ISSN: 2378-2951

Ferreira et al. Int J Clin Cardiol 2022, 9:269
DOI: 10.23937/2378-2951/1410269
Volume 9 | Issue 5
Open Access

International Journal of Clinical Cardiology

REVIEW ARTICLE

Multimodality Imaging Applied to Dilated Cardiomyopathy

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Abstract

Dilated cardiomyopathy is a heterogeneous group of diseases, in which imaging modalities are important for diagnosis, guiding therapy and prognostic assessment. Given the plethora of imaging techniques available, each one with its strengths and limitations, it is of crucial importance to appropriately select which ones to use based on the clinical context. This article intends to review the main applications of echocardiography, computed tomography, magnetic resonance and nuclear imaging in the field of dilated cardiomyopathy.

Keywords

Dilated cardiomyopathy, Multimodality imaging, Echocardiography, Computed tomography, Magnetic resonance, Nuclear imaging

Introduction

Dilated cardiomyopathy (DCM) is a heterogeneous group of diseases, being, as a group, one of the most frequent etiologies of heart failure with reduced ejection fraction and the most frequent indication for heart transplantation worldwide [1]. Its correct and timely recognition and management is therefore crucial. Its diagnosis presupposes the exclusion of coronary disease (of severity and/or extension that is considered to be sufficient to justify cardiac dysfunction), as well as the exclusion of abnormal load conditions (hypertension or valvular disease) [2].

Given the heterogeneity of this group, both in terms of etiologies, clinical presentation and possible specific treatments depending on the etiology, it is understandable that in imaging terms it is often necessary to use more than one imaging method to guide the diagnosis, plan the treatment and maintain follow-up of these patients. However, the use of different imaging methods must be tailored to each patient in a personalized way. In this way, this article intends to briefly address the role of each of the most commonly used imaging techniques in terms of their applicability in DCM.

Echocardiography

Transthoracic echocardiography is (as in many other cardiac pathologies) the first-line imaging modality in the evaluation of patients with DCM, given its high accessibility, portability, low cost and safety. Not only is it a first-line modality, but it is also a fundamental test for the follow-up of these patients, namely in the assessment of response to established therapies.

The echocardiographic examination must be complete [3], with assessment of morphology and global and regional ventricular systolic function, diastolic function assessment, multiparametric assessment of associated valvular heart disease, detection of desynchrony, assessment of atrial function and morphology, evaluation of the probability of pulmonary hypertension, assessment of the pericardium and great vessels, as well as extracardiac findings with potential clinical relevance, such as the detection and quantification of pleural effusion. The use of echocardiographic contrast agents should be used whenever necessary/relevant, such as, for example, for exclusion of mural thrombus or accurate quantification of ventricular volumes and function in patients with a suboptimal echocardiographic window. Advanced echocardiographic modalities should be used whenever available, such as:

Citation: Ferreira JB, Beringuilho M, Fialho I, Passos M, Lopes J, et al. (2022) Multimodality Imaging Applied to Dilated Cardiomyopathy. Int J Clin Cardiol 8:269. doi.org/10.23937/2378-2951/1410269

Accepted: October 01, 2022: **Published:** October 03, 2022

- 3D echocardiography as it allows a more accurate and reproducible assessment of ventricular volumes and function [4], and, consequently, of the left ventricular ejection fraction, which is an extremely important parameter for the definition of therapies to be instituted, thus being a parameter that must be evaluated as accurately and reproducibly as possible;
- Assessment of myocardial deformation through global longitudinal strain by 2D speckle tracking, of particular importance in the detection of disease in the preclinical phase since it is currently the most studied parameter for the detection of subclinical disease, with the added advantage of being a highly reproducible parameter [5,6]; also derived from myocardial strain, the assessment of mechanical dispersion may be of clinical interest since it has been suggested as a marker of arrhythmic events [7,8]; also the evaluation of the longitudinal strain of the right ventricle may be of clinical interest, which has been demonstrated as an independent predictor of right ventricular failure after implantation of a left ventricular assist device [9];
- Assessment of myocardial work, a parameter calculated based on the strain curves associated with blood pressure at the time of the examination, which is currently mainly a research parameter, however with potential utility, for example, in the evaluation of response to cardiac resynchronization therapy [10].

Transesophageal echocardiography also plays an important role in several scenarios regarding patients with DCM, examples of which are the more accurate assessment of valvular heart disease (with particular emphasis on the assessment of secondary mitral regurgitation that can act both as a consequence of DCM as well as a contributing mechanism to the progression of dilation and disfunction) and guidance during percutaneous valve interventions, as well as exclusion of atrial thrombi before interventional or cardioversion procedures.

Stress echocardiography may also play an important role in the complementary assessment of certain valvular heart diseases as well as in the diagnosis of DCM in terms of ruling out significant coronary disease. It also has a prognostic role since the contractile reserve assessed by stress echocardiography has been shown to have a predictive value for the existence of reverse remodeling and functional recovery [11].

Computed Tomography

The main role of computed tomography (CT), namely through CT angiography, falls within the scope of the diagnosis of DCM itself, as it is a highly valuable exam in the exclusion of significant epicardial coronary disease [12]. More recently, the possibility of performing functional assessment of coronary stenosis by CT (FFRct) complements the purely angiographic approach to the exclusion (or detection) of hemodynamically significant coronary disease [13,14].

In addition to this indication, CT angiography also has excellent accuracy for the detection or exclusion of atrial thrombi in patients with atrial fibrillation, as well as for cardiac morphological assessment when planning the implantation of devices such as valve prostheses, circulatory assist devices or as guide for implantation of left ventricular lead in cardiac resynchronization devices [15]. Finally, CT may have a role in the assessment of ventricular volumes and function, however, due to the lower temporal resolution and use of ionizing radiation and iodinated contrast, it has a limited role in cases where echocardiography has a suboptimal image and magnetic resonance is contraindicated.

Magnetic Resonance

Cardiac magnetic resonance imaging (CMR) is currently an increasingly indispensable imaging method in the evaluation of patients with DCM, given its ability to accurately and reproducibly assess ventricular volumes, function and mass, in a way that obviates many of the limitations of other imaging methods, namely echocardiography. It is the gold-standard imaging method for the assessment of ventricular volumes and systolic function, obtained through cine sequences [16]. Furthermore, the tissue characterization of the myocardium that CMR allows to perform in a non-invasive way is undoubtedly an added value of CMR in the imaging evaluation of patients with DCM. For these reasons, in addition to the fact that CMR is an exam without the use of ionizing radiation and with the use of gadolinium-based contrast, which are generally considered safe (for the non-linear compounds, currently in use in clinical practice), make this examination of great importance for the etiological characterization of patients with MCD.

Myocardial late gadolinium enhancement is currently the gold-standard noninvasive technique for assessing the presence and extent of myocardial fibrosis [16]. The late enhancement pattern helps in the etiological diagnosis of the dysfunction and, first of all, given its value in the etiological diagnosis, one must differentiate between late enhancement with an ischemic (subendocardial or transmural) or non-ischemic (mid-mural or subepicardial) pattern; in the case of late enhancement of an ischemic pattern, its presence does not exclude by itself the diagnosis of DCM, since it must be of sufficient extension to justify the ventricular dysfunction. Within the patterns of non-ischemic late gadolinium enhancement, the distribution of late enhancement itself may point to a specific etiology, such as the involvement of basal segments (mainly the basal septum and lateral wall) in sarcoidosis,

or mid-mural enhancement with different locations in cases of genetic, inflammatory, or idiopathic MCD; It is worth noting the case of amyloidosis in which, although the typical pattern of enhancement is a subendocardial enhancement pattern, it has a diffuse and circumferential distribution (not compatible with a coronary territory), a finding that in correlation with other imaging and clinical findings usually establishes the diagnosis. In addition to its etiological diagnostic value, late enhancement also has a robust prognostic value (and additive to the ejection fraction), in which its presence is a marker of future adverse events [17,18]; this occurs in a continuous way, as the greater the extension of the enhancement, the worse the prognosis in terms of all-cause mortality, hospitalization or sudden cardiac death [19]. The absence of late myocardial enhancement has been associated with a good prognosis, namely with a higher probability of reverse remodeling after the institution of therapies [20,21]. In addition to late enhancement, the possibility of performing a myocardial perfusion study with contrast [with a diagnostic accuracy similar to that of positron emission tomography (PET) and superior to single photon emission computed tomography (SPECT) [22]] aids in the detection or exclusion of significant coronary disease.

Late enhancement can also play an important role in the therapeutic orientation of these patients, namely in the selection and orientation of patients for resynchronization and defibrillation devices. The DANISH study [23] questioned the benefit of ICD implantation in patients with DCM in the same way as in patients with ischemic dysfunction, having led to a class reduction in the recommendation of ICD implantation in primary prevention in patients with DCM in the most recent European recommendations [24]. Considering the hypothesis that patients with delayed enhancement may be those who will benefit most from ICD implantation, studies have been developed with the purpose of testing this theory, however, with conflicting results so far [25,26]. Still with regard to resynchronization through CRT implantation, the distribution of late enhancement can help to define the optimal positioning for the left ventricular lead, given that to obtain myocardial stimulation it must be positioned close to a zone of viable myocardium [27]; this can be even more critical in view of the results of a study that showed an increased risk of cardiovascular death when positioning the aforementioned electrode over myocardial scar areas [28].

In addition to late gadolinium enhancement, myocardial mapping techniques have been gaining preponderance, as they contribute to tissue characterization beyond late enhancement, especially because they do not require the administration of contrast. Through mapping techniques, the values of myocardial T1, T2 and $T2^*$ can be assessed, which represent intrinsic tissue properties that are altered in disease processes [29]. T1 mapping has shown a good correlation with the presence of late gadolinium enhancement, allowing the assessment of the presence and extent of fibrosis (without the need for administration of a gadolinium-based contrast agent) when a high native T1 value is evidenced, also having an associated prognostic value [30]. On the other hand, low T1 values may also raise suspicion of certain etiologies, such as myocardial iron deposition cardiomyopathy or Anderson-Fabry disease. In addition to native T1 mapping (without contrast), the assessment of T1 mapping after contrast administration, together with the hematocrit value, allows the assessment of myocardial extracellular volume, which is particularly useful for the quantification of amyloid deposition in patients with cardiac amyloidosis (both ATTR and AL), adding additional prognostic value to late enhancement or native T1 mapping [31]. T2 mapping makes it possible to quantitatively assess the presence and extent of myocardial edema, particularly useful in situations of active inflammation, such as in the acute phase of myocarditis, or in phases of exacerbation/flares of inflammatory cardiomyopathy (such as, for example, sarcoidosis) [32]. $T2^*$ mapping is the method of choice for non-invasive assessment of the presence and extent of myocardial iron deposition, having a well-established role in both diagnosis and follow-up of these patients, with regard to the assessment of response to iron chelation therapy [33].

Still in regard to therapeutic guidance, namely cardiac resynchronization therapy and the assessment of ventricular desynchrony, CMR is a reference method for the assessment of cardiac movement and deformation through the tagging technique [34]. However, this technique involves complex post-processing which limits its clinical applicability.

The assessment of myocardial strain through feature tracking has been suggested as an additional prognostic marker [35,36], being a technique that, when available, can be applied through post-processing of the regularly acquired cine images, thus not requiring additional sequences that would lead to an increase in image acquisition time.

Finally, a note for the evaluation of the right ventricle whose volumes and function are often difficult to assess by echocardiography, and also because right ventricular function in patients with DCM has been shown to be an independent predictor of survival after cardiac transplantation [37].

Given all the previously mentioned advantages of CMR, there is increasing evidence that CMR should be offered to all patients with a diagnosis or suspicion of DCM (provided there are no contraindications) at an early stage of the evaluation, with the aim of diagnosis, prognosis and consequent therapeutic guidance.

Nuclear Imaging

SPECT may play a role in the diagnosis by allowing the assessment of myocardial perfusion, thus enabling the detection of areas of ischemia and/or necrosis that point to a diagnosis of ischemic cardiomyopathy and not DCM. The use of gated-SPECT also allows the assessment of left ventricular volumes and function, although it has a limited role in this context. Nuclear imaging may also play an important role in detecting specific etiologies in patients with an established diagnosis of MCD.

^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET is particularly useful for the diagnosis of sarcoidosis, as it is the most sensitive method for detecting areas of active inflammation as well as detecting areas of inflammation in extracardiac territories [38].

SPECT with ^{99}mTc-3,3-disphosphono-1,2-propanodicarboxylic acid (^{99}mTc-DPD) has an established role in the diagnosis and quantification of cardiac amyloidosis by transthyretin deposition (ATTR) [39,40], which is of increasing interest in recent times given the emergence of a therapy with demonstrated results to delay the progression of the disease [41].

SPECT with ^{123}Imetaiodobenzylguanidine (^{123}I-MIBG), which is a substance analogous to norepinephrine, is a technique with prognostic value as it allows the assessment of sympathetic innervation at the cardiac level, which has been shown to be associated with arrhythmic events and disease progression [42-44].

Conclusion

The aim of this article was to make a general review of the applicability of the various imaging techniques regarding the evaluation of patients with (or suspected) DCM. Thus, it intended to take a different approach from the one applied in a current consensus document that presents the applicability of the various imaging techniques according to the clinical purpose [45]. It can easily be understood that in most cases it will be necessary to use more than one imaging modality to achieve the best diagnosis, prognosis and therapeutic guidance for these patients, with information that complements each other. A special emphasis is given to CMR, which is an increasingly important exam in these cases. However, the limitations of accessibility to certain techniques, cost and exposure to radiation and/or contrast in certain imaging techniques dictate that the choice of exams to be performed must be carried out in a judicious way and applied individually to each patient. In conclusion, there are still several techniques under development and many of the ones already available for use in imaging laboratories still lack further studies that allow their validation and use in a clear and routine way in clinical practice.

Conflicts of Interest

None to declare.

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