# Medium-Term Changes in Myocardial Perfusion and Ventricular Remodeling Following Acute Myocardial Infarction

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The mortality of patients with acute myocardial infarction has obviously decreased in recent years, probably because of faster, more frequent administration of reperfusion treatment and greater use of add-on drugs with beneficial effects on the prognosis.[1] However, some patients still experience a poor clinical outcome, which, among other factors, is closely linked to infarct size and onset of heart failure in the acute phase.[1,2] One of the main risks faced by patients with extensive infarctions infarctions who survive the hospitalization the hospitalization phase is the development of progressive ventricular dilation and dysfunction in the following months.[3] Although this left ventricular remodeling process could have a compensatory purpose, it often occurs in association with the development or worsening of heart failure and leads to greater mortality.[3]

In addition, a high percentage of patients with acute myocardial infarction and apparently successful revascularization treatment on angiography have altered myocardial perfusion.[4-11] This finding has been associated with a lack of functional recovery and progressive expansion of the infarct area and overall ventricular dilation and dysfunction, as well as a higher incidence of clinical complications during follow-up.[4-11]

The extent to which the residual tissue perfusion abnormality after revascularization treatment in an acute myocardial infarction is a mere reflection of massive necrosis in the area at risk, or can itself have deleterious effects on myocyte survival, is still a subject of debate. The first interpretation is supported by experimental models in which massive tissue damage is already observed in the first few hours, and even minutes, after

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reperfusion,[12-14] as well as the fact that areas with perfusion defects tend to show a lack of viability.[4,5] In addition, progressive deterioration of microvascular perfusion has been observed in experimental animals in the first few hours after infarction,[15] indicating that this factor may have an influence on the final size of necrosis and, in itself, be a potential target for therapeutic interventions. Furthermore, in some studies, microvascular obstruction predicted the onset of complications, regardless of infarction size.[5] However, strategies aimed at reducing microvascular damage after reperfusion have shown disparate results.[13,14,16,17]

Apart from these controversial therapeutic implications, it is clear that assessment of myocardial perfusion after infarction has prognostic connotations and therefore, has been the subject of considerable attention in recent years. Although rapid, complete resolution of ST segment elevation in the electrocardiogram after reperfusion treatment is clearly indicative of normalized tissue perfusion, more sophisticated methods are available to estimate perfusion, such as coronary flow pattern analysis or, more directly, imaging techniques such as angiography, contrast echocardiography and cardiac magnetic resonance (CMR).[4-11,14,18]

Although there are few doubts as to the adverse prognostic implications of inadequate myocardial perfusion immediately after revascularization treatment for infarction, the mid- to long-term evolution of tissue perfusion and its associated clinical connotations are uncertain. By analyzing first-pass gadolinium images obtained from cardiac MRI in animal models, it has been described that hypoperfusion areas increase in the first 48 h of reperfusion[15] and remain stable until the ninth day.[19] In humans studied using the same technique, Taylor et al[8] observed an improvement in microvascular perfusion 3 months postinfarction with respect to the examination done in the first few hours.[8] Bodí et al[11] recently described perfusion normalization at 6 months in 62% of the segments that were hypoperfused after the first week, whereas the alterations persisted in the remaining segments. Additionally, in a small number of segments, perfusion within this interval even worsened.[11] Similar results have been obtained with echocardiography after

intracoronary or intravenous contrast injection: in a varying percentage of patients, improvement of regional myocardial perfusion has been observed between the time immediately after reperfusion and the ninth day[6] or at one month,[4] and also between the first day and the month after infarction.[7] However, there are reports that perfusion defects observed in the acute phase of infarction within areas of increased gadolinium enhancement in delayed MRI sequences disappear in the following months.[9]

In this issue of *Revista Española de Cardiología*, Bodí et al[20] present data on the evolution of myocardial perfusion as analyzed by intracoronary myocardial contrast echocardiography in patients with a successfully reperfused first infarction, normal coronary flow in the acute phase and at the sixth month, and an uncomplicated clinical course. In the initial examination performed a few days after infarction, myocardial perfusion abnormalities were observed in 20 patients, 10 of whom had normal perfusion at the sixth month and 10 of whom had persistent alterations. These proportions are very similar to those observed by Galiuto et al[7] in a smaller number of patients studied by intravenous myocardial contrast echocardiography and, obviously, are also consistent with the observations based on first-pass MRI studies conducted recently by the authors of this article in a large subgroup of patients included in the current series.[11]

Unlike some previous studies,[4,6-8,10] in this study the initial abnormal perfusion was not significantly associated with greater left ventricular dilation or poorer functional evolution between the first and second examination. Although we cannot rule out the possibility that a larger series would have found differences, no trend appears to exist in this regard. It is likely that the time point at which the initial examination was performed may have influenced this aspect, since the first examination was earlier in most of these previous studies, within the first 24 hours,[4,6-8] whereas in this study it was done 4 days after the infarction on average, a time at which the end-diastolic volume was already significantly greater in patients with abnormal perfusion than in the others. Regarding functional evolution, only data on the overall ejection fraction is available, with no detailed, segment-to-segment analysis that could have shown differences.

A key finding of this study is that patients with persistent defects tended to present ventricular enlargement during follow-up, whereas those who achieved normal perfusion showed the opposite trend. Although these differences were not significant, they are in line with the results obtained in previous studies[7] and indicate that persistent abnormal perfusion could influence ventricular remodeling. However, this association alone cannot safely establish a cause-and-effect relationship, and it cannot be ruled out that both phenomena are in parallel in the evolution of infarctions, or even that in some cases the presence of late perfusion defects may be secondary to the ventricular dilation itself, which is frequently associated with very high diastolic pressures that could hinder microvascular perfusion, particularly in the subendocardium.

The authors should be congratulated on the rigorous selection of patients and the comprehensive study, which enabled them to obtain a great deal of valuable information. However, as they themselves acknowledge, these selection criteria limit extrapolation of the results to general patient populations with infarction.

In conclusion, along with some previous studies, these results clearly show, as highlighted by the authors, that a perfusion abnormality can persist at mid-term in reperfused acute myocardial infarction. Perhaps the greater sensitivity of echocardiography versus MRI and of first-pass techniques over delayed sequences may explain why this chronic perfusion alteration is observed in studies that have used these techniques[6-8,11,20] and the systematic disappearance of the defects described in late MRI detection.[9] In our opinion, it is also important to note that perfusion improves from the fourth day to the sixth month in approximately half the patients. The reasons why this improvement occurs in some patients and not in others are not clear; however, based on the association of late perfusion with the evolution of ventricular volumes, the field of study is of interest. An awareness of the mechanisms of late improvement of perfusion could be useful in developing therapeutic strategies that could enhance this favorable evolution. The authors point out that late assessment of myocardial perfusion could be used in the future to screen patients eligible for cellular treatment. This would be desirable; however, for the time being, until there is a consensus on the methodology and the indications of this new, promising therapeutic modality,[21] we should continue to treat patients who have extensive infarctions with the various drugs proven to be useful in improving prognosis and limiting ventricular remodeling, regardless of the status of microvascular perfusion.[1,3]

## REFERENCES

1. Heras M, Marrugat J, Arós F, Bosch X, Enero J, Suárez MA, et al. Reducción de la mortalidad por infarto agudo de miocardio en un período de 5 años. Rev Esp Cardiol. 2006;59:200-8.
2. Cequier A, Bueno H, Augé JM, Bardají A, Fernández-Ortiz A, Heras M. Características y mortalidad del infarto agudo de miocardio tratado con intervencionismo coronario percutáneo primario en España: resultados del Registro TRIANA 1 (Tratamiento del Infarto Agudo de miocardio eN Ancianos). Rev Esp Cardiol. 2005;58:341-50.
3. Opie LH, Commerford PJ, Gersh BJ, Pfeffer MA. Controversies in ventricular remodelling. Lancet. 2006;367:356-67.
4. Ito H, Iwakura K, Oh H, Masuyama T, Hori M, Higashino Y, et al. Temporal changes in myocardial perfusion patterns in patients with reperfused anterior wall myocardial infarction: their relation to myocardial viability. Circulation. 1995;91:656-62.
5. Wu KC, Zerhouni EA, Judd RM, Lugo-Olivieri CH, Barouch LA, Schulman SP, et al. Prognostic significance of microvascular

obstruction by magnetic resonance imaging in patients with acute myocardial infarction. Circulation. 1988;97:765-72.

6. Brochet E, Czitrom D, Karila-Cohen D, Seknadji P, Faraggi M, Benamer H, et al. Early changes in myocardial perfusion patterns after myocardial infarction: relation with contractile reserve and functional recovery. J Am Coll Cardiol. 1998;32:2011-7.

7. Galiuto L, Lombardo A, Maseri A, Santoro L, Porto I, Cianflone D, et al. Temporal evolution and functional outcome of no reflow: sustained and spontaneously reversible patterns following successful coronary recanalisation. Heart. 2003;89:731-7.

8. Taylor AJ, Al-Saadi N, Abdel-Aty H, Schulz-Menger J, Messroghli DR, Friedrich MG. Detection of acutely impaired microvascular reperfusion after infarct angioplasty with magnetic resonance imaging. Circulation. 2004;109:2080-5.

9. Hombach V, Grebe O, Merkle N, Waldenmaier S, Höher M, Kochs M, et al. Sequelae of acute myocardial infarction regarding cardiac structure and function and their prognostic significance as assessed by magnetic resonance imaging. Eur Heart J. 2005;26: 549-57.

10. Serra V, Pérez de Isla L, Zamorano J, Almería C, Rodrigo JL, Pérez M, et al. Utilidad de la ecocardiografía de contraste miocárdico con cuantificación basada en imagen paramétrica para la predicción de la recuperación funcional de segmentos acinéticos en pacientes con infarto agudo de miocardio sometidos a angioplastia primaria. Rev Esp Cardiol. 2005;58:649-56.

11. Bodí V, Sanchis J, López-Lereu MP, Núñez J, Sanz R, Palau P, et al. Microvascular perfusion 1 week and 6 months after myocardial infarction by first-pass perfusion cardiovascular magnetic resonance imaging. Heart. 2006;92:1801-7.

12. Padilla F, García-Dorado D, Agulló L, Inserte J, Paniagua A, Mirabet S, et al. L-Arginine administration prevents reperfusion-induced cardiomyocyte hypercontracture and reduces infarct size in the pig. Cardiovasc Res. 2000;46:412-20.

13. Barrabés JA, García-Dorado D, Mirabet M, Lidón RM, Soriano B, Ruiz-Meana M, et al. Lack of effect of glycoprotein IIb/IIIa blockade on myocardial platelet or polymorphonuclear leukocyte accumulation and on infarct size after transient coronary occlusion in pigs. J Am Coll Cardiol. 2002;39:157-65.

14. Barrabés JA, García-Dorado D, Mirabet M, Inserte J, Agulló L, Soriano B, et al. Antagonism of selectin function attenuates microvascular platelet deposition and platelet-mediated myocardial injury after transient ischemia. J Am Coll Cardiol. 2005;45:293-9.

15. Rochitte CE, Lima JAC, Bluemke DA, Reeder SB, McVeigh ER, Furuta T, et al. Magnitude and time course of microvascular obstruction and tissue injury after acute myocardial infarction. Circulation. 1998;98:1006-14.

16. Eisenberg MJ, Jamal S. Glycoprotein IIb/IIIa inhibition in the setting of acute ST-segment elevation myocardial infarction. J Am Coll Cardiol. 2003;42:1-6.

17. Frangogiannis NG, Smith CW, Entman ML. The inflammatory response in myocardial infarction. Cardiovasc Res. 2002;53:31-47.

18. Bertomeu-González V, Bodí V, Sanchis J, Núñez J, López-Lereu MP, Peña G, et al. Limitaciones del blush miocárdico para el análisis del la perfusión miocárdica en pacientes con infarto agudo de miocardio y flujo TIMI 3. Rev Esp Cardiol. 2006;59:575-81.

19. Wu KC, Kim RJ, Bluemke DA, Rochitte CE, Zerhouni EA, Becker LC, et al. Quantification and time course of microvascular obstruction by contrast-enhanced echocardiography and magnetic resonance imaging following acute myocardial infarction and reperfusion. J Am Coll Cardiol. 1998;32:1756-64.

20. Bodí V, Sanchis J, Núñez J, López-Lereu MP, Mainar L, Bosch MJ, et al. Perfusión miocárdica alterada tras un infarto en pacientes con flujo TIMI 3 mantenido: ¿sólo un fenómeno agudo? Rev Esp Cardiol. 2007;60:486-92.

21. Nadal-Ginard B, Torella D, Ellison G. Medicina regenerativa cardiovascular en la encrucijada: es urgente basar los ensayos clínicos sobre terapia celular en datos sólidos obtenidos en animales experimentales relevantes para los humanos. Rev Esp Cardiol. 2006;59:1175-89.