

Original Research

The Greek Cardiac Magnetic Resonance Experience: A Comparison with the EuroCMR Registry

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Introduction: We carried out an evaluation of Greek cardiovascular magnetic resonance (CMR) data in order to analyse the indications, safety, quality, and impact on management, in comparison with the EuroCMR registry.

Methods: A retrospective analysis was performed of Greek CMR data from patients referred from 6 Greek cardiac clinics to 6 different MRI units in Athens that offer CMR services. A total of 10,000 CMR examinations carried out from 1995 to 2010 were evaluated retrospectively and included in the study.

Results: Fifty percent of patients underwent evaluation for thalassaemic syndromes. In the remaining 50%, the most important indications were: a) workup of myocarditis/cardiomyopathies (40%), b) assessment of viability (5%), and c) congenital heart disease (5%). Image quality was good in 75%, moderate in 15%, and inadequate in 10% of cases. Complications occurred in 0.02%, including allergic reactions, dyspnoea, and panic attack. No death or cardiac complication was observed during or due to CMR; however, stress testing was not used in any of the cases. In 65% of all CMR studies, the initial diagnosis made by a non-SCMR-trained person had no impact on the patients' management and did not offer any diagnostic contribution to referral clinicians, discouraging them from referring for CMR again. However, after the re-evaluation performed by an SCMR-trained person, the results of the Greek CMR were capable of satisfying all imaging needs in a percentage of patients equivalent to that presented in the EuroCMR registry (83% vs. 86%, $p=NS$), so that no further non-invasive imaging procedures would be required after CMR.

Conclusions: Thalassaemia and myocarditis were the most frequent CMR indications in Greece. However, the lack of training according to SCMR guidelines lowers the diagnostic efficacy significantly and leads to under-use of the technique.

Cardiovascular magnetic resonance (CMR) is a new non-invasive, non-radiating imaging technique that provides high-resolution images with information about heart morphology, function, perfusion and fibrosis.¹ Using a combination of different sequences, CMR can give a robust answer to the majority of cardiac questions during a single examination. In this context, cine-CMR,

using a steady-state-free precession (SS-FP) sequence provides information about cardiac morphology, function and contractile reserve.² Perfusion CMR, evaluating the first pass of gadolinium using a T1 sequence with and without vasodilators, can provide reliable information about myocardial perfusion.³⁻⁶ Furthermore, the application of gadolinium, using an inversion recovery sequence, can be used for fibro-

sis detection in both infarct and myocarditis.⁷ Additionally, T2 and T2 star provide heart-liver iron evaluation in multiple transfused patients.⁸⁻¹⁷

Although CMR has a broad spectrum of clinical indications and is increasingly used in daily clinical practice, detailed information about the general use of this technique in the clinical routine, its safety, and its impact on patients' management is available only in the European Cardiovascular Magnetic Resonance (EuroCMR) registry. However, the EuroCMR registry represents the CMR experience in some very specialised centres in Germany, Europe and the USA, and does not give any information about the situation in other European countries with different clinical queries, training level and legislation with regard to who is responsible for performing and interpreting the CMR examination.

Our aim was to evaluate retrospectively the CMR data of 10,000 patients referred by 6 cardiac clinics to 6 different MRI units offering CMR services in Athens. The evaluation included indications, image quality, safety and impact on patient management after CMR. The results were compared with those presented in the EuroCMR registry.¹⁸

Methods

Study population

The study was retrospective and included 10,000 patients who were referred for CMR by 6 Greek cardiac centres located in Athens (Onassis Cardiac Surgery Centre, Hippokraton University Hospital, Laikon University Hospital, "Alexandra" University Hospital, Agia Sofia Children's Hospital, Pentelis Children's Hospital) between 1995-2010 (20% from 1995 to 2000, 30% from 2000 to 2005, and 50% from 2006 to 2010). Coronary artery disease (CAD), myocarditis, cardiomyopathies and heart failure due to both ischemic and non-ischaemic heart disease were referred from Onassis Cardiac Surgery Centre, Hippokraton University Hospital, Laikon University Hospital and "Alexandra" University Hospital. Patients with heart failure due to thalassaemia were referred only from Laikon and Agia Sofia Children's Hospitals. Patients with congenital heart disease were referred only from Agia Sofia Children's Hospital. Paediatric patients with myocarditis and cardiomyopathies were referred only from Agia Sofia Children's Hospital and Pentelis Children's Hospital. Patients were selected retrospectively and included in

the study according to the consensus appropriateness criteria for CMR imaging endorsed by the American College of Cardiology Foundation, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance (SCMR), American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology.¹⁹ All CMR data were initially evaluated by a non SCMR-trained person and were re-evaluated retrospectively by a senior doctor who had fulfilled the SCMR Level 3 criteria (2 years' full-time training). Finally, the Greek CMR data were compared with those of the EuroCMR registry.

Variable evaluation

All variables assessed were collected from medical records. Variables included anonymous demographic data, history, indication for CMR, procedural parameters, complications, results of CMR and the impact of CMR on patients' management.

Complications of CMR

Death, resuscitation, or any other condition that took place during the CMR and required the patient's admission for at least 1 night after the CMR examination (e.g. allergic shock, arrhythmias, etc.) were considered as severe complications. Dyspnoea, chest pain, allergy without shock, panic attack, etc., were considered as mild complications.¹⁸

CMR image quality

Images that did not allow answering of the clinical question were graded as poor. Images that allowed complete answering of the referrer's questions, but created some doubts due to artefacts, were graded as moderate. Images with optimal quality allowing complete answering of the clinical question were graded as good. A change of patient management was reported if CMR resulted in a new diagnosis that was not suspected before (e.g. acute myocarditis found during workup of suspected dilated cardiomyopathy) or if the results of CMR initiated a change in medication.¹⁸

Statistics

Since the objectives of this registry were descriptive in

nature, no formal hypothesis testing was done. Absolute numbers and percentages were computed to describe the patient population and expressed as mean \pm standard deviation. Categorical values were compared by chi-square test or Fisher's exact test, and continuous variables were compared by 2-tailed Wilcoxon rank sum test. Values of $p < 0.05$ were considered significant.

Results

Use of CMR in the clinical routine in Greece and most common indications

The most important indications for CMR in this cohort were: 1) thalassaemia (50%); 2) myocarditis /cardiomyopathies (40%); 3) assessment of viability (5%); and 4) congenital heart disease (5%). Dividing the analysis cohort into subgroups, internal referrals represented 30% and external 70% of the cases. In the internal subgroup the 3 most important indications were 1) myocarditis/cardiomyopathies, 2) myocardial viability, and 3) congenital heart disease; while in the external subgroup the 3 most important indications were 1) thalassaemia evaluation, 2) myocarditis/cardiomyopathies, and 3) congenital heart disease.

From 1995 to 2000 the referrals included 1000 patients with thalassaemia and 100 patients with cardiomyopathies, from 2000 to 2005, 1500 patients with thalassaemia and 400 with myocarditis/cardiomyopathies, and finally from 2006 to 2010, 2500 patients with thalassaemia, 3500 with myocarditis/cardiomyopathies, 500 with congenital heart disease and 500 for viability assessment. It is important to mention that the CMR evaluation of thalassaemia was requested by haematologists, who use the technique to validate chelation therapy, and not by cardiologists, who still consider echocardiography as the best technique to evaluate iron overload.

In comparison to the EuroCMR registry, where the most important CMR indications were workup of myocarditis/cardiomyopathies, risk stratification in suspected CAD/ischaemia, and assessment of myocardial viability,¹⁸ the Greek CMR examinations were mainly oriented towards the assessment of thalassaemia and myocarditis. The evaluation of viability constituted only a small percentage and the evaluation of ischaemia by CMR was completely absent.

Regarding the use of contrast agent, there is a significant difference between the Greek patients who received a gadolinium-based contrast agent compared

to the EuroCMR registry patients (50% vs. 88%, $p < 0.001$).¹⁸ This difference is due to the fact that the majority of Greek CMR studies were performed for iron evaluation in thalassaemia patients and the application of contrast agent was considered not to be necessary. However, the median contrast dose was 1.4 mmol/kg (1.2-1.6 mmol/kg) and did not differ significantly from that used in the EuroCMR.¹⁸ Patients' baseline characteristics are presented in Table 1. Primary indications for CMR are given in Table 2.

Imaging procedures before CMR

Before undergoing CMR, all patients had undergone a transthoracic echocardiography study, 50% cardiac catheterisation, 10% (2/3 with congenital heart disease and 1/3 with cardiomyopathies) transoesophageal echocardiography, 1% cardiac computed tomography, and 50% single-photon emission tomography (SPECT) imaging.

In comparison to the EuroCMR registry, where before undergoing CMR, 64.1% of patients had undergone transthoracic echocardiography, 25.1% cardiac catheterization, 1.9% transoesophageal echocar-

Table 1. Patients' baseline characteristics.

All patients	10,000
Sex	Male 60%, Female 40%
Age (years)	40 \pm 10 (20-60)
Body mass index (kg/m ²)	27 \pm 2 (24-29)
Field	1.5-T 100%, 3.0-T 0%
Stress testing	Not used
Reader:	
SCMR-trained person	100%
Team of cardiologist and radiologist	0%
Non SCMR-trained person	100%

Table 2. Primary indications for cardiovascular magnetic resonance.

Thalassaemia	50%
Myocarditis/cardiomyopathies	40%
Assessment of viability	5%
Congenital heart disease	5%
Suspected CAD/ischaemia in known CAD	0%
Valvular heart disease	0%
Aortic disease	0%
Ventricular thrombus	0%
Cardiac masses	0%
Pulmonary vessels	0%
Coronary vessels	0%
Other than above	0%

CAD – coronary artery disease.

diography, 1.8% cardiac computed tomography, and 0.3% SPECT imaging,¹⁸ in Greece all patients had as a main investigation a transthoracic echocardiogram and half of them also a SPECT and a cardiac catheterisation. Although CMR was the first imaging procedure ordered in 23.1% of the Euro CMR registry, in Greece, CMR was never the first imaging procedure ordered in any of the patients.

Procedural safety in the clinical routine

Complications occurred in 0.02% of patients, and included allergic reactions, dyspnoea and panic attack. No patient died during or due to CMR, however, it should be emphasised that stress testing was not used in any case.

Image quality in the clinical routine

The image quality in the Greek CMR studies was significantly lower compared to that mentioned by the EuroCMR registry.¹⁸ It was good in 75% vs. 90.1% ($p < 0.001$), moderate but still diagnostic in 15% vs. 8.1% ($p < 0.05$), and poor in 10% of the Greek CMR studies vs. 1.8% in the EuroCMR registry ($p < 0.001$).

Impact of CMR on patient management in the clinical routine

In 65% of all the CMR cases, the initial diagnosis made by a non SCMR-trained person was just a description of images, that had no impact on the patients' prognosis and management and did not offer any diagnostic contribution to the referral clinicians. However, after the re-evaluation performed by an SCMR-trained person, the results of the Greek CMR studies were capable of satisfying all imaging needs in a percentage of patients equivalent to that presented in the EuroCMR registry (83% vs. 86%, $p = \text{NS}$), so that no further non-invasive imaging procedure would be required after CMR. However, since CMR was never the first and only examination in any of the patients, conclusions about the impact of CMR in this regard cannot be drawn. Furthermore, since stress CMR data were not available, the possible impact of stress CMR on the patients' diagnosis and management remains unknown.

Cost analysis

There is a great variation regarding the cost of CMR studies between different centres in Greece, with

prices starting from 180 to 700 euros, without stress application, depending on the centre's individual policy. We should mention that officially there is no price for stress, because at the moment it is not included in patients' clinical work-up by the Greek Ministry of Health, and the only stress CMR studies done by our team were part of research protocols.¹⁹ Although we did not perform a cost analysis of integrating CMR into the clinical routine, given the inability of CMR reporting, by non SCMR-trained people, to offer clinically useful information, it seems unlikely that integrating the technique into the clinical routine would be cost effective.

Discussion

In this retrospective analysis, after the re-evaluation of 10,000 Greek CMR studies, we found that 50% of them were performed for the assessment of iron overload, although only two of the referring centres had thalassaemic patients, 40% for myocarditis/cardiomyopathies, 5% for viability, and 5% for congenital heart disease. Furthermore, although CAD was the main interest of 4/6 referring centres, only 5% of patients were referred for viability evaluation. Image quality was good in 75%, moderate in 15%, and inadequate in 10% of cases. In the initial reports produced by a non SCMR-trained person, 65% of the CMR data had no impact on patients' management and did not offer any diagnostic contribution to referral clinicians, which would be likely to discourage them from referring patients again for CMR. However, after the re-evaluation by an SCMR-trained person, CMR was capable of satisfying all imaging needs in 83% of patients.

Complications occurred only in a very small percentage that was lower compared to the EuroCMR registry. However, stress testing was not used in any patient. This was expected, due to the lack of use of stress studies in Greek CMR. Concerning the image quality of CMR examinations, it was also lower compared to the EuroCMR registry, probably because of the lack of training of both doctors and technicians, and quality controls in different MRI units, given the inadequate legislation in this field in Greece.

On the basis of these findings, we have demonstrated an increase in the routine use of CMR. However, the inadequate training according to SCMR guidelines and the descriptive nature of the reporting of the Greek CMR studies, without any clinically important conclusions, do not allow the technique to re-

veal its usefulness over the whole spectrum of cardiovascular medicine.

Another important finding is that echocardiography is the first and the *sine qua non* imaging approach to all cardiac patients in Greece. This is to be expected, because echocardiography, with its flexibility, availability, speed, low cost and clinically oriented diagnostic information (in Greece it is performed and interpreted exclusively by cardiologists), remains the imaging technique of first choice for all cardiac patients, as recommended by current guidelines.²⁰ However, CMR can add to the echocardiographic findings, especially in the workup of cardiomyopathies and myocarditis,^{21,22} in suspected CAD,²³ and for the assessment of myocardial viability.²¹

We must also emphasise the importance of CMR in the evaluation of cardiac iron overload in thalassaemia patients, which is the most frequently CMR examination performed in Greece. Indeed, CMR has completely changed the diagnosis and treatment of these patients in Greece.⁹ However, there are still problems in the application and interpretation of imaging protocols in different centres and different machines that suggest the necessity of multi-centre and multi-vendor studies in Greece in order to evaluate the inter- and intra-observer variability and establish a “common language” for the evaluation of iron overload.

In comparison to the EuroCMR registry, where the most important indications for CMR were workup of myocarditis/cardiomyopathies and risk stratification in suspected CAD,¹⁸ in the Greek CMR examinations the most important indications were the assessment of thalassaemia and myocarditis, with only a small percentage for CAD risk stratification. This is the result of the inadequate CMR training of Greek cardiologists, who still believe that CMR is a rather “exotic” examination and has no place in CAD evaluation, the “holy grail” of cardiology. Additionally, CMR training according to European Guidelines has not yet been included in the “core curriculum” of Greek cardiologists.²⁵ Furthermore, Greek cardiologists believe that they can answer all their queries about coronary artery disease and cardiomyopathies using exclusively echocardiography, a cheap, widely available technique that is already in their hands. This widely accepted opinion in Greece (and in many other European countries) underestimates the lower image quality and the important inter-observer variability of echocardiography, especially in stress studies.

Regarding the examinations done before the CMR, all Greek patients had an echocardiogram and

almost half of them a cardiac catheterisation and a SPECT study. This is mainly due to the fact that, although Greek cardiologists are very familiar with echocardiography, they are completely “immune” to CMR, traditionally considered as a radiological field in Greece. Consequently, they refer to CMR only these cases in which the rest of the techniques were unable to give reliable results. The most interesting finding of our study was that, although CMR is the gold standard for viability,¹⁸ it was not considered as a reliable tool for the evaluation of myocardial scar by the majority of Greek cardiologists and its use was restricted to a very small percentage of cases, referred only by cardiac surgeons. In contrast, there is a rapid increase in the use of stress echocardiography, even though it presents a lot of reproducibility problems due to its flexibility, because it is performed and interpreted by well trained and experienced cardiologists. Additionally, the high percentage of SPECT and catheterisations in Greek patients, compared to the EuroCMR registry, contributed to an increase of 3-5 times in cost and of 2-3 times in radiation quantity for the evaluation of cardiac diseases in Greece.

The most striking finding was that in 65% of Greek CMR studies the initial diagnosis made by a non SCMR-trained person had no impact on the patient’s management and did not give clear diagnostic information to referral clinicians, discouraging them from referring patients for CMR again. It is obvious that a strong diagnostic technique like CMR can contribute more to confusion than to real solutions if it is used in the wrong way. Interestingly, after the re-evaluation performed by an SCMR-trained person, the CMR study was capable of satisfying all imaging needs in 83% of patients, so that no further non-invasive imaging procedure would be required after CMR, as has already been proved by the EuroCMR registry.¹⁸ Although many publications about CMR have appeared recently in this Journal,²⁵⁻²⁸ the lack of SCMR credentialing, the complete exclusion of cardiologists from the field in Greece, even if they are SCMR-trained, the lack of laboratory quality control, the inadequate training of both cardiologists and radiologists, and the lack of collaboration between the two specialties do not allow CMR to prove its real diagnostic capability.

The current study presents the following limitations.

- a) It was a retrospective analysis including patients evaluated over a long period of time, during which great progress was made in CMR technology

place; as a consequence the older data were of inferior quality compared to the more recent. Additionally, the grading of image quality was based rather on the ability of CMR to answer the clinical queries the scan was ordered for than on the quality of the images *per se*.

- b) The sample analysed presents the CMR experience of some distinguished cardiac centres in Athens, but not the CMR experience in the rest of the country. Additionally, it did not represent the results of a centre of excellence with the active participation of cardiologists and radiologists who are well trained in CMR, because at the moment there is no such centre in Greece. The old style Greek legislation, considering CMR as a technique exclusively performed and interpreted by radiologists, discourages cardiologists from improving their knowledge about CMR indications and performance.
- c) Despite the fact that the patients were included in the study according to the internationally accepted consensus appropriateness criteria for CMR,²⁹ the retrospective design of the study did not allow monitoring comparable to a prospective study.
- d) The current data were retrospective and did not include a head-to-head comparison of CMR with other imaging modalities with regard to diagnostic performance or prognostic implications.

In conclusion, the findings of the EuroCMR registry, based on the experience of some centres of excellence in Germany, other European countries and the USA, do not necessarily represent the reality in the rest of Europe, particularly countries like Greece, where the SCMR-guidelines for training are not applied and there is old legislation that is unable to satisfy the new scientific needs in the field. Serious and persistent efforts by both the European and Greek Societies of Cardiology and Radiology will be needed to reverse this situation and contribute to reliable CMR diagnosis and cost effectiveness over the whole spectrum of cardiovascular medicine.

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