Prognostic value of myocardial fibrosis on cardiac magnetic resonance imaging in patients with ischemic cardiomyopathy: A systematic review

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Background The use of cardiac magnetic resonance imaging (c-MRI) in risk stratification for clinical outcomes of patients with ischemic cardiomyopathy (ICM) remains low. This systematic review investigated the prognostic value of myocardial fibrosis as assessed by late gadolinium enhancement (LGE) on c-MRI in patients with ICM for ventricular tachyarrhythmia, sudden cardiac death (SCD), or all-cause mortality.

Methods We conducted a systematic review of the electronic databases Pubmed and Embase for relevant prospective English-language studies published between January 1990 and February 2019. All included articles were prospective studies that comprised of human participants older than 18 years with ICM and a primary or secondary prevention implantable cardioverter/defibrillator (ICD); had a sample size >30 participants; had at least 6 months of follow-up; and reported on ventricular tachyarrhythmia, SCD, and all-cause mortality. A total of 90 articles related to ICM were identified and were subsequently screened independently by 2 authors. Pooled sensitivity and specificity of LGE were calculated using random-effects model.

Results Eight studies with 1,085 participants were included in the final analysis. The mean age of patients varied from 43 to 83 years, with most patients being men. The most common comorbidities reported included history of diabetes mellitus (22%-62%), hyperlipidemia (40%-86%), and hypertension (35%-88%). The ejection fraction of each study was reported as mean or median and varied from 22% to 35%. During a follow-up that ranged from 8.5 to 65 months, there were 110 ventricular arrhythmic events reported. The pooled sensitivity and specificity of LGE for ICD therapy delivered for ventricular arrhythmias were 0.79 (95% CI: 0.66-0.87) and 0.28 (95% CI: 0.14-0.46), respectively. For all-cause mortality, the pooled sensitivity and specificity of LGE were 0.76 (95% CI: 0.40-0.93) and 0.41 (95% CI: 0.14-0.75), respectively. Although SCD was of significant interest to our review, only 1 of the studies reported on the association between LGE and SCD, leading to the subsequent exclusion of SCD from the end point analysis.

Conclusions LGE has high prognostic value in predicting adverse outcomes in patients with ICM and may provide helpful information for clinical decision making related to SCD prevention. Our findings illustrate how LGE may improve *current* risk stratification, prognostication, and selection of patients with ICM for ICD therapy. (Am Heart J 2020;229:52-60.)

What is already known about this subject?
Myocardial fibrosis in ischemic cardiomyopathy (ICM) results from scar tissue in the setting of prior myocardial infarction and is considered an important substrate for the genesis of spontaneous ventricular arrhythmia. However, the prognostic implication of myocardial scar burden for spontaneous ventricular tachyarrhythmia, sudden cardiac death, and all-cause mortality remains unclear.
What does this study add?

This systematic review demonstrates that myocardial fibrosis has high prognostic value in predicting adverse outcomes (spontaneous ventricular tachyarrhythmia and all-cause mortality) in patients with ICM.

How might this impact on clinical practice?

Our findings have the potential to improve current risk stratification and selection of patients with ICM for ICD therapy. Additionally, our study may help to further identify vulnerable subgroups of patients who otherwise do not meet current indications for ICD therapy.

Ischemic cardiomyopathy (ICM) is the most common cause of heart failure (HF) due to systolic dysfunction in the Western hemisphere, and it results in a number of comorbid complications and increased mortality. ICM also poses a high risk for sudden cardiac death (SCD), and ischemic heart disease (IHD) is the most common underlying substrate associated with SCD (42% of SCDs are due to IHD).[1] Implantation of an implantable cardioverter/defibrillator (ICD) is recommended for both primary and secondary prevention in appropriately selected patients at high risk of SCD.[1] Although ICD implantation has been shown in multiple trials to improve survival due to its termination of ventricular arrhythmia, risk stratification and identification of patients who stand to benefit the most from ICD placement remain a challenge as only one third of patients with an ICD receive appropriate therapy (ie, therapy delivered for ventricular arrhythmias) within 3 years after implantation.[2] Additionally, how to identify high-risk patients who do not meet current clinical indications for ICD therapy but yet remain at risk for SCD and sudden cardiac arrest (SCA) and stand to potentially benefit from appropriate ICD therapy is uncertain. Over the past decades, several clinical risk factors and tests have been investigated as potential tools to risk stratify vulnerable participants for SCD and ventricular arrhythmias; however, few have been found to have enough discriminative and predictive power.

One test that has been proposed for SCD risk stratification is the cardiac magnetic resonance imaging (c-MRI) which is used to detect myocardial fibrosis and can characterize scar burden and distribution.[3] Myocardial fibrosis in ICM signifies scar tissue from a prior myocardial infarction[1] and is an important substrate for the genesis of spontaneous ventricular arrhythmias.[4-6]It has been shown that, in patients with ICM, ventricular tachycardia (VT) results from scar-related reentry, and the scar can be visualized and assessed using late gadolinium enhancement (LGE) on c-MRI.[7,8]

There is paucity of contemporary data on the utility of the detected myocardial fibrosis on c-MRI in the risk stratification for clinical outcomes, particularly in relation to its prognostic significance in ICM. Although a few studies have suggested an association between myocardial fibrotic burden on c-MRI in patients with ICM and mortality and other cardiovascular outcomes,[9-11] these studies were limited by their small sample size, limited follow-up, and retrospective design. Also, previous reviews on this topic have combined data on participants with inducible and those with spontaneous ventricular tachyarrhythmias, making it difficult to derive meaningful potential conclusions about the role of LGE in predicting spontaneous ventricular arrhythmias. In this systematic review, we aim to investigate the prognostic value of myocardial fibrosis as assessed by LGE in patients with ICM for spontaneous ventricular tachyarrhythmias, SCD, or all-cause mortality.

Methods

Database and search strategies

We searched various electronic databases including Pubmed and Embase and published bibliographies for relevant prospective English-language studies from January 1990 to February 2019. Search terms included *cardiac magnetic resonance imaging or c-MRI, LGE, arrhythmia, hypertrophic cardiomyopathy, ICM, NICM, cardiac ventricular tachycardia, ventricular fibrillation/tachycardia or death, sudden death, cardiac death, cardiac defibrillators, implantable defibrillator or implantable device intervention*. This initial search was conducted using the software Distiller, the world's most used systematic review software. The search was subsequently narrowed and limited to prospective studies comprised of human participants older than 18 years with ischemic cardiomyopathy (ICM) and a primary or secondary prevention ICD, had a sample size >30 participants, and had at least 6 months of follow-up. Additionally, only studies on ICM that report on sustained and spontaneous ventricular arrhythmias were included in this analysis. Editorials, case reports/series, editorial articles, session presentations, systematic review articles, letters to the editor, and comments were excluded. Patients or the public WERE NOT involved in the design, or conduct, or reporting, or dissemination of our research. Lastly, our study and all original studies included herein were conducted prior to the current COVID-19 pandemic and thus do not include any known subjects with SARS-CoV-2.

Study selection and data collection

A total of 2,646 articles were identified (Figure 1). Two authors extracted selected studies independently for relevant studies on ICM, nonischemic (NICM), and hypertrophic cardiomyopathy. A total of 2,340 articles were excluded after reading the title and abstract. A total of 306 articles were then retrieved; fully reviewed; and
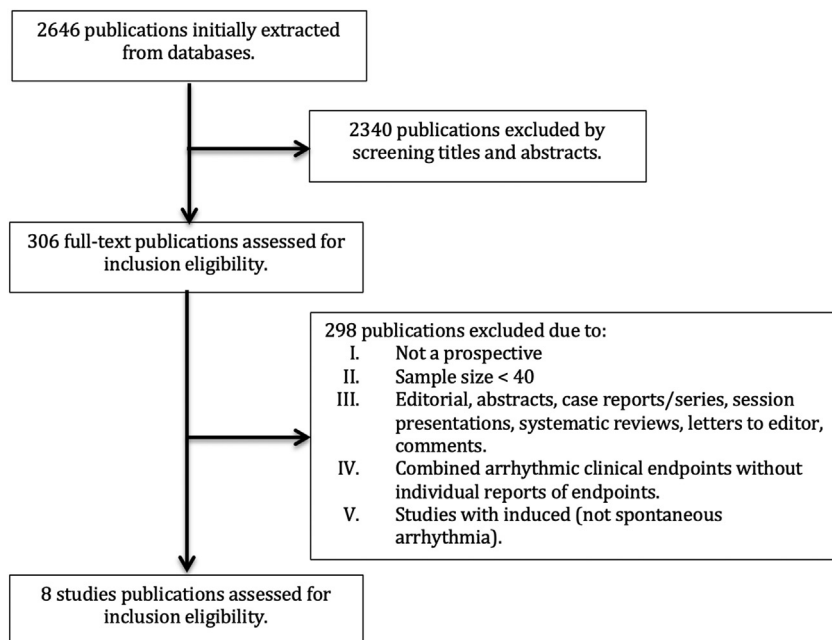
Flow diagram of articles.

categorized as pertaining to hypertrophic, ICM, or NICM. When disagreement arose, the authors met and discussed any discrepancies to reach consensus. A total of 8 studies met all of our inclusion criteria and were included in the final analysis. The first author thoroughly reviewed the 8 studies and extracted pertinent details including baseline demographic and clinical characteristics and clinical outcomes from each study. Specifics regarding the approach used for data collection are detailed in Figure 1.

Outcomes of interest were SCD, sustained and spontaneous ventricular tachyarrhythmias such as ventricular tachycardia, ventricular fibrillation, aborted SCD, appropriate ICD therapy including shocks and antitachycardia pacing, and all-cause mortality. We included studies with composite primary or secondary outcomes/events if they reported separately on the individual outcomes. Data from those studies were then extracted and collected for the analysis. Studies with composite primary or secondary outcomes of interest that did not report separately on the individual outcomes of interest were not included in the pooled analysis. Studies that reported on inducible arrhythmias during an electrophysiology study were also excluded. Of special interest to us were aspects of the myocardial scar that the investigators found to be most predictive of outcomes and the reported pattern of scar.

Statistical analysis

Patient's baseline characteristics are reported using median with interquartile range and mean +/− SD, as reported in the original studies. Follow-up periods are reported in months, and clinical outcomes including the ventricular arrhythmic events were extracted and reported as simple counts. To estimate the importance of myocardial fibrosis across various studies, pooled sensitivity and specificity analyses were conducted using a random-effects model (DerSimonian-Laird estimator). Proportions (sensitivity and specificity) were converted to corresponding log odds and summarized on this scale. Subsequently, the summary values were converted back to the reported proportions. Heterogeneity statistics for the meta-analysis were also generated. Individual study sensitivities and specificities were displayed with exact 95% CIs. Meta-analysis was performed with the "metafor" package (version 2.0) within R statistical software version 3.4.2 (The R Foundation, Vienna, Austria, 2017). Institutional review board approval was not needed for this study.

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Results

Clinical and demographics data

Eight studies comprised of 1,085 participants with median/mean follow-up of 8.5-64.8 months were included in the final analysis. The total population age and male gender percentage ranged from 43 to 83 years and 64% to 88%, respectively (Table I).

The most commonly reported comorbidities were prior history of diabetes (22%-62%), hyperlipidemia (40%086%),

Table I. Baseline characteristics and LGE–c-MRI scar parameters most predictive of end points of studies

First author	Study site	Year	Patients	Follow-up*	Male (%)	LVEF[†]	Events[‡]	Scar definitions	Scar parameters most predictive of end points
Demirel et al[12]	Netherlands	2014	94	64.8	86	31.9% ± 9.3%	34	Core scar: ≥50% maximal SI. Peri-infarct zone: SI ≥35% and <50% of maximal SI	Ratio of peri-infarction mass/infarction core mass >0.60
Roes et al[4]	Netherlands	2009	91	8.5	81	28% ± 9%	18	Core scar: ≥50% maximal SI. Gray zone: SI ≥35% and <50% of maximal SI	Infarct gray zone or peri-infarct zone >16.7 g
Boye et al[19]	Germany	2011	52	41.2	NA	30% ± 9%	13	Core scar: >5 SD above remote myocardium. Gray zone/peri-infarct: range of definitions	Relative infarct transmurality ≥43%
Bernhardt et al[13]	Germany	2011	41	39.5	83	35% ± 12%	12	Core scar/presence of LGE. Total myocardial volume, % of hyperenhanced myocardium, and scar coronary distribution were all assessed quantitatively.	Core/total scar aka presence of LGE
Gao et al[18]	Canada	2012	59 ICM (124 total)	21.1	83	~26%	10	Core/total scar: <2 SD above that of a remote noninfarcted myocardium. Gray or peri-infarct zone: difference of total hyperenhancement measured by ≥2 SD and ≥3SD thresholds	Total or core scar ≥38.7 g
Iles et al[14]	Australia	2011	42 ICM (103 total)	19.1	88	27% ± 8%	6	Core/total scar: ≥2 SD above that of a remote noninfarcted myocardium	Core/total scar aka presence of LGE
Puntmann et al[15]§	UK, Germany, Australia	2018	665	17	64	NA[§]	15	Core/total scar: ≥2 SD above the mean of the reference range (for normal/abnormal myocardium)	Core/total scar aka presence of LGE
Fernández-Armenta et al[16]	Spain	2012	41 ICM (78 total)	25	83	22%	2	Core scar: >50% maximal SI above that of a remote noninfarcted myocardium. Gray zone or border zone: >2 SD and <50% maximal SI	Late gadolinium presence, core scar mass percentage >16%, border zone/gray zone >9.5 g

LVEF (left ventricular ejection fraction), ICM (ischemic cardiomyopathy), ICD (implantable cardioverter defibrillator), VF/VT (ventricular fibrillation/ventricular tachycardia), SCD (sudden cardiac death).
* Follow-up duration is in median or mean of months.
† Left ventricular ejection fraction is reported in median or mean according to the original studies.
‡ *Events* refer to arrhythmic events such as appropriate ICD discharge for sustained VF/VT and SCD in ICM subjects. Mortality data were not captured in the events.
§ This study also includes subjects with coronary artery disease but normal ejection fraction percentage (118 patients had ejection fraction ≤35%).

and hypertension (35%-88%). The ejection fraction was reported as mean or median in each study, and it varied from 22% to 35% (Table I). The rate of use of β-blockers ranged from 49% to 94%, whereas the rate of use of angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers ranged from 51% to 100%. The rate of use of aldosterone antagonists was reported in 5 of the 8 studies and ranged from 13.8% to 56%.[12-16] All studies included participants meeting criteria for primary prevention ICDs.[12-19] Three of the 8 studies also enrolled patients receiving secondary prevention ICD.[4,15,18] The study that reported the number of patients with primary and secondary prevention ICDs included only 10 out of 91 patients with a secondary prevention ICDs[4]. The remaining 2 studies did not provide specific breakdown of patients with primary
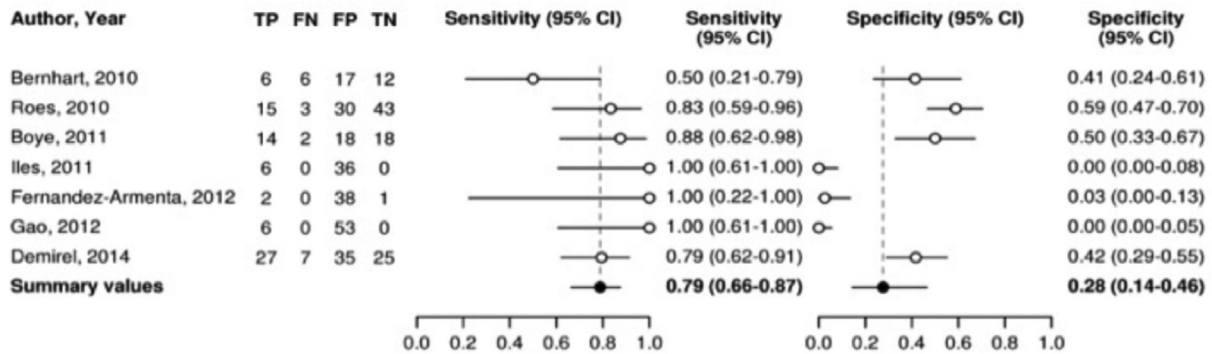
versus secondary prevention ICDs.[15,18] Interestingly, all of the studies were conducted in European countries or Australia, with 1 study also enrolling participants from North America.[15]

LGE c-MRI characteristics

Various scar parameters were used to describe aspects of the myocardial fibrotic burden visualized on c-MRI. Five studies use the core scar extent, 2 studies use the peri-infarct zone, and 1 study uses the relative infarct transmularity (Table I). For our analysis, scar parameters found by the investigators to be the strongest predictors of primary and/or secondary end points were included. Additionally, studies noted that all included subjects underwent c-MRI testing prior to ICD implantation and

Figure 2

Appropriate ICD therapy

Author, Year	TP	FN	FP	TN	Sensitivity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Specificity (95% CI)
Bernhart, 2010	6	6	17	12		0.50 (0.21-0.79)		0.41 (0.24-0.61)
Roes, 2010	15	3	30	43		0.83 (0.59-0.96)		0.59 (0.47-0.70)
Boye, 2011	14	2	18	18		0.88 (0.62-0.98)		0.50 (0.33-0.67)
Iles, 2011	6	0	36	0		1.00 (0.61-1.00)		0.00 (0.00-0.08)
Fernandez-Armenta, 2012	2	0	38	1		1.00 (0.22-1.00)		0.03 (0.00-0.13)
Gao, 2012	6	0	53	0		1.00 (0.61-1.00)		0.00 (0.00-0.05)
Demirel, 2014	27	7	35	25		0.79 (0.62-0.91)		0.42 (0.29-0.55)
Summary values						**0.79 (0.66-0.87)**		**0.28 (0.14-0.46)**

0.0 0.2 0.4 0.6 0.8 1.0   0.0 0.2 0.4 0.6 0.8 1.0

TP: true positive, FN: false negative, FP: false positive, TN: true negative

Forest plot of the composite arrhythmic end point in patients with ICM.

that follow-up was conducted during clinic visits and device interrogation via remote transmission. Study participants did not undergo repeat c-MRI following ICD implantation.

Summary statistics

A total of 110 arrhythmic events occurred among the 1,085 participants where arrhythmic event is described as sustained and spontaneous ventricular tachyarrhythmia such as ventricular tachycardia, ventricular fibrillation, aborted SCD, and appropriate ICD discharge/therapy including antitachycardia pacing. The pooled sensitivity and specificity of LGE for ICD therapy delivered for ventricular arrhythmias were 0.79 (95% CI: 0.66-0.87) ($I^2 = 20.7\%$, $Q = 7.6$, $P = .27$) and 0.28 (95% CI: 0.14-0.46) ($I^2 = 83.3\%$, $Q = 36.0$, $P < .001$), respectively. For all-cause mortality, the pooled sensitivity and specificity of LGE were 0.76 (95% CI: 0.40-0.93) ($I^2 = 67.7\%$, $Q = 6.2$, $P = .045$) and 0.41 (95% CI: 0.14-0.75) ($I^2 = 91.5\%$, $Q = 23.5$, $P < .001$), respectively. Although SCD was of significant interest to our review, only 1 of the studies reported on the association between LGE and SCD, leading to the subsequent exclusion of SCD from the end point analysis. The forest plots for appropriate ICD therapy/discharge and mortality are displayed in Figures 2 and 3, respectively. Heterogeneity testing summary is reported above using the I^2 symbol.
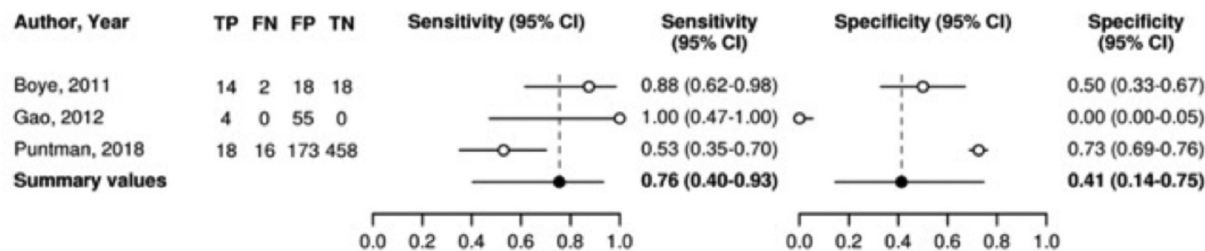
Discussion

Through our meta-analysis which included 1,085 participants, we have shown that LGE has high prognostic value in predicting adverse outcomes in patients with ICM. Although previous meta-analyses have assessed the role of LGE in ICM,[20,21] to our knowledge, this is the first meta-analysis to include *only prospective studies*, *studies with only ICM*, and *studies of participants with spontaneous sustained ventricular arrhythmias excluding inducible ventricular arrhythmias*. We believe that these differentiating factors are paramount to eliminating the known potential bias of retrospective studies and studies containing mixed ICM/NICM, and to reducing the uncertain clinical interpretation of inducible ventricular arrhythmia during electrophysiological testing. The former issues were evident in a recent review by Disertori et al that included both prospective and retrospective studies and studies containing mixed ICM/NICM population, which rendered it challenging to deduct a more definite conclusion regarding the role of LGE in ICM.[22] The latter point was evident in one study by Klem et al that included 105 (77%) participants undergoing electrophysiological testing where inducible monomorphic ventricular tachycardia was not found to be an independent predictor of the primary end point (all-cause mortality or appropriate ICD discharge for ventricular tachycardia or fibrillation) or secondary end points (all-cause mortality alone, and SCD or appropriate ICD discharge) in the multivariable analysis.[23] By incorporating *prospective* studies of ICM participants reporting on *spontaneous* sustained ventricular arrhythmias, we avoided the pitfalls of prior meta-analyses on this topic and conducted a robust analysis.

In all the studies included in our systematic review, increased myocardial fibrotic burden strongly correlated with adverse events regardless of the scar parameters examined. Although LGE appears to be associated with outcome, it is not clear if it is additive to other factors (eg, left ventricular ejection fraction [LVEF]). Nonetheless, it

Figure 3

All-cause mortality

Author, Year	TP	FN	FP	TN	Sensitivity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Specificity (95% CI)
Boye, 2011	14	2	18	18		0.88 (0.62-0.98)		0.50 (0.33-0.67)
Gao, 2012	4	0	55	0		1.00 (0.47-1.00)		0.00 (0.00-0.05)
Puntman, 2018	18	16	173	458		0.53 (0.35-0.70)		0.73 (0.69-0.76)
Summary values						**0.76 (0.40-0.93)**		**0.41 (0.14-0.75)**

TP: true positive, FN: false negative, FP: false positive, TN: true negative

All-cause mortality forest plot.

does appear to confer a more complete prognostic implication beyond existing conventional parameters and continued contemporary improvement of ICM management. For instance, LGE correlated with worse outcomes in 2 of the included studies that consisted of ICM subjects on optimal medical therapy[12,13] and in the other studies with subjects being optimized on various components of guideline-directed medical therapy (GDMT). The specific rates of use of medical therapy of the studies, as informed by contemporary guidelines, are provided above. Moreover, a recent study revealed that infarcted myocardial tissue as measured by c-MRI may help to better identify patients at risk for monomorphic VT when combined with LVEF.[13] The key finding in our study is that ventricular scar burden as visualized on CMR portends a *high* risk of adverse outcomes including ventricular tachyarrhythmia and mortality in patients with ICM beyond conventional risk stratification parameters. The fact that the association remains in spite of the heterogeneity of the scar parameters further bolsters the prognostic value of LGE on c-MRI in clinical settings.

Although most recent studies use a binary approach by detecting the presence of scar to investigate the role of LGE in predicting outcomes, a more granular approach characterizing and grading the severity of diseased myocardium of infarct tissue heterogeneity may add to the prognostic discriminating power of LGE beyond that noted in our study. Presently, it remains unknown if certain scar parameters provide more discriminating power beyond the absolute presence/absence as compared to others. Specifically, does the extent of scar matter more than the location? Or does transmurality confer worse prognosis than subendocardial scar? Or does the density matter more than the transmurality of the scar? What threshold of the scar or fibrotic aspect of T1 mapping confer worse prognosis? Also, how does the selection of contrast agents or MRI vendors impact quantification of scar? Can LGE eventually be also used for

CRT selection? Now that our study has illustrated that the mere presence of LGE correlates with adverse outcomes in prospective ICM participants, future randomized studies are needed to address the aforementioned questions and potential prognostic role of various scar parameters.

In relatively few small studies, both myocardial infarct size and peri-infarct border size were linked to mortality in patients with ICM.[11,24] However, as previously noted, studies use various methods to characterize scar parameters and to quantify fibrotic burden. These methods range from presence or absence of fibrosis to characterization of scar using transmural scar percentage, core infarct zone, total scar zone, peri-infarct zone or "gray" zone, and distribution of the scar. One reason for the heterogeneity in reporting is the lack of a national and international standardized protocol for reporting c-MRI scar. Among studies in our review, some have found the core infarct zone to be more predictive of worse outcomes, whereas others have found the peri-infarct zone to be more important. For instance, both Gao et al and Iles et al found the core infarct zone to be of significant prognostic potential for ventricular arrhythmia and SCD.[14,18] Meanwhile, Roes et al reported on the peri-infarct scar mass and found it to be predictive of worse outcomes,[4] whereas Demirel et al found the peri-infarct to core infarct ratio to be the most predictive of appropriate ICD therapy and all-cause mortality.[12] However, regardless of the parameters used, LGE correlates with arrhythmic events, SCA or SCD, and mortality.

Recently, myocardial fibrosis noted on other imaging modalities has been correlated with poor outcomes. Borger van der Burg et al reported that extensive scar tissue visualized on technetium Tc 99m tetrofosmin scintigraphy is an independent predictor of death or recurrent VT in patients with ICM.[25] However, use of those other imaging modalities has been limited because of their inability to adequately assess the size, transmural extent, distribution, and density of myocardial scar. c-MRI

is the best imaging modality to assess and to accurately characterize myocardial scar burden because it provides information on the aforementioned scar parameters that other modalities cannot provide. As such, it is unclear what additional diagnostic or prognostic information other imaging modalities would provide beyond that of c-MRI.

Our study demonstrated that LGE provides prognostic value in the prediction of ventricular tachyarrhythmia and all-cause mortality in participants with ICM. Specifically, LGE has a high sensitivity for the prediction of the aforementioned outcomes. Although the specificity of LGE in our findings is low and indiscriminate, if the LGE can be coupled with other tests with low sensitivity but high specificity, false positives may be correctly identified as negative. Therefore, LGE is not the end-all factor but rather one that contributes to the prediction of bad outcomes in patients with ICM and could potentially help improve current stratification and selection of patients for ICD implantation in ICM. Furthermore, in clinical settings, c-MRI scar parameters can be used to identify vulnerable subgroups of patients at risk of adverse outcomes who otherwise do not meet current clinical indications for ICD preventative therapy. Presently, ICD placement is indicated for primary prevention of SCD in patients who are at increased risk of life-threatening VT/ ventricular fibrillation (VF) in spite of optimal medical management and for secondary prevention of SCD in patients with prior sustained VT/VF or resuscitated SCD secondary to VT/VF[1]. However, only one third of patients with an ICD receive appropriate therapy (ie, therapy delivered for ventricular arrhythmias) within 3 years after implantation.[2] Also, inappropriate ICD shocks occur in approximately 10%-20% of ICD recipients.[26-31] As such, patient selection for ICD therapy may be improved by using c-MRI to further identify vulnerable subgroups of patients as demonstrated in our analysis. Additionally, extending beyond the current ICD indications to cover patients with an LVEF >35% and a positive LGE on c-MRI should be considered in future studies. More widespread use of MRI to inform clinical decision making is contingent on future randomized clinical trials showing improvement in outcomes with an ICD implanted on the basis of LGE detected on c-MRI.

Limitation

First, all of the studies were conducted in European countries or Australia, with 1 study also enrolling participants from North America. As such, generalizability of our findings to the US population may be limited. Second, study sites used different protocols for conducting the LGE-CMR studies, and thus, the heterogenous assessment of the myocardial scar burden should be interpreted with care. Yet, regardless of the considerable heterogeneity across studies, the magnitude and directionality of the prognostic implication of ventricular scar burden appear to be consistent across the studies and in our analysis. Third, because of the lack of patient-level data, our study could not adjust for confounders or other pertinent contributing factors. Studies collected data on various factors, and not all studies collected data on all the same factors. Studies also made use of various different definitions of variables and defined outcomes. We attempted to account for this considerable amount of heterogeneity by conducting and reporting heterogeneity testing summaries in the "Results" section above, which were negative. Fourth, our end point analysis is a composite of arrhythmic events which is rather a heterogeneous composite given that some studies report arrhythmic events as any appropriate ICD therapy including antitachycardia pacing (which itself is dependent on device settings), whereas others report only appropriate ICD shock for ventricular arrhythmias. This inherent issue with report of arrhythmic events is unavoidable and one that is difficult to adjust for because manuscripts do not always provide specific details regarding "appropriate" ICD therapy, which in turn may significantly impact the results of systematic review. Fifth, our end point analysis was calculated using binary findings (presence/absence) as reported from the original studies, and thus, a dose-response relationship was not assessed. As noted above, future studies should investigate potential dose-response relationship of ventricular scar parameters and arrhythmic events. Sixth, our analysis included subjects with both primary and secondary prevention ICDs, which may affect the application of our findings for potential improvement of stratification of patients for ICD implantation.

Conclusion

In this meta-analysis of 8 prospective studies of c-MRI in patients with ICM, we found that ventricular scar burden poses a high risk of ventricular tachyarrhythmia and all-cause mortality in participants with ICM. As such, c-MRI may improve risk stratification of ICM patients and aid in patient selection for ICD therapy. Future studies should examine the role of the c-MRI in patients who otherwise do not meet current indications for an ICD.

CRediT authorship contribution statement

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