

Diagnosis and Treatment of Acute Myocardial Infarction: Where do we Stand?

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In the leading article entitled “Current criteria for the diagnosis and treatment of acute myocardial infarction”, Claribel Plain Pazos., et al. [1] gave an outline of epidemiologic situation, diagnostic possibilities, and management of patients with acute myocardial infarction (AMI) in Cuba. Diagnosis was typically established by a conventional triad of symptoms, electrocardiographic (ECG) changes and rise of biomarkers. They strongly recommended early myocardial reperfusion to avoid consequent adverse events.

Over the past decades, cardiovascular disease (CVD) has remained a universal health problem associated with huge expenditures. For example, coronary artery disease (CAD) claimed 862.017 deaths among men and 903.330 among women in Europe in 2014 [2]. Since then the CVD mortality has started to decrease in most European countries, though the long-term trends in Central and Eastern Europe have been less consistent. In Cuba, the CVD mortality has been similarly disadvantageous with a total of 24.462 deaths in 2014, 44% of them due to the AMI [1]. Unfortunately, death rates there have recently shown an upward turn [3]. The unfavorable tendencies were attributed to unhealthy trends in physical activity, obesity, smoking, and delayed adoption of effective medication (e.g. aspirin, β -blockers, ACE inhibitors, statins) as well as myocardial reperfusion (e.g. thrombolysis and percutaneous coronary interventions [PCI]) [4,5]. On the other hand, developed countries experience a CVD mortality reduction, more than half of which was explained by changes in risk factors in the population, primarily the decrease in cholesterol and blood pressure levels, and smoking cessation [6]. It seems that rigorous implementation of primary and secondary preventive measures would, along the same lines, appear as one of the most effective means to control the CVD mortality in Cuba as well.

Patients with detected myocardial injury belong to a largely heterogeneous group and may need, as a consequence, extensive diagnostic workup and adjusted treatment. Cardiac troponins (cTn) are preferred biomarkers and high-sensitivity assays are recommended for routine use. Elevations of the cTn values above the 99th percentile upper reference limit are defined as the myocardial injury. Clinical definition of the AMI denotes the presence of myocardial injury in the setting of acute myocardial ischemia [7]. However, injuries from non-ischemic causes may arise secondary to many cardiac (e.g. myocarditis) and non-cardiac conditions (e.g. renal failure). The AMI is typically caused by a sudden, critical obstruction of the culprit coronary artery (AMI types 1, 3, 4 a-c, and 5). The final event is usually related to the occlusive thrombus. On the other hand, AMI type 2 results from a mismatch between oxygen supply and demand; stable CAD is a common, though not a mandatory finding. In those patients, it is advisable to treat the underlying imbalance with appropriate measures (e.g. volume adjustment, blood pressure management, administration of blood products, heart rate control, and respiratory support). Consequently, patients with the AMI frequently require additional investigations beyond the traditional diagnostic triad, such as supplemental laboratory tests, non-invasive cardiac examination, and coronary angiography. Not surprisingly, immediate myocardial reperfusion may sometimes prove redundant in the AMI cases.

Overall, prognosis of patients with any documented myocardial injury is unfavorable. In addition to some universal clinical markers of risk (e.g. advanced age, diabetes, and renal insufficiency), the initial clinical presentation and the resting 12-lead ECG are highly predictive of early prognosis. Patients with recurrent or ongoing chest pain resistant to medical treatment, hemodynamic instability or cardiogenic shock, life-threatening arrhythmias or cardiac arrest, mechanical complications of the AMI, and acute heart failure are very high risk patients and need close surveillance and early invasive strategy [8]. Based on the ECG changes, the AMI patients are divided into those with persistent ST-segment elevations (STEMI) and those without them (NSTEMI). The fundamental study of De Luca, et al. [9] convincingly demonstrated that indeed every minute of delay in reperfusion for STEMI significantly affected the 1-year mortality; therefore, all efforts should be made to shorten the total ischemic time. Currently, the average hospital mortality in STEMI patients varies between 4% and 12% in Europe, while reported 1-year mortality after hospital discharge is approximately 10% [10]. In contrast, hospital mortality in NSTEMI patients is lower, from 3% to 5%; however, at 6 months the mortality rates in both AMI groups practically come together [8]. Compared to European data, the death rates in Cuba, derived from selected literature data, seem much worse. In a cohort of 251 STEMI patients admitted to the same medical institution, hospital mortality was reported to be 13% [11]. Armas, *et al.* [12] calculated annual mortality for the AMI patients from the case-fatality analyses in 14 Cuban provinces over the years 2004 - 2008. There were 81.8 deaths per 100.000 population which resulted in the annual mortality of 49%.

Immediate treatment goals in the AMI patients are relieving pain and distress, improving coronary blood flow, and restoring heart function as quickly and as best as possible. Long-term goals are improving overall heart function, managing risk factors and lowering risk of a repeat heart attack. A combination of drugs and revascularization procedures may be used to meet these goals. In the previous article [1], a comprehensive description of the drug treatment was given. However, coronary revascularization requires some additional thoughts.

Myocardial reperfusion can be achieved by chemical (i.e. thrombolysis) or mechanical means (i.e. PCI). Thrombolysis regains the arterial lumen by dissolving the occlusive fibrin clot, leaving the atherosclerotic plaque essentially unchanged. At present, fibrin specific agents are used (e.g. tenecteplase, alteplase, or reteplase). The largest benefit of thrombolysis is seen when treatment is administered within 2h after the symptom onset. If timely PCI cannot be performed after the STEMI diagnosis, thrombolytic therapy is an acceptable alternative within 12h of symptom onset in patients without contraindications. Invasive strategy (i.e. angiography followed by PCI) is recommended between 2 and 24h after successful thrombolysis. Immediate PCI is indicated when thrombolysis has failed or in the case of recurrent ischemia [10].

Primary PCI is preferably performed using radial approach. After the coronary anatomy is recognized and passage through the culprit lesion assured, new generation drug-eluting stents are deployed into the diseased artery. Somewhat unexpectedly, the role of routine use of thrombus aspiration has been questioned in STEMI [10] as well as in NSTEMI patients [13]. Randomized clinical trials in high volume hospitals have repeatedly shown that, if delay to treatment is similar, primary PCI is superior to thrombolysis in reducing mortality, re-infarction, or stroke [14]. Hence, primary PCI is the preferred reperfusion strategy in the STEMI patients within 12h of symptom onset, provided it can be performed expeditiously by an experienced team.

Early invasive strategy with coronary angiography, followed, if indicated, by revascularization, is carried out in the majority of NSTEMI patients in regions with well-developed healthcare systems. The indication for an invasive approach, the timing for myocardial revascularization and the selection of the revascularization modality depend on numerous factors, including clinical presentation, comorbidities, risk stratification, presence of high-risk features specific for a revascularization modality, frailty, cognitive status, estimated life expectancy, and functional and anatomic severity of the CAD [8].

The time from symptom onset until reperfusion occurs is an estimate of total ischemic time. Apparently, STEMI patients with long ischemic times have very little myocardium left for salvage. Several experimental and human clinical studies have confirmed that infarct size and mortality are strongly correlated with the total ischemic time, and much less so with its subintervals like door-to-balloon time. The goal should be to get rid of all unnecessary steps in the care of STEMI patients and develop the systems of care with the focus of decreasing the total ischemic time [15]. It is recommended that the pre-hospital management of STEMI patients is based on regional networks designed to deliver reperfusion therapy expeditiously and effectively, with efforts made to make primary PCI available to as many patients as possible. However, these networks are liable to many predictable or unpredictable delays so that considerable efforts on supervision and education are needed to make them run smoothly. The recommended mode of a patient's presentation is by alerting the emergency medical system calling the national emergency number (e.g. 112 or 911). This period depends on the ability of the patient to realize the seriousness of the problem. The ultimate duration of the arrival of medical help involves the performance of emergency medical services systems. Management of STEMI starts from the point of first medical contact. A working diagnosis of STEMI, based on symptoms and ECG signs, must be made in less than 10 minutes [10]. When STEMI diagnosis is made in the pre-hospital setting, the appropriate catheterization must be activated; clear definition of geographic areas of responsibility needs to be established. It is indicated to bypass non-PCI hospitals as well as emergency department at the waiting hospital, so that the patients should be brought straight to the catheterization laboratory. In the geographic areas where the expected transfer time to the primary PCI center makes it impossible to achieve the maximal allowable delays, the emergency medical services should develop systems for rapid thrombolysis with subsequent immediate transfer to primary PCI center. Shared written protocols, based on risk stratification and transportation by a trained physician, nurse, or paramedic staff in appropriately equipped ambulances or helicopters should be used. To maximize staff experience, primary PCI centers should perform the procedure systematically on a 24/7 basis for all STEMI patients. It should be considered that primary PCI for STEMI be performed by trained operators with annual volumes of ≥ 75 procedures at institutions performing ≥ 400 PCI per year [16]. Maximum time from STEMI diagnosis to primary PCI (i.e. guidewire crossing) should be ≤ 120 minutes, maximum time from STEMI diagnosis to bolus or infusion start of thrombolysis in patients unable to meet primary PCI target times ≤ 10 minutes, time delay from start of thrombolysis to evaluation of its efficacy 60 - 90 minutes and time delay from start of fibrinolysis to angiography (if thrombolysis is successful) 2 - 24h [10]. For example, urgent coronary angiography and a primary PCI strategy, together with 24-hour 7-day call for interventional cardiology, was introduced in our hospital in 2000. Hospital mortality rates significantly decreased from 13% in the first year to 3.9% and 6.7% in subsequent years [17].

Conclusion

Patients with the AMI belong to a heterogeneous group. Diagnosis is usually established from symptoms, ECG changes and cTn rise and fall. In some patients, extended diagnostic workup is needed along with the adjusted treatment. Prognosis is overall unfavourable, particularly in STEMI and very high-risk NSTEMI patients. Timely access to invasive strategy (angiography followed by PCI) in 24/7 catheterization laboratories has proved to be lifesaving. Finally, rigorous implementation of primary and secondary preventive measures has the potential to be one of the most effective means to control the CVD mortality.

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