The Importance of Evaluating Remodeling

La importancia de evaluar el remodelado

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Adverse left ventricular remodeling is a myocardial maladaptive process characterized by morphological changes in the structure and shape of the chamber with subsequent impaired function.

It is a common cause of heart failure occurring in up to 30% of anterior infarctions and 17% of inferior infarctions, according to some series. (1)

From a pathophysiological perspective, the process involves a sequence that could be divided in two stages: an early acute stage in the site of acute myocardial infarction (AMI), and a second late stage of remodeling at least a month after the event. The latter is potentially reversible and includes both structural and biochemical changes, occurs in sites other than site of infarction, and involves viable cardiomyocytes. (2)

As a result, noninfarcted remote myocardial tissue becomes hypertrophic and undergoes adaptive dilatation in response to increased wall stress; this is not necessarily the case in all infarctions and is not necessarily progressive. (3,4)

The connection among extensive infarction, remodeling, and the rate of cardiovascular events is well known. It has been interesting to read the article *Left Ventricular Remodeling After Infarction: A Perspective from Gated-Spect Myocardial Perfusion Imaging*, where L. San Miguel et al. (5) evaluate risk factors associated with adverse remodeling after a non-extensive infarction. This model identifies diabetes as a risk factor independently associated with adverse remodeling in less extensive infarctions.

While no clinical endpoints were evaluated, pathophysiological evidence supports this finding and identifies diabetes as a factor related to adverse remodeling.

As suggested by this article, gated-SPECT myocardial perfusion at rest is an accessible, less complex method with a shorter time of acquisition than magnetic resonance imaging, and can be used to evaluate adverse remodeling through the association between necrotic burden and left ventricular ejection fraction.

While this is a retrospective work sensitive to potential unidentified confounders, it suggests, like many others, the importance of more aggressive treatment for heart failure in diabetic patients.

This information, together with other method-related aspects –such as AMI localization and degree of motility–, provide a wider view for clinical cardiologists when considering other variables and, therefore, enable enhancement of the relevant treatment for the benefit of the patient.

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AUTHORS' REPLY

We deeply appreciate our colleagues' interest in our article. As above stated, the association between diabetes and left ventricular remodeling has been described in previous articles. Our report from a nuclear cardiology department database was our modest contribution and shows that SPECT myocardial perfusion imaging may provide valuable information on this subject. We believe that these concepts may specially help colleagues who are unable to perform other more complex cardiologic images.

Lucas San Miguel MTSAC,

N-acetyl Cysteine and Post-infarction Remodeling

N-acetil cisteína y remodelado post infarto

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Ischemic cardiomyopathy is the main cause of worldwide mortality. Despite progress in the strict control of risk factors and in anti-ischemic and antithrombotic treatment, patients suffering from acute myocardial infarction (AMI) present with a worse prognosis. A concept supporting the unfavorable outcome of these patients is cardiac remodeling following the irreversible loss of cardiac muscle, with the resulting increase in the risk of heart failure and sudden death. (1)

Pathophysiologically, during AMI there is an increase of oxidative stress, triggered by the over production of oxygen-derived free radicals (2) which are deleterious for the cardiomyocytes and lead to a reduction of their viability, greater hypertrophy, and ventricular remodeling. (3)

In their interesting study, M Rodriguez et al. used an experimental AMI model in rabbits with the aim of reducing this oxidative stress by increasing antioxidant species, through N-acetyl cysteine (NAC) administration in animals with AMI induced by ligation of the left coronary artery. (4) N-acetyl cysteine is a precursor of cysteine, an amino acid catabolized by gamma-glutamyl cysteine synthetase producing glutathione, the main endogenous antioxidant system of the organism against oxidative stress. (5)

After a 28-day follow-up period, the AMI group treated with NAC significantly reduced non-infarcted zone thinning, left ventricular (LV) dilation, the increase of LV diastolic pressure and ejection fraction impairment.

The results of this study support the importance of targeting post AMI ventricular remodeling and suggest that antioxidant therapy, as NAC administration, could provide significant benefits to improve the prognosis of patients, with a favorable effect in the initial stages of cardiac remodeling. However, studies in humans, applicable to the general population, as well as randomized clinical trials, are necessary to extend this knowledge and reproduce these results.

These findings highlight the need to continue the research in this field to develop new therapeutic strategies that benefit the affected population.

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AUTHORS' REPLY

On behalf of the research team, I wish to express our most sincere thanks to Drs. María Florencia Pérez, Juan Manuel Pérez and Joaquín Pérez, for their interest and thorough and valuable comments on our study: *Administration of N-acetylcysteine Attenuates Post-Myocardial Infarction Remodeling*. Their observations and analysis enrich our publication.

As mentioned in the article, post myocardial infarction remodeling refers to the structural changes that take place in the heart after a myocardial infarction (MI), affecting its geometry. In its chronic evolution, it provokes progressive functional impairment and heart failure, significantly affecting patient quality of life and increasing the long-term risk of adverse events. Management of ventricular remodeling includes strategies to reduce the working load of the heart, improve the contractile function and prevent complications. However, even with available therapeutic resources, an unfavorable outcome occurs in a high number of patients. Therefore, it is necessary to develop new strategies to modify this harmful situation.

Oxidative stress increasingly emerges as a pathophysiological mechanism of myocardial injury, involved in different pathological processes. Recent experimental animal and clinical studies, have pointed out that during post MI remodeling and heart failure, oxidative stress due greater oxygen-derived free radical production plays a key role, in both early as late stages. The search for alternative therapies that decrease myocardial damage caused by oxidative stress have led to consider N-acetylcysteine as an antioxidant agent. Its use as such in other medical areas is a very active field of research. Though studies in the cardiovascular area are scarce, the results are promising.

The search for new therapeutic resources can start knowing the mechanisms involved in the development and/or maintenance of pathological processes, as attempted in our study. Unfortunately, this type of work usually goes unnoticed or does receive careful attention. However, preclinical findings frequently set the foundations for future clinical progress and improved patient care.

As expressed by Dr. Pérez et al., human studies are necessary to confirm our results and benefit the affected population. Nevertheless, their comment endorsing the importance of targeting ventricular remodeling after an acute myocardial infarction encourages us to persist in a more detailed study of this field and to continue exploring the afore-mentioned and new strategies.

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