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Review

Evaluation of inflammatory pericardial syndromes by multimodality imaging: a narrative review

Evaluación de los síndromes pericárdicos inflamatorios mediante imágenes multimodales: una revisión narrativa

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ABSTRACT. Inflammatory pericardial disease is a group of diseases that include acute pericarditis, constrictive pericarditis, pericardial effusion and tamponade. Clinical diagnosis is really a challenge, and multiple imaging tools are needed to complement each other and provide information for diagnosis, treatment and prognosis of diseases. In this narrative review we will discuss the main multimodal imaging techniques (echocardiography, tomography, magnetic resonance and positron emission tomography) and their real applications in the approach of this entity.
Key words: Pericarditis, echocardiography, tomography, magnetic resonance imaging, positron emission tomography.

RESUMEN. *La enfermedad pericárdica inflamatoria es un conjunto de enfermedades que incluyen la pericarditis aguda, pericarditis constrictiva, derrame pericárdico y tamponade. Su adecuado diagnóstico por clínica es realmente un reto, y se necesitan múltiples herramientas de imagen que se complementan y brindan información tanto para el diagnóstico, guiar el tratamiento y pronóstico. En esta revisión narrativa abordaremos las principales técnicas de imagen multimodal (ecocardiograma, tomografía, resonancia magnética y tomografía por emisión de positrones) y sus aplicaciones reales en el abordaje de dicha entidad.*
Palabras clave: *Pericarditis, ecocardiografía, tomografía, resonancia magnética, tomografía emisión positrones.*

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The pericardium is a sac composed of two walls and a virtual space between them, which in normal conditions contains a certain amount of fluid. It surrounds the heart and the great vessels. Its functions, in summary, are fixation, protection and lubrication of the heart. Pericardial syndromes consist of a spectrum of alterations with different pathophysiologies. The most prevalent disease worldwide is acute pericarditis. Despite being a relatively common disease in the cardiology clinic, there are no reliable statistics, due to few epidemiological data. Other disorders included in the pericardial syndromes are chronic pericarditis, constrictive pericarditis, pericardial effusion, cardiac tamponade and pericardial tumors (primary and metastatic). In recent years, the multimodal imaging approach has been standardized and recent management guidelines ultimately recommend it.[1,2] Multimodal imaging includes echocardiogram, computed tomography (CT), cardiac magnetic resonance (CMR) and positron emission tomography (PET). This article will review the uses and indications of each of these diagnostic modalities in the evaluation of inflammatory pericardial syndromes.

ACUTE PERICARDITIS

Acute pericarditis is a multietiological inflammatory pericardial disorder, which can occur as an isolated entity or as part of a systemic disease, it can present with or without a pericardial effusion. Most cases are self-limited, and occasionally, it can turn recurrent or chronic.

Echocardiography: It is recommended to perform an echocardiogram in all patients with suspected pericarditis. Although many patients may have normal results, if pericardial effusion is present, it supports the diagnosis. The amount of effusion may vary between trivial or mild to large, causing the so-called swinging heart. Myocardial ischemia or injury (like myopericarditis) is excluded when no wall motion abnormalities are found. We may also find increased pericardial brightness, thickening of pericardial layers, and in isolated cases, septal bounce, suggestive of constrictive physiology. If fibrinous strands are present, inflammatory etiology should be suspected.

CMR: The pericardium is defined as a hypo intense curvilinear line between the myocardium and the pericardial fat in cine sequences. It is best visualized in the middle third of the free wall of the right ventricle. In acute pericarditis, an increase in the thickness (>2.5mm) and intensity of the pericardium is usually observed. Findings that might be associated with acute inflammation are: 1) increased signal in the pericardium in T2 weighted sequences (edema), 2) post gadolonium enhancement in early cine sequences, and 3) late enhancement *(Figure 1)*.[3,4] Besides its clinical use for diagnosis, CMR has a prognostic value for two reasons: a) diagnosing coexistence of myocarditis, and b) a greater extension of late enhancement, suggests a greater recurrence at six months.[5] Both findings modify the subsequent treatment.

CT: This technique can easily visualize the pericardium. Like CMR, thickness >2.5mm suggest acute pericarditis. In addition, the existence of irregular contours can be observed. In the context of patients with acute chest pain and intermediate risk of coronary artery disease, the diagnosis of pericarditis remains exclusionary, so CT may be the ideal initial approach.

PET: Because it allows direct visualization of the inflammatory activity; PET/CT image using [18F] FDG allows us to use it for diagnosis, risk stratification and therapeutic monitoring of pericarditis.[6]

CONSTRICTIVE PERICARDITIS

Constrictive pericarditis can occur after any pericardial disease process, mostly inflammatory; and by consequence the pericardium thickens, scars, stiffens and even calcifies, turning it into a non-compliant heart, and ultimately limiting its diastolic filling. It is frequently underdiagnosed or confused with restrictive cardiomyopathy due to similar clinical findings. Time from initial pericardial injury up to onset of constriction is variable, specific risk of progression depends on etiology, it rarely occurs after viral or idiopathic pericarditis but is relatively common in bacterial pericarditis, mostly with purulent pericarditis. Tuberculosis is highly related with this process in underdeveloped countries like Mexico. Diagnosis is suggested when data of right heart failure is present along with preserved biventricular function. The physiopathology of constrictive pericarditis is explained as diastolic filling is restricted by an inelastic, non-compliant pericardium after an initial expansion of the myocardium; early diastolic filling is more rapid than normal because the restraining effect happens until mid-diastole, limiting ventricular filling, even with atrial contraction. As constriction becomes deeper, total diastolic volume is

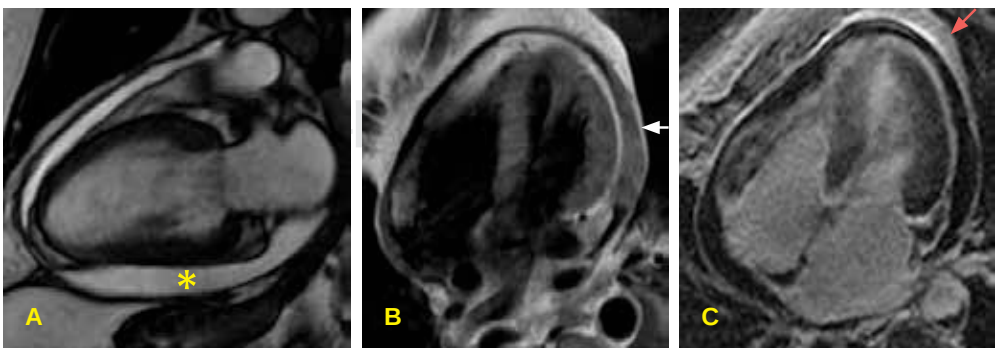

Figure 1: CMR of acute pericarditis. **A.** Cine imaging showing pericardial effusion (*) and thickness of pericardium. **B.** T2w imaging showing increased signal in the pericardium (white arrow), consistent with edema and acute inflammation. **C.** Late gadolinium enhancement of the pericardium (red arrow).

reduced, causing a decrease in cardiac output, and, at the same time, systemic venous pressures increase resulting in blood return to the adjacent inferior vena cava and hepatic veins. As seen with cardiac tamponade, ventricular interdependence becomes exaggerated, manifested as an inspiratory bulging of the interventricular septum to the left, having an additive effect on decreasing the cardiac output during inspiration.

Echocardiography: It is cost effective in these cases. All the different techniques used in echocardiography allow us to differentiate between restrictive cardiomyopathy, constrictive pericarditis and other conditions. It should be noticed that there are not absolute sensitive or specific echocardiographic indicators of constriction, therefore, all data found must be correlated.

With 2D a M modes we can find pericardial thickening and calcification, but it is not mandatory; increased pericardial thickness is suggested by parallel motion of the visceral and parietal pericardium, separated by a relatively echo-free space. If effusion is also present, it makes easier to appreciate the thickened pericardium (>3mm). Shadowing below the pericardium suggests the presence of calcification. The augmented ventricular interdependence appears as exaggerated septal shifts according to the respiratory cycle, or as an abrupt posterior motion of the interventricular septum in early diastole with inspiration (bounce), most evident with M-mode rather than 2D. Also, a diastolic endocardial flattening of the posterior wall endocardium can be present. Imaging of the inferior vena cava shows dilation and a decrease, or even absence, of collapse.

Doppler echocardiography is essential. The classic Doppler finding is an augmented E/A ratio of mitral valve inflow with a short deceleration time, as seen in any disease with restrictive or constrictive physiology, but what makes the difference and establishes the diagnosis is an exaggerated respiratory variability in E-wave velocity (a drop >25% in the first beat after inspiration) with variation >20% in pulmonary vein diastolic forward flow. The propagation velocity of early diastolic trans mitral flow on color M-mode is usually increased as often as >100cm/s.

Doppler tissue imaging is particularly useful. Normally, the lateral mitral annular velocity (e') exceeds the one of the medial annulus in a ratio >1.2, but with constriction, stiff pericardium limits the motion of the lateral annulus with no effect on the medial annulus. There is therefore both preservation of medial velocities and a compensatory augmentation of apex to base shortening of the septum relative to the lateral wall. This increases the medial annulus velocity (>7-8cm/s) situation called «*annulus paradoxus*» and therefore shifting the ratio <1.2 («annulus reverses») which has been documented as a reliable sign of constrictive pericarditis.

Novel techniques in echocardiography are promising in this particular scenario and may help distinguishing between constrictive pericarditis and restrictive cardiomyopathy. Circumferential strain, torsion, and early diastolic untwisting reduce, as global longitudinal strain has no change in constriction, whereas longitudinal strain reduces in restrictive cardiomyopathy. Speckle-tracking techniques have shown significant differences between the strain of the right or left ventricle free walls and the septum.

CMR: Calcifications can be observed as an increase in signal intensity in the pericardium. The thickening of the pericardium is suggestive of constriction when it exceeds 4mm, with sensitivity of 88% and specificity of 100%.[7] The abnormal septal motion, which is the septal protodiastolic flattening, showed sensitivity of 81% and specificity of 100% for the diagnosis of contrition.[8] Moderate to intense delayed enhancement (affecting the entire pericardium) has been associated with a greater proportion of progression to constriction.[9] Speaking of findings of functional constriction, CMR can evaluate the respirophasic changes in real-time sequences, observing the septal excursion to the left ventricle at the beginning of inspiration, and trans mitral and trans tricuspid flows can be quantified simultaneously, with cut-off points of its respiratory variation of more than 25% for the mitral (area under curve [AUC]: 1.0) and more than 45% for the tricuspid (AUC: 0.98).[10] Other indirect constriction data include dilation of the inferior vena cava, suprahepatic veins, right atrium, as well as the coexistence of splenomegaly, ascites and pleural effusion.

CT: Is the ideal method to observe pericardial calcifications, either partial or total. Ring calcifications are also observed as a cause

of constriction. Like the CMR, the pericardial thickness >4mm is highly suggestive, with sensitivity of 86% and specificity of 75%. Dilation of the inferior vena cava with a VCI-aortic radius >1.6 showed sensitivity of 86% and specificity of 75% for this diagnosis.[11]

PET: Inflammation of the pericardium can reach a degree that limits the diastolic ventricular filling, with subsequent fibrosis also known as constrictive pericarditis. The importance lies in the natural evolution of acute pericarditis, since, if detected in early stages of inflammation, the natural progression can be stopped, and therefore avoid fibrosis (transient pericarditis). In a study by Chang et al[12] the use of [18F] FDG in PET was hypothesized to predict the reversibility of transient pericarditis with the use of steroids. It was found that after three months of steroid treatment, the standardized maximal uptake value (SUVmax) was reduced compared to the baseline parameters (2.1±0.8, p<0.001). All patients who responded to treatment had SUVmax >3. This determined that if we use a SUVmax cutoff point of 3.0, we will obtain sensitivity of 100%, specificity of 71% to predict treatment response. This would allow us to avoid surgeries and unnecessary steroid treatments with a very high level of certainty *(Figure 2)*.

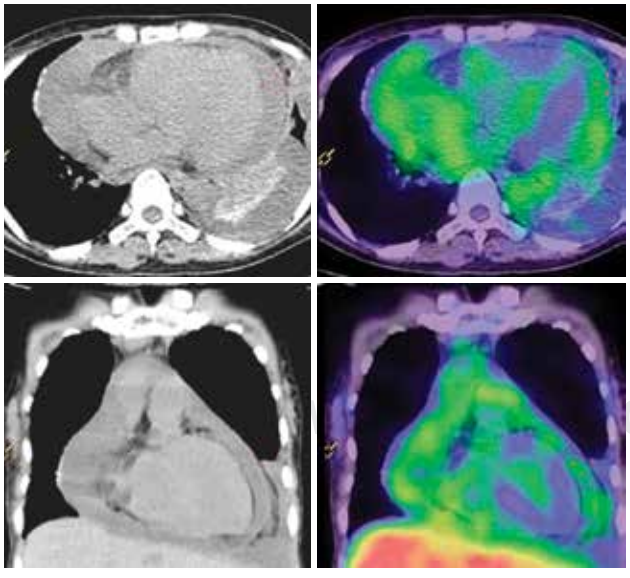

Figure 2: PET of a pericardial effusion with hypermetabolic activity of the fluid, consistent with an exudate.

PERICARDIAL EFFUSION

It is defined as an accumulation of >50mL of fluid inside the pericardial space. As any other pericardial disease it is multietiological. It can be formed either as an increase of production of pericardial fluid, causing an exudate, or by a decrease in the reabsorption, usually generated by an increment of the venous pressure and therefore forming a transudate. Blood in pericardial space may be related with trauma, aortic dissection or with cardiac procedures.

Echocardiography: M and 2D modes show pericardial effusion like an echo free space between both layers of pericardium throughout the cardiac cycle. Using all possible views reliably help to determine the extent of effusion. Left pleural effusion may confused with pericardial effusion; in a 2D parasternal long axis view, if there is fluid between descending aorta and the heart, it should be considered of pericardial origin rather than pleural. 3D echo has shown no difference in this particular case. It's important to note that a specific amount of effusion can't accurately be measured with echocardiography, since there are multiple variations between the effusion and the irregular shape of the heart, and because the possibility of loculations, etc. With echocardiographic data, effusions can be classified according to hemodynamic repercussion (none, mild, severe-cardiac tamponade) and size, measuring the separation between visceral and parietal pericardial layers (mild effusions <10mm, moderate 10-20mm, and large effusions >20mm). When we find an effusion and the heart seems to be dancing in the pericardial space («swinging heart») it is by definition a large effusion. Size also may be an etiological clue, in which small effusions are related with pericarditis while large ones are related with neoplasia or TB. It should be noted that size does not correlate with hemodynamic repercussion, since small increases in an acute onset increase intrapericardial pressure in a short amount of time deriving in hemodynamic instability (cardiac tamponade), whereas, slow increases of fluid elevate the pericardial pressure in the same velocity, allowing cardiac compensatory mechanisms to counteract the hemodynamical effects of the amount of effusion.

CMR and CT: In addition to the uses already described in acute and constrictive pericarditis, CMR and CT contribute little to the approach of these patients. Its use is limited when echocardiography is not diagnostic or in cases where it is necessary to evaluate structures close to the heart, such as trauma or neoplasms *(Figures 3 and 4)*. CT can also suggest the etiology of the effusion, especially when the density is >30 HU, which is very suggestive of hemorrhagic etiology. In cases of significant pericardial effusion, these methods can better visualize the extent of the effusion to guide the pericardiocentesis.

CARDIAC TAMPONADE

Cardiac tamponade is a life threatening condition, with a slow or rapid onset, caused by an accumulation of fluid in the pericardial sac due to inflammation, trauma, rupture of myocardial structures, cardiac devices and procedures, etc., resulting in compression of cardiac chambers and abnormal filling. Considering the pericardial stiffness, as the pressure in the pericardial sac increases due to the effusion, cardiac chambers are compressed and become smaller, reducing diastolic compliance and decreasing systemic venous return. Normally, during inspiration systemic venous return increases distending the right ventricle, however, in tamponade, increased intrapericardial pressure limits this distension and is therefore transmitted to the interventricular septum bulging it to the left, reducing left ventricle compliance and therefore compromising its filling, which at the end results in a decrease of preload, and therefore, of cardiac output and subsequently in hypotension. Ergo, increased intrapericardial pressure and limitation of cardiac volumes causes an exaggerated ventricular interdependence, the physiological basis of clinical pulsus paradoxus. It should be noted that tamponade is the «last drop» of the phenomena of increasing intrapericardial pressure, and it is related with the exhaustion of cardiac compensatory mechanisms. The use of echocardiography is a class I indication in cardiac tamponade and can be also used in guiding pericardiocentesis increasing safety and efficacy.

Even though cardiac tamponade is a clinical diagnosis, there are several helpful echocardiographic findings. Not all of them have to be present to suggest hemodynamic compromise. We must aim to demonstrate an effusion that ultimately causes reduced cardiac output, elevated central venous pressure and chamber collapse. Special considerations must be taken in patients with significant left or right ventricle hypertrophy, situations that mask typical findings. First of all, a pericardial effusion should be present and not necessarily has to be a large one; small but of rapid onset may compromise patients stability further more than those with a slow onset with large pericardial effusion. With M and 2D modes we can find diastolic collapse of the right atrium and ventricle when intrapericardial pressure exceeds intracavitary pressures. Duration of

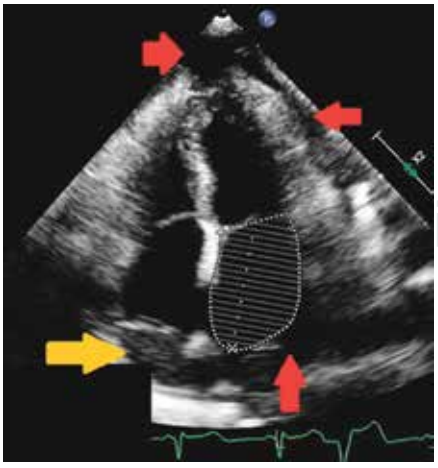

Figure 3:

Female with a global pericardial effusion (red arrows) with no hemodynamic compromise, and an incidental finding of a mass inside the pericardial sac (yellow arrow) which turned to be a malignant mesotelyoma.

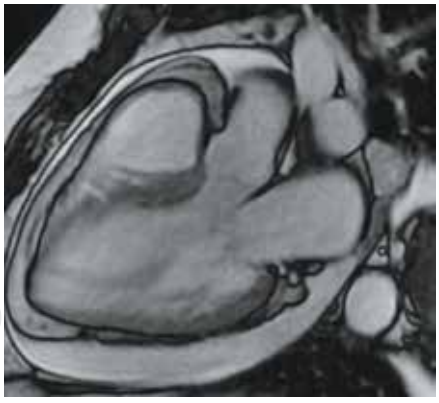

Figure 4: CMR of a patient with asymptomatic pericardial effusion without hemodynamic compromise. Note the normal pericardium thickness and a mass next to left atrium (red arrow).

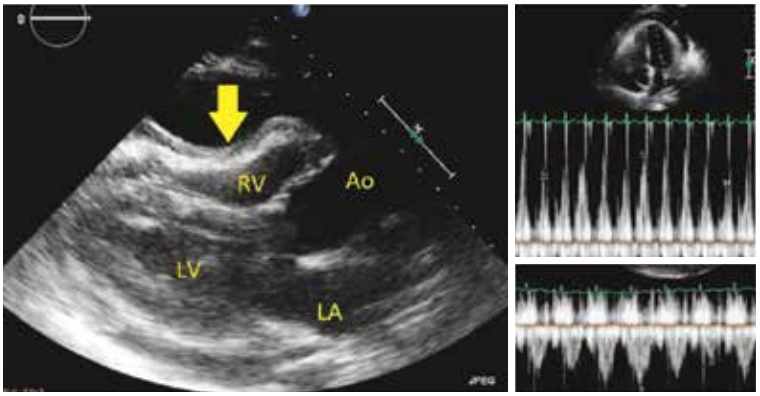

Figure 5: Young male with relapsing pericarditis who presented to the ER with hypotension and tachycardia, pulsus paradoxus, among other clinical manifestations. Echocardiogram performed in the ER, showed diastolic collapse of the right cavities (yellow arrow) and significant respiratory variation in both aortic outflow (down right) a mitral inflow velocities (upper right), echocardiographic findings suggestive of cardiac tamponade. Echo guided pericardiocentesis was performed and a few moments after decompressing the pericardium, patient became hemodynamic stable.

right atrium collapse more than one third of the cardiac cycle is very sensitive and specific. During inspiration we can see bulging to the left of the interventricular septum. This causes a variation of aortic outflow (echocardiographic demonstration of pulsus paradoxus) than can be assessed with Doppler in the left ventricle outflow tract. Also with Doppler we can document exaggerated phasic respiratory variations both in mitral and tricuspid inflow. An exaggerated respiratory variability (>25%) in mitral inflow velocity might be seen, with inspiratory decrease and expiratory increase, also seen in pulmonary vein diastolic forward flow. The opposite happens in the right heart. It can also be appreciated a respiratory variation in ventricular chamber size. Inferior vena cava dilatation with <50% reduction in diameter during inspiration is another very sensitive but poor sensible finding, and with Doppler we can find that its flow into the right atrium becomes predominantly during systole *(Figure 5)*. The use of other imaging techniques in this scenario is exceptional and is not recommended.

As seen above, there is a multimodality diagnostic, and even prognostic approach to evaluate pericardial disease. We must confidently rely in each of them to increase each of their diagnostic value, and as mentioned, before, one must make use of a combination of modalities to increase the diagnostic power of imaging in pericardial disease. As with echocardiographic findings alone, all data found in the different imaging modalities must be correlated.

REFERENCES

1. Cosyns B, Plein S, Nihoyanopoulos P et al. European Association of Cardiovascular Imaging (EACVI) position paper: multimodality imaging in pericardial disease. Eur Heart J Cardiovasc Imaging. 2014; 16: 12-31.
2. 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 (9): 965-1012.e15.
3. Yared K, Baggish AL, Picard MH et al. Multimodality imaging of pericardial diseases. J Am Coll Cardiol Img. 2010; 3: 650-660.
4. Wang ZJ, Reddy GP, Gotway MB et al. CT and MR imaging of pericardial disease. Radiographics. 2003;23:S167-S180.
5. Kumar A, Sato K, Yzeiraj E et al. Quantitative pericardial delayed hyperenhancement informs clinical course in recurrent pericarditis. Available in: http://dx.doi.org/10.1016/j.jcmg.2016.10.020
6. Treglia G et al. A 'Ring of Fire' around the heart: pericarditis detected by FDG-PET/CT. Cardiovascular Medicine, EMH Media, 19 Sept. 2018. Available in: cardiovascmed.ch/en/article/doi/cvm.2018.00576/
7. Masui T, Finck S, Higgins CB. Constrictive pericarditis and restrictive cardiomyopathy: evaluation with MR imaging. Radiology. 1992; 182: 369-373.
8. Giorgi B, Mollet N, 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.
9. 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.
10. Thavendiranathan P, Verhaert D, Walls MC et al. Simultaneous right and left heart real-time, free-breathing cmr flow quantification identifies constrictive physiology. J Am Coll Cardiol Img. 2012; 5: 15-24.
11. Hanneman K, Thavendiranathan P, Nguyen ET et al. Cardiovascular CT in the diagnosis of pericardial constriction: predictive value of inferior vena cava cross-sectional area. J Cardiovasc Comput Tomogr. 2014; 8 (2): 149-157.
12. Chang SA et al. [18F] Fluorodeoxyglucose PET/CT predicts response to steroid therapy in constrictive pericarditis. J Am Coll Cardiol. 2017; 69 (6): 750-751.

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