Hyperviscosity and high thrombus burden: Is it time to re-evaluate an old but still gold pathophysiological concept?

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The existence of an association between hyperviscosity and acute myocardial infarction (AMI) has been previously analyzed and reported, in particular in young patients, either in the acute phase [1] and during follow-up [1, 2].

In AMI patients, thrombotic lesions are a common finding on angiography and can increase the rate of procedural complications and the incidence of in-hospital major adverse cardiac events, thus affecting short- and long-term outcomes [3]. The prediction of high thrombus burden (HTB) in the infarct-related artery could help to improve procedural success and related clinical outcomes in these patients.

The article by Çınar et al. [4] reports an association between high values of whole blood viscosity (WBV) at both high and low shear rates and HTB on angiography in non-ST elevation myocardial infarction (NSTEMI) patients. Moreover, patients with HTB also exhibited higher values of hematocrit, triglycerides, baseline cardiac troponin I, and total protein. These results are consistent with a previous study performed in our Institution in which, among the hemorheological variables analyzed (WBV at high and low shear rates, plasma viscosity, and the erythrocyte deformability index), higher values of hematocrit and of WBV at low shear rate were found in patients with ST-elevation myocardial infarction (STEMI) with respect to NSTEMI and unstable angina. This suggests a role of these parameters in favoring STEMI occurrence during acute coronary syndromes (ACS) [5]. Our results and those by Çınar et al. [4] strengthen the concept that hemorheological variables play an important role in the pathogenesis of ACS. Moreover, these results are also supported by previous histologic findings showing that transmural AMI was frequently associated with the presence of reddish thrombi, rich in erythrocytes and fibrin, while unstable angina was characterized more often by whitish or greyish thrombi, rich in platelets [6], which suggests a role of high hematocrit values in the formation of complete thrombotic occlusions.

The need for a simple and reliable tool in everyday clinical practice to predict the amount of thrombus on angiography is a heartfelt theme for cardiologists and is also confirmed by the validation of the CHA2DS2-VASc score for predicting HTB in patients with either STEMI [7] or NSTEMI [8], regardless of the presence of atrial fibrillation.

In particular, in NSTEMI patients, receiver-operating characteristics analysis revealed the cut-off value of CHA2DS2-VASc score >2 as a predictor of HTB with a sensitivity of 74% and a specificity of 61% with an area under curve of 0.71. In that study, increased baseline serum C-reactive protein levels, lower serum albumin levels (representing the counterpart of increased values of acute phase proteins) and decreased lymphocyte counts (indicating the left shift of the formula due to the increase
in neutrophils) were also additional independent predictors of HTB [8].

Another interesting finding of the study by Çınar et al. [4] is that, in patients with HTB, hyperviscosity is not only a determinant factor in thrombus pathogenesis but can also affect microvascular perfusion. In fact, in that study HTB was associated with an increased risk of distal embolization, no-reflow phenomenon, and a lower percentage of postprocedural thrombolysis in myocardial infarction (TIMI) flow >II and of TIMI Myocardial Blush Grade >II. This suggests that hemorheological variables can contribute to the occurrence of the no-reflow phenomenon after successful restoration of epicardial coronary blood flow, possibly causing greater myocardial damage. These results are in line with another study performed by our group, in which we demonstrated, in STEMI patients, a correlation between blood viscosity and infarct size, expressed by the peak values of 2 cardiac biomarkers, creatine kinase, and cardiac troponin I [9]. In this latter study, we also hypothesized that increased neutrophils in response to myocardial necrosis could cause further myocardial damage also by contributing to the no-reperfusion phenomenon, as previously demonstrated [10, 11] and recently confirmed in a cardiac magnetic resonance study conducted in STEMI patients [12]. Furthermore, in agreement with data reported by Çınar et al. [4] we also demonstrated that alterations of hemorheological variables were found in relation to the achievement of a final TIMI flow less than 3, which in turn was associated with an increased infarct size [5].

In conclusion, the study by Çınar et al. [4] reinforces previous evidence on the role of hemorheological variables in ACS patients and underlies the possible impact of an alteration of blood viscosity in patients with NSTEMI and, in particular, the importance of pre-operative evaluation in these patients.

Moreover, the article by Çınar et al. [4] together with those performed in our Institution could also have an important impact on primary prevention during cardiological evaluations, guiding the search for primary or secondary causes of polycythemia, and their possible treatment. Finally, it may also aid the search for other determinants of blood viscosity in order to reduce the risk of STEMI or at least of procedural complications in case of ACS.

**Article information**

**Conflict of interest:** None declared.

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**REFERENCES**