MSD MANUAL
Professional Version

Restrictive Cardiomyopathy

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Restrictive cardiomyopathy is characterized by noncompliant ventricular walls that resist diastolic filling; one (most commonly the left) or both ventricles may be affected. Symptoms include fatigue and exertional dyspnea. Diagnosis is by echocardiography and cardiac catheterization. Treatment is often unsatisfactory and is best directed at the cause. Surgery is sometimes useful.

A cardiomyopathy is a primary disorder of the heart muscle (see also Overview of Cardiomyopathies).

Restrictive cardiomyopathy is the least prevalent form of cardiomyopathy.

Restrictive cardiomyopathy can affect one or both ventricles. Either type may be diffuse or nondiffuse (when the disorder affects only one ventricle or part of one ventricle unevenly).

Restrictive cardiomyopathies can be classified into 4 etiologic categories:

- Infiltrative (eg, amyloidosis, sarcoidosis)
- Non-infiltrative (eg, idiopathic, systemic sclerosis)
- Storage diseases (eg, Fabry disease, hemochromatosis)
- Endomyocardial disorders (eg, endomyocardial fibrosis, hypereosinophilic syndrome, carcinoid syndrome, metastatic cancer, drugs [hydroxychloroquine, ergotamine, methysergide])

Primary restrictive cardiomyopathies include idiopathic restrictive cardiomyopathy and endomyocardial fibrosis while the others are considered secondary forms. Some of these are inherited, and others are acquired (1).

In patients with hypereosinophilic syndrome and extensive endocardial fibrosis, thrombus can form in the apices and inflow tracts ventricles compromising the size of the ventricular cavities. This type of restrictive cardiomyopathy is termed obliterative.

General reference

1. Gowda SN, Ali HJ, Hussain I. Overview of Restrictive Cardiomyopathies. *Methodist Debakey Cardiovasc J* 2022;18(2):4-16. Published 2022 Mar 14. doi:10.14797/mdcvj.1078

Etiology of Restrictive Cardiomyopathy

Restrictive cardiomyopathy is not always a primary cardiac disorder. Although the cause is usually unknown, it may arise as the consequence of systemic or genetic disorders; identified causes are listed in the table Causes of Restrictive Cardiomyopathy.

Some disorders that cause restrictive cardiomyopathy also affect other tissues (eg, amyloidosis, hemochromatosis). Some myocardial infiltrative disorders also affect other cardiac tissue. Rarely, amyloidosis affects coronary arteries. Sarcoidosis and Fabry disease may also affect nodal conduction tissue. Löffler syndrome (a subcategory of hypereosinophilic syndrome with primary cardiac involvement), which occurs in the tropics, begins as an acute arteritis with eosinophilia, followed by thrombus formation on the endocardium, chordae, and atrioventricular (AV) valves, progressing to fibrosis. Endocardial fibroelastosis (EFE), which occurs in infants and children, affects only the left ventricle. Endomyocardial fibrosis (EMF) occurs commonly in tropical regions and affects both the left and right ventricles.

TABLE

Some Causes of Restrictive Cardiomyopathy

Cause	Examples
Endomyocardial disorders	Carcinoid tumors Endocardial fibroelastosis Endomyocardial fibrosis (EMF) Hypereosinophilic syndrome (including Löffler syndrome) Metastatic cancer Medications (eg, hydroxychloroquine, ergotamine, methysergide)

Data from Gowda SN, Ali HJ, Hussain I. Overview of Restrictive Cardiomyopathies. *Methodist Debakey Cardiovasc J* 2022;18(2):4-16. Published 2022 Mar 14. doi:10.14797/mdcvj.1078

Cause	Examples
	Radiation
Infiltrative disorders	Amyloidosis Sarcoidosis
Non-infiltrative disorders	Idiopathic restrictive cardiomyopathy Pseudoxanthoma elasticum Systemic sclerosis
Storage diseases	Fabry disease Glycogen storage diseases Hemochromatosis

Data from Gowda SN, Ali HJ, Hussain I. Overview of Restrictive Cardiomyopathies. *Methodist Debakey Cardiovasc J* 2022;18(2):4-16. Published 2022 Mar 14. doi:10.14797/mdcvj.1078

Pathophysiology of Restrictive Cardiomyopathy

Endocardial thickening or myocardial infiltration (sometimes with death of myocytes, papillary muscle infiltration, compensatory myocardial hypertrophy, and fibrosis) may occur in one, typically the left, or both ventricles. As a result, the mitral or tricuspid valves may malfunction, leading to regurgitation. If nodal and conduction tissues are affected, the sinoatrial (SA) and atrioventricular node malfunction, sometimes causing various grades of SA block and AV block.

The main hemodynamic consequence is diastolic dysfunction with a rigid, noncompliant ventricle, impaired diastolic filling, and high filling pressure, leading to pulmonary venous hypertension. Systolic function may deteriorate if compensatory hypertrophy of infiltrated or fibrosed ventricles is inadequate. Mural thrombi can form, resulting in systemic emboli.

Symptoms and Signs of Restrictive Cardiomyopathy

Symptoms of restrictive cardiomyopathy are exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea, and peripheral edema. Fatigue results from a fixed cardiac output due to resistance to ventricular filling. Atrial and ventricular arrhythmias and AV block are common; angina and syncope are uncommon. Symptoms and signs closely mimic those of constrictive pericarditis.

Physical examination detects a quiet precordium, a low-volume and rapid carotid pulse, pulmonary crackles, and pronounced neck vein distention with a rapid *y* descent (see figure Normal Jugular Vein Waves). A third heart sound (S3) and/or a fourth heart sound (S4) may occur and must be differentiated from the precordial knock of constrictive pericarditis. In some cases, a murmur of functional mitral or tricuspid regurgitation results because myocardial or endocardial infiltration or fibrosis changes chordae or ventricular geometry. Pulsus paradoxus does not occur.

Diagnosis of Restrictive Cardiomyopathy

- ECG, chest x-ray, and echocardiography
- MRI
- Sometimes left and right heart catheterization, including cardiac biopsy
- Laboratory tests and biopsy of other organ systems as needed

Restrictive cardiomyopathy should be considered in patients with heart failure and preserved ejection fraction, particularly when a systemic disorder known to lead to restrictive cardiomyopathy has already been diagnosed. However, the underlying disorder may not be obvious on presentation.

ECG, chest x-ray, and echocardiography are required.

The ECG is usually nonspecifically abnormal, showing ST-segment and T-wave abnormalities and sometimes low voltage. Pathologic Q waves, not due to previous myocardial infarction, sometimes occur. Left ventricular hypertrophy due to compensatory myocardial hypertrophy or abnormalities of conduction, including AV block, sometimes occurs.

On chest x-ray, the heart size is often normal or small but can be enlarged in late-stage amyloidosis or hemochromatosis.

Echocardiography shows normal left ventricular ejection fraction. Tissue Doppler imaging frequently suggests elevated LV filling pressures, and strain imaging can show impaired longitudinal contraction despite the normal ejection fraction. Other common findings include dilated atria and myocardial hypertrophy.

In amyloidosis an unusually bright echo pattern from the myocardium may be observed. Technetium-99m pyrophosphate cardiac imaging is also useful in differentiating immunoglobulin light chain (AL) from transthyretin (ATTR) cardiac amyloid. Strongly positive scans are specific for ATTR amyloid. Weakly positive scans may occur with AL amyloid, recent myocardial infarction, or significant chronic kidney disease. Because scan results are not always specific, AL amyloid should be ruled out using serum light chain and urine/serum immunofixation studies. Identifying the type of amyloid has implications for treatment, genetic counseling, and overall prognosis (1).

If the diagnosis is still in doubt, MRI can show abnormal myocardial texture in disorders with myocardial infiltration (eg, by amyloid or iron). MRI as well as cardiac CT can detect pericardial thickening, which can help diagnose pericardial constriction, which can clinically mimic restrictive cardiomyopathy.

Cardiac FDG PET (fluorodeoxyglucose positron emission tomography) assessment may be useful to identify inflammatory myocardial disorders such as cardiac sarcoidosis, which may manifest similarly to other causes of restrictive cardiomyopathy.

If a definitive diagnosis is not evident after noninvasive testing, invasive work-up with cardiac catheterization and endomyocardial biopsy should be considered. Catheterization detects high atrial pressure in restrictive cardiomyopathy with a prominent *y* descent and an early diastolic dip followed by a high diastolic plateau in the ventricular pressure curve. Diastolic pressure is usually a few mm Hg higher in the left ventricle than in the right, in contrast to constrictive pericarditis where pressure in the ventricles is equal. Biopsy can detect endocardial fibrosis and thickening, myocardial infiltration by iron, myocardial infiltration by amyloid, chronic myocardial fibrosis, or in the case of Fabry disease, inclusions in vascular endothelial cytoplasm. Coronary angiography is normal, except when amyloidosis affects epicardial coronary arteries.

Laboratory tests and biopsies of other organ systems for the most common causes of restrictive cardiomyopathy (eg, fat pad biopsy for amyloidosis, iron tests or liver biopsy for hemochromatosis) should be done.

Diagnosis reference

1. Bokhari S, Castaño A, Pozniakoff T, et al: (99m)Tc-pyrophosphate scintigraphy for differentiating light-chain cardiac amyloidosis from the transthyretin-related familial and senile cardiac amyloidoses. *Circ Cardiovasc Imaging* 6:195–201, 2013. doi: 10.1161/CIRCIMAGING.112.000132

Treatment of Restrictive Cardiomyopathy

- Cause treated
- Diuretics considered

If the diagnosis is made at an early stage, specific treatment of some underlying causes, such as amyloidosis, hemochromatosis, sarcoidosis, and Löffler syndrome, may help.

Diuretics may be used for patients with edema or pulmonary vascular congestion but must be given cautiously because they can lower preload; the noncompliant ventricles depend on preload to maintain cardiac output.

Digoxin does little to alter hemodynamic abnormalities and may cause serious arrhythmias in cardiomyopathy due to amyloidosis, in which extreme digitalis sensitivity is common. If heart rate is elevated, beta-blockers or rate-limiting calcium channel blockers may be used cautiously in low doses. Afterload reducers (eg, nitrates) may cause profound hypotension and usually are not useful.

Left ventricular assist device (LVAD) and transplantation are sometimes recommended (1).

Treatment reference

1.Muchtar E, Blauwet LA, Gertz MA: Restrictive cardiomyopathy: Genetics, pathogenesis, clinical manifestations, diagnosis, and therapy. *Circ Res* 121:819–837, 2017. doi: 10.1161/CIRCRESAHA.117.310982

Prognosis for Restrictive Cardiomyopathy

Prognosis is poor (see table Diagnosis and Treatment of Cardiomyopathies) because the diagnosis is often made at a late stage. No treatment is available for most patients; symptomatic, supportive care can be provided.

Standard therapies that are used in dilated cardiomyopathy (eg, angiotensin-converting enzyme [ACE] inhibitors, digoxin, beta-blockers) are poorly tolerated in restrictive cardiomyopathy. Patients with restrictive cardiomyopathy may also have autonomic dysfunction (especially in amyloid heart disease) or low systemic blood pressure. There is a high rate of conduction system disease, heart block, and sudden death.

Key Points

- In restrictive cardiomyopathy, endocardial thickening or myocardial infiltration leads to a rigid, noncompliant ventricle and thus diastolic dysfunction; systolic function is normal until late in the disease.
- Sometimes, valvular tissue or the conduction system is involved, causing valvular regurgitation or heart block and arrhythmias.
- Etiology is usually unknown, but some cases are caused by potentially treatable disorders, including amyloidosis, hemochromatosis, or sarcoidosis.
- Diagnosis is by echocardiography plus testing for cause.
- Treatment is often unsatisfactory unless the cause can be addressed; diuretics may benefit patients with edema or pulmonary vascular congestion but must be used cautiously to avoid lowering preload.
- Standard treatments for dilated cardiomyopathy (eg, ACE inhibitors, digoxin, beta-blockers) are poorly tolerated in restrictive disease.