EDITORIAL

Distinguishing Constrictive Pericarditis From Restrictive Cardiomyopathy—An Ongoing Diagnostic Challenge

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Constrictive pericarditis (CP) and restrictive cardiomyopathy (RCM) are serious disorders that share common pathophysiologic elements including biventricular diastolic dysfunction, elevated biatrial pressures, and reduced resting cardiac output. Yet, while these 2 disorders have similar clinical presentations, they are caused by very different pathologic processes, which have distinct implications for treatment. CP is potentially curable by surgical pericardiectomy, whereas therapeutic options for RCM are limited. A mistakenly undertaken surgical pericardiectomy in a patient with RCM would be highly inappropriate. Consequently, accurate differentiation between these 2 superficially similar disorders is of paramount clinical importance. The report by Jain et al[1] in this issue of *JAMA Cardiology* describes a simplification of an established technique that aids in distinguishing these 2 groups of disorders.

Related article page 100

Distinctions Between CP and RCM

RCM is a family of myocardial disorders with the common element of decreased ventricular myocardial diastolic compliance. These include hypertrophic, infiltrative, and fibrotic disorders. Pure CP is a disorder in which a functionally normal heart is encased in a stiff fibrotic and potentially calcified pericardium that extrinsically determines its maximum diastolic volume. RCM and CP can coexist, particularly in patients who have had prior radiation therapy with or without concomitant cardiotoxic chemotherapy.[2]

The foundational physiological phenomenon that distinguishes CP from RCM is the presence of enhanced ventricular interaction, also commonly termed *ventricular interdependence* and *ventricular discordance*. It reflects competition between the ventricles for the constrained diastolic volume.

In RCM, ventricular diastolic compliance is determined by each chamber's intrinsic myocardial diastolic stress/strain relationship. While the ventricles share the interventricular septum, the diastolic distensibility of their free walls is a major determinant of their individual pressure-volume relationships and the left ventricle (LV) and right ventricle (RV) compete, at most, only modestly for their respective end diastolic volumes.

In contrast, in CP, the heart's maximum end diastolic volume is fixed by its pericardial encasement. Thus, any increment in 1 ventricle's end diastolic volume occurs at the obligatory expense of the other ventricle.

Over a respiratory cycle, the normal reciprocal changes in systemic and pulmonary venous return cause modest corresponding changes in RV and LV preload and, correspondingly, stroke volume. In CP, because of the total ventricular end diastolic volume constraint and elevated filling pressures, this phenomenon is exaggerated. This was first reported by Hatle et al.[3] They combined observations from echocardiogram/Doppler transvalvular flow velocity measurements and ventricular pressure recordings to demonstrate greater respiratory phasic changes in diastolic inflow and ventricular systolic pressure in patients with CP compared with patients with RCM. Subsequently, Talreja et al[4] reported a refinement of the hemodynamic observations by Hatle et al,[3] showing enhanced respirophasic reciprocal variation of the planimetered systolic area of micromanometer RV and LV pressure recordings in CP compared with RCM and other disorders. Using the ratio of RV to LV systolic area (in mm Hg × seconds) they defined a dimensionless parameter (systolic area index) as the ratio of the 2 ratios measured during inspiration and expiration: systolic area index = (inspiration RV area / LV area) / (expiration RV area / LV area), in which the area units are mm Hg × seconds.

In their series, this parameter, which may be considered to be a surrogate for relative changes in stroke volume, was 97% sensitive and 100% specific at distinguishing between CP and RCM.

While this concept was widely adopted for the hemodynamic assessment of suspected CP, most cardiac catheterization laboratories are not equipped to replicate the technique that Talreja et al[4] used to measure systolic area index. Consequently, laboratories commonly adopted a crude approximation using visual inspection of fluid-filled catheter recordings. This simplification cannot be expected to have sufficient precision to replicate the findings by Talreja et al[4] exactly.

The current report by Jain et al[1] provides a simplified strategy for detecting enhanced ventricular interaction. This analysis substitutes pulmonary artery and aortic ejection times (also documented to reflect stroke volume) for the systolic area index. The findings are similarly discriminatory, albeit in a smaller patient sample. It is also noteworthy that, as is the case in the planimetered ventricular systolic area parameter, the change magnitudes are dominated by changes in pulmonary artery ejection time although aortic ejection time, while not varying as much as pulmonary artery ejection time, also changes inversely with respiration.

As these parameters can be easily measured from good-quality fluid-filled catheter recordings, they can be applied in clinical cardiac catheterization laboratories more readily than the measurements used to calculate ventricular systolic area index.

Challenges in the Diagnostic Distinction of CP From RCM

While distinguishing between CP and RCM is often straightforward, in some cases, ambiguities in the overall clinical picture present major diagnostic challenges. This problem has spawned considerable clinical research studying a variety of structural and functional parameters in an effort to define population differences between patients with CP and RCM.[5] Unfortunately, none of the many potentially distinguishing criteria is 100% sensitive and specific. A given patient may have inconsistent findings with some parameters, suggesting CP while others favor RCM.

To reach a correct diagnosis requires integrating the findings of multiple diagnostic modalities applying a thorough understanding of the differences between the 2 conditions' pathologies and pathophysiologies to adjudicate nondiagnostic and potentially inconsistent findings. Because CP and RCM involve structural abnormalities that are responsible for the functional abnormalities, it is important to aggregate structural and functional information. Imaging modalities can supply both to complement hemodynamic measurement data.

Structural features that can differentiate CP from RCM include ventricular architecture, myocardial structure, and pericardial thickness and tethering. Functional parameters include ventricular inflow velocity patterns, ventricular septal displacement and abnormal diastolic septal motion, abnormal atrioventricular valve annular motion, and abnormal myocardial strain.

Doppler echocardiography with tissue Doppler imaging and speckle tracking ventricular strain imaging is the initial test of choice because it provides a wealth of structural and functional information. Physiologic measurements made either by echocardiogram/Doppler or by direct hemodynamic recordings are interrelated by basic principles of physics. Accordingly, they should be congruent and confirmatory of each other.

Cardiac magnetic resonance and computed tomography can provide additional structural information including myocardial tissue characterization and pericardial structure. Ideally, the aggregate of all structural and functional data will be sufficiently consistent to permit arriving at a distinguishing diagnosis. If hemodynamic and echocardiogram/Doppler data are inconsistent, the cause of the discrepancy should be identified.

Pitfalls in the Distinction Between CP and RCM

Distinguishing between CP and RCM can be complicated by numerous interpretive pitfalls. Each disorder has a spectrum of severities and early presentations of mild to moderate severity of disease may be misinterpreted. While positive findings make a particular diagnosis more likely, few patients demonstrate all the findings consistent with their diagnosis. Negative findings may not be exclusionary. For example, while imaging demonstration of extensive pericardial thickening and calcification is highly suggestive of CP, in 1 series, 18% of patients with surgically confirmed CP had pericardial thicknesses of 2 mm or less on computed tomographic imaging.[6] While enhanced ventricular interaction is a foundational parameter, it is an enhancement of a normal phenomenon and the boundary between normal and abnormal values is not absolute. Pseudo ventricular interaction can occur in the settings of respiratory distress or other circumstances of increased work of breathing. Atrial fibrillation, with variable diastolic intervals, will alter beat to beat ventricular stroke volumes, making respirophasic assessment more complex.

The availability of multiple sophisticated diagnostic modalities provides a wealth of anatomic and functional information to apply to the assessment of the patient suspected of having either CP or RCM. However, sorting through the complexity and variability of these 2 groups of disorders can still be a major clinical challenge requiring an in-depth understanding of both disorders and thoughtful interpretation of the totality of all available diagnostic information.

ARTICLE INFORMATION

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