

Trombophilic Screening in Young Adults with Myocardial Infarction: Utility or Futility?

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ARTICLE INFO

Received: 📅 June 06, 2019

Published: 📅 June 19, 2019

ABSTRACT

Citation: Carmelo Buttà, Giuseppe Miceli. Trombophilic Screening in Young Adults with Myocardial Infarction: Utility or Futility?. Biomed J Sci & Tech Res 18(5)-2019. BJSTR. MS.ID.003229.

Introduction

It is widely accepted that several cardiovascular Risk Factors (RFs) contribute to the occurrence of Myocardial Infarction (MI) and most of them are frequently encountered in elderly population. However, occasionally MI can affect young subjects who do not present the abovementioned RFs. In these setting, thrombophilic mechanisms are often called into question to justify MI etiology. Thrombophilia describes an inherited or acquired condition which can increase the risk of venous or arterial thrombosis. The utility of testing for thrombophilia to guide prevention and treatment decisions is controversial [1], especially in patients with arterial thrombosis. Nevertheless, in the 1980s and 1990s thrombophilia testing became common in unselected patients and their relatives [2]. Even today, thrombophilia testes are frequently performed, particularly in young patients, with a not indifferent impact for health spending.

Thrombophilic Disorders

The most studied thrombophilic disorders in young patients with MI are: Factor V Leiden (FVL) and Factor II (FII) G20210A mutation. The relationship between FVL and risk of MI has led to conflicting results, therefore the association appears stronger in young subjects. A study by Butt et al. [3] showed that FVL was higher exclusively in MI patients younger than or equal to 50 years, with 3.9- fold higher prevalence in young patients than in patients older than 50 years and 2.7-fold higher than in age matched control subjects. A systematic review showed that FVL does not significantly correlate with MI (OR 1.26, 95% CI 0.94 to 1.67), but the decision

to include in the study young patients (<55 years) contributed to make the association significant (OR 1.29, 95% CI 1.03 to 1.61) [4]. A meta-analysis showed that FVL was not associated with MI but correlation was stronger in patients younger than 55 years of age affected by MI, ischemic stroke or complicated Peripheral Vascular Occlusive Disease (PVD) (OR, 1.37; 95% CI, 0.96–1.97) [5]. However, the large Italian Atherosclerosis Thrombosis and Vascular Biology Study found no evidence for an association between FVL and MI at age younger than 45 years [6].

Even the relationship between the FII G20210A mutation and risk of MI is controversial but this association appears more solid in young population. Furthermore, Butt et al found that the prevalence of FII G20210A was higher in MI patients than in controls (OR 3.3, 95% CI 2.6-4), particularly in younger than 51 years (5.6-fold higher than in age-matched control subjects) [3]. A study by Rallidis et al. showed that FII G20210A was more frequent in ST Elevation Myocardial Infarction (STEMI) patients ≤ 35 years of age than in controls (OR 2.2, 95% CI 1.1-4.2) and the risk increased substantially in presence of smoking as a RF [7]. Another study indicated that the FII G20210A was the only genetic prothrombotic RF associated with the risk of developing MI under the age of 36 years [8]. Finally, in the meta-analysis of Kim and Becker, the relationship between MI and FII G20210A was slightly stronger than the association with FVL (OR 1.28; 95% CI, 0.94 to 1.73) and it seemed to become stronger in subjects younger than 55 years of age with MI, ischemic stroke or complicated PVD (OR, 1.66; 95% CI, 1.13–2.46) [5]. However, the large Atherosclerosis Thrombosis and

Vascular Biology Study among survivors of MI at age younger than 45 years did not confirm this association [6].

Merely some case reports reported Protein C (PC), Protein S (PS) e Antithrombin (AT) III deficiencies in young patients with MI. Unfortunately, very few studies have investigated these thrombophilic disorders in a large population. Two studies by Rallidis et al found no difference in AT, PC, and PS plasma levels between patients with STEMI or MI under the age of 36 years and the controls [7,8]. Therefore, evidence for an association between deficiency of these factors and the risk of MI are inadequate.

Extensive evidence support the hypothesis that the Antiphospholipid (APL) syndrome is associated with risk of MI [9,10]. Since the diagnosis of the APL syndrome is possible if it is present at least one clinical criterion and one laboratory criterion [11], in our opinion, it is justified search for APL antibodies in young patients with MI without other cardiovascular RFs.

Conclusion

In conclusion, evidence about the relationship between thrombophilia and juvenile MI are still inadequate. FII G20210A and FVL are the only thrombophilic disorders that showed an association with MI in young patients although with some controversial results. Nevertheless, some randomized trials conducted in patients with hyperhomocysteinemia (considered a RF for atherosclerosis) showed that reducing serum homocysteine levels through B vitamins administration in patients with cardiovascular diseases does not modify prognosis [12,13]. Therefore, association is not synonymous of RF.

As long as some valuable trials do not demonstrate the efficacy of different therapeutic strategy (like using of anticoagulant or prolonged double anti-aggregation) in improving prognosis of MI in young population with positive thrombophilic screening, thrombophilic testing in these patients will be worthless and expensive. As things stand today, in patients with juvenil MI the only useful test that seems to be worth performing is APL antibodies test, even if MI is not a frequent event in APL syndrome [11-13].

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2019.18.003229

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