cardiac cycle with agitated saline injection). The others had large PFO and atrial septal aneurysm, with mean ejection fraction  $60.3 \pm 2.37$  SD. The mean serum level of coagulative factors is summarized in Table 1.

Laboratory data did not show sign of hypercoagulation state in any of the patients.

## Discussion

As mentioned previously overall 25% of the normal population have PFO. Embolic CVA in the patients may be due to paradoxical emboli. However, despite high prevalence of PFO, the rate of embolic CVA is low. Since, the rate of PFO in patients with cryptogenic CVA was high,<sup>8</sup> the relationship between such entities may be affected by some other cofactors. Hypercoagulation disorders cause several neurological deficits and are usually treated with anticoagulant medications.<sup>9</sup>

Shutov, et al in their study on 150 patients with embolic stroke found 4 patients with hypercoagulation,<sup>10</sup> and suggested that hypercoagulation factors be checked in such patients.

We investigated the effect of hypercoagulation as a co- factor in CVA patients with PFO and found that none of the patients studied had any stages of hypercoagulation. It therefore seems that hypercoagulation in our patients is not a direct risk factor for embolic CVA at least any higher than for normal

**Table 1.** Mean serum level of coagulative factors in patients under study

Serum level of coagulative factors	Count	Minimum	Maximum	Mean	SD
Protein C	40	69.60	242.00	112.4	30.4
Protein S	40	81.20	156.00	116.3	16.9
Anti thrombin	40	67.10	134.00	101.5	17.0
factor v leiden	40	2.75	4.00	3.1	0.18
Lupus anticoagulant	40	30.10	41.30	35.4	4.5
Anticardiolipin Antibody	40	0.10	2.30	1.5	2.3
B2glycoprotein1	40	4.40	16.00	13.9	51.8
platelet count	40	112.00	395.00	229.1	55.9
Homocystein level	40	5.20	18.10	11.3	6.5

population.

have no conflicts of interest.

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