MYOCARDIAL DISEASE

Clinical use of multimodality imaging in the assessment of dilated cardiomyopathy

João Silva Marques, Fausto J Pinto

► Additional references are published online only. To view please visit the journal online (http://dx.doi.org/10.1136/heartjnl-2013-304539).

Department of Cardiology, University Hospital Santa Maria, Lisbon Academic Medical Centre, CCUL, University of Lisbon, Lisbon, Portugal

Correspondence to
Professor Fausto J Pinto, Faculty of Medicine of Lisbon University, Cardiology Department, University Hospital Santa Maria/CHLN, Av Prof Egas Moniz, Lisbon 1649-028, Portugal; faustopin@gmail.com

SCOPE OF THE PROBLEM AND CHALLENGES TO THE CLINICIAN

Dilated cardiomyopathy (DCM) is a heart muscle disorder that frequently leads to heart failure. It is defined by the presence of left ventricular (LV) dilatation and LV systolic dysfunction in the absence of abnormal loading conditions or extensive coronary artery disease (CAD).[1] In that regard, the accurate and reproducible assessment of cardiac dimensions and function is paramount, but there is also a need to fully characterise valve function and the presence and functional consequences of CAD. This is particularly important because coronary heart disease is considered the most frequent cause for finding a dilated, dysfunctional heart in clinical practice. Also, LV enlargement and dysfunction are late features of chronic volume or pressure overload that are seen in patients with severe valve disease. Therefore, multimodality cardiac imaging aims to correctly identify DCM from the wider pool of patients with reduced ejection fraction (EF).

The prevalence of DCM in the general population remains undefined but it is considered to be the most common cardiomyopathy worldwide,[w1] with an estimated incidence of 4.5/100 000/year.[w2] A broad spectrum of entities may cause DCM. Traditionally, familial and genetic causes were thought to account for a small percentage of cases but are now increasingly recognised.[w3] The other aetiologies are grouped into non-familial DCM, that comprises idiopathic DCM when there is no identifiable cause, and acquired DCM, when ventricular dysfunction is a complication of other disorders that afflict the myocardium. Imaging modalities may contribute valuable information for reaching a probable diagnosis of acquired DCM.

The prognosis in patients with DCM and symptoms of heart failure is very poor.[w4] However, the clinical course of the disease is not always predictable based on these variables. Indeed, EF is considered an important imaging measurement in DCM, not only because of its diagnostic and prognostic relevance but also because most clinical trials selected patients based on it. Therefore, treatment strategies are often dependent on EF calculation. Although it is such an important parameter, EF calculation is still a challenge for cardiovascular imaging.

Also, most patients who have a clear indication for implantable cardioverter-defibrillator (ICD) implantation will never experience an appropriate discharge, and about one third of patients who receive cardiac resynchronisation therapy (CRT) do not improve. In that regard, multimodality imaging approaches may be necessary to better stratify the individual risk of the patient.

Ultimately, the last frontier in DCM imaging may be the individualisation of therapy using multimodality molecular imaging to identify the mechanisms responsible for the disease in each patient.

MORPHOLOGIC DIAGNOSIS OF DCM

Echocardiography, cardiac magnetic resonance (CMR), cardiac CT, single photon emission CT (SPECT), and positron emission tomography (PET) can be used for anatomic and functional imaging of the heart and may be valuable tools in the diagnosis of patients with DCM. Table 1 summarises the strengths and weaknesses of each imaging modality.

Echocardiography is the cornerstone of diagnostic imaging in DCM because it is accurate, widely available, and lacks ionising radiation (figure 1). Diagnostic criteria have relied on the identification of an EF <45%, in association with an LV end-diastolic dimension >112% of the predicted value corrected for age and body surface area.[2] The apical biplane method of summation of discs (modified Simpson's rule) is the recommended method for measuring EF. The role of echocardiography is also emphasised in current guidelines as the imaging modality of choice for evaluating patients with heart failure.[w5] [w6] However, there are some difficulties particularly related to wide inter- and intra-observer measurements variability.[w7] Additionally, obtaining images of sufficient quality for diagnostic purposes may be difficult in patients with poor acoustic windows. In those cases, ultrasonographic contrast for cavity opacification significantly improves the accuracy and reproducibility of EF measurements.[3] Nevertheless, contrast echocardiography is not able to prevent other classic pitfalls such as reliance on geometric assumptions and foreshortening of the LV. Not surprisingly, it lacks accuracy compared with other imaging modalities.[w8] Recently, real-time three dimensional (3D) echocardiography has emerged and eliminates the need for geometric modelling and the errors caused by foreshortened views. In fact, semi-automated quantification of EF using 3D echocardiography allows rapid, accurate, and reproducible LV measurements, that are superior to conventional 2D echocardiography.[4] However, despite high correlation to gold standard techniques, volumes may be underestimated using this modality.[w9] Furthermore, a poor acoustic window continues to be a limitation and a small angle of data acquisition may be problematic, particularly in patients with very large heart chambers.

Table 1 Comparison of imaging modalities for the evaluation of dilated cardiomyopathy

	2D echo	3D echo	CMR	CT	SPECT	PET
LV volumes and function	++	+++	++++	+++	++	++
Valvular disease	++++ (TOE optimal)	++++ (TOE optimal)	+++	+	–	–
Ischaemia/perfusion	+++	+++	+++	+	+++	++++
Morphology of the coronary arteries	–	–	++	+++	–	–
Imaging fibrosis	– (suspected using speckle tracking)	–	++++	++	–	++
Myocyte metabolism	–	–	++	–	++	++++
Clinical validation of prognostic tools	++++	++	+++	+	++	++
Spatial resolution	+++	++	+++	+++	++	++
Temporal resolution	++++	+++	++	+	+	+
Limitations	Operator dependence, acoustic window	Operator dependence, acoustic window	Availability, incompatible devices, renal failure	Availability, radiation, renal failure	Availability, radiation	Availability, radiation

CMR, cardiac magnetic resonance; echo, echocardiography; PET, positron emission tomography; SPECT, single photon emission CT; TOE, transoesophageal echocardiography.

In patients with suboptimal echocardiographic image quality the use of other imaging modalities is paramount for diagnostic purposes (figure 1). The accuracy of CMR calculated LV volumes has been validated both in vitro and in vivo. Therefore, CMR is considered the gold standard for accurate and reproducible assessment of ventricular volumes and EF. Cardiac CT can also assess cardiac structure and function with excellent correlation with other imaging modalities.[5] However, few studies were performed in patents with DCM and the accuracy is not unequivocally established. For intermodality comparison it is important to bear in mind that CT may overestimate LV volumes and underestimate EF compared with CMR.[w10] ECG gated SPECT ventricular angiography by myocardial perfusion or by blood pool techniques provides highly accurate, reproducible and prognostically validated measurements of LV volumes and EF.[w11] However, SPECT as well as

PET scans are not primarily used to determine LV function. Additionally, unlike the other imaging modalities discussed, nuclear techniques do not allow direct assessment of valvular structure and function. Also, radiation exposure is a limitation. Furthermore, all imaging methods that rely on gated acquisitions may be biased in patients with cardiac arrhythmias, which are common in DCM. Therefore SPECT and PET should be used primarily when other modalities are not available or if information on myocardial ischaemia and viability is clinically relevant.

AETIOLOGY ASSESSMENT IN DCM

By definition it is critical to exclude valvular disease and severe CAD in patients with suspected DCM. Figure 2 provides a proposed diagnostic algorithm for patients with clinical suspicion of DCM. Transthoracic echocardiography is the standard tool for the assessment of valvular heart
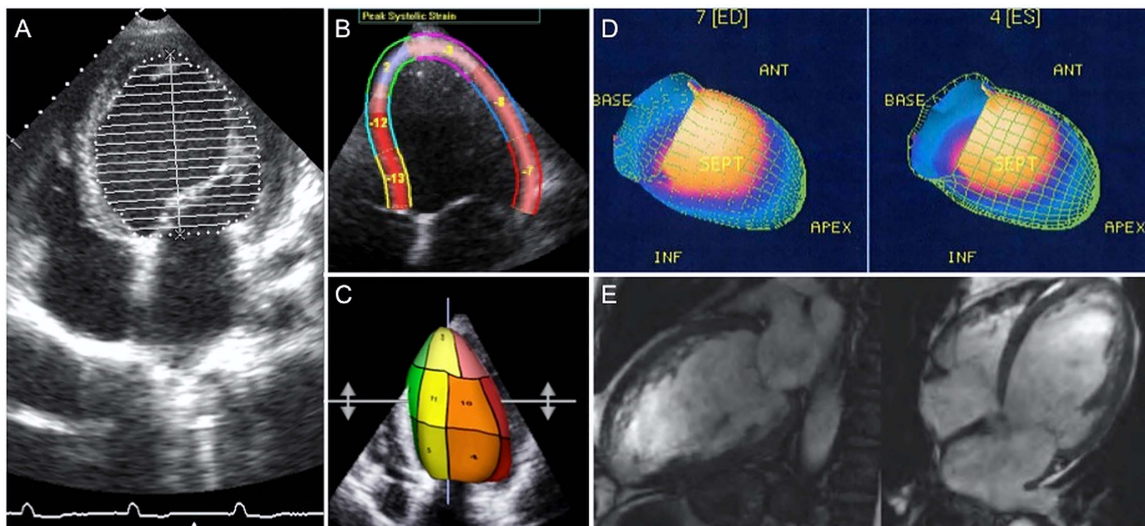

Figure 1 Clinical examples of imaging modalities that may be used for assessing left ventricular (LV) dimensions and function in patients with suspected dilated cardiomyopathy. Transthoracic echocardiography assessment of LV ejection fraction is the cornerstone for the diagnosis (A). Speckle tracking analysis currently provides global and segmental evaluation of LV function (B). However, real-time 3D echocardiography provides more accurate estimation of LV volumes (C). In patients with a poor acoustic window, single photon emission CT imaging may assess LV function (D). Nevertheless, when available, cardiac MRI provides highly accurate and reproducible characterisation of LV morphology and function (E).
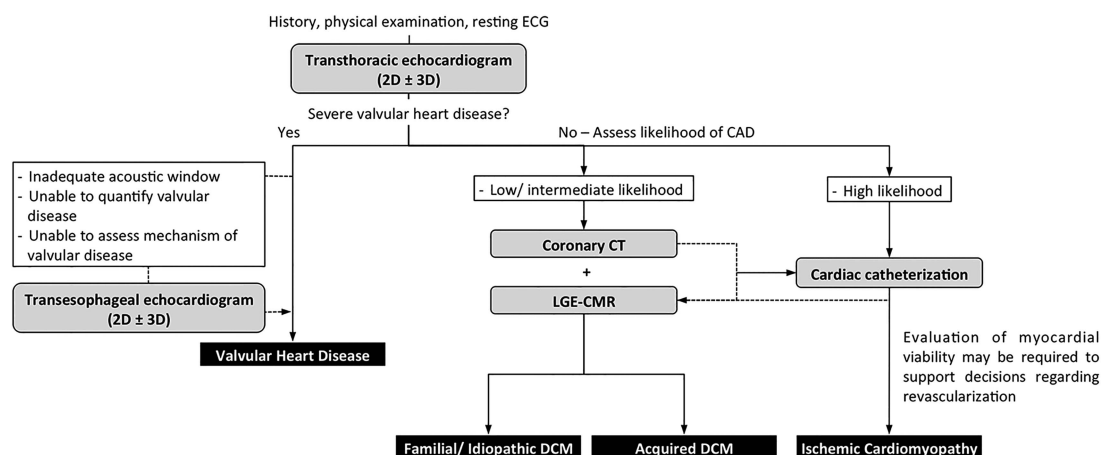
Figure 2 Proposed diagnostic imaging algorithm for the aetiologic evaluation of patients with suspected dilated cardiomyopathy (DCM). CAD, coronary artery disease; LGE-CME, late gadolinium enhancement-cardiac magnetic resonance.

disease. Transoesophageal echocardiography may improve diagnostic accuracy, particularly in patients with complex disease or in congenital heart disease. CMR is a reasonable alternative. Although it has lower temporal resolution for imaging structures that are thin and highly mobile, CMR provides qualitative and quantitative measurements of valve stenosis and regurgitation.[6] CT is also emerging as an alternative technique to evaluate cardiac valve structure and function.[w12] However, at present, valve assessment should not be a routine clinical indication for CT as it lacks temporal resolution and uses radiation.

In clinical practice, identifying ischaemic aetiology is important because patients with severe ischaemia may benefit from coronary revascularisation.[7] For assessing CAD as the cause of a dilated, failing heart the same modalities that are used to assess morphology and function may be employed. Nevertheless, complementary information may be provided by other tests that specifically assess coronary anatomy or ischaemia. Because of the prognostic and therapeutic implications of finding severe CAD in patients with systolic heart failure, coronary angiography is recommended in the assessment of DCM, particularly in patients with angina.[w5 w6] In fact, there is historic evidence that clinical data and the results of non-invasive tests may fail to recognise extensive CAD in a significant proportion of patients.[w13] However, developments in cardiac CT imaging allow detection of significant stenosis with high negative predictive value. In fact, CT is feasible, safe and accurate for detecting coronary stenosis in patients with suspected DCM and may represent an alternative to coronary angiography, particularly in patients with a low or intermediate likelihood of CAD.[8]

Imaging can also identify myocardial scar as a surrogate for previous myocardial infarction. Late gadolinium enhancement (LGE)-CMR is a powerful technique to distinguish systolic dysfunction related to CAD from DCM,[9] even in patients without previous clinical suspicion of CAD.[10] Thus, LGE-CMR may be a valid alternative to invasive tests for detecting CAD in patients who are undergoing CMR for the assessment of LV function. More recently, it was recognised that CT contrast agents may be used to identify infarct.[11] However, this modality is less validated than CMR and increases radiation exposure. Nevertheless, the combination of LGE-CMR for detection of myocardial scar, with the coronary anatomic details provided by CT angiography, may effectively and non-invasively exclude CAD as the cause of DCM in patients with low or intermediate likelihood of disease. The coronary anatomy information provided by CT is incremental because it may effectively exclude proximal coronary lesions that may impact prognostic and treatment strategies. In highly calcified vessels and when there is conflicting information coming from non-invasive imaging modalities, invasive coronary angiography should be performed.

A different approach to evaluating CAD includes the assessment of ischaemia and viability. It may be particularly important to distinguish incidental CAD in DCM from ischaemic cardiomyopathy and to support decisions regarding revascularisation. Dobutamine stress echocardiography is able to detect CAD in DCM patients, but the wall motion analysis may be troublesome in patients with left bundle branch block (LBBB).[w14] However, the use of tissue Doppler assessment may increase the sensitivity and specificity of the test.[w15] In patients with a poor acoustic window dobutamine stress CMR may be a good alternative.[12] It may be used as an add-on feature in patients undergoing LGE-CMR, increasing the clinical information provided while minimising the time taken to reach a clinical decision. SPECT is also able to identify ischaemia in DCM.[w16] However, the performance of cardiac scintigraphy may be suboptimal, particularly in patients with LBBB. Even though it is not a routine test in DCM, the integrated diagnostic information of PET-CT may be very useful in challenging cases.[w17] Indeed the diagnostic capabilities of hybrid imaging may be further expanded with future developments and incorporation of other imaging modalities.

The contribution of imaging for establishing the diagnosis of DCM is not limited to exclusion of CAD and valvular heart disease. Indeed, the probable diagnosis of acquired DCM may be established using cardiac imaging in the appropriate clinical setting. Although echocardiography has a prominent role in the diagnosis of DCM, the role in diagnosing specific acquired forms of DCM is less impressive, with most of the findings being unspecific. For this purpose CMR is the imaging modality of choice because it is able to characterise tissue abnormalities that previously could only be identified using histology. CMR imaging allows characterisation of acute versus chronic injuries, quantification of intramyocardial iron deposition, and provides data regarding identification, location and pattern of myocardial fibrosis using LGE. In fact, emerging data suggest that some forms of DCM have a predilection for particular patterns of myocardial fibrosis and that information may provide useful insights about the likely cause of DCM (figure 3).

Myocarditis may be found in a significant proportion of patients with DCM.[w18] CMR imaging is currently considered the most accurate, non-invasive, diagnostic test for myocarditis. It incorporates the evaluation of LV function and wall motion abnormalities with myocardial characterisation in terms of oedema, capillary leakage and necrosis (figure 4).[13] Myocardial oedema can be detected and quantified using T2 weighted CMR and is considered an unspecific marker of acute myocardial injury. Increased signal on T1 weighted spin-echo images after gadolinium administration is considered to be associated with capillary leakage. Additionally, several studies have shown that the presence of LGE, as a surrogate for myocardial necrosis, is associated with myocarditis at biopsy. The most common patterns of LGE in myocarditis include, but are not limited to, an intramural rim-like pattern and a subepicardial patchy pattern. Preliminary data, using speckle tracking echocardiography in patients with myocarditis, suggest that longitudinal deformation may be used to identify wall segments with LGE in CMR (figure 4).[w19] Therefore, this new echocardiographic technique holds promise for the assessment of patients with myocarditis.

Infiltrative cardiomyopathies such as amyloidosis, haemochromatosis and sarcoidosis may present as DCM and they convey a significantly poorer prognosis.[w18] Typical morphological features when combined with widespread LGE of the subendocardium or a transmural pattern involving the interatrial septum and right ventricle are accurate for diagnosing cardiac amyloidosis.[w20] In sarcoidosis, the use of LGE-CMR may increase sensitivity for determining cardiac involvement compared to consensus criteria.[14] Many LGE patterns may be recognised in sarcoidosis, but basal and subepicardial myocardial involvement is typical.[15] Additionally, T2 weighted imaging may localise areas of myocardial inflammation. Unlike the other infiltrative cardiomyopathies, fibrosis is infrequent in iron overload cardiomyopathy.[w21] Instead, the T2* technique is able to identify cardiac iron overload.[16]

In other challenging clinical cases, when echocardiography is not able to provide a definitive diagnosis, CMR may be helpful for identifying the dilated phase of hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, and LV non-compaction.

DETERMINING THE PROGNOSIS: LOOKING BEYOND EF

In routine cardiology practice, critical decision making over matters such as defibrillator implantation and biventricular pacing treatment of
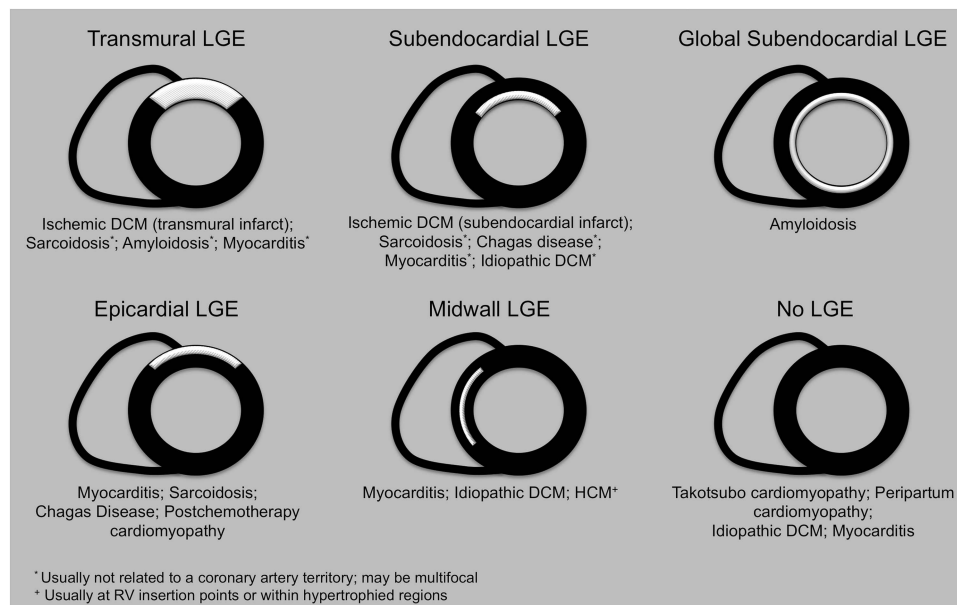

Transmural LGE
Ischemic DCM (transmural infarct);
Sarcoidosis*; Amyloidosis*; Myocarditis*

Subendocardial LGE
Ischemic DCM (subendocardial infarct);
Sarcoidosis*; Chagas disease*;
Myocarditis*; Idiopathic DCM*

Global Subendocardial LGE
Amyloidosis

Epicardial LGE
Myocarditis; Sarcoidosis;
Chagas Disease; Postchemotherapy
cardiomyopathy

Midwall LGE
Myocarditis; Idiopathic DCM; HCM+

No LGE
Takotsubo cardiomyopathy; Peripartum
cardiomyopathy;
Idiopathic DCM; Myocarditis

* Usually not related to a coronary artery territory; may be multifocal
+ Usually at RV insertion points or within hypertrophied regions

Figure 3 Schematic representation of possible late gadolinium enhancement (LGE) patterns in cardiac MRI of dilated cardiomyopathy (DCM) patients and possible aetiologies that should be considered. HCM, hypertrophic cardiomyopathy; RV, right ventricle.

Figure 4 Imaging in a 42-year-old man presenting with acute Q fever myocarditis. T2 weighted cardiac MRI showed nodular enhancement in the mid lateral wall, mainly affecting subepicardium (A, yellow arrows). After gadolinium, transmural nodular late enhancement with a central core of unaffected myocardium was recognised in the same location (B, yellow arrows). Speckle tracking strain analysis showed abnormal systolic deformation in mid basal lateral wall (C) in the location of myocardial inflammation detected by cardiac magnetic resonance (D, yellow arrow).
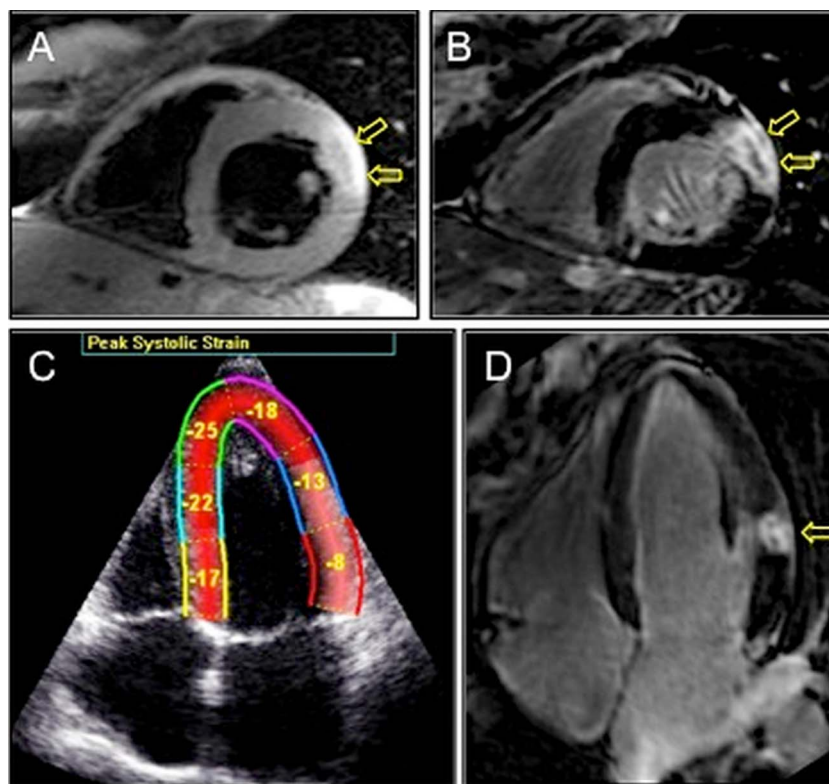
congestive heart failure is based heavily on EF. It is considered one of the most powerful predictors of prognosis in DCM. As previously discussed, there are some specific advantages and hurdles associated with each imaging modality that should be considered when selecting the method to assess EF in clinical practice. However, several other indexes may be obtained using multimodality imaging that may add relevant information for prognostic purposes.

Transthoracic echocardiography provides several prognostic tools that should be used routinely in the assessment of patients with DCM. They include the assessment of LV morphology,[w22] left atrial volume,[w23] and right ventricular function.[w24] Similarly, LV diastolic function[w25] and estimation of pulmonary artery pressure[w26] are some important haemodynamic parameters for assessing prognosis. In fact, there are a myriad of echocardiographic parameters that have been shown to predict individually the prognosis in DCM. However, finding those tools that provide incremental risk prediction when combined is clinically imperative. In that regard, end-systolic volume index, left atrial volume index, mitral E wave deceleration time, tricuspid annular peak systolic excursion, and pulmonary artery systolic pressure were included in an echocardiographic risk score to predict mortality in systolic heart failure patients.[17]

Tissue Doppler imaging provides evaluation of myocardial motion and deformation. One of the most relevant prognostic parameters is mitral annulus velocity measured in early diastole, that provides incremental value to predict cardiac mortality compared with clinical data and standard echocardiographic measurements.[w27] Systolic mitral annular velocity is also a strong independent echocardiographic predictor of prognosis.[w28] However, speckle tracking does not have angle dependency, and tissue deformation is easier to evaluate than using tissue Doppler. Therefore it is promising for assessing LV function and possibly predicts the prognosis in DCM. Indirect evidence for prognostic relevance comes from a study of unselected, consecutive individuals undergoing echocardiography to investigate LV impairment, that showed speckle tracking derived global longitudinal strain may be a superior predictor of all-cause mortality compared to EF.[w29] Importantly, in a mainly non-ischaemic DCM population, global longitudinal strain provided risk stratification with greater accuracy than EF.[18] Recently, a broad number of tissue deformation parameters have been associated with heart failure prognosis, including longitudinal and circumferential strain and strain rate, and radial strain.[w30] Although these measures may reflect different aspects of deformation, future studies should explore which of them are more closely associated with clinical outcomes in DCM.

Currently, the use of 3D echocardiography for predicting prognosis in DCM is not based on large, prospectively collected data of clinical outcomes. However, this imaging technique may provide more accurate and reproducible assessment of cardiac volumes and function that may lead to changed categorisation with potential impact in clinical decisions.[w31] Also, 3D speckle tracking is an emerging clinical application of this imaging modality.[w32]

Stress echocardiography may provide important information to the clinician because contractile

reserve predicts a good response to therapy.[w33] Several indexes for the assessment of LV contractile reserve have been prognostically validated in long term follow-up and include the wall motion score, change in EF, end-systolic pressure to volume ratio, and cardiac power output.[w34] Combining the information provided by baseline Doppler echocardiography with stress echocardiography may further stratify patients into a high risk category when restrictive filling pattern and no contractile reserve are simultaneously present.[19] Preliminary prognostic data on the use of 3D echocardiography combined with a dobutamine stress test is emerging. In that regard, an increase in systolic dyssynchrony index during stress may predict cardiovascular events.[w35] Similarly, 3D speckle tracking may be used to assess contractile reserve and prognosis.[w36]

Other modalities may assist in the stratification of prognosis. The presence of mid wall fibrosis with LGE-CMR imaging has been shown to be an independent predictor of prognosis beyond EF.[20] In fact, LGE-CMR is particularly useful for identifying arrhythmic outcome and sudden cardiac death.[w37] Nevertheless, there is growing evidence that, similar to echocardiography, CMR may provide morphologic information that is relevant for assessing the prognosis in DCM. Recently, detection of right ventricular systolic dysfunction in CMR (right ventricular EF $\leq 45\%$) was shown to independently predict transplant-free survival in DCM patients, with significant impact on risk stratification.[21]

Regional perfusion–metabolism mismatches can be evaluated with SPECT or PET and can help to predict the prognosis. Moreover, the combined results of LGE-CMR and perfusion–metabolism SPECT warrant accurate prediction of cardiac events in patients with DCM.[w38]

GUIDING DEVICE THERAPY

CRT in patients with DCM and electrocardiographic evidence of ventricular dyssynchrony improves the prognosis. Nevertheless, about one third of patients do not improve with this therapy.[w39] In small, single centre studies several echocardiographic parameters of mechanical dyssynchrony were able to distinguish CRT responders from non-responders. However, the PROSPECT trial failed to identify baseline echocardiographic parameters to predict response to CRT.[w40] Furthermore, the EchoCRT study—a randomised trial to evaluate the effect of CRT in patients with otherwise class I indication except for a QRS duration <130 ms and echocardiographic evidence of LV dyssynchrony—was stopped as it was proving to be futile.[w41] Therefore, cardiac dyssynchrony based on currently studied echocardiographic parameters cannot be recommended to predict treatment response or to exclude patients from conventional indications for CRT. Recently, a large number of mechanical dyssynchrony indexes have emerged based on 3D echocardiography,[w42] CMR,[w43] CT,[w44] SPECT,[w45] and PET/CT.[w46] They currently lack the temporal resolution of echocardiography but may be more reproducible. However, it is still to

Multimodality imaging in dilated cardiomyopathy: key points

Screening and morphologic diagnosis
- Echocardiography is the cornerstone of diagnostic imaging in dilated cardiomyopathy (DCM).
- Ultrasonographic contrast for cavity opacification improves accuracy and reproducibility of EF measurements.
- 3D echocardiography allows LV measurements that are more accurate than 2D echocardiography.
- Cardiac magnetic resonance (CMR) is the gold standard for the assessment of ventricular volumes and EF.
- CT and nuclear techniques are limited by the use of radiation.

Aetiology
- By definition it is critical to exclude valvular disease and severe coronary artery disease (CAD) in patients with suspected DCM.
- Transthoracic echocardiography is the standard tool for the assessment of valvular disease.
- Coronary angiography is recommended when there is high likelihood of CAD.
- The combination of late gadolinium enhancement (LGE)-CMR and CT angiography may be used in patients with low or intermediate likelihood of CAD. They combine tissue characterisation information with coronary anatomy detail.
- CMR is the imaging modality of choice in the diagnosis of acquired DCM. It allows characterisation of acute injuries, quantification of intramyocardial iron deposition, and identifies patterns of myocardial fibrosis using LGE.

Prognosis
- Transthoracic echocardiography provides several prognostic tools that should be used routinely in the assessment of the patients with DCM.
- Tissue Doppler and speckle tracking imaging provide prognostic information beyond EF.
- Detection of LV contractile reserve at stress echocardiography is prognostically relevant.
- The identification and extent of myocardial fibrosis using LGE-CMR predicts sudden cardiac death or ventricular tachycardia.

Guiding device therapy
- Cardiac dyssynchrony based on currently studied echocardiographic parameters cannot be recommended to predict treatment response or to exclude patients from conventional indications for cardiac resynchronisation therapy (CRT).
- CT or CMR may characterise coronary venous anatomy that may be used for planning LV lead placement in CRT implantation.
- Transthoracic echocardiography may be used to optimise parameters of CRT treatment, particularly in non-responders.
- CMR may be useful for stratifying the risk of sudden cardiac death of patients with DCM and borderline criteria for implantable cardioverter-defibrillator implantation.

be determined if any of these modalities will have an impact on clinical practice.

Notwithstanding, imaging may assist in the implantation of a CRT device. Namely, coronary venous anatomy, which is used for planning LV lead placement, may be depicted non-invasively using CMR[w47] and CT.[w48]

Imaging may also be used to optimise parameters of CRT treatment. However, there is no consensus that it should be used routinely because clinical results have been mixed.[w49–w53] Nevertheless, CRT optimisation may be particularly attractive in patients considered to be non-responders. In that regard, a CRT optimisation programme, that included echocardiographic assessment of intraventricular dyssynchrony and optimal atrioventricular (AV) interval, led to an improved prognosis.[22]

ICD devices are used to prevent sudden cardiac death in patients with DCM. Although current guidelines only emphasise the role of EF in the imaging selection of patients, there is a considerable proportion of patients who have an ICD implanted who will never receive appropriate device therapy. Myocardial fibrosis is considered to be the substrate basis for re-entry—the principal mechanism of ventricular arrhythmias in DCM. Therefore, the use of imaging to identify myocardial fibrosis may help to stratify the risk of sudden death of DCM patients. Myocardial ultrasonic integrated backscatter imaging is considered an investigational tool to assess fibrosis.[w54] LGE-CMR is also a useful clinical tool for identifying myocardial fibrosis. In fact, finding significant fibrosis (26–75% of wall thickness) using CMR predicts inducible ventricular tachycardia at electrophysiology testing.[w55] Also, the identification of mid wall fibrosis predicts sudden cardiac death or ventricular tachycardia.[23] The extent of fibrosis may also provide additive

information.[w56] Altogether, these findings suggest that CMR may be useful for stratifying the risk of sudden cardiac death in patients with DCM and borderline criteria for ICD. However, in order to integrate stratification flowcharts for ICD implantation, CMR potential should be further demonstrated in larger prospective studies.

Given the recent developments in the treatment of functional mitral regurgitation that include transcatheter treatment, there are some additional roles for imaging that go beyond diagnosis. Indeed transoesophageal echocardiography, particularly using 3D imaging, may offer a valuable contribution in planning and guiding the procedures.[w57]

WHERE DO WE GO FROM HERE? THE QUEST FOR MORE SELECTIVE MOLECULAR IMAGING TOOLS

Although not readily and widely available, molecular imaging has the potential to impact future clinical cardiovascular care profoundly, particularly in the population with DCM. It extracts the most out of multimodality imaging by incorporating morphologic and tissue characterisation capabilities of several imaging modalities. Multiple molecular targets are being developed for use with current imaging modalities including echocardiography, CMR, CT, and scintigraphic methods.

The myocardial renin–angiotensin–aldosterone and the adrenergic systems have been closely linked to major maladaptive responses that lead to LV remodelling. However, the differential pathophysiological contribution of these systems in the individual patient is not clinically available and therefore the current treatment goals are population based rather than addressing the specificities of each individual patient. In the future this scenario may be changed by the use of molecular imaging methods. In fact, myocardial angiotensin converting enzyme and angiotensin II type 1 receptors[w58 w59] as well as presynaptic[w60] and postsynaptic[w61] cardiac sympathetic function can be monitored using SPECT or PET radiotracers.

Other possible targets for molecular imaging in DCM include myocardial apoptosis,[w62 w63] fibrosis,[w64] and inflammation[w65 w66] that may become useful for monitoring and predicting cardiac remodelling.

CONCLUSION
In the assessment of DCM, multiple imaging modalities may contribute toward determining the diagnosis, prognosis, and approach to treatment. However, each imaging modality may provide relevant information regarding more than one of these clinical needs. Therefore, to explore fully the potential impact of imaging, the strategy should be individualised according to the specific clinical needs.

Provenance and peer review Commissioned; externally peer reviewed.

REFERENCES

1. Elliott P, Andersson B, Arbustini E, *et al*. Classification of the cardiomyopathies: a position statement from the European Society Of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J* 2008;29:270–6.
2. Thomas DE, Wheeler R, Yousef ZR, *et al*. The role of echocardiography in guiding management in dilated cardiomyopathy. *Eur J Echocardiogr* 2009;10:iii15–21.
   ▸ Comprehensive review on the role of echocardiography in the assessment of patients with DCM.
3. Malm S, Frigstad S, Sagberg E, *et al*. Accurate and reproducible measurement of left ventricular volume and ejection fraction by contrast echocardiography: a comparison with magnetic resonance imaging. *J Am Coll Cardiol* 2004;44:1030–5.
4. Jacobs LD, Salgo IS, Goonewardena S, *et al*. Rapid online quantification of left ventricular volume from real-time three-dimensional echocardiographic data. *Eur Heart J* 2006;27:460–8.
5. Butler J. The emerging role of multi-detector computed tomography in heart failure. *J Card Fail* 2007;13:215–26.
6. Cawley PJ, Maki JH, Otto CM. Cardiovascular magnetic resonance imaging for valvular heart disease: technique and validation. *Circulation* 2009;119:468–78.
7. Yusuf S, Zucker D, Peduzzi P, *et al*. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet* 1994;344:563–70.
8. Andreini D, Pontone G, Pepi M, *et al*. Diagnostic accuracy of multidetector computed tomography coronary angiography in patients with dilated cardiomyopathy. *J Am Coll Cardiol* 2007;49:2044–50.
   ▸ Pivotal investigation showing accuracy and feasibility of cardiac CT for detecting CAD in patients with DCM.
9. McCrohon JA, Moon JC, Prasad SK, *et al*. Differentiation of heart failure related to dilated cardiomyopathy and coronary artery disease using gadolinium-enhanced cardiovascular magnetic resonance. *Circulation* 2003;108:54–9.
10. Soriano CJ, Ridocci F, Estornell J, *et al*. Noninvasive diagnosis of coronary artery disease in patients with heart failure and systolic dysfunction of uncertain etiology, using late gadolinium-enhanced cardiovascular magnetic resonance. *J Am Coll Cardiol* 2005;45:743–8.
    ▸ Comparative study of coronary angiography and late gadolinium enhanced cardiac magnetic resonance (LGE-CMR) for CAD in patients with DCM without clinical suspicion of CAD that showed LGE-CMR is a valid clinical tool for that purpose.
11. Lardo AC, Cordeiro MA, Silva C, *et al*. Contrast-enhanced multidetector computed tomography viability imaging after myocardial infarction: characterization of myocyte death, microvascular obstruction, and chronic scar. *Circulation* 2006;113:394–404.
12. Lipinski MJ, McVey CM, Berger JS, *et al*. Prognostic value of stress cardiac magnetic resonance imaging in patients with known or suspected coronary artery disease: a systematic review and meta-analysis. *J Am Coll Cardiol* 2013;62:826–38.
    ▸ Systematic review and meta-analysis on the role of stress CMR imaging for risk stratification of patients based on contemporary studies that included a large number of patients with assessment of prognosis.
13. Skouri HN, Dec GW, Friedrich MG, *et al*. Noninvasive imaging in myocarditis. *J Am Coll Cardiol* 2006;48:2085–93.
    ▸ Comprehensive review of imaging modalities that may assist in the diagnosis of myocarditis.
14. Patel MR, Cawley PJ, Heitner JF, *et al*. Detection of myocardial damage in patients with sarcoidosis. *Circulation* 2009;120:1969–77.
15. Ichinose A, Otani H, Oikawa M, *et al*. MRI of cardiac sarcoidosis: basal and subepicardial localization of myocardial lesions and their effect on left ventricular function. *AJR Am J Roentgenol* 2008;191:862–9.
16. Kirk P, Roughton M, Porter JB, *et al*. Cardiac T2* magnetic resonance for prediction of cardiac complications in thalassemia major. *Circulation* 2009;120:1961–8.
    ▸ This large study established a significant role for CMR in identifying patients with thalassaemia major at high risk of heart failure and arrhythmia. Therefore, T2* imaging may be used for the early identification of patients at risk of developing DCM.
17. Carluccio E, Dini FL, Biagioli P, *et al*. The 'Echo Heart Failure Score': an echocardiographic risk prediction score of mortality in systolic heart failure. *Eur J Heart Fail* 2013;15:868–76.
    ▸ A large prospective study investigating the association between 14 transthoracic echocardiography parameters and death in DCM patients that showed end-systolic volume index, left atrial volume index, mitral E wave deceleration time, tricuspid annular peak systolic excursion, and pulmonary artery systolic pressure are independent predictors of mortality.
18. Mignot A, Donal E, Zaroui A, *et al*. Global longitudinal strain as a major predictor of cardiac events in patients with depressed left ventricular function: a multicenter study. *J Am Soc Echocardiogr* 2010;23:1019–24.
    ▸ A multicentre study that showed global longitudinal strain is feasible and allows better risk stratification than EF in patients with systolic heart failure.
19. Pratali L, Otasevic P, Rigo F, *et al*. The additive prognostic value of restrictive pattern and dipyridamole-induced contractile reserve in idiopathic dilated cardiomyopathy. *Eur J Heart Fail* 2005;7:844–51.
20. Gulati A, Jabbour A, Ismail TF, *et al*. Association of fibrosis with mortality and sudden cardiac death in patients with nonischemic dilated cardiomyopathy. *JAMA* 2013;309:896–908.
    ▸ Prospective study of LGE-CMR imaging for predicting total mortality in patients with DCM, showing that the presence and extent of fibrosis are independently associated with prognosis after adjustment for EF.
21. Gulati A, Ismail TF, Jabbour A, *et al*. The prevalence and prognostic significance of right ventricular systolic dysfunction in nonischemic dilated cardiomyopathy. *Circulation* 2013;128:1623–33.
22. Mullens W, Grimm RA, Verga T, *et al*. Insights from a cardiac resynchronization optimization clinic as part of a heart failure disease management program. *J Am Coll Cardiol* 2009;53:765–73.
    ▸ Study of a protocol driven approach to treat patients non-responsive to cardiac resynchronisation therapy that included echocardiography guided device optimisation which resulted in fewer events in those patients with changed device settings or treatment.
23. Assomull RG, Prasad SK, Lyne J, *et al*. Cardiovascular magnetic resonance, fibrosis, and prognosis in dilated cardiomyopathy. *J Am Coll Cardiol* 2006;48:1977–85.