

Left ventricular diastolic dysfunction

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Introduction

Left ventricular (LV) diastolic dysfunction is an entity that has gained importance in the last two decades compared to LV systolic failure or LV failure with reduced ejection fraction. The term diastolic heart failure has been termed Heart Failure with normal Ejection Fraction (HF_nIEF) to contrast it with LV systolic heart failure which has reduced EF (HF_rEF). The prevalence of HF_nIEF in the heart failure population is about 50-55%. Since patients with diastolic heart failure are at high risk of decompensation in the perioperative period or during an ICU stay, anaesthetists should be familiar with the pathophysiology of diastolic heart failure

Natural History

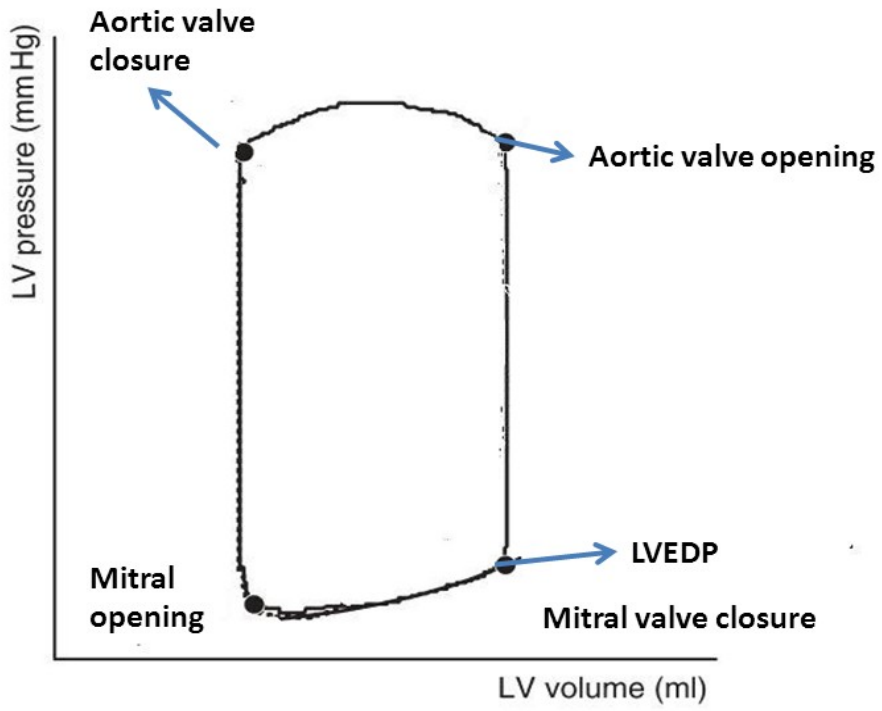
Large studies show that the mortality rate for HF_nIEF is about the same as the mortality in heart failure in those with reduced ejection fraction. The rates of hospital admission and other forms of morbidity are similar in both these groups

The features of Diastole

Normal diastolic function is dependent on compliance, distensibility and relaxation properties of the ventricles. Examining the pressure volume loops provide data regarding diastolic function. First of all a detailed examination of the diastolic phase of the cardiac cycle is in order. For this the pressure-volume plot of the cardiac cycle is a must in aiding understanding. (See figure 1)

Diastole extends from closure of the aortic valve to the closure of the mitral valve. It is composed of four phases

- i. Isovolumetric relaxation
- ii. Early filling
- iii. Diastasis
- iv. Atrial systole



Figure

Figure 1: The normal pressure volume loop showing the different phases of the cardiac cycle

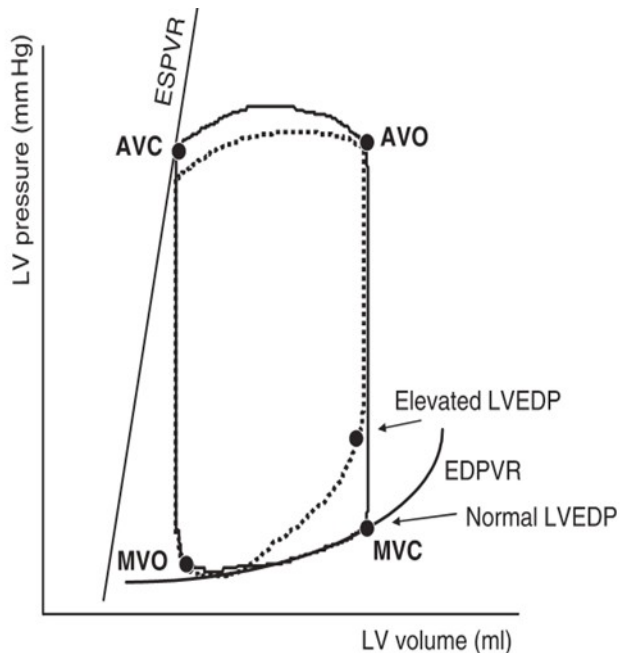


Figure 2: The loop with the solid line is the normal pressure volume loop and the loop with the dotted line is the pressure-volume loop in diastolic dysfunction. In diastolic dysfunction the end-diastolic pressure volume relationship (EDPVR) is shifted upwards whereas the ends systolic pressure volume relationship (ESPVR), which is an indicator of systolic function, is not affected

Isovolumetric relaxation: This commences from the closure of aortic valve and extends to the opening of mitral valve. Ventricular volume remains the same and there is rapid fall in intra-cavitary pressure due to the active relaxation. The Isovolumetric relaxation time (IVRT) is prolonged in any condition that impairs active relaxation (e.g. myocardial ischemia). IVRT is shortened by raise in LA pressure. This is because raise in LAP causes early opening of the mitral valve.

Early diastolic filling: this begins with the opening of the mitral valve. Ventricular pressure declines during this phase despite ventricular filling. The cause for this is active relaxation of the ventricles. The pressure gradient between the LA and LV is greatest in this phase. This phase accounts for 80% of the ventricular filling. The main determinants of this phase are rate of active relaxation, the recoil of myocardial elastic elements and the LAP. Early diastolic filling can be characterized (invasively) by the rate of volume change of the LV, the dV/dt

Diastasis: Ventricular filling slows in mid diastole as the transmitral pressure gradient declines. The main determinant of the LV filling at this time is the LV chamber compliance dV/dP or its inverse the chamber stiffness. The chamber compliance is dependent on the

- a) intrinsic myocardial stiffness
- b) ventricular mass
- c) ventricular volume –distended chamber has lower compliance than a normal one

- d) pericardial restraint,
- e) RV volume
- f) loading conditions

Atrial systole: This increases the transmitral gradient. In the normal conditions it is responsible for 15-20% of the LV filling. Under conditions that impair active relaxation the contribution to LV filling increases up to 35%

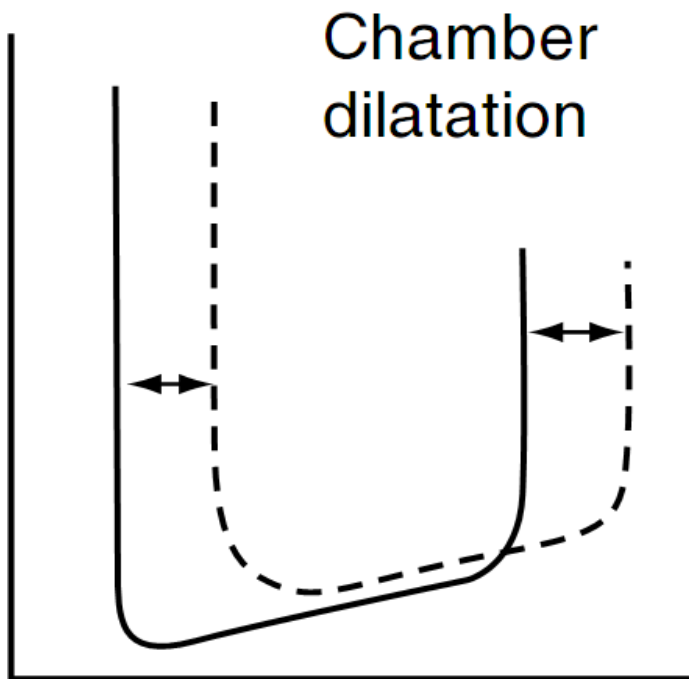


Figure 3: The effect of chamber dilatation on the normal P/V loop of the heart. The solid loop is the chamber with normal LV function and the dotted line with diastolic dysfunction. With the onset of chamber dilatation the P/V loop is shifted to the left i.e. higher end-diastolic pressure

LV COMPLIANCE AND RELAXATION

Compliance: Compliance or distensibility is defined as the ratio of volume change to the corresponding pressure change or as the slope of the volume–pressure (dV/dP) relationship. Elastance or stiffness is the inverse of compliance (dP/dV). Decreased compliance or increased stiffness is thus defined as an increase in the steepness of the pressure–volume plot. There are two causes of poor diastolic compliance.

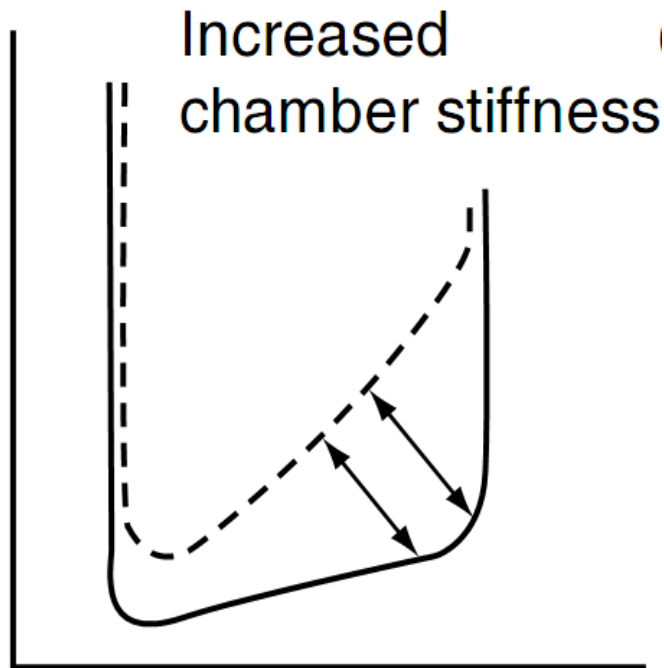


Figure 4: P/V relationship in LV with increased chamber stiffness. The normal P/V loop is represented by the solid line

Increased chamber stiffness: This occurs in aortic stenosis or systemic hypertension. In these cases, there is an increase in the amount of myocardial tissue due to concentric LV hypertrophy. Diastolic compliance of the ventricle is diminished despite that fact that the compliance of the individual muscle units is normal.

Increased muscle stiffness: This occurs in restrictive cardiomyopathies due to amyloidosis and hemochromatosis. In these cases, the compliance of the individual muscle units is diminished due to an infiltrative process.

Distensibility: Decreased ventricular distensibility is defined as an increased diastolic pressure at a given volume. This would be represented in a diastolic pressure volume diagram by a parallel upward shift of the entire pressure–volume relation. Decreased distensibility can occur from intrinsic and extrinsic causes.

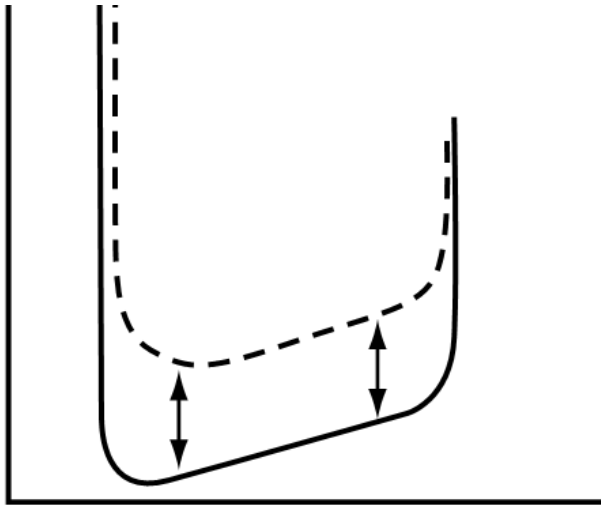


Figure 5: Schematic of the P/V loop in diastolic dysfunction due to reduced distensibility. The solid loop is the normal curve.

Intrinsic causes: Coronary artery disease is one of the important reasons for diastolic dysfunction. There is diminished distensibility which is seen even earlier than systolic dysfunction. For a given diastolic volume the diastolic pressure will be higher

Extrinsic causes: Decreased distensibility may be caused by extrinsic limitations to ventricular expansion in diastole. Diminished distensibility occurs due to ventricular interdependence via an intact ventricular septum and the restraining effect of the pericardium. For example, distension of the right ventricle with a leftward septal shift will result in diminished distensibility of the left ventricle. In addition, reduced distensibility may occur due to restrictive pericarditis or pericardial tamponade or fluid filled pericardium

Relaxation: Ventricular relaxation is energy consumptive process. Adenosine triphosphate (ATP) is required for calcium sequestration back into the sarcoplasmic reticulum and for detachment of actin-myosin cross-bridges. When isovolumic relaxation is delayed, early diastolic filling is impeded. When relaxation is incomplete, filling is impeded throughout diastole. Relaxation is impaired during myocardial ischemia and in patients with hypertrophic and congestive cardiomyopathies. Normally, the right ventricular end-diastolic pressure (RVEDP) is 1–2mmHg greater than the mean right atrial pressure (RAP), and the left ventricular end-diastolic pressure (LVEDP) is 2–3mmHg greater than the mean LAP. These small differences in pressure are due to the volume added to the ventricle by atrial systole. When LV compliance is poor, the A wave produced by atrial systole will be large and the additional volume provided by the atrial kick in end-diastole will result in a large increase in LVEDP. In these patients, the peak A-wave pressure in the LAP or pulmonary wedge pressure (PCWP) is a better measure of LVEDP because the mean LAP or PCWP pressure will underestimate LVEDP. Even large A waves only slightly

elevate mean LAP because their duration is short. Thus, well-timed atrial contraction results in a large elevation of LVEDV with only a small elevation of mean LAP and limited pulmonary venous congestion. For patients who chronically function on a steep portion of the compliance curve, a large A wave, left atrial enlargement on electrocardiogram (ECG) and an S4 on physical examination are expected findings

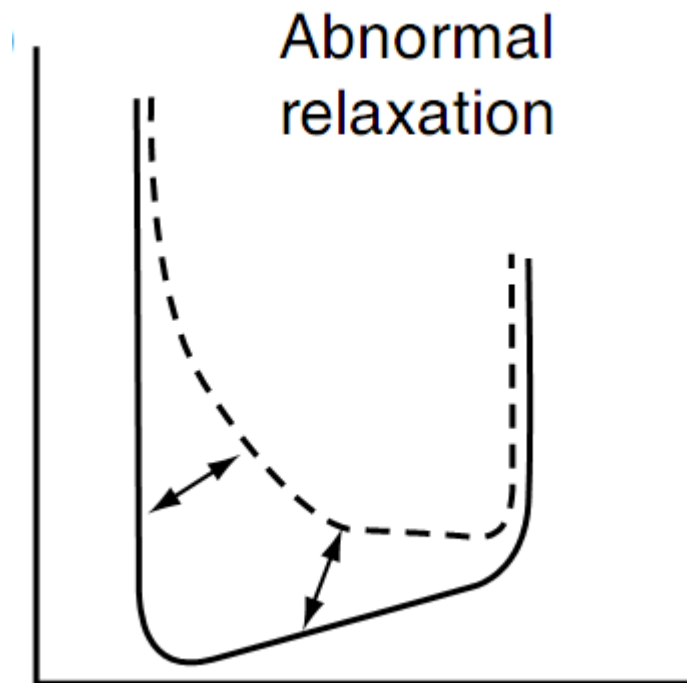


Figure 6: Diastolic pressure volume relationship when the ventricular relaxation is impaired

Clinical Features

Demographic features: Elderly. Female>Male

Underlying cardiac disease: Hypertension, coronary heart disease, diabetes and atrial fibrillation

Comorbidities: Obesity and renal dysfunction

Echocardiographic features:

LV size: normal to reduced. Small subset it may be increased

LVH: LVH is common but not always present. Relative wall thickness > 0.45

Left atrium: enlarged

Diastolic dysfunction Grade: I-IV

Other features: Pulmonary hypertension, wall motion abnormality, RV enlargement

Pertinent negatives: Rule out valve disease, pericardial disease, ASD

Brain Natriuretic Peptide or N-terminal-pro-BNP: Increased but less than that in HFrEF

Exercise testing: Decreased peak Oxygen uptake (VO₂). Exaggerated hypertensive response. Inability to increase the heart rate (chronotropic incompetence)

Chest radiogram: Similar to HFrEF, Cardiomegaly, pulmonary venous hypertension, edema, pleural effusion

Electrocardiogram: variable

Table 1: Features of heart with reduced versus normal EF

	Altered ejection fraction	Preserved ejection fraction
Dyspnoea	Chronic	Transient mainly
Heart rate	Increased	Increased
Mitral regurgitation	Present	Rare
S3/S4 gallop	S3 > S4	S4 mainly
Rales	Present	Present
Peripheral oedema	Present	Rare
Cardiomegaly	Constant	Inconstant
LV dilatation	Nearly constant	Absent
ECG abnormal	Constant	Inconstant
BNP	Markedly increased	Often mildly increased

Features of heart failure including Diastolic Heart failure

The Framingham criteria for diagnosis of heart failure. This requires two major and one minor criterion

Major criteria:	Paroxysmal Nocturnal Dyspnea or orthopnea Jugular venous distension of CVP > 16 mm Hg Rales or acute pulmonary edema Cardiomegaly Hepatojugular reflex Response to diuretic (weight loss > 4.5 Kg in 5 days)
Minor criteria:	Ankle edema Nocturnal cough Exertional dyspnea Pleural effusion Vital capacity < 2/3 of normal Hepatomegaly Tachycardia > 120 bpm

Diagnosis of definite probable and possible diastolic heart failure

Definite: Clinical evidence of heart failure + echocardiography shows preserved LVEF within 72 hours of the heart failure events documented diastolic dysfunction

Probable: Clinical evidence of heart failure + echocardiography preserved LVEF within 72 hours of the heart failure events but no documentation of diastolic dysfunction

Possible: Clinical evidence of heart failure + echocardiography shows preserved LVEF but no documentation of diastolic dysfunction

Condition is most possibly diastolic heart failure if: SBP > 160 and DBP > 100 mm Hg during the episode of LV failure. Echo shows concentric LVH *without* wall motion abnormalities. Precipitation by tachyarrhythmia or clinical improvement in response to treatment directed at diastolic dysfunction (e.g. control of heart rate, lowering of BP, restoring atrial booster mechanism)

Echocardiographic diagnosis of diastolic dysfunction

The two events that occur during the diastole that is of interest during echocardiography are

- a. The blood flow from the LA to the LV across the mitral valve i.e. the *transmitral flow*
- b. The blood flow from the pulmonary veins to the LA

So studying these two events provide the greatest amount of clue regarding diastolic dysfunction

Transmitral flow:

There are two peaks in the Doppler flow during the transmitral flow

- i. The large 'E' wave that corresponds to early diastolic filling
- ii. The small 'A' wave that corresponds to atrial systole

Normal: the E/A ratio is more than 1

Variables that can be measured during this time include the Isovolumic Relaxation Time (IVRT), maximum E wave velocity (Emax), E wave deceleration time (Edec), maximum A wave velocity (Amax), A wave velocity time integral (AVTI) and the ratio of E/A wave amplitude.

Impaired relaxation by Echo (grade 1 diastolic dysfunction): The IVRT is prolonged. The LV pressure is maintained longer than normal in diastole. This decreases the transmitral gradient and reduces the diastolic flow resulting in prolonged low-velocity E wave. The E/A ratio < 1

'Pseudonormal filling' by Echo (grade 2 diastolic dysfunction): With diastolic dysfunction the initial pattern is impaired relaxation with normal LAP. However the LAP increases with time and because of this the mitral valve opens earlier, shortening the IVRT. The initial gradient for filling is higher leading to a higher Emax. The mid-diastolic LV pressure rises and this shortens the Edec and reduces Amax. The result is a "normal" looking Doppler wave form with the E/A greater than 1

Restrictive filling by Echo (grade 3 diastolic dysfunction) : This pattern is seen with the onset of reduced chamber compliance in association with severely elevated LAP. During the early filling phase the elevated LAP leads to increased transmitral gradient, increased E wave velocity, increasing the Emax and duration of E wave. Later in the diastole, the reduced compliance leads to rapid increase in the ventricular pressure as the LV fills. This shortens the Edec and decrease the magnitude of the A wave (decreased Amax and AVTI). The E/A ratio is >2

Pulmonary venous Doppler waveforms

Normal Pulmonary venous Doppler waveforms: Forward flow from the pulmonary veins occur during systole and diastole leading to two positive peaks, the 'S' and the 'D' wave. There is brief reversal of flow in the late diastole due to atrial contraction (A wave) The 'S' wave has two components the S1 and S2.

The parameters of clinical interest are the maximum height of the S, D and A wave and the S/D ratio. The normal S/D ratio is approximately 1.

Abnormal waveforms: Abnormal relaxation causes reduction in the D wave. The S/D ratio is >1 . Pseudonormalization and restrictive filling produce a progressive increase in the D wave in parallel with the increase in LAP and the transmitral Emax. The S/D ratio is <1 . There is increase in reverse flow into the pulmonary veins during the atrial systole producing an increase in the reverse A wave.

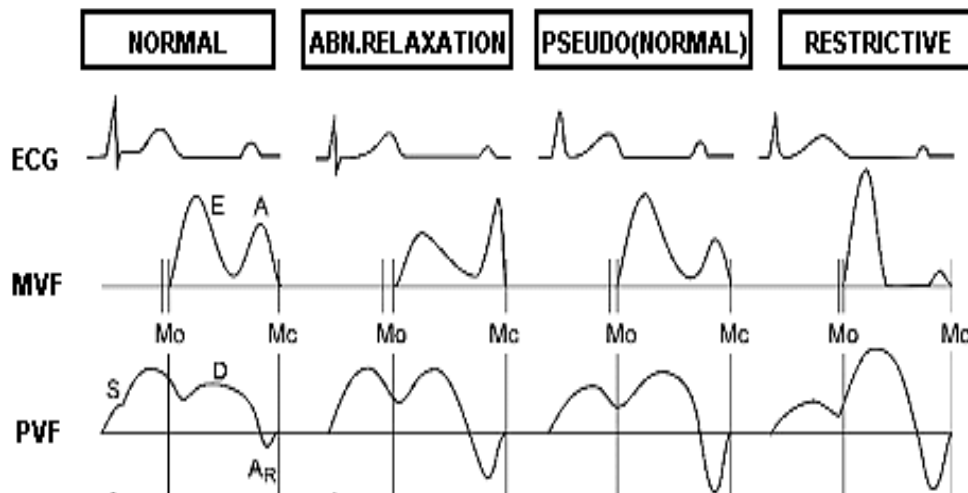


Figure 7: The transmitral flow and the pulmonary venous flow Doppler in different phases of diastolic dysfunction. See text for details.

Diastolic heart failure in clinical practice

Many factors including uncontrolled hypertension, atrial fibrillation, myocardial ischemia, anemia, renal insufficiency, and non-compliance with treatment may precipitate overt systolic and diastolic heart failure. However, uncontrolled hypertension is involved in more than 50% of the cases of acute (decompensated) diastolic heart failure. Anaesthetists may have to deal with acute decompensated diastolic heart failure during the perioperative period, in the ICU or in the emergency department.

Perioperative setting

The perioperative period carries a risk of decompensation of chronic diastolic heart failure or induction of acute diastolic dysfunction. Therefore, it is important to identify high-risk patients and situations and drugs likely to adversely affect LV diastolic function and be able to prevent and treat acute decompensation. Preoperative screening should focus on the detection of:

- (i) history of diastolic heart failure or structural factors potentially associated with an impaired LV diastolic function: LV hypertrophy (except in young athletes) and atrial arrhythmia affecting LV 'active filling';
- (ii) factors carrying a higher risk of diastolic heart failure: female, age more than 70 yr old, history of untreated hypertension, ischaemic heart disease, or diabetes mellitus;
- (iii) clinical signs of heart failure, especially dyspnoea on exertion;
- (iv) Specific measures from echocardiography: LV hypertrophy, impairment of diastolic function, preserved LVEF.

Particular attention should be paid in patients with potential LV diastolic dysfunction to avoid a further deterioration of diastolic function, especially hypovolaemia, tachycardia, and rhythms other than sinus. For elective surgery, patients with definite diastolic heart failure group would benefit from a cardiologist opinion and their treatment checked to optimize diastolic function before surgery.

Haemodynamic changes affecting diastolic time, such as arrhythmia and myocardial ischaemia, worsen pre-existing diastolic dysfunction. Tachycardia shortens diastole and is likely to impair LV filling. Rhythm disturbances can be precipitated by hypo or hyperkalaemia, anaemia, or hypovolaemia. Treatment with beta-blockers or non-dihydropyridine calcium channels blockers can be tried to prevent tachycardia and improve LV filling.

Myocardial ischaemia or acute increases in cardiac loading (volume loading or changes in position) may slow myocardial relaxation. Myocardial ischaemia may also induce rhythm disturbances that will further aggravate LV diastolic dysfunction. Beta-blockers still remain the first choice drugs in this situation.

Action of anesthetic drugs: The volatile agents like isoflurane, sevoflurane and opioids do not appear to affect LV relaxation and compliance. Both regional and or general anesthesia is acceptable and there is no evidence for superiority of either technique.

Recovery room and ICU setting

The postoperative period is the time of greatest hemodynamic stress characterized by tachycardia and hypertension. This provides sufficient substrate for vulnerable patients to manifest with diastolic failure. There is evidence to suggest that even patients with systolic dysfunction may present with features of diastolic failure during this period

Myocardial ischemia

Myocardial ischaemia is one of the main mechanisms of LV diastolic dysfunction in the early postoperative period, and several factors, including pain-induced sympathetic activation (tachycardia, hypertension), shivering, anaemia, hypovolaemia, and hypoxia, may alter myocardial oxygen balance.

Sepsis

Increasing evidence suggests that both systolic and diastolic functions are affected in severe sepsis and septic shock. Increased free radical production, especially peroxynitrite overproduction, seems to play a major role in the nitration and therefore the deterioration of protein function in septic patients.

Management of Diastolic heart failure

Preventive:

Treat systolic and diastolic hypertension

Coronary artery disease should be appropriately treated

Treat atrial fibrillation as patients with diastolic dysfunction are dependent on the “atrial kick” for optimal loading

Ventricular rate should be controlled in those with atrial fibrillation. Heart rate is the primary determinant of diastolic filling. Tachycardia is poorly tolerated. Beta blockers and calcium channel blockers improve diastolic filling

Patients with diastolic dysfunction may be on angiotensin receptor blockers as they are known to reduce LV hypertrophy and lead to improved LV filling through afterload reduction. Angiotensin converting enzyme inhibitors are also used in these patients to treat hypertension, LV hypertrophy, diabetes and coronary artery disease

Nitrates may provide symptomatic relief.

Diuresis to reduce pulmonary congestion and peripheral edema. Many patients require elevated filling pressure for adequate stroke volume and hence caution must be exercised against over diuresis

Acute decompensated diastolic heart failure

The management of acute decompensated diastolic heart failure is based on a reduction in pulmonary congestion and a correction of the precipitating factors, such as a hypertensive crisis, myocardial ischaemia, acute rhythm disturbances, and sepsis. Specific treatment of precipitating factors should always be considered: vasodilators for hypertensive crisis, coronary revascularization, restoration of sinus rhythm, and haemodynamic optimization in septic shock.

A hypertensive crisis can be managed by i.v. calcium antagonists such as nifedipine or nitrendipine (sublingual nifedipine is not recommended). High-dose nitrates i.v can decrease both preload and afterload. Sodium nitroprusside can also produce balanced vasodilatation, but may result in severe unloading or hypotension in these non-dilated ventricles. Caution is advised with the use of sodium

nitroprusside. Angiotensin converting enzyme inhibitors are not useful in the acute phase because of their slower onset of action. Beta-adrenergic blockers or diltiazem may be used in acute heart failure related to rapid atrial fibrillation or severe myocardial ischaemia.

Pulmonary congestion can be reduced by controlling blood volume or improving LV filling. Because of the steepness of the LV diastolic pressure/volume relationship, a small decrease in LVEDV can lead to a marked decrease in LVEDP. The reduction in the blood volume can be achieved either by nitrates or by diuretics, in order to reduce venous return and decrease LVEDV. Nevertheless, diuretics should be carefully considered in the context of acute hypertensive crisis, as blood volume is often already decreased by chronic hypertension or the long-term use of diuretics. As contractile function is preserved, the role of sympathomimetic inotropes is limited. Digoxin is useful only to slow the heart rate in rapid atrial fibrillation. Digoxin has not been shown to reduce mortality

Treatment for acute diastolic heart failure

In addition to measures described above such as diuresis, use of nitrates to decrease the preload, control of hypertensive crisis, and control of tachycardia, inotropes need to be considered in the treatment of acute diastolic heart failure

Except in the presence acute diastolic heart failure, positive chronotropic and inotropic agents should be avoided as they worsen the diastolic function by increasing the contractile force and heart rate, or by increasing calcium concentrations in diastole. Short term management of acute diastolic heart failure such as following cardiopulmonary bypass, epinephrine is useful as they decrease the relative load of the LV and improve the LV systolic function.

Drugs with specific facilitator action on the diastolic phase (positive lusitropic effect) are also considered during this time. Such drugs include dobutamine, milrinone and levosimendan. In cardiac failure, the positive lusitropic effect is likely to be more preserved than the inotropic effect of these drugs.

Acknowledgements

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