

Short-Term Prognosis of Juvenile Myocardial Infarction: Role of Plasma Viscosity

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In our early research¹ regarding the hemorheological pattern in patients with acute myocardial infarction (AMI) with a mean age of 61.45 ± 10.99 years, we showed that the major hemorheological parameters were almost normalized 2 weeks after the acute event. In the last decade, we focused on hemorheological parameters in juvenile myocardial infarction (JMI), defined as AMI in patients aged ≤ 45 years, in the “Sicilian study on juvenile myocardial infarction”.^{2,3}

Juvenile myocardial infarction is responsible for 2% to 10% of all cases with AMI in different surveys.^{4,5} Juvenile myocardial infarction presents a typical pattern of risk factors^{6,7} and shows clinical, angiographic, and prognostic characteristics.⁵ Regarding risk factors, cigarette smoking is by far the most common, followed by family history of coronary artery disease and hypercholesterolemia, while arterial hypertension and diabetes mellitus are less frequent. Juvenile myocardial infarction may be associated with the use of oral contraceptives, pregnancy, or cocaine abuse as well as with congenital coronary artery abnormalities. Concerning the clinical picture, patients with JMI reach hospital earlier than older patients, enhancing the effectiveness of revascularization procedures and treatment of complications. In JMI, the absence of coronary stenosis is often demonstrated or just 1 coronary vessel is affected; 2- or 3-vessel disease is infrequent. Generally, patients with JMI have a lower incidence of complications, such as early and late heart failure, angina, reinfarction, and atrioventricular block; mortality during hospitalization and after 6 months is significantly reduced.

In the Sicilian study, we observed a pattern of inflammatory polymorphisms in patients with JMI.⁸ A higher prevalence of proinflammatory polymorphisms (SNP A2080G of pyrin gene, SNP Gly670Arg of PECAM gene, C1019T of Cx 37 gene, and SNP G1059C of PCR gene) and a lower prevalence of anti-inflammatory polymorphisms (Asp299Gly of TLR4 gene, SNP – 1082 G/A of IL10 gene, CCR5 Δ 32) were present.

We revisited plasma viscosity (PV) in our survey of patients with JMI and considered 2 aspects in particular. The first is the potential role played by PV in the dynamics of myocardial microcirculation (namely, in the phenomenon of coronary slow flow) that may be secondary to AMI⁹⁻¹¹; the second aspect was life expectancy.

Plasma viscosity is dependent on the plasma protein concentration, although the contribution of different proteins (fibrinogen, α_2 -macroglobulin, immunoglobulins, haptoglobin, and ceruloplasmin) differs in relation to their molecular size and shape; the plasma protein composition can also change due to pathophysiological processes.¹² The PV plays a pivotal role, together with erythrocyte deformability and platelets, in microcirculatory blood flow.¹³

In this editorial, we describe the behavior of PV in 120 patients with JMI (109 men; mean age 39.4 ± 5.8 years); the time interval between AMI onset and the first hemorheological evaluation was 13 ± 7 days. Using fasting venous blood, we measured PV at the shear rate of 450 s^{-1} using the cone-and-plate viscometer Wells-Brookfield mod $\frac{1}{2}$ LVT (Middleboro, Massachusetts). We reexamined this parameter 3 ($n = 83$) and 12 ($n = 70$) months after AMI.

At the initial stage, PV was increased compared to controls (CS 1.259 ± 0.125 vs JMI 1.519 ± 0.108 mPa-s, $P < .001$). The PV did not differ between ST-segment elevation myocardial infarction (STEMI) and non-STEMI as well as in 3 subgroups of the patients with JMI subdivided according to the number of cardiovascular risk factors (39 had 0 or 1 risk factor, 39 had 2 risk factors, and 42 had ≥ 3). Coronary angiography was performed in 103 patients; no significant coronary stenosis was demonstrated in 23, 46 had a single vessel disease, and 34 had multi-vessel disease. The PV did not differ between the 3 subgroups. At 3 and 12 months after AMI, PV was persistently increased compared to controls (at 3 months 1.466 ± 0.119 mPa-s and at 12 months 1.475 ± 0.009 mPa-s, respectively).

Although the literature has described a low incidence of cardiovascular complications in JMI,⁵ in our survey, follow-up carried out for as long as 18 months showed that 5 patients developed heart failure, 15 a new ischemic event (angina in 12

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and reinfarction in 3), and 4 had an ischemic event associated with heart failure. The drugs prescribed at hospital discharge were in agreement with current recommendations (antiplatelet agent in 96.69%, statin in 75.31%, and a beta-blocker in 64.45%); however, enrollment started in 2001 and at that time the use of 2 antiplatelet agents after AMI was not common.

Considering the number of patients who developed cardiovascular complications, we reexamined PV measured at the initial stage, in patients with JMI with ($n = 24$) and without ($n = 74$) cardiovascular events (CEs). The PV was initially higher in the subgroup that subsequently developed CE (JMI without CE 1.500 ± 0.107 vs JMI with CE 1.555 ± 0.094 mPa-s, $P < .05$).

Considering that several studies investigated the neutrophil to lymphocyte ratio (NLR) in patients with AMI not selected for age,^{14,15} we subdivided our patients with JMI into 2 subgroups according to the median NLR value. In the subgroup with high NLR, PV was higher (JMI + low NLR 1.492 ± 0.097 vs JMI + high NLR 1.545 ± 0.113 mPa-s, $P < .01$, respectively).

While the subdivision of patients with JMI according to the NLR supports the role of PV as part of the acute-phase reaction,¹⁶ its behavior in the patients subdivided according to short-term cardiovascular outcomes suggests an influence on coronary microcirculation. The regulation of myocardial microcirculation has been extensively analyzed,¹⁷ and blood viscosity was shown to be linked to the hemodynamic profile in small and large vessels.¹⁸ The association of a significantly increased PV with small-vessel occlusion was also described in ischemic cerebral disease.¹⁹

Some studies showed a link between PV and the risk of cardiovascular diseases^{20,21} as well as a relationship between PV and the severity of coronary artery disease.^{22,23} It has been recently observed that PV was positively associated with the incidence of cardiovascular and noncardiovascular death during the long-term follow-up of a male population.²⁴ Similar to what was described in patient with unstable angina,²⁵ transmural myocardial infarction,²⁶ and in no-reperfusion STEMI who had undergone primary coronary intervention,²⁷ PV also seemed to have a prognostic value in our survey. Therefore, the persistence of a hemorheological alteration can be detrimental to coronary hemodynamics, contributing to the phenomenon of secondary coronary slow flow.⁹⁻¹¹ Since the increase of PV in patients with JMI persisted after 12 months, monitoring the hemorheological profile and its possible response to drugs should be given further attention.

Declaration of Conflicting Interests

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