#### **BIBLIOGRAPHIC REVISION**



# The usefulness of nuclear magnetic resonance to assess prognosis in patients suffering from heart failure

## La utilidad de la resonancia magnética nuclear para la evaluación del pronóstico de pacientes con insuficiencia cardíaca

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#### ABSTRACT

**Introduction:** the role of nuclear magnetic resonance in heart failure is much discussed in the etiologic and prognostic assessment of this disease. Therefore, a description of the usefulness of nuclear magnetic resonance would show its role in assessing prognosis in patients suffering from heart failure of diverse etiologies.

**Objective:** describe the use of nuclear magnetic resonance to assess prognosis in patients suffering from heart failure.

**Methods:** a narrative bibliographic review was done by searching databases such as PubMed, Scopus, Elsevier and Springer.

**Results:** cardiac magnetic resonance is superior to echocardiography to assess the volumes and the function of the left ventricle with better reproducibility, also when analyzing systolic anomalies and characterizing the viable myocardial tissue as well as the one with the presence of myocardial fibrosis. Precisely detecting myocardial fibrosis helps predict adverse occurrences in patients suffering from heart failure.

**Conclusions:** nuclear magnetic resonance helps identify a disease undetected in previous circumstances and nosological entities challenging to diagnose. So its use relates to better diagnostic performance and, therefore, to better predicting adverse effects in patients suffering from heart failure.

Key words: Heart Failure; Cardiomyopathy; Cardiovascular Magnetic Resonance.

#### RESUMEN

**Introducción:** el rol de la resonancia magnética nuclear en la insuficiencia cardíaca es muy discutido, tanto en la evaluación etiológica y pronóstica de esta enfermedad. Por lo que, una descripción sobre cuál es la utilidad de la resonancia magnética nuclear mostraría el rol de esta para la evaluación del pronóstico en pacientes con insuficiencia cardíaca de diversas etiologías.

**Objetivo:** describir la utilidad de la resonancia magnética nuclear para la evaluación del pronóstico en pacientes con insuficiencia cardíaca.

**Metodología:** se realizó una revisión bibliográfica narrativa, mediante la búsqueda en bases de datos como PubMed, Scopus, Elsevier y Springer.

**Resultados:** la resonancia magnética cardíaca es superior a la ecocardiografía para evaluar los volúmenes y la función del ventrículo izquierdo con mejor reproducibilidad, también al analizar anomalías sistólicas y caracterizar el tejido miocárdico viable, así como aquel con presencia de fibrosis miocárdica. Precisamente, la detección de fibrosis miocárdica posee un valor predictor de eventos adversos en pacientes con insuficiencia cardíaca.

Conclusiones: la resonancia magnética nuclear es útil para identificar una enfermedad no detectada en

previas circunstancias y entidades nosológicas de difícil diagnóstico. Por lo que su uso se asocia a un mejor rendimiento diagnóstico y, por lo tanto, un mejor predictor de efectos adversos en pacientes con insuficiencia cardíaca.

Palabras clave: Insuficiencia Cardiaca; Miocardiopatía; Resonancia Magnética Cardiovascular.

#### **INTRODUCTION**

Heart failure (HF) is a significant health problem due to the number of hospitalizations that, in addition to generating high costs, cause severe social adverse effects. This disease is more commoner in the adult population, with a significant increase in prevalence from 70 years on.<sup>(1)</sup> Besides, it is a severe cause of morbidity and mortality, with a mortality rate of 5 years is around 50 %.<sup>(2)</sup> Nowadays, there has been some progress in its management, emphasizing meeting the goals of optimizing the clinical condition, improving the functional capacity, reducing the number of hospitalizations and reducing mortality. In developed countries, the global prevalence of HF ranges from 1,5 % to 4 %. This figure is increasing due to the aging world population beyond 75 years. Currently, there are no significant differences between European and Asian countries.<sup>(3)</sup> In the general adult population, the prevalence of HF is estimated to range from 1 % to 2 %, with those with preserved left ventricular ejection fraction (LVEF) amounting to more than half of said population. As regards the incidence of this disease, in western developed countries, it ranges from 1 to 9 cases for every 1 000 persons. In Latin America, there is little epidemiological information on HF; most data come from a few individual studies. A meta-analysis performed by Ciapponi et al. to estimate the load of HF in Latin America out of studies conducted in this region showed a combined prevalence of 1,01 %, the ages 51 to 69 being the most affected, i.e. the elderly population.<sup>(4)</sup> Ecuador is no exception since we only know out of multicentric pieces of research; for instance, one done in five health houses in Quito City, where 6,1 % of all patients hospitalized in the clinic and surgery area have an HF condition and also that mortality exceeds neoplastic diseases with 7,01 % of deaths every 4,882 hospitalizations in 2013.<sup>(5,6)</sup>

The main means of study through images can identify and characterize the cardiac tissue with similar degrees of accuracy; besides, they provide a way to monitor the different processes of the disease. These processes are changes or alterations in the tissue, such as those for support. These alterations manifest as changes in the heart's geometry, tissue mass and pumping function; all these processes become concrete in the term cardiac remodeling (CR), meaning the physiopathologic mechanism that justifies the clinical syndrome.<sup>(7)</sup> Currently, other more specialized imaging methods like nuclear magnetic resonance (NMR) make it possible to characterize cardiac lesions, and they become very relevant as they focus on the etiopathologic and physiopathologic aspects of the disease, thus generating a better decision on treatment and implementation of a specific and individualized therapy.<sup>(8)</sup> On the other hand, the usefulness of cardiac computed tomography consists in being an accurate alternative for the study of HF in patients with susceptible devices in NMR.<sup>(9)</sup> However, cardiac magnetic resonance (CMR) helps quantify the volumes of the cardiac ventricle and valve morphology and to characterize and determine the degree of functionality of the myocardium.<sup>(10,11,12)</sup> Finally, NMR provides strategic information to assess the prognosis in patients suffering from HF according to their etiology.<sup>(13)</sup>

Images are the golden standard when assessing MR; nevertheless, monitoring LVEF via conventional echocardiography has several limitations; for instance, it does not provide a detailed profile without access to good information on the prognosis, and consequently, it is impossible to benefit from therapies focused on each phenotype. Many times, these findings relate to the changes after therapy is implemented.<sup>(14)</sup>

Because of the above, this piece of research aims to describe the usefulness of nuclear magnetic resonance to assess prognosis in patients suffering from heart failure.

#### **METHODS**

A narrative and descriptive bibliographic review was done, and an exploration of specialized and updated scientific literature on the usefulness of NMR in assessing prognosis in patients suffering from HF. There was a search for scientific articles, the quartiles of which were established from Q2 to Q1 and published from 2011 to 2021.

The PRISMA method was used to assess and choose the articles. Primary and secondary information sources are found in scientific databases such as Springer (BMC), PubMed, Elsevier and Scopus, with adjusted scientific up-to-datedness. Research articles, controlled and randomized clinical trials, systematic reviews and metaanalyses were included. Together with the above, the Boolean operators "And", "Or" and "Not" will be used.



Figure 1. Process for article selection

## RESULTS

A piece of research was found in the etiologic study, which was based on three different independent groups: 1) with CMR, 2) with conventional X-ray angiography, and 3) a group with a different that accessed all clinical and image data for their review.<sup>(15)</sup> Another study, with the use of stress tests and subsequent images with late gadolinium enhancement (LGE), studied the proportion of new clinical diagnoses in patients suffering from heart failure with preserved ejection fraction (HFpEF).<sup>(16)</sup>

As regards the implication of CMR to assess the predictive value of prognosis in patients suffering from HF, a study used the image with LGE to determine the presence or absence of myocardial fibrosis in 180 patients for the later therapeutic decision.<sup>(17)</sup> On the other hand, a multicentered analysis performed on 1,247 patients with a history of myocardial infarction with an elevation of segment ST and with preserved LVEF assessed the volumes and function of the left ventricle (LV) to assess the predictive value of the risk factors of the clinic, the myocardial lesion and the microvasculature via CMR.<sup>(18)</sup>

Garget al.<sup>(19)</sup> demonstrated the value of CMR to stratify pulmonary hypertension with HFpEF via noncontrasted image and flow. However, the characterization of the tissue with diffuse myocardial fibrosis via LGE showed higher rates of associations with death due to all the causes as well as a higher risk of hospitalization (table 1).<sup>(20,21,22)</sup>

#### DISCUSSION

Minimally invasive cardiac images are an important pillar in the clinical assessment of patients suffering from different heart conditions, especially HF. It is indispensable to quantify the volumes and the degree of myocardial functionality. In this context, echocardiography undoubtedly intervenes due to its advantages regarding its availability in habitual clinical practice;<sup>(8,9)</sup> however, the benefits of CMR are notably remarkable at the time of providing more accurate when assessing the same parameters. We should emphasize that CMR allows us both to identify the characteristics of the cardiac tissue and to differentiate the ischemic or non-ischemic state of a coronary event and, therefore, the degree of fibrosis in the affected myocardium.<sup>(10)</sup>

Author/place/ year	Title	Population	Study	Results
Roy et al. <sup>(21)</sup> , Lovaina, Bélgica, 2018	Associations and prognostic significance of diffuse myocardial fibrosis by cardiovascular magnetic resonance imaging in heart failure with preserved ejection fraction.	118	Prospective	Patients with HFpEF, high extracellular volume (ECV), likely reflecting abnormal diffuse myocardial fibrosis, was associated with a higher rate of all-cause death and first HF hospitalization at short-term follow- up.
Kato et al. <sup>(22)</sup> , Kanagawa, Japón, 2015	Prognostic significance of quantitative assessment of focal myocardial fibrosis in patients with heart failure with preserved ejection fraction.	111	Prospective	During a mean follow-up of 851 ± 609 days, 10 events were observed (two cardiovascular deaths, eight hospitalizations for heart failure decompensation). The area under the LGE % receiver operating characteristics curve for detection of future events was 0,721 (95 % CI 0,628-0,802).
Garg et al. <sup>(19)</sup> , South Yorkshire, Inglaterra, 2021	cardiovascular magnetic resonance imaging predicts all-cause mortality in pulmonary hypertension associated with heart failure with preserved ejection fraction.	116	Retrospective	In this study, 116 patients with pulmonary hypertension-HFpEF were identified. During a mean follow-up of $3 \pm 2$ years, 61 patients with pulmonary hypertension-HFpEF died (53 %).
Kanagala et al. <sup>(16)</sup> , Leicester, Inglaterra, 2018	Diagnostic and prognostic utility of cardiovascular magnetic resonance imaging in heart failure with preserved ejection fraction: implications for clinical trials.	42	Prospective	CMR diagnosed significant new pathology in 27 % of patients with HFpEF. These patients were at increased risk of death and hospitalization for heart failure.
Lin et al. <sup>(17)</sup> , Shangqiu, China, 2022	Diagnostic value of cardiac magnetic resonance imaging for myocardial fibrosis in patients with heart failure and its predictive value for prognosis.	180	Retrospective	Levosimendan combined with ivabradine hydrochloride can effectively alleviate MF in patients with MF, and RMRC has a good predictive value for MF in such patients, which is worthy of clinical promotion.
Reindl et al. <sup>(18)</sup> , Innsbruck, Aus- tria, 2021	Cardiac magnetic resonance imaging improves the prognostic stratification of patients with ST-segment elevation myocardial infarction and preserved ejection fraction.	1 247	Prospective	C-statistics revealed that the addition of CMR predictors (GLS and MVO) to clinical predictors (female sex and TIMI risk score) resulted in a significantly (P = 0,02) higher AUC [0,76 (95 % CI 0,73-0,79)] compared to clinical predictors alone [AUC 0,65 (95 % CI 0,62-0,69).
Chun et al. <sup>(18)</sup> ,Seúl, Corea del Sur, 2022	Prognostic cardiac magnetic resonance markers of left ventricular involvement in arrhythmogenic cardiomyopathy to predict heart failure outcomes.	60	Retrospective	Assessment of LV myocardium by CMR with LGE and native T1, T2 and extracellular volume markers was significantly associated with the risk of HF-related events in patients with MCA.
Assomull et al. <sup>(15)</sup> , Inglaterra, 2011	Role of cardiovascular magnetic resonance imaging as a gatekeeper for invasive coronary angiography in patients with heart failure of unknown etiology.	120	Prospective	We found that CMR-LGE correctly identified all 29 patients to whom CAD was attributed as the underlying cause. In 2 of these patients, a CAD etiology was attributed despite unobstructed coronary arteries. Of the patients with a diagnosis of DCM, 25 had a pattern of midwall fibrosis.

 Table 1. Value of cardiac magnetic resonance concerning the etiology of HF and its prognosis

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Thus, as evidenced in the prospective study by Assomull et al.<sup>(15)</sup>, using CMR in patients suffering from HF is beneficial when detecting a scarcely clear etiology assessed with conventional methods. Concretely, that study demonstrated that LGE exceeds coronary angiography in costs and risks of exposure to ionizing radiation; nevertheless, CMR is currently restricted to studying the origins and trajectories of the coronary vessels.

Employing CMR, tissues with fibroadipose infiltration are characterized, a finding enabling diagnosis of cardiomyopathies challenging to be diagnosed. In a retrospective analysis of a patient suffering from arrhythmogenic cardiomyopathy, Chun et al.<sup>(20)</sup>, evidenced that the main CMR markers (LGE, native mapping of T1, T2 and extracellular volume) related to events consonant with HF in these patients. Besides, thanks to the volumetric measurements of the ventricles that can be assessed via CMR, Garg et al.<sup>(19)</sup> developed a tool and, consequently, a CMR helpful model to evaluate the right ventricle and the seriousness of pulmonary hypertension in patients suffering from heart failure with preserved ejection fraction (HFpEF). This demonstrates that CMR plays an essential role in assessing HF since the assessment of the tissue contributes new information that was hidden or scarcely evident before.

Once the capability of CMR to elucidate new findings had been demonstrated, which is helpful in the significant heterogeneity of underlying etiologies, in this line, Kanagalaet al.<sup>(16)</sup> identified patients suffering from coronary arterial disease and microvascular malfunction without any previous echocardiographic diagnosis, which suggest the possibility of implementing better risk stratification.

The prognostic resonance value has a fundamental importance in assessing patients suffering from HF. As the current evidence refers, the quantification of myocardial fibrosis via CMR with late gadolinium enhancement (LGE) has palpable prognostic implications. In this area, Kato et al.<sup>(22)</sup> demonstrated that a larger size of LGE massively relates to a high rate of future adverse events, which shows the previously discussed usefulness. In contrast to the benefit of LGE, Roy et al.<sup>(21)</sup> assessed the existence, the relations and the predictive value of studying the extracellular volume (ECV) with CMR and found a correlation between high values of ECV and abnormalities proper to the extracellular matrix.

On the other hand, a multicentric analysis performed by Reindl et al.<sup>(18)</sup> demonstrates an approach based on findings of microvascular obstruction and global longitudinal tension as parameters in CMR predicted major adverse cardiovascular events (death, congestive HF and reinfarction) with more prognostic validity than the markers used in habitual clinical practice. However, in the last years' HF has benefitted from many clinical trials aimed at reducing its morbidity and mortality; nevertheless, said patients continue needing reiterated hospitalizations, and it is because of them that methods for early detection of symptoms are still required. Henceforward, Lin et al.<sup>(17)</sup> aimed to determine, via a trial with 180 patients suffering from HF, the predictive value of CMR for myocardial fibrosis in this entity; for that purpose, LVEF and the end-systolic diameter of LV were used as indicators of cardiac function at the end-systolic volume of LV. After the pharmacotherapeutic intervention, said indicators demonstrated they have potential when predicting myocardial fibrosis, which positively supports the predictive value of CMR in patients suffering from HF. However, there is a need for more prospective randomized trials supporting the routine use of CMR to characterize risk in habitual clinical practice.

#### **CONCLUSIONS**

Cardiac magnetic resonance efficiently identifies diseases undetected in previous circumstances and is challenging to diagnose. It is the only image technique that makes it possible to assess cardiac function, structure (tissue characteristics), perfusion and viability without ionizing radiation. It also enables predicting adverse effects in patients suffering from heart failure.

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#### **CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest.

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