# Practical diastology

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## Abbreviations used

CPB cardiopulmonary bypass
$ETCO_2$ end-tidal carbon dioxide
ICU intensive care unit
IVRT isovolumic relaxation time
LV left ventricular
MACE major adverse cardiac events
NIRS near-infrared spectroscopy
OR operating room
PA pulmonary artery
PCWP pulmonary capillary wedge pressure
PVF pulmonary venous flow
PW pulsed wave
RV right ventricular
TEE transesophageal echocardiography
TTE transthoracic echocardiography
$V_p$ propagation velocity

## Is it important to evaluate diastolic function?

There have been several studies showing the importance of diastolic dysfunction in cardiology [1]and in cardiac surgery[2;3]. Most of these studies were limited to the evaluation of baseline left ventricular (LV) diastolic function. Patients were followed post-operatively or on a long term basis. These studies have shown a clear relationship between the presence and severity of diastolic dysfunction and their primary end-point which could have been difficult separation from cardiopulmonary bypass (CPB)[4;5] or survival [2]. Baseline assessment of LV diastolic function is relevant because it can be use to stratify patients. In order to illustrate the importance of the pre-operative evaluation of diastolic function a study by Lee *et al* [6] was published in 2012 in Anesthesiology. This was an observational study that included 1,048 consecutive adults undergoing elective off-pump coronary artery bypass graft surgery in which the E/e' was measured preoperatively. The primary outcome was occurrence of major adverse cardiac events

(MACE), defined as a composite of death, myocardial infarction, malignant ventricular arrhythmia, cardiac dysfunction, or need for new revascularization. Using logistic regression and survival analyses, the authors found that an E/e' ratio more than 15 was independently associated with 30-day MACE (odds ratio 2.4, 95% CI 1.4-3.9) and 1-yr MACE (hazard ratio 2.1, 95% CI 1.4-3.1), irrespective of underlying LV ejection fraction. This study is important not only because it re-confirms the association between abnormal LV diastolic function and mortality but also because it stresses the incremental importance of also evaluating LV systolic function. But can we apply these concepts in the operating room (OR) and the intensive care unit (ICU)?

## Can we monitor diastolic function intraoperatively or in the intensive care unit?

It is possible to evaluate LV diastolic function in both the OR and the ICU. In the majority of cases, the evaluation will be obtained following the induction of general anesthesia using transesophageal echocardiography (TEE). However there are numerous pitfalls. One of them is the effect of anesthesia on diastolic function. In a study of 50 patients with pre-operative LV diastolic function, Couture *et al*. compared the transthoracic echocardiographic (TTE) examination obtained before induction of anesthesia to the TEE exam after[7]. Both bi-atrial and bi-ventricular dimensions and diastolic function were analyzed. Following induction of anesthesia, the heart rate decreased, while the mean arterial pressure remained unchanged. There were significant changes in bi-atrial diameter. Opposite changes in LV and right ventricular (RV) were observed. Reduction in RV systolic function but no changes in LV systolic function was also documented. Most Doppler velocities decreased. In 42% of patients, improvement in LV diastolic function was observed. Therefore when evaluating diastolic function in the OR and in the ICU, it is important to realize that it may not correspond to the pre-operative awake state.

In addition in order to monitor a signal, ideally it has to be continuous. This is not the case for our current method of evaluating diastolic function. The word monitoring comes from the Latin “monere” which means warning. For instance, several studies have shown that diastolic function is one of the earliest sign of myocardial ischemia. [8]. Abnormal diastolic function could precede electrocardiographic changes however it would be very difficult to monitor continuously diastolic function in the OR and the ICU. Which parameters should be monitored? The information is also displayed in a different screen which can be close or away from the more vital hemodynamic data. In addition, several factors could alter Doppler velocities such as surgical manipulation, bleeding, hemodynamic derangements etc. This would make any diastolic indices very sensitive but poorly specific in the diagnosis of intraoperative myocardial ischemia for instance. How do we evaluate diastolic function and are there other non-echo based monitoring alternatives that could indicate abnormal diastolic function?

## Echocardiographic and non-echocardiographic bedside indices of diastolic function

Several guidelines on the evaluation of diastolic function have been published [9-11]. A review article by Matyal *et al*. in Anesthesia Analgesia 2011 gives an excellent overview of the subject[12]. Echocardiographically, LV diastolic dysfunction has been classified as mild (impaired LV relaxation), moderate (pseudonormal pattern), and severe (LV restrictive filling). In addition, LV diastolic function evaluation allows the estimation of LV filling pressures. Algorythms used in the presence or the absence of LV systolic dysfunction have been proposed[12]. We use a combination of Doppler-derived variables in the diagnosis of LV diastolic dysfunction (Figure 1) [10] and we have developed a diagnostic algorithm which has been validated (Figure 2) [5;5]. The major advantage of TEE compared to TTE in the evaluation of diastolic function is the availability in the majority of patients of an adequate pulmonary venous flow (PVF) signal.

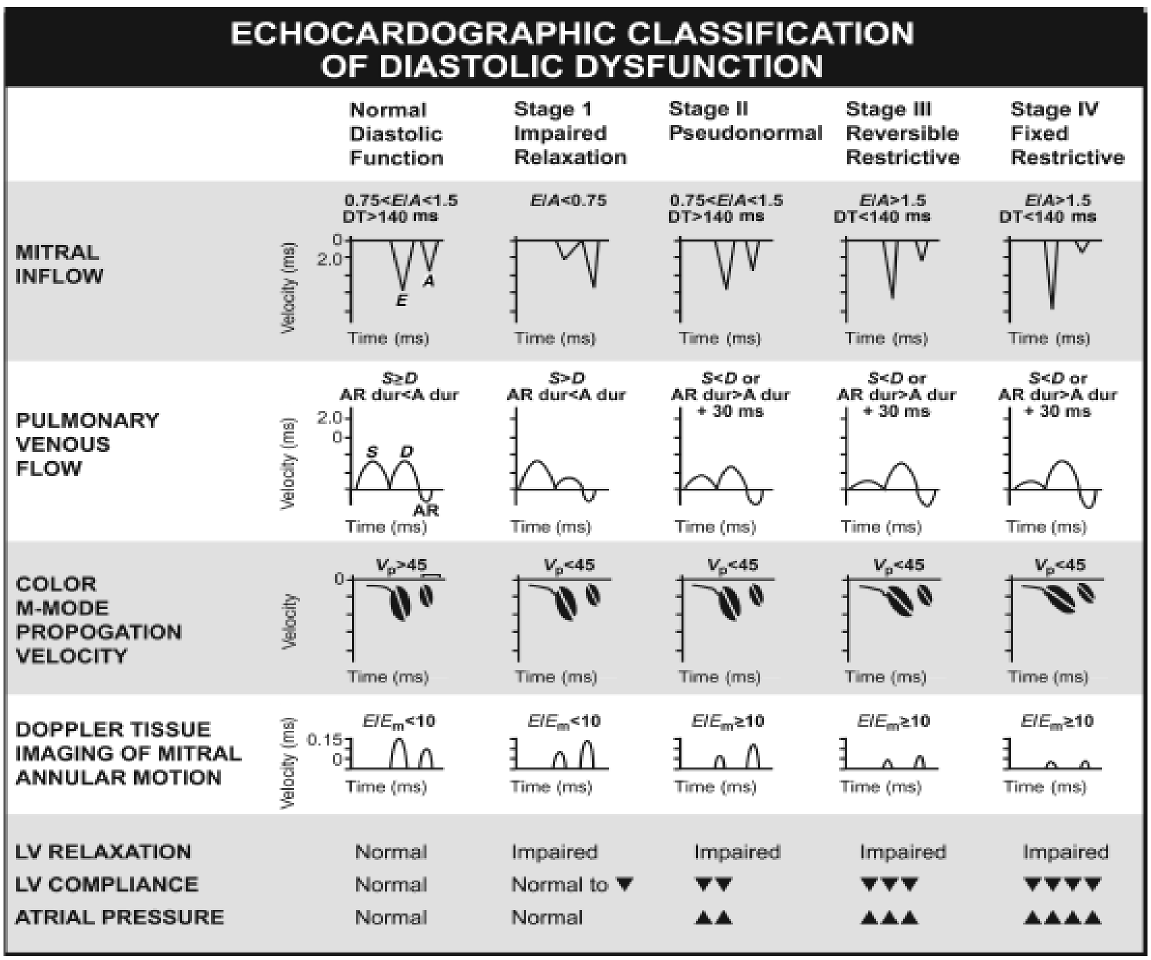


Figure 1 Diastolic function classification. Echocardiographic classification of diastolic dysfunction adapted for transesophageal echocardiography is shown. *Abbreviations*: A, peak late diastolic transmitral flow velocity; A dur, duration of mitral inflow A-wave; AR dur, peak pulmonary venous atrial reversal flow velocity duration; D, peak diastolic pulmonary venous flow velocity; DT, deceleration time; *E*, peak early diastolic transmitral flow velocity; *E*m, peak early diastolic myocardial velocity; LV, left

ventricle; S, peak systolic pulmonary venous flow velocity; Vp, flow propagation velocity. *Source*: Adapted from Ref. [10] with permission of Denault at al.[13].

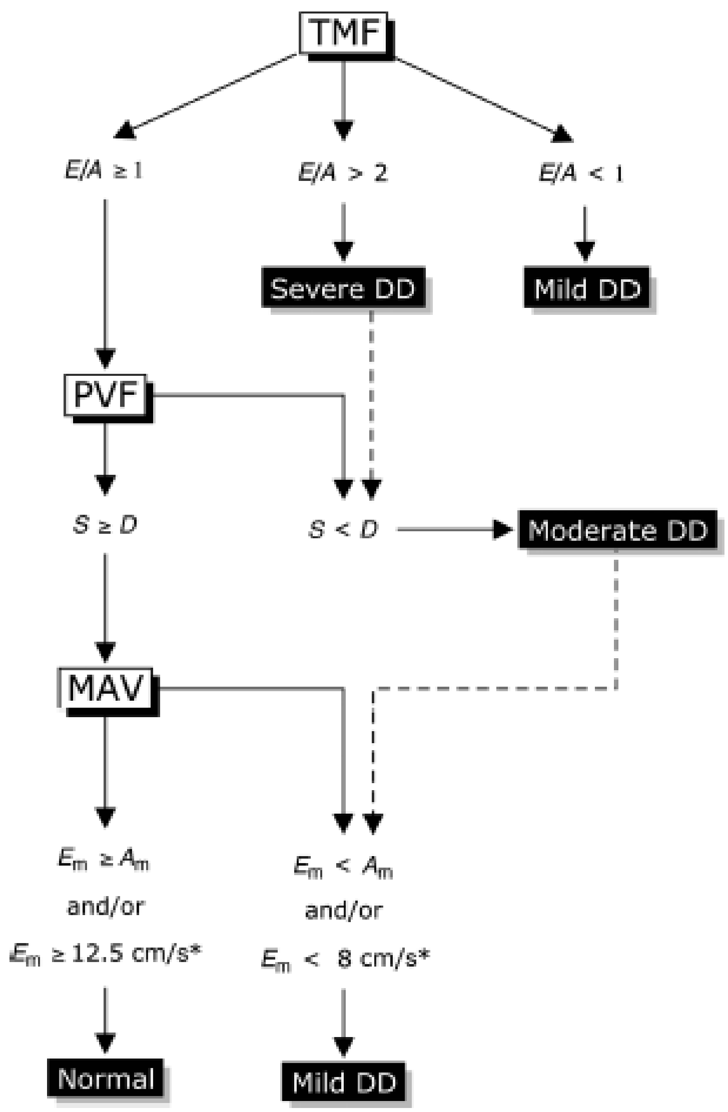


Figure 2 LV diastolic dysfunction algorithm. LV diastolic function is classified using pulsed wave Doppler of the TMF, PVF and tissue Doppler examination of MAV. Patients with a pacemaker, atrial fibrillation, non-sinus rhythm, mitral stenosis, severe mitral and aortic regurgitation are excluded from analysis. *Normal *E*m is

within an 8–12.5 cm/s interval. *Abbreviations*: *A*, peak late diastolic TMF velocity; *A*m, peak late diastolic MAV; *D*, peak diastolic PVF velocity; DD, diastolic dysfunction; E, peak early diastolic TMF velocity; *E*m, peak early diastolic MAV; LV, left ventricle; MAV, mitral annular velocity; PVF, pulmonary venous flow; *S*, peak systolic PVF velocity; TMF, transmitral flow. *Source*: [5]. with permission of Denault at al.[13].

Diastolic dysfunction alters the pressure-volume relationship and could explain some of the observed changes between filling pressure and ventricular volume observed after CPB. Impaired or delayed relaxation (mild diastolic dysfunction) results in decreased LV pressure decay during diastole and prolonged isovolumic relaxation time (IVRT). This will be reflected with higher diastolic filling pressure for the same LV volume. Echocardiographic evaluation of abnormal relaxation using pulsed-wave (PW) Doppler interrogation of the mitral valve will demonstrate prolonged IVRT, prolonged E-wave deceleration time, and a reduction of the *E*/*A* ratio. The PVF PW Doppler signal will show an increased *S*/*D* ratio. Tissue Doppler of the mitral annulus will demonstrate an $E_m/A_m$ ratio <1 while on color M-mode, propagation velocity ($V_p$) will be decreased. The delayed relaxation abnormality is the most common form of diastolic dysfunction (64% in our practice)[5]. It is commonly associated with LV hypertrophy either due to hypertension or aortic stenosis.

In patients with relaxation abnormalities and increased filling pressure, a moderate or intermediate form of diastolic dysfunction called the pseudonormal pattern is seen. The expression “pseudonormal” is a consequence of the normal looking PW Doppler mitral inflow signal while the PVF pattern is clearly abnormal ($S/D < 1$). With a pseudonormal pattern, the pressure-volume diagram will demonstrate moderate upward elevation of the diastolic waveform. Echocardiographically, it is characterized by reduced IVRT, a pseudonormal *E/A* ratio and deceleration time, PVF with inverted *S*/*D* ratio < 1 and atrial reversal wave velocity exceeding 40 cm/s, abnormal tissue Doppler of the mitral annulus with a reduced $E_m/A_m$ ratio and abnormally low color M-mode $V_p$ .

Left ventricular restrictive filling abnormality represents a more severe degree of diastolic dysfunction. This is associated with an upward shift of the diastolic pressure-volume curve. In these patients the following echocardiographic findings are observed: PW Doppler of the mitral inflow reveals shortened IVRT and E-wave deceleration time, a high *E*/*A* ratio >2; PW Doppler interrogation of the PVF shows predominant diastolic flow, while tissue Doppler imaging of the mitral annulus demonstrates reduced $E_m$ velocity and decreased color M-mode propagation velocity. This type of abnormality is commonly seen in hemodynamically unstable patients before or after cardiac surgery.

There are however several other elements that are important to assess in order to evaluate LV diastolic function. The patient has to be in sinus rhythm. The heart rate has to be normal because tachycardia by itself can impede filling. The use of a pacemaker will alter filling patterns particularly if only the ventricle is paced. The hemodynamic conditions have to be stable otherwise the Doppler parameters will vary significantly. Finally pericardial disease and right ventricular dysfunction have to be ruled-out. They can significantly influence LV diastolic parameters.

Other non-echocardiographic parameters can also be present in the presence of diastolic dysfunction. Filling pressures will be typically proportional to the severity of diastolic function. In a study where we evaluated LV diastolic function of 179 consecutive patients we observed that patients with pseudonormal and restrictive patterns had higher pulmonary capillary wedge pressure (PCWP) than those with normal or mild diastolic function[5]. Restrictive diastolic dysfunction is encountered in less than 5% of our patients undergoing cardiac surgery. In these patients pulmonary hypertension is typically present with “v” waves that are not associated with significant mitral regurgitation (Figure 3). In patients with normal or mild diastolic dysfunction, no predominant “v” waves will be present. Often an “a” wave will be seen on the PCWP tracing.

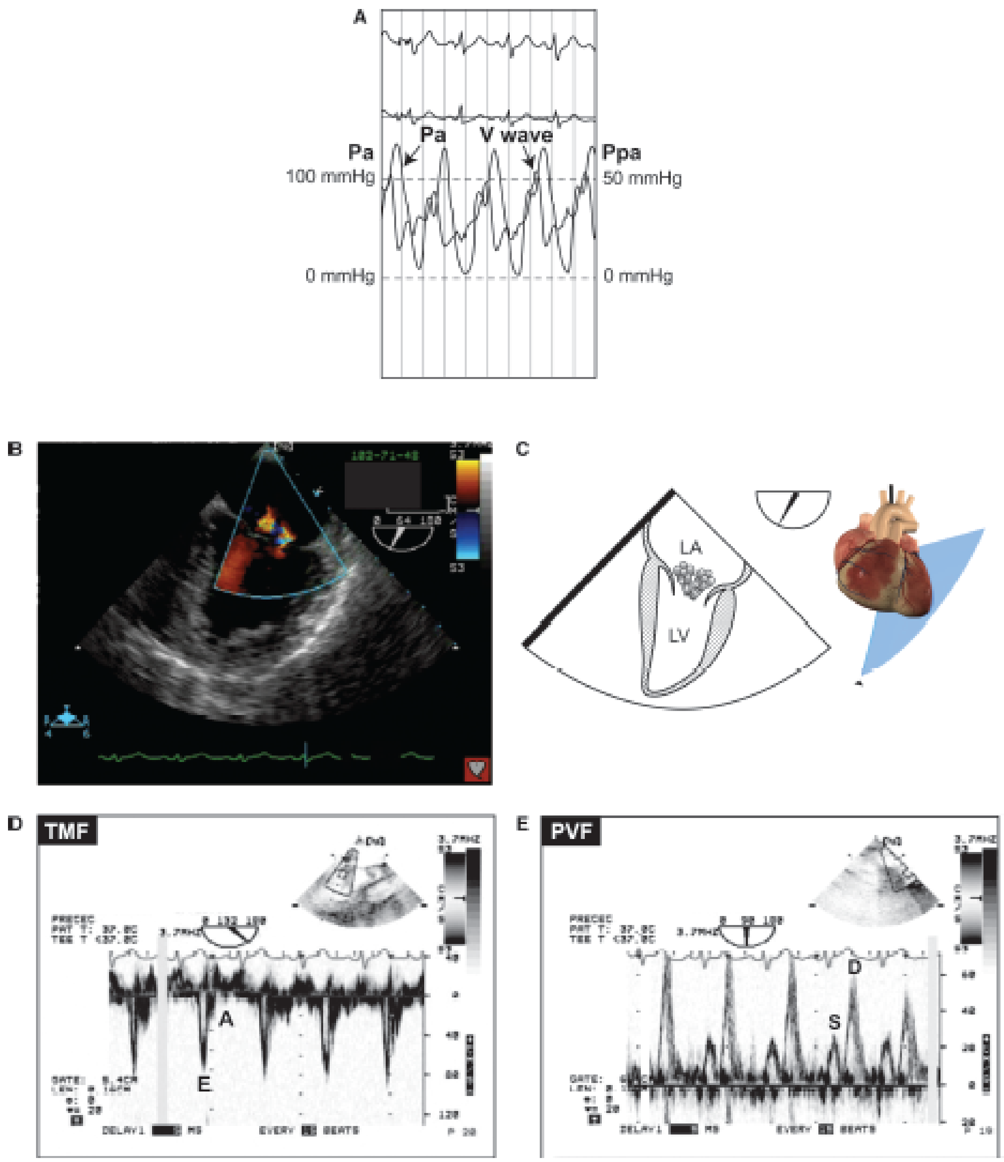


Figure 3 Stage III LV diastolic dysfunction (restrictive filling). A 61-year-old woman with cardiogenic shock is brought to the operating room for emergency coronary revascularization. (A) She was hemodynamically unstable on an intra-aortic balloon pump and vasoactive support. A 50 mmHg "V" wave on the wedged pulmonary artery catheter tracing was seen without any significant mitral regurgitation on color flow imaging (B,C). (D) TMF showed an E/A ratio >2 with a deceleration time <60 ms and isovolumic relaxation time of 40 ms. (E) The left upper PVF showed an abnormal *S/D* ratio with *S* wave blunting. *Abbreviations: A*, peak late diastolic TMF velocity; *D*, peak diastolic PVF velocity; *E*, peak early diastolic TMF velocity; LA, left atrium; LV, left ventricle; Pa, arterial pressure; Ppa, pulmonary arterial pressure; PVF, pulmonary venous flow; *S*, peak systolic PVF velocity; TMF, transmitral flow.

There are two other markers of diastolic dysfunction that we are currently using. One is the presence of B lines that can be obtained with the use of lung ultrasound[14]. The other is related to the use of near-infrared spectroscopy or NIRS[15]. Discussion on the use of lung ultrasound is beyond the scope of this article but reviews can be consulted [14;16;17], The presence of B lines or the so-called comet tail artifact are associated with alveolar-interstitial syndrome. They are typically present in pulmonary edema however the origin of pulmonary edema can be cardiogenic of non-cardiogenic. A paper by Frassi *et al*. in 340 patients has shown a linear relationship between the severity of diastolic function and the number of B lines on lung examination [18]. Another indirect indicator suggestive of abnormal diastolic function can be obtained using NIRS. In a study by Heringlake *et al* published in Anesthesiology in 2011, 1178 patients undergoing cardiac surgery were evaluated pre-operatively in order to obtain baseline NIRS values[19]. The authors observed that patients with NIRS values below 50% have increased risk of one-year mortality. The NIRS values correlated directly with ejection fraction but inversely with the N-terminal pro-B-type natriuretic peptide which is elevated typically in either systolic or diastolic dysfunction. In that regard, Paquet *et al* completed a study in 2008 in 99 cardiac surgical patients comparing NIRS with the TEE examination. Patients with moderate and severe form of diastolic function had lower NIRS values than those with normal or mild forms[20]. This suggests that abnormal diastolic function was associated with reduced cardiac output.

**Is left more important than right ventricular diastolic function evaluation?**

There has been much more literature and interest in LV than RV diastolic function however the interest in RV systolic and diastolic function is growing[21-23]. In 2010 guidelines for the evaluation of RV function were published by Rudski *et al*. [24]. In that article, some parameters were proposed to evaluate RV diastolic function. We have been interested in RV diastolic function for the last 10 years since our first publication in 2002 on unstable patients in the ICU[25]and in 2005 on the significance of abnormal hepatic venous flow (HVF) before cardiac surgery [26]. In order to study RV diastolic function, an algorithm was developed (Figure 4) and validated[5]. In several of our studies, we observed that hemodynamically unstable patients commonly had abnormal RV filling abnormalities[25]. Initially we were able to attribute the abnormal HVF as a consequence of pulmonary hypertension [26]. However as we gain more experience in the evaluation of RV function, we observed that the use of RV myocardial performance index (RVMPI) which is a dual indicator of RV systolic and diastolic function, was the best predictor of post-operative cardiac failure and mortality in patients undergoing cardiac surgery[27]. Indeed, pulmonary hypertension became non-significant when RV function parameters were considered. Therefore as more severe form of LV diastolic dysfunction are associated with pulmonary hypertension, only those associated with impairment of RV function were associated with poor outcome.

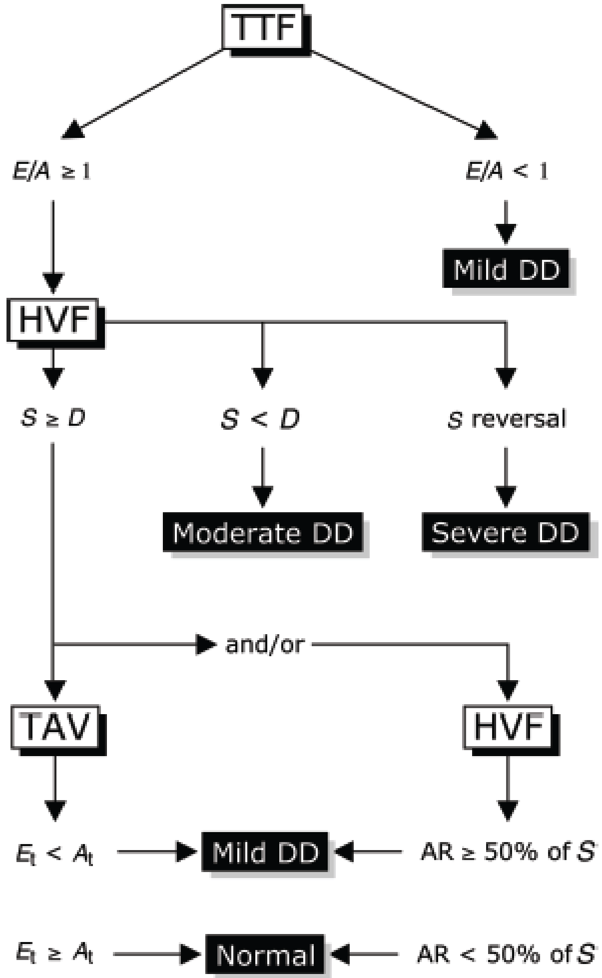


Figure 4 RV diastolic dysfunction algorithm. Diastolic function is classified by pulsed wave Doppler of the TTF, HVF and tissue Doppler imaging of the TAV. Patients with a pacemaker, atrial fibrillation, non-sinus rhythm, moderate to severe tricuspid regurgitation and tricuspid annuloplasty are excluded from analysis. *Abbreviations*: *A*, peak late diastolic TTF velocity; AR, peak atrial reversal HVF velocity; $A_t$, peak late diastolic TAV; DD, diastolic dysfunction; *D*, peak diastolic HVF velocity; *E*, peak early diastolic TTF velocity; $E_t$, peak early diastolic TAV; HVF, hepatic venous flow; RV, right ventricle; *S*, peak systolic HVF velocity; TAV, tricuspid annular velocity; TTF, transtricuspid flow. *Source:* [5]. *with permission of Denault at al.*[13].

In 2006 we reported the use of RV pressure monitoring in the diagnosis of RV outflow tract obstruction (RVOTO) in 800 consecutive patients[28]. Following this study, we started to routinely monitor RV pressure waveform[29-32]. This method was described several years ago in the diagnosis of RV ischemia [33;34] but not as a continuous monitoring modality. Our group has been using continuous RV pressure waveform monitoring in order to detect changes in RV function during cardiac surgery. The diagnosis of RV systolic dysfunction, diastolic dysfunction and RVOTO can be obtained instantaneously, in a dynamic fashion, using a pulmonary artery (PA) catheter and continuously transducing the RV port [Paceport, Edwards Lifescience, Irvine, CA] [28]. The normal RV diastolic slope is typically horizontal due to the normal RV compliance, which is much higher than LV compliance [23]. When RV pressure is combined with PA pressure monitoring, there should also be no significant differences between the peak systolic PA pressure and the systolic RV pressure (Figure 5).

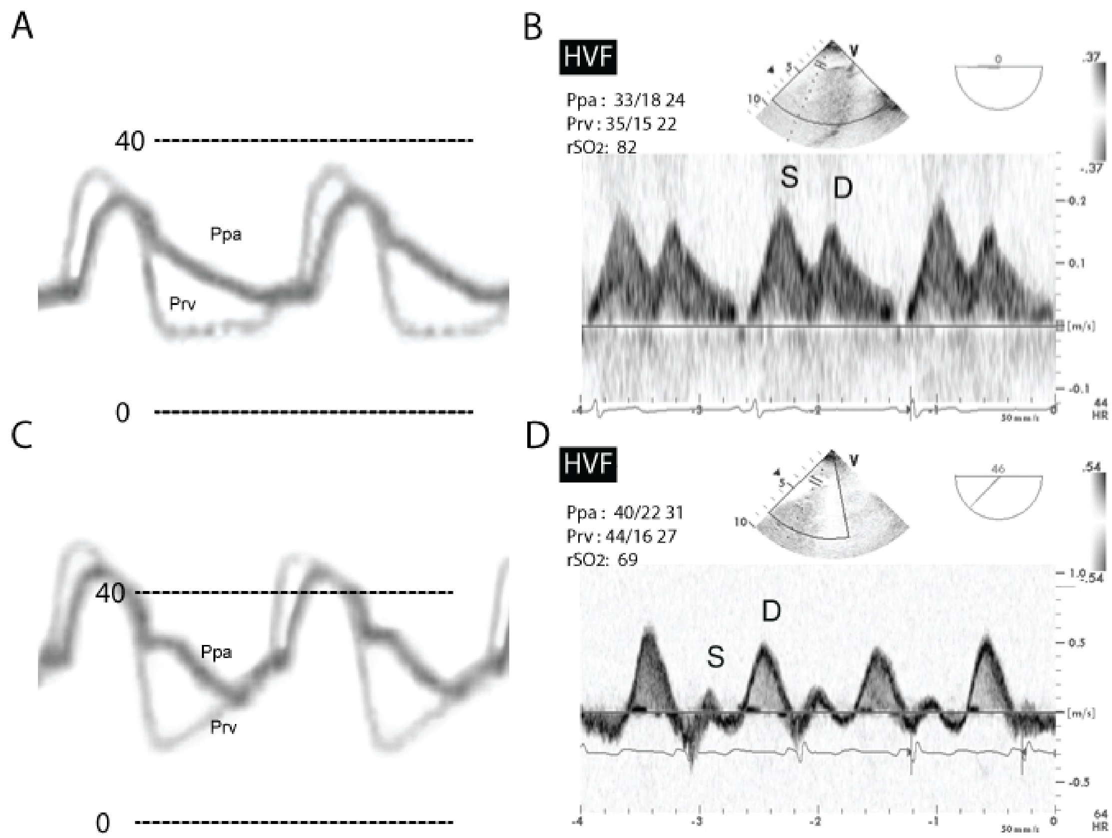


Figure 5. Zoomed right ventricular pressure (Prv) and pulmonary artery pressure (Ppa) with their corresponding Doppler hepatic venous flow (HVF) before (A,B) and after cardiopulmonary bypass (CPB). Note the change in the diastolic slope of the Prv waveform and the corresponding change in the systolic (S) to diastolic (D) ratio of the

HVF. After CPB, the regional oxygen saturation of the brain (rSO2) was lower, but still within normal limits (60±5%). [32]

In RV dysfunction, a progressive change from a horizontal to an oblique diastolic slope will be observed (Figure 5). As RV function deteriorates, it will change to a square root slope and then equalisation of the RV to PA diastolic pressure. This will correlate with changes in HVF or RV diastolic function. With severe RV systolic dysfunction delayed systolic upstroke (or RV pulsus tardus) and reduction in RV pulse pressure will be observe.  As mentionned previously, another useful diagnosis that can be instantaneously made with RV pressure waveform monitoring is RVOT obstruction (RVOTO). This is readily seen whenever the RV systolic pressure is 6 mmHg or more above the PA systolic pressure. The mechanism of RVOTO can be dynamic or mechanical. Dynamic RVOTO with gradients above 25 mmHg are observed in 4% of patients undergoing cardiac surgery and they are associated with hemodynamic instability [28]. In this situation (which is analogous to dynamic LV outflow tract obstruction associated with systolic anterior motion of the mitral valve), inotropic agents would be contra-indicated however volume and beta-blocking agents can be used if the RVOTO is non-mechanical. In the operating room, we simultaneously display both the PA and the RV pressure waveform throughout surgery. This technique may be the fastest and easiest way to diagnose hemodynamic instability resulting from RV systolic or diastolic dysfunction or RVOTO. However, when RV dysfunction is suspected, both cardiac and pulmonary echocardiography will be instrumental in determining the etiology and consequences. With RV dysfunction, NIRS values will remain normal (Figure 5). However with RV failure, both abnormal diastolic slope and reduced NIRS values will be observe (Figure 6).

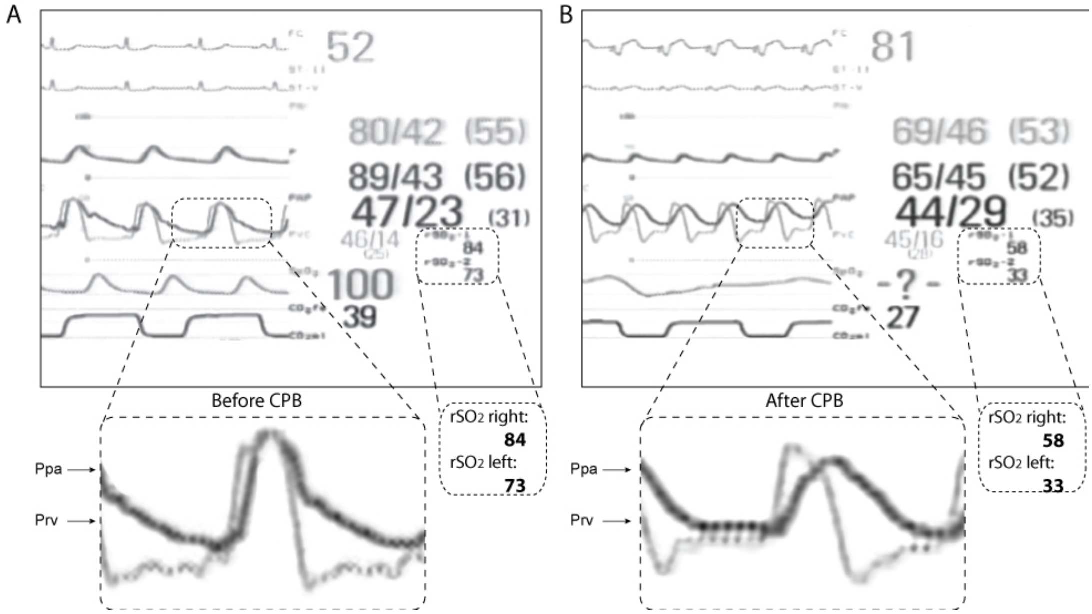


Figure 6. Hemodynamic waveforms combined with regional near infrared spectroscopy (NIRS) values obtained before (A) and after cardiopulmonary bypass (CPB) (B). The upper NIRS value was obtained from the right lower extremity and the lower NIRS value is from the brain. Note that after CPB, both values were reduced significantly. This was associated with failure to wean from CPB and significant hemodynamic instability. The etiology was a result of acute right ventricular (RV) failure, demonstrated on the right ventricular pressure (Prv) waveform. Note the change Prv from a normal shape before CPB to a square root sign, with diastolic equalisation after CPB. Note also that the pulmonary artery pressure (Ppa) systolic values were lower after CPB and non diagnostic of acute RV failure. The right atrial pressure was 16 mmHg compared to 14 mmHg before CPB. ($ETCO_2$ ,end-tidal carbon dioxide; Paf, femoral arterial pressure; Par, radial arterial pressure; Ppa, pulmonary artery pressure; $SaO_2$, oxygen saturation)[32]

**How we approach it in the operating room and in the intensive care unit.**

In the OR and in the ICU, the approach to diastolic function evaluation will be different if the exam is performed in an elective fashion or during an emergency situation. After the induction of anesthesia, in elective cases, as part of our cardiac examination, we will routinely include the evaluation of both LV and RV diastolic function. RV diastolic function using pressure waveform will also be displayed continuously. As we work in a teaching hospital, the components of the evaluation of diastolic function has to be transmitted to trainees especially if they are considering taking the National Board of Echocardiography Perioperative TEE examination. When we perform TEE examination, I will insist that the hemodynamic conditions, the end-tidal carbon dioxide ($ETCO_2$) (as it correlates with cardiac output[35]) and minute ventilation, the NIRS values and the drugs used at that precise moment be noted beside the echocardiographic images. This information allows us to better interpret the TEE images for systolic, diastolic and valvular assessment. In a critical situation, the TTE or TEE exam will be focused[13;36]. If there are no elevated pulmonary artery pressure, normal RV diastolic waveform, no B lines, normal oxygen saturation and the size of both left and right atria is normal, diastolic function is unlikely to be significantly abnormal. In that situation both NIRS values and $ETCO_2$ will be used to evaluate continuously the effect of the interventions.

## How to treat diastolic function?

In the most recent guidelines on diastolic function[12], very little information is provided on the treatment of diastolic function. In fact diastolic function is often a result of an underlying process whether ischemic or not. There are however some situations in which information on the severity of diastolic function can help the clinician in managing an unstable patient in the OR and ICU. Fluid responsiveness for instance tends to more important in patients with normal or mild diastolic function[37]. If ischemia is associated with diastolic dysfunction, resolution of ischemia will be associated with improvement of diastolic parameters[38]. Agents such as milrinone have been proposed to improve lusitropy[39] however we could not confirm this finding in patients with pre-op diastolic function[40]. Interestingly, when LV diastolic function is secondary to RV systolic dysfunction, improvement in the latter can lead to resolution of the LV diastolic abnormalities[41].

## Conclusion

In summary, the evaluation of both LV and RV diastolic function are important to appreciate. Their prognostic significance is well demonstrated. The endpoint however in dealing with an hypoxic or unstable patients it to maintain adequate oxygen transport. Oxygen transport is the product of arterial oxygen content and cardiac output[42]. Abnormal diastolic function with elevated filling pressure can alter both of these components. Abnormal oxygenation though elevated filling pressure can be easily diagnosed using bedside lung ultrasound and detecting B lines. Detection of B lines is easier than measuring the E/e' ratio. If B lines are present, then LV diastolic function evaluation might be relevant in order to determine the cardiogenic or non-cardiogenic nature of pulmonary edema. In the presence of reduced cardiac output, LV diastolic function evaluation might not be as relevant as RV systolic and diastolic function evaluation. The latter can be assessed continuously using RV pressure waveform and the efficacy of the treatment confirmed non-invasively using $ETCO_2$ and NIRS.

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