

Evaluation of Chronic Myocardial Ischemic Scarring Through Strain Analysis Derived from Cardiac Magnetic Resonance Feature Tracking: Review Article

Mohammed Mousa*¹, Islam Z. Mahmoud², Tarek H. Elkammash¹, Azza A. Gad¹, Radwa A. Noureldin¹

Departments of ¹Diagnostic and Interventional Radiology and

²Cardiovascular Medicine, Faculty of Medicine, Suez Canal University, Egypt

*Corresponding author: Mohammed Mousa, **Mobile:** (+20)01145674233, **Email:** m-a-mousa@live.com

ABSTRACT

Background: Despite improvements in medical treatment, ischemic heart disease (IHD) is still a major cause of death and disability worldwide. Among the most important diagnostic and therapeutic tools for IHD, cardiac magnetic resonance (CMR) offers detailed information about the structure, function, and viability of the heart muscle. Myocardial viability, function, and the presence of problems such as microvascular blockage and ventricular thrombi can be better understood with the use of CMR imaging techniques like cine imaging, late gadolinium enhancement (LGE), and perfusion imaging. Myocardial strain analysis, including feature tracking, quantifies myocardial deformation and provides sensitive and specific markers of ischemia and dysfunction. Strain analysis has demonstrated prognostic value in predicting adverse cardiac events.

Objective: This review aimed to summarize the current understanding of IHD pathophysiology, CMR techniques for IHD assessment, and the role of myocardial strain analysis in the evaluation of IHD.

Methods: Using the following keywords: Ischemic heart disease, cardiac magnetic resonance, myocardial strain, feature tracking and myocardial infarction were all searched through Science Direct, Google Scholar, and PubMed. The writers also reviewed relevant literature references, although they only included the most recent or comprehensive study. Documents in languages other than English have been excluded due to lack of translation sources. Unpublished papers, oral presentations, conference abstracts, dissertations, and other works that were outside the scope of large-scale scientific studies were excluded.

Conclusion: In order to properly assess and treat IHD, CMR is essential. The capacity of strain analysis to evaluate both local and systemic myocardial function provides important clues regarding the severity and prognosis of illness. Continued research and technological advancements will further enhance the clinical utility of CMR in optimizing the care of patients with IHD.

Keywords: Ischemic heart disease, Cardiac magnetic resonance, Myocardial strain, Feature tracking, Myocardial infarction.

ISCHEMIC HEART DISEASE

INTRODUCTION

The high rates of morbidity and mortality caused by IHD make it a major public health issue on a worldwide scale. The global economic impact of this major public health concern is substantial. An estimated 126.5 million instances of IHD have been reported globally, indicating a considerable frequency. In addition, IHD is still one of the leading causes of death worldwide, accounting for more than 9 million fatalities every year⁽¹⁾.

IHD is still a major killer of adults in industrialized countries, even though IHD mortality rates have dropped significantly in the last few decades due to effective public health campaigns and new therapeutic interventions like thrombolytic agents, early revascularization, angiotensin-converting enzyme inhibitors, and beta-blockers. In addition, the incidence of IHD is expected to keep climbing⁽²⁾.

Survivors of an initial acute myocardial infarction (MI) exhibit an increased risk of subsequent mortality from IHD, primarily attributed to the development of heart failure and late cardiac events. Furthermore, the escalating average lifespan within the population will likely contribute to an increased incidence of cardiovascular disease and a corresponding rise in heart disease-related mortality. Other significant contributors to the growing prevalence of IHD include a rising

incidence of type 2 diabetes, a decline in physical activity levels, and an increase in obesity rates^(2,3). The escalating prevalence of IHD necessitates a judicious and resource-conscious approach to both diagnostic and therapeutic interventions. A critical challenge in this context lies in the establishment and ongoing refinement of appropriateness criteria for cardiac imaging modalities^(1,2).

In the last twenty years, MRI has become an essential tool for diagnosing and predicting the prognosis of IHD in both clinical and preclinical settings⁽⁴⁾.

Pathophysiology

Coronary artery disease (CAD) is the main cause of IHD because atherosclerosis can narrow the coronary arteries, which provide blood to the heart⁽⁵⁾. Plaque rupture, thrombosis, myocardial dysfunction, and necrosis are the hallmarks of the acute coronary syndromes and chronic stable angina that make up the spectrum of disorders known as CAD⁽⁵⁾. If left untreated, myocardial ischemia sets off a chain reaction that, if left unchecked, can cause cell death⁽⁵⁾. The amount of myocardial necrosis is affected by variables such as the length and intensity of ischemia, the amount of blood flow that remains after the ischemia has ended, and the demand for oxygen by the heart muscle⁽²⁾. Timely reperfusion strategies, such as primary

percutaneous coronary intervention (PCI), are crucial to salvage viable myocardium and limit infarct size ⁽²⁾. However, reperfusion itself can induce myocardial reperfusion injury, contributing to microvascular obstruction and adverse outcomes ^(6,7).

Post-infarction left ventricular (LV) remodeling involves a complex interplay of acute and chronic changes, including infarct expansion, scar formation, and LV dilatation ^(8,9). These changes can lead to adverse LV remodeling, a significant determinant of long-term prognosis and the development of heart failure ⁽⁹⁾. Recognizing different patterns of myocardial dysfunction, such as stunned myocardium, hibernating myocardium, and areas of irreversible necrosis, is crucial for optimizing therapeutic interventions and improving patient outcomes ^(6,10).

The concept of "ischemic preconditioning" highlights the heart's ability to adapt to brief ischemic episodes, providing a degree of protection against subsequent, more prolonged ischemia ⁽¹⁾. Differentiating between viable and nonviable myocardium, particularly in patients with chronic CAD, is crucial for guiding therapeutic decisions, such as choosing between PCI and coronary artery bypass grafting (CABG) ⁽⁶⁾.

CMR evaluation of IHD

Cardiac magnetic resonance (CMR) has emerged as a valuable tool for the comprehensive evaluation of IHD, offering a multiparametric approach that encompasses functional assessment, myocardial tissue characterization, and the detection of complications ⁽¹¹⁾. CMR utilizes various techniques, including cine imaging for functional assessment, late gadolinium enhancement (LGE) for identifying myocardial fibrosis, and T2-weighted imaging for detecting myocardial edema. Furthermore, first-pass perfusion imaging with vasodilators allows for the assessment of inducible ischemia and the detection of microvascular obstruction (MVO) ⁽¹²⁾.

In order to better understand acute myocardial damage, CMR imaging with early gadolinium enhancement (EGE) is quite beneficial. Microvascular occlusion (MVO) and ventricular thrombi are two conditions that can be detected by electrocardiogram (ECG) as perfusion deficiencies inside the perfused myocardium ⁽¹³⁾.

In the acute phase of IHD, LGE on CMR imaging shows areas of increased extracellular space, which reflects myocardial edema and necrosis. In the chronic phase, LGE transitions is good identifier to myocardial fibrosis ⁽¹³⁾. Depending on the region of the coronary arteries that are affected, ischemic left ventricular end-ejection (LGE) tends to be distributed either subendocardially or transmurally. When measuring myocardial viability, the amount of fibrosis, as measured by LGE, is of the utmost importance. Functional compromise becomes apparent when the fibrosis surpasses 50%, and especially when it approaches 75% ⁽¹¹⁾.

Areas with weak signals within LGE regions denote MVO. Within hours following an acute ischemia event, MVO becomes observable. Its measurement and quantification are most effective between 2 and 9 days after the event, when it reaches a plateau ⁽¹³⁾. Scar thickness at 6 months is inversely proportional to the severity of MVO ⁽¹¹⁾. Unfavorable remodeling and worse prognosis are two outcomes that can be predicted independently by myocardial bleeding and myocardial vein occlusion (MVO) ⁽¹⁴⁻¹⁶⁾.

Advantages of CMR imaging over other imaging modalities include better spatial resolution, more accurate evaluation of biventricular function, and more exact characterization of myocardial scar and viability ⁽¹⁷⁾. When evaluating inducible ischemia, studies have shown that CMR has a better diagnostic accuracy than single-photon emission computerized tomography (SPECT) ⁽¹⁸⁻²¹⁾. Patients at increased risk for arrhythmias may also be identified by the presence of severe LGE, especially perilesional fibrosis ⁽¹¹⁾.

When evaluating individuals with suspected or confirmed IHD, stress CMR is highly recommended by international guidelines. For individuals with an intermediate illness likelihood, stress CMR should be performed as a first-line diagnostic test, according to the 2013 ESC guidelines ⁽²²⁾. Stress CMR is becoming more and more acknowledged as a useful tool for risk stratification and directing therapeutic decision-making, even though exercise testing and SPECT are preferred by American standards ⁽²³⁾.

Studies such as CE-MARC and MR-IMPACT II have demonstrated the clinical utility of stress CMR, highlighting its potential to reduce the need for unnecessary coronary angiography and improve patient outcomes ^(18,19,24).

Myocardial strain analysis

The strain on the myocardium is a measure of the tissue's deformation throughout the cardiac cycle, which is caused by variations in the fibers' length, thickness, and orientation ⁽²⁵⁾. The relative change in tissue length or thickness between the end-diastolic and end-systolic states is called Lagrangian strain ⁽²⁵⁾, and it is the most widely used measure. Negative values are ascribed to shortening, thinning, and counterclockwise rotation, and positive values to thickening and clockwise rotation, according to convention ⁽²⁶⁾.

The complex three-dimensional motion of the myocardium involves distinct strain patterns. Myocardial fibers exhibit a helical orientation, with subepicardial fibers oriented left-handedly, subendocardial fibers oriented right-handedly, and mid-myocardial fibers oriented circumferentially ^(26,27). Longitudinal strain reflects shortening along the long axis of the heart, circumferential strain reflects shortening around the circumference, and radial strain reflects thickening of the ventricular wall ⁽²⁶⁾.

Ventricular torsion, a key aspect of myocardial function, arises from the opposing rotational movements of subepicardial and subendocardial fibers.

Twist angle, defined as the difference in rotational angles between the base and apex, is a commonly used measure of torsion^(28, 29). Torsion can also be described as the circumferential-longitudinal shear angle between short-axis slices⁽²⁹⁾.

Feature tracking

A modern CMR strain method, feature tracking (FT) examines steadily state free precession (SSFP) cine pictures that are recorded routinely. Following the principles of optical flow, FT uses maximum likelihood algorithms to trace the displacement of tiny tissue areas between consecutive frames⁽³⁰⁾. For precise tracking, you need high-resolution photos that can pick up on even the most minute changes in tissue mobility⁽³⁰⁾.

First, the endocardial and epicardial borders are manually or automatically delineated on cine pictures. Then, these outlines are propagated throughout the cardiac cycle for the FT analysis⁽³⁰⁾. You can measure longitudinal strain by looking at it from the long axis, circumferential strain from the short axis, and radial strain by combining the two. By using three-dimensional FT, all three strain components may be estimated at the same time⁽³⁰⁾.

Accelerating FT analysis can be achieved through post-processing using artificial intelligence approaches. Nevertheless, FT has certain limitations. One of these is that it may not be able to catch fast cardiac events as well as echocardiography due to its poorer temporal resolution. While FT does a good job of differentiating between the endocardial and epicardial boundaries, the small pixel sizes make it difficult to precisely follow features inside the myocardium. Further sources of artefacts include blood movement close to the endocardium and 2D acquisitions with through-plane motion⁽³⁰⁾.

Strain Analysis in Ischemic Heart Disease

Circumferential strain in particular is an extremely sensitive indicator of myocardial ischemia. It has been shown that CMR-based feature tracking (FT) can identify ischemia segments with impaired circumferential strain. Without stress agents or intrusive procedures, techniques like myocardial tagging and single-beat fast-Strength-encoded imaging (SENC) with global longitudinal strain (GLS) and global circumferential strain (GCS) have demonstrated potential in diagnosing myocardial ischemia. When it comes to myocardial infarction, strain measures are really helpful. The degree of myocardial injury is strongly associated with strain, which correlates directly with infarct size and inversely with risk area. Strain analysis also outperforms wall thickness measurements in distinguishing between transmural and subendocardial infarctions. In addition, strain can detect functionally intact segments during myocardial infarction, which may indicate a chance of recovery. Strain analysis has emerged as a powerful prognostic marker in IHD. It has demonstrated superior predictive

value for major adverse cardiac events compared to traditional risk factors such as left ventricular ejection fraction, infarct size, and microvascular obstruction⁽³⁰⁾.

CONCLUSION

This review highlighted the critical role of CMR in the evaluation and management of patients with IHD. From assessing myocardial viability and detecting complications such as microvascular obstruction and ventricular thrombi for quantifying the extent of myocardial fibrosis and guiding therapeutic decisions, CMR provides invaluable insights into the pathophysiology and progression of IHD. Strain analysis, a powerful tool within the CMR armamentarium, offers unique advantages. By quantifying myocardial deformation, strain provides a good marker of myocardial ischemia and dysfunction. Techniques such as feature tracking have shown promise in diagnosis, risk stratification, and prognostication in patients with IHD. Still, we need further studies to standardize and improve CMR methods, to find the best ways to take pictures, and to create reliable algorithms for automated analysis. Improving the accuracy, efficiency, and therapeutic value of CMR in the management of IHD will depend heavily on continued breakthroughs in artificial intelligence and machine learning.

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REFERENCES

1. **Khan M, Hashim M, Mustafa H et al. (2020):** Global Epidemiology of Ischemic Heart Disease: Results from the Global Burden of Disease Study. *Cureus*, 12 (7): e9349. doi: 10.7759/cureus.9349.
2. **Lippi G, Franchini M, Cervellin G (2013):** Diagnosis and management of ischemic heart disease. In: *Seminars in thrombosis and hemostasis*. *Semin Thromb Hemost.*, 39 (2): 202-13.
3. **Antman E, Braunwald E (2020):** Managing stable ischemic heart disease. Vol. 382, *New England Journal of Medicine*. Mass Medical Soc., 20: 1468-70.
4. **Buffa V, Di Renzi P (2020):** CMR in the diagnosis of ischemic heart disease. *Radiol Med.*, 125 (11): 1114-23.
5. **Marzilli M, Merz C, Boden W et al. (2012):** Obstructive coronary atherosclerosis and ischemic heart disease: an elusive link! *J Am Coll Cardiol.*, 60 (11): 951-6.
6. **Kloner R (2020):** Stunned and Hibernating Myocardium: Where Are We Nearly 4 Decades Later? *J Am Heart Assoc.*, 9(3):e015502. Kloner R (2020): Stunned and Hibernating Myocardium: Where Are We Nearly 4 Decades Later? *J Am Heart Assoc.*, 9 (3): e015502.
7. **Futterman L, Lemberg L (2000):** Hibernating myocardium, stunning, ischemic preconditioning: clinical relevance. *Am J Crit Care*, 9 (6): 430-6.
8. **Anzai T (2013):** Post-infarction inflammation and left ventricular remodeling: a double-edged sword. *Circ J.*, 77 (3): 580-7.

9. **Taylor A, Chan W (2015):** Post-Infarction LV Remodeling: Remote Changes Do Not Necessarily Occur Remotely From Time of Infarction. *JACC Cardiovascular Imaging*, 8 (7): 790-792
10. **Heusch G, Schulz R (2017):** Characterization of hibernating and stunned myocardium. *Eur Heart J.*, 18: 102–10.
11. **Baritussio A, Scatteia A, Bucciarelli-Ducci C (2018):** Role of cardiovascular magnetic resonance in acute and chronic ischemic heart disease. *Int J Cardiovasc Imaging*, 34 (1): 67–80.
12. **Motwani M, Swoboda P, Plein S et al. (2018):** Role of cardiovascular magnetic resonance in the management of patients with stable coronary artery disease. *Heart*, 104 (11): 888–94.
13. **Beek A, van Rossum A (2010):** Cardiovascular magnetic resonance imaging in patients with acute myocardial infarction. *Heart*, 96 (3): 237–43.
14. **Romero J, Lupercio F, Diaz J et al. (2016):** Microvascular obstruction detected by cardiac MRI after AMI for the prediction of LV remodeling and MACE: a meta-analysis of prospective trials. *Int J Cardiol.*, 202: 344–8.
15. **Kidambi A, Mather A, Motwani M et al. (2013):** The effect of microvascular obstruction and intramyocardial hemorrhage on contractile recovery in reperfused myocardial infarction: insights from cardiovascular magnetic resonance. *J Cardiovasc Magn Reson.*, 15 (1): 1–9.
16. **Husser O, Monmeneu J, Sanchis J et al. (2013):** Cardiovascular magnetic resonance-derived intramyocardial hemorrhage after STEMI: influence on long-term prognosis, adverse left ventricular remodeling and relationship with microvascular obstruction. *Int J Cardiol.*, 167 (5): 2047–54.
17. **Imazio M, Andriani M, Bondoni L et al. (2019):** Learning Cardiac Magnetic Resonance - A Case Based Guide. Springer, Pp: 99-115. DOI:10.1007/978-3-030-11608-8
18. **Greenwood J, Maredia N, Younger J et al. (2012):** Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. *Lancet*, 379 (9814): 453–60.
19. **Schwitzer J, Wacker C, Wilke N et al. (2012):** Superior diagnostic performance of perfusion-cardiovascular magnetic resonance versus SPECT to detect coronary artery disease: The secondary endpoints of the multicenter multivendor MR-IMPACT II (Magnetic Resonance Imaging for Myocardial Perfusion Assessm. *J Cardiovasc Magn Reson.*, 14 (1): 1–10.
20. **Jaarsma C, Leiner T, Bekkers S et al. (2012):** Diagnostic performance of noninvasive myocardial perfusion imaging using single-photon emission computed tomography, cardiac magnetic resonance, and positron emission tomography imaging for the detection of obstructive coronary artery disease: a meta-anal. *J Am Coll Cardiol.*, 59 (19): 1719–28.
21. **Li M, Zhou T, Yang L et al. (2014):** Diagnostic accuracy of myocardial magnetic resonance perfusion to diagnose ischemic stenosis with fractional flow reserve as reference: systematic review and meta-analysis. *JACC Cardiovasc Imaging*, 7 (11): 1098–105.
22. **Montalescot G, Sechtem U, Achenbach S et al. (2014):** 2013 ESC guidelines on the management of stable coronary artery disease. *Türk Kardiyol Derneği Arşivi.*, 42: 73–134.
23. **Alfakih K, Greenwood J, Plein S (2017):** The 2016 update to NICE CG95 guideline for the investigation of new onset stable chest pain: More innovation, but at a cost? *Clin Med.*, 17 (3): 209-11.
24. **Greenwood J, Ripley D, Berry C et al. (2016):** Effect of care guided by cardiovascular magnetic resonance, myocardial perfusion scintigraphy, or NICE guidelines on subsequent unnecessary angiography rates: the CE-MARC 2 randomized clinical trial. *JAMA.*, 316 (10): 1051–60.
25. **Amzulescu M, De Craene M, Langet H et al. (2019):** Myocardial strain imaging: review of general principles, validation, and sources of discrepancies. *Eur Hear Journal-Cardiovascular Imaging*, 20 (6): 605–19.
26. **Zhang X, Haynes P, Campbell K et al. (2015):** Numerical evaluation of myofiber orientation and transmural contractile strength on left ventricular function. *J Biomech Eng.*, 137 (4): 44502. doi: 10.1115/1.4028990.
27. **Torrent-Guasp F, Kocica M, Corno A et al. (2004):** Systolic ventricular filling. *Eur J cardio-thoracic Surg.*, 25 (3): 376–86.
28. **Scatteia A, Baritussio A, Bucciarelli-Ducci C (2017):** Strain imaging using cardiac magnetic resonance. *Heart Fail Rev.*, 22: 465–76.
29. **Rüssel I, Tecelão S, Kuijjer J et al. (2009):** Comparison of 2D and 3D calculation of left ventricular torsion as circumferential-longitudinal shear angle using cardiovascular magnetic resonance tagging. *J Cardiovasc Magn Reson.*, 11 (1): 1–7.
30. **Schuster A, Hor K, Kowallick J et al. (2016):** Cardiovascular magnetic resonance myocardial feature tracking: concepts and clinical applications. *Circ Cardiovasc Imaging*, 9 (4): e004077. doi: 10.1161/CIRCIMAGING.115.004077.