Expert Review of Cardiovascular Therapy

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ierk20

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To cite this article: Katia Menacho Medina, Andreas Seraphim, Diana Katekaru, Amna Abdel-Gadir, Yuchi Han, Mark Westwood, J Malcolm Walker, James C Moon & Anna S Herrey (2021): Non-invasive Rapid Cardiac Magnetic Resonance for the Assessment of Cardiomyopathies in Low-Middle Income Countries, Expert Review of Cardiovascular Therapy, DOI: 10.1080/14779072.2021.1915130

To link to this article: https://doi.org/10.1080/14779072.2021.1915130

Accepted author version posted online: 09 Apr 2021.

Publisher: Taylor & Francis & Informa UK Limited, trading as Taylor & Francis Group

Journal: *Expert Review of Cardiovascular Therapy*

DOI: 10.1080/14779072.2021.1915130

Non-invasive Rapid Cardiac Magnetic Resonance for the Assessment of Cardiomyopathies in Low-Middle Income Countries

Katia Menacho Medina[1,2], Andreas Seraphim[1,2], Diana Katekaru[3], Amna Abdel-Gadir[1], Yuchi Han[4], Mark Westwood[2], J Malcolm Walker[1,5,6], James C Moon[1,2], Anna S Herrey[1,2]

[1]Institute of Cardiovascular Science, University College London, United Kingdom;
[2]Barts Heart Centre, Saint Bartholomew's Hospital, London, United Kingdom;
[3]Dos de Mayo Hospital, Lima, Peru,
[4] Departments of Medicine (Cardiovascular Division) and Radiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA,
[5]University College London Hospitals NHS Foundation Trust, London, United Kingdom;
[6]The Hatter Cardiovascular Institute, University College London Hospital, London, United Kingdom

Corresponding author:
Dr Anna Herrey
Barts Heart Centre, Saint Bartholomew's Hospital
London EC1A 7BE
E-mail: a.herrey@nhs.net
Phone number: +44 203 4656114
Fax: +44 203 465 7932

Abstract:

Introduction: Cardiac Magnetic Resonance (CMR) is a crucial diagnostic imaging test that redefines diagnosis and enables targeted therapies, but the access to CMR is limited in low-middle Income Countries (LMICs) even though cardiovascular disease is an emergent primary cause of mortality in LMICs. New abbreviated CMR protocols can be less expensive, faster, whilst maintaining accuracy, potentially leading to a higher utilization in LMICs.

Areas covered: This article will review cardiovascular disease in LMICs and the current role of CMR in cardiac diagnosis and enable targeted therapy, discussing the main obstacles to prevent the adoption of CMR in LMICs. We will then review the potential utility of abbreviated, cost-effective CMR protocols to improve cardiac diagnosis and care, the clinical indications of the exam, current evidence and future directions.

Expert opinion: Rapid CMR protocols, provided that they are utilized in potentially high yield cases, could reduce cost and increase effectiveness. The adoption of these protocols, their integration into care pathways, and prioritizing key treatable diagnoses can potentially improve patient care. Several LMIC countries are now pioneering these approaches and the application of rapid CMR protocols appears to have a bright future if delivered effectively.

Keywords: Cardiac MRI, abbreviated protocols, Low-Middle Income Countries, Cardiomyopathy.

Article Highlights:

- CMR is a key diagnostic imaging test, accepted by international guidelines, that can improve cardiac care for specific indications.

- Rapid CMR protocols could be based on the principle that critical information cannot be obtained by any other imaging modalities: cardiac function, scar assessment and cardiac iron quantification.
- The access of Cardiac Magnetic Resonance is still limited in Low-Middle Income Countries, with less data available on the current use of CMR in these countries.
- The adoption of abbreviated CMR protocols can potentially increase access of CMR in LMICs, potentially improving cardiac care.
- There are some pilot studies that have run abbreviated CMR protocols in single centers in LMICs. However, there is still much to do for improving the accessibility of CMR throughout the world.

1. Introduction

Non-communicable diseases are a major problem worldwide causing 73% of global deaths in 2017 (1). Within this, cardiovascular disease (CVD) is the leading cause of morbidity and mortality, with 17.8 million deaths in 2017 (2), and CVD has increased by 21% since 2007 in high-income countries. (2) However, it is not well publicised that 80% of CVD occur in low and middle-income countries (LMICs), representing 30% of global deaths. (3, 4) This is an economic burden, modelled to reduce gross domestic product (GDP) by up to 2% (5). The projected economic burden of CVD in LMICs countries is expected to be dramatic, encompassing significant costs on existing health care systems and budgets (6, 7). Scarce resources and limited health infrastructure compound this disproportionate CVD burden on LMICs. To treat established disease, resources are often unevenly distributed and frequently poorly targeted with suboptimal central distribution and few national guidelines. Disease prevention and cardiac health promotion are also low in LMICs (8) where geopolitical and socio-economic problems constitute a pivotal barrier to CVD control including insufficient investment in health promotion and disease prevention, unequal distribution, low health budgets, divided health care systems, and poor coordination. Unstable political environments and other vested interests such as food, alcohol, and tobacco industries, along with uneven population service delivery, compound the problem(8, 9).

2. Diagnostic Tests in Low-Middle Income Countries:

One key aspect of cardiovascular care is the availability of diagnostic testing. An accurate diagnosis is necessary for targeted, often life-preserving therapy. In general, for every US dollar spent on diagnosis, ten are spent on treatment. Some therapies available in LMICs (bypass surgery, stenting) are expensive and effective, but only if targeted to the right patients. Appropriateness of any diagnostic test depends on disease prevalence, pre-test probability, therapeutic options, and diagnostic test performance, availability, and cost, particularly incremental cost and cost-benefit for each care pathway. (10)

Resource constraints in LMIC limit the availability of some diagnostic tests, resulting in less accurate diagnoses and ineffective treatment, which may lead to increased cost to the individual and the society. Morbidity and mortality of heart failure, for example, can be reduced to half with relatively inexpensive medical therapy and prevention of recurrent hospital admissions, provided that it is diagnosed and treated early.

Echocardiography is the mainstay of cardiac diagnostic imaging. For a select number of pathologies, CMR can play a unique role by adding diagnostic accuracy safely without ionizing radiation, providing prognostic information, and guiding patient management (11-14). Change in therapeutic strategies following CMR can result in better outcomes for patients (15, 16). Example scenarios for CMR are listed in table 1.

3. Cardiac Magnetic Resonance in Low-middle Income Countries: Figure 1

Because of its cost, CMR to date is a modality frequently used in high-income countries (HICs), which is reflected in the origin of published evidence, expert consensus and standard protocols. CMR's unique contribution to tissue characterisation is the focus of most guidelines, consensus statements and publications, with additional applications constantly being added as the science progresses (17, 18).

In the HICs, easy access to CMR and rapid technical progress can lead to four critical problems identified by our group. These problems can be applied to a wide range of advanced imaging modalities, and should be avoided when trying to implement the use of these advanced imaging modalities in LMICs (19) – See Figure 1

(1) *Single modality overuse*: one service becoming locally dominant through internal resource competition exacerbating the imbalance (19).
(2) *Protocol complexity*: Because CMR can provide multiparametric imaging assessment (function, scar, perfusion, flow, mapping), scans gradually increase in length with reducing yield and increasing costs (19).
(3) *Multiple modality over-testing*: Multiple scans are requested concurrently – this can occur through referrer uncertainty, differential confidence in local services, access barriers, or disconnection within diagnostic imaging provision or follow-up structures. (19).
(4) *Short interval repeat testing*: maximum yield from a diagnostic testing is the initial assessment to secure the primary diagnosis. Subsequent interval scanning, particularly at a short time interval, is less cost-effective (19).

Although there are MRI units available in LMICs in rapidly increasing numbers (20), there is little access to CMR (21). A lack of local expertise and access to training, may result in inappropriate referrals, limited understanding of its usefulness and additional diagnostic value, and increased reluctance to use CMR. This pattern, together with long and therefore costly scan, is a major barrier to more widespread use of CMR in LMICs (22).

4. Improving the access to Cardiac Magnetic Resonance in Low-Middle Income Countries. See figure 1

Considering these obstacles in LMICs, the next step is to maximise cost-benefit and access to CMR in those countries. The approach displayed here may be of value in HICs also, with new centers starting their CMR service or facing increasing demand on scans:

1) *Focused CMR protocols – Rapid CMR*: Based on the principle that critical information cannot be obtained from any other imaging test:

a) Cardiac function (using cine images sequences), CMR is the gold standard exam for assessing cardiac volume, mass, and systolic function (18).
b) Scar imaging (using a standard late gadolinium enhancement technique - LGE). This type of sequence is available on most MRI scanners worldwide (11, 23).

c) Iron Quantification: CMR - T2* is the technique to assess cardiac iron levels. It is easy to standardize, highly reproducible, and guideline supported (24) (25) in high prevalence regions of iron overload cardiomyopathy.

2) *Assessment of cost-effectiveness:* A faster, less expensive, and easier protocol will lead to a cost-effective use of the modality.

3) *Explore new fields of research in LMICs:* Aiming to generate new scientific hypotheses, research, evidence, and global impact (8). CMR can be used to address specific research questions in LMICs, and explore opportunities that may not be available in HICs (26-28).

4) **Rapid CMR protocols: Clinical Practice Experience in Low-Middle Income Countries:**

CMR's core utility is the combination of cardiac function and tissue characterization with LGE. (29). These properties have led to the implementation of CMR in multiple international guidelines, providing vital diagnostic and prognostic information in multiple different pathologies and disease states (30, 31).

Examples of this unique application include differentiation of ischemic (32) and non-ischemic cardiomyopathies (33), such as hypertrophic cardiomyopathy (34, 35), infiltrative heart diseases (amyloid/Fabry disease/cardiac sarcoidosis/iron) (36-39), myocarditis (40), and other forms of inherited cardiomyopathies (41).

One of the critiques of CMR is the speed of acquisition. However, CMR can be performed faster. One approach is sequence development to speed up image acquisition. Examples include the use of parallel imaging (42), compressed sensing (43), and CMR multitasking (44). The main limitations of these techniques is the requirement of state-of-the-art scanner models and software, access to which may be limited in LMICs. Thus, these solutions are mainly being adopted in HICs (45).

Alternatively, imaging protocols can be shortened, aiming for an optimal balance between maximising diagnostic performance and limiting scan time. These abbreviated examinations have been piloted and implemented in LMICs and the initial data is promising for their clinical application.

(1) <u>Contrast Rapid CMR scan for the assessment of cardiomyopathies:</u>

Menacho and colleagues (46) designed a short CMR contrast protocol for the assessment of a wide-spectrum of cardiomyopathies in a 1.5T scanner, initially piloted in the United Kingdom and then performed in Lima – Peru. After a short

period of training and by deploying standard sequences (localisers, cine images and scar assessment with LGE) (47). The average scan time was 18 ± 7 minutes and the final cost assessment was $150 per scan. The investigators scanned nighty-eight patients in two centers, 25 patients per day, embedding their project within a local training and education program. The clinical impact of this was significant. In 19% cases a new diagnoses was reached and in 56% of cases the result of the CMR study had altered the clinical management when this was re-evaluated at 1-year of follow-up (Figure 2). Examples of clinical cases where the abbreviated protocol played an essential role in diagnosis and management are shown in Figure 3. Since the pilot study in Peru, in partnership with local and international scientific societies such as Society of Cardiovascular Magnetic Resonance (SCMR), the project has been extended to more centers in Peru (five public hospitals - three cities), one center in La Havana – Cuba, two centers in Buenos Aires - Argentina, one center in Cape Town-South Africa with a total 650 patients scanned using the rapid CMR protocol (48). International CMR guidelines have recently incorporated the contrast rapid CMR protocol, suggesting that the protocol minimizes exam times and maximizes cost-effectiveness (18).

(2) *Non-contrast Rapid CMR scan for the assessment of cardiac iron:*

Thalassemia is the most common monogenetic disorder worldwide, with 23,000 cases of B-thalassemia major in newborn infants annually (49). Unless regularly transfused, most patients do not survive beyond seven years of age. Although transfusion allows survival into teenage years, it leads to organ iron accumulation, and without chelation treatment, results in significant morbidity and mortality in early adulthood. However, chelation therapy is expensive and potentially toxic (25, 50). It is therefore crucial not only to assess the amount of myocardial and hepatic iron, but also to monitor treatment effectiveness. Serum ferritin assesses total body iron stores and continues to be used as a relatively cheap surrogate parameter to guide chelation therapy, however, correlation with myocardial iron concentration is limited. (51). The use of CMR-T2* measurement, on the other hand, has had a major impact on outcomes in patients with iron-overload cardiomyopathies. This has been reflected in guidelines, which have incorporated CMR as the gold standard test for

cardiac iron evaluation (18). CMR - T2* is easy to standardize, reproducible, and guideline supported (52). Only limited additional analysis is needed, either on the scanner or with several free tools available (53). If therapy is applied appropriately, guided by tissue iron using CMR, studies reported a >70% reduction in mortality can occur in Thalassemic patients (39). Unfortunately, LMICs underuse CMR in this context. Consequently, care is based on inadequate iron loading information and the use of expensive and scarce resources, including chelators and transfusion, based on less reliable clinical and laboratory measurements.

CMR cardiac T2* protocols can be highly abbreviated. Thalassemia "camps" can be set up with up to 50 patients scanned using a single magnet in one day, demonstrating that CMR T2* can permit a rapid assessment of cardiac and liver iron, making this technology more accessible to patients and cost saving to health care systems (54, 55). See table 2.

(3) Rapid CMR perfusion protocol for the assessment of Coronary Artery Disease:

Another major indication for CMR is the assessment of ischemic heart disease (IHD), both from a diagnostic point-of-view as well as for risk stratification. Recent multicenter trials in patients with stable coronary artery disease (CAD) have shown that CMR is superior, and it is cost-effective when compared to SPECT (56), with comparable accuracy to FFR (57). However, the main limitations of stress perfusion CMR are longer scan times (around 45-60 minutes), the requirement for advanced training for radiographers and the need for specialized equipment, usually expensive. Foley et al, however, have demonstrated that perfusion CMR can also be accelerated (58). The investigators scanned 18 patients with new chest pain and IHD, The average scan time was 17.2 ± 0.5 minutes. The authors reduced the scan time using the two following approaches: 1) speeding up the acquisition using novel CMR sequences such as 3D mDIXON LGE, and 2) by using only one IV cannula, acquiring only stress perfusion images, which is known to provide the highest diagnostic yield (18, 58, 59).

This study's results are encouraging, suggesting that ischaemia assessment by CMR may take as little as 20 minutes. Such an abbreviated protocol not only increases efficiency, but may also impact positively on the patient experience. However, the wider application of such protocols in LMICs is currently limited for a

number of reasons. Firstly, access to newer scanner models and software is required. Secondly, there is a need for specialised equipment and local expertise. In contrast, many LMICs continue to rely on alternative methods of ischaemia or coronary artery evaluation, which may be more easily accessible or cheaper or more familiar, or all of the above. Examples include exercise treadmill tests, scintigraphy, cardiac CT, or proceed straight to angiography. This reduces the likelihood of adoption of stress perfusion CMR into clinical practice in LMICs.

(4) Rapid CMR protocols for other indications:

Additional sequences in CMR, such as parametric mapping (60), velocity encoded flow, and angiography, are more complex with a higher training requirements for both scanning and reporting. These sequences may potentially reduce the incremental benefit of CMR if not selectively applied (19). However, parametric T1 mapping is particularly useful in diagnosing cardiac amyloidosis (high native T1) (61) and Anderson-Fabry disease (low native T1) (62) without the need for contrast. If a T1 mapping sequence is available and there is a high suspicion of either of these two pathologies, one or multiple T1 mapping slices can be acquired as part of the CMR protocol.

Cardio-oncology is another field, which could potentially benefit from rapid CMR protocols. There is an increasing awareness of the heart and circulation as potential targets for damage associated with cancer treatment, with cardio-toxicity often being the main determinant of treatment selection and patient outcome (63). In the future, CMR is likely to play an increasing important role in the early diagnosis of heart involvement, patient selection, and monitoring of cardio-protective strategies (64, 65). In the exceedingly busy schedule of current day oncology patients, the use of abbreviated CMR protocols is an attractive proposition and currently under active investigation (66). The COVID-19 pandemic has further increased resource constraints on healthcare systems worldwide, providing care to patients with and without COVID-19. In this context, diagnostics tests, including CMR, need to be adapted to allow for safe practices of urgent studies, especially where CMR may be used to detect cardiovascular involvement in patients with COVID-19 infection. Rapid CMR protocols, using standard sequences and tailored to clinical indications, are recommended by international guidelines (67, 68)

5) Recommended Rapid CMR Protocols in Low-Middle Income countries:

These protocols are for guidance only and can be adapted in accordance to scanner and software availability. Due to technical developments, the protocols below may change. See figure 4

GENERAL STRUCTURE OF THE PROTOCOL (46)

A. **Localizer**
B. **Anatomy:** A transverse bright blood single shot-fast spin-echo stack for anatomic evaluation (optional ungated)
C. **Pilots** 2 chamber, 5 slices short axis stack
D. **Volume and cardiac structure assessment - Longitudinal axis:** Four, two, three-chamber cine acquisitions) ± aortic valve (optional)* (19)

** This protocol can be used for Cardio-Oncology patients (± 1 mid-SAX T1 mapping/ T2w or T2 mapping if sequences are available) (65, 69).

RAPID CMR IRON OVERLOAD PROTOCOL: 8-12 minutes (54, 55) See figure 4

Follow steps A to D

E. **Volume and cardiac structure assessment - SAX cine stack** (8mm slice thickness, 2mm interslice gap) **– either optional or conditional – done if the 4 and 2chamber cine suggest impairment***
F. **Iron Assessment:** Cardiac (T2*) - 1 mid SAX slice, Liver(T2*) - 1 single slice. Move forward before volumes assessment in scenarios where imaging may stop early (19)

Tips and suggestions:

Acquisition and scanning: (18)

- T2* heart: Multiecho gradient echo with 6-9 echo times equally ranging from ~2ms to ~18ms – 1.5T (increment ~2ms). For liver: ~1ms, increment ~1ms, up to 12ms. A single mid-ventricular short-axis image is acquired

Optional: In patients with severe iron overload, a pulse sequence with shorter echo spacing could be helpful to accurately determine at ~1ms and extending to 1~2ms, with each echo iteratively spaced by ~1ms.

*For patients unable to cooperate with the necessary breath-hold, patients with arrhythmias and to speed-up the scan length, consider sequences included in Table 3, if available. To improve optamisation of workflow surrounding the abbreviated CMR protocol, see Table 4.

Post-processing and iron quantification analysis: (17)

- Complete analysis in the mid-ventricular septum.
- Consider including T1 mapping (single slice - mid SAX) for the heart if available (70)
- Be cautious in measuring the liver in particular if high iron levels are present and point truncation is needed (19, 24)

CONTRAST RAPID CMR CARDIOMYOPATHY PROTOCOL - 20 minutes (46, 47)

See figure 4

Follow steps A to D ± T2w / T2 mapping (if available) for specific indications (60)

- contrast injection by hand (dose 0.1mmol/kg) gadoterate meglumine/ gadobutrol

E. **Volume and cardiac structure assessment - SAX cine stack:** 8-mm slice thickness, 2 mm interslice gap)*

F. **Scar imaging:** repeating cine views as needed, followed by an optional sequence to determine the optimal inversion time and segmented k-space late gadolinium enhancement acquisitions in multiple planes with Phase Sensitive Inversion Recovery sequence (PSIR) and magnitude reconstructions (MAGIR)* (19)

Tips and suggestions: A low dose of contrast before cine imaging acquisition: The minimum dose of contrast suggested at 0.1mmol/kg: Endocardial definition is adequate after contrast performing accurate measurement if left ventricular mass and volumes. (47) Ventricular segmentation from base to apex in diastole.

*For poor breath-holders, patients with arrhythmia or to speed-up the scan length, consider sequences included in Table 3, if available (19). To improve optamisation of workflow surrounding the abbreviated CMR protocol, see Table 4.

CONTRAST RAPID CMR ISCHEMIC HEART DISEASE PROTOCOL (58) (17)

Follow steps A to D

F. **Stress perfusion:** 140 µg/kg/min (option to increase to 170 or 210 µg/kg/min in the absence of symptoms or adequate hemodynamic response). Stress agent. E.g.: Adenosine. Sequence: Typically, saturation-recovery imaging with bSSFP, gradient-echo (GRE) in 3 short-axis slices, slice thickness 8-10mm, in-plane resolution, <3mm, after IV bolus of contrast (dose 0.05mmol/kg) gadoterate meglumine/ gadobutrol) followed by 20ml saline flush (5ml/s) via injector pump.*

G. **A further contrast intravenous bolus** of 0.05 mmol/kg, followed immediately by optional early gadolinium enhancement imaging.

H. **Volume and cardiac structure assessment - SAX cine stack:** 8-mm slice thickness, 2 mm interslice gap)**

I. **Scar imaging:** repeating cine views as needed, followed by an optional sequence to determine the optimal inversion time and segmented k-space late gadolinium enhancement acquisitions in multiple planes with PSIR and MAGIR (19)

* Continuously monitoring the heart rate and blood pressure of the patient using MR conditional monitors.

Tips and suggestions:

- Stress and safety equipment in place: monitoring equipment (blood pressure, ECG and intercom to communicate with the patient) with emergency resuscitation policy in place and crash cart appropriately prepared; regular practice runs.
- LV function performed immediately after GBCA infusion may reduce the contrast of the blood-endocardium interface.

**For patients less able to hold their breath, patients with arrhythmia or to speed-up the scan length, consider sequences included in Table 3, if available.

- Post-processing software required for analysis and interpretation (17, 19)

Conclusion: There is a high and increasing burden of CVD in LMICs, currently the leading cause of mortality and morbidity. A key aspect of cardiovascular care is the appropriate use of diagnostic testing. CMR is an established advanced imaging

technology for the anatomical, functional, and tissue characterization of a wide range of cardiac pathologies. There are specific indications where CMR adds incremental diagnostic value, which no other imaging technique can provide. Rapid CMR protocols propose to be faster, cheaper, and easier while allowing for accurate diagnosis in specific cardiovascular pathologies, with most of the scans acquired in less than 20 minutes. The abbreviated protocols may be the key to more widespread implementation of CMR in LMICs and worldwide, leading to better patient care. Ongoing evaluation of this proof-of-principle is required to make the wider adoption of CMR a reality.

Expert Opinion:

LMICs carry a high burden of cardiovascular disease globally at a significant individual and societal cost. The lack of access to good healthcare, which includes appropriate diagnostic tests to establish the correct diagnosis and access to the right treatment, remains a major barrier. Low healthcare budgets in LMICs, divided and poorly coordinated health care systems, unstable political environments, ill-targeted healthcare policies, and lack of training and education to healthcare providers further contribute to the problem.

Echocardiography is the first-line imaging technique that is portable, cost-effective, and widely recommended in international guidelines. In some instances, however, echocardiography may not be sufficient to establish the correct diagnosis, confirm early disease involvement, or to assess reversibility and treatment progress.

CMR is a crucial diagnostic imaging test, which can improve cardiac care if applied to the right patient cohorts, and is therefore recommended in a number of international guidelines. CMR is very well adapted and widely in HICs, but its adoption remains limited in LMICs. CMR is commonly considered an expensive, complicated and slow test, and in some cases where understanding of the technique is limited, may not add to the diagnostic armamentarium.

The core utility of CMR is the combination of cardiac functional assessment and tissue characterization (scar/fibrosis/iron). Based on this principle, implementation of abbreviated protocols can potentially increase access as well as acceptance of CMR in LMICS, thereby making this technology available to patients whose treatment may be altered as a consequence. Furthermore, the post-processing imaging analysis of the rapid CMR sequences are mainly focused on the assessemtent of

coventional volumes, mass and quantification of ejection fraction, as well as the qualitative assessment of presence of scar and distribution, and cardiac iron quantification with T2*. Most of the commercial post-processing protocols have these options of analysis.

More advanced parameters of measuring cardiac function can be obtained from the standard rapid CMR protocol, such as Feature Tracking with Global Longitudinal Strain (GLS), which is a fast and robust technique, carrying important clinical information in many circumstances(71), but requires additional software.

There is also a potential utility of automated machine learning post-processing analysis for a faster analysis with similar precision to expert human analysis,, which can aid especially where local expertise may be missing (72).

Pilot studies in the field have shown that abbreviated protocols can be implemented in a single center and improve patient care. Three primary principles are important: 1) A partnership program including stakeholders at a healthcare system level with national/international expert support, 2) A continuous program of education and training for local imagers/referrers to deliver the technology and to use CMR only when indicated and 3) an abbreviated protocol, focusing on the essential strategy of rapid CMR – faster, easier, and cheaper.

A correct diagnosis is only the first step towards better patient outcomes, and whether access to crucial diagnostics such as CMR will result in better targeted or improved treatment, and ultimately a reduction of morbidity and mortality in LMICs, remains to be seen.

Funding:

KM is funded by The Peruvian Scientific, Technological Development and Technological Innovation (FONDECYT) and Global Engagement Office, University College London. JMW receives support from the National Institute for Health Research University College London Hospitals Biomedical Research Centre and UCLH Charity - Greenbaum/ McClean Legacy.

Declaration of interest:

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject

matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.□

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Figures

Figure 1: Barriers and Potential Strategies for Improving the Access of Advanced Cardiac Magnetic Resonance in Low-Middle Income Countries HICs: High-income countries, CMR: Cardiac Magnetic Resonance, LGE: Late gadolinium enhancement, MRI: Magnetic Resonance Imaging, LMICs: Low-Middle Income Countries.

Figure 2: Contrast-abbreviated Cardiac Magnetic Resonance (CMR) protocol to evaluate cardiomyopathies in an Upper-Middle-Income country, Peru. The project implemented a $150 – 18-minute protocol in 2 centers in Lima, following the participants to assess clinical impact in diagnosis and management. Images reprinted with permission of the authors (48).

Figure 3: Three clinical scenarios where the Use of the Rapid CMR protocol impacted patients' diagnosis and change of treatment. Note that the length of the scans was below 20 minutes. Images reprinted with permission of the authors. CMR: Cardiac Magnetic Resonance, HCM Hypertrophic cardiomyopathy, DCM: Dilated cardiomyopathy. Images reprinted with permission of the authors (48).

Figure 4: Rapid CMR Protocols: All protocols start with localizer sequences and longitudinal axis volume cine ± aortic valve cine, followed by 1) ***Cardiomyopathy Contrast Protocol*** – SAX cine volume cine and late gadolinium enhancement sequences. The average length of the scan: 20 minutes, 2)*T2** ***Non-Contrast Protocol*** – T2* for cardiac and liver iron ± SAX cine sequences. Average length scan 11 minutes.

Tables:

Clinical Indications for Rapid Cardiac Magnetic Resonance	
Clinical Scenarios	Examples
Myocardial infarction with nonobstructive coronary arteries (MINOCA)	Acute myocarditis Takotsubo cardiomyopathy
Uncommon diseases/scenarios	Iron cardiac overload Multisystem diseases (cardiac amyloidosis, Fabry)
Where "normal" is not known:	Abnormal anatomy (pectus excavatum) Athletic training Dual pathology
Where other tests don't work	The apex in apical HCM Poor acoustic windows
High pre-test probability without a diagnosis	Familial disease: normal echocardiogram, ECG abnormal
To target expensive, complex interventions	Three-vessel disease with poor left ventricle function, ICD decisions Combination chelation regimes for iron overload
Has there been an infarct ever?	Assess myocardial viability
Critical Scenarios where Rapid Cardiac Magnetic Resonance not indicated	
Screening and low pre-test probability	
Untreatable disease	
Where results will not change care	
When therapy is not available (e.g., ICD is unaffordable for a patient)	

	Rapid Cardiac MRI protocols to assess Cardiac and Liver Iron Overload	
Where other te		
To avoid a decision		
Lead	Abdel-Gadir et al. (54)	Fernandes et al. (55)
Serial scanning at an inappropriately short interval		
Researcher		

Table 1: Main clinical indications for a Rapid Cardiac Magnetic Resonance protocol. Reprinted from Rapid Cardiac MRI protocols Feasibility and Potential Applications by Menacho Ket al.l Curr Radiol Rep (2020) 8:2 (19)

Country	Thailand (one center)	India (7 centers)
Sequences included in the protocol	Pilot localizers T1 mapping - mid short axis T2* mapping – mid short axis Transverse dark blood single shot fast spin echo stack for anatomic evaluation Cine function: Longitudinal axis cine	Orthogonal Localizer (30 seconds) 2CH Localizer (15 seconds) T2* mapping heart (1 minute) T1 mapping heart (1 minute) Liver T1 (1 minute) Liver T2* (1 minute) Compressed sensing cine (15 seconds – optional)
Length of Scan	8.3 ± 2.4minutes	5.2 minutes (4 – 7 min) 7.5±1.8min (with cine)
Number of participants	97	179
Comparison of automated vs. manual analysis	Automated Analyses only	-1.2ms (95% CI -1.7 to -0.8ms)
Cardiac iron by T2* <20ms (participant %)	15 (15.5)	Not available
Impact on management	Not available	Not available

Table 2: Two Rapid CMR protocols (T2*) for quantification of cardiac and liver iron, implemented in two low-middle income countries (54, 55). The length of the scans was less than 10 minutes. The table was reprinted with the permission of the authors.

A) Imaging Poor Breath – Holders - Cine Sequences (73)	
Acceleration Technique (74)	**Comment**
Reduce the number of phases for each breath-hold: - By reducing the acquisition matrix - By reducing the field of view (FOV)	Reduces Signal-noise ratio (SNR) Increases spatial resolution
Increase voxel size	Decrease spatial resolution
Use parallel imaging	Prone to artifact
Acquire imaging in inspiration	Varying slice position with each breath-hold
Compressed sensing (43)	Improves spatial resolution but requires advanced software and the latest model scanner
CMR Multitasking	Enables acquisition of data without ECG or breath-hold but requires advanced software
B) Imaging Patients with arrhythmia – Cine Sequences	
Heart rate and rhythm control before scanning	Use beta-blockers or other antiarrhythmic medication
Use Prospective triggering (44)	Reduces SNR
Use Real-time imaging	Reduces temporal, spatial resolution and SNR
C) Imaging Poor Breath-Holders and patients with arrhythmia – Late Gadolinium Enhancement	
Single-shot Inversion Recovery (IR) (75)	A single breath-hold. Moderately lower contrast-to-noise ratio (CNR), allowing fast and accurate determination of scar with a high spatial resolution
Single breath-hold 3D mDIXON LGE (76)	Cover the whole LV in a single breath-hold with comparable image quality to 2D LGE. It requires an

	advanced software package.

Table 3: Modification Rapid CMR sequences Protocol for poor breath-holders, patients with arrhythmia, and to speed-up CMR scan. Reprinted from Rapid Cardiac MRI protocols Feasibility and Potential Applications by Menacho K et al.l Curr Radiol Rep (2020) 8:2 (19)

	Optimisation of workflow surrounding the abbreviated CMR protocol – Rapid CMR

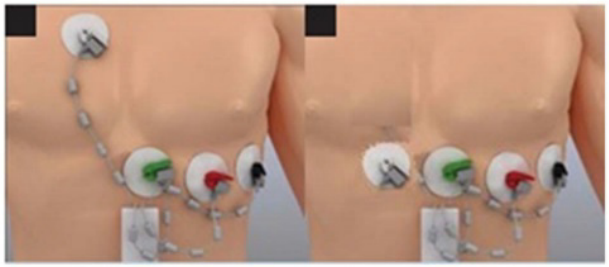
Pre-Scanning Preparation	On arrival, patient changes into hospital gown, open to the front, and hospital trousers as appropriate
	Record patient height and weight on a form (e.g. safety questionnaire)
	Trained staff to check safety questionnaire and address any concerns
	Trained staff to cannulate for gadolinium injection
	Ensure ECG leads are placed in an 'L' or box position, achieving a minimum of 3/5 bars for a reliable ECG trace 
	Practice breath holding commands with the patient (images usually acquired in with few exceptions)
During the Scanning	Ensure the protocol is set it up on the scanner in advance, with patient details including height and weight
	Have gadolinium contrast prepared for manual injection, suggested dose is 0.1mmol/kg ref (single dose of 0.1mL/kg for gadobutrol and 0.2mL/kg for gadoterate meglumine)
After the CMR Scan	Have at least two trained staff ready to aid the patient out of the scanner
	Verify ECG stickers and cannula have been removed from the patient in the preparation room.

Table 4: Tips for improvement of workflow surrounding the Abbreviated CMR Protocol. For CMR scan workflow and adjustment for COVID-19 scans see reference (68)

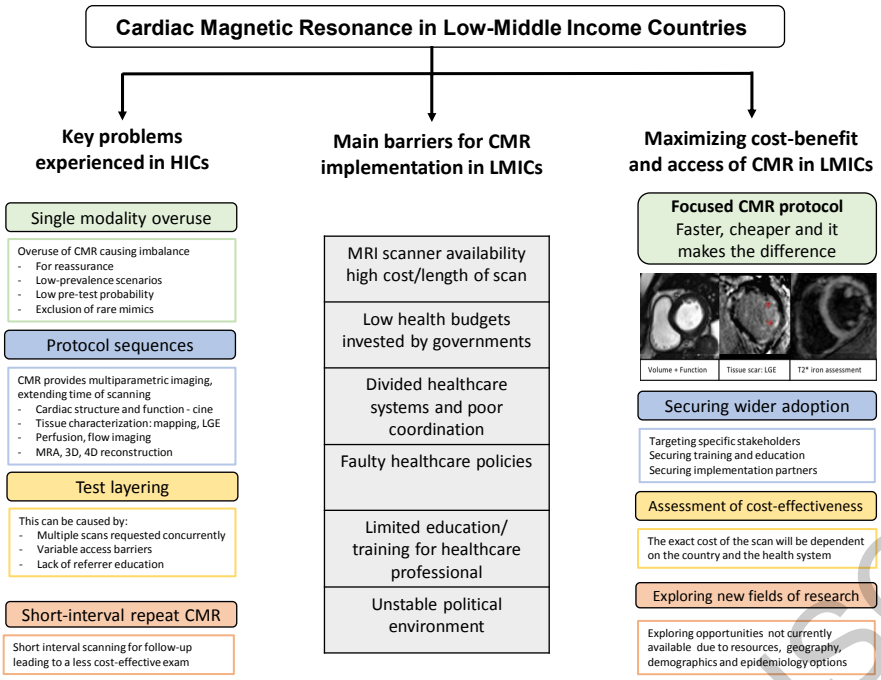


fig 1

Fig 2

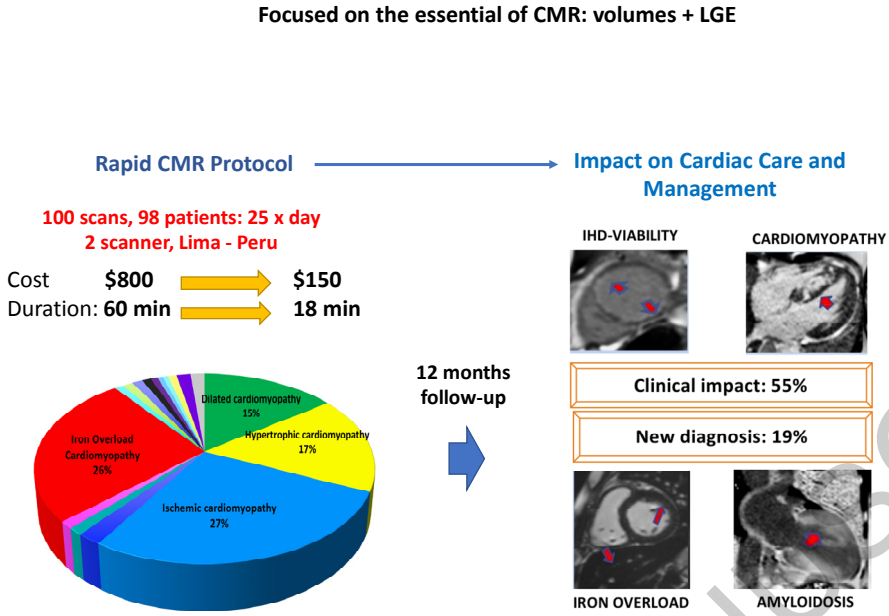


Fig 3

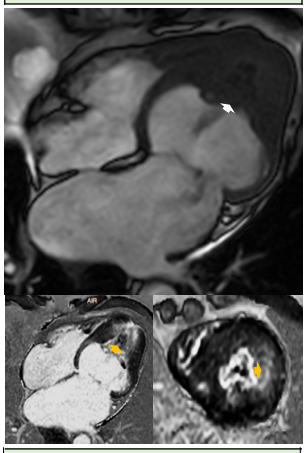
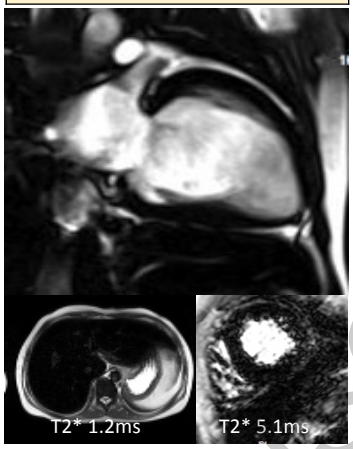
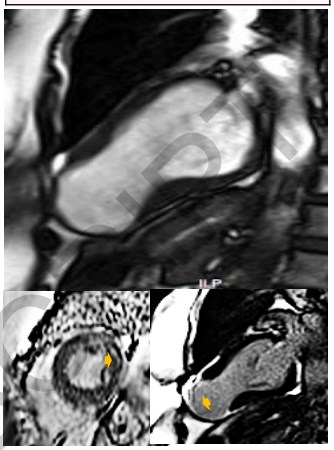
Length of scan	**20 min scan**	**11 min scan**	**19 min scan**
Pre rapid- CMR indication	69 year old lady, apical HCM	29 year old lady, Beta-thalassaemia	76 year old lady, non-ischaemic DCM
Rapid CMR scan findings			
Post rapid-CMR results	Endomyocardial fibrosis + thrombus and calcification. Patient died 3 months later	Severe cardiac and liver iron overload and dysfunction. Dual chelation therapy started	Chagas cardiomyopathy (positive by serological assessment) Patient underwent ICD, medical treatment

Fig 4