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## Diastolic Heart Failure After Cardiac Surgery

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### 1. Introduction

It appears that for some time diastole was taken for granted and largely ignored. Systole was thought of as the only function that truly predicted cardiac risk. The fact that diastolic heart failure (DHF) was referred to at one point as “heart failure with normal ejection fraction (EF)” lends credence to this assumption. It has been proven since that cardiac relaxation is an active energy-dependent process that begins in late systole and extends into early or mid-diastole (Shah & Pai, 1992). The fact that diastolic dysfunction contributes to up to half of the cases of heart failure dispelled the myth that systolic function is the only factor to consider in cardiac risk assessments (Bhatia et al., 2006, Owan et al., 2006, Vasan et al., 1995). Cardiologists are ahead of surgeons in recognizing the importance of diastolic function in clinical practice. They have noticed that changes in diastolic filling pattern are of a prognostic value following myocardial infarction. Left ventricular remodeling following acute myocardial infarction (AMI) is a well known phenomenon occurring in the earliest post infarction phase and continuing for weeks or months. A restrictive transmitral filling pattern which is a marker of diastolic dysfunction provides significant information in these patients. A short initial deceleration time (DT) < 150 ms obtained as early as 1 day after AMI can identify patients who are likely to undergo LV remodeling in the following year (Otasević, 2001). Remodeling is a precursor of heart failure and a strong predictor of mortality. Therefore, an early restrictive filling pattern as evidenced by a short DT identifies patients who are likely to develop progressive LV dilation and dysfunction. Persistence of a restrictive filling pattern is the most powerful independent predictor of severe dilation and late mortality (Temporelli et al., 2004, Whalley et al., 2006). The importance of diastolic dysfunction to the surgeon became apparent when it was established that it is a predictor of difficult weaning off cardiopulmonary bypass and mortality (Bernard et al., 2001, Salem et al.,

2006). Finally, the impact of diastolic dysfunction affects the anesthesiologist as these patients may tolerate acute preload reduction with induction of anesthesia poorly leading to low cardiac output and hypotension. This patient population presents difficult anesthetic challenges and places these patients at high risk of perioperative morbidity and mortality (Couture et al, 2009 Sanders et al 2009). In short, diastolic dysfunction has touched every facet of clinical practice. This chapter will predominantly focus on DHF (with normal EF) as distinct to the combined systolic and diastolic failure.

## 2. Clinical spectrum

Diastolic dysfunction can be defined as the inability of the left ventricle to adequately fill at low or normal atrial pressures unrelated to intrinsic valve disease or pericardial pathology. This dysfunction can result either from an impairment in LV compliance (passive mechanism) or from an alteration in LV relaxation (active process).

Since not all patients who undergo heart surgery have a normal EF, the classical definition of DHF of heart failure with normal EF does not always apply. It is therefore necessary not to overlook the status of the preoperative EF when assessing the DHF in the postoperative heart. With this understanding DHF in the postoperative state is better defined as a clinical syndrome of heart failure with a preserved left ventricular EF in the absence of major valve disease or pericardial pathology (Vasan & Levy, 2000 Vasan, 2003). It is associated with abnormalities of diastolic distensibility, filling, or relaxation of the left ventricle (Gaasch & Zile, 2004) clinically; DHF is usually accompanied by severe reduction of exercise capacity, neuroendocrine activation, and poor quality of life. Typically the ventricle has thick walls and a small cavity (increased left ventricular mass/volume ratio) (Kitzman et al, 2000). In contrast to systolic heart failure, DHF affects women more frequently. DHF can occur alone or in combination with systolic heart failure. In isolated DHF (characterized as a small stiff heart), the only abnormality in the pressure-volume relationship occurs during diastole, when there are increased diastolic pressures with a low end diastolic volume. In systolic heart failure, the abnormalities in the pressure-volume relationship during systole include decreased EF, stroke volume and stroke work. If there are in addition, changes in the diastolic portion of the pressure-volume relationship that leads to increased diastolic pressures, the implication then is that there is both systolic and diastolic cardiac failure (Zile & Brutsaert, 2002; Deswal, 2005; Burkoff et al. 2003). These concepts are depicted in Figure 1, using simplified pressure-volume loops, and showing the left ventricular end-diastolic pressure-volume curves. The normal left ventricle is shown with (LVEDP) < 16 mmHg. For DHF, the loop is smaller indicating reduced stroke volume, and shifted up and to the left, with LVEDP > 16 mmHg. It is important to note, that the end-diastolic volume in DHF is at the lower range of normal. In contrast, the end-diastolic volume in patients with systolic failure is increased.

## 3. Mechanics of diastole

Ventricular relaxation is an active energy-dependent process that begins in late systole and extends into early or mid-diastole (van Kraaij et al.2003). Relaxation can be defined as the time period during which the myocardium loses its ability to generate force and further shortening, and returns to an unstressed length and force (Zile & Brutsaert, 2002) Diastole begins at the closure of the aortic valve and lasts until closure of the mitral valve

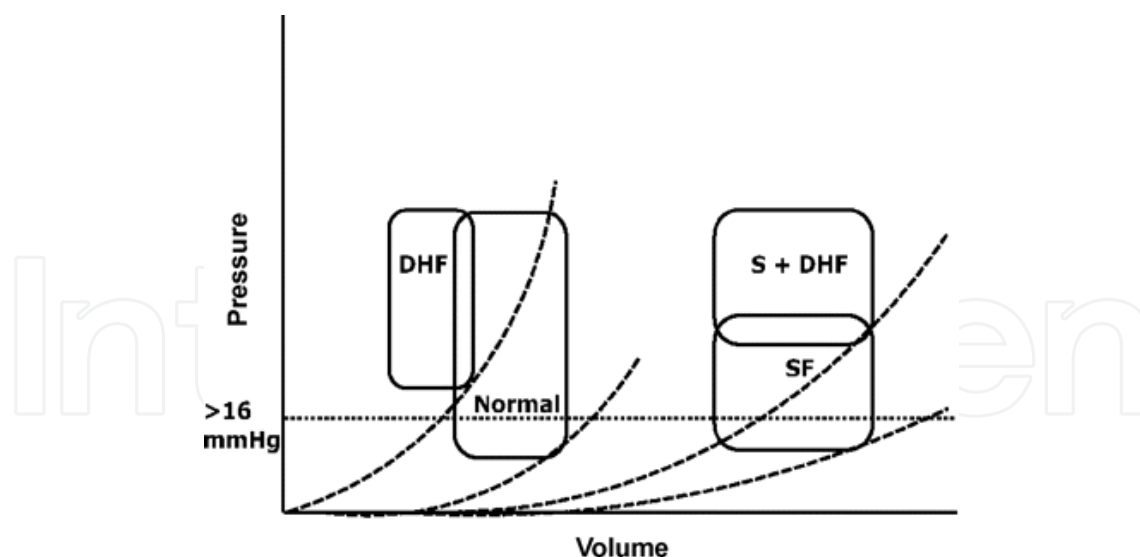


Fig. 1. Pressure-volume loop diagram indicating the position of the end-diastolic pressure-volume on curve for DHF; normal diastolic function (Normal); systolic failure (SF), and systolic and diastolic failure (S+DHF). A horizontal dashed line at >16 mmHg indicates division between normal and raised end-diastolic pressure. Adapted with permission from Elsevier Publishing (Alsaddique et al 2009)

(Kawaguchi et al, 2003). Broadly speaking, diastole can be looked at as two phases; isovolumetric relaxation corresponds to LV pressure decline at constant volume, that lasts from the closure of the aortic valve to opening of the mitral valve. The second phase is auxotonic relaxation corresponding to LV filling lasting until closure of the mitral valve. LV filling depends mainly on the pressure gradient between the LA and LV which is influenced by ventricular compliance, active relaxation, and augmented by atrial contraction towards end-diastole. Traditionally however, diastole is divided into four distinct phases: isovolumetric relaxation, early rapid ventricular filling, diastasis and atrial systole. The isovolumetric relaxation time is a continuum of systole and is dependent on it. The early rapid ventricular filling phase is dependent on LV relaxation and compliance. Diastasis is dependent on both the heart rate and chamber compliance. The atrial contraction depends on the chamber compliance, left atrial (LA) function and the conduction system of the heart. At the cellular level, diastole begins when adenosine triphosphate hydrolyzes and actin-myosin cross bridges unlink, leading to sarcomeric relaxation. This is related to decreases in cytoplasmic  $\text{Ca}^{2+}$  and the subsequent dissociation of  $\text{Ca}^{2+}$  from troponin C. The majority of cytosolic  $\text{Ca}^{2+}$  is actively resequenced into the sarcoplasmic reticulum via the sarcoplasmic reticulum  $\text{Ca}^{2+}$ -ATPase (SERCA2). The remaining cytosolic calcium is removed by the sarcolemmal sodium calcium exchanger and other mechanisms (Groban, 2005). Diastolic function depends on the passive elastic recoil properties of the LV as well as active relaxation. Impaired active myocardial relaxation causes a slow decline in the left ventricular intracavity pressure. The mitral valve opens later, as left atrial filling needs to increase in order to provide a positive gradient across the mitral valve. In severe cases, an increased left atrial pressure state is developed so as to exceed the (increased) left ventricular intracavity pressure (Aurigemma & Gaasch, 2004). An increase in passive chamber compliance can also produce the same pattern and result in elevated LVEDP, thereby necessitating an increased left atrial pressure to provide a driving gradient (Zile et

al, 2004). The mechanisms that cause diastolic dysfunction are multifactorial (Kiss et al, 2004). However, they can be broadly categorized as intrinsic (that is affecting the ventricular muscle) or extrinsic (any process that can cause external compression of the left ventricle). A summary of these causes is shown in Table 1. Whilst many of these causes are not reversible in the short term, it is important for clinicians to understand potentially reversible causes so that they can be readily identified and treated. An example of extrinsic pathology is a distended abdomen caused by dilated stomach and bowels actively pushing on the diaphragm, compressing the heart and interfering with cardiac filling, thereby leading to or exacerbating the development of DHF. The major factors that affect diastolic function are ventricular relaxation and compliance. Other factors that influence diastolic function to a lesser degree include systolic function, left atrial pressure, the pericardium, and intrathoracic pressure (Wu & Yu, 2005). In diastolic dysfunction relaxation abnormalities appear early and the inability of the left ventricle to fill in early diastole significantly affect the rapid filling phase resulting in a compensatory increase in filling with atrial contraction. The other factor that determines LV filling is chamber compliance (distensibility of the ventricles), defined as the change in volume over the change in pressure ( $dV/dP$ ). It can be derived using the relationship between changes in end diastolic pressure (EDP) and end diastolic volume (EDV) by using the formula:

$$\text{Compliance} = \Delta \text{EDV} / \Delta \text{EDP} \text{ (Gilbert \& Glantz, 1989; Lewis \& Gotsman, 1976)}$$

When ventricular compliance begins to decrease the EDP rises, but the EDV remains unchanged. The increase in EDP reduces the pressure gradient across the mitral valve leading to reduced ventricular filling culminating in decreased cardiac output. Diastolic relaxation is more sensitive to ischemia than systolic contraction, and may lead to subtle relaxation abnormalities without systolic impairment (Garcia-Fernandez et al, 1999). In coronary artery disease, ventricular relaxation as reflected in the early diastolic filling rate may be impaired at rest.

#### 4. Contributing factors

Primary diastolic failure is typically seen in patients with hypertensive or valvular heart disease as well as in hypertrophic or restrictive cardiomyopathy but can also occur in a variety of other clinical situations. The main risk factors for this form of heart failure are advancing age, hypertension, and diabetes mellitus (- Zile & Gaasch 2001). There is a high incidence of diastolic dysfunction among normotensive patients with diabetes mellitus (Boyer et al, 2004). Increased matrix collagen, interstitial fibrosis, myocardial microangiopathy, and myocytes hypertrophy are common findings in the diabetic heart that can lead to diastolic dysfunction. Tight glycemic control decreases the risk of heart failure in patients with diabetes (Iribarren et al, 2001; Liu et al, 2001). The defect in DHF is a combination of impaired ventricular relaxation and a decrease in passive ventricular distensibility (Aurigemma & Gaasch, 2004; Zile et al, 2004). The low cardiac output associated with DHF is due to inadequate ventricular filling, not impaired systolic contraction, and is an important point to remember when managing these patients. LV filling depends mainly on the pressure gradient between the LA and LV which is influenced by compliance, active relaxation, and at end diastole by atrial contraction (Appleton et al, 2000). There are number of predisposing factors that can contribute to DHF in the postoperative cardiac surgical patient. The mechanisms by which these factors exert their



Intrinsic causes	
Cause	Comment
Delay in active relaxation	Any cause that interferes with myofilament cross-bridge detachment. Includes poor calcium sequestration, abnormal calcium sensitivity, myocardial ischemia, abnormal sodium/calcium exchanger or alteration in the myocyte calcium-handling proteins
Abnormal “cardiac spring”	During contraction, molecular springs such as Titan molecules are compressed, and during diastole contribute to chamber expansion via mechanical elastic recoil. Abnormalities of these molecules may cause diastolic heart failure. It also underlines the importance of systolic function in early diastolic recoil.
Myocardial fibrosis	Abnormalities of collagen, or other infiltrative processes (such as amyloid), may increase ventricular wall stiffness by a variety of mechanisms
Left ventricular hypertrophy	This is associated but not necessarily causative of diastolic dysfunction. Chronic increased load such as hypertension or aortic stenosis may also cause changes in collagen composition.
Acute myocardial ischemia	Active relaxation is highly energy dependent, and acute myocardial ischemia will lead to (reversible) diastolic dysfunction
Extrinsic causes	
Right ventricle pressure or volume overload	The right ventricle physically compresses the left ventricle. In severe cases, the left ventricle becomes D-shaped rather than O-shaped. Any course of pressure or volume overload, including pulmonary hypertension will exacerbate left-sided diastolic dysfunction.
Pericardium	Pericardial fluid or restrictive pericardial disease will limit ventricular filling or physically compress the left ventricle.
Pleural fluid	A large pleural effusion may compress the heart
Hyper inflated lungs	Pressure from the lungs is transmitted via the pericardium to the heart. Severe lung hyperinflation mimics pericardial tamponade. High levels of PEEP are similar.
Distended abdomen	Fluid, fat, or gaseous distension can cause myocardial compression, particularly in the supine patient

Table 1. Causes of diastolic dysfunction

effect are briefly explained. Atrial fibrillation is a common occurrence in the postoperative period. It causes loss of atrial contraction that results in impaired diastolic filling. Myocardial hypertrophy is another predisposing factor found in some of the valvular lesions and in hypertensive patients. Its presence interferes with the passive late phase of diastolic filling of the LV contributing to diastolic dysfunction. Myocardial ischemia in the postoperative cardiac surgical patient significantly slows active myocardial relaxation during early diastole. It may also lead to rhythm disturbances that will further aggravate LV diastolic dysfunction. Tachyarrhythmias impair LV filling by shortening the diastolic phase of the cardiac cycle resulting in impaired LV filling (- Zile & Brutsaert, 2002). The effect of positive pressure ventilation (to which virtually all of open heart surgery patients are subjected to postoperatively) on cardiac performance is complex involving changes in preload and afterload for both right and left ventricles. Positive pressure ventilation can lower ventricular filling, and may also reduce afterload, enhancing ventricular emptying during systole. The effect on cardiac output depends on whether the effect on preload or afterload predominates. If the patient is normovolemic and intrathoracic pressure are within normal the effect on afterload reduction predominates resulting in an increase in the cardiac output. The increase in stroke volume leads to increase in systolic blood pressure during lung inflation results in a phenomenon known as reverse pulsus paradoxus. The beneficial effects of positive pressure ventilation on cardiac output are reversed by hypovolemia leading to decreased cardiac output and hypotension (Pinsky , 2005 2007)]. Pericardial constriction or tamponade causes increased resistance to diastolic filling and physiologically is “acute severe extrinsic diastolic failure” whereby the heart becomes physically compressed by the pericardial effusion. Renal insufficiency results in volume overload that leads to a slowing of myocardial relaxation potentially contributing to DHF (Tsuyuk et al, 2001). Chronic anemia is usually accompanied by an increase in cardiac mass due to volume overload. In the animal model, chronic anemia resulted in increased left ventricular end-diastolic pressure and decreased functional reserve which in turn can lead to diastolic dysfunction. It can also lead to tachycardia that it turn shortens diastole resulting in diastolic dysfunction. The anemia that is seen in the postoperative period due to excessive postoperative blood loss is transient, acute and is often rapidly corrected in these patients leading to very little if any effect on the diastolic function (Rakusan, et al 2001). Chronically uncontrolled hypertension is by far the most common predisposing factor in for DHF. It can lead to DHF through a number of ways; one of them is by causing LV hypertrophy that can results in a delayed LV relaxation with all its attendant effects on diastolic filling. The other mechanism is related to a reduced arterial compliance that can also contribute to diastolic dysfunction (Mottram et al, 2005). Hypertension that is seen at times in the postoperative period is usually transient is quickly managed and therefore does not pose the same risk of the more common form of hypertension. At times one may need to pace the heart in the post operative period; as most pacing wires placed at surgery are ventricular, pacing under these circumstances would affect diastolic filling bringing about diastolic dysfunction or could even trigger DHF in some instances. This is largely due to the loss of the atrial contribution to LV filling (Alsaddique, 2008). It is therefore better to keep this possibility in mind and make the extra effort of placing both atrial and ventricular wires for sequential pacing. There seems to be some evidence that Nitric Oxide (NO) metabolism plays a role in acute diastolic dysfunction following episodes of ischemia and reperfusion. It is thought that NO could have a beneficial role as pretreatment with cyclic guanosine monophosphate (cGMP)

donors, or with NO donors protects myocytes from relaxation failure in animal models (Schlüter et al, 1994; Draper & Shah, 1997; du Toit et al, 1998).

## 5. Assessment of diastolic function

### 5.1 Echocardiography evaluation

Transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE) play a major role in the assessment of diastolic function. A combination of 2-dimensional echocardiography, pulsed wave Doppler, Color M-mode (CMM) and Tissue Doppler imaging (TDI) are used in combination to categorize the grade of diastolic dysfunction.

2-D echocardiography is used to assess ventricular dimensions, LV mass, EF and LA size. Pulsed wave Doppler (PWD) measures the velocity of blood at the cursor position. The mitral inflow Doppler spectral display is composed of an E (early) wave for passive diastolic filling followed by an A (atrial) wave for atrial systole. Mitral blood flow is affected by LV relaxation, LV compliance, and the LA-LV pressure gradient. PWD is used to assess transmitral flow velocity recording and pulmonary vein flow velocity variables in the evaluation of diastolic dysfunction (Hunt et al, 2001; Vasan & Levy, 2000). The four useful variables from mitral flow are: peak early diastolic transmitral flow velocity (E), peak late diastolic transmitral flow velocity (A), early filling deceleration time (DT) and A wave duration [Adur] (Myśliński et al, 2002; Appleton et al, 1988). A normal E/A ratio is considered to be between 0.75 and 1.5. Early filling DT reflects LV compliance in early diastole. The normal DT is usually less than 200 milliseconds in young patients and may exceed 200 ms in patients over 60 years of age (Garcia et al, 1998). Pulmonary venous (PV) flow is composed of systolic and diastolic waves, and an atrial contraction reversal wave. The normal pattern is systolic predominance, but this is reversed when the LAP is elevated. In high LAP, the atrial reversal wave increased in duration such that it exceeds the mitral A wave duration. The major problem with the use of PV flow variables is the difficulty in obtaining adequate measurement when using TTE. The Doppler flow parameters are influenced by a variety of factors including altered loading conditions and heart rate, and not all patients "fit the pattern" (Appleton et al, 2001; Pirracchio et al, 2007). In the operative and critical care settings, the loading conditions and heart rates change frequently, and the patterns may alter without significant change in chamber compliance. Therefore, the results from these measurements may be inconsistent and accordingly inconclusive in the postoperative cardiac surgical patient. Color M-mode (CMM) Doppler flow propagation velocity (Vp) is an easily obtained diastolic index. It displays velocity information along a line that extends from the mitral valve to the LV apex, providing superior temporal resolution (5 milliseconds), spatial resolution (1mm) and velocity resolution (5 cm/s). The commonly used variable for CMM Doppler is the Vp into the LV which is the velocity at which the blood travels from the mitral valve to the LV apex. In sinus rhythm CMM is characterized by 2 distinct waves, one corresponds to the E wave and the second one to the A wave.

Vp relates well to LV relaxation and is claimed to be relatively load independent. A Vp value of less than 45 cm / s is consistent with diastolic dysfunction in patients older than 30 years of age < 55 cm/s in patients less than 30 years of age (Onose et al, 1999; Dumesnil et al, 1991). However, a major limitation of Vp is that it is heart rate dependent and in the perioperative setting, heart rate changes frequently.

Tissue Doppler imaging (TDI) is an ultrasound imaging modality that directly measures myocardial velocity during the cardiac cycle and allows wall movement to be directly



analyzed (Vitarelli &, Gheorghiade, 1998; Dokainish, 2004). The myocardial portion commonly studied is above the mitral annulus at either the septal or lateral walls. Three wave forms are described, Peak systolic wave, early diastolic wave (Ea) and the end diastolic wave (a') related to the atrial contraction. The Ea wave is relatively independent of loading state and is used to assess LV relaxation, a cut off of 8 cm /s for septal Ea or < 10 cm/s for lateral wall Ea measurement is now widely accepted as a sign of diastolic dysfunction (Sohn et al, 1997). It is easy to perform and available in the majority of patients even if the 2-D imaging is poor, and holds promise as a method to quantify change in diastolic function. When measuring TDI, Khouri and associates measure only early diastolic myocardial velocity (e') at the lateral corner of the mitral annulus, because it has been noted that the lateral annular velocity is more reproducible than the septal annular velocity (Khouri et al, 2004). Figure 2 reveals Echocardiographic findings typical of DHF pattern. Transthoracic echocardiography (TTE) is not always possible in the postoperative situation, due to hemodynamic instability, mediastinal air, the close proximity to a fresh surgical wound, presence of drains and dressings, or due to the inability to position the patient in an optimum way. In addition, mechanical ventilation with high positive end-expiratory pressure, pacing wires, ECG leads further add to the obstacles for the desired examination window resulting in a poor image quality.

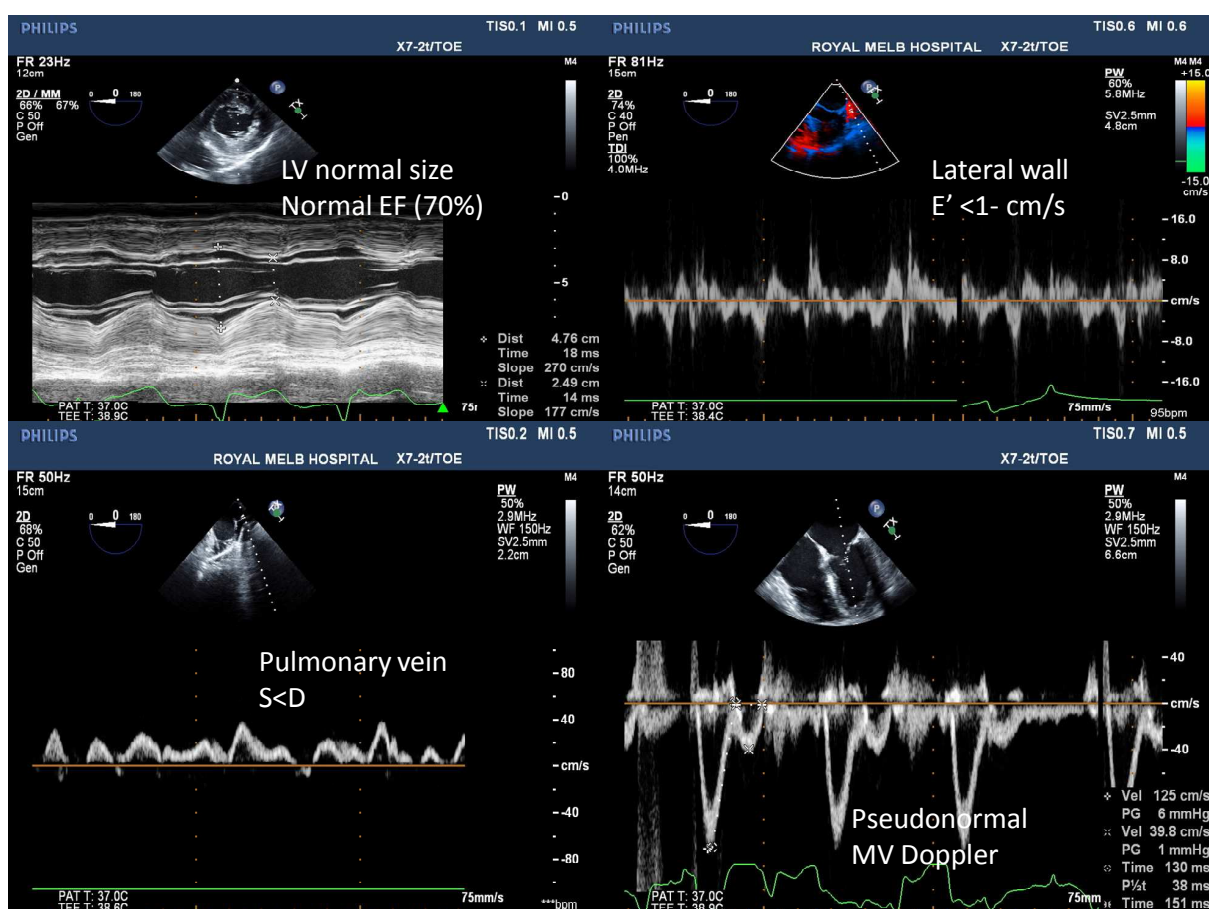


Fig. 2 Typical diastolic failure (small stiff heart) typically Grade 2 American Society of Echocardiography (ASE).

This is a common pattern in the perioperative setting. Typically Cardiac Index (CI ) 1.8-2.2 l/min/m<sup>2</sup> Pulmonary Artery Wedge Pressur( PCWP) > 15 mmHg

5.2 Use of Transesophageal Echocardiography (TEE)

TEE has a well established role in cardiac surgery as it has proved to be a valuable tool for intraoperative decisions particularly in valve surgery (Eltzschig et al, 2008). In addition, it has also proved to be useful in the field of intensive care for the assessment of hemodynamics and to track its variations after therapeutic interventions. Repeated measurements of left ventricular end-diastolic dimension are recommended in order to accurately track the hemodynamic changes, as a single determination is not felt to be reliable. TEE can adequately assess right ventricular function and left ventricular filling pressure using combined Doppler modalities (Vignon, 2005). The same parameters that are described for assessing diastolic function utilizing TTE can be achieved using TEE (Groban& Dolinski , 2005; Klein et al, 1999) though caution should be exercised as many of the Doppler parameters have not been extensively validated in sedated and ventilated patients.

5.3 Identifying a high left atrial pressure

A simple way to conceptualize diastolic failure is to recognize that if high left atrial pressure is present, then clinically important diastolic failure is present, as the body has had to adapt to a stiff ventricle by raising the LAP sufficient to provide an adequate transmitral driving gradient to fill the LV. Figure 3 High LAP can be diagnosed by invasive monitoring (such as a pulmonary artery catheter), or non-invasively with TTE or TEE. A simple pattern that can be easily recognized is that of a tense left atrium, evident by a fixed curve of the interatrial septum pointing from the left to the right atria. When the LAP is normal, the interatrial septum changes direction to point to the left atrium during mid-systole. Once a high LAP is detected, then echocardiography is focused on the chamber dimensions and EF to determine if it is DHF (small LV with normal EF), or systolic and diastolic failure (large heart with reduced EF).

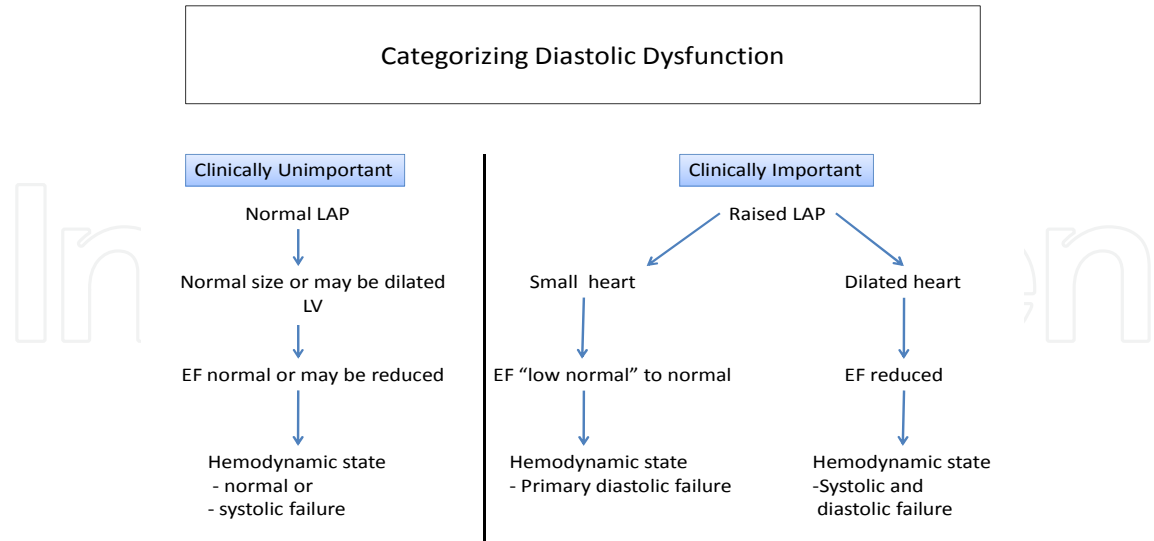


Fig. 3. Flow chart to categorize diastolic dysfunction. Clinically important diastolic failure is associated with raised left atrial pressure. Diastolic dysfunction with normal left atrial pressure does not usually affect hemodynamic stability. The key is to identify high LAP and then identify if the LV volume is small to normal or dilated, in order to differentiate primary diastolic failure from systolic and diastolic failure.

#### 5.4 Natriuretic peptides

B-type Natriuretic peptide (BNP) is a marker of systolic left ventricular dysfunction and heart failure. It however increases in subjects with diastolic dysfunction (mean  $20.3 \pm 4.7$  pg/ml vs. control  $9.6 \pm 0.5$  pg/ml,  $p < 0.001$ ). A normal BNP level virtually excluded the presence of diastolic dysfunction and concomitant left ventricular hypertrophy (LVH). Increased BNP concentrations in subjects with diastolic dysfunction are strongly related to LVH (Lukowicz et al, 2005).] In patients with normal systolic function, elevated BNP levels and diastolic filling abnormalities might help to reinforce the diagnosis diastolic dysfunction (Lubien et al, 2002; Krishnaswamy et al, 2001) A-type atrial, natriuretic peptide (ANP) is secreted from the atria in response to dilatation. Brain-type (B-type) natriuretic peptide (BNP) is a neurohormone that is released by the cardiac myocytes when left ventricular wall stress increases. After secretion the pro-hormone is cleaved to the biologically active hormone (BNP) and an inactive N-terminal fragment (N-BNP) Plasma levels of BNP increase in direct relation to increase in ventricular end-diastolic volume and end-diastolic pressure of both right and left side (Stewart, 2005). A rise in BNP produces vasodilatation and increase in renal sodium excretion (Maisel et al, 2002). Atrial natriuretic peptide and brain natriuretic peptide are known to be indices for heart failure. Postoperative ANP plateaus on the third postoperative day and decreases gradually down to the preoperative level by one month Postoperative BNP plateaus, showing very slow decrease and it never returning to the preoperative level (Song et al, 2004; Bail et al, 2004)]. This pattern of changes in the BNP and ANP levels after cardiac surgery makes it rather impractical to use them as markers for heart failure in the immediate postoperative setting of these patients.

#### 5.5 Cardiac catheterization

The characteristic finding of DHF is an elevated left ventricular end diastolic pressure (LVEDP) over 16 mm Hg in the presence of a normal LV chamber size (van Heerebeek et al 2006; Kitzman et al, 2002) Vasan and Levy recommended cardiac catheterization as a prerequisite for making the diagnosis of a definite DHF (Vasan & Levy 2000). In the post-operative setting of a fresh open heart surgery cardiac, catheterization is probably not warranted and the diagnosis can be made by less invasive means.

#### 5.6 Multidetector CT (MDCT) of the heart

Cardiac MDCT is most commonly performed for the purpose of noninvasive cardiac angiography. Image data are acquired continuously during a single breath-hold scan, typically 10 to 15 seconds in duration. Contrast is required for angiography and for endocardial border definition, with typical doses in the range of 60 to 80 mL per scan, quite comparable to a diagnostic cardiac catheterization. Patients with cardiomyopathies of all etiologies represent a large and growing population that stands to benefit from advanced imaging techniques (Sibley & Lima, 2008). Electron-beam computed tomography (EBCT) has been shown to be a reliable tool for the assessment of ventricular diastolic function and to detect constrictive filling pattern (Kloeters et al, 2008; Rumberger, 2000). These tools cannot be utilized in the assessment of the post operative heart for logistical reasons

#### 5.7 Cardiac magnetic resonance

Cardiac magnetic resonance (CMR) is the latest addition to the diagnostic tools. The specific advantage of cardiac magnetic resonance (CMR) over echocardiography is the possibility to

acquire images in any selected plane or along any selected axis. A routine CMR examination in the setting of heart failure will acquire short access images covering the entire heart from base to apex in addition, to the long access slices. It can also provide a range of LV filling parameters almost similar to those obtained by echocardiography (Rademakers & Bogaert, 2006; Hauser et al, 2004). CMR is considered as a valid alternative for echocardiography when an adequate echocardiographic assessment cannot be obtained. It is the diagnostic modality of choice for assessing small changes in LA or LV volumes and in LV mass (Rademakers, 2003). Clinical use of CMR is expanding and starting to address diastolic LV dysfunction. It is not of course practical to obtain CMR in the fresh postoperative cardiac surgical patient suspected to have DHF.

## 6. Diagnosis of DHF in postoperative heart

In an ICU environment, the diagnostic criteria are usually based on invasive hemodynamic measurements. As ventricular compliance begins to decrease, the end-diastolic pressure (EDP) rises but the end-diastolic volume (EDV) remains unchanged. The increase in EDP reduces the pressure gradient necessary for ventricular filling and this eventually leads to a lower EDV resulting in a decrease in cardiac output via the Frank-Starling mechanism. The usual method of assessing cardiac failure by the relationship between ventricular filling pressure and stroke volume does not distinguish between systolic and DHF. The end-diastolic pressure (EDP) is elevated in both types of heart failure. The end-diastolic volume (EDV) is increased in systolic heart failure and is decreased in DHF thus it is the parameter that will distinguish systolic from DHF (Aurigemma & Gaasch, 2004). The measurement that is most often utilized to distinguish between diastolic and systolic heart failure is the EF. The EF is normal or near normal in patients with DHF and is reduced in systolic heart failure.

Pulmonary artery catheter with a fast response thermistor can measure the EF of the right ventricle. These catheters are able to register the temperature (T) changes during each cardiac cycle. The change in temperature is due to dilution of the indicator fluid by venous blood that fills the ventricle during diastole. The amount of blood that fills the ventricle during diastole is equal to the stroke volume, the temperature differences between each plateau on the curve ( $T_1 - T_2$ ) is the thermal equivalent of the stroke volume (SV) (Figure 4). Temperature  $T_1$  is the thermal marker for end-diastolic volume (EDV). The EF becomes equivalent to the ratio  $T_1 - T_2 / T_1$  or  $[SV/EDV]$  (Spinale et al, 1990,1991). Once the EF is measured the stroke volume can be calculated by dividing the cardiac output by heart rate. The EDV can be determined by rearranging the EF formula  $EDV = SV/EF$ . The normal RV Right ventricular (RV) EF using thermodilution method is 0.45 to 0.50 which is about 10% lower than the EF measured by radionuclide imaging (Kay et al, 1983). The accepted normal for RVEDV is [80 to 140ml/m<sup>2</sup>] (Siniscalchi et al, 2005).

The chief points to help in the diagnosis of DHF in the postoperative heart are: (1) Hemodynamic evidence of heart failure (2) Mean pulmonary capillary wedge pressure >12 mmHg (Paulus et al, 2007) (3) Echocardiographic evidence of raised left atrial pressure (LAP) as evidenced by a distended LA with the interatrial septum displaying a fixed curvature towards the right atrium (Kusumoto et al 1993; Royse et al, 2004). (4) Echocardiographic evidence of a small LV in the absence of hypovolemia and valvular heart disease (5) Low EDV as determined by the pulmonary artery catheter (6) EF better or similar to the preoperative one. Table 2.



<ul style="list-style-type: none"><li>• Increased PACWP</li><li>• <math>EF \geq \text{Preop}^a</math></li><li>• Evidence of raised LAP<sup>a</sup></li><li>• Small LV<sup>a</sup></li><li>• Low EDV<sup>b</sup></li><li>• Absence of significant pericardial effusion<sup>a</sup></li></ul>
<sup>a</sup> Revealed by echocardiography. <sup>b</sup> As determined by pulmonary artery catheter.

Table 2. Features that would suggest DHF in a postoperative heart. PACWP: pulmonary artery capillary wedge pressure; CI: cardiac index; LAP: left atrial pressure; EF; EDV: end diastolic volume. Adapted with permission from Elsevier Publishing (Alsaddique, 2008)

Indeed according to the European criteria, a normal cardiac index in the face of pulmonary edema suggests DHF (Paulus et al, 2007). Echocardiography is a useful tool to diagnose DHF. In the postoperative heart suspected to have DHF it is not always possible to get an adequate assessment. In addition, air trapped within the postoperative mediastinum creates poor acoustic windows through which ultrasounds waves cannot pass. An echocardiography study that would simply establish that the left ventricular function has not deteriorated compared to the preoperative one and rules out the presence of cardiac tamponade or significant pericardial effusion can usually be done and would probably suffice under the circumstances. If the hemodynamics allow, one can probably use TEE to diagnose of DHF, it remains however an invasive procedure that should only be carried out by an experienced operator. Published guidelines for performance of TEE should be followed (Nihoyannopoulos et al, 2007; Cheiltin et al, 2003; Benjamin et al, 1998). The information gained by TEE should be integrated with the rest of the hemodynamic parameters (pulmonary artery occlusion pressures or pulmonary artery end-diastolic pressures), LA dimensions, and conventional Doppler imaging of mitral inflow in conjunction with TDI of the lateral mitral annular wall.

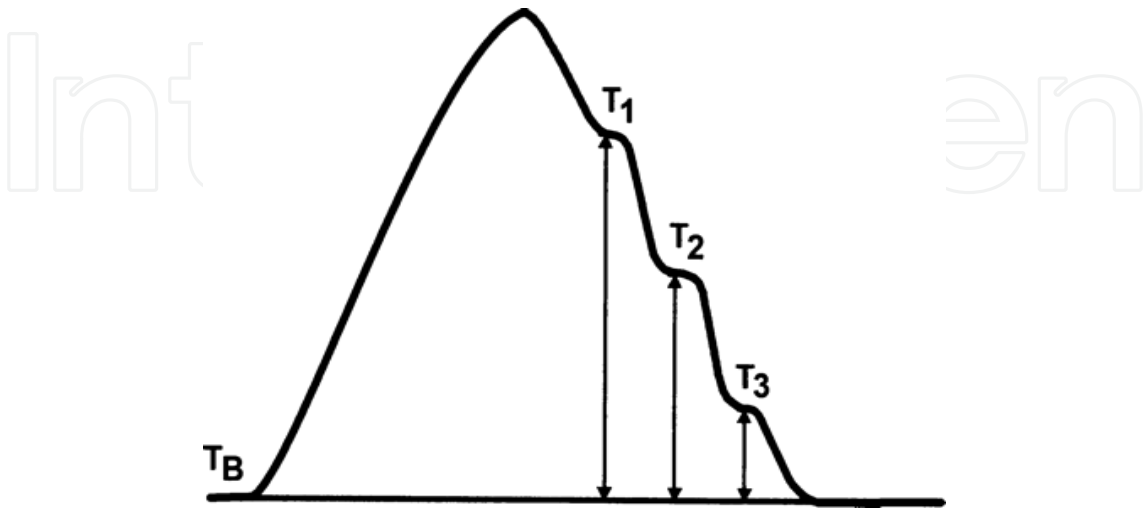


Fig. 4. Thermodilution EF for the right ventricle.  $T_B$  baseline blood temperature.  $T_1$ ,  $T_2$  and  $T_3$  are successive temperature plateaux. (Adapted with permission from Elsevier)



As it has been determined that objective measurement of LV diastolic function serves to confirm rather than establish the diagnosis of DHF. The diagnosis of DHF can be assumed without the measurement of the various parameters that reflect LV diastolic function in the presence of acute pulmonary edema associated with indirect signs of elevated left atrial pressure (Zile et al, 2001).

## 7. Perioperative management of DHF

Management begins by anticipating the problem before it actually happens. In the preoperative period, it is important to identify patients who may have or are at risk of DHF. Any prior history of DHF is important to identify and attention should be paid to patients who are likely to develop it in order to prevent any further deterioration of diastolic function in the post operative period. Chronically uncontrolled hypertension is a common cause of DHF it should be sought and aggressively treated prior to surgery to reduce the risk of perioperative heart failure (Kostis et al, 1997). Hypertension leads to DHF because of LV hypertrophy and decreased arterial compliance (Mottram et al, 2005). Diabetes mellitus, especially with poor glycemic control, is independently associated with abnormal LV relaxation, is similar in severity to that associated with systemic hypertension. The combination of diabetes and hypertension is associated with greater abnormality than patients with either condition alone. Aggressive control of diabetes, as well as of hypertension, should be considered an important component of the management in the pre operative period. Tight glycemic control decreases the risk of heart failure in patients with diabetes (Iribarren et al, 2001; Liu et al, 2001). It is helpful to avoid hypovolemia, tachycardia and tachyarrhythmias as they impair LV filling by shortening the diastolic phase of the cardiac cycle resulting in suboptimal LV filling (Zile & Brutsaert, 2002). Any reversible predisposing factors is to be corrected prior to surgery. Echocardiography is helpful in the preoperative assessment of patients especially those with compromised cardiac performance in order to identify the nature of heart failure. Risk factors for DHF include elderly patients, the female gender, hypertension, increased left ventricular mass, diabetes, obesity, and ischemic heart disease (Klapholz et al, 2004).

## 8. Intraoperative and postoperative management

The key to managing DHF is to maintain preoperative parameters as closely as possible. Managing DHF is analogous to walking on a tightrope. Any minor deviation from the “normal parameters tightrope” could lead to hypotension and low cardiac output, or pulmonary venous congestion. The second key principle is to maintain operating volume. As shown in Figure 1, the left ventricle with DHF operates at “just adequate” volume. If the volume is reduced, then a marked reduction in stroke volume will occur leading to low cardiac output and hypotension. It is also important to realize that it is difficult to achieve normal volume in DHF because of the relaxation abnormality. Although the left ventricular volume appears low, it is in the setting of an elevated left atrial pressure. Management of DHF is therefore a process of maintaining a delicate balance and avoiding the contributing and triggering factors that can lead to poor hemodynamic outcome. A summary of these contributing factors is shown in Figure 5. Reduced LV volume (such as blood loss or vasodilation) rapidly leads to hypotension. Tachycardia shortens the diastolic filling time, thereby reducing left ventricular volume and stroke volume (Zile & Brutsaert, 2002). High-

dose inotropes initially may increase blood pressure, but as tachycardia ensues, it would cause progressive reduction in left ventricular volume producing a hyperdynamic empty ventricle. High levels of positive end expiratory pressure (PEEP), obesity, pericardial or pleural effusions cause extrinsic compression of the heart and worsen diastolic function. Conversely, excessive administration of fluid in an attempt to improve cardiac output may not produce an increase in stroke volume but will produce an increase in end-diastolic pressure. This may exacerbate pulmonary venous congestion. Excessive hypertension or vasoconstriction will reduce EF and increase left ventricular end-diastolic volume. This has the effect of shifting up the end-diastolic pressure-volume curve where a small increase in volume will produce a large increase in end-diastolic pressure, increasing the risk of pulmonary edema. Bradycardia increases diastolic filling time, and will lead to an increase in the peak LVEDP. DHF can lead to pulmonary hypertension due to elevated pressure transmitted back through the pulmonary veins (Owan et al, 2006). Hypercapnea and hypoxia are potent causes of pulmonary hypertension in the perioperative setting.

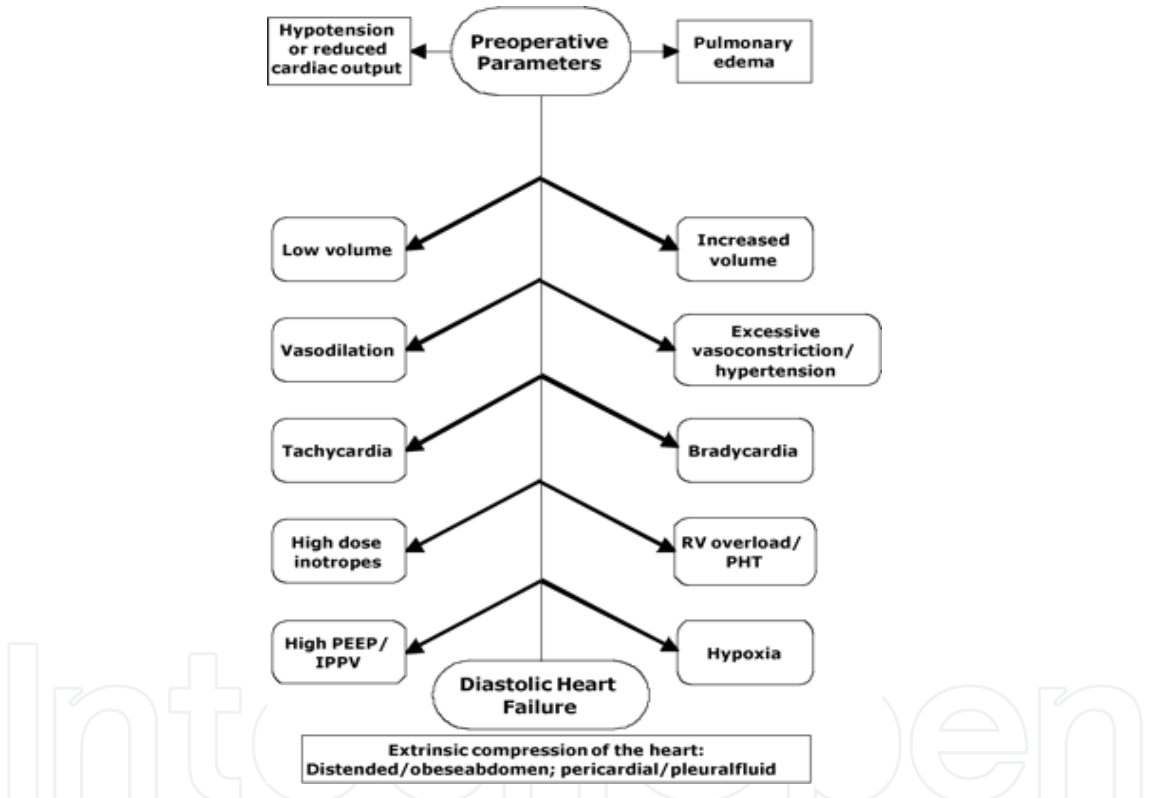


Fig. 5. Contributing factors to hemodynamic instability in patients with DHF. Deviation from normal parameters can lead to either hypotension/reduced cardiac output, or to pulmonary edema. (Adapted with permission from Elsevier)

### 9. Management strategies

A summary of clinical strategies is shown in Figure 6. The mainstay of treatment is to be realistic about hemodynamic goals, and to return the patient to normal preoperative parameters. Potential reversible causes (particularly extrinsic causes) should be identified and managed like pericardial tamponade and significant pericardial effusion as they cause resistance to LV filling leading to acute DHF. These conditions should therefore be suspected

in the event of unexplained DHF in the postoperative patient. Echocardiography is the most effective clinical tool to diagnose and monitor DHF. It can even gives indications about the hemodynamic profile of the patient, a raised left atrial pressure can be identified by enlarged atria, and a fixed curvature of the interatrial septum bowing from left to right (Royse et al 2001). One has to assess the different hemodynamic parameters of the patient to find out the cause for the imbalance that led to failure. For example, in the setting of reduced volume, administration of fluids, avoidance of tachycardia and reducing high dose inotropes will improve left ventricular end-diastolic volume. Vasoconstrictors may be required to counteract the effect of vasodilation which is seen during and immediately after cardiac surgery, thereby returning systemic vascular resistance to normal. Mechanical ventilation may affect hemodynamic performance in DHF. The mechanism is complex involving changes in preload and afterload for both right and left ventricles. Positive pressure ventilation may reduce venous return thereby reducing preload; and it also may reduce afterload enhancing ventricular ejection. This may have a variable effect on cardiac output. If the patient is normovolemic and intrathoracic pressure is normal, then the effect on afterload reduction may increase cardiac output. The beneficial effects of positive pressure ventilation on cardiac output are reversed by hypovolemia leading to decreased cardiac output and hypotension. Mechanical ventilation is beneficial in order to avoid hypercapnea, and PEEP can help reduce pulmonary venous congestion (Pinsky 2005, 2007). The use of continuous positive airway pressure (CPAP) by a face mask in the spontaneously breathing patient is reported to be effective in the treatment of diastolic dysfunction and may therefore be a useful ventilatory support under these circumstances (Benjelid etal, 2005; Moritz etal, 2003; Bersten etal, 1991)

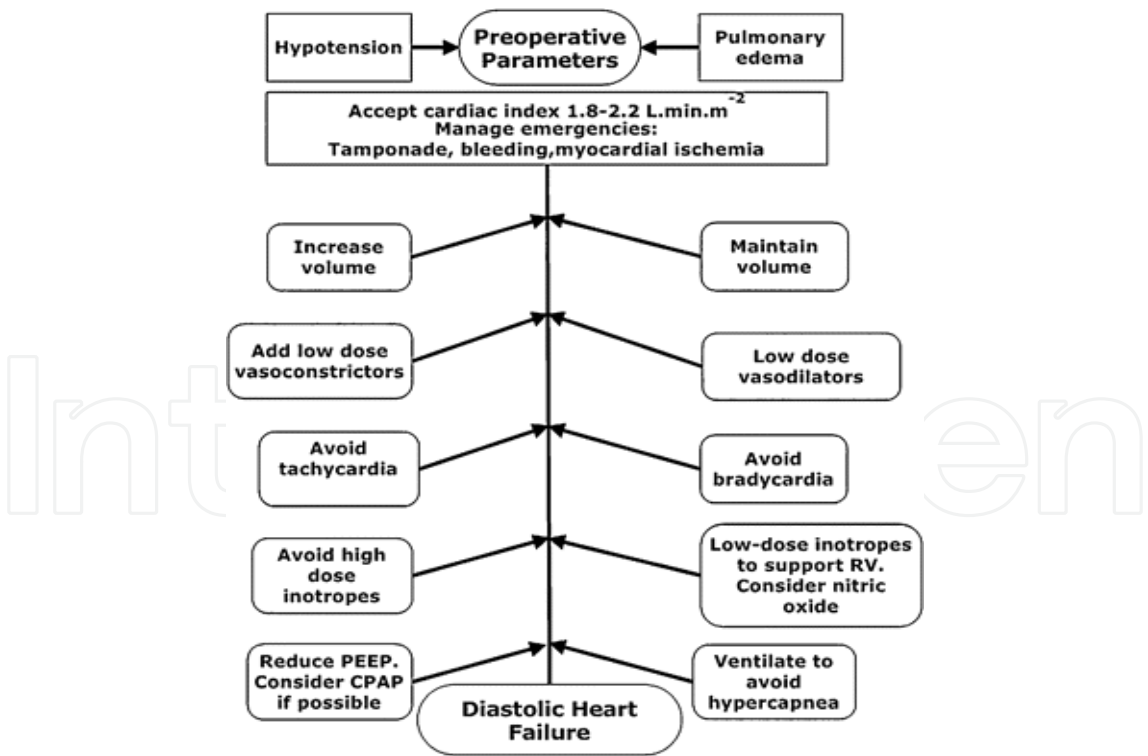


Fig. 6. Strategies to treat DHF in the perioperative setting. Treatment strategies are aimed to return to preoperative parameters. RV is right ventricle, PEEP is positive end-expiratory pressure; CPAP is continuous positive airway pressure. (Adapted with permission from Elsevier)

## 10. The contributing factors

Acute renal failure leads to volume overload and can trigger DHF (Tsuyuki et al 2001). Excessive fluid administration has the same effect and can be a contributing factor for postoperative DHF. Atrial fibrillation (AF) leads to loss of effective atrial contraction, changes LV filling pattern and results in a slowing of myocardial relaxation thereby triggering DHF. Pharmacological or electrical cardioversion may be necessary to restore sinus rhythm or at least rate control. In the postoperative coronary artery bypass patient unexplained DHF should lead to the suspicion of acute graft malfunction, which could happen in the absence of any signs of ischemia. Postoperative myocardial ischemia is an important reversible cause of diastolic dysfunction in the postoperative period as ischemia significantly slows active myocardial relaxation during early diastole affecting thereby LV filling. Ischemia could also lead to rhythm disturbances that will further aggravate LV diastolic dysfunction. It is well known that tachycardia and dysrhythmias shorten diastole leading to impaired left ventricular filling. Restoration of sinus rhythm should always be a priority in management (Zile & Brutstaert, (Piaarcchio 2002). If pacing is required, then atrio-ventricular sequential pacing will enhance ventricular filling. Ventricular pacing alone leads to loss of the atrial contribution (Alsaddique, 2008) and right ventricular pacing may induce dyssynchronous contraction. Pain may induce tachycardia and hypertension with the potential of triggering DHF through these mechanisms. Sepsis can exacerbate DHF, as it affects both systolic and diastolic function of the heart. In case of DHF developing late in the postoperative period sepsis should be considered as one of the possibilities. The role of sepsis in causing diastolic failure was identified by using pressure-volume loops in anesthetized endotoxemic rabbits. Left ventricular diastolic properties were shown to be altered; with prolonged relaxation, decreased compliance leading to increased end-diastolic pressure. Diastolic dysfunction can contribute to the development of cardiogenic septic shock (Pirracchio et al, 2007). Other factors that can contribute to DHF include a large pleural effusion or any other process that causes extrinsic compression of the heart or that could potentially impair or delay ventricular filling could contribute to or trigger DHF. This includes pericardial tamponade which is in effect “acute extrinsic DHF”.

## 11. Additional management considerations

The incidence of pure DHF in the postoperative heart is not known. Many cases of failure that are thought of as systolic failure are in reality diastolic in nature. There is no consensus on management of diastolic failure in the postoperative heart or intensive care environment in general. Echocardiography can be used not only to diagnose but also to monitor therapy and the hemodynamic changes. These points deserve emphasis:

1. The management of DHF is based on the strategy of avoiding pulmonary congestion whilst maintaining adequate cardiac output, and correction of any predisposing factors. As the systolic function is maintained in diastolic failure positive inotropes have little role in the management. The exception is where there is “low normal” EF or evidence of RV dysfunction or RV strain in the setting of pulmonary hypertension. In these situations, **low dose** inotrope therapy may improve cardiac output and hemodynamic stability. High dose inotrope therapy will induce tachycardia, and shorten diastolic filling time, leading to progressive reduction in LV preload and deterioration in hemodynamics.
2. In diastolic failure ventricular filling is impaired, diuretic therapy leads to volume depletion that will further impair ventricular filling resulting in a more reduction of the cardiac output.

3. Vasodilation is the enemy of DHF. Though vasodilation facilitates ejection, the heart empties but is unable to adequately re-fill, leading to progressive reduction in preload and deterioration in hemodynamic conditions. Normalizing systemic vascular resistance with a vasoconstrictor helps to maintain hemodynamic stability and normotension.
4. Many patients with DHF also have pulmonary hypertension. Hypotension in this setting leads to compromise of RV blood flow and relative RV ischemia, thereby causing RV failure. The RV fails by dilating, which leads to further compression of the LV and worsening DHF. This can lead to a spiral of progressive hypotension. In these circumstances a vasoconstrictor to preserve blood pressure and maintain LV preload, and in addition low dose inotrope (such as dobutamine) to support RV function, can improve hemodynamic stability. If the situation remains refractory it is worth considering nitric oxide (NO) to selectively treat right ventricular pressure overload. There is to our knowledge no published work on the use NO in DHF but it remains as an option if all else fails (Granton & Moric, 2008; Natori et al, 2003).

## 12. Use of diuretics

Diuretics should be used with caution, as high filling pressure is required to maintain cardiac output. Diuresis may result in hypotension in patients with DHF because of the steep shape of the left ventricular end-diastolic pressure-volume relationship, where small changes in end-diastolic volume will lead to reduced stroke volume. The use of diuretics must be countered by increased vigilance of hemodynamic variables, as indiscriminate use can be counter-productive (Zile & Burstaert, 2002; Aurigemma & Gaasch 2004).

## 13. Antiarrhythmics

Intravenous digoxin is a commonly used therapy for the management atrial fibrillation and paroxysmal atrial tachycardia. Other therapeutic agents include calcium antagonists such as verapamil, beta-blockers such as esmololol sotalol for acute rhythm control, or amiodarone. The current evidence supports the use of amiodarone for AF occurring after cardiac surgery. Amiodarone also reduces perioperative ventricular tachyarrhythmias and strokes, and helps reduce duration of hospitalization (Bagshaw et al, 2006; Saltman, 2003). Nevertheless digoxin continues to be valuable in long-term therapy of atrial flutter and fibrillation. More recently digoxin has been the subject of different studies to determine its effects on all forms of heart failure (HF). It has been shown that digoxin at serum concentration of 0.5-0.9 ng/mL reduces mortality and hospitalizations in all HF patients, including those with DHF. At higher serum levels, digoxin reduces HF hospitalization but has no effect on mortality or all-cause hospitalizations (Ahmed et al, 2006). The recommendation went further to suggest that the results of the DIG trial may provide support for the use of digoxin in patients who have heart failure with preserved EF, because a trend toward reduction in hospitalizations for heart failure was observed with digoxin in the ancillary trial (Ahmed, 2006)]. However the guidelines of the American College of Cardiology–American Heart Association Task Force for the management of heart failure and the Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology do not recommend the use of digoxin in patients who have heart failure with preserved EF (Hunt et al 2005; Swedberg et al, 2005).



### 13.1 Use of inotropes

Aggressive use of positive inotropic agents have little role in the management of DHF, though low dose inotropes may improve stability in the setting of low-normal EF or where there is pulmonary hypertension as described earlier [such as a combination of 3-5mcg/kg/min dobutamine and norepinephrine 3-5 mcg/min] (Little & Brucks, 2005; Wu & Yu, 2005). This is a very common pattern in DHF in the perioperative setting and may be exacerbated by poor cardioprotection (especially to the right heart), myocardial edema or reperfusion injury. Pharmacologically, the use of high dose inotropes leads to an increase in heart rate, which causes shortening of diastolic filling time leading to reduced ventricular volume and a gradual worsening of cardiac output. Therefore, in DHF it is probably wise to accept less than ideal hemodynamics provided adequate perfusion is maintained. It is therefore suggested that a cardiac **index between 1.8 and 2.2 L.min.m<sup>-2</sup>** is acceptable. Aiming for higher levels of cardiac index may not be readily achieved, and the strategy used would necessitate higher doses of inotropes and volume, with potential for greater pulmonary venous congestion. The danger of increasing inotrope use is that if the patient deteriorates, the typical response is to increase the inotropic dose leading to further tachycardia and shortened diastolic filling, thereby further reducing stroke volume and worsening cardiac performance, effectively creating a vicious circle of deterioration. The art of managing these patients is to achieve the delicate balance between hypotension and pulmonary venous congestion by judicious use of vasopressors, low-dose inotropes and fluids, such that their baseline hemodynamic state is maintained until the recovery processes following surgery abate.

### 13.2 Role of Vasodilators

It is important to appreciate that vasodilators facilitate ventricular ejection, and in the setting of a stiff left ventricle, makes it difficult to re-fill. This is especially important if there is associated tachycardia, as this will further exacerbate the inability to adequately refill the ventricle. If vasodilators are used they could make the ventricle operate at a lower end-diastolic volume further contributing to the low cardiac output. Under these circumstances a vasoconstrictor may actually be helpful by reducing EF and increasing the end diastolic volume. Vasodilators (especially inodilators) are appropriate for secondary DHF (systolic and diastolic failure). It is important to remember, however, the goal of maintaining preoperative hemodynamics, which means that the level of vasodilation should not depart considerably from baseline. In practice, most patients will have a vasodilation state after surgery, and are already excessively dilated. Vasodilator use in this setting can be counterproductive. If using inodilators, then add norepinephrine to control excessive vasodilation, and return it towards normal.

### 13.3 Role of vasoconstrictors:

Vasoconstrictors should be considered as part of the management of DHF, if vasodilation is manifest in the postoperative course. Vasodilation is common both during and immediately after cardiac surgery, and is part of the sterile inflammatory response syndrome seen following cardiac surgery. Diastolic abnormality prevents adequate filling of the left ventricle so that the end-diastolic volume progressively declines. Low-dose vasoconstrictors are protective in this setting with the aim of normalizing but not increasing vascular resistance.

### 13.4 Other pharmacological agents.

The value of beta-blockers in the perioperative period has recently been questioned because of the POISE trial that has examined their effect on non-cardiac surgery patients (POISE study group, 2008). Nevertheless one could extrapolate that the same would probably happen in a cohort of cardiac surgery patients. Beta blockers offer cardiac protection in the shape of a reduction of myocardial infarction (Andersen et al, 2008; Everly et al, 2004). Conversely, the incidence of stroke and its resulting patient disability was increased in the treatment group leading to increased mortality (Sear et al, 2008). Caution should be exercised with aggressive use of perioperative beta blockade. Beta blockers in the postoperative heart are used for control of tachycardia in the presence of adequate volume. An ultra short acting agent given intravenously (e.g. esmolol or landiolol that have a very short half life can be helpful (Mitchell et al, 2002; Kirshenbaum et al 1985; Yoshida et al, 2008). They can also help in case of fast atrial fibrillation to achieve an initial rate control in the process of stabilizing the hemodynamics (Kobayashi et al, 2004). Verapamil, a calcium channel blocker, can also be used intravenously to control heart rate and to treat fast atrial fibrillation (Abernethy & Schwartz, 1999). Calcium channel blockers in general are effective in DHF caused by idiopathic hypertrophic cardiomyopathies (Setaro et al 1990), but they do not offer the same benefits to diastolic failure caused by other factors (Nishimura et al, 1993). There are no drugs specifically marketed for the treatment of diastolic dysfunction. Inodilators may improve diastolic function in systolic and DHF, or bi-ventricular failure, as they will maintain stroke volume at a lower left ventricular end-diastolic volume. This has the effect of the heart working at a lower end-diastolic pressure. Unloading of the right ventricle will reduce the effect of left ventricular compression via the interventricular septum.

Long-term (outpatient) treatment that addresses myocardial remodeling includes ACE-inhibitors and angiotensin receptor blockers, calcium channel blockers, careful use of diuretics such as spironolactone, carvedilol, control of hypertension and treatment of myocardial ischemia (Yip et al, 2008; Yamamoto et al, 2005; Bergstrom et al, 2004; Yoshida et al, 2004). Future strategies are likely to address disorders of calcium handling, as well as modulating myocardial proteins and collagen subtypes (Kass et al, 2004).

### 13.5 Cardiac resynchronization therapy

Cardiac-resynchronization therapy (CRT) has been shown to improve the rate of survival, quality of life, exercise capacity, and functional status in patients with a prolonged QRS interval and moderate-to-severe heart failure that is resistant to optimal medical therapy. CRT is thought to improve the left ventricular EF and functional status by minimizing regional left ventricular delay caused by prolonged ventricular conduction, reducing mitral regurgitation and left ventricular reverse remodeling, and normalizing neurohormonal factors. Current guidelines support the use of CRT in patients with an EF of 35% or less, moderate or severe heart failure (New York Heart Association [NYHA] class III or IV), and a prolonged QRS interval [ $\geq 120$  msec] (Abraham et al, 2002; Leclercq et al, 2002). CRT did not improve peak oxygen consumption in patients with moderate-to-severe heart failure with narrow QRS intervals providing evidence these patients may not benefit from this form of therapy (Beshai et al, 2007). The effects on diastolic function have been the subject of recent studies by load-dependent pulsed-wave Doppler transmitral indices. A number of studies have shown that in heart failure patients receiving CRT, improvement in LV diastolic

function is coupled to the improvement in LV systolic function (Waggoner et al, 2005). The specific value of CRT for the treatment of the DHF as distinct from systolic and diastolic failure has not however, been extensively investigated.

## 14. Summary

5. DHF is “ a small stiff heart” with high left atrial pressure, whereas systolic and diastolic failure is a dilated heart with reduced EF and a high left atrial pressure, and echocardiography is the best way to differentiate these two conditions.
6. The key operating principle in DHF is to maintain their preoperative haemodynamic state and maintain operating volume
7. The key operating principle of systolic and diastolic failure is to improve stroke volume at a lower operating volume
8. The cardiac index in DHF is not great - but is enough. Do not “shoot for the stars”.
9. Low dose inotropes and enough vasoconstrictors to normalise vascular resistance can improve hemodynamic stability
10. High dose inotropes are often counterproductive
11. Excessive vasodilation is the enemy of DHF.

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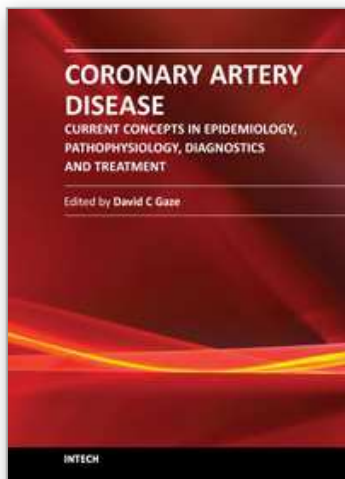
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## **Coronary Artery Disease - Current Concepts in Epidemiology, Pathophysiology, Diagnostics and Treatment**

Edited by Dr. David Gaze

ISBN 978-953-51-0262-5

Hard cover, 272 pages

**Publisher** InTech

**Published online** 16, March, 2012

**Published in print edition** March, 2012

Cardiovascular disease is ranked as the leading cause of death world wide, responsible for 17.1 million deaths globally each year. Such numbers are often difficult to comprehend. Heart disease kills one person every 34 seconds in the USA alone. Although the leading killer, the incidence of cardiovascular disease has declined in recent years due to a better understanding of the pathology, implementation of lipid lowering therapy new drug regimens including low molecular weight heparin and antiplatelet drugs such as glycoprotein IIb/IIIa receptor inhibitors and acute surgical intervention. The disease burden has a great financial impact on global healthcare systems and major economic consequences for world economies. This text aims to deliver the current understanding of coronary artery disease and is split into three main sections: 1. Epidemiology and pathophysiology of coronary artery disease 2. Coronary artery disease diagnostics and 3. Treatment regimens for coronary artery disease

### **How to reference**

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Ahmed A. Alsaddique, Colin F. Royse, Mohammed A. Fouda and Alistair G. Royse (2012). Diastolic Heart Failure After Cardiac Surgery, *Coronary Artery Disease - Current Concepts in Epidemiology, Pathophysiology, Diagnostics and Treatment*, Dr. David Gaze (Ed.), ISBN: 978-953-51-0262-5, InTech, Available from: <http://www.intechopen.com/books/coronary-artery-disease-current-concepts-in-epidemiology-pathophysiology-diagnostics-and-treatment/diastolic-heart-failure-after-cardiac-surgery>

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