Response to Campbell: Is This a Case of Constriction?

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The patient presented by Dr Patricia Campbell1 from the Advanced Heart Disease Section of Brigham and Women’s Hospital exemplifies challenges that surround the possible diagnosis of constrictive pericarditis. Constrictive pericarditis is a pericardial compressive syndrome due to fibrosis, scarring, and occasionally calcification of the pericardium. The primary pathophysiological consequence is impairment of ventricular filling. The hemodynamic abnormalities are characterized by elevation of both right and left ventricular filling pressures and equalization of right and left ventricular diastolic pressures. It should be appreciated, however, that there are a number of pathological conditions that can be associated with equalization of ventricular diastolic pressures (Table)

Differential Diagnosis

The best-recognized differential diagnosis for equalization of ventricular diastolic pressures is presented by the pair of constrictive pericarditis and restrictive cardiomyopathy. Cardiac catheterization and measurements of intracardiac pressures frequently are performed to distinguish between these 2 conditions.

Constrictive pericarditis can be caused by infection, such as tuberculosis, noninfectious inflammatory disorders, and collagen vascular diseases such as systemic lupus erythematosus. It can also occur as a complication of radiation therapy or traumatic hemorrhagic pericardial effusion. In the patient under discussion, there was no history suggesting tuberculosis, collagen vascular disease, or previous symptomatic pericarditis and no prior radiation or chest trauma.

Constrictive pericarditis, however, is being increasingly encountered after open heart surgery. In ≈2% of patients after coronary artery bypass surgery, constrictive pericarditis develops. The patient under discussion had previous triple-vessel coronary artery bypass surgery, and thus, constrictive pericarditis needs to be considered in his differential diagnosis, which was particularly relevant in this patient referred to a cardiac surgeon for consideration of a pericardial stripping procedure. Presentation of constrictive pericarditis within 6 months of cardiac surgery would be unusual, however, and some exertional dyspnea had preceded surgery.

Restrictive cardiomyopathy is a myocardial disease, primarily one of the left ventricle. Left ventricular end-diastolic pressures usually are elevated in patients with restrictive cardiomyopathy. Because of a passive increase in left atrial and pulmonary venous pressures, pulmonary artery pressure increases. Postcapillary pulmonary hypertension may cause right ventricular failure with increased right ventricular end-diastolic pressure. In advanced patients with biventricular failure, equalization of the diastolic pressures also can occur. In restrictive cardiomyopathy, impairment of ventricular filling results from increased myocardial stiffness and decreased myocardial relaxation. Amyloidosis is the most common cause of restrictive cardiomyopathy. Other causes are eosinophilic myocarditis, radiation heart disease, and endomyocardial fibrosis, which were not present in this patient. There was no history of radiation and no suggestive echocardiographic or clinical features to suggest endomyocardial fibrosis. Familial or idiopathic restrictive cardiomyopathy cannot be excluded but are rare and usually present in younger patients.

Severe tricuspid valve regurgitation also may be associated with equalization of diastolic pressures. The right atrium and right ventricle are markedly dilated, and the pericardial constraint can produce equalization of diastolic pressures. A related mechanism for equalization of diastolic pressures has been demonstrated in acute right ventricular myocardial infarction.2 It is very likely that in patients with acute massive or submassive pulmonary embolism with right ventricular failure, pericardial constraint also can lead to equalized diastolic pressures. Cardiac tamponade, right ventricular myocardial infarction, and massive or submassive pulmonary embolism associated with equalization of diastolic pressures generally should be suspected from the presentation and echocardiographic appearance, in most cases without recourse to invasive measurement of intracardiac pressures.

Dilated heart failure with low left ventricular ejection fraction generally is associated with higher left ventricular than right ventricular filling pressures. However, if the original etiology or a complicating event such as a right ventricular infarction affected the right ventricle more than the left, there can be equalization of elevated diastolic filling pressures. The hemodynamic and echocardiographic profiles clearly distinguish this from either constrictive or restrictive disease.

There is increasing recognition of heart failure with preserved left ventricular ejection fraction (HFpEF). This condition can be associated with marked elevations in pulmonary venous pressures, particularly with exertion, and secondary...
Chronic Restrictive cardiomyopathy revealed jugular venous pressure of the clinical assessment at the time of initial evaluation does not seem prone to develop primary failure with normal close to normal, with dilation of the left and right atria and the failure, the left ventricular volume and ejection fraction are mon in HFpEF. In HFpEF with secondary right ventricular hypertrophy, diabetes, older age, and obesity that are com-
strable systolic dysfunction, and the predisposing factors of associated with restrictive cardiomyopathy, the absence of demon-
strable systolic dysfunction, and the predisposing factors of hypertension, diabetes, older age, and obesity that are common in HFpEF. In HFpEF with secondary right ventricular failure, the left ventricular volume and ejection fraction are close to normal, with dilation of the left and right atria and the right ventricle. (Unlike the left ventricle, the right ventricle does not seem prone to develop primary failure with normal ventricular volume and ejection fraction.)

Clinical Assessment
The clinical assessment at the time of initial evaluation revealed jugular venous pressure of \( \approx 15 \) to 16 mm Hg. In the absence of tricuspid valve stenosis, jugular venous pressure reflects right atrial pressure, which in turn reflects right ventricular diastolic pressure. The patient under discussion also had a positive Kussmaul sign, which is defined as an increase or lack of fall in the jugular venous pressure during inspiration. Although classically associated with constrictive pericarditis, a Kussmaul sign also can occur in restrictive cardiomyopathy, tricuspid regurgitation, pulmonary embolism, and right ventricular failure. A prominent right ventricular impulse (left parasternal lift) usually indicates right ventricular failure, which may reflect an increased volume load as in tricuspid regurgitation or pressure overload as pulmonary hypertension. In constrictive pericarditis, the prominent left parasternal impulse is appreciated in diastole rather than systole. In this patient, the prominent systolic left parasternal impulse was probably due to right ventricular volume and pressure overload.

A “prominent crisp sound in early diastole, of higher pitch than the usual third heart sound” may indicate a pericardial knock, which is highly suggestive of constrictive pericarditis. Other early diastolic sounds are the opening snaps associated with tricuspid and mitral valve stenosis. It should be appreciated that a relatively higher pitched third heard sound in patients with systolic or diastolic heart failure may mimic a pericardial knock.

In the patient under discussion, there was no palpable hepatic pulsation. Absence of hepatic pulsation favors the diagnosis of constrictive pericarditis rather than tricuspid regurgitation or restrictive cardiomyopathy. However, in patients with moderately severe tricuspid regurgitation or restrictive cardiomyopathy, systolic hepatic pulsation may be absent. The absence of physical findings of pulmonary hypertension, such as a loud pulmonic component of the second heart sound (P2), also favors the diagnosis of constrictive pericarditis or primary tricuspid regurgitation. The physical findings of ascites and lower-extremity edema that were present in the patient are consistent with severely elevated right-sided pressures and do not distinguish among constrictive pericarditis, restrictive cardiomyopathy, or other causes of right ventricular failure and tricuspid regurgitation.

In this patient, an ECG showed atrial fibrillation and normal QRS voltage. It is of interest that atrial fibrillation is present in almost 30% of patients with constrictive pericarditis. However, it occurs in about one third of all patients with advanced symptoms of heart failure with either low or preserved ejection fraction.

Echocardiography
Echocardiography is the first cardiac laboratory examination to be performed. It should always be reviewed carefully and repeated if necessary for further assessment before cardiac catheterization is undertaken in patients with suspected constrictive pericarditis or restrictive cardiomyopathy. In the patient under discussion, both right and left atria appeared enlarged, with normal left ventricular diastolic volumes and dimensions. Biatrial enlargement is rare in constrictive pericarditis but very common in restrictive cardiomyopathy. In constrictive pericarditis, right ventricular dimension and volume remain normal. In heart failure with either low or preserved ejection fraction, however, the right ventricle may dilate with right ventricular failure secondary to postcapillary pulmonary hypertension. In this patient, estimated pulmonary artery systolic pressure was \( \approx 48 \) mm Hg, and the right ventricle was dilated. These findings favor the diagnosis of myocardial disease rather than constriction but could be seen both in restrictive disease and in HFpEF physiology without primary restrictive etiology.

Left ventricular wall thickness remains normal in constrictive pericarditis and some restrictive cardiomyopathies, and moderate left ventricular hypertrophy is often but not always seen in HFpEF. In restrictive cardiomyopathy due to amyloidosis, left ventricular wall thickness is increased due to “pseudohypertrophy.” In this patient, amyloidosis is an unlikely diagnosis because both QRS voltage and left ventricular wall thickness were normal. Left ventricular ejection fraction remains normal in constrictive pericarditis and is normal or mildly reduced in restrictive cardiomyopathy. Left ventricular ejection fraction in this patient was between 45% and 50%, which can be normal for his age. Doppler echocardiographic studies to assess diastolic function reveal an increased E/a ratio, a decreased deceleration time (<150 ms), and a restrictive filling pattern in both constrictive pericarditis and restrictive cardiomyopathy. In this patient, the E/a ratio was increased, and restrictive transmural flow pattern was

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<td>Cardiac tamponade</td>
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<td>Severe tricuspid regurgitation</td>
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<td>Dilated LV failure with primary or secondary RV failure</td>
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<td>Left-sided heart failure with preserved ejection fraction complicated by secondary RV failure</td>
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LV indicates left ventricular; RV, right ventricular.

Table. Examples of Conditions That Can Cause Equalization of Ventricular Diastolic Pressures
present. However, the other echocardiographic findings, such as right ventricular enlargement and flattening of the interventricular septum, favor the diagnosis of restrictive cardiomyopathy or HFP EF with secondary right ventricular failure. The estimated pulmonary artery systolic pressure of 48 mm Hg would be consistent with elevated left-sided filling pressures causing pulmonary venous and pulmonary arterial hypertension that could increase right ventricular afterload. The D-shaped appearance of the left ventricle seen in the short-axis view during initial echocardiographic evaluation of this patient indicated right ventricular pressure or volume overload.

Invasive Hemodynamic Study
After admission to the referral center, the patient underwent cardiac catheterization. Both left and right heart catheterization along with coronary angiography were performed. Selective coronary angiography revealed patent coronary arteries after the prior interventions. Simultaneous right and left ventricular pressure tracings also were performed, which showed a dip-and-plateau pattern. There was also suggestion of equalization of the diastolic pressures. The hemodynamic findings, however, weigh strongly against a diagnosis of constriction. In constrictive pericarditis, the end-systolic pressure is close to 0 mm Hg, but it never reached 0 mm Hg in this patient, varying between 5 and 30 mm Hg. In constrictive pericarditis, the right and left ventricular diastolic pressures are similar from the end of the rapid filling phase to the end of diastole, not differing >5 mm Hg. Even with effective left atrial contraction during the atrial filling phase, there is very little further separation of left and right ventricular diastolic pressures. In contrast, in this patient, there was a gradual increase in both right and left ventricular diastolic pressures beginning from the termination of the rapid filling phase until end diastole. Furthermore, left ventricular end-diastolic pressure consistently exceeded right ventricular end-diastolic pressure by >5 mm Hg. These hemodynamic findings weigh against the diagnosis of constriction.

In restrictive cardiomyopathy, there is a gradual increase in left and right ventricular diastolic pressures during mid- and end-diastolic filling phases. In constrictive pericarditis, the right ventricular end-diastolic pressure usually exceeds one third of the peak systolic pressure, which it did in this patient. However, right ventricular peak systolic pressure exceeded 50 mm Hg, which is uncommon in constrictive pericarditis.

Response to Therapy
After admission to the heart failure unit after the cardiac catheterization, intensive therapy was begun. After continuous intravenous infusion of furosemide for 12 days, the patient lost 13 lb. It should also be noted that the substantial diuresis coincided with discontinuation of pioglitazone. This hypoglycemic agent had been started 18 months before the patient lost 13 lb. It should also be noted that the substantial elimination of pioglitazone may well have caused increased volume status at the new lower level. After admission to the heart failure unit after the cardiac catheterization, intensive therapy was begun. After continu-

Considerable clinical improvement occurred with a decrease in dyspnea and increase in exercise tolerance. Repeat hemodynamic evaluation showed the pulmonary capillary wedge pressure reduced to within normal range, with clear separation of left ventricular and right ventricular pressures throughout the cycle. The Doppler echocardiographic studies after diuretic therapy showed normalization of right ventricular size and absence of flattening of the interventricular septum. It should be appreciated that in constrictive pericarditis, diuretic therapy usually does not change hemodynamic abnormalities.

After all these discussions, I still need to answer the question, “Is it constriction?” Of constriction and restriction, the evidence clearly leans away from constriction and more toward restriction. First, the echocardiographic findings of right ventricular enlargement and flattening of the interventricular septum favor restriction and not constriction. Second, simultaneous determinations of right and left ventricular diastolic pressures did not demonstrate equalization of diastolic pressures. Third, left ventricular end-diastolic pressure was significantly higher than right ventricular end-diastolic pressure. Thus, the final diagnosis cannot be constriction. If forced to choose between the classic dichotomy of constriction and restriction, the answer would have been restriction. However, since these physiological distinctions were originally drawn, there has been increasing recognition of the HFP EF syndrome. Ongoing physiological investigation is providing new insights into the relationship of HFP EF, secondary pulmonary hypertension, and right heart dysfunction.

The marked clinical improvement in this patient was achieved by careful reduction of elevated circulating volume and ongoing attention to control of hypertension. It should be noted that the elimination of pioglitazone may well have diminished the patient’s tendency to fluid retention, thus helping to stabilize his volume status at the new lower level after discharge to home. Surgical intervention would not have revealed a substrate for pericardial stripping and likely would have been complicated by an arduous postoperative course in the setting of his right-sided heart failure. This case demonstrates the importance of meticulous, systematic investigation and management of patients with advanced heart failure, guided by humility and respect for the history and future of each patient as an individual.

Acknowledgments
I thank Dr Campbell for her lucid presentation, which provides a glimpse of her knowledge and expertise. I also want to thank Dr Lynne Stevenson for honoring me by the invitation to contribute this brief commentary about the differential diagnosis of constrictive physiology.
Disclosures

None.

References


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