

Magnetic Resonance Imaging of Myocardial Strain After Acute ST-Segment–Elevation Myocardial Infarction A Systematic Review

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Abstract—The purpose of this systematic review is to provide a clinically relevant, disease-based perspective on myocardial strain imaging in patients with acute myocardial infarction or stable ischemic heart disease. Cardiac magnetic resonance imaging uniquely integrates myocardial function with pathology. Therefore, this review focuses on strain imaging with cardiac magnetic resonance. We have specifically considered the relationships between left ventricular (LV) strain, infarct pathologies, and their associations with prognosis. A comprehensive literature review was conducted in accordance with the PRISMA guidelines. Publications were identified that (1) described the relationship between strain and infarct pathologies, (2) assessed the relationship between strain and subsequent LV outcomes, and (3) assessed the relationship between strain and health outcomes. In patients with acute myocardial infarction, circumferential strain predicts the recovery of LV systolic function in the longer term. The prognostic value of longitudinal strain is less certain. Strain differentiates between infarcted versus noninfarcted myocardium, even in patients with stable ischemic heart disease with preserved LV ejection fraction. Strain recovery is impaired in infarcted segments with intramyocardial hemorrhage or microvascular obstruction. There are practical limitations to measuring strain with cardiac magnetic resonance in the acute setting, and knowledge gaps, including the lack of data showing incremental value in clinical practice. Critically, studies of cardiac magnetic resonance strain imaging in patients with ischemic heart disease have been limited by sample size and design. Strain imaging has potential as a tool to assess for early or subclinical changes in LV function, and strain is now being included as a surrogate measure of outcome in therapeutic trials. (*Circ Cardiovasc Imaging*. 2017;10:e006498. DOI: 10.1161/CIRCIMAGING.117.006498.)

Key Words: angiotensin-converting enzyme inhibitor ■ coronary artery disease ■ heart failure
■ magnetic resonance imaging ■ ST-segment–elevation myocardial infarction

In recent years, survival has been improving after an acute ST-segment–elevation myocardial infarction (STEMI). In the United States, the mean predicted 10-year risk of death for coronary heart disease among adults aged 30 to 74 years decreased from 7.2% (1999–2000) to 6.5% (2009–2010).¹ Consequently, more individuals who survive an acute STEMI have residual infarct pathology that predisposes them to the subsequent development of LV dysfunction and heart failure, which remain the major causes of death post–myocardial infarction (MI).² In fact, despite improvements in survival, the incidence of heart failure after acute MI has not decreased in the past several years.^{3,4}

Identifying individual patients who are at risk of heart failure post-MI remains problematic.^{5,6} Reductions in left ventricular ejection fraction (LVEF; mild, moderate, and severe) are prognostically important^{7,8} and used in evidence-based guides for treatment stratification, for example, angiotensin-converting enzyme

inhibitor therapy^{6,8} and implantable defibrillator devices.^{6,9} However, LVEF is a global index that reflects changes in dimensions rather than contractility, and LVEF may not account for regional variations in myocardial contractility.

Strain, the change in length per unit length of tissue, reflects myocardial deformation and is more closely linked with myocyte metabolism and contractility than LVEF.¹⁰ Strain imaging has high potential for prognostication in the setting of post-MI risk assessment.¹⁰ Strain is a tensor that can be largely described using 3 principal strains (E_1 , E_2 , and E_3), or more commonly for the heart, in a cylindrical coordinate system as strains in the radial, circumferential, and longitudinal directions. Tissue shortening is reflected by a negative strain value, which is typical during systole for circumferential and longitudinal directions, whereas radial strain is typically positive because LV thickening occurs in the radial direction with contraction.

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Cardiac Magnetic Resonance for Estimation of Myocardial Strain

There are several techniques for assessing myocardial strain with cardiac magnetic resonance (CMR; Figures 1 and 2). The bespoke strain methods include myocardial tagging,¹¹ strain-encoding imaging (SENC),^{12,13} phase-contrast imaging,¹⁴ displacement encoding with stimulated echoes,^{15–17} and cine-derived strain.^{18–22}

Bespoke Strain Acquisitions

Myocardial tagging measures strain based on the imaging and tracking of tissue markers (tags) induced by changes to the tissue magnetization.^{11,23} Tagging has good intraobserver agreement,^{24,25} has moderate interobserver agreement,²⁶ and is considered by some as a gold-standard reference method.²⁷ However, tagged CMR has some limitations, with the most notable being time-consuming analysis that typically involves manual planimetry.

Harmonic phase analysis²⁸ provides rapid analysis of tagged images but at the expense of reduced spatial resolution and strain accuracy.²⁹ Cine phase-contrast velocity-encoded imaging is another long-standing magnetic resonance imaging method,

which is well-suited to the assessment of strain rate,^{30,31} but requires the integration of data to compute strain, which may decrease strain accuracy. This technique encodes tissue velocity directly into the phase of the signal by the application of a bipolar magnetic field gradient. SENC is effective for the quantification of through-plane strain, as the tag planes are oriented parallel to the imaging plane, but is limited in its ability to thoroughly assess radial and circumferential strains with good spatial coverage and measuring other parameters such as twist and torsion.^{12,13}

Displacement encoding with stimulated echoes^{15–17} encodes myocardial tissue displacement into the phase of the magnetic resonance imaging signal. Displacement encoding with stimulated echoes has equivalent or better accuracy and reproducibility of strain as compared with tagging,^{32,33} while providing simple and rapid strain analysis.^{34–36}

Retrospective Estimation of Strain Using Cine CMR Images

Feature tracking (FT) involves retrospective motion tracking of steady-state free precession cine images. However, the

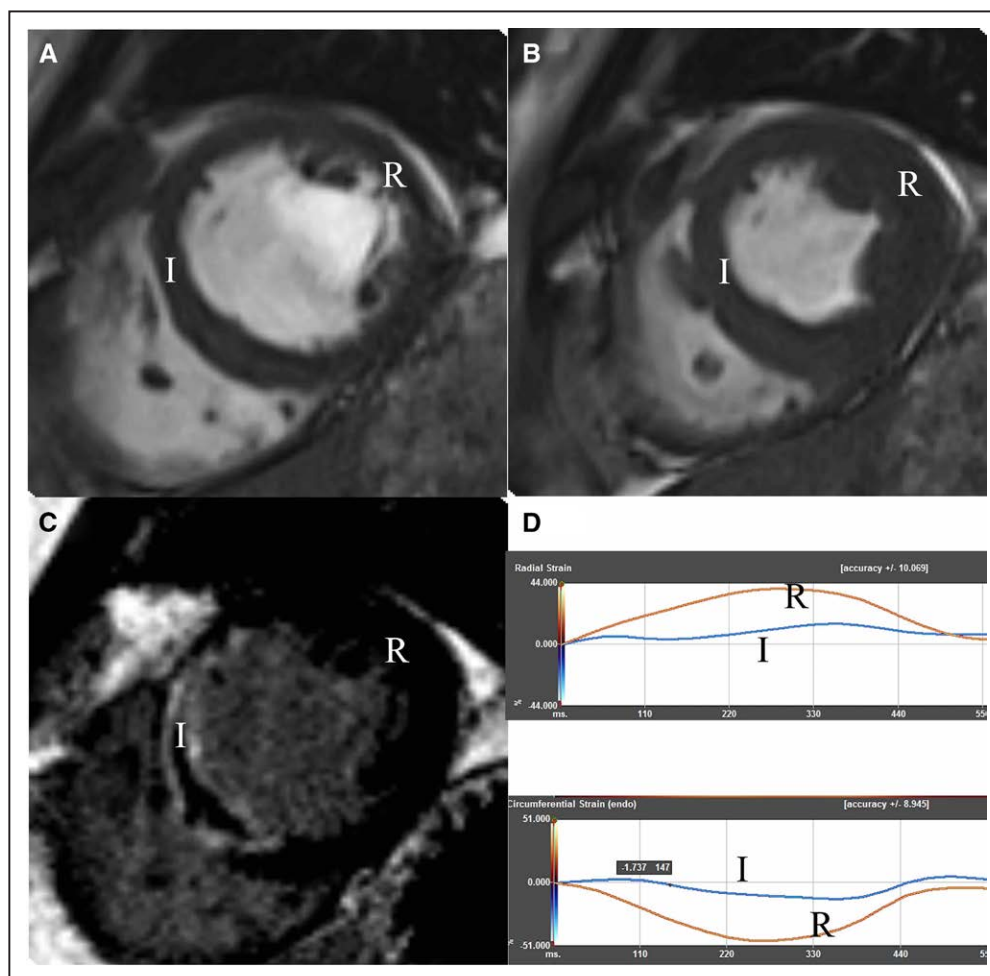


Figure 1. Feature tracking–derived strain. A 48-y-old male patient presented with acute anterior ST-segment–elevation myocardial infarction. He underwent cardiovascular magnetic resonance 2 d after primary percutaneous angioplasty to his proximal left anterior descending artery, with restoration of normal antegrade coronary flow (thrombolysis in myocardial infarction flow grade 3). **A**, End-diastole mid-left ventricular short-axis cine acquisition. I denotes infarct region, and R denotes remote. **B**, End-systole cine acquisition, with noticeable thickening in the R region but not in the I region. **C**, Matched mid-diastolic late gadolinium enhancement depicting a transmural septal scar with microvascular obstruction. **D**, Peak radial and circumferential strain, with I being over the anteroseptal segment, which shows reduced radial and circumferential strain and R being within normal ranges.

method mainly derives strain by tracking the displacement of the endocardial border,¹⁸ rather than the full thickness of the myocardial tissue, with potentially lower accuracy and greater measurement variability compared with dedicated strain methods.^{21,22,37} FT measurements will be less reliable when endocardial border definition is unclear³⁸ especially for segmental strain, when measurement error can be problematic.²² Peak strain values may vary according to the technique used, with some techniques such as FT generating higher peak strain values compared with other techniques such as tagging.^{26,39,40}

New techniques in how strain can be derived from cine imaging have recently been developed. Tissue tracking¹⁹ incorporates strain derived from both the endo- and epicardial borders, whereas deformation tracking is a noncommercial software using an intensity-based b-spline deformable image registration method.²¹ Both methods have been reported to generate lower magnitudes of strain than FT.

Temporal resolution (≈ 50 ms) is generally similar between these methods. Ideally, strain values would be consistent regardless of the method used though differences in CMR acquisition methods, and analysis techniques are likely to result in intertechnique variability.

Which Approach to Strain Imaging Is Preferred?

Given the contemporary drive for time-efficient imaging, short scans, and patient comfort, retrospective cine-strain imaging without the need for additional breath-hold scans is appealing for routine clinical practice. For research imaging, where accuracy and precision are key considerations, a dedicated strain scan may be preferred to estimates of strain from cine scans. In this case, for patients early post-MI, a single midventricular and longitudinal breath-hold scan may provide sufficiently meaningful data as a pragmatic trade-off against additional scans intended to gain more extensive LV coverage, especially when other components of the imaging examination may involve multiple breath-holds.

Methods

Eligibility Criteria

Our aims were to (1) assess the relationships between strain and infarct characteristics in patients after an acute STEMI and in those with stable ischemic heart disease (SIHD), (2) assess the relationships between strain and LV outcomes in patients after an acute STEMI and in those with SIHD, and (3) determine whether CMR-derived strain is a predictor of clinical outcome in patients following an acute MI.

We limited our search to peer-reviewed journals and human participants. Studies with fewer than 10 patients or those not published in English were excluded. Twenty-four publications were identified that described the relationship between myocardial strain and infarct characteristics (Table 1 in the [Data Supplement](#)).

Search Strategy

A systematic literature review was performed according to the PRISMA⁴¹ and MOOSE⁴² guidelines by 2 independent researchers (K.M. and C.M.; Figure 3) who independently searched PubMed and EMBASE using the following keywords and variations on them: myocardial infarction, infarct, coronary artery disease, ischemic cardiomyopathy, myocardial strain, strain rate, magnetic resonance imaging, cardiac magnetic resonance, outcome, MACE, mortality, infarct, and infarct characteristics ([Data Supplement](#)).

Study Selection

Abstracts of all potential titles were reviewed by K.M. and C.M. References of relevant reviews and all full articles were searched to retrieve any additional articles, repeating the process until no new articles were found.

CMR Strain Parameters and Infarct Characteristics

Relationships Between Regional Strain and Infarct Characteristics

Tagging^{43,44} and SENC⁴⁵ discriminate patients with MI from healthy volunteers based on regional differences in myocardial contractility. Early post-MI, the infarct zone contains heterogeneous pathology including edema, inflammatory cell infiltrates, hemorrhage, and viable and dead tissue. For these reasons, infarct size by late gadolinium enhancement is initially typically larger compared with repeat assessments months later.⁴⁶ Not surprisingly, there is only a moderate correlation between global indices of strain (circumferential or longitudinal) and infarct size when assessed early post-STEMI.²⁶

Reductions in global peak circumferential,^{26,45,47–55} radial,^{54,56} and longitudinal strain,^{45,51,54} as well as radial phase dispersion⁵⁷ and circumferential strain rate,⁵⁸ can discriminate transmural infarction from nontransmural infarction and non-infarcted remote zones in patients with recent MI, SIHD, and ischemic cardiomyopathy (Table 1). Compared with longitudinal strain, circumferential strain has greater discriminative value for assessment of the transmural extent of infarction in patients with recent²⁶ and chronic MI.^{51,54}

In patients with SIHD, circumferential strain imaging with CMR⁴⁸ can reveal subtle reductions in LV contractile function that are attributable to infarct pathology and which otherwise would not be apparent if assessed using standard measures of LV systolic function such as LVEF or fractional shortening.

Comparative Analyses of Strain and Surrogate LV Outcomes

In patients with acute STEMI, global circumferential strain,^{59,60} strain rate,⁶² and global longitudinal strain⁶¹ are predictive of adverse remodeling in the longer term in most, but not all, studies⁴⁰ (Table 1). Sample size is an important consideration because only a limited proportion of patients (eg, <10%) will experience adverse remodeling when defined in binary terms, for example, $\geq 20\%$ increase in LV end-diastolic or end-systolic volume index at 6 months from baseline.⁴⁰ When FT-derived circumferential strain and longitudinal strain have been compared in prognostic studies, only circumferential strain has proven to be a multivariable associations of LV function post-MI.⁵⁹ This difference is clinically relevant because global circumferential strain predicts functional recovery after coronary revascularization.⁶³ Circumferential myofibers are typically located on the epicardial aspect of the heart, whereas longitudinal myofibers are typically located in the midendocardium, and these anatomic differences may explain the potentially superior clinical significance of circumferential strain measurements in post-MI patients.⁴⁴ Still, the available clinical evidence is limited, and further research is warranted.

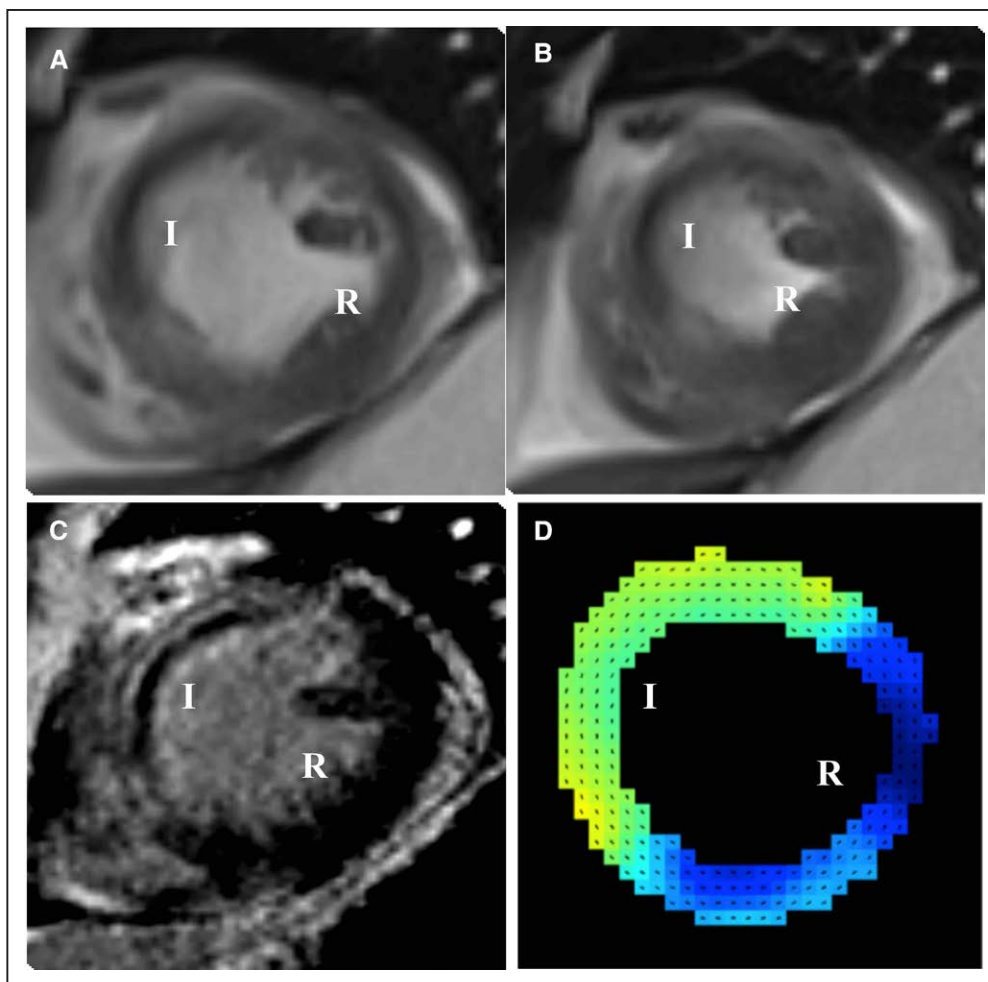


Figure 2. Displacement ENcoding with Stimulate Echoes (DENSE) derived strain. A 52-y-old male patient presented with anterior ST-segment-elevation myocardial infarction. Cardiovascular magnetic resonance scan was performed 2 d after primary percutaneous angioplasty to his proximal left anterior descending artery. **A**, End-diastole mid-left ventricular short-axis cine acquisition. I denotes infarct region, and R denotes remote. **B**, End-systole cine acquisition. **C**, Matched mid-diastolic late gadolinium enhancement depicting a transmural septal scar. **D**, DENSE-derived circumferential strain map, with lower magnitudes of strain depicted as green pixels (I region), and higher magnitudes depicted as blue pixels (R region).

SENC-derived circumferential strain rate has similar prognostic value compared with the extent of late gadolinium enhancement for the prediction of recovery of LV systolic function after acute MI.⁶² Regional circumferential strain derived from tagging,⁶⁴ rather than FT,⁶⁰ has incremental prognostic use in predicting segmental functional recovery (by wall-motion scoring) in the longer term after an acute STEMI. Compared with FT-derived strain, tagging-derived strain would seem to be more robust based on reduced variance and increased predictive accuracy for identifying myocardial segments with the potential for contractile recovery post-MI.^{21,22}

Microvascular obstruction^{62,65} and intramyocardial hemorrhage^{61,65} are associated with reduced circumferential strain and a reduced likelihood of recovering circumferential contractile function in affected segments. On the contrary, edematous segments without infarction may generally generate less circumferential strain,⁶⁶ but contractile function may recover in the longer term.⁶⁷

In patients with SIHD with or without chronic MI, the transmural extent of late gadolinium enhancement in

individual myocardial segments is inversely associated with the changes in midventricular circumferential strain as revealed by CMR tagging after coronary revascularization,⁶³ unlike LVEF that may not reflect any parameter of the segmental extent of infarct scar.⁶³ Therefore, compared with global LVEF, strain imaging enables a more detailed assessment of the effects of therapeutic interventions. The threshold in the transmural extent of scar ($\geq 25\%$) varies between study populations and imaging methods.⁶³ Given the importance of revascularization decisions for individual patients, we think more work is needed to clarify the relevant thresholds to inform therapy.

Is Myocardial Strain a Predictor of Clinical Outcome Post-Myocardial Infarction?

There is a gap in knowledge about whether or not myocardial strain assessed by CMR is independently associated with health outcomes post-MI, including major adverse cardiac events and mortality.⁶⁸ In a group of patients referred for CMR (31% with SIHD, 13% with previous MI), lateral

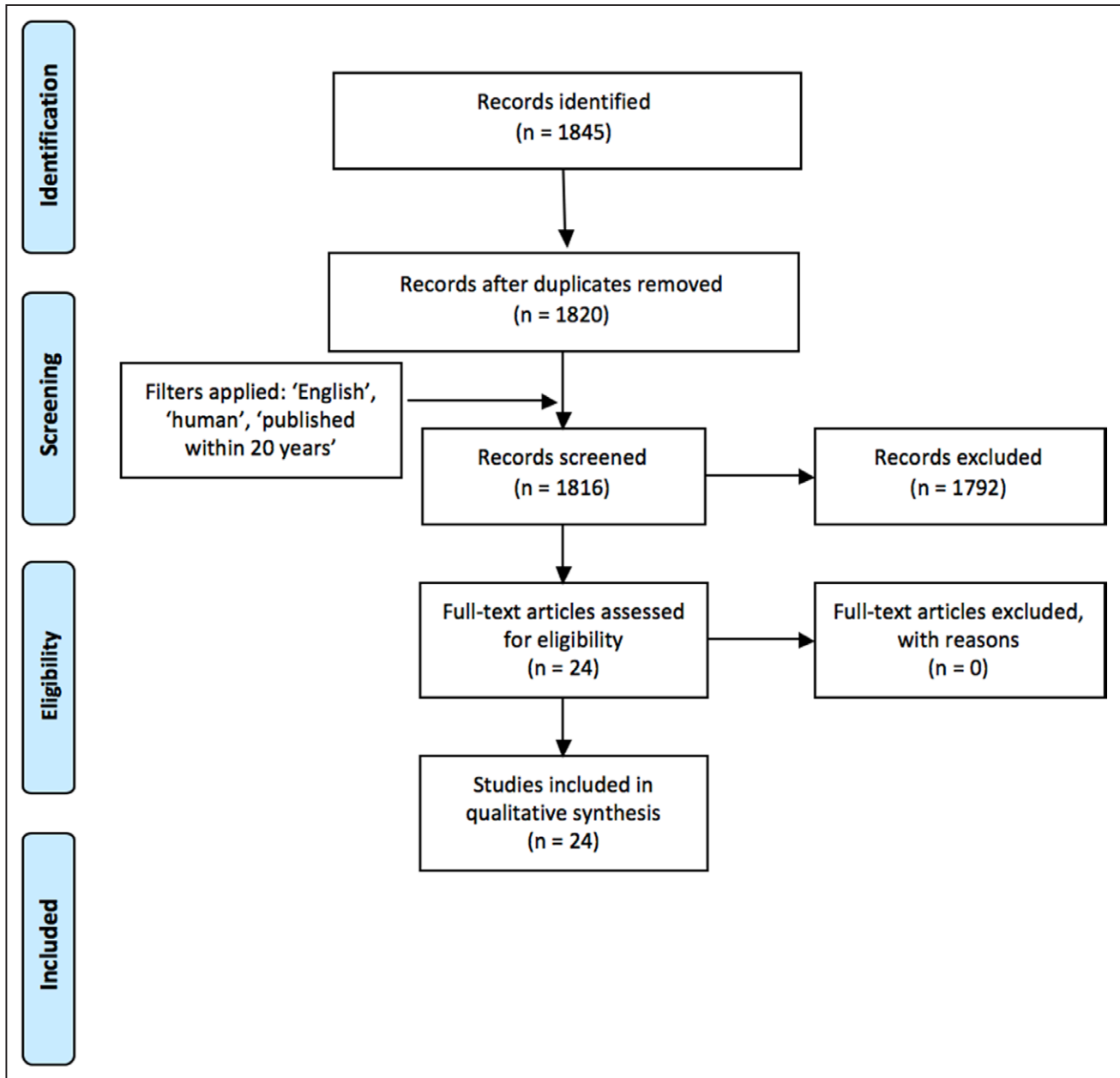


Figure 3. Literature search flow diagram.

mitral annular plane systolic excursion was a univariate and multivariate predictor of major adverse cardiac events. Mitral annular plane systolic excursion is a surrogate for LV longitudinal function reflecting long-axis LV shortening during systole.⁶⁹ In a similar all-comers group⁷⁰ (11% with coronary artery disease), tagging-derived global circumferential strain was a multivariate predictor of major adverse cardiac events.

Infarct size revealed by CMR is independently associated with health outcomes post-STEMI.⁷¹ Renal impairment is common after acute MI,⁷² rendering some patients ineligible for gadolinium-contrast examinations. Further studies are required to assess whether strain imaging might serve as an alternative tool for prognostication in post-MI patients who are ineligible for contrast imaging.

Clinical Perspective

Strain provides more direct information on regional and global LV function in patients with acute MI or SIHD than LV ejection fraction or wall-motion score. Initial infarct size may overestimate the true extent of irreversibly damaged myocardium,^{46,73,74} which may limit its prognostic accuracy early post-MI (the time most relevant to clinicians). Accordingly, myocardial strain has emerging potential for predicting LV recovery post-MI. Strain imaging may also be useful when infarct size cannot be assessed because of intolerance of gadolinium-contrast media.

Strain imaging may be useful as an early biomarker of subclinical impairment in systolic function before LV function may become globally impaired.⁷⁵ Strain may be measured to assess treatment efficacy in clinical trials of therapeutic

Table 1. Strengths and Limitations of Available Data for Post-STEMI Strain Using CMR

Strengths	Limitations
Relationship of strain with infarct size	
Strain (E_{CC} ^{26,45,47–55} E_{RR} ^{54,56} E_{LL} ^{45,51,54}) is reduced in infarcted tissue when compared with remote myocardium	Small sample sizes (most $n < 50$), observational studies. Not all studies assessed intra- and interobserver variability
E_{CC} can discriminate infarct transmuralities ⁵⁹	E_{LL} cannot discriminate infarct transmuralities ⁵⁹
Strain correlates with infarct size ^{26,55}	E_{CC} provides no additional benefit to segmental infarct size to predict recovery ⁶⁰
Relationship of strain with LV remodeling post-STEMI	
E_{LL} is a modest predictor of adverse remodeling ⁶¹	Adverse remodeling occurs in a small set of patients with STEMI, requiring a larger sample size
E_{CC} can predict LV function at 6 months ^{59,62}	
Relationship of strain with health outcomes	
	No data has been published as yet assessing strain with health outcomes

E_{CC} indicates circumferential strain; E_{LL} , longitudinal strain; E_{RR} , radial strain; LV, left ventricle; and STEMI, ST-segment–elevation myocardial infarction.

interventions in IHD patients predicated on improved precision and accuracy compared with LVEF (Clinicaltrials.gov search date, February 7, 2017: Remote Ischemic Preconditioning to Prevent Dialysis Induced Cardiac Injury [NCT02630355] and Intensive Statin Therapy in Patients With Acute MI [NCT01923077]).

Strain is superior to wall motion scoring for dobutamine stress testing in patients with SIHD^{76–79} (Data Supplement).

Going forward, for the diagnostic value of strain imaging to be realized in the clinic, the techniques should be straightforward to learn and implement, ideally across vendors, with acceptable accuracy and precision and short, automated postprocessing.

Practical Limitations to Measuring Strain With CMR in the Acute Setting

Historically, CMR vendors did not include strain analysis options within their software, and this gap may have served as a stimulus for third-party software providers. When strain analysis is not possible on the CMR workstation, then workflow issues may emerge, as Digital Imaging and Communications in Medicine images must be transferred from the scanner to other computers. Thankfully, this circumstance is changing, and commercially available strain analysis methods are becoming more accessible and integrated within imaging platforms. Postprocessing times vary from minutes with feature tracking and displacement encoding with stimulated echoes^{26,35,36} to somewhat longer with myocardial tagging.²⁶ Including all of the steps from image transfer to the final read-out, LV strain analysis with FT may involve half an hour per patient and more than 1 hour for tagging,²⁶ which is clearly a

Table 2. Advantages and Limitations of Echocardiography, When Compared With CMR for Post-STEMI Strain Measurement

Advantages	Limitations
Portability, lower cost, current standard of care ⁶	Has lower precision and accuracy than CMR ⁸⁰
Higher temporal resolution	Lower spatial resolution than CMR
Shorter scanning time	CMR enables comparison of strain with coregistered infarct characteristics
Significant contraindications to CMR ⁸¹	Study quality depends on good thoracic windows
Evidence base for echocardiography is stronger than with CMR ^{82–88} for post-STEMI strain assessment	...

CMR indicates cardiovascular magnetic resonance; and STEMI, ST-segment–elevation myocardial infarction.

limiting factor for the day-to-day assessment of strain in routine clinical practice.

Limitations and Lack of Data Showing Incremental Value of CMR-Derived Strain in Clinical Practice

Most of the CMR studies evaluating strain in patients with recent MI or SIHD have been limited by small sample size (usually ≤ 50 participants) and short durations of follow-up (< 1 year; Table 1; Table I in the Data Supplement). Few studies of strain imaging have described quality assurance parameters, for example, repeatability, and none have described the impact of treatment decisions based on strain values in relation to health outcomes.

Strain Derived from Echocardiography

Strain by speckle-tracking echocardiography is emerging as an alternative to LVEF and wall motion for the assessment of myocardial function (Table 2). Most of the echocardiographic literature relates to longitudinal strain because short-axis acoustic windows that would be necessary for circumferential strain are commonly limited.

In patients with recent STEMI, strain derived from speckle-tracking echocardiography predicts adverse remodeling,⁸² has the potential to assess viability,⁸³ and correlates with infarct size.^{84,85} Speckle-tracking echocardiography–derived global longitudinal strain has the potential to discriminate patients with obstructive CAD during stress^{86–88} or even at rest,^{86–88} reflecting the early consequences of the ischemic cascade on myocardial contractility.

Tissue Doppler imaging can be used to derive strain indirectly⁸⁹ based on tissue velocity measurements provided that the direction of myocardial motion is along the ultrasound probe scan lines. Speckle-tracking echocardiography makes use of speckle-generating targets,⁹⁰ which are tracked through the cardiac cycle. A variety of software options have emerged,⁹¹ leading to a lack of standardization.⁹² Because this technique tracks speckles from one frame to the next, the results are influenced by image quality, with reverberations and signal dropout distally being important issues. Because the speckles are generated by the interaction of reflected ultrasound off myocardial tissue, these speckles may not be stable,

because contracting myocardium changes the angle at which ultrasound waves are reflected and moving in and out of the plane of view, with related measurement errors.⁹¹

Three-dimensional speckle-tracking echocardiography is now available⁹³; however, measurement accuracy and precision are uncertain.⁹⁴ Disadvantages include a longer acquisition time, over multiple heartbeats, and a bulkier hand-held probe, making it reliant on good echo windows. The main advantage of 3D speckle tracking is that through-plane motion is discounted.

Echocardiography and CMR-Derived Strain

In an all-comers study of 106 patients, strain values estimated with speckle-tracking echocardiography and CMR-FT were moderately well correlated.⁹⁵ In patients with SIHD, regional circumferential strain revealed by tagging and speckle tracking are at best moderately correlated,⁵² but small sample size (n=23) limits firm conclusions. In a study of layer-specific myocardial deformation in 29 patients with ischemic cardiomyopathy, Altiok et al,⁴⁹ noted that endocardial strain (the inner half of the myocardium) by SENC was only weakly correlated ($r=0.50$; SE of the estimate=5.2%) with the magnitude of endocardial strain by 2D speckle-tracking echocardiography, and the magnitude of strain was underestimated by SENC as compared with echocardiography. The prognostic value of global longitudinal strain^{96–99} and global circumferential strain¹⁰⁰ as revealed by echocardiography in STEMI survivors is fairly well established.

Echocardiography is the standard of care in clinical practice because of its portability, lower cost, safety, and higher temporal resolution, when compared with CMR. Strain can also be retrospectively estimated from routinely acquired echocardiograms, provided image quality is sufficient. On the contrary, CMR has higher precision and accuracy than echocardiography,⁸⁰ is not limited by acoustic windows, and permits spatial registration of strain with infarct pathology.

Conclusions

We have conducted a systematic review of the literature on imaging myocardial strain in patients with coronary heart disease. For practical applications in the clinic, strain imaging with echocardiography and CMR are emerging options for the detection of early impairment in myocardial contractility before a reduction in global LVEF in patients with SIHD. In patients with borderline LVEF values, strain imaging may also be clinically useful to examine contractility in greater detail.

Multiple factors influence the decision to use echocardiography or CMR, not least cost and logistics. CMR offers the additional advantage of integrating myocardial function with pathology. On the basis of the available evidence, global circumferential strain has superior prognostic value compared with global longitudinal strain in post-MI patients.

Critically, strain imaging studies have been limited by design, that is, cross-sectional, small sample size, short duration of follow-up, lack of blinding, and, in prognostic studies, use of surrogate outcomes rather than hard health outcomes. Looking to the future, further studies should involve larger numbers of participants to increase precision. More information is needed on whether parameters of myocardial strain

have incremental prognostic value for the prediction of LV surrogate and health outcomes in post-MI patients, compared with standard imaging parameters. Should this be the case then strain imaging early post-MI may emerge as a new tool in the clinic and for measurement of surrogate outcomes in clinical trials.

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Disclosures

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