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ORIGINAL ARTICLE

Use of rapid cardiac magnetic resonance imaging to guide chelation therapy in patients with transfusion-dependent thalassaemia in India: UMIMI study

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Aims To explore the impact of incorporating a faster cardiac magnetic resonance (CMR) imaging protocol in a low–middle-income country (LMIC) and using the result to guide chelation in transfusion-dependent patients.

Methods and results A prospective UK–India collaborative cohort study was conducted in two cities in India. Two visits 13 months apart included clinical assessment and chelation therapy recommendations based on rapid CMR results. Participants were recruited by the local patient advocate charity, who organized the patient medical camps. The average scanning time was 11.3 ± 2.5 min at the baseline and 9.8 ± 2.4 min ($P < 0.001$) at follow-up. The baseline visit was attended by 103 patients (mean age 25 years) and 83% attended the second assessment. At baseline, 29% had a cardiac T_2^* < 20 ms, which represents significant iron loading, and 12% had left ventricular ejection fraction <60%, the accepted lower limit in this population. Only 3% were free of liver iron ($T_2^* \geq 17$ ms). At 13 months, more patients were taking intensified dual chelation therapy (43% vs. 55%, $P = 0.002$). In those with cardiac siderosis (baseline $T_2^* < 20$ ms), there was an improvement in T_2^*—10.9 ± 5.9 to 13.5 ± 8.7 ms, $P = 0.005$—and fewer were classified as having clinically important cardiac iron loading ($T_2^* < 20$ ms, 24% vs. 16%, $P < 0.001$). This is the first illustration in an LMIC that incorporating CMR results into patient management plans can improve cardiac iron loading.

Conclusion For thalassaemia patients in an LMIC, a simplified CMR protocol linked to therapeutic recommendation via the patient camp model led to enhanced chelation therapy and a reduction in cardiac iron in 1 year.

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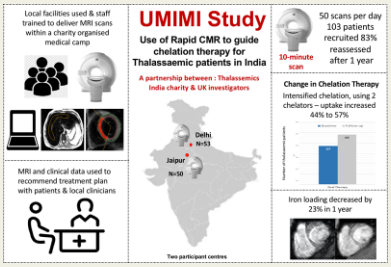
Graphical Abstract Graphical representation of the study, illustrating the design, implementation and the summarised findings.



Keywords Cardiac magnetic resonance • Myocardial iron overload • Thalassaemia • Low–middle-income country • India

Introduction

In India, there are over 100 000 thalassaemia patients and 17 000 homozygous births annually.[1] Thalassaemia care has been designated to be of national strategic importance in India, but there are still many areas of concern, including access to diagnostics and appropriate use of chelation therapy.[2] Transfusion allows survival,[3] but it leads to iron accumulation and without effective chelation treatment there is a high risk of iron toxicity.[4] Transfusions in India have been available in an organized fashion for over 20 years[5,6] and all three chelators [deferoxamine (DFO); deferiprone (DFP); and deferasirox (DFX)] are available.[7] Successful chelation can be difficult to achieve in practice and effective clinical care requires targeting therapy to those individuals most at risk.[8,9] Current practice in India relies on serum ferritin (SF) concentrations to identify iron loading; however, the correlation of SF with myocardial iron is variable[10] and over-reliance on SF is suboptimal.[9] Cardiac magnetic resonance (CMR) is the accepted standard for detection and management of iron loading,[11,12] but training and standardization are needed.[13] When therapy is guided by CMR T_2^*, a >70% reduction in mortality has been reported[14] and this CMR-guided approach is routinely available in high-income countries (HICs),[3] but has been underused in low–middle-income countries (LMICs), including India, despite magnetic resonance imaging (MRI) scanners being widely available.[15] Obstacles to uptake include lengthy scan times, high costs, a lack of training and standardization, as well as poor integration of results into care pathways due to a lack of appreciation of the potential to reduce mortality.[16]

Thalassaemia 'medical camps', where patients from local and distant centres gather over a number of days for a concentrated effort of clinical assessment, often with experts gathered together from abroad, have been employed in India for many years[6] and the UK investigators (J.M.W., E.A., A.A.-G., and J.K.W.) have been contributors to these camps, some for more than two decades. However, this is the first time CMR scanning has been integrated into the assessments, driven by an appreciation of the historical inadequacy of clinical data available for decision-making for attendees at the camps. Previously, the feasibility of rapid CMR (rCMR) in LMICs has been demonstrated using existing equipment, by undertaking up to 50 CMR scans per day.[17–19] Here, we exploit that experience in a study that brought together local patient advocates (the patient and family charity Thalassemics India (TI); https://www.thalassemicsindia.org) and local haematology leadership, supported by expertise from the UK, at two sites over two days. We assessed a care model adapted to local circumstances, which would be applicable to many LMICs. This incorporated rCMR, immediate reporting, and a clinical review, with treatment recommendations based on published international guidelines.

We tested success by evidence of reduced cardiac iron, a process likely to be associated with improved outcomes, and changes in reported chelation usage.

Methods

Ethics

Ethical approval was obtained from three sites, in the UK: University College London (UCL REC project ID/title: 11255/001); in India: Institutional Ethics Committee—Clinical Studies, New Delhi (reg. ECR/5/Inst/DL/2013/RR-16) and Jaipur (N–IEC/2019/01). All subjects had been referred for a clinical CMR by their haematologists. A team of six from the UK travelled to India for each visit to train/partner with local personnel, help undertake assessments, and support CRM scanning, which was also assisted by staff from the All India Institute of Medical Science (AIIMs), New Delhi.

Patients

Thalassaemic patients, aged over 16 and known to TI through their regular programme of patient medical camps,[6] were invited to attend an assessment, which was to include an MRI scan. They were sent a patient information leaflet, translated from an original approved by the ethical committees. The sample size was pragmatic, based on our previous experience and availability of local MRI scanner time (one working day per centre: 25 patients per half-day session). The follow-up visit was 13 months later, in January 2020.

Study implementation

All participants provided written consent to participation in the study (see Supplementary material online, *Figure S1*). Patients were requested to bring their medical records to the camp.

Demographic data, previous clinical care, and medical assessments were undertaken by the local haematologists with the support of the

UK visiting doctors (J.M.W. and E.A.) and detailed clinical data in six domains were recorded using a browser-based software (REDCap—Research Electronic Data Capture).[20] The transfusion regimes for patients were assessed by history, and an estimate of the iron loading rate was calculated on the reported number and frequency of transfusions assuming a uniform red blood cell content (RBC) of the transfused units, {[(units of blood per year) × 200]/(weight)/365}.[21]

All patients underwent an electrocardiogram (ECG) (CardioSecur-Pro, Personal MedSystems GmbH, Frankfurt, Germany) and an abbreviated CMR scan. The cardiac and liver T_2^* values, as well as cardiac function [left ventricular ejection fraction (LVEF)], were available for the clinical review. All patients received a written record of their results and the recommendations for treatment. Three chelation therapy options (DFX, DFP, and DFO) were recommended to patients, following internationally agreed standards of care[9]—(1) ejection fraction >60%, cardiac T_2^* >20 ms (no cardiac iron): no change in treatment; (2) ejection fraction >60%, T_2^* 10–20 ms (moderate/mild cardiac iron overload): increase doses of current drug or change chelator(s) to improve adherence; (3) ejection fraction <60% or T_2^* <10 ms (severe cardiac iron overload), or liver T_2^* <2.0 ms (severe liver iron overload): recommend combination therapy at guideline-recommended doses, the precise combinations to be determined by the patient's haematologist (see *Figure 1*).

All the patients who attended the first clinic were invited to attend for review, where assessments were repeated. Non-attendees were contacted by telephone. Each attendee received an updated report (see *Figure 1*).

Abbreviated rapid cardiac magnetic resonance protocol (see Supplementary material online, *Figure S2*)

The protocol (cardiac volumes, function, and cardiac/liver iron assessment) was imported and archived in each 1.5 T MRI scanner under the supervision of the physicist (R.B.)—centre 1: GE Healthcare Signa HDxt; centre 2: Siemens Avanto Syngo MR B17. The protocol included

A. a pilot three-place localizer.
B. pilots: two chambers, five-slice short-axis stack.
C. anatomy: a transverse bright blood single-shot fast spin-echo stack for anatomic evaluation (optional ungated).
D. volume and cardiac structure assessment: four, two, three chambers and short-axis cine acquisitions. Short-axis cine stack (7 mm slice thickness, 3 mm interslice gap).
E. iron assessment: cardiac (T_2^*)—one mid-short-axis slice; liver (T_2^*)—one single slice.[11]
   i. T_2^*: heart—single breathold, gradient-echo, multiecho scan with a series of eight echo times equally ranging from 3 to 18 ms at 1.5 T (with each echo iteratively spaced by 1.5–2 ms).[11,22]
   ii. T_2^* liver: a non-ECG-gated image was acquired in the axial orientation through the mid-portion of the liver (a gradient-echo, multiecho scan starting at 0.8–1.3 ms up to 12 ms, with each echo iteratively spaced by 0.8–1 ms).

An expert radiographer (L.M.) oversaw scanning, supported by local radiographers, who were trained to acquire images. Scan time was defined from the time stamp of the first image to the last image acquired.

Rapid cardiac magnetic resonance analysis (see Supplementary material online, *Figure S2*)

Images were analysed using cvi42 (version 5·11·4–1559, Circle Cardiovascular Imaging Inc., Calgary, Canada).

Cardiac function and volume. End diastolic (ED) and end systolic (ES) phases were defined as the largest and smallest long-axis ventricular volumes visually at mid-ventricular level. Contiguous short-axis slices were segmented using a semi-automated thresholding technique in ED (endocardium first and then epicardium) and ES (endocardium) to derive left ventricle (LV) end diastolic volume (EDV), end systolic volume (ESV), stroke volume (SV), ejection fraction (EF), and LV mass, with allometric scaling using body surface area. To address basal slice variability, blood volume was included if there was over 50% of LV myocardium surrounding blood pool, and a long-axis atrioventricular plane correction was used. The left ventricular outflow tract was included in the blood volume and LV papillary muscles were included as part of LV mass and excluded from the volume.[11]

T_2^* CMR post-procession analysis. The post-processing CMR analysis was restricted to the septum, drawing a full-thickness region of interest (ROI) by limiting the epicardial and endocardial border. Liver T_2^* analysis was restricted to a liver parenchymal area, drawing a full-thickness ROI and avoiding the inclusion of blood vessels. A truncation method was applied to calculate iron values and discard the late 'plateau' points and fit each curve to a monoexponential equation.[23] Anonymized scans were reported immediately after acquisition, with reports completed by two level 3 CMR European Association of Cardiovascular Imaging (EACVI)–European Society of Cardiology (ESC) trained doctors with at least 4 years of experience in reporting CMR (K.M.M. and J.B.A). Reports were made blind to the patient's clinical status. The imaging reports were translated appropriately and incorporated into the medical records, by study administrators (T.S. and J.K.W.).

Statistical analysis

Data were analysed using SPSS (version 24·0, Statistical Package for the Social Sciences, International Business Machines, Inc., Armonk, NY, USA). Continuous data were expressed in mean with standard deviation and categorical data presented as absolute numbers and percentages. Normal distribution was formally tested using the Shapiro–Wilk test. Comparisons of baseline and follow-up cardiac function and iron parameters were only analysed in the participants who completed the study; for this cohort, continuous data were compared using two-sided Student's *t*-tests and categorical variables were compared using the χ^2 test or Fisher's exact test as appropriate. Statistical significance was defined as a two-sided p value < 0·05.

Results

Characterization of the study population

One hundred and three patients attended the baseline assessment, 53 at centre 1 and 50 at centre 2 (*Table 1*). The average age was 25 years (15–46 years), 52% being male; 28% of patients had had a splenectomy. The prevalence of reported diabetes was 8% and thyroid disease 13%. The average blood pressure was 116 ± 11.7/79 ± 9.5 mmHg, heart rate 88 ± 12.7 b.p.m., with normal ECGs in 60%, borderline changes of uncertain clinical significance in 33%, and abnormalities in five patients (4.8%). These abnormalities were QTc interval >440 ms in three male patients, nodal rhythm in one patient, and right bundle branch block (RBBB) with QRS duration (QRSd) >120 ms in one patient. No patients were in atrial fibrillation. History of heart failure was reported by 9.7% of the participants and other cardiac morbidity by 6.7%. Seventy six per cent of the patients

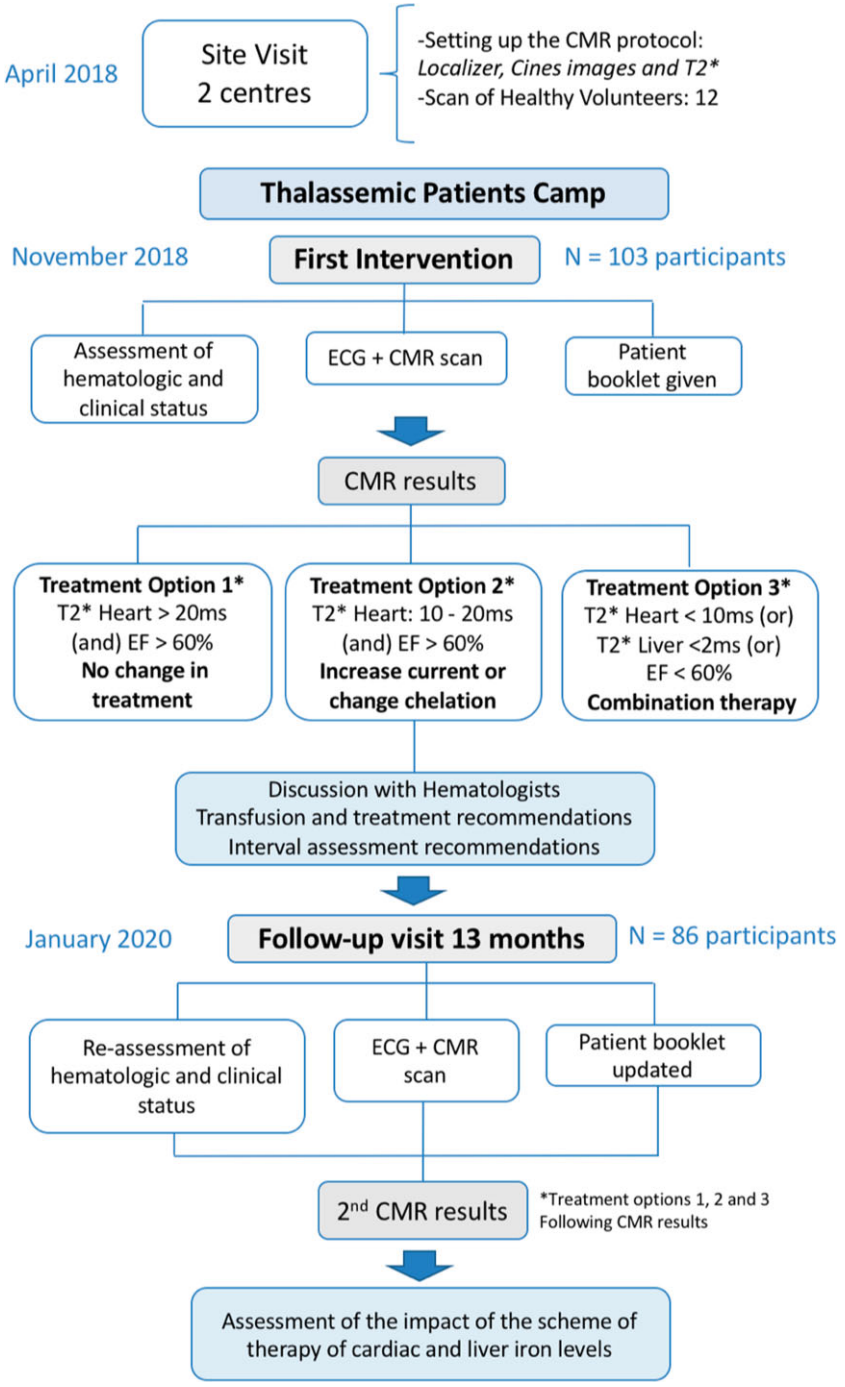


Figure 1 The time line and patient pathway for subjects in the UMIMI study.

reported having had a previous MRI scan (87% centre 1 vs. 60% centre 2; $P = 0.002$); however, scan results were available for only seven participants (7%), despite 95% having their detailed medical records at the review. The median baseline ferritin level was 1750 mcg/L (IQR 1859 mcg/L). All the patients were receiving chelation therapy and the average doses being taken are shown in *Table 1*. The proportion of patients taking DFX monotherapy was higher in the centre 1 cohort (45% vs. 12%, $P = 0.001$). Combination therapy, using two chelators, was similar in both centres (DFO + DFP: 6% vs. 10%, P = NS; DFO + DFX: 19% vs. 18%, P = NS; DFP + DFX: 19% vs. 23%, P = NS). Iron loading rate was within the internationally recommended average 0.3–0.5 mg/kg/day: 0.43 ± 0.1 mg/kg/day in centre 1 vs. 0.34 ± 0.1 mg/kg/day in centre 2.

Cardiac magnetic resonance results

All attendees were scanned without complication at both sites and both visits.

Table 1 Demographic, clinical, and cardiac magnetic resonance data—UMIMI study Baseline first visit data

Clinical Data	Total	Centre 1	Centre 2	*P*-value
Demographic				
Total (%)	103 (100%)	53 (52%)	50 (48%)	
Age (mean ± SD)	25 ± 7	26.7 ± 6.7	23.2 ± 7	0.013
Gender male (%)	54 (52%)	30 (57%)	24 (48%)	NS
BSA (m^2) (mean ± SD)	1.49 ± 0.2	1.55 ± 0.21	1.42 ± 0.2	0.0006
Thalassaemic details				
Ferritin level (ng/dl) median ± IQR	1750 ± 1859	1846 ± 2431	1700 ± 2241	NS
Diabetes, *n* (%)	8 (8%)	7 (13%)	1 (2%)	0.034
Thyroid, *n* (%)	13 (13%)	11 (20%)	2 (4%)	0.01
Normal ECG (%)	62 (60%)	33 (62%)	29 (58%)	NS
Previous cardiac MRI (%)		6 (11%)	1 (2%)	0.001
Iron loading rate mg/kg/day (mean ± SD)[a]	0.38 ± 0.1	0.43 ± 0.1	0.34 ± 0.1	0.0002
Chelation therapy				
Desferrioxamine (DFO) *n* (%) Mean dose (32 ± 13 mg/kg/day)	3 (3%)	1 (2%)	2 (4%)	NS
Deferipone (DFP) *n* (%) Mean dose (70 ± 25 mg/kg/day)	22 (21%)	6 (10%)	16 (33%)	0.001
Deferasirox (DFX) *n* (%) Mean dose (33 ± 9.5 mg/kg/day)	30 (29%)	24 (45%)	6 (12%)	0.001
Combined (DFO + DFP) *n* (%)	8 (8%)	3 (6%)	5 (10%)	NS
Combined (DFO+ DFX) *n* (%)	19 (19%)	10 (19%)	9 (18%)	NS
Combined (DFP+DFX) *n* (%)	21 (21%)	10 (19%)	11 (23%)	NS

SD, standard deviation; ECG, electrocardiogram; MRI, magnetic resonance imaging; BSA, body surface area; NS, non significant; IQR, interquartile range.
[a] Iron loading rate estimate: {[(units of blood per year) × 200]/(weight)/365}.

Table 2 Baseline cardiac iron and cardiac structure and function results

CMR variable	All patients	Centre 1	Centre 2	*P*-value
Total (%)	103 (100%)	53 (52%)	50 (48%)	
Time of scanning (min) (mean ± SD)	11.3 ± 2.5	13.2 ± 4.2	10.6 ± 2.4	<0.052
Heart T_2^* (ms) (mean ± SD)	29.1 ± 11.9	29.5 ± 12.1	30.8 ± 11.6	0.12
Heart T_2^* <20 ms, *N* (%)	30 (29%)	21 (40%)	9 (18%)	<0.02
Heart T_2^* <10 ms, *N* (%)	13 (6%)	8 (15%)	5 (10%)	<0.019
Liver T_2^* (ms) (mean ± SD)	4.8 ± 4.2	4.9 ± 4.2	4.7 ± 5.5	0.84
LVEF (%) (mean ± SD)	65 ± 4.8	65.9 ± 5	66.9 ± 4.9	0.23
RVEF (%) (mean ± SD)	67.1 ± 6.1	66.7 ± 6.9	67.6 ± 5.8	0.051

CMR, cardiac magnetic resonance; SD, standard deviation; LVEF, left ventricular ejection fraction; RVEF, right ventricular ejection fraction.

The average scanning time was 11.3 ± 2.5 min at the baseline and 9.8 ± 2.4 min ($P < 0{\cdot}001$) at follow-up. Extracardiac findings were common (29%) and included: small pericardial effusions in 10% of the participants. Within the group of patients with a spleen, 77% had splenomegaly. Extramedullary haematopoiesis (e.g. paravertebral, retrosternal, and rib expansion location) was found in 13% of the patients. Other incidental findings were cirrhotic fibrotic liver in one patient (already known), remnant spleen in two patients, and kidney cysts in two patients.

Baseline T_2^* CMR analysis was completed in 103 patients; overall cardiac T_2^* value was 29.2 ± 11.9 ms, with a mean LVEF of 64.5 ± 5.7%. At the first visit, 30 patients (29%) had cardiac T_2^* <20 ms; 13 patients (6%) had severe cardiac iron ($T_2^* < 10$ ms), and 12 patients (12%) had an LVEF <60%. Seven patients (6%) had cardiac T_2^* <20 ms plus an LVEF <60%. Between the two participant centres, the prevalence of cardiac T_2^* values <20 ms was 21 (40%) in centre 1 vs. 9 (18%) in centre 2, $P < 0.02$. Data are summarized in *Table 2*.

The mean liver T_2^* was 4.8 ± 4.2 ms; 48% had severe liver iron overload ($T_2^* < 2.2$ ms) and only three patients had no liver iron ($T_2^* > 17$ ms), with no differences between centres. Twelve healthy volunteers were scanned (six in each participant centre): overall cardiac T_2^* was 37.5 ± 3.5 ms (37.4 ± 3.2 ms for centre 1 vs. 38 ± 4.6 ms for centre 2; $P = 0.7$) and LVEF of 66.6 ± 5.9% (66.4 ± 4.5% for centre 1 vs. 66.9 ± 5.8% for centre 2, $P = 0.1$).

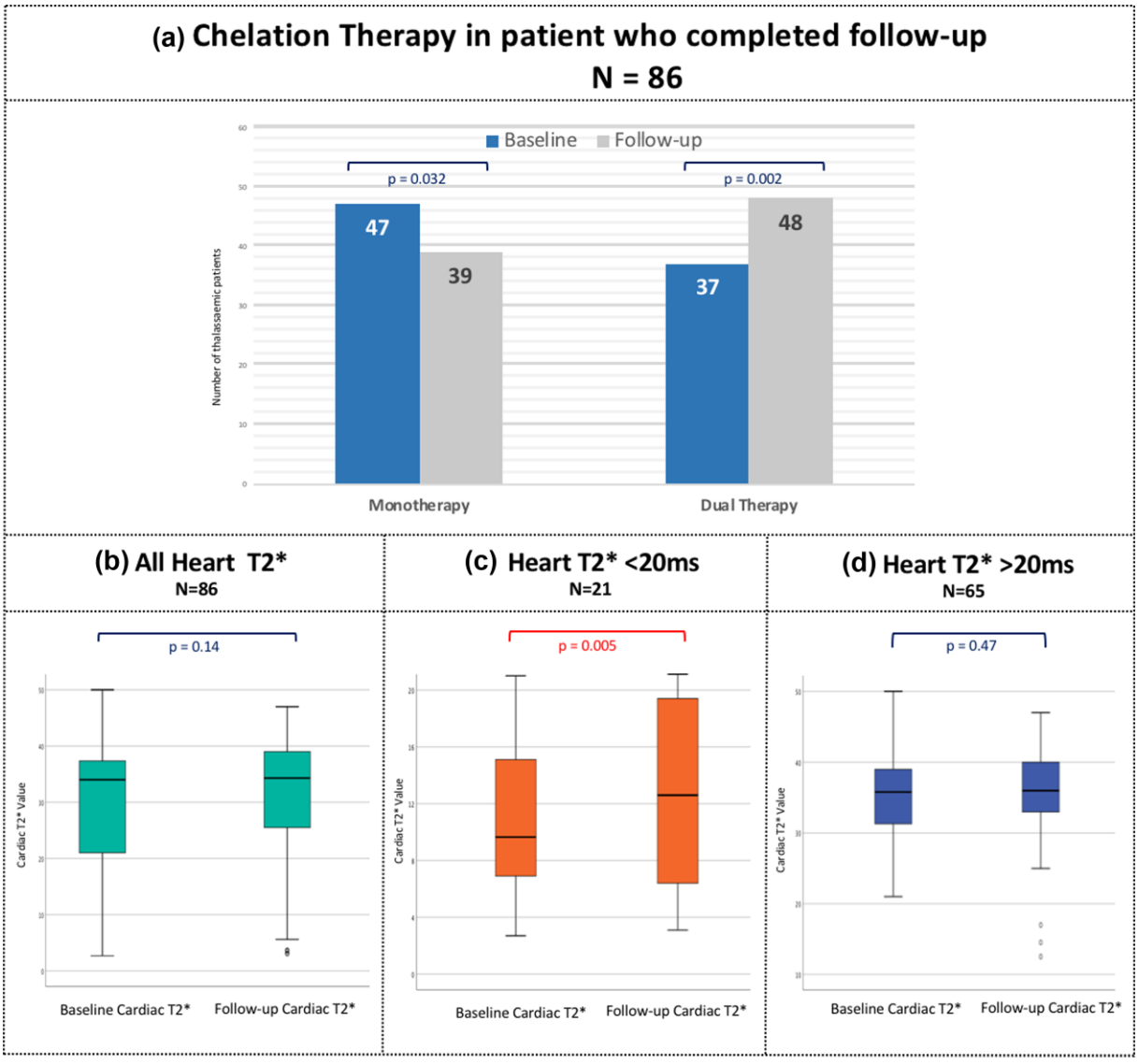


Figure 2 Panel (a) shows the number of patients at baseline and follow up who were taking single agent chelation therapy—monotherapy and those taking combinations of two chelators, dual therapy. Panels (b), (c) and (d) illustrate the mean, interquartile range and standard error for the MRI cardiac T2* for all patients, for those with significant iron loading (T2* <20 ms) and those with no cardiac iron (T2* > 20 ms), respectively.

Follow-up results

At 13-month follow-up visit, 86 (83%) attended. Ten patients could not attend on either of the two days offered, but were successfully contacted and clinical data obtained. None had suffered any adverse events. Six patients were lost to follow-up and one died in the follow-up period; this individual had presented at the baseline exam in overt cardiac failure attributed to iron overload and had failed to respond to intensive inpatient therapy.

The dominant change between the first and second visits was the reduction in the use of monotherapy [47 (55%) vs. 39 (45%), $P = 0.032$] and increase in the use of combined oral chelators [48 (43%) vs. 39 (55%), $P = 0.002$] (*Figure 2* and Supplementary material online, *Table S3*).

The average doses used changed little: DFO (-11 ± 14.9 mg/kg/day, $P = 0.01$), DFP ($+2.8 \pm 23$ mg/kg/day, $P =$ NS), and DFX ($+2.5 \pm 9.5$ mg/kg/day, $P = 0.03$).

For the whole group, overall average cardiac T_2^* and LVEF did not change significantly [cardiac T_2^* at 29.1 ± 11.8 ms at baseline vs. 30.2 ± 11.7 ms at follow-up ($P = 0.12$) and LVEF 65.1 ± 5.3% at baseline vs. 66 ± 4.8% at follow-up ($P = 0.06$)].

The liver T_2^* did not change (4.8 ± 4.2 ms vs. 4.9 ± 4.5 ms, $P = 0.61$) (*Table 3*).

Twenty-one participants with clinically significant iron loading ($T_2^* < 20$ ms) completed both visits. Cardiac T_2^* increased significantly from 10.9 ± 5.9 ms at baseline to 13.5 ± 8.7 ms at the follow-up visit ($P = 0.005$). Given the linearity of R_2^*

Table 3 Cardiac magnetic resonance iron status and left ventricle systolic function data—comparison between basal and 13-month follow-up—UMIMI study

	Baseline	Follow-up	*P*-value
All participants who completed follow-up, $N = 86$			
Heart T_2^* (ms) (mean ± SD)	29.2 ± 11.8	30.2 ± 11.7	0.14
Heart T_2^* <20 ms, *N* (%)	21 (24%)	14 (16%)	<0.001
Severe heart iron (<10 ms), *N* (%)	10 (12%)	6 (7%)	<0.001
Liver T_2^* (ms) (mean ± SD)	4.8 ± 4.2	4.9 ± 4.5	0.61
LVEF (%) (mean ± SD)	65 ± 5.3	66 ± 4.8	0.06
Cardiac T_2^* <20 ms, $N = 21$			
Heart T_2^* <20 ms (mean ± SD)	10.9 ± 5.9	13.5 ± 8.7	0.005
LVEF (%) (mean ± SD)	65 ± 8.1	66 ± 7.3	0.61
Cardiac T_2^* >20 ms, $N = 65$			
Heart T_2^* >20 ms (mean ± SD)	34.7 ± 6.4	35.4 ± 6.9	0.47
LVEF (%) (mean ± SD)	66 ± 4.2	66 ± 3.8	0.06

SD, standard deviation; LVEF, left ventricular ejection fraction.

(1/ T_2^*) to iron concentration, this represents a 23% reduction in cardiac iron. Of the entire cohort who completed the follow-up, cardiac T_2^* became normal ($T_2^* > 20$ ms) in seven (8%) patients and three participants (2%) with no cardiac iron overload at the first visit became abnormal ($T_2^* < 20$ ms) at the second visit.

Discussion

In India, ineffective transfusion, infections, and lack of appropriate chelation continue to be significant risk factors for mortality in beta thalassaemia.[24] Cardiac MRI T_2^* is a key test for diagnosis, guiding therapy, and its adoption is associated with improved outcomes.[5,9] The implementation of CMR has been difficult in countries such as India,[1,2,16,18,25] impeding the delivery of optimal care. There are several barriers that block CMR delivery, including the perception by healthcare providers that it is a time-consuming, expensive, and intricate technique.

We did four things to make CMR more accessible and relevant to the local conditions:

1. We embedded our project in a locally organized thalassaemic medical camp.
2. We used an agreed, structured clinical evaluation, which included an MRI scan, to guide therapy.
3. We implemented an average 10 min rCMR protocol.
4. We trained the local care providers to enable them to undertake the rCMR scans.

The Ultrafast MRI for Iron Management in India (UMIMI) project was undertaken in two centres in India on regularly transfused TDT patients, referred for cardiac iron and clinical assessment by their local haematologists. The selection of patients was controlled by the local advocate charity TI and was thus not a random selection within the region. All the components for the patients' clinical and imaging assessment were completed at the visit and recommendations for management were based on the result of the rCMR and discussed with the patient, with a written record for their haematologist (Supplementary material online, *Figures S4 and S5*). At the follow-up visit, those patients with clinically significant cardiac iron loading ($T_2^* < 20$ ms at baseline) had improved and the prevalence of cardiac $T_2^* < 20$ ms fell from 24% to 16%. No changes in LVEF were seen in this young population, which was not unexpected; it would be unusual to see changes in cardiac function in this age group,[26] despite cardiac iron overload. There was only one patient in cardiac failure at the baseline visit and, despite intensive therapy, this individual did not survive to the follow-up.

In this study, we embedded CMR scanning in a familiar patient medical camp scenario and found that a third of participants had cardiac iron overload and 97% of patients had liver iron. We have previously shown that CMR to assess cardiac and liver iron could be performed rapidly and less expensively in Thailand[17] and India.[18] However, the impact of such rapid CMR protocols on patients' therapy and tissue iron loading has not previously been investigated. For our study, the average time of scanning was only 10 min, with the overall time improved progressively once local radiographers gained experience (e.g. on our second visit, the average scan time was 9 vs. 11 min for the first visit).

This study represents a collaboration between the UK team, the local haematologists, and the patient advocate charity (TI) and it was felt to be unethical to include a comparable non-intervention group in this study. Patients attended the TI-organized medical camp specifically to have a cardiovascular assessment. This group of TDT patients and their advocates were aware of the importance placed on CMR scans in management guidelines, and keen to avail themselves of the opportunity to access this investigation. Thus, they might represent a more motivated group than other less supported patients in India. We formally incorporated in a one-stop clinic format the results of the CMR scans in the treatment recommendation given to each patient and made available to the local haematologists, some of whom were part of the patient camp medical team. We have not assessed whether adoption of the recommendations depended on the presence of the haematologist at the camp, or

whether it was taken up equally for those patients from more remote centres.

Although note was taken of liver iron loading, the main emphasis of this study and clinical assessment was biased towards the heart. Patients with very severe liver iron loading (T_2^* < 2.0 ms) were advised to increase their chelation intensity. The lack of improvement in liver iron assessed by T_2^* in this group may be due to the very severe nature of the liver iron loading and changes within the liver iron content being difficult to reliably detect by our methods.

The UMIMI intervention was associated with an increase in the intensity of chelator therapy, with more patients receiving combination treatment with the two oral chelators. It is highly likely that improved chelation was responsible for the improvement in cardiac T_2^* over a relatively short time. Subgroup analysis to establish which chelation regime provided the best response was not prespecified or attempted in this small group studied over such a short interval. The adoption of regular MRI scanning for T_2^* measurement and intensified chelation has previously been credited with improving mortality in TDT, via improved cardiac iron loading,[3,27,28] so it is not unreasonable to suggest that this result in India is consistent with previous experience. Demonstrating a practical method to incorporate rCMR scanning into the routine care of thalassaemic patients in India has been achieved. The next steps require that this methodology be adopted more widely and determining whether the benefit can be sustained and clinical outcomes improved.

Conclusions

These data demonstrate that a faster and simpler CMR protocol can be successfully embedded into patients' care within the thalassaemic medical camp model in an LMIC and that improvements in cardiac iron loading follow. In those countries where cardiac iron has been improved, there has been a demonstrable improvement in survival for TDT patients and it would be reasonable to predict that similar outcomes could be achievable in India by wider adoption of this approach.

Supplementary material

Supplementary material is available at *European Heart Journal—Quality of Care and Clinical Outcomes* online.

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Author contributions

J.M.W. conceptualized the study, acquired funding, collected, analysed, and interpreted the data, and co-wrote the article. K.M. collected, analysed, and interpreted the data and co-wrote the article. A.A-.G. and E.A. collected and analysed data. K.G., V.O., S.P., A.R., and S.P. supported acquisition of data. R.B., L.McG. and N.M. guided the study method and acquired data. V.K., A.M., R.B., H.M., and V.M. provided resources and supported acquisition of data. J.W. and S.T. acquired data and undertook project administration. J.M. guided the study method and supported interpretation of data. All co-authors were involved in reviewing and editing the final article.

Data availability

The data used for the current study are all anonymized and are available to other researchers upon reasonable request and approval of the collaborative groups.

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