FIC Federazione Italiana di Cardiologia
Italian Federation of Cardiology

Multimodality imaging of pericardial diseases

Massimo Imazio[a,b], Patrizia Pedrotti[c], Giuseppina Quattrocchi[c], Alberto Roghi[c], Luigi Badano[d], Riccardo Faletti[b,e], Jan Bogaert[f] and Fiorenzo Gaita[a,b]

J Cardiovasc Med 2016, **17**:774–782

Keywords: cardiac magnetic resonance, cardiac tamponade, computed tomography, constrictive pericarditis, echocardiography, imaging, pericardial effusion, pericarditis, pericardium

[a]University Cardiology, Department of Medical Sciences, AOU Città della Scienza e della Salute, [b]University of Torino, Torino, Italy, [c]Department of Cardiology, Cardiovascular Magnetic Resonance Unit, Niguarda Cà Granda Hospital, Milano, [d]Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, [e]University Radiology, Department of Surgical Sciences, AOU Città della Scienza e della Salute, Torino, Italy and [f]Department of Radiology, UZ Leuven, Leuven, Belgium

Correspondence to Massimo Imazio, MD, FESC, Cardiology Department, Maria Vittoria Hospital and Department of Public Health and Pediatrics, University of Torino, Torino, Italy
E-mail: massimo_imazio@yahoo.it; massimo.imazio@unito.it

Received 10 January 2016 **Revised** 21 July 2016
Accepted 24 July 2016

Pericardial diseases are common diseases encountered in clinical practice either as an incidental finding or part of a known heart or systemic disease.[1,2]

The cause is varied and may be infectious [especially viral or bacterial with tuberculosis (TB) as leading cause all over the world and especially in developing countries] or noninfectious (systemic inflammatory diseases, post-cardiac injury syndromes, cancer, metabolic, posttraumatic and drug-related).[3] In many cases, pericardial response to different causes may be relatively nonspecific with acute inflammation and increase of pericardial fluid production manifested as pericardial effusion. Chronic processes (>3 months) may lead to organization, fibrosis and calcification of the pericardium, which may exert a 'constrictive' action on the cardiac chambers.

Although survival is possible in the absence of the pericardium, it has several functions as mechanical barrier to the spread of infections and pathological processes from the surrounding organs and structures. The pericardium has additional mechanical functions including fixation of the heart and allowing cardiac motions without attrition; it has mild compressive effects on right chambers and regulates the interaction between right and left chambers.[4]

Few clinical syndromes have been reported: pericarditis, pericardial effusion, cardiac tamponade, constrictive pericarditis and pericardial masses.

Many cases have a self-limited course, but significant morbidity and mortality can occur if pericardial disease is not recognized and treated.

On this basis, multimodality imaging is an integral part of contemporary management of pericardial diseases that is recommended in all patients with suspected pericardial disease.[5] Main imaging modalities include echocardiography, computed tomography (CT) and cardiac magnetic resonance (CMR).

In 2013, the American Society of Echocardiography has issued a consensus statement on multimodality cardiovascular imaging of pericardial diseases that has been endorsed by the Society of Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography.[6] In 2014, an European position paper has been also published by the European Association of Cardiovascular Imaging and European Society of Cardiology (ESC) Working Group on myocardial and pericardial diseases.[7] Aim of the present focused review is to compare the two documents and provide essential key messages for implementation of multimodality imaging in clinical practice also by nonexperts in cardiovascular imaging.

The American consensus statement

The American consensus statement is a comprehensive, updated review of the main imaging methods for the study of pericardial diseases.[6] The main structure of the article consists of a brief review of the anatomy and pathophysiology of the pericardium, with description of the pericardial syndromes (acute pericarditis, recurrent pericarditis, pericardial effusion, cardiac tamponade, constrictive pericarditis, pericardial masses and congenital abnormalities of the pericardium) including essential data on the cause, diagnosis and therapy of each syndrome besides detailed statements on multimodality imaging. The final part includes future techniques, applications and key points for each pericardial syndrome.

Main strengths and weaknesses of echocardiography, CT and CMR are reviewed. The clinical evaluation should guide the decision of which diagnostic test should be performed to avoid unnecessary testing and costs. Echocardiography remains the first imaging modality for the diagnosis and follow-up of patients with a suspected or known pericardial disease. The main reasons are the wide availability, the limited costs and possibility to assess basic anatomic and functional data. In clinical practice, data from echocardiography are integrated with the clinical evaluation and other basic tests (e.g. ECG, chest radiograph and blood chemistry) and are sufficient for the

DOI:10.2459/JCM.0000000000000427

clinical management of the vast majority of patients without resorting to additional imaging techniques in most cases.[6] Nevertheless, although echocardiography is widely available and cheap, it has several important limitations also linked to the fact that not all echolaboratories (e.g. in peripheral hospitals) are capable of performing a comprehensive echocardiographic evaluation for the assessment of specific pericardial diseases such as constrictive pericarditis. Furthermore, some echocardiographic manifestations, such as the presence of pericardial effusion in the setting of a suspected pericarditis, may be misleading and may require further assessment to reach the correct diagnosis by additional clinical, laboratory and imaging techniques.

The normal pericardium consists of an inner layer (the visceral pericardium or epicardium that consists of a layer of mesothelial cells in contact with the myocardium or epicardial-fat-containing vessels and nerves) and an outer layer (the parietal pericardium particularly rich in collagen fibres). The anatomical thickness of the pericardium is 0.8–1.0 mm, and it appears as a curvilinear density on CT, with an intermediate signal intensity delineated by surrounding fat on CMR. Its measure ranges from 0.7 to 1.2 mm on CT and 1.2–1.7 mm on CMR (abnormal values usually are >2–3 mm).[8–12] Transthoracic echocardiography is not reliable for the measure of pericardial thickness, whereas limited studies have found the measures on transoesophageal echocardiography (TOE) to be reliable and correlated to those reported by CT.[13] Specific recommendations and considerations on pericardial syndromes are reviewed and summarized in the subsequent paragraphs.

Specific recommendations

Acute and recurrent pericarditis

According to the document, diagnostic criteria for acute pericarditis include four clinical criteria: pericarditic chest pain, pericardial rubs, ECG changes (ST-segment elevation and/or PR depression) and new or worsening pericardial effusion. The diagnosis is performed when at least two out of four criteria are detected. Supportive findings to be considered in case of atypical or doubtful presentations according to traditional diagnostic criteria include the elevation of inflammatory markers and 'evidence of pericardial inflammation' by imaging.[6] The American document especially supports the use of CMR to detect pericardial oedema on T2-weighted images and pericardial late gadolinium enhancement (LGE) as organizing pericarditis. Imaging of pericardial inflammation may also be helpful in selected cases to monitor the response to anti-inflammatory therapy.[6]

Echocardiography is the first imaging method for the diagnosis and detection of pericardial effusion and cardiac tamponade (overall 3% of cases). Additional features that can be assessed by echocardiography include increased pericardial brightness, intrapericardial fibrinous strands (inflammatory cause or clotted blood), septal bounce (in case of constrictive physiology) and pericardial masses.

Echocardiography should be performed within 24 h from the beginning of symptoms. In case of 'poor prognostic features' (high fever >38 °C, indolent course and failure to respond to therapy),[14] CT and CMR should be considered as well as in patients with inconclusive echocardiographic findings, atypical presentations, suspicion of constriction, associated chest trauma or concomitant diseases [e.g. myocardial infarction (MI), chest and lung diseases].[6] CMR is the most sensitive test for the comprehensive evaluation of pericardial anatomy and function, for the detection of pericardial inflammation and to highlight the features of constrictive physiology.[10–12]

At CT, the inflamed pericardium is thickened and contrast-enhanced. If pericardial fluid is present, exudative fluid has increased density [e.g. 20–60 Hounsfield unit (HU)] compared with transudates (<10 HU).[8,9,11] At CMR, the inflamed pericardium is thickened, shows increased signal intensity on T2-weighted short-tau inversion recovery (STIR) images (oedema) and enhances at late postcontrast images as expression of inflammation. Inflammatory pericardial fluid with high protein content shows higher signal on T1-weighted images. Pericardial adhesions between inflamed visceral and parietal pericardial layers can be assessed using dynamic tagging at CMR study.[8,9,11]

Similar considerations apply to recurrent pericarditis.[14]

Pericardial effusion

A quantitative classification of the effusions is proposed as small between 50 and 100 ml, moderate from 100 up to 500 ml and large if more than 500 ml.[6] The size of the effusion is poorly correlated with its haemodynamic effect, whereas the speed of accumulation is much more important as the pericardium is rather stiff and rapidly accumulating effusions may quickly become symptomatic (e.g. haemopericardium with cardiac tamponade) compared with slowly accumulating effusions that may become large without symptoms (e.g. hypothyroidism).[15–19] Pericarditis is commonly associated with small effusions if uncomplicated[20–22]; moderate effusions have several possible causes, whereas large effusions are especially related to neoplasms, TB or hypothyroidism.[15–19] Uncomplicated small effusions related to pericarditis may be managed in an outpatient setting, whereas patients with moderate-to-large pericardial effusions should be admitted for evaluation, monitoring and possible drainage for diagnostic and/or therapeutic purposes.[5,6,15–19]

Imaging is indicated whenever a pericardial effusion is suspected (e.g. pericarditis, aortic dissection, after MI and in patients developing hypotension or haemodynamic

instability after surgical or percutaneous cardiac procedures).

Echocardiography is the first imaging modality for the diagnosis and evaluation of pericardial effusions.[6] On M-mode, a systolic-only separation of pericardial layers is considered a 'trivial' and clinically insignificant amount of pericardial fluid. A small pericardial effusion (>50 ml) is manifested by a systo-diastolic separation of pericardial layers. A left pleural effusion may be distinguished by pericardial fluid on the parasternal long axis view as pericardial fluid is between the descending aorta and the heart, whereas pleural effusion is posterior to the descending aorta. Epicardial fat may be distinguished from pericardial fluid as it is brighter than the myocardium and moving in concert with the heart.[6] Semiquantitative assessment of the pericardial effusion considers the size of the echo-free space between pericardial layers at end-diastole: only systolic separation is considered trivial, in small pericardial effusion the separation is less than 10 mm, in moderate effusion it is between 10 and 20 mm, and it is more than 20 mm in large or more than 25 mm in very large effusions.[6,16,19]

When the pericardial effusion is complex or loculated or clot is present, CT is an important adjunct study to be performed. On CT, attenuation levels may be helpful to give a suggestion of the type of effusion: low attenuation values close to those of fat (−60 to −80 HU) have been reported in case of chylopericardium, attenuation values close to water (<10 HU) can be found in transudates, whereas attenuation values between 20 and 60 HU suggest possible exudates. Effusions with attenuation values more than 60 HU suggest haemorrhage.[8,9,11] CMR is helpful for an attempt of tissue characterization and differentiation of pericardial thickening from fluid and especially in complex, loculated effusions or when a haematoma is suspected.[10–12]

Cardiac tamponade

The haemodynamic spectrum of cardiac tamponade varies from mild to severe and life-threatening.[15,16] In addition, cardiac tamponade may be either low pressure (or occult) or regional due to loculated effusion or compressive blood clot.

Echocardiography is the initial imaging modality in the suspect of cardiac tamponade: the most important echocardiographic findings include the presence of pericardial effusion, a dilated inferior vena cava (IVC) (IVC plethora: dilated IVC > 21 mm with <50% reduction in diameter during inspiration), abnormalities of the hepatic veins (usually showing a biphasic normal hepatic venous flow with systolic velocity greater than diastolic velocity and a reduced forward velocity or small reversal during atrial contraction; in case of tamponade, the diastolic component is reduced or abolished in more severe cases), right heart diastolic chamber collapse, inspiratory bulge or 'bounce' of the interventricular septum and abnormal respiratory changes at Doppler flow velocity recordings (e.g. >30% inspiratory reduction in mitral peak E wave velocity is considered diagnostic).[23–31]

For diastolic right chamber collapse, it is important to note that because the right atrium (RA) is a thin-walled structure, a brief collapse may occur even in the absence of tamponade in moderate-to-large pericardial effusions. The duration of RA collapse is important: if it exceeds one-third of the duration of the cardiac cycle, it is nearly 100% sensitive and specific for clinical cardiac tamponade. M-mode study placing a cursor through the affected wall is an excellent method to assess timing and duration of chamber collapse.[25] The absence of any chamber collapse has a more than 90% negative predictive value for clinical cardiac tamponade.

Diastolic right chamber collapse may be affected by basal levels of chambers pressure and it could be delayed in case of right ventricular (RV) hypertrophy, pulmonary hypertension and on the opposite it could be anticipated in hypovolaemia.[6]

TOE may be helpful in assessing regional tamponade in postoperative and postprocedural cardiac tamponade. CT and CMR do not have a role in the emergency and urgent setting of cardiac tamponade. CT may be valuable in case of subacute cardiac tamponade due to a loculated effusion.[6]

Constrictive pericarditis

Constrictive pericarditis is not always due to a thickened pericardium: in surgically proven forms about 20% of cases have a pericardial thickness less than 3 mm.[32] Echocardiography is the first imaging modality in all patients with a suspicion of pericardial constriction.[6] Pericardial thickness cannot be reliably assessed by echocardiography but pericardial constriction can be suspected in case of parallel motion of the pericardial layers, which are usually separated by an echo-free space. Additional findings include diastolic flattening of the left ventricular (LV) posterior wall, abrupt posterior motion of the ventricular septum in early diastole with inspiration (septal bounce) and occasionally premature opening of the pulmonary valve. The 'septal bounce' is a very specific sign of pericardial constriction due to the exaggerated interventricular interdependence occurring in the setting of constrictive pericarditis. The rigid pericardium fixes the maximal volumes of ventricles; thus, the increased size of the RV during inspiration (due to increased venous return) can occur only with a shift of the septum to the left side and subsequent reduction of the size of the LV, the reversal changes occur during expiration. On two-dimensional echocardiography, IVC plethora and septal bounce are evident signs of elevated RA pressure.[6] Characteristic Doppler flow velocity recordings reflect exaggerated interventricular

interdependence with more than 25% respiratory variation for peak mitral E wave and more than 40% respiratory variation of tricuspid E wave.[33,34] The propagation velocity of early diastolic transmitral flow on colour M-mode is normal or increased (>100 cm/s).[35] On Doppler tissue imaging, E′ velocity is normal or even elevated at the septum (thus the usual positive linear relation between E/E′ ratio and left atrial pressure is reversed in most patients with constriction: the so-called annulus paradoxus), but might be decreased at the lateral mitral annulus (annulus reversus) as constriction worsens, due to a limitation of the possible longitudinal movements of the ventricle by the rigid pericardium.[6,35–40] On the contrary, the E′ velocity is reduced in restrictive cardiomyopathy as it is a primary disease affecting the myocardium: this feature is particularly useful for the clinicians for the differential diagnosis between constrictive pericarditis and restrictive cardiomyopathy. Strain imaging may be helpful to distinguish constriction from restriction as the reduction in global strains areas more pronounced in the circumferential direction for patients with constriction, whereas it is more pronounced in the longitudinal direction in patients with restrictive cardiomyopathy.[6,41–43]

CT is highly accurate to assess pericardial thickness (thickened parietal pericardium is usually >4 mm), and it is the best diagnostic test for the assessment of calcifications (about 50% of patients with pericardial constriction have calcifications). Both features are very helpful for the surgical planning of pericardiectomy.[8,9,11] Contrast-CT may allow better delineation of cardiac chambers and depict pericardial enhancement as sign of pericardial inflammation.[43]

CMR allows the measurement of pericardial thickness (pathologic if >4 mm), the differentiation of pericardial effusions from pericardial thickening, the assessment of pathologic interventricular interdependence (cine-real time imaging during free breathing) and the identification of IVC plethora.[11–13,44,45] Moreover, pericardial LGE might be helpful to predict possible reversibility of constriction after anti-inflammatory therapy. Patients with pericardial LGE have greater fibroblasts proliferation, chronic inflammation, neovascularization and thickening compared with those without LGE.[43]

In addition, CMR myocardial tagging sequences can demonstrate pericardial–myocardial adherence (adhesions blunt or abolish tag deformation).[6]

Nowadays, the advances in imaging techniques (e.g. use of CMR) allow early diagnoses of constrictive pericarditis before advanced forms with calcifications.

Pericardial masses

Pericardial masses can be readily identified by echocardiography, which remains the first imaging technique to approach this issue. CT and CMR are the second-level imaging modalities usually required for further assessment of the masses. CMR is superior to other imaging techniques for tissue characterization.[6]

The European position paper

The European position paper briefly describes and summarizes the different imaging modalities (chest radiograph, echocardiography, cardiac CT and CMR) with their strengths and limitations, normal anatomy, physiology and imaging findings. The use of noninvasive imaging is briefly reviewed with a specific focus on recommendations.[7]

Echocardiography is recommended when pericarditis is suspected as the presence of pericardial effusion is a diagnostic criterion.[1,2,21,22] No additional imaging techniques are required in case of absent or mild effusion and uncomplicated course.

Echocardiography is recommended also for follow-up studies and to guide and monitor pericardiocentesis when needed (therapeutic pericardiocentesis in cardiac tamponade and large symptomatic pericardial effusions or diagnostic pericardiocentesis in moderate-to-large pericardial effusions and suspicion of a nonidiopathic cause).[6]

CMR is recommended when concomitant myocarditis is suspected to detect myocardial involvement.[46,47] TOE is recommended in case of transthoracic echocardiography images of poor quality.

In case of moderate-to-large pericardial effusion or complicated course or suspicion of nonidiopathic cause, additional imaging is needed. CT and CMR are particularly recommended for these cases.[7]

CT allows the assessment of pericardial thickness and calcifications and of the composition of pericardial effusion (transudate vs. exudate vs. haematoma according to attenuation values expressed in HU). CMR is superior for tissue characterization as well as for the evaluation of pericardial and myocardial inflammation.[8,9,11,12,43]

The main recommendations of the European document include

(1) **Recommendations for acute pericarditis with small or no effusion (noncomplicated course)**: transthoracic echocardiography (TTE) to confirm clinical diagnosis and CMR to confirm clinical diagnosis if clinical context of myocarditis.
(2) **Recommendations for acute pericarditis with complicated course and/or moderate-to-severe effusion and no tamponade**: TTE to confirm clinical diagnosis, TOE if poor TTE quality of imaging, TTE to indicate, contraindicate pericardiocentesis, TTE to guide and for follow-up of pericardiocentesis, CMR to confirm clinical diagnosis in case of myocarditis. It

is considered reasonable: CT/CMR to confirm clinical diagnosis in case of high suspicion of aortic dissection, CT/CMR to confirm the clinical diagnosis in case of trauma or associated disorders, CT/MRI to confirm clinical diagnosis if echocardiography inconclusive, CMR for follow-up of pericardiocentesis and TTE for follow-up.

(3) **Recommendations for cardiac tamponade and pericardiocentesis:** TTE to confirm clinical diagnosis, TOE if poor TTE quality of imaging, TTE to indicate, contraindicate pericardiocentesis. It is reasonable: TTE to guide and for follow-up of pericardiocentesis, CT/CMR to confirm clinical diagnosis in case of high suspicion of aortic dissection, CT/CMR to confirm the clinical diagnosis in case of trauma and CMR for follow-up of pericardiocentesis. It is not recommended: CT/CMR to confirm clinical diagnosis if echocardiography inconclusive.

(4) **Recommedations for constrictive pericarditis:**

4.1 **Chronic constrictive pericarditis**: it is recommended: TTE to confirm clinical diagnosis, TOE if poor TTE quality of imaging (thickness of pericardium), CMR for planning pericardiotomy (degree of myocardial fibrosis and atrophy, lung damage), and TTE for follow-up. It is reasonable: CT/CMR to confirm clinical diagnosis if echocardiography inconclusive, CT for planning a pericardiotomy (calcification, coronary arteries, lung damage, previous CT surgery), CMR for follow-up.

4.2 **Effusive-constrictive pericarditis**: it is recommended: TTE to confirm clinical diagnosis and for follow-up postpericardiocentesis. It is reasonable: CT/CMR to confirm clinical diagnosis if echocardiography inconclusive, CMR with contrast to evaluate inflammation, and CMR for follow-up.

(5) **Pericardial masses of the pericardium**: it is recommended: TTE to confirm clinical diagnosis, TOE if poor quality of imaging, and CT/CMR to confirm clinical diagnosis and for further evaluation of the mass and lymphadenopathy detection.

For pericardial cysts and diverticula: it is recommended: TTE to confirm clinical diagnosis and follow-up, and CT/CMR to confirm clinical diagnosis. It is reasonable: contrast echocardiography to exclude anomalous systemic vein. It is not recommended CT for follow-up.

Overall, the two documents provide similar indications and recommendations regarding the use of different imaging techniques with a main difference represented by a more detailed description of the findings in the American document and a more detailed listing of recommendations with a more concise description of the findings in the European document. We summarize the main differences of the two documents in Table 1.

Table 1 Main similarities and differences between the American[6] and European position papers[7]

Feature	American position paper	European position paper
Document pages	63	20
Figures (main text)	58	21
References	215	87
Description of anatomy and pathophysiology	Detailed	Summary
Specific sections on main pericardial syndromes[a]	Yes	Yes
Detailed list of recommendations for each syndrome (as list/table)	No	Yes
Discussion and list of main strengths and weaknesses of main imaging modalities (TTE, CT and CMR)	Yes	Yes

CMR, cardiac magnetic resonance; CT, computed tomography; TTE, transthoracic echocardiography. [a] Pericarditis, pericardial effusion, cardiac tamponade, constrictive pericarditis and pericardial masses.

The 2015 European Society of Cardiology guidelines on the diagnosis and management of pericardial diseases

The new 2015 ESC guidelines on the diagnosis and management of pericardial diseases summarize the role of multimodality imaging of pericardial diseases as a modern and comprehensive approach for the evaluation of patients with high-risk features and when echocardiography is not sufficient for the final diagnosis.[5]

These guidelines are consistent with the American and European consensus documents.[6,7] The main recommendations for the imaging of pericardial diseases are summarized in Tables 2 and 3.

Additional considerations have been added on the role of nuclear medicine techniques.[5] In selected cases, PET alone, or preferably in combination with CT (PET/CT) can be performed to assess the metabolic activity of pericardial disease.[48–50] Increased pericardial uptake of (18)F-fluorodeoxyglucose (FDG) can be demonstrated in patients with solid cancers and lymphoma and is indicative of (malignant) pericardial involvement, thus providing essential information in the diagnosis, staging and assessment of therapeutic response. The uptake is usually intense and often associated with a focal soft-tissue mass. PET/CT is also of value in identifying the nature of inflammatory pericarditis. In particular, tuberculous pericarditis yields higher FDG uptakes than idiopathic forms.[48–51] Nevertheless, this application of PET/CT is limited to specific cases in which second-level imaging techniques (e.g. CT and CMR) are not diagnostic. It should be underlined that in most cases, the presence of active inflammatory pericarditis can be easily diagnosed using MR (thickened pericardial layers with positive T2-STIR and LGE) or also with contrast-enhanced CT (enhancement of pericardial layers).

Key messages for clinical practice

Echocardiography is the first-level imaging test to be performed in a patient with suspected pericardial disease.

Table 2 General diagnostic workup of pericardial diseases (from 2015 European Society of Cardiology guidelines)[5]

Recommendation	Class	Level
In all cases of suspected pericardial disease the first diagnostic evaluation is recommended with auscultation; ECG; transthoracic echocardiography; chest radiograph; routine blood tests, including markers of inflammation (i.e. CRP and/or ESR), white blood cell count with differential count, renal function, liver tests and cardiac enzymes (creatine kinase and troponins)	I	C
Independent predictors of an identifiable and specifically treatable cause of pericarditis (i.e. bacterial, neoplastic pericarditis and systemic inflammatory diseases) can identify patients at high risk of complications. Major factors include:	I	B
Fever >38 °C, subacute course (symptoms developing over several days or weeks), large pericardial effusion (diastolic echo-free space >20 mm in width), cardiac tamponade and failure of aspirin or NSAIDs		
CT and/or CMR are second-level testing for diagnostic workup in pericarditis	I	C
Pericardiocentesis or surgical drainage is indicated for cardiac tamponade or suspected bacterial and neoplastic pericarditis	I	C
Percutaneous or surgical pericardial biopsy may be considered in selected cases of suspected neoplastic or tuberculous pericarditis	IIb	C
Further testing is indicated in high-risk patients (defined as above) according to the clinical conditions	I	C

CMR, cardiac magnetic resonance; CRP, c reactive protein; CT, computed tomography; ESR, erythrocyte sedimentation rate.

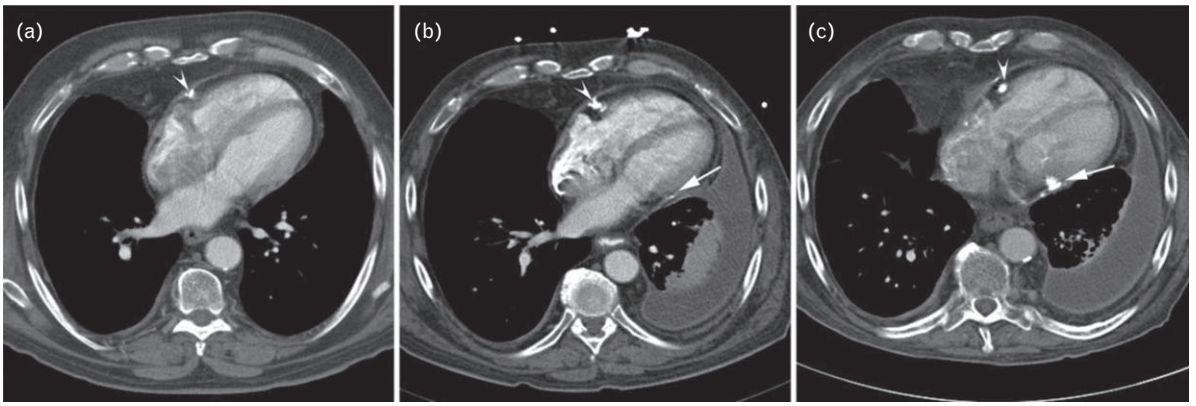
Table 3 First-level and second-level investigation for pericarditis according to 2015 European Society of Cardiology guidelines[5]

Level	Investigation
First level (all cases)	Markers of inflammation (i.e. ESR, CRP and white blood cell count). Renal function and liver tests, thyroid function. Markers of myocardial lesion (i.e. troponins and CK). ECG echocardiography chest radiograph
Second level (if first level not sufficient for diagnostic purposes)	CT and/or CMR; analysis of pericardial fluid from pericardiocentesis, or surgical drainage, for cardiac tamponade; or suspected bacterial, neoplastic pericarditis; or symptomatic moderate-to-large effusions not responding to conventional anti-inflammatory therapy
	Additional testing should be directed to specific causes according to clinical presentation (presence of high-risk clinical criteria)

CMR, cardiac magnetic resonance; CK, creatine kinase; CRP, c reactive protein; CT, computed tomography; ESR, erythrocyte sedimentation rate.

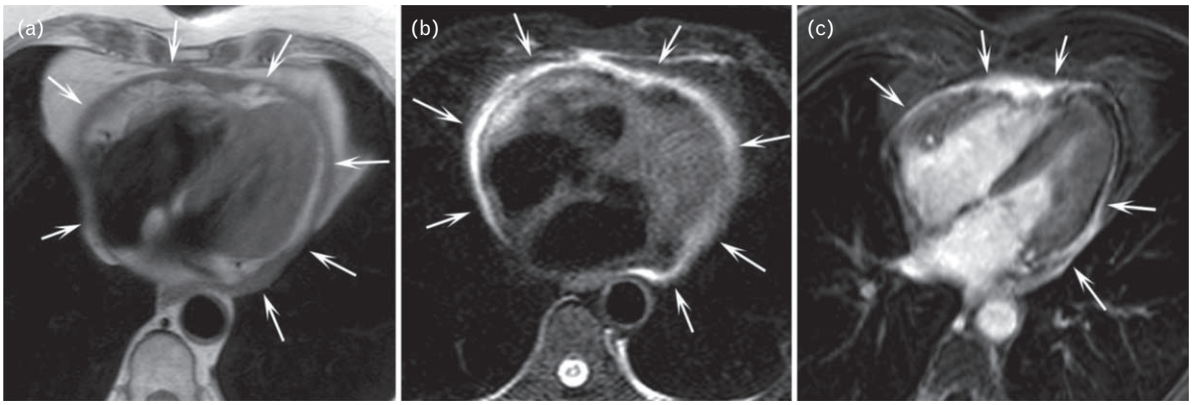
The main strengths of this imaging modality include its wide availability, low cost and portability; it can be performed at bedside or in urgent settings as well as with a respirometer to detect respiratory changes of chamber, vessels size and flows. Nevertheless, echocardiography has a limited window with a narrow field of view and may be also limited in specific conditions (i.e. obesity, chronic obstructive pulmonary disease and postoperative patient). It is also operator-dependent with little tissue characterization capability and cannot accurately assess pericardial thickening (unless TOE is considered) and calcifications. On the contrary, CT may allow the detection of concomitant pleuropulmonary disease, pericardial thickening and calcifications (Fig. 1), but it is more expensive, requires ionizing radiation and may be limited for functional evaluation, in case of arrhythmias, or in clinically unstable conditions. CMR allows better tissue characterization, allowing the non-invasive detection of pericardial inflammation (Fig. 2) and of concomitant myocardial involvement as well as the differentiation between pericardial effusion and pericardial thickening. Main weaknesses include the higher

Fig. 1



Constrictive pericarditis in a 71-year-old man. The presence of calcifications along the left lateral heart border invading the myocardium and right-sided calcifications is evident. There is also concomitant left-sided pleural effusion.

Fig. 2



Recurrent pericarditis on cardiac MRI. A 61-year-old woman with recurrent pericarditis. On cardiac MRI, there is evidence of a thickened, oedematous and strongly enhancing pericardium without evidence of effusive component.

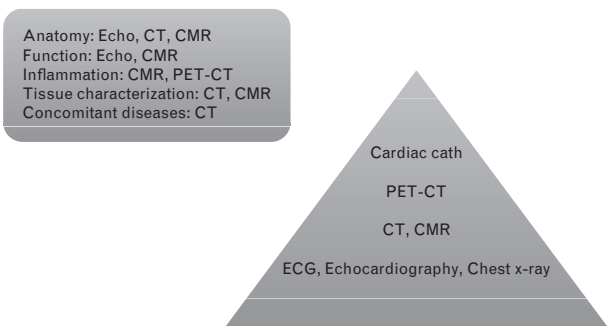
costs, the long acquisition and postprocessing times, the evaluation of patients with arrhythmias, or clinically unstable, and use of gadolinium contrast (discouraged in patients with glomerular filtration rates <30 ml/min).[52] Moreover, as for CT, this imaging technique requires breath-holding at specific times, and the quality of the images is affected in patients unable to breath-hold. Overall, CT and CMR represent second-line techniques especially indicated in cases that are not completely defined by echocardiography, have high-risk clinical features and do not respond to usual therapies, or in case of clinically suspected concomitant pleuropulmonary or systemic disease. A summary of the comparison of the relative main strengths and weaknesses of the different techniques is reported in Table 4.

Table 4 Comparison of noninvasive imaging modalities to study the pericardium

	TTE	CT	CMR
Technical aspects			
Availability	+++	++	+
Cost	Low	Moderate	High
Exam duration (min)	15–30	10	30–40
Safety	+++	+[a]	++[b]
Patient access and monitoring	+++	++	+/−
Pericardium			
Pericardial thickness	−	+++	+++
Pericardial calcifications	−	+++	+/−
Pericardial inflammation	+/−	++	+++
Motion of layers (adhesions)	++	+	+++
Effusion detection	++	+++	+++
Effusion characterization	−	++	++
Pericardial masses	+	+/++	++/+++
Guiding/monitoring pericardiocentesis	+++	−	−
Cardiac morphology (including tissue characterization)	+	++	+++
Cardiac function			
Systolic	++	++[c]	+++
Diastolic function	+++	−	++
Septal motion (coupling)	+++	+/−	+++
Respiratory changes	++	+/−	++

(−) not possible or poor, (+) moderate, (++) good, (+++) excellent. CMR, cardiac magnetic resonance; CT, computed tomography; TTE, transthoracic echocardiography. [a] Ionizing radiation, potential nephrotoxicity of contrast medium, allergic reactions to contrast. [b] Contraindicated in patients with non-MR conditional devices, insulin pumps, metal foreign bodies in the eye, use of gadolinium-based contrast agent discouraged in patients with severe renal impairment (creatinine clearance <30 ml/min), restricted only to haemodynamically stable patients. [c] Use of ECG-synchronized data and spiral acquisition with retrospective reconstruction is also needed. Effusion characterization, systolic function and cardiac tissue characterization may be all available in a CT report, but only with peculiar CT acquisition protocols and with significantly different X-ray exposures. Use of ECG gating with retrospective data acquisition is needed to assess systolic cardiac function, however, at the expense of a significantly higher radiation exposure, and as a consequence is not routinely performed.

Fig. 3



Multimodality imaging for pericardial diseases. Each technique may provide complementary features to complete the puzzle and select the best management and therapy for the specific clinical case. The figure highlights the pyramidal approach to pericardial imaging: basic techniques include ECG, echocardiography and chest radiograph and are for all patients with a suspicion of pericardial diseases; additional techniques should be added in more complicated cases and with specific indications (e.g. for a suspicion of constrictive pericarditis, computed tomography is especially helpful to detect pericardial thickening and calcifications, cardiac magnetic resonance is useful to assess thickening, inflammation and constrictive physiology, whereas cardiac catheterization is at the apex of the pyramid as it is indicated only when the diagnosis cannot be definitely concluded by noninvasive techniques or when they provide conflicting data).

Multimodality imaging of pericardial diseases guided by clinical judgement is essential for the diagnosis and correct therapy of pericardial diseases.[5–7] Each technique has specific advantages, disadvantages as well as indications and contraindications and should be considered in the clinical context (Fig. 3). For instance, in a patient with a suspicion of constrictive pericarditis, the first suspicion is clinical (signs and symptoms of right heart failure in a patient with a possible history of previous pericarditis or cardiac surgery or irradiation). Echocardiography confirms the clinical suspicion, and additional techniques should be selected according to the features to be evaluated: CT and CMR for the assessment of pericardial thickening, CT for the assessment of the presence and extension of calcifications, CMR to differentiate the possible presence of small pericardial effusion vs. pericardial thickening and for the evaluation of possible pericardial inflammation that may suggest that anti-inflammatory therapy should be tried before resorting to pericardiectomy.

Each technique may provide complementary features to complete the puzzle and select the best management and therapy for the specific clinical case and should not be considered as mutually exclusive and antagonist. Such multimodality evaluation has currently reduced the need for cardiac catheterization to cases that cannot be definitely concluded by noninvasive techniques or when they provide conflicting data.

References

1 Imazio M, Gaita F. Diagnosis and treatment of pericardis. *Heart* 2015; **101**:1159–1168.
2 Imazio M, Gaita F, LeWinter M. Evaluation and treatment of pericarditis: a systematic review. *JAMA* 2015; **314**:1498–1506.
3 Ntsekhe M, Mayosi BM. Tuberculous pericarditis with and without HIV. *Heart Fail Rev* 2013; **18**:367–373.
4 Imazio M. *Myopericardial diseases*. Springer; 2016.
5 Adler Y, Charron P, Imazio M, *et al.*, Authors/Task Force Members. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: the task force for the diagnosis and management of pericardial diseases of the European Society of Cardiology (ESC) endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2015; **36**:2921–2964.
6 Klein AL, Abbara S, Agler DA, *et al.* American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. *J Am Soc Echocardiogr* 2013; **26**:965–1012.
7 Cosyns B, Plein S, Nihoyanopoulos P, *et al.*, European Association of Cardiovascular Imaging (EACVI); European Society of Cardiology Working Group (ESC WG) on Myocardial and Pericardial diseases. European Association of Cardiovascular Imaging (EACVI) position paper: multimodality imaging in pericardial disease. *Eur Heart J Cardiovasc Imaging* 2015; **16**:12–31.
8 Verhaert D, Gabriel RS, Johnston D, *et al.* The role of multimodality imaging in the management of pericardial disease. *Circ Cardiovasc Imaging* 2010; **3**:333–343.
9 Yared K, Baggish AL, Picard MH, *et al.* Multimodality imaging of pericardial disease. *JACC Cardiovasc Imaging* 2010; **3**:650–660.
10 Misselt AJ, Harris SR, Glockner J, *et al.* MR imaging of the pericardium. *Magn Reson Imaging Clin N Am* 2008; **16**:185–199.
11 Bogaert J, Francone M. Pericardial disease: value of CT and MR imaging. *Radiology* 2013; **267**:340–356.
12 Bogaert J, Francone M. Cardiovascular magnetic resonance in pericardial diseases. *J Cardiovasc Magn Reson* 2009; **11**:14.
13 Ling LH, Oh JK, Tei C, *et al.* Pericardial thickness measured with transesophageal echocardiography: feasibility and potential clinical usefulness. *J Am Coll Cardiol* 1997; **29**:1317–1323.
14 Alraies MC, AlJaroudi W, Yarmohammadi H, *et al.* Usefulness of cardiac magnetic resonance-guided management in patients with recurrent pericarditis. *Am J Cardiol* 2015; **115**:542–547.
15 Spodick DH. Acute cardiac tamponade. *N Engl J Med* 2003; **349**:684–690.
16 Imazio M, Adler Y. Management of pericardial effusion. *Eur Heart J* 2013; **34**:1186–1197.
17 Sagristà-Sauleda J, Mercé J, Permanyer-Miralda G, Soler-Soler J. Clinical clues to the causes of large pericardial effusions. *Am J Med* 2000; **109**:95–101.
18 Soler-Soler J, Sagristà-Sauleda J, Permanyer-Miralda G. Management of pericardial effusion. *Heart* 2001; **86**:235–240.
19 Imazio M, Mayosi BM, Brucato A, *et al.* Triage and management of pericardial effusion. *J Cardiovasc Med (Hagerstown)* 2010; **11**:928–935.
20 Imazio M, Cecchi E, Demichelis B, *et al.* Indicators of poor prognosis of acute pericarditis. *Circulation* 2007; **115**:2739–2744.
21 Imazio M, Bobbio M, Cecchi E, *et al.* Colchicine in addition to conventional therapy for acute pericarditis: results of the COlchicine for acute PEricarditis (COPE) trial. *Circulation* 2005; **112**:2012–2016.
22 Imazio M, Brucato A, Cemin R, *et al.*, ICAPInvestigators. A randomized trial of colchicine for acute pericarditis. *N Engl J Med* 2013; **369**:1522–1528.
23 Himelman RB, Kircher B, Rockey DC, Schiller NB. Inferior vena cava plethora with blunted respiratory response: a sensitive echocardiographic sign of cardiac tamponade. *J Am Coll Cardiol* 1988; **12**:1470–1477.
24 Singh S, Wann LS, Klopfenstein HS, *et al.* Usefulness of right ventricular diastolic collapse in diagnosing cardiac tamponade and comparison to pulsus paradoxus. *Am J Cardiol* 1986; **57**:652–656.
25 Gillam LD, Guyer DE, Gibson TC, *et al.* Hydrodynamic compression of the right atrium: a new echocardiographic sign of cardiac tamponade. *Circulation* 1983; **68**:294–301.
26 Schiller NB, Botvinick EH. Right ventricular compression as a sign of cardiac tamponade: an analysis of echocardiographic ventricular dimensions and their clinical implications. *Circulation* 1977; **56**:774–779.
27 Leimgruber PP, Klopfenstein HS, Wann LS, Brooks HL. The hemodynamic derangement associated with right ventricular diastolic collapse in cardiac tamponade: an experimental echocardiographic study. *Circulation* 1983; **68**:612–620.
28 Rifkin RD, Pandian NG, Funai JT. Sensitivity of right atrial collapse and right ventricular diastolic collapse in the diagnosis of graded cardiac tamponade. *Am J Noninvasive Cardiol* 1987; **1**:73–80.
29 Leeman DE, Levine MJ, Come PC. Doppler echocardiography in cardiac tamponade: exaggerated respiratory variation in transvalvular blood flow velocity integrals. *J Am Coll Cardiol* 1988; **11**:572–578.
30 Appleton CP, Hatle LK, Popp RL. Cardiac tamponade and pericardial effusion: respiratory variation in transvalvular flow velocities studied by Doppler echocardiography. *J Am Coll Cardiol* 1988; **11**:1020–1030.
31 Appleton CP, Hatle LK, Popp RL. Superior vena cava and hepatic vein Doppler echocardiography in healthy adults. *J Am Coll Cardiol* 1987; **10**:1032–1039.
32 Talreja DR, Edwards WD, Danielson GK, *et al.* Constrictive pericarditis in 26 patients with histologically normal pericardial thickness. *Circulation* 2003; **108**:1852–1857.
33 Hatle LK, Appleton CP, Popp RL. Differentiation of constrictive pericarditis and restrictive cardiomyopathy by Doppler echocardiography. *Circulation* 1989; **79**:357–370.
34 Oh JK, Hatle LK, Seward JB, *et al.* Diagnostic role of Doppler echocardiography in constrictive pericarditis. *J Am Coll Cardiol* 1994; **23**:154–162.
35 Rajagopalan N, Garcia MJ, Rodriguez L, *et al.* Comparison of new Doppler echocardiographic methods to differentiate constrictive pericardial heart disease and restrictive cardiomyopathy. *Am J Cardiol* 2001; **87**:86–94.
36 Garcia MJ, Rodriguez L, Ares M, *et al.* Differentiation of constrictive pericarditis from restrictive cardiomyopathy: assessment of left ventricular diastolic velocities in longitudinal axis by Doppler tissue imaging. *J Am Coll Cardiol* 1996; **27**:108–114.
37 Ha JW, Ommen SR, Tajik AJ, *et al.* Differentiation of constrictive pericarditis from restrictive cardiomyopathy using mitral annular velocity by tissue Doppler echocardiography. *Am J Cardiol* 2004; **94**:316–319.
38 Sohn DW, Kim YJ, Kim HS, *et al.* Unique features of early diastolic mitral annulus velocity in constrictive pericarditis. *J Am Soc Echocardiogr* 2004; **17**:222–226.
39 Ha JW, Oh JK, Ling LH, *et al.* Annulus paradoxus: transmitral flow velocity to mitral annular velocity ratio is inversely proportional to pulmonary capillary wedge pressure in patients with constrictive pericarditis. *Circulation* 2001; **104**:976–978.

40 Reuss CS, Wilansky SM, Lester SJ, *et al.* Using mitral ''annulus reversus'' to diagnose constrictive pericarditis. *Eur J Echocardiogr* 2009; **10**:372–375.
41 Veress G, Feng D, Oh JK. Echocardiography in pericardial diseases: new developments. *Heart Fail Rev* 2013; **18**:267–275.
42 Welch TD, Ling LH, Espinosa RE, *et al.* Echocardiographic diagnosis of constrictive pericarditis: Mayo Clinic criteria. *Circ Cardiovasc Imaging* 2014; **7**:526–534.
43 Feng D, Glockner J, Kim K, *et al.* Cardiac magnetic resonance imaging pericardial late gadolinium enhancement and elevated inflammatory markers can predict the reversibility of constrictive pericarditis after antiinflammatory medical therapy: a pilot study. *Circulation* 2011; **124**:1830–1837.
44 Giorgi B, Mollet NR, Dymarkowski S, *et al.* Clinically suspected constrictive pericarditis: MR imaging assessment of ventricular septal motion and configuration in patients and healthy subjects. *Radiology* 2003; **228**:417–424.
45 Francone M, Dymarkowski S, Kalantzi M, *et al.* Assessment of ventricular coupling with real-time cine MRI and its value to differentiate constrictive pericarditis from restrictive cardiomyopathy. *Eur Radiol* 2006; **16**:944–951.
46 Imazio M, Brucato A, Belli R, *et al.* Colchicine for the prevention of pericarditis: what we know and what we do not know in 2014 – systematic review and meta-analysis. *J Cardiovasc Med (Hagerstown)* 2014; **15**:840–846.
47 Imazio M, Brucato A, Spodick DH, Adler Y. Prognosis of myopericarditis as determined from previously published reports. *J Cardiovasc Med (Hagerstown)* 2014; **15**:835–839.
48 Lobert P, Brown RK, Dvorak RA, *et al.* Spectrum of physiological and pathological cardiac and pericardial uptake of FDG in oncology PET-CT. *Clin Radiol* 2013; **68**:e59–e71.
49 Dong A, Dong H, Wang Y, *et al.* (18)F-FDG PET/CT in differentiating acute tuberculous from idiopathic pericarditis: preliminary study. *Clin Nucl Med* 2013; **38**:e160–e165.
50 Salomäki SP, Hohenthal U, Kemppainen J, *et al.* Visualization of pericarditis by fluorodeoxyglucose PET. *Eur Heart J Cardiovasc Imaging* 2014; **15**:291.
51 Alter P, Figiel JH, Rupp TP, *et al.* MR, CT, and PET imaging in pericardial disease. *Heart Fail Rev* 2013; **18**:289–306.
52 Dill T. Contraindications to magnetic resonance imaging: noninvasive imaging. *Heart* 2008; **94**:943–948.