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Original article

Prognostic Value of Myocardial Ischemia and Necrosis in Depressed Left Ventricular Function: a Multicenter Stress Cardiac Magnetic Resonance Registry

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ABSTRACT

Introduction and objectives: The incremental prognostic value of inducible myocardial ischemia over necrosis derived by stress cardiac magnetic resonance in depressed left ventricular function is unknown. We determined the prognostic value of necrosis and ischemia in patients with depressed left ventricular function referred for dipyridamole stress perfusion magnetic resonance.

Methods: In a multicenter registry using stress magnetic resonance, the presence (≥ 2 segments) of late enhancement and perfusion defects and their association with major events (cardiac death and nonfatal infarction) was determined.

Results: In 391 patients, perfusion defect or late enhancement were present in 224 (57%) and 237 (61%). During follow-up (median, 96 weeks), 47 major events (12%) occurred: 25 cardiac deaths and 22 myocardial infarctions. Patients with major events displayed a larger extent of perfusion defects (6 segments vs 3 segments; $P < .001$) but not late enhancement (5 segments vs 3 segments; $P = .1$). Major event rate was significantly higher in the presence of perfusion defects (17% vs 5%; $P = .0005$) but not of late enhancement (14% vs 9%; $P = .1$). Patients were categorized into 4 groups: absence of perfusion defect and absence of late enhancement (n = 124), presence of late enhancement and absence of perfusion defect (n = 43), presence of perfusion defect and presence of late enhancement (n = 195), absence of late enhancement and presence of perfusion defect (n = 29). Event rate was 5%, 7%, 16%, and 24%, respectively (P for trend = .003). In a multivariate regression model, only perfusion defect (hazard ratio = 2.86; 95% confidence interval, 1.37-5.95]; $P = .002$) but not late enhancement (hazard ratio = 1.70; 95% confidence interval, 0.90–3.22; $P = .105$) predicted events.

Conclusions: In depressed left ventricular function, the presence of inducible ischemia is the strongest predictor of major events.

Valor pronóstico de la isquemia miocárdica y la necrosis en pacientes con la función ventricular izquierda deprimida: un registro multicéntrico con resonancia magnética cardiaca de estrés

Palabras clave:
Resonancia magnética cardiaca de estrés
Dipiridamol
Función ventricular izquierda deprimida
Pronóstico

RESUMEN

Introducción y objetivos: No se conoce el valor pronóstico incremental que aporta la isquemia miocárdica inducible respecto a la necrosis determinada por resonancia magnética cardiaca de estrés en pacientes con función ventricular izquierda deprimida. Se determina el valor pronóstico de la necrosis y la isquemia en pacientes con función ventricular izquierda deprimida remitidos a exploración por resonancia magnética de estrés con perfusión de dipiridamol.

Métodos: En un registro multicéntrico basado en el uso de resonancia magnética de estrés, se determinó la presencia (≥ 2 segmentos) de realce tardío de contraste y defectos de perfusión y su asociación con eventos mayores (muerte cardiaca e infarto no mortal).

Resultados: De un total de 391 pacientes, se identificó defecto de perfusión o realce tardío en 224 (57%) y 237 (61%). Durante el seguimiento (mediana, 96 semanas), se produjeron 47 eventos mayores (12%): 25 muertes cardiacas y 22 infartos de miocardio. Los pacientes con eventos mayores presentaron mayor

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extensión de los defectos de perfusión (6 frente a 3 segmentos; p < 0,001), pero no del realce tardío (5 frente a 3 segmentos; p = 0,1). La tasa de eventos mayores fue significativamente superior en presencia de defectos de perfusión (el 17 frente al 5%; p = 0,0005), pero no cuando había realce tardío (el 14 frente al 9%; p = 0,1). Se clasificó a los pacientes en los cuatro grupos siguientes: ausencia de defecto de perfusión y ausencia de realce tardío (n = 124), presencia de realce tardío y ausencia de defecto de perfusión (n = 43), presencia de realce tardío y presencia de defecto de perfusión (n = 195), y ausencia de realce tardío y presencia de defecto de perfusión (n = 29). Las tasas de eventos fueron del 5, el 7, el 16 y el 24% respectivamente (p de tendencia = 0,003). En un modelo de regresión multivariable, solamente el defecto de perfusión predijo los eventos clínicos (*hazard ratio* = 2,86; intervalo de confianza del 95%, 1,37-5,95; p = 0,002), pero el realce tardío no (*hazard ratio* = 1,70; intervalo de confianza del 95%, 0,90-3,22; p = 0,105).

Conclusiones: En los pacientes con la función ventricular izquierda deprimida, la isquemia inducible es el más potente predictor de futuros eventos mayores.

Abbreviations

CMR: cardiac magnetic resonance
LGE: late gadolinium enhancement
LV: left ventricular
PD: perfusion defect

INTRODUCTION

Depressed left ventricular (LV) function is present in about 50% of patients with heart failure[1] and the prognosis with ischemic origin is worse than with nonischemic etiology.[2] The evaluation for inducible myocardial ischemia appears valuable to discern ischemic from nonischemic etiology of depressed LV function. In normal LV function, prognosis is associated with the presence and amount of ischemia reduction;[3] however, the prognostic role of ischemia has not been specifically shown for patients with depressed LV function. Moreover, differentiation between necrotic LV dysfunction vs ischemic LV dysfunction might have important implications since the latter is potentially reversible and thus its reversal may confer symptomatic and prognostic benefit.

Dipyridamole stress perfusion cardiac magnetic resonance imaging (CMR) appears as the ideal noninvasive clinical tool to discriminate ischemic from nonischemic etiology of heart failure. In one examination, CMR allows for a simultaneous assessment of inducible ischemia[4,5] and necrosis.[6,7] However, apart from these diagnostic considerations, risk stratification in this patient population remains challenging. For that purpose, most studies have focused on myocardial necrosis, but recently it has been demonstrated that the presence of inducible ischemia offers incremental prognostic value.[8] However, this issue has not been specifically addressed and a simultaneous assessment of necrosis and ischemia has not been carried out in patients with depressed LV function. Recent studies have pointed out the importance of viability; nevertheless, results were not as decisive as expected and it has been suggested that inducible ischemia might play an important prognostic role.[9,10]

In a multicenter registry with consecutive patients referred for further diagnostic workup of depressed LV function, we assessed the prognostic value of stress perfusion CMR-derived inducible ischemia and necrosis in terms of major events (cardiac death and nonfatal myocardial infarctions.)

METHODS

Study Group

This is a multicenter registry conducted in 1 community hospital and 2 university hospitals from January 2003 to June 2010. All baseline data, CMR characteristics, and outcome were collected prospectively according to pre-defined endpoints. Data of patients with depressed LV function, although prospectively collected, were retrospectively reviewed and included: *a)* consecutive patients with depressed LV function on echocardiography referred for stress perfusion CMR for unclear etiology (ischemic vs nonischemic), and *b)* patients with depressed LV function and known ischemic heart disease referred for therapeutic decision-making.

Left ventricular ejection fraction was determined on echocardiography using the biplane method of discs (modified Simpson rule) and depressed LV function was defined as < 45%, considered moderately abnormal under current guidelines.[11]

Patients with acute coronary syndromes, valvular or congenital heart disease, hypertrophic and restrictive cardiomyopathies on echocardiography, as well as acute myocarditis or any contraindications to CMR or dipyridamole, were not included in the study.

Figure 1 shows the patient flow through the study. Of all included patients, 66 were excluded due to insufficient image quality or an incomplete study. Patients with a final diagnosis of a valvular or congenital heart disease or hypertrophic or restrictive cardiomyopathies previously unrecognized by echocardiography were also excluded.

A CMR-related coronary angiography (prompted by or carried out within 3 months of the CMR examination)[4,5] was performed in 122 patients (27%) and was abnormal in 89 cases. To avoid the confounding effect on spontaneous outcome, patients undergoing CMR-related revascularization (37 percutaneous coronary intervention and 20 coronary artery bypass graft) were excluded from analysis. Therefore, the final study population comprised 391 patients.

All baseline characteristics were prospectively recorded upon patient arrival to the CMR facilities by two experienced cardiologists. Management and medical treatment was left at the discretion of the patients' cardiologists, who were aware of the CMR results. The local ethics committee at each institution approved the study protocol and all subjects gave written informed consent.