

# Introduction

Italo de Luca, Alessandro Boccanelli\*, Francesco Fedele\*\*

Department of Cardiology, Azienda Policlinico, Bari, \*Division of Cardiology, San Giovanni-Addolorata Hospital, Rome, \*\*Department of Cardiovascular and Respiratory Sciences, "La Sapienza" University, Rome, Italy

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## Address:

Dr. Italo de Luca

Divisione di Cardiologia  
Ospedaliera  
Azienda Policlinico  
Piazza Giulio Cesare, 11  
70124 Bari  
E-mail: itadelu@tin.it

"Cardiologia 2000" is an international meeting held annually in Ostuni (Italy) where recent scientific questions are discussed by cardiologists and heart surgeons. The eighth edition, held in 2003, focused on the theme "From acute myocardial infarction to left ventricular dysfunction" which we believed should be presented in this Supplement of the *Italian Heart Journal*.

Acute myocardial infarction is the leading cause of heart failure and its prevention and cure would lead to a drastic reduction in social and medical costs.

As Prof. Robert O. Bonow stressed in his editorial comment, in preventing cardiovascular diseases there are many challenges to be met in the 21st century and one of these is to ensure that recommended guidelines, such as those developed jointly by the American College of Cardiology and the American Heart Association, are adhered to. Indeed, as he says, "if 75% of patients with acute myocardial infarction were enrolled in *Get with the Guidelines* at discharge with an 85% adherence rate to secondary prevention guidelines, it is estimated that 80 000 lives would be saved annually". This represents one third of our goal of reducing cardiovascular deaths by 25%.

Definition of acute myocardial infarction is another challenge to be met. Troponins are widely accepted as highly sensitive biochemical markers and specific for myocardial necrosis. In September 2000, the Joint European Society of Cardiology and American College of Cardiology Committee established the revised criteria for acute myocardial infarction: typical rise and gradual fall (troponin) or a more rapid rise and fall (creatin kinase-MB) of biochemical markers of myocardial necrosis, with at least one of the following: a) is-

chemic symptoms; b) development of pathologic Q waves on the ECG; c) ECG changes indicating ischemia (ST-segment elevation or depression); d) or coronary artery intervention (e.g. coronary angioplasty).

Dr. Giuseppe Di Pasquale and colleagues re-assess the advantages of the re-definition of myocardial infarction over the previous World Health Organization (WHO) criteria. However they discuss the problems related to using troponin indiscriminately due mainly to the high number of false positives. They clarify the major problems with the new myocardial infarction definition regarding the biomarker diagnostic cut-off controversy, focus the criticism on the epidemiological and health care impact, on the lack of recommendation for any implementation strategy and in particular on the lack of attention in situations where troponin levels cannot be determined. Moreover, the authors point to the Italian Federation of Cardiology recommendations that post-procedural myocardial infarction diagnosis should still follow conventional WHO criteria. As they say, there is much work to be done to ensure that assays are of an appropriate standard and to educate patients, doctors and society to these substantial changes.

Amongst the new cardiovascular risk factors is hyperhomocysteinemia. Indeed, it has been estimated that for every increase of 5 mmol/l in fasting plasma homocysteine concentrations, the incidence of coronary disease increased from 1.6 to 1.8. Prof. Raffaele De Caterina and his colleagues confirm the role of fasting homocysteine in the prediction of vascular events. Their study on a population in Friuli leads them to suggest that homocysteine and vitamin B6 are independent and additive cardiovascular risk factors.

Echocardiography is taking on a greater and greater role in the diagnosis and prognosis of myocardial infarction. Dr. Paolo Colonna and colleagues analyze the novel echocardiographic technique (myocardial contrast echocardiography, contrast opacification of the left ventricle, coronary flow reserve study, integrated backscatter, tissue Doppler and strain rate imaging) and try to assess their actual clinical weight in every pathophysiological status. The aim is to achieve a correct diagnosis of the extension of myocardial necrosis which takes into consideration the transmural wavefront development, the amount of viable myocardium and/or the presence of microvascular damage.

Prof. Fausto J. Pinto analyzes the contribution given by the new echocardiographic methodologies to improve the conventional echocardiographic accuracy in the evaluation of left ventricular dysfunction. These methodologies include: second harmonics, which is becoming a standard in most equipments; contrast echo, which improves left ventricular opacification and endocardial border definition; color kinesis, which allows automated segmental motion analysis; tissue Doppler imaging, which can help in the assessment of regional and diastolic function; strain and strain rate which could quantify local myocardial deformation, shown to be a potential strong marker of ischemia. Moreover, he concludes, echocardiography could research myocardial viability and identify the candidates that will benefit from revascularization.

The paper of Dr. Maria Frigerio and Dr. Giovanni Aguggini reports many recommendations regarding the echocardiographic assessment of left ventricular diastolic dysfunction and useful suggestions for therapeutic treatment. Treatment must be based on the pathophysiology of the syndrome and requires precise use of diuretics, angiotensin-converting enzyme inhibitors, nitrates and digoxin. Confusion in interpretation of data is generated by the cut-off value for definition of "normal" or "preserved" left ventricular ejection fraction (from 40 to 50%) that varies among authors. We share Maria Frigerio's opinion that, since normal left ventricular ejection fraction is  $\geq 50\%$ , an appropriate definition of diastolic heart failure could be "heart failure syndrome occurring in patients with left ventricular ejection fraction  $\geq 50\%$ ".

Dr. Leonardo de Luca and Prof. Mihai Gheorghiade discuss the problems of patients hospitalized with worsening chronic heart failure. Interestingly, although in-hospital mortality in these patients is very low ( $< 2-3\%$ ), the readmission rate within 60 days is as high as 30%. The immediate goal is to improve symptoms and signs of congestion and then to implement long-term life-saving therapies. The authors describe data from recent large clinical trials involving more than 10 000 patients, examine the utility and safety of established therapies (e.g. intravenous diuretics, digitalis, milrinone), examine new therapies aimed at treating these patients (e.g. levosimendan, nesiritide, tolvaptan), and

compare existing and new therapies (e.g. dobutamine and levosimendan). For patients with worsening chronic heart failure a large armamentarium of non-pharmacological, pharmacological, electrical, and/or surgical therapies is available but it is extremely underused.

Dr. Leonardo De Luca and colleagues also present a review of three drugs, milrinone, vesnarinone and levosimendan, which respectively represent the three classes of inotropic agents evaluated in randomized clinical trials in patients with acute heart failure. These three classes are: 1) agents that increase the intracellular concentration of cyclic adenosine monophosphate by stimulating the beta-adrenergic receptor or inhibiting phosphodiesterase; 2) drugs that increase the intracellular sodium concentration; 3) the new calcium-sensitizing drugs. The authors conclude that levosimendan, a new calcium-sensitizing drug, may well represent a new frontier in the treatment of acute heart failure.

The available pharmacological strategies have recently been completed by new electrical therapies including implantable cardioverter-defibrillators for "MADIT II" patients and cardiac resynchronization for the 30% of heart failure patients with concomitant intraventricular conduction delay. The wide variety of available heart failure medications, comment Dr. Giuseppe Augello and colleagues, provides ample evidence that we have not yet succeeded in this effort. The authors have prospectively conducted a clinical pilot study to assess mid-term safety and preliminary efficacy of chronically implanted generators of non-excitatory signals, referred to as cardiac contractility modulation signals, in patients with chronic systolic heart failure. Safe and effective inotropic electrical therapy could be a useful addition to our therapeutic armamentarium and could become useful to symptomatic drug-refractory heart failure patients.

Today primary angioplasty constitutes the "standard of care" for patients with acute myocardial infarction within 12 hours of onset, affirm Charles X. Kim and Charles J. Davidson. This procedure not only increases short-term and long-term survival but also reduces in-hospital complications and rehospitalization with notable advantages in terms of health service costs. More research, the authors consider, is necessary to define the role of pharmacological therapy adjunctive to primary angioplasty, in particular thrombolytics and the glycoprotein IIb/IIIa inhibitors and their combined therapy, in the "strategy of reperfusion".

Moreover, data in the literature, explain Dr. Francesco Bovenzi and colleagues, suggest that primary angioplasty produces greater advantages in terms of mortality in patients with acute myocardial infarction at high risk due to advanced age or the coexistence of diabetes mellitus, renal failure, or obesity, especially if precociously hospitalized.

In the cases of extensive acute myocardial infarction  $> 5$  leads and/or cardiogenic shock with multivessel disease or left main coronary stenosis, surgical solution

permits a complete and definitive revascularization with protection of the whole myocardium at risk. In the “De Gasperis” Department in Milan, surgical intervention of these patients is held as the first choice option. Unfortunately, Dr. Ettore Vitali and colleagues remind us, the same guidelines end up placing the surgical option in class I only in failed cases of coronary angioplasty with hemodynamic instability and persistent ischemia refractory to medical therapy and the surgical option only in class IIa for cardiogenic shock with an anatomy favorable to surgery.

Dr. Michele De Bonis and colleagues report their experience and their considerations on the role of the “conventional” procedures which are under development for the surgical treatment of ischemic cardiomyopathy: myocardial revascularization, that decreased the risk of death when viable myocardium could be demonstrated; left ventricular surgical restoration for post-infarction akinetic scar or dyskinetic aneurysm, which provides gratifying results in terms of survival and clinical improvements; mitral valve repair, using different reconstructive approaches for the specific treatment of functional ischemic mitral regurgitation; passive containment devices, which in preliminary clinical experience seem able to halt ventricular dilation promoting reverse remodeling and improving cardiac function; surgical ablation of atrial fibrillation, which seems to represent an advance in the treatment of atrial fibrillation in heart failure patients. Since heart transplantation represents a realistic option just for a limited number of patients, significant changes and improvements should be waited over the next few years

for patients with advanced ischemic heart failure as some of the above described procedures are refined and more data become available.

The limitations of medical and surgical approaches stimulate investigations on the potential role of stem cells as a source for repairing damaged myocardium. These investigations are the focus of the review of Prof. Sergio Chierchia and Dr. Luca Deferrari. Encouraging results have been obtained in experimental ischemic and non-ischemic heart disease. On the other hand, the authors conclude, myocardial cell replacement therapy for the treatment of patients with postinfarction heart failure still needs more study: for instance, the optimal model of stem cell delivery, the best timing for implant, the number and the type of cells and the characteristics of patients who are going to benefit most from the treatment are still to be established.

The clinical and social importance of post-infarction heart failure is documented by the high incidence of this condition which is destined to increase due to the aging of the population and the higher survival rate of patients. The proceedings of the Ostuni meeting are an annual update for cardiologists to see the current status and opinions of leading experts on this problem.

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