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Cardiac magnetic resonance assessment of diastolic dysfunction in acute coronary syndrome

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Abstract

Chest pain is an important presenting symptom. However, few cases of chest pain are diagnosed as acute coronary syndrome (ACS) in the acute setting. This results in frequent inappropriate discharge and major delay in treatment for patients with underlying ACS. The conventional methods of assessing ACS, which include electrocardiography and serological markers of infarct, can take time to manifest. Recent studies have investigated more sensitive and specific imaging modalities that can be used. Diastolic dysfunction occurs early following coronary artery occlusion and its detection is useful in confirming the diagnosis, risk stratification, and prognosis post-ACS. Cardiac magnetic resonance provides a single imaging modality for comprehensive evaluation of chest pain in the acute setting. In particular, cardiac magnetic resonance has many imaging techniques that assess diastolic dysfunction post-coronary artery occlusion. Techniques such as measurement of left atrial size, mitral inflow, and mitral annular and pulmonary vein flow velocities with phase-contrast imaging enable general assessment of ventricular diastolic function. More novel imaging techniques, such as T2-weighted imaging for oedema, T1 mapping, and myocardial tagging, allow early determination of regional diastolic dysfunction and oedema. These findings may correspond to specific infarcted arteries that may be used to tailor eventual percutaneous coronary artery intervention.

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Introduction

Chest pain is the most important presenting symptom of coronary artery disease (CAD). However, only 15%–20% of patients with chest pain are diagnosed with acute coronary syndrome (ACS) based on an electrocardiogram (ECG) and cardiac enzyme (CE) levels at presentation.[1] This lack of diagnosis is predominantly due to the delay in pathophysiological manifestation of ACS, from arterial occlusion to overt ECG and/or a rise in CE. The consequences are manifold and up to 10% of patients with eventual myocardial infarction (MI) are misdiagnosed and inappropriately sent home.[2] This also results in a major delay in treatment and inadequate risk stratification of patients, eventually resulting in progression to MI and/or complications arising from MI.

Therefore, there is an urgent need for a simple, but efficacious, investigative modality that enables rapid assessment, diagnosis, and risk stratification of ACS in patients presenting to the emergency department with chest pain. In the last 20 years, there has been an evolutionary shift in research and funding away from conventional investigations, such as ECG and CE measurement, towards cardiovascular imaging tools, such as echocardiography. More recently, computed tomography (CT)- and magnetic resonance imaging (MRI)-based investigative modalities have been used to diagnose ACS.[3]

ACS

ACS refers to a variety of clinical presentations ranging from unstable angina to MI. These presentations result from underlying myocardial ischaemia subsequent to acute thrombosis induced by a ruptured coronary artery plaque.[4–7] The main impediment to rapid and accurate assessment, diagnosis, and risk stratification of ACS is the apparent lag between coronary artery occlusion and manifestation of symptoms. This is complicated by the heterogeneous nature of the clinical presentation itself.

Within 10 to 20 seconds following coronary artery occlusion, the myocardial relaxation time begins to shorten, resulting in diastolic dysfunction and a rise in left ventricular (LV) end-diastolic pressure. Wall motion abnormalities then occur 15 to 30 seconds later, followed by a fall in LV ejection fraction. Subsequently, electrical signs and ischaemic symptoms may begin to manifest (Figure 1).[3,8] However, these manifested symptoms are also dependent on the patients' age, sex, and any underlying comorbidities, such diabetes mellitus, which may delay and/or attenuate the symptoms.

The earliest detectable abnormality in ACS is either a reduction or cessation of coronary blood flow and altered myocardial perfusion. This has been the subject of many studies on the use of rest and/or stress myocardial perfusion imaging using single-photon emission CT, positron emission tomography, and cardiac magnetic resonance (CMR).[9–14] These imaging modalities provide a high negative predictive value in patients with suspected ACS. Unfortunately, CT-based imaging techniques involve the use of radionuclide perfusion agents and the cost of setting up an acute perfusion imaging service in the emergency department is prohibitive. There is also a lack of sufficient diagnostic and prognostic data for greater use of CMR perfusion imaging in the emergency setting.[3–5]

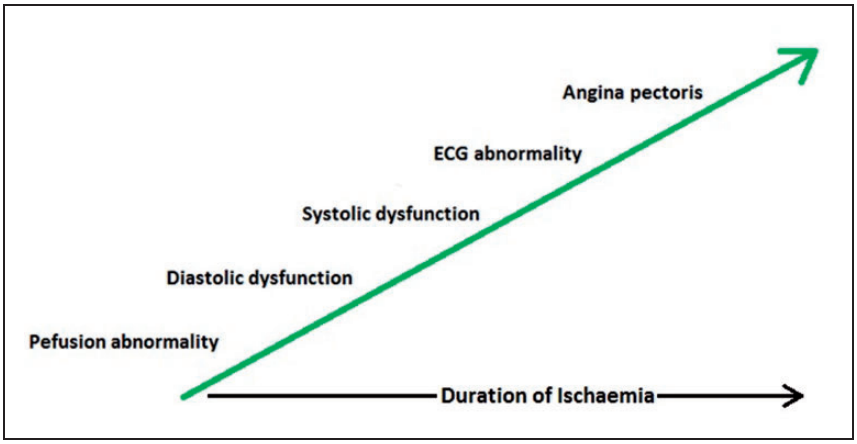

Figure 1. Cascade of events following coronary artery occlusion (adapted from Gani F et al., 2007)

Diastolic dysfunction

Ventricular relaxation during diastole is an active process that is related to calcium uptake from contracted myocytes. Normal relaxation allows the left ventricle to fill at rest and during exercise without an increase in end-diastolic pressure. Diastolic dysfunction occurs when there is ischaemia-induced abnormality in LV relaxation and compliance.[15]

Assessment of diastolic dysfunction post-ACS is important because it is correlated with infarct size, confers a higher risk of mortality, and is associated with a poorer prognosis, independent of LV systolic function.[16–19] Furthermore, in the acute setting, diastolic dysfunction portends a higher likelihood of progression to MI in the absence of any electrocardiographic or serological evidence of coronary artery occlusion, which occurs later in the temporal cascade of events.[14–16]

The typical assessment modality for diastolic dysfunction is echocardiography. Echocardiography is usually performed prior to discharge to identify patients at higher risk of complications, and thus a poorer prognosis, to enable optimization of treatment. Therefore, although echocardiography is relatively inexpensive and easy to use, its use in the acute setting of assessment of ACS is limited. The main limitations to echocardiography are anatomical, reduced endocardial definition, inter-observer variability, and lack of tissue characterization.

An advantage of CMR is that it can potentially provide relevant incremental information during the acute assessment stage. CMR provides the possibility of accurately diagnosing ACS, eliminating potential differentials, and risk-stratifying patients with a single investigative modality. This in turn affects management and reduces time wastage, unwarranted referrals, and inappropriate discharge.

CMR imaging

In the emergency department, the difficulty in managing patients with chest pain is accurate early diagnosis and early, efficacious institution of treatment. CMR imaging offers high spatial resolution, enabling a detailed volume and functional assessment. Early diastolic dysfunction, which indicates the presence of

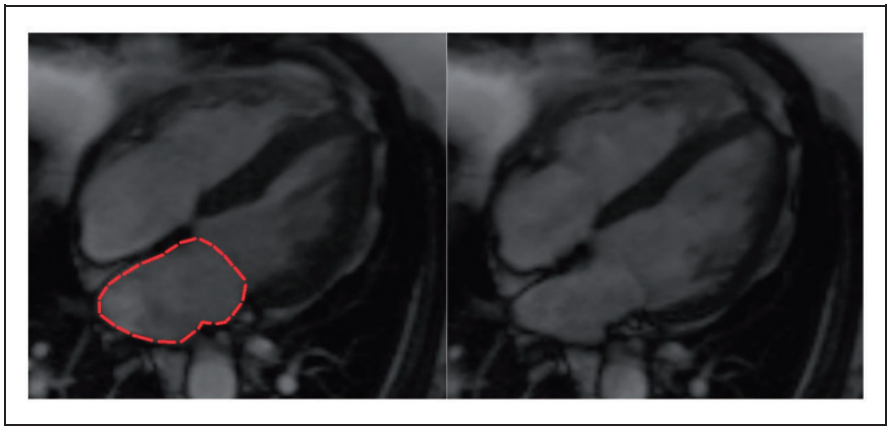

Figure 2. Planimetry is performed by manually tracing the LA endocardial wall at end-systole of a cine sequence (left image: end-systole, right image: end-diastole)

significant CAD, can then be coupled with late gadolinium enhancement imaging for excellent tissue characterization, and permits exceptional prognostic capacity. CMR techniques are able to provide a more accurate diagnosis of ACS compared with standard clinical assessment. Furthermore, the use of new imaging techniques, such as T2-weighted sequences for detection of oedema and T1 mapping, can be extended to patients with an intermediate to high risk for ACS.[14,20,21]

Assessment of diastolic function

Initial rest cine MRI uses steady-state free precession (SSFP) sequences to acquire a series of consecutive, breath-hold, long- and short-axis slices. These are used for assessment of ventricular wall motion, ventricular volume, ejection fraction, myocardial mass, and anatomy of extracardiac structures.

Left atrial size

The left atrium (LA) is directly affected by LV filling pressure and is a reliable indicator of the duration and severity of diastolic dysfunction.[22] Chronic elevation in LV filling pressure results in LA dilatation and this is associated with an increased risk of death post-ACS.[23–25] ACS may also affect atrial function by direct ischaemic injury.[26] In the clinical setting, although LA volume is a better prognostic indicator, LA diameter and area are simpler to acquire, and thus easily measured.[27]

The LA is visualized in the horizontal long-axis view (four-chamber view), at maximal size during end-systole, and just prior to opening of the mitral valve. Planimetry is performed by manually tracing the LA endocardial wall at end-systole of a cine sequence (SSFP) (Figure 2). The SSFP technique is used because it enables excellent contrast and good image quality.[27] The LA is dilated when the planimetry area is greater than 24 cm^2.[27,28]

Transmitral flow

Transmitral (TM) flow represents an immediate indicator of the filling gradient between the LA and LV. TM flow is normally assessed via transthoracic echocardiography (TTE), which records the filling pattern from which the degree of diastolic dysfunction is inferred. CMR uses through-plane, phase-contrast, velocity-encoded imaging to determine TM velocities.

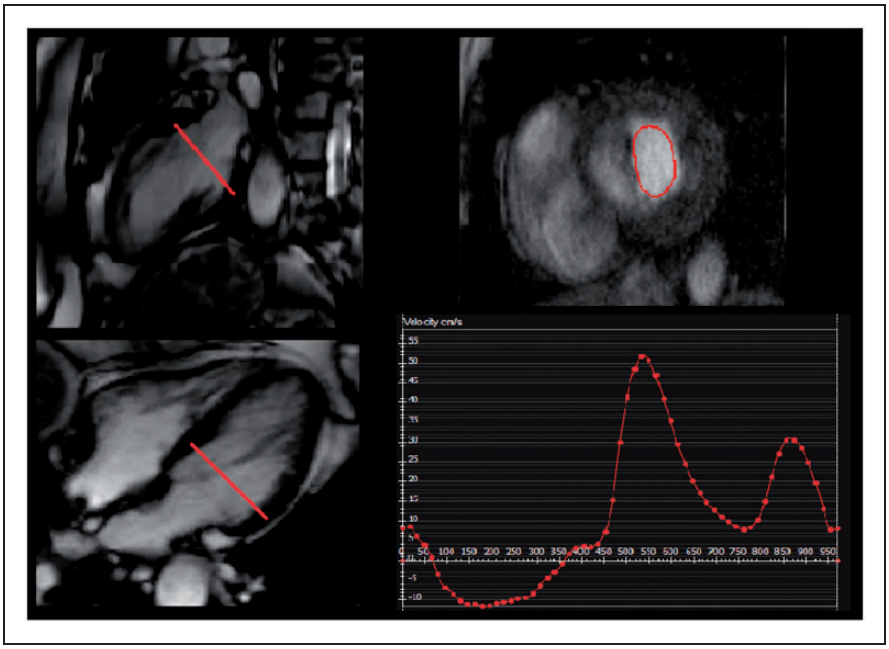

Figure 3. Cross-sectional MV inflow requires positioning of the sample plane along the tips of the MV in at least two orthogonal planes

Phase-contrast imaging is a validated technique for evaluating velocity, the velocity gradient, volume, and the pattern of blood flow.[29,30] Although CMR-based phase-contrast imaging underestimates peak mitral E (early diastolic) and A (atrial contraction) velocities compared with TTE, the linear correlation between the two modalities is excellent.[31–33]

To acquire cross-sectional TM flow, an imaging plane is planned parallel to the mitral annular plane at the level of the mitral leaflet tips from the LV outflow tract, vertical long-axis, or horizontal long-axis views (Figure 3). Phase-contrast, velocity-encoded data sets are then acquired with the velocity sensitivity set at 150 cm/s. A region of interest is manually drawn on one frame to encircle the cross-section of mitral valve (MV) leaflets as previously described.[34,35] This is then propagated using a semi-automated contouring mode with manual override, yielding maximum velocity versus time graphs (Figure 3).

Pulmonary vein flow

Pulmonary venous (PV) flow wave form analysis is an important tool for evaluating LV diastolic function. The PV flow wave form is affected by LV filling and compliance, LA preload, and contractility.[36] The main utility of measuring the PV wave form is that it is useful in differentiating between normal and pseudo-normal TM flow patterns.[37,38]

Although there is no dedicated processing tool for PV flow, its wave form when compared with the TM flow pattern and LA area ensures optimal assessment of diastolic dysfunction in the acute setting. Furthermore, assessment of PV flow in CMR is almost guaranteed when compared with TTE assessment of PV flow. Assessment

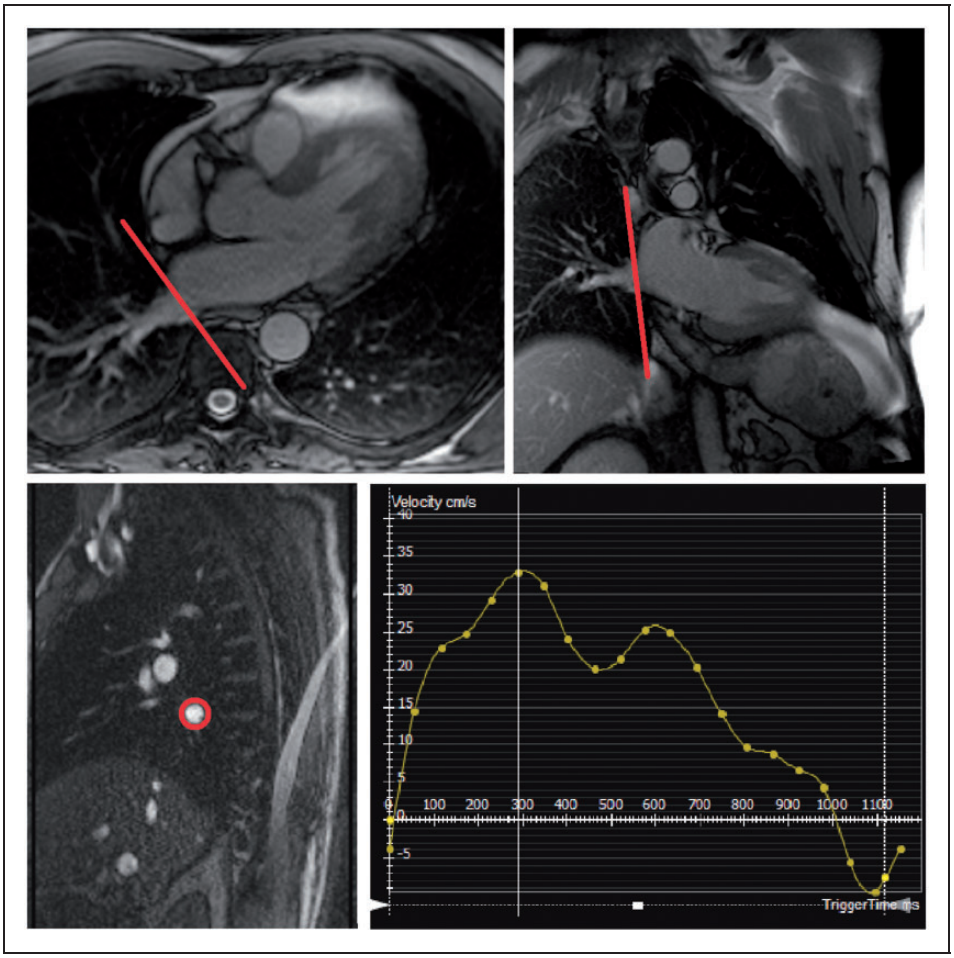

Figure 4. Cross-sectional PV flow acquisition sequences and luminal region of interest, and resultant velocity versus time graph

of PV flow by TTE is only achievable in approximately 60% of cases because of anatomical and physical restrictions in attaining optimal views. Moreover, there is good correlation between TTE and CMR techniques for assessment of PV flow.[34,37]

Cross-sectional PV flow is acquired by placing an imaging plane 0.5 to 1 cm distal to the ostium, and perpendicular to the level of the right superior PV.[39,40] A region of interest is then manually drawn on one frame to encircle the lumen of the PV and it is then propagated using a semi-automated contouring mode with manual override. This then yields the familiar velocity curve over time (Figure 4). Diastolic dysfunction can then be classified into four grades based on the E/A and S/D wave forms (Figure 5).

Myocardial tissue phase-contrast imaging

Tissue phase-contrast imaging is the CMR equivalent of TTE-based tissue Doppler imaging (TDI).[41,42] Mitral annular velocity measurement by tissue phase-contrast imaging represents the rate of change in the LV

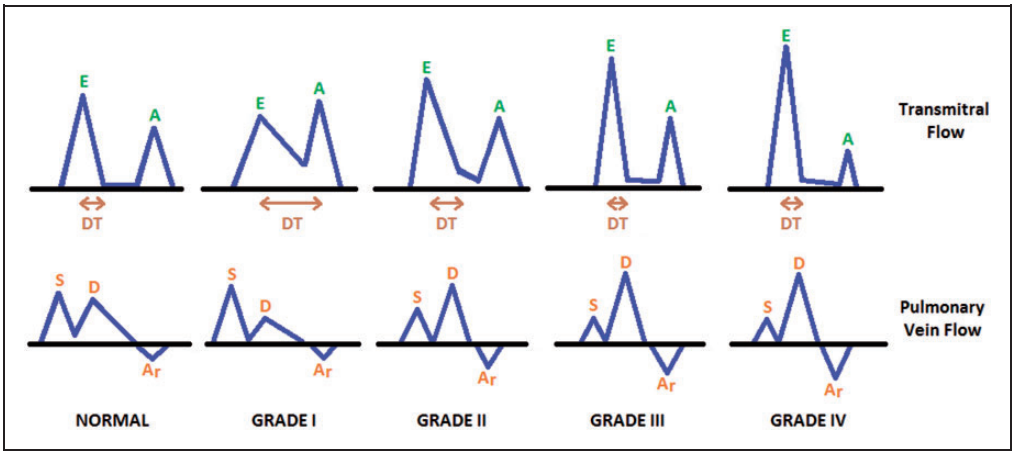

Figure 5. Classification of diastolic dysfunction grades (I–IV) E - early diastolic flow, A - atrial or late diastolic flow, DT- deceleration time, S - systolic flow, D - diastolic flow, Ar - atrial reversal flow.

long-axis dimension and impaired relaxation results in a reduced early mitral annular velocity (e′). The ratio of early TM flow velocity (E) to early diastolic mitral annular velocity (E/e′) accurately predicts elevated LV filling pressure.[42,43] An E/e′ ratio of > 15 has been shown to be a strong predictor of decreased survival after acute ACS.[44] CMR-derived E/e′ is also well correlated with TDI and pulmonary capillary wedge pressure measurements.[39,45]

To acquire mitral annular velocity, an imaging plane is planned perpendicular to the LV base from the vertical long-axis and horizontal long-axis views. Phase-contrast, velocity-encoded data sets are then acquired with the velocity sensitivity set at 30 cm/s. A region of interest is manually drawn on one frame to encircle the inferior septal basal region, which is then propagated, yielding maximum velocity versus time graphs (Figure 6).[45]

Myocardial tagging

Myocardial tagging involves placement of a grid of radiofrequency tags on the myocardium, which then distorts with myocardial movement during systole and diastole.[46,47] The deformation and displacement of these radiofrequency tags allows comprehensive analysis of diastolic strain and strain rate with good temporal and spatial resolution.[48–50] The LV strain rate and torsion recovery rate directly reflect diastolic dysfunction. More importantly, myocardial tagging enables accurate assessment of regional diastolic dysfunction and has shown delayed infarction, hibernating myocardium, and transmural ischaemia.[51]

Late gadolinium enhancement imaging is acquired via inversion-recovery segmented gradient echo T1-weighted sequences. Three sequential short-axis slices (basal, mid, and distal) are then obtained with six segments per slice corresponding to the coronary territory. Sequential grid-tagged images with identical slice positions are obtained using a two-dimensional turbo field-echo sequence with rest grid pulse for myocardial strain analyses, as previously described (Figure 7).[49,52]

Harmonic phase analysis is used by placing a mesh around the epicardial and endocardial contours of the LV short-axis slices in each phase of the cardiac cycle (Figure 8). Lagrangian circumferential shortening strain is then computed, yielding

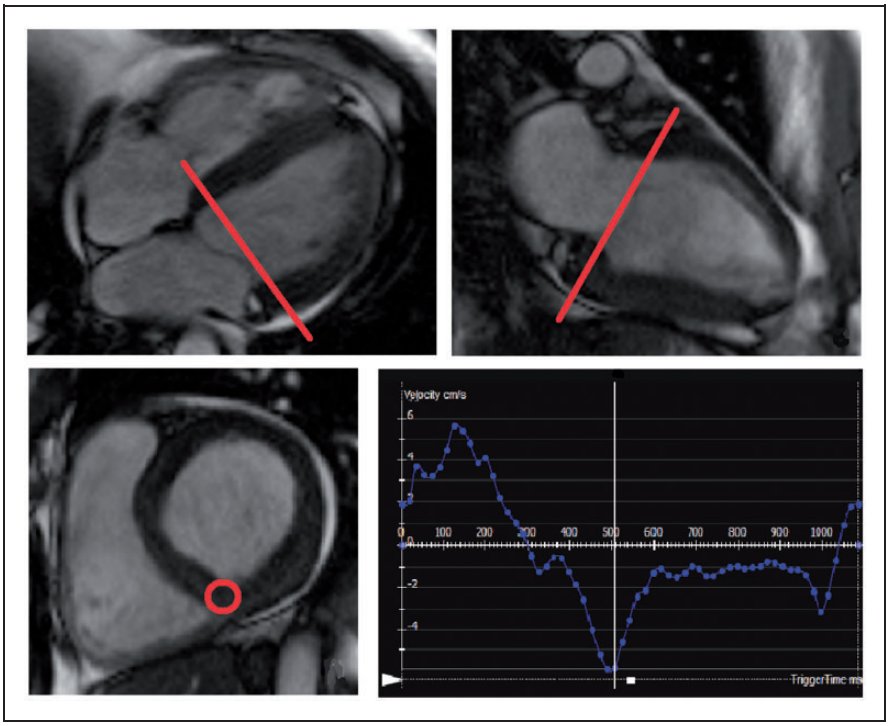

Figure 6. Cross-sectional mitral annular velocity measurement requires positioning of the sample plane perpendicular to the LV base in at least two orthogonal planes

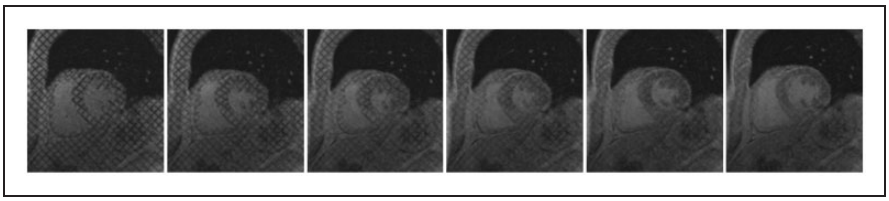

Figure 7. Sequential grid-tagged images showing LV deformation during systole and diastole

time-strain curves (Figure 9). Peak diastolic strain (%) and strain rate (1/s) are then used for assessment of diastolic LV deformation.

Future direction and prospects for clinical studies

The use of phase-contrast imaging for flow assessment, myocardial tissue phase-contrast imaging, and myocardial tagging is gaining greater recognition and proving to be helpful for assessing of diastolic dysfunction by CMR. Moreover, detection of diastolic dysfunction in the setting of acute chest pain in patients with a moderate to high risk of CAD should indicate the need for further imaging sequences to adequately rule out CAD.

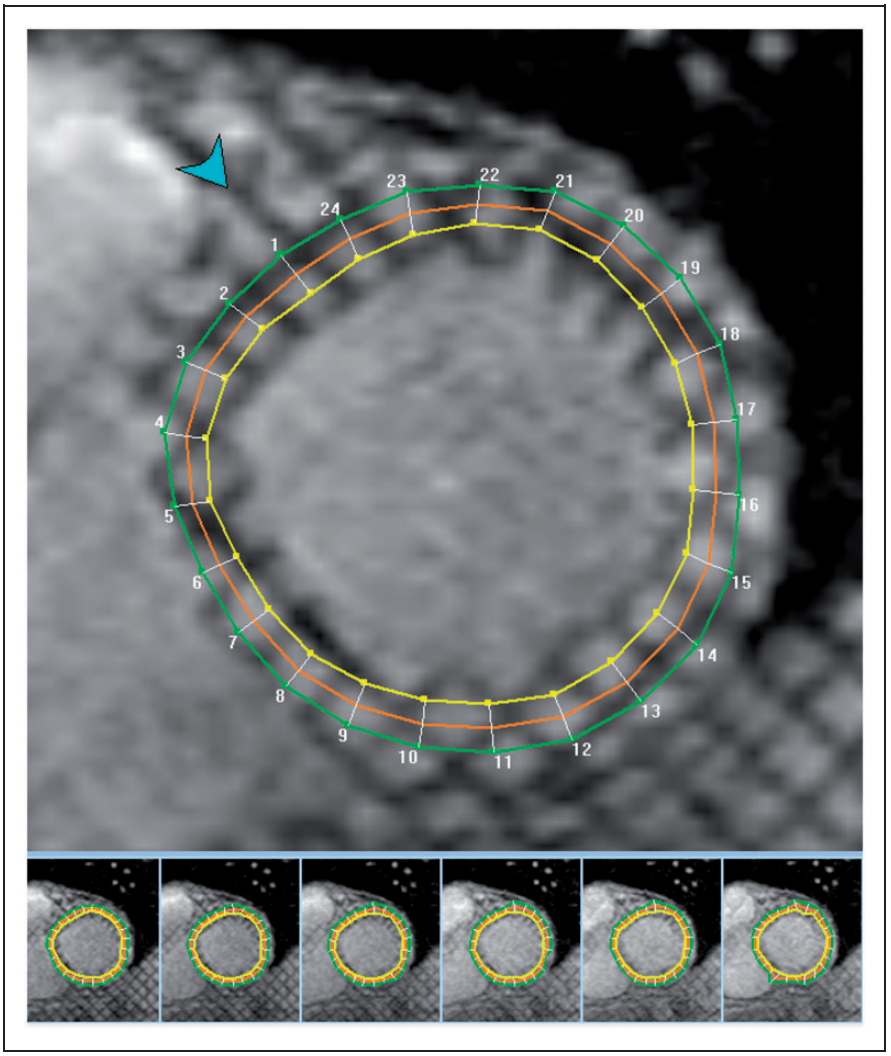

Figure 8. A mesh is placed around the epicardial and endocardial contours of the LV short-axis slices in each phase of the cardiac cycle

Other novel imaging sequences include T2-weighted imaging for oedema or haemorrhage and T1 relaxation times with modified look-locker imaging. T2-weighted imaging using T2-short Tau inversion recovery (T2-STIR) is able to detect small changes in tissue composition of unbound intracellular water following an acute ischaemic event.[53,54] These changes can be detected as early as 20 minutes following ischaemic injury and enable differentiation between acute and chronic myocardial infarcts compared with delayed gadolinium enhancement.[55] T1 mapping allows accurate and reliable voxel-by-voxel mapping of infarcted myocardium. This obviates the need for delayed gadolinium enhancement and enables CMR use in patients who are otherwise contraindicated to gadolinium infusion.[56,57] These two novel imaging

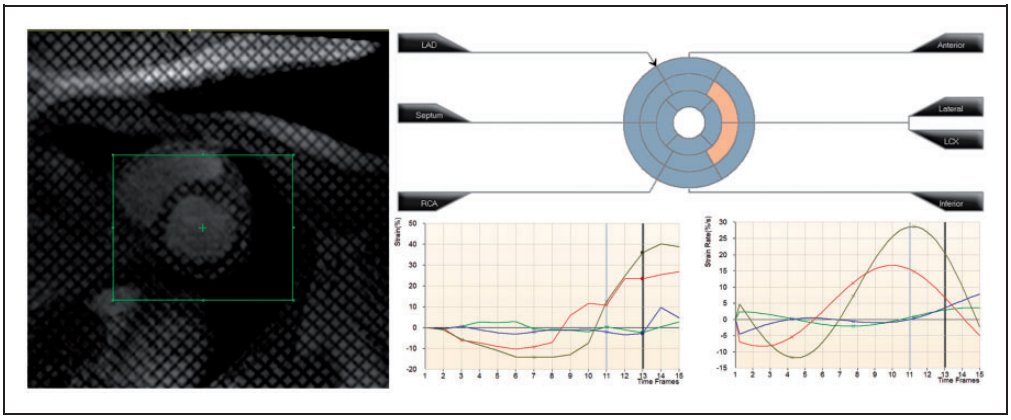

Figure 9. Lagrangian circumferential shortening strain is computed, yielding time-strain curves

sequences, when paired with regional diastolic dysfunction assessment by myocardial tagging, may allow segment-by-segment evaluation of ischaemia in ACS and guide eventual percutaneous coronary intervention.

Patients presenting with ACS can undergo volume and functional assessment, T2-STIR for imaging of oedema, measurement of TM flow velocity for universal diastolic function, myocardial tagging for regional systolic and diastolic dysfunction, confirmatory first-pass myocardial perfusion assessment, and delayed gadolinium enhancement. These imaging modalities provide sufficient diagnostic and prognostic information for adequately assessing a patient presenting to the emergency department with chest pain and suspected of having ACS. These modalities take the same time that it takes to send and receive the results of any routine CE profile that is sent from the same department. Positive findings in any or a combination of these imaging modalities result in immediate referral for coronary intervention it is indicated. A negative finding results in immediate discharge from the emergency department, thereby reducing wastage and delay.

The main limitation to routine use of CMR imaging in ACS is the cost in terms of hardware and human resources. Additionally, newer imaging protocols may lengthen the scan time beyond what is acceptable for revascularization targets, and thus rule out the relevance of CMR in the emergency setting. Therefore, further research is required to establish the cost-effectiveness of CMR use in routine clinical practice.

Conclusion

Current clinical tools for comprehensive assessment of patients presenting to the emergency department with chest pain are useful, but not optimal. CMR imaging has the ability to accurately and reliably diagnose, risk stratify, and prognosticate ACS, especially with its multimodal ability to assess diastolic dysfunction. Despite the manifold benefits of CMR, its wider use in routine clinical assessment is limited, and more studies are required for assessing its cost-effectiveness.

Declaration of conflicting interest

The Authors declare that there is no conflict of interest.

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References

1. Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: executive summary and recommendations. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (committee on the management of patients with unstable angina). *Circulation* 2000; 102: 1193–1209.
2. Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med* 2000; 342: 1163–1170.
3. Gani F, Jain D and Lahiri A. The role of cardiovascular imaging techniques in the assessment of patients with acute chest pain. *Nucl Med Commun* 2007; 28: 441–449.
4. Hamm CW, Bassand JP, Agewall S, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2011; 32: 2999–3054.
5. Wright RS, Anderson JL, Adams CD, et al. 2011 ACCF/AHA focused update incorporated into the ACC/AHA 2007 guidelines for the management of patients with unstable Angina/Non-ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines developed in collaboration with the American academy of family physicians, society for cardiovascular angiography and interventions, and the society of thoracic surgeons. *J Am Coll Cardiol* 2011; 57: e215–e367.
6. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics–2011 update: a report from the American Heart Association. *Circulation* 2011; 123: e18–e209.
7. Fox KA, Birkhead J, Wilcox R, et al. British cardiac society working group on the definition of myocardial infarction. *Heart* 2004; 90: 603–609.
8. Teixeira R, Lourenço C, Baptista R, et al. Left ventricular end diastolic pressure and acute coronary syndromes. *Arq Bras Cardiol* 2011; 97: 100–110. [in Portuguese, Spanish, Abstract in English].
9. Patel AR, Bhave NM and Mor-Avi V. Myocardial perfusion imaging with cardiac computed tomography: state of the art. *J Cardiovasc Trans Res* 2013; 6: 695–707.
10. Coelho-Filho OR, Rickers C, Kwong RY, et al. MR myocardial perfusion imaging. *Radiology* 2013; 266: 701–715.
11. Becker A and Becker C. CT imaging of myocardial perfusion: possibilities and perspectives. *J Nucl Cardiol* 2013; 20: 289–296.
12. Udelson JE, Beshansky JR, Ballin DS, et al. Myocardial perfusion imaging for evaluation and triage of patients with suspected acute cardiac ischemia: a randomized controlled trial. *JAMA* 2002; 288: 2693–2700.
13. Radensky PW, Hilton TC, Fulmer H, et al. Potential cost effectiveness of initial myocardial perfusion imaging for assessment of emergency department patients with chest pain. *Am J Cardiol* 1997; 79: 595–599.
14. Kwong RY, Schussheim AE, Rekhraj S, et al. Detecting acute coronary syndrome in the emergency department with cardiac magnetic resonance imaging. *Circulation* 2003; 107: 531–537.
15. Zile MR and Brutsaert DL. New concepts in diastolic dysfunction and diastolic heart failure: Part II: Causal mechanisms and treatment. *Circulation* 2002; 105: 1503–1508.
16. Barbieri A, Bursi F, Politi L, et al. Echocardiographic diastolic dysfunction and magnetic resonance infarct size in healed myocardial infarction treated with primary angioplasty. *Echocardiography* 2008; 25: 575–583.
17. Khumri TM, Reid KJ, Kosiborod M, et al. Usefulness of left ventricular diastolic dysfunction as a predictor of one-year rehospitalization in survivors of acute myocardial infarction. *Am J Cardiol* 2009; 103: 17–21.
18. Poulsen SH, Jensen SE, Gøtzsche O, et al. Evaluation and prognostic significance of

left ventricular diastolic function assessed by Doppler echocardiography in the early phase of a first acute myocardial infarction. *Eur Heart J* 1997; 18: 1882–1889.
19. Nijland F, Kamp O, Karreman AJ, et al. Prognostic implications of restrictive left ventricular filling in acute myocardial infarction: a serial Doppler echocardiographic study. *J Am Coll Cardiol* 1997; 30: 1618–1624.
20. Cury RC, Shash K, Nagurney JT, et al. Cardiac magnetic resonance with T2-weighted imaging improves detection of patients with acute coronary syndrome in the emergency department. *Circulation* 2008; 118: 837–844.
21. Miller CD, Hwang W, Hoekstra JW, et al. Stress cardiac magnetic resonance imaging with observation unit care reduces cost for patients with emergent chest pain: a randomized trial. *Ann Emerg Med* 2010; 56209.e2–219.e2.
22. Simek CL, Feldman MD, Haber HL, et al. Relationship between left ventricular wall thickness and left atrial size: comparison with other measures of diastolic function. *J Am Soc Echocardiogr* 1995; 8: 37–47.
23. Tsang TS, Abhayaratna WP, Barnes ME, et al. Prediction of cardiovascular outcomes with left atrial size: is volume superior to area or diameter? *J Am Coll Cardiol. 2006* 47: 1018–1023.
24. Moller JE, Hillis GS, Oh JK, et al. Left atrial volume. A powerful predictor of survival after acute myocardial infarction. *Circulation* 2003; 107: 2207–2212.
25. Beinart R, Boyko V, Schwammenthal E, et al. Long-term prognostic significance of left atrial volume in acute myocardial infarction. *J Am Coll Cardiol* 2004; 44: 327–334.
26. Pinar M, Gulel O, Kucuksu Z, et al. Evaluation of biatrial size and functions by different echocardiographic parameters in patients with acute coronary syndromes. *Int J Cardiovasc Imaging* 2013; 29: 1725–1732.
27. Maceira AM, Cosín-Sales J, Roughton M, et al. Reference left atrial dimensions and volumes by steady state free precession cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2010; 12: 65.
28. Anderson JL, Horne BD and Pennell DJ. Atrial dimensions in health and left ventricular disease using cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2005; 7: 671–675.
29. Chatzimavroudis GP, Zhang H, Halliburton SS, et al. Clinical blood flow quantification with segmented k-space magnetic resonance phase velocity mapping. *J Magn Reson Imaging* 2003; 17: 65–71.
30. Tang C, Blatter DD and Parker DL. Accuracy of phase-contrast flow measurements in the presence of partial-volume effects. *J Magn Reson Imaging* 1993; 3: 377–385.
31. Hartiala JJ, Mostbeck GH, Foster E, et al. Velocity-encoded cine MRI in the evaluation of left ventricular diastolic function: measurement of mitral valve and pulmonary vein flow velocities and flow volume across the mitral valve. *Am Heart J* 1993; 125: 1054–1066.
32. Karwatowski SP, Brecker SJ, Yang GZ, et al. Mitral valve flow measured with cine MR velocity mapping in patients with ischemic heart disease: comparison with Doppler echocardiography. *J Magn Reson Imaging* 1995; 5: 89–92.
33. Mohiaddin RH, Gatehouse PD, Henien M, et al. Cine MR Fourier velocimetry of blood flow through cardiac valves: comparison with Doppler echocardiography. *J Magn Reson Imaging* 1997; 7: 657–663.
34. Rathi VK, Doyle M, Yamrozik J, et al. Routine evaluation of left ventricular diastolic function by cardiovascular magnetic resonance: a practical approach. *J Cardiovasc Magn Reson* 2008; 10: 36.
35. Azarisman SM, Wong DT, Richardson JD, et al. Evaluation of mitral inflow velocity profile: Optimal Through Plane Location for Mitral Inflow Assessment with Cardiac Magnetic Resonance. *Exp Clin Cardiol* 2014; 20: 975–1001.
36. Westenberg JJ. CMR for assessment of diastolic function. *Curr Cardiovasc Imaging Rep* 2011; 4: 149–158.
37. Caudron J, Fares J, Bauer F, et al. Evaluation of left ventricular diastolic function with cardiac MR imaging. *Radiographics* 2011; 31: 239–259.

38. Tabata T, Thomas JD and Klein AL. Pulmonary venous flow by doppler echocardiography: revisited 12 years later. *J Am Coll Cardiol* 2003; 41: 1243–1250.
39. Daneshvar D, Wei J, Tolstrup K, et al. Diastolic dysfunction: improved understanding using emerging imaging techniques. *Am Heart J* 2010; 160: 394–404.
40. Keren G, Bier A, Sherez J, et al. Atrial contraction is an important determinant of pulmonary venous flow. *J Am Coll Cardiol* 1986; 7: 693–695.
41. Karwatowski SP, Brecker SJ, Yang GZ, et al. A comparison of left ventricular myocardial velocity in diastole mea- sured by magnetic resonance and left ventricular filling measured by Doppler echocardiography. *Eur Heart J* 1996; 17: 795–802.
42. Ommen SR, Nishimura RA, Appleton CP, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. *Circulation* 2000; 102: 1788–1794.
43. Nagueh SF, Middleton KJ, Kopelen HA, et al. Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. *J Am Coll Cardiol* 1997; 30: 1527–1533.
44. Hillis GS, Møller JE, Pellikka PA, et al. Noninvasive estimation of left ventricular filling pressure by E/e' is a powerful predictor of survival after acute myocardial infarction. *J Am Coll Cardiol* 2004; 43: 360–367.
45. Paelinck BP, de Roos A, Bax JJ, et al. Feasibility of tissue magnetic resonance imaging: a pilot study in comparison with tissue Doppler imaging and invasive measurement. *J Am Coll Cardiol* 2005; 45: 1109–1116.
46. Zerhouni EA, Parish DM, Rogers WJ, et al. Human heart: tagging with MR imaging - a method for noninvasive assessment of myocardial motion. *Radiology* 1988; 169: 59–63.
47. Axel L and Dougherty L. MR imaging of motion with spatial modulation of magnetization. *Radiology* 1989; 171: 841–845.
48. Edvardsen T, Rosen BD, Pan L, et al. Regional diastolic dysfunction in individuals with left ventricular hypertrophy measured by tagged magnetic resonance imaging: the Multi-Ethnic Study of Atherosclerosis (MESA). *Am Heart J* 2006; 151: 109–114.
49. Azevedo CF, Amado LC, Kraitchman DL, et al. Persistent diastolic dysfunction despite complete systolic functional recovery after reperfused acute myocardial infarction demonstrated by tagged magnetic resonance imaging. *Eur Heart J* 2004; 25: 1419–1427.
50. Sengupta PP, Tajik AJ, Chandrasekaran K, et al. Twist mechanics of the left ventricle: principles and application. *JACC Cardiovasc Imaging* 2008; 1: 366–376.
51. Paelinck BP, Lamb HJ, Bax JJ, et al. Assessment of diastolic function by cardiovascular magnetic resonance. *Am Heart J* 2002; 144: 198–205.
52. Wong DT, Weightman MJ, Baumert M, et al. Electro-mechanical characteristics of myocardial infarction border zones and ventricular arrhythmic risk: novel insights from grid-tagged cardiac magnetic resonance imaging. *Eur Radiol* 2012; 22: 1651–1658.
53. Higgins CB, Herfkens R, Lipton MJ, et al. Nuclear magnetic resonance imaging of acute myocardial infarction in dogs: alterations in magnetic relaxation times. *Am J Cardiol* 1983; 52: 184–188.
54. Knight RA, Ordidge RJ, Helpern JA, et al. Temporal evolution of ischemic damage in rat brain measured by proton nuclear magnetic resonance imaging. *Stroke* 1991; 22: 802–808.
55. Abdel-Aty H, Zagrosek A, Schulz-Menger J, et al. Delayed enhancement and T2-weighted cardiovascular magnetic resonance imaging differentiate acute from chronic myocardial infarction. *Circulation* 2004; 109: 2411–2416.
56. Messroghli DR, Walters K, Plein S, et al. Myocardial T1 mapping: application to patients with acute and chronic myocardial infarction. *Magn Reson Med* 2007; 58: 34–40.
57. Ghugre NR, Ramanan V, Pop M, et al. Quantitative tracking of edema, hemorrhage, and microvascular obstruction in subacute myocardial infarction in a porcine model by MRI. *Magn Reson Med* 2011; 66: 1129–1141.