Université de Montréal

Intraoperative hemodynamic instability during and after separation from cardiopulmonary bypass: importance, mechanism and prevention

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Thèse présentée à la Faculté des études supérieures

en vue de l'obtention du grade de PhD

en Sciences Biomédicales (3-484-1-0)

Septembre 2009

Université de Montréal
Faculté des études supérieures

Cette thèse intitulée:

Difficult separation from cardiopulmonary bypass:
Importance, mechanism and prevention

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a été évaluée et défendue le 17 décembre 2009
Pour voir la vidéo de la présentation :
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Abstract

Every year, 1 million to 1.25 million patients worldwide undergo cardiac surgery. [1] Up to 36,000 cardiac surgeries are performed each year in Canada and close to 8000 in Quebec (http://www.ccs.ca). Because of the aging of the population, cardiac surgery will increasingly be offered to patients at a higher risk of complications. Indeed, elderly patients have increased co-morbidities, and aging is also a significant risk factor in the prevalence of coronary artery disease. [2] The consequence is a reduced physiologic reserve, hence an increased risk of mortality. These issues will have a significant impact on future healthcare costs, because our population undergoing cardiac surgery will be older and more likely to develop postoperative complications. One of the most dreaded complications in cardiac surgery is difficult separation from cardiopulmonary bypass (CPB). The definition of difficult separation from CPB includes the time period from when CPB is initiated and until the patient leaves the operating room. When separation from CPB is associated with right ventricular failure, the mortality rate will range from 44% to 86%. [3-7] Therefore the diagnosis, the preoperative prediction, the mechanism, prevention and treatment of difficult separation from CPB will be crucial in order to improve the selection and care of patients and to prevent complications for this high-risk patient population. The hypotheses of this thesis are the following: 1) difficult separation from CPB is an independent factor of morbidity and mortality, 2) the mechanism of difficult separation from CPB can be understood through a systematic approach, 3) inhaled milrinone is a preventive and therapeutic approach in the patient at risk for difficult weaning from CPB after cardiac surgery.

Keywords : Right ventricle; Cardiopulmonary bypass; Cardiac surgery; Hemodynamic instability; Transesophageal echocardiography; Pulmonary hypertension.

Chapter 3 Mechanisms of difficult separation from cardiopulmonary bypass

As we have previously observed, difficult separation from CPB is an important and independent cause of morbidity and mortality. Therefore, it is of crucial importance to understand that mechanism precisely in order to initiate appropriate treatment. Difficult separation from CPB will result in a reduction in cardiac output, which will in turn result in hemodynamic instability. In order to describe this mechanism, the use of the concept of venous return as described by Guyton, [54] combined with that of biventricular pressure-volume relationship, can help us understand this critical condition. The use of TEE has allowed us to document the various causes of hemodynamic instability, and examples from the MHI TEE database (n = 15,000 exams) will be used to illustrate this concept.

3.1 Mechanism of hemodynamic instability

The various components of hemodynamic instability can be explained using the classical concept of venous return as described by Guyton. [54] In simple terms, venous return (VR) is determined by a pressure gradient. This gradient corresponds to the difference between the mean systemic venous pressure (Pms) in the periphery and the right atrial pressure (Pra). This pressure gradient difference is divided by the resistance to venous return (Rvr).

$$VR = \frac{\mathbf{Pms - Pra}}{\mathbf{Rvr}} \qquad \text{(Equation 1)}$$

Therefore venous return and, consequently, cardiac output, will be reduced if: 1) the right atrial pressure is elevated, 2) the mean systemic pressure is low, and/or 3) the resistance to venous return is increased. There are several ways to illustrate this relationship. The classical approach to describe venous return and cardiac output is illustrated in Figure 13. [156]

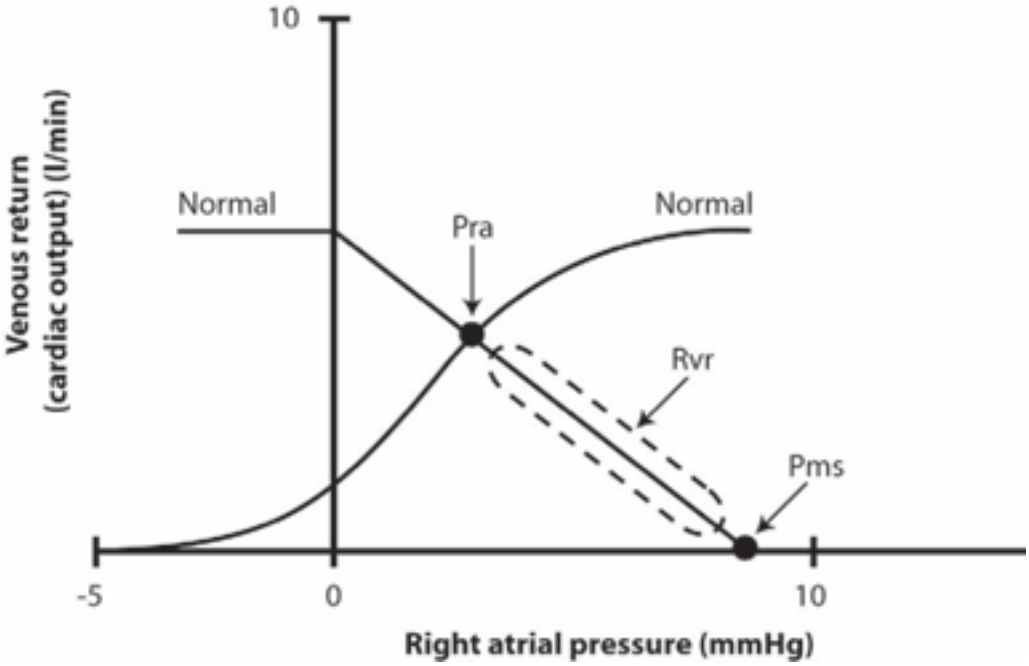

Figure 13 Venous return and cardiac output

The venous return and cardiac output (*y* axis) and its relation with right atrial pressure (*x* axis) is shown. The intersection of both curves will correspond to the right atrial pressure (Pra) at which, in a steady state, an individual will have an unique venous return and cardiac output. The mean systemic pressure (Pms) corresponds to the point where the venous return = 0. The venous return curve is linked to the resistance to venous return (Rvr) (dotted lines) (Adapted from Jacobsohn [156]).

The pressure-volume relationship is used to describe a single cardiac cycle (Figure 14).

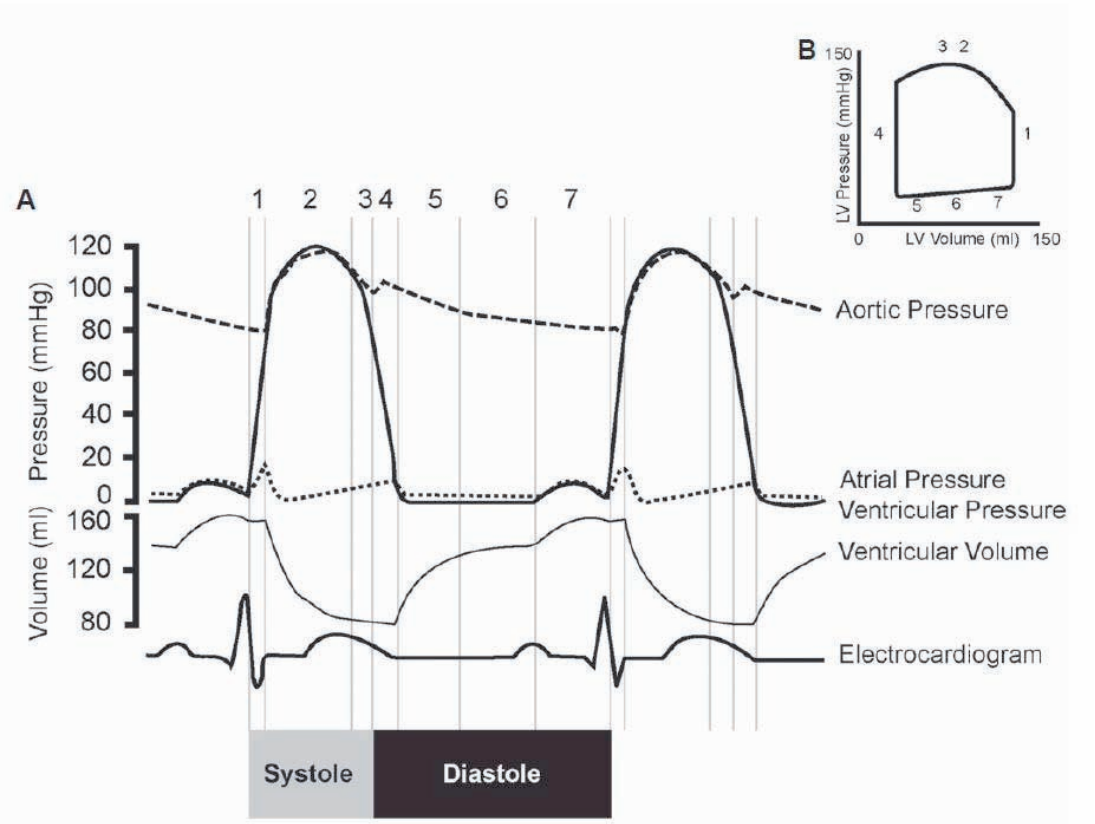

Figure 14 Pressure and volume during a cardiac cycle

(A) Changes in aortic, atrial, ventricular pressure, and ventricular volume in relation to the electrocardiogram. Left ventricular (LV) pressure and volume over time during a cardiac cycle is characterized by seven time-related events. Isovolumic contraction [1] is followed by early [2] and late [3] ejection. Diastole starts with isovolumic relaxation, [4] followed by the early filling phase after the opening of the mitral valve, [5] diastasis, [6] and atrial contraction. [7] (B) Corresponding LV pressure-volume relationship during one cardiac cycle (With permission of Denault *et al.* [12]).

The pressure-volume relationship is typically described for the left ventricle but has also been used to evaluate right ventricular function. [157] The major difference between both ventricles is the reduced pressure in the right compared to the left ventricle. [48] In order to integrate the pressure-volume relationship to the venous return concept, we used a simplified alternative approach illustrated in Figure 15.

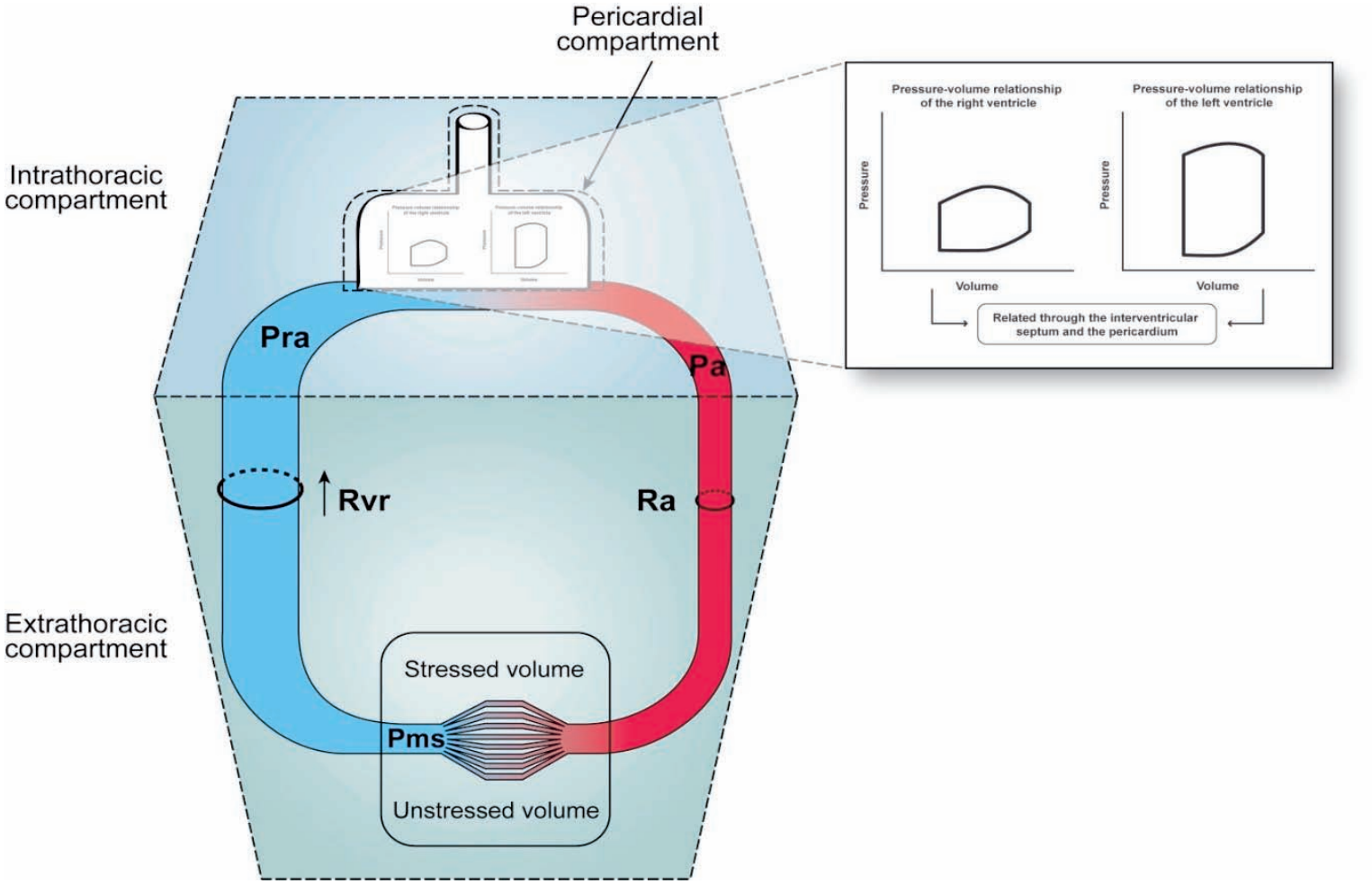

Figure 15 Venous return and pressure-volume loop concept

The circulatory system can be divided into an intrathoracic and an extrathoracic compartment. Illustrated in red is the arterial system and in blue, the venous system. Most of the blood volume (~70%) lies in the venous system. The mean systemic pressure (Pms) is determined by the stressed volume (~30% of blood volume). The cardiac pump has two components, the right and the left ventricles, defined by their respective pressure-volume loops (simplified). Both ventricles are connected together through the pericardium and the interventricular septum. The function and interaction between both ventricles will determine right atrial pressure (Pra). Blood returning back to the heart, i.e. venous return, will be dependent on the pressure gradient between the peripheral pressure, or Pms, and the central pressure, or Pra. Furthermore, any conditions increasing the resistance to venous return (Rvr), for instance compression of the inferior vena cava, will reduce venous return and consequently cardiac output. (Pa, systemic arterial pressure; Ra, arterial resistance) (With permission of Deslauriers *et al*. [158])

The combination of conventional hemodynamic monitoring and TEE allows the determination of the causes of hemodynamic instability. [44] However, so far, a systematic approach in the diagnosis of difficult separation from CPB using conventional hemodynamic and TEE has not been performed in cardiac surgery. This combined approach can be used to determine the causes of difficult separation from CPB. The causes of hemodynamic instability resulting in reduced venous return or cardiac output and leading to difficult separation from CPB are a reduction in Pms, an increase in Pra and an increase in Rvr (Table 11).

Table 11 Mechanism of hemodynamic instability in cardiac surgery

1) Reduction in mean systemic pressure:
- Reduction in stressed volume:
  - Hemorrhagic shock:
    - External hemorrhage
    - Internal: hemothorax, peritoneal hemorrhage, retroperitoneal hemorrrhage, gastrointestinal hemorrhage
- Increased in compliance
  - Sepsis and overwhelming shock [137]
  - Drug-induced vasodilation
  - Anaphylaxis
  - Vasoplegic syndrome
  - Adrenal insufficiency

2) Increased right atrial pressure
- Left and right ventricular systolic dysfunction
- Left and right ventricular diastolic dysfunction
- Left and right outflow tract obstruction
- Left and right embolism
- Aortic and mitral patient-prosthesis mismatch
- Hypoxemia and hypercapnia
- Pulmonary reperfusion syndrome

3) Increased resistance to venous return
- Compartment syndrome
  - Pericardial tamponade
  - Mediastinal: post cardiopulmonary bypass
  - Pleural: hemothorax and pneumothorax
  - Abdominal: intrinsic, extrinsic or parietal
- Vena cava syndrome
  - Inferior
  - Superior

3.1.1 Reduction in mean systemic pressure

The mean systemic pressure, or Pms, will depend on the amount of blood contributing to maintain a specific venous pressure. [156] This can be expressed by the following equation:

$$Pms = \frac{\mathbf{V - V_0}}{\mathbf{Compliance\ of\ the\ venous\ reservoir}} \qquad \text{(Equation 2)}$$

where V is the total volume of the venous reservoir and $\mathbf{V_0}$ the unstressed volume. The difference between V and V_0 is equal to the stressed volume. Consequently, a reduction in Pms will be caused by a loss of stressed volume, such as hemorrhagic shock, or an increase in compliance of the venous reservoir, such as can be the case following drug-induced vasodilation. Reduction of Pms results in a reduction in venous return and cardiac output from a parallel medial shift of the venous return curve. Pressure and volume of both ventricles will be reduced (Figure 16).

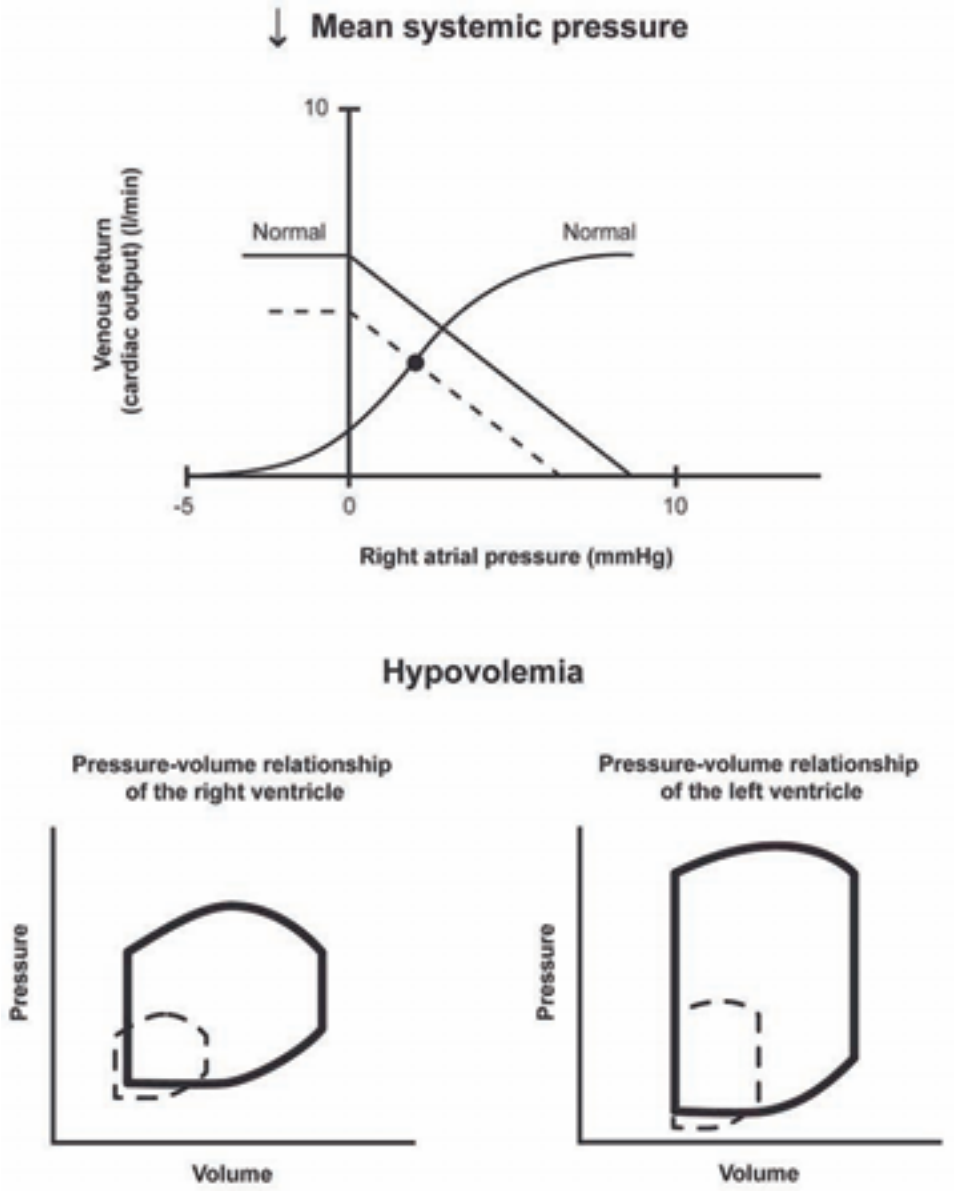

Figure 16 Reduction in mean systemic venous pressure

Reduction in mean systemic venous pressure will result in a medial shift of the venous return curve. In such a situation, pressure and volume of the right and left ventricles will be reduced. This diagnosis can be made with conventional hemodynamic monitoring alone. In such a situation, filling pressure, venous return and cardiac output will be reduced. There are two basic mechanisms: a reduction in the stressed volume and an increase in venous compliance. Both conditions will be associated with a reduction in both left- and right-sided cardiac dimensions; however, some specific echocardiographic findings can suggest rather one mechanism or the other.

3.1.1.1 Reduction in stressed volume

During cardiac surgery, hemorrhagic shock is a common mechanism of reduced Pms that occurs because of a loss of blood volume and, consequently, hemoglobin. Hemorrhagic shock can be defined as internal or external. The latter is easy to diagnose; the former can however prove more difficult to recognize. There are two conditions of internal blood losses that can be diagnosed during cardiac surgery. The first is massive pleural effusion secondary to a hemothorax. We have encountered this condition following traumatic perforation of the superior vena cava during the insertion of a central venous catheter. The diagnosis can easily be made using TEE, as both right and left pleural cavity can be seen using TEE). The mechanism of hemodynamic instability of a hemothorax can also result from an increase in the resistance to venous return, as will be discussed later. In such a situation, right atrial pressure might not be reduced, as the hemothorax can externally compress the right atrium.

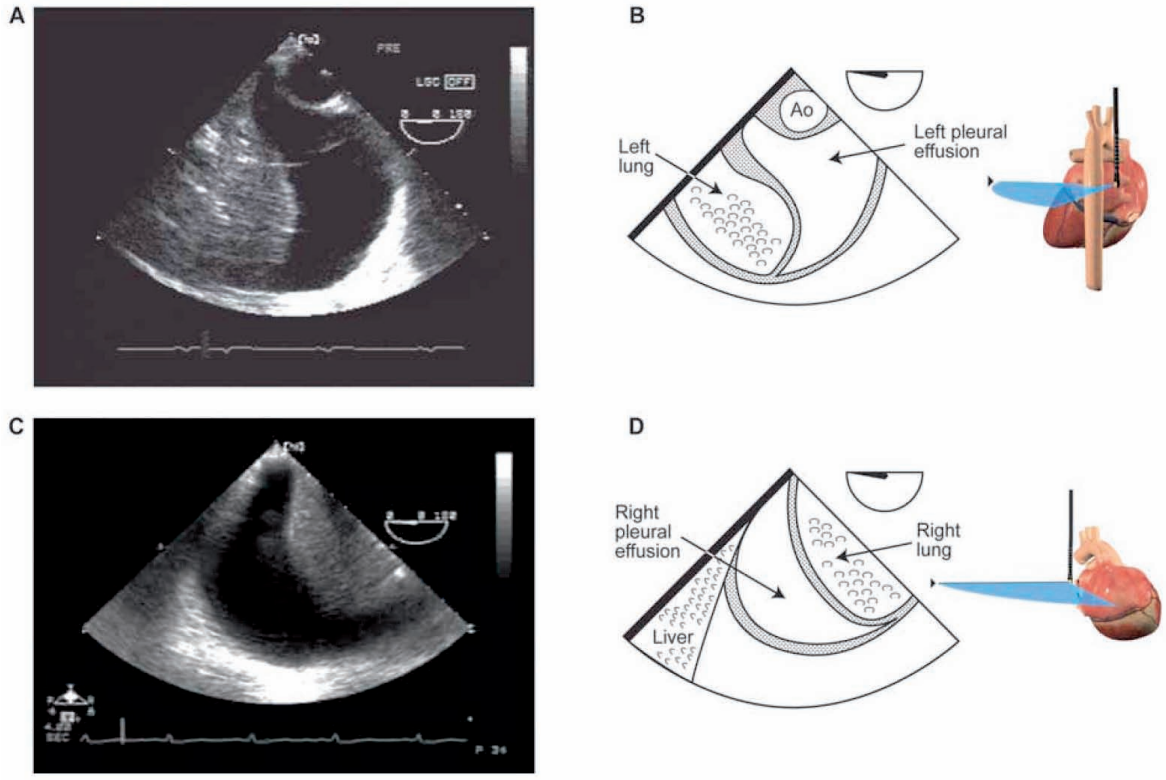

Figure 17 Bilateral pleural effusions

(A, B) The left pleural effusion is typically posterior to the descending aorta (Ao) and seen on the right side of the screen. (C,D) The right pleural effusion is on the left side of the screen where part of the liver can be seen. A total of 2500 mL of pleural fluid was removed from the right (900 mL) and left pleural (1400 mL) cavities (With permission of Denault *et al.* [13]).

Another cause of hemodynamic instability easily diagnosed in the operating room is peritoneal hemorrhage. This can result from abdominal aortic or iliac rupture, which can occur during manipulation of these structures. This situation has been encountered during the emergency insertion of an IABP. The diagnosis is based on the new onset of fluid collection in the abdomen. The echocardiographic image is similar to that of ascitis (Figure 18).

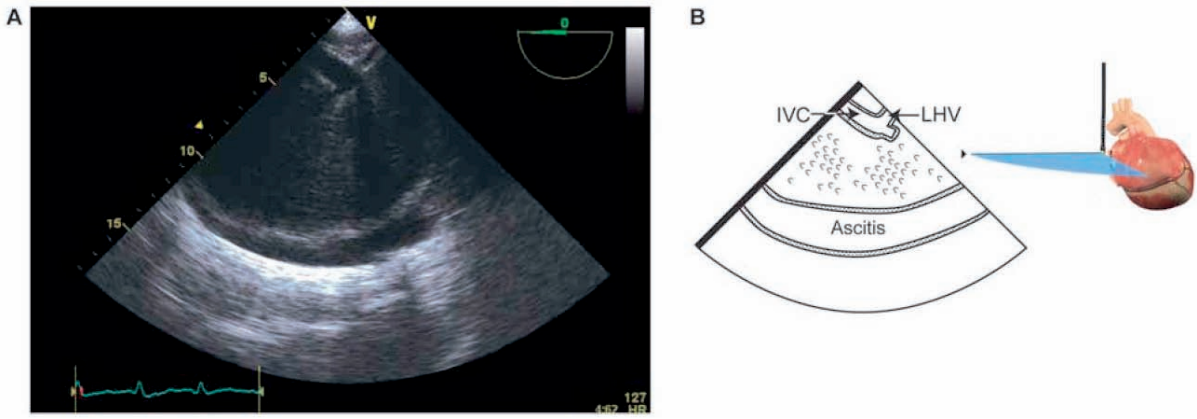

Figure 18 Abdominal examination using transesophageal echocardiography

(A,B) Presence of ascitis in a 58-year-old woman. (IVC, inferior vena cava, LHV, left hepatic vein) (Courtesy of Denault *et al.* [13]).

Other sites of bleeding include the gastrointestinal tract and the retroperitoneal space. Such a diagnosis would require other modalities, such as gastrointestinal endoscopy and computed tomography.

3.1.1.2 Increase in venous compliance

The second mechanism involved in a reduction in Pms is an increased compliance of the vascular system. This diagnosis can also be suggested by some specific echocardiographic signs evocative of an infectious process, for instance. Increased venous compliance can develop following the use of several drugs during cardiac surgery, during the vasoplegic syndrome and, in some cases, sepsis. [137]

The use of preoperative angiotensin-converting enzyme inhibitors has been associated with vasodilatory shock in cardiac surgery. [159] In such a case, vasopressin has been proposed as a drug of choice. [160;161] Drug-induced vasodilation can occur shortly following the induction of anesthesia and is often rapidly reversible. Anaphylactic reaction can also occur, particularly during the administration of blood products, aprotinin and protamine, and in patients previously exposed to these agents. Adrenaline or even vasopressin can be used in such a situation. [162] Similarly, the administration of protamine can be associated with acute pulmonary hypertension combined with right ventricular failure. [163] In these situations heparine, methylene blue [163] or inhaled prostacyclin [164] have been used to manage unstable patients. Patients exposed to or under corticosteroids can also present a predisposition to adrenal insufficiency, another cause of increased venous compliance. [165]

The term “vasoplegic syndrome” has been used to describe a severe systemic inflammatory response syndrome occurring after CPB [166] and, in rare instances, in patients without CPB. [136] Vasoplegic syndrome is defined as a mean arterial pressure < 60 mmHg, a cardiac output greater than 4.0 L/min, and low systemic vascular resistance (600 dyne/s/cm^5) under an intravenous norepinephrine infusion (0.5 µg/kg/min)[·]. [167] This condition can occur in up to 5% of patients undergoing cardiac surgery and is associated with an increased morbidity and mortality going up to 5.6%. Treatment with methylene blue has been shown to be effective in 94% of cases. [167] The mechanism of the vasoplegic syndrome is thought to be related to surgical trauma, contact of blood

[·] This is equivalent to 130 mL/hr of norepinephrine (4 mg/250 mL) for a 70 kg patient.

components with the artificial CPB circuit and lung reperfusion injury. [168] This effect will trigger a cytokine-mediated activation of platelets and leukocytes. Both tumor necrosis factor α (TNF-α) and interleukin-6 levels are related to the degree of surgical stress. [169] A high level of TNF-α will promote the secretion of nitric oxide (NO) and platelet-activating factor (PAF). The release of NO will reduce systemic vascular resistance and increase compliance; PAF is partially responsible for the increased permeability in sepsis and shock. [170]

Finally, emergency operation in patients already hemodynamically unstable on vasoactive medication is a well-known risk factor for LCOS [75;78] and mortality. [141] These patients may already show an increase in venous compliance from sepsis. Active endocarditis for instance, with the associated sepsis, is an important predictor of outcome in the Parsonnet score [100] and EuroSCORE. [101;141] In such conditions, the requirement for vasoactive medication can be the result not only of an increased venous compliance but is also often associated with other mechanisms.

3.1.2 Increased right atrial pressure

Increased right atrial pressure can result from left and right systolic dysfunction, diastolic dysfunction, outflow tract obstruction and embolism. In addition, certain biochemical conditions can increase pulmonary vascular resistance, such as hypoxemia, hypercapnia and the pulmonary reperfusion syndrome (see Chapter 6). Aortic and mitral patient-prosthesis mismatch are other factors that can contribute to an increase in right atrial pressure. These conditions, along with their definitions, mechanisms and echocardiographic signs, will be reviewed.

3.1.2.1 Left ventricular systolic dysfunction

One of the most common causes of elevated right atrial pressure is left ventricular systolic dysfunction. During cardiac surgery, left ventricular systolic dysfunction can result from ischemia, poor protection during CPB and air embolism. In a situation where systolic

dysfunction appears either to the left or the right, a right-sided (or lateral) shift of the pressure-volume relationship will be observed. Biventricular volumes will be increased, while ventricular pressure is typically normal or high (Figure 19).

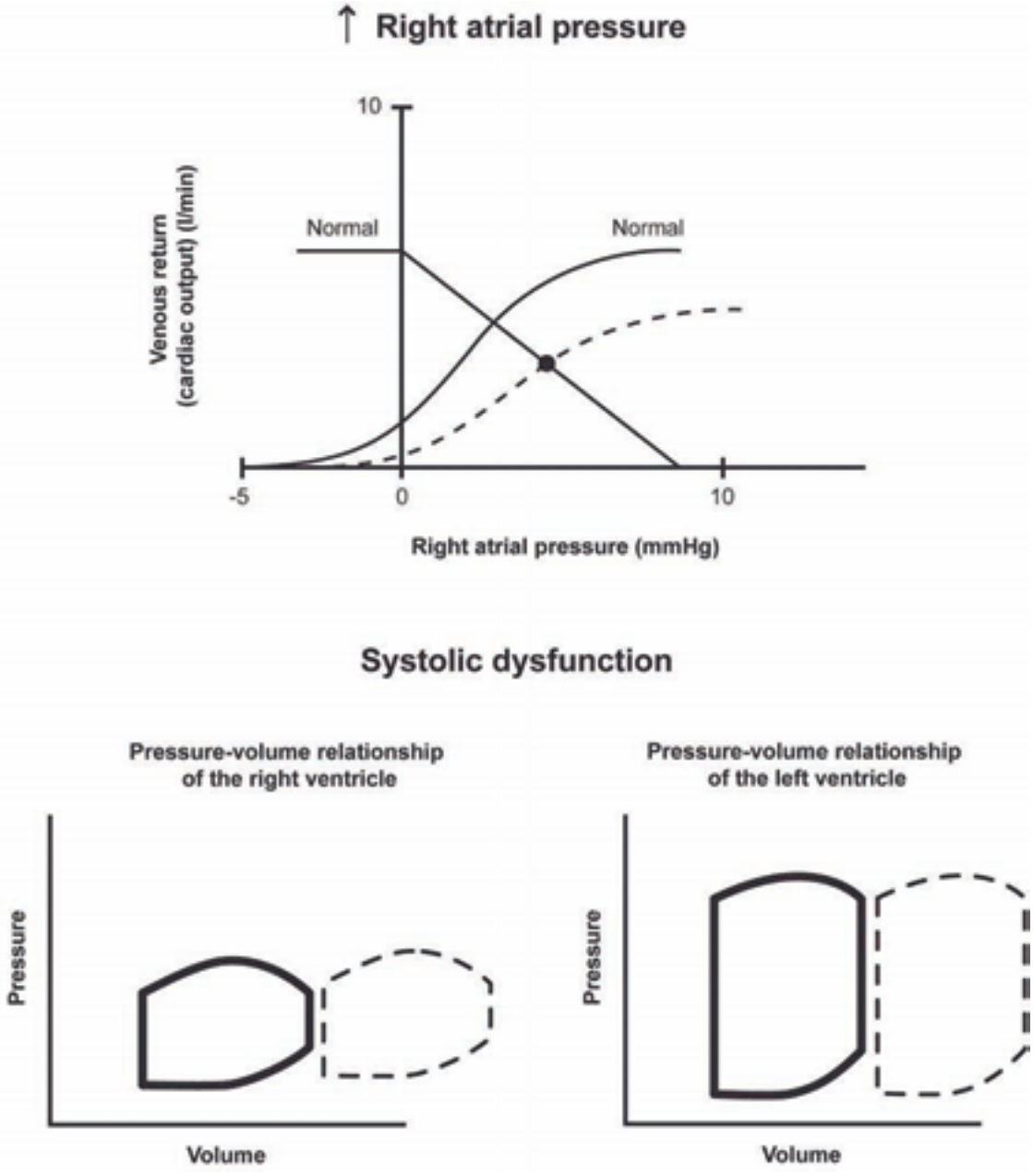

Figure 19 Biventricular systolic dysfunction

Biventricular systolic dysfunction will be associated with a reduction in venous return and cardiac output. The right atrial pressure will increase. In that situation, the pressure and volume of the right and left ventricles will shift laterally.

Echocardiographically, signs of left ventricular dysfunction include a reduced left ventricular ejection fraction measured either using a mid-esophageal view (Figure 20) or transgastric view (Figure 21).

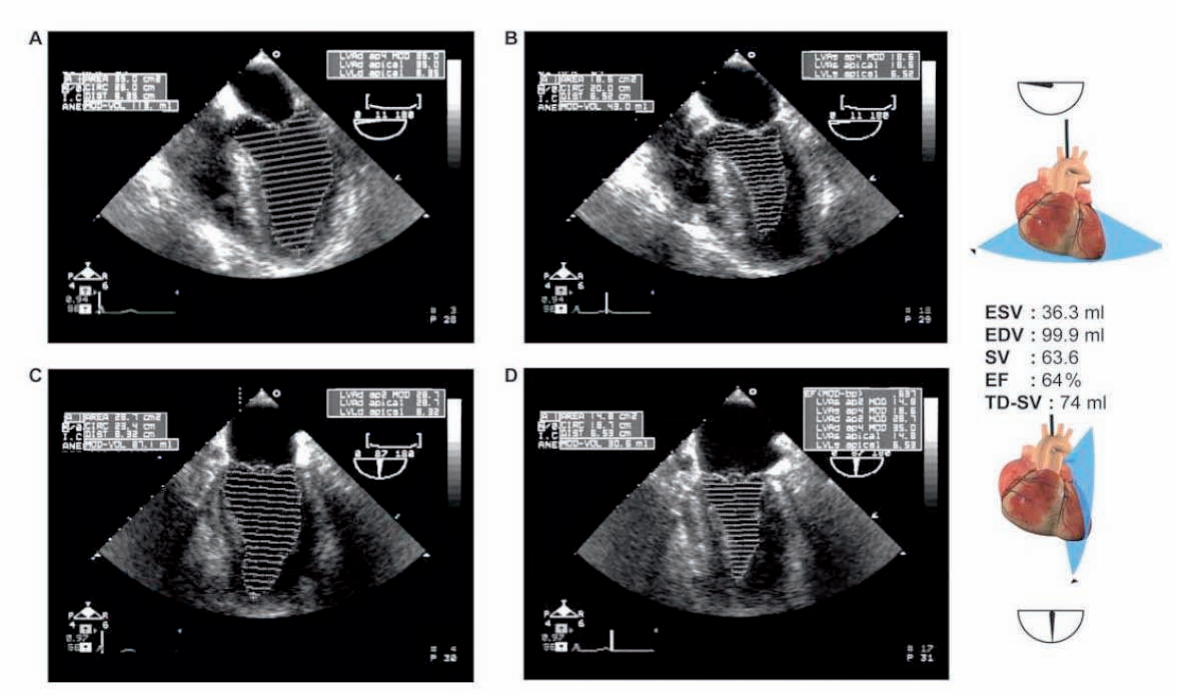

Figure 20 Simpson's method of discs

Measurement of left ventricular volumes by modified Simpson's biplane method using mid-esophageal four- (A,B) and two-chamber (C,D) views. The calculated echocardiographic stroke volume (SV) was slightly different from the SV measured with thermodilution (TD) (EDV, end diastolic volume; EF, ejection fraction; ESV, end systolic volume). (With permission of Denault *et al.* [13])

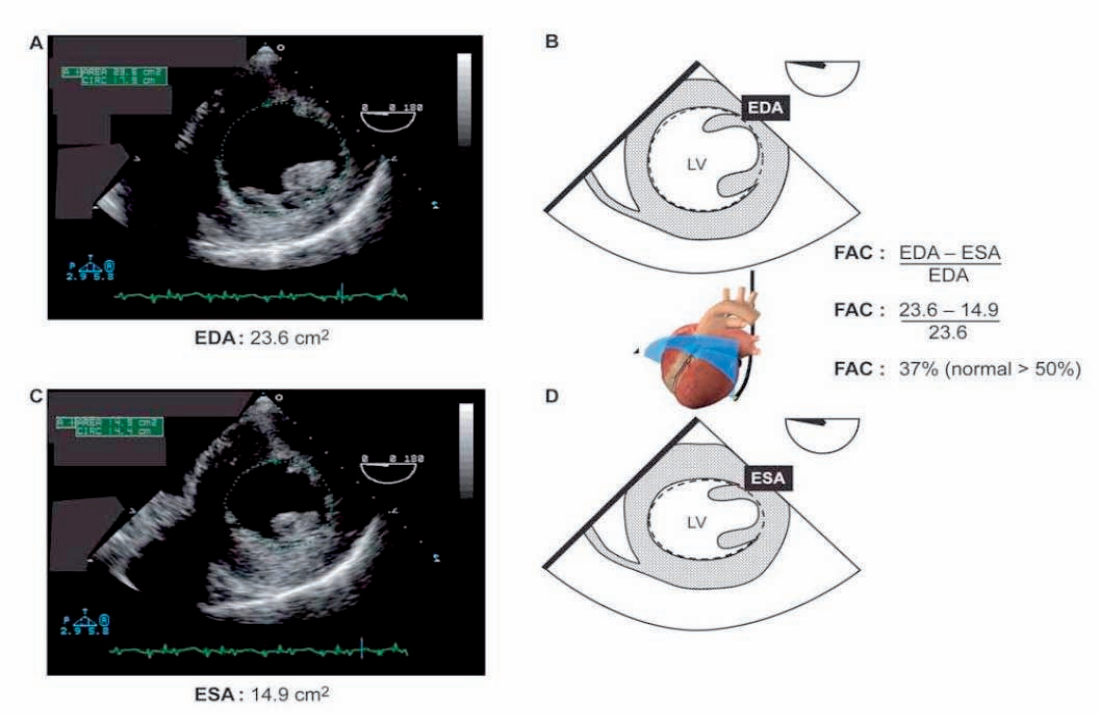

Figure 21 Left ventricular fractional area change

Measurement of fractional area change (FAC) in a 75-year-old man with unstable angina undergoing emergency revascularization. A transgastric mid-papillary view of the left ventricle (LV) in diastole (A,B) and in systole (C,D) provides the measurements to calculate the FAC, which was 26%. Note the exclusion of the papillary muscles during tracing of the areas. (EDA, end diastolic area; ESA, end systolic area). (With permission of Denault *et al.* [12])

Left ventricular systolic dysfunction originating from either coronary artery disease, cardiomyopathy, or associated with valvular heart disease, will be associated with an elevated left ventricular filling pressure and, consequently, post-capillary pulmonary hypertension. In cardiac surgery, left ventricular systolic dysfunction can be present before or after the procedure.

When present before the procedure, left ventricular systolic dysfunction, defined as reduced LVEF or associated with regional wall motion abnormalities (RWMA), is a known predictor of perioperative mortality in cardiac surgery. [73] This observation was well described in the Coronary Artery Surgery Study (CASS) in 1983. [171] This study

analyzed 7658 patients who underwent isolated coronary revascularization, irrespective of age, and examined whether an age of 65 years or older was an independent predictor of perioperative mortality. The variables selected, in order of significance, were: congestive cardiac failure score; left main coronary artery stenosis and a left-dominant circulation; age of 65 years or older; left ventricular wall motion score; gender; and history of unstable angina pectoris. [171] When left ventricular dysfunction before cardiac surgery is associated with mortality, the mechanism involved is most likely hemodynamic instability. Indeed, in a smaller study of 128 patients undergoing coronary revascularization, Royster *et al.*, [58] using logistic regression analysis, observed that LVEF was significantly lower and the most significant factor ($p = 0.0022$) associated with the requirements for inotropes after cardiac surgery.

Left ventricular dysfunction can occur after cardiac surgery and will be associated with a worse outcome. Leung *et al.* [172] found that postoperative RWMA, as demonstrated by TEE, was the most reliable predictor of operative outcome. Six of 18 patients with postoperative RWMA had an adverse outcome, defined as myocardial infarction, severe left ventricular dysfunction requiring inotropic therapy, or cardiac death, whereas none of the 32 patients without postoperative RWMA showed any adverse outcome.

In summary, reduced left ventricular dysfunction is associated with worse outcome after cardiac surgery when it is present before or after the procedure. Post-capillary pulmonary hypertension is the consequence of left ventricular dysfunction; however, an elevation of LVEDP will appear before elevated left atrial pressures reach the pulmonary circulation. In addition, elevated LVEDP can be present without reduced left ventricular systolic function. This condition is named left ventricular diastolic dysfunction.

3.1.2.2 Left ventricular diastolic dysfunction

Diastolic dysfunction is evaluated and diagnosed by an accepted classification and recommended guidelines (Figure 22). [173;174] These guidelines are based on Doppler signals obtained at the mitral valve leaflet, namely the transmitral flow (TMF) early (E) and

atrial (A) velocities, the pulmonary venous flow (PVF) systolic (S) and diastolic (D) velocities and the myocardial wall velocities measured at the mitral annulus, so-called the mitral annular velocities (MAV). The latter are composed of Em (early component of the MAV) and Am (late or atrial component of the MAV). In patients undergoing cardiac surgery, we have used the following criteria to define diastolic function: normal (TMF E/A >1, PVF S/D >1, MAV Em/Am >1), mild diastolic dysfunction (E/A < 1, S/D >1, MAV Em/Am <1), moderate diastolic dysfunction (E/A ≥ 1, S/D <1, MAV Em/Am <1), and severe diastolic dysfunction (E/A >2, S/D <1, MAV Em/Am < or >1).

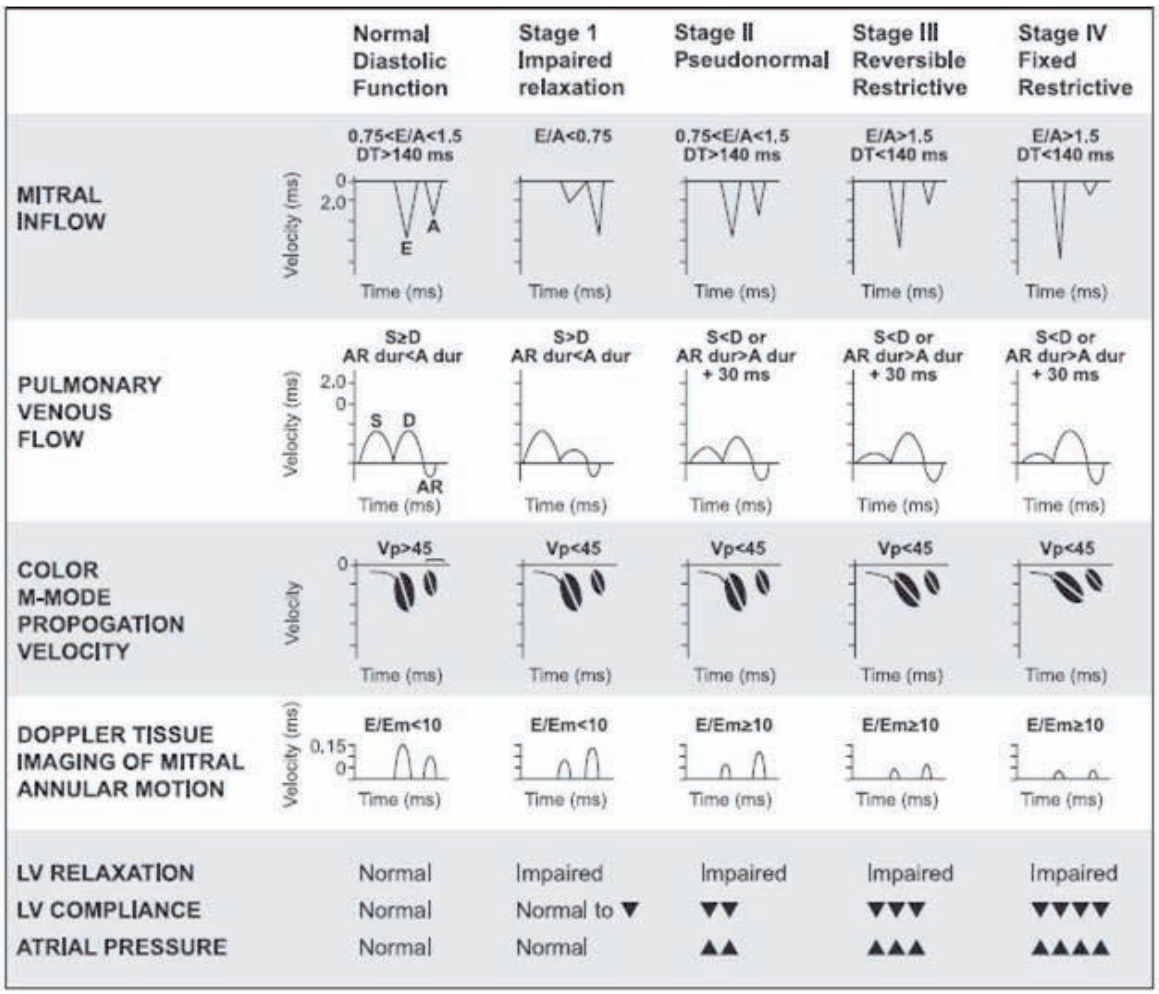

Figure 22 Echocardiographic classification of diastolic dysfunction

(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; Em, peak early diastolic myocardial velocity; LV, left ventricular; S, peak systolic pulmonary venous flow velocity; Vp, flow propagation velocity). (With permission of Denault *et al.* [12]).

Diastolic dysfunction of both the left and right ventricles will be associated with a normal or reduced volume requiring an increased filling pressure (Figure 23).

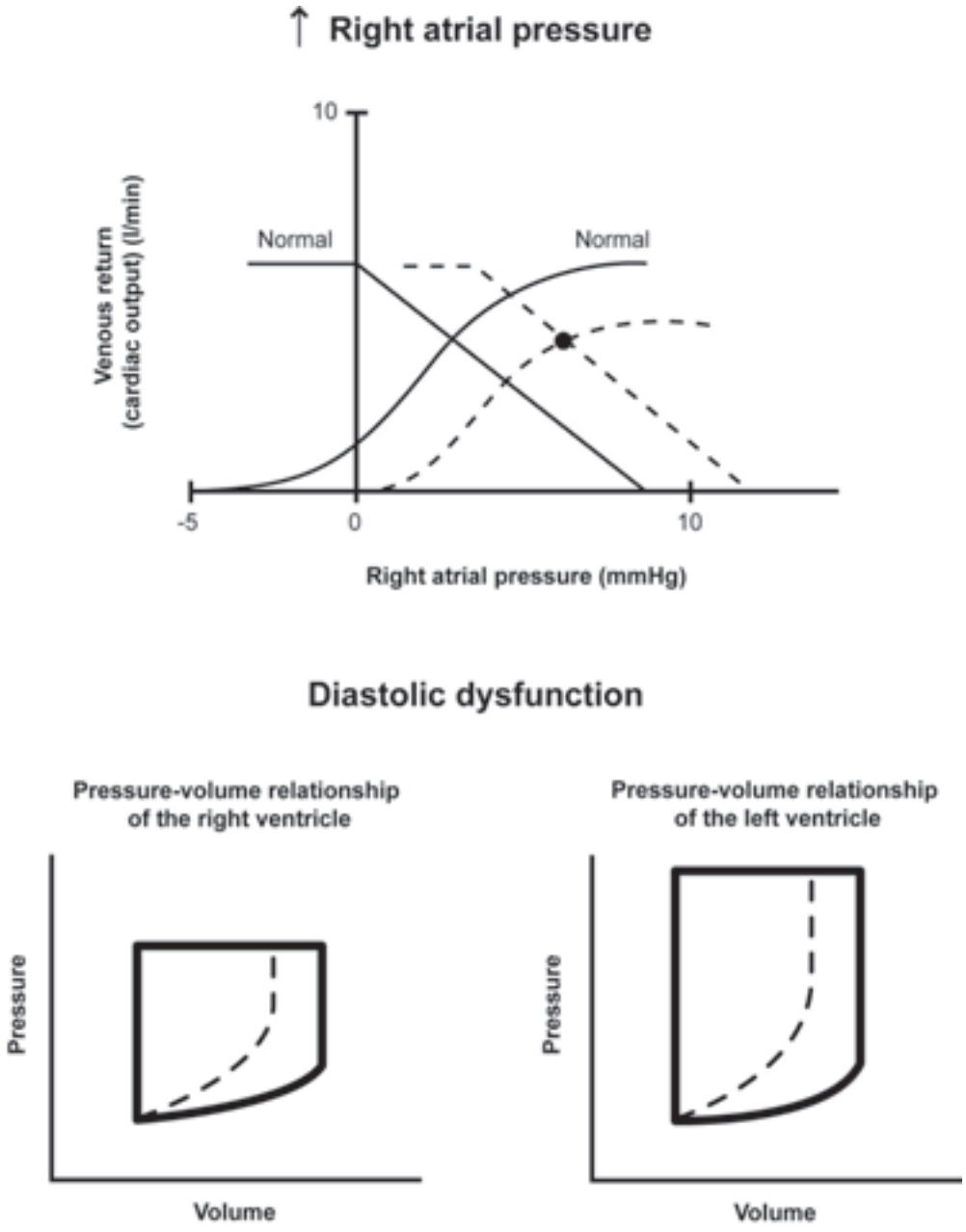

Figure 23 Biventricular diastolic dysfunction

Biventricular diastolic dysfunction will be associated with a maintained venous return and cardiac output. However, the right atrial pressure will increase from a parallel rightward shift of the venous return curve. In that situation, the filling pressure will increase and ventricular volume can be normal or reduced.

The recognition that left ventricular diastolic dysfunction plays a central role in the pathophysiology of cardiac disease has been compared to the discovery of the Rosetta Stone, which played a key role in understanding 1000 years of Egyptian history. [175] This new understanding was triggered by developments in echocardiography that allowed for a simple, rapid and non-invasive assessment of cardiac function. However, before echocardiography was routinely used in cardiology, several clinicians observed that elevated LVEDP *per se* was associated with mortality. In 1983, in the CASS study, Gersh *et al.* [171] reported their results on 1086 patients of 65 years of age or older who underwent isolated coronary artery bypass grafting. Using a stepwise linear discriminant analysis, the authors identified five variables predictive of perioperative mortality. The first was the presence of 70% or more stenosis of the left main coronary artery and a left-dominant circulation, and the second most important factor was LVEDP.

There is a growing interest in the evaluation of diastolic dysfunction. Diastolic dysfunction is associated with reduced survival in patients with congestive heart failure, [176;177;177-179] sepsis [180] and following acute myocardial infarction. [181;182] This is consistent with the observation that preoperative elevated LVEDP increases the incidence of postoperative inotropic support [58;104] and mortality. [8;11;183] It also supports the hypothesis that diastolic dysfunction before cardiac surgery could have an impact on survival and postoperative complications. [17;39;155;184;185]

The hypothesis that patients with diastolic dysfunction are at higher risk of hemodynamic instability after cardiac surgery is supported by a study by Bernard *et al.* [17] that included 66 patients, of whom 52 underwent coronary revascularization alone. The factors associated with an increased need for vasoactive support after CPB were: female gender, diastolic dysfunction and prolonged duration of CPB. Diastolic dysfunction was more significant than systolic dysfunction in predicting difficult separation from CPB and vasoactive requirement after surgery. The importance of preoperative diastolic dysfunction as an independent predictor of hemodynamic complications and survival in cardiac surgery was reconfirmed by four other investigations. [39;155;184;185]

In summary, diastolic dysfunction will predispose to hemodynamic instability because the impairment of the left ventricle to accommodate volume and the consequent elevated LVEDP can predispose to pulmonary edema, pulmonary hypertension and right ventricular dysfunction. Finally, when hemodynamic instability occurs after cardiac surgery, it is almost invariably associated with filling abnormalities. [19]

3.1.2.3 Right ventricular systolic dysfunction

There are several ways to evaluate right ventricular function, and these methods were reviewed by Haddad *et al.* [48] Right ventricular function is commonly measured with 2D or Doppler echocardiography following published guidelines. [186] Right ventricular fractional area change (normal ≥ 35%) (Figure 24), right ventricular myocardial performance index (Figure 25) and tricuspid annular plane systolic excursion (Figure 26) [44] can be obtained to evaluate right ventricular function. The right ventricular myocardial performance index is stratified as $<$ or $\geq$ 50%, as previously described. [187;188]

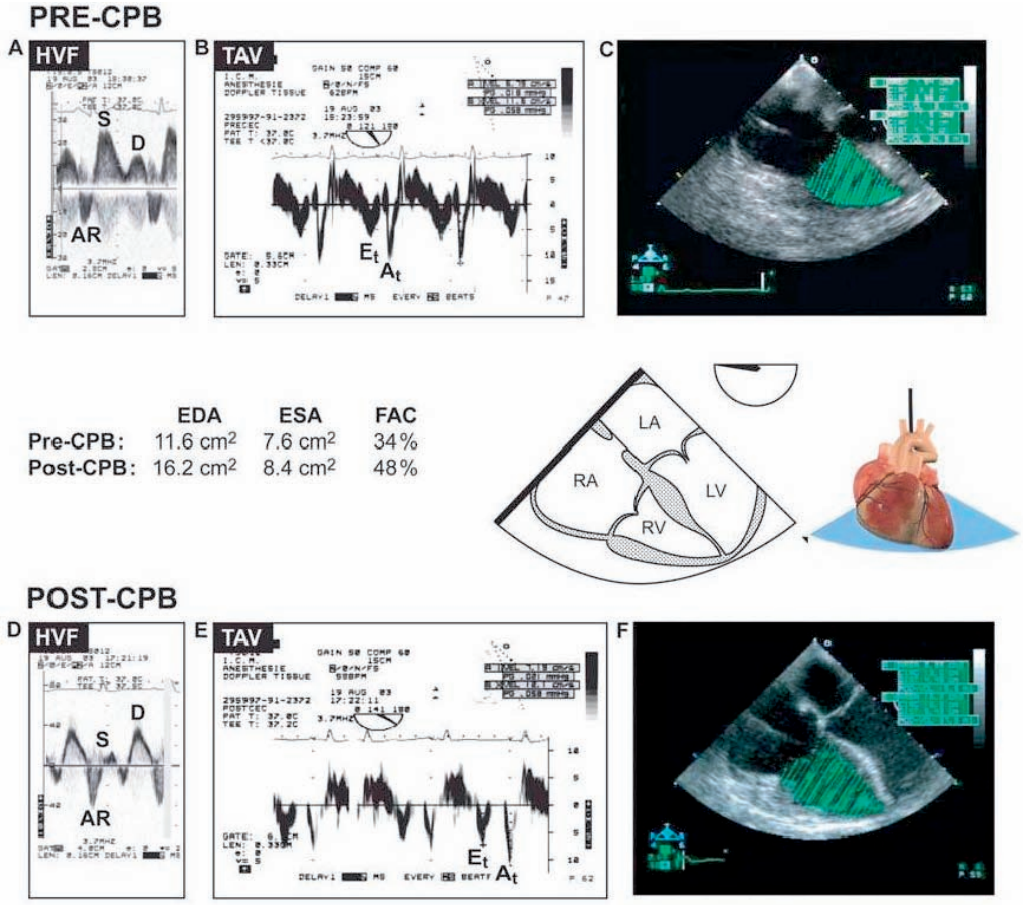

Figure 24 Right ventricular systolic and diastolic function

A 65-year-old man with previous inferior myocardial infarction scheduled for coronary revascularization. (A–C) Before cardiopulmonary bypass (CPB) the ejection fraction of the left ventricle (LV) is 20% with a low cardiac index of 1.5 L/min per m². (A) Pulsed wave Doppler hepatic venous flow (HVF) shows systolic flow (S) predominance. (B) Tricuspid annular velocities (TAV) by tissue Doppler shows a E_t/A_t ratio < 1 (E_t = 5.7 and A_t = 11.5 cm/sec). Both suggest mild diastolic dysfunction of the RV. (C) The fractional area change (FAC) of the RV is 34%. (D–F) Post-CPB. (D) The HVF showed new blunting of the systolic flow. (E) The TAV are increased with a similar ratio (E_t = 7.1 and A_t = 12.1 cm/sec). This suggests decreased RV compliance. (F) Right ventricular FAC increased to 48% consistent with the surgeon's visual appreciation of improved right ventricular function. Upon arrival to the intensive care unit, the cardiac index was 3.0 L/min per m² (AR, atrial reversal; EDA, end-diastolic area; ESA, end-systolic area; LA, left atrium; RA, right atrium). (With permission of Denault *et al.* [12])

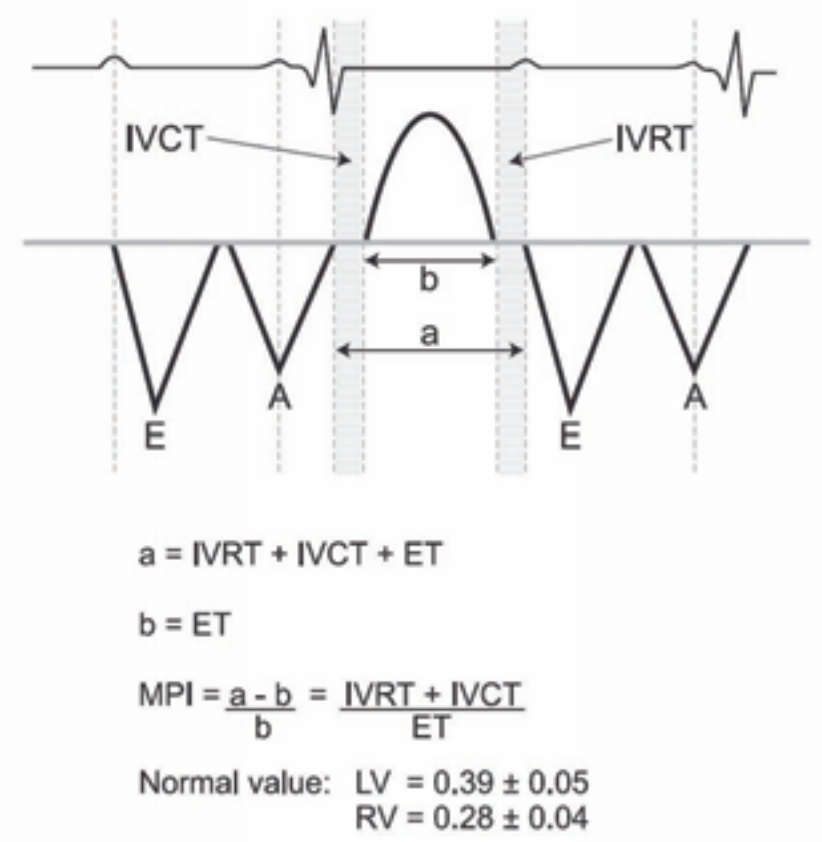

Figure 25 Myocardial performance index (MPI)

Measurement of MPI or Tei index. (1) For the MPI of the left ventricle (LV), the transmitral inflow is used for measurement of the duration "a" from the end of atrial contraction (A-wave) to the beginning of LV filling (E-wave). (2) The ejection time (ET) or "b" is measured from a deep transgastric long-axis view Doppler interrogation of the left ventricular outflow tract. The MPI of the right ventricle (RV) is similarly obtained using the transtricuspid flow and the mid-esophageal ascending aorta short-axis view for the right ventricular outflow tract (IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time). (With permission of Denault *et al.* [12])

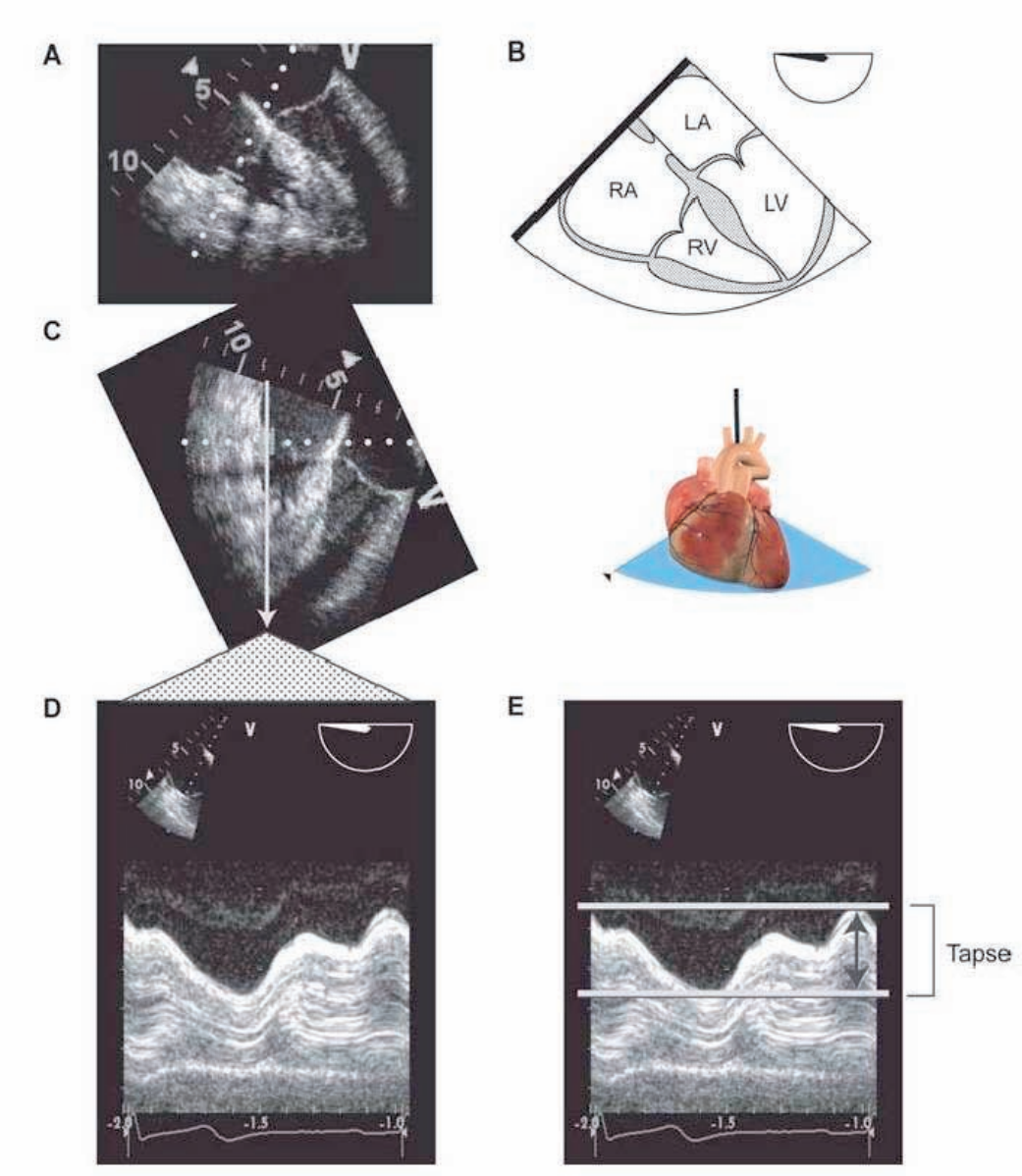

Figure 26 Tricuspid annular plane systolic excursion (TAPSE)

Steps in the measurement of the TAPSE measured using anatomic M-mode. First a four-chamber view is obtained (A-B). Then the M-mode cursor is positioned along the plane of the TAPSE motion (C). An M-mode figure of this excursion or displacement is obtained (D). The lower point corresponds to the maximal systolic excursion and the upper point is the atrial contraction. The TAPSE is equal to the total systolic excursion of the tricuspid annulus (E). Normal TAPSE should be 20-25 mm. (With permission of Denault *et al.* [12])

Right ventricular systolic dysfunction can be associated or not with left ventricular systolic dysfunction. The mechanism of biventricular systolic dysfunction was illustrated in Figure 27 However, isolated right ventricular systolic dysfunction can lead to left ventricular diastolic dysfunction and left ventricular outflow tract obstruction (Figure 27). In severe cases, this can lead to the opening of a patent foramen ovale and worsening hypoxemia. Hypoxemia will further increase pulmonary hypertension and thus lead to a deterioration of the right ventricular function if the cycle is uninterrupted.

There is growing evidence that morbidity and mortality associated with pulmonary hypertension (discussed in more detail in Chapter 6) are dependent on right ventricular adaptation to disease rather than on the absolute value of pulmonary arterial pressure. [46;189-191] Survival and outcome in idiopathic pulmonary arterial hypertension are more related to elevated mean right atrial pressure and reduced cardiac output than to pulmonary arterial pressure values alone. [189;192]

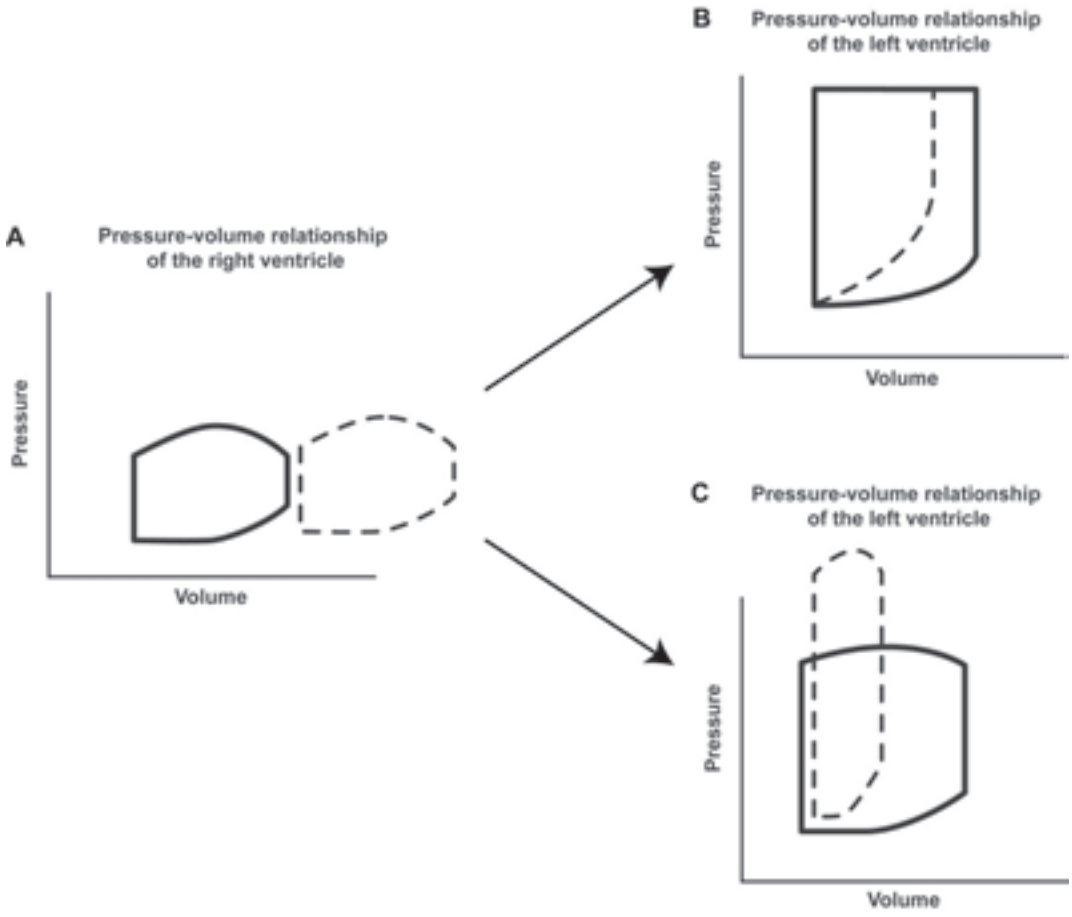

Figure 27 Isolated right ventricular systolic dysfunction

Isolated right ventricular systolic dysfunction (A) can alter the geometry of the left ventricle via the common pericardium and the interventricular septum through 2 mechanisms. The most frequent is a filling abnormality (B). This is associated with a reduction in left ventricular volume and an increase in left ventricular pressure. The second mechanism can appear in very severe right ventricular dysfunction. This will also be associated with a reduction in left ventricular volume, an increase in left ventricular pressure but also left ventricular outflow tract obstruction (C). In the latter situation, the use of inotropes could exacerbate the left ventricular outflow tract obstruction.

The importance of right ventricular function in cardiac surgery has been demonstrated in a variety of clinical settings such as high risk coronary or valvular heart disease, congenital heart disease, heart transplantation, in patients requiring mechanical assist devices and in the unstable postoperative patient (Table 12).

Table 12 Prognostic value of right ventricular function in cardiac surgery

Study	Population	Study Design	RV dysfunction	Results
Reitchert *et al.* [3]	Unstable postoperative patients	Prospective *n* = 60	RVFAC < 35%	RV dysfunction associated with high mortality rates
Pinzani *et al.* [193]	Mitral and combined mitro-aortic surgery	Retrospective *n* = 382	Clinical definition	Postoperative RV failure is the strongest predictor of postoperative mortality
Cullen *et al.* [194]	Tetralogy of Fallot	Prospective *n* = 35	Restrictive RV physiology	Restrictive physiology predicts longer intensive care unit stay post repair and lower cardiac output
Gatzoulis *et al.* [195]	Tetralogy of Fallot	Prospective *n* = 41	Restrictive RV physiology	Restrictive physiology predicts smaller RV and better exercise tolerance
Kromos *et al.* [196]	LVAD and RV failure	Retrospective *n* = 31	Clinical mean RVEF = 11.8%	Preoperative clinical factors such as fever, pulmonary edema, and intraoperative blood transfusions were associated with RVAD need
Hosenpud *et al.* [197]	Heart Transplantation	Retrospective International Society for Heart & Lung transplantation *n* = 69,205	RV failure associated with circulatory failure	RV failure accounts for up to 20% of early deaths

Study	Population	Study Design	RV dysfunction	Results
Oehiai *et al.* [6]	LVAD	Retrospective *n* = 245	RV failure requiring RVAD	23 patients (9%) required RVAD. The need for circulatory support, female gender, and non-ischemic etiology were predictors of RVAD need.
Maslow *et al.* [112]	CAD undergoing coronary bypass surgery with LVEF < 25%	Retrospective *n* = 41	RVFAC < 35%	RV dysfunction is associated with decreased long term survival
Therrien *et al.* [198]	Tetralogy of Fallot	Prospective *n* = 17	RV remodeling	Severe RV dilatation (RVEDV >170 mL/m² or RVESV > 85 mL/m²) associated with incomplete RV remodeling
Webb *et al.* [199]	Atrial septal defect	Retrospective series	RV remodeling	Older age at repair and abnormal RV myocardial relaxation were associated with incomplete RV remodeling
Denault *et al.* [38]	Patients undergoing bypass surgery	Retrospective and prospective *n* = 800	Dynamic obstruction of RVOT (Gd > 25 mmHg)	Incidence: 4%, dynamic obstruction of RVOT was associated with a higher incidence of difficult weaning from bypass
Haddad *et al.* [46]	High-risk valvular surgery	Prospective *n* = 50	RVFAC < 32% or RVMPI > 0.50	Preoperative RV dysfunction was associated with a higher incidence of postoperative circulatory failure

CAD: coronary artery disease, Gd: gradient, LV: left ventricular, LVAD: left ventricular assist device, RV: right ventricular, RVAD: right ventricular assist device, RVES: right ventricular end-systolic volume, RVED: right ventricular end-diastolic volume, RVEF: right ventricular ejection fraction, RVFAC: right ventricular fractional area change, RVMPI: right ventricular myocardial performance index, RVOT: right ventricular outflow tract obstruction (From Haddad *et al.* [49])

However, most of the evidence that supports the importance of right ventricular function is based on retrospective or small prospective studies. To date, parameters of right ventricular function have not been included in large-scale risk stratification models and therefore their incremental value to the Parsonnet score or the EuroSCORE have not been well established. [100;103;200;201] A recent panel from the National Institutes of Health has stressed the importance of research in the understanding of right ventricular failure. [191] Right ventricular dysfunction can be present before or after the surgical procedure.

In patients presenting with severe aortic stenosis, Boldt *et al.* [202] have demonstrated that preoperative right ventricular dysfunction was associated with a greater requirement of postoperative inotropic support. In a retrospective study including patients undergoing mitral and mitral-aortic valvular surgery, Pinzani *et al.* [193] demonstrated that preoperative right ventricular failure was associated with perioperative mortality. In this same study, postoperative right ventricular failure was the most important independent predictor of late survival. In a small prospective study of 14 patients with severe non-ischemic mitral regurgitation and high-risk descriptors (LVEF ≤ 45% or RV ejection fraction (RVEF) ≤ 20%), Wencker *et al.* [203] found that preoperative RVEF ≤ 20% predicted late postoperative death. In patients undergoing coronary revascularization, Maslow *et al.* [112] showed that right ventricular dysfunction defined by a right ventricular fractional area change (RVFAC) of less than 35% in the context of severe left ventricular systolic dysfunction (LVEF ≤ 25%) and non-emergent coronary revascularization was associated with an increased risk of postoperative morbidity and mortality. In this retrospective study ($n = 41$), patients with right ventricular dysfunction had a higher prevalence of diabetes mellitus and renal disease, as well as a higher incidence of postoperative inotropic or mechanical support, longer intensive care unit and hospital stay and a decreased short-term and long-term survival.

The presence of right ventricular failure after CPB is associated with a mortality rate ranging from 44% to 86%. [4] The incidence of post-cardiotomy acute refractory right ventricular failure ranges from 0.04 to 0.1%. Acute refractory right ventricular failure has also been reported in 2-3% patients after a heart transplant and in almost 20-30% patients

who received a left ventricular assist device support, with a reported initial salvage rate of only 25-30%. [5]

3.1.2.4 Right ventricular diastolic dysfunction

The mechanism of right ventricular diastolic function was illustrated in Figure 23. Normal right ventricular diastolic function [204] is defined using normal values reported for Doppler transtricuspid flow early (E) and atrial (A) velocities, [205] hepatic venous flow (HVF) systolic (S), diastolic (D) and atrial reversal (AR) velocities [113;114;206] and tissue Doppler imaging (TDI) of the tricuspid annulus. [207;208] The latter are composed of the Et (early component of the TDI) and At (late or atrial component of the TDI). Right ventricular diastolic function is classified as normal (TTF E/A >1, HVF S/D >1, Et/At >1), mild diastolic dysfunction (E/A <1, or reversed AR >50% of S wave measured on HVF, or Et < At when both E/A and S/D >1), moderate diastolic dysfunction (E/A ≥ 1, S/D <1, Et/At <1), and severe diastolic dysfunction (S wave reversal on HVF, irrespective of the E/A and S/D ratio).

Right ventricular diastolic dysfunction could constitute an additional marker to identify populations at higher risk of requiring vasoactive support, and potentially other clinical outcomes. We have previously documented that in hemodynamically unstable patients in the intensive care unit, abnormal right ventricular filling abnormalities were the most common echocardiographic observation. [19] We also noted, in a pilot study, that abnormal hepatic venous flow, when present before cardiac surgery, was associated with an increased need for vasoactive support after cardiac surgery. [34] In these two previous studies, patients were also not graded according to the severity of right ventricular diastolic dysfunction; however, in a recent study, [39] we were able to confirm that moderate to severe right ventricular diastolic dysfunction is associated with lower cardiac index and an increased risk of difficult separation from CPB.

3.1.2.5 Left ventricular outflow tract obstruction

With the increasing use of echocardiography, both in the operating room and in critically ill patients, left ventricular outflow tract obstruction (LVOTO) is being diagnosed more frequently. Left ventricular outflow tract obstruction can be defined as an obstruction to blood flow, either fixed or dynamic, usually located below the aortic valve but sometimes involving regions up to the ventricular apex. The term mid-cavitary or apical obstruction is then used. [209;210]

The diagnosis of LVOTO is critical because although the clinical manifestations are similar to those of left ventricular systolic dysfunction, the treatment and management are based on a completely different rationale. [211] Indeed, inotropic support, pharmacological or mechanical afterload reduction, and volume restriction used in heart failure would significantly deteriorate the hemodynamics of a patient presenting with a low output state resulting from LVOTO. Despite known risk factors for LVOTO, such as ventricular septal thickness > 13 mm, long posterior mitral leaflet, anteriorly displaced coaption point and mitro-aortic angle > 90 degrees, [212] we have seen this condition in numerous scenarios and believe that it has the potential to occur in almost every type of hemodynamically unstable patient presenting with a significantly reduced left ventricular preload. In LVOTO, elevated left ventricular filling pressure will be present with flow turbulence in the left ventricular outflow tract. In some patients, this turbulence can lead to a suctioning (Venturi effect) or drag effect [213] of the anterior leaflet of the mitral valve into the left ventricular outflow tract, the so-called SAM: systolic anterior motion. This will lead to mitral regurgitation, which is typically excentric (Figure 28).

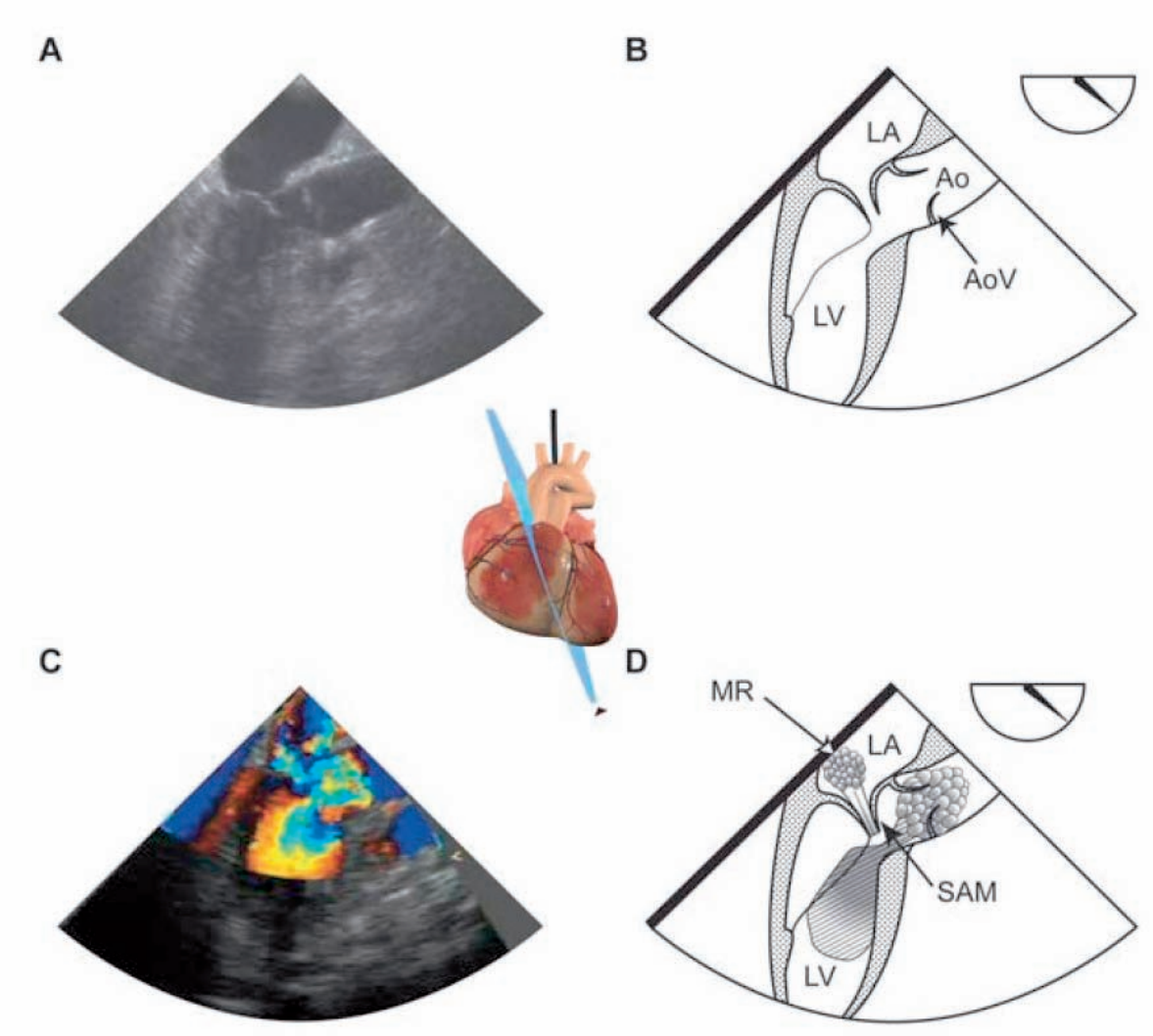

Figure 28 Dynamic left ventricular outflow tract (LVOT) obstruction

Mid-esophageal long-axis view in a 38-year-old man with hemodynamic instability. (A, B) Part of the anterior mitral valve leaflet is obstructing the LVOT. (C, D) This was associated with mitral regurgitation (MR). His hemodynamic condition improved with fluid and ß-blockade (Ao, aorta; AoV, aortic valve; LA, left atrium; LV, left ventricle; SAM, systolic anterior motion). (With permission of Denault *et al.* [12])

The consequence of a left or right ventricular outflow tract obstruction will be a reduction in stroke volume and cardiac output with an elevated filling pressure (Figure 29).

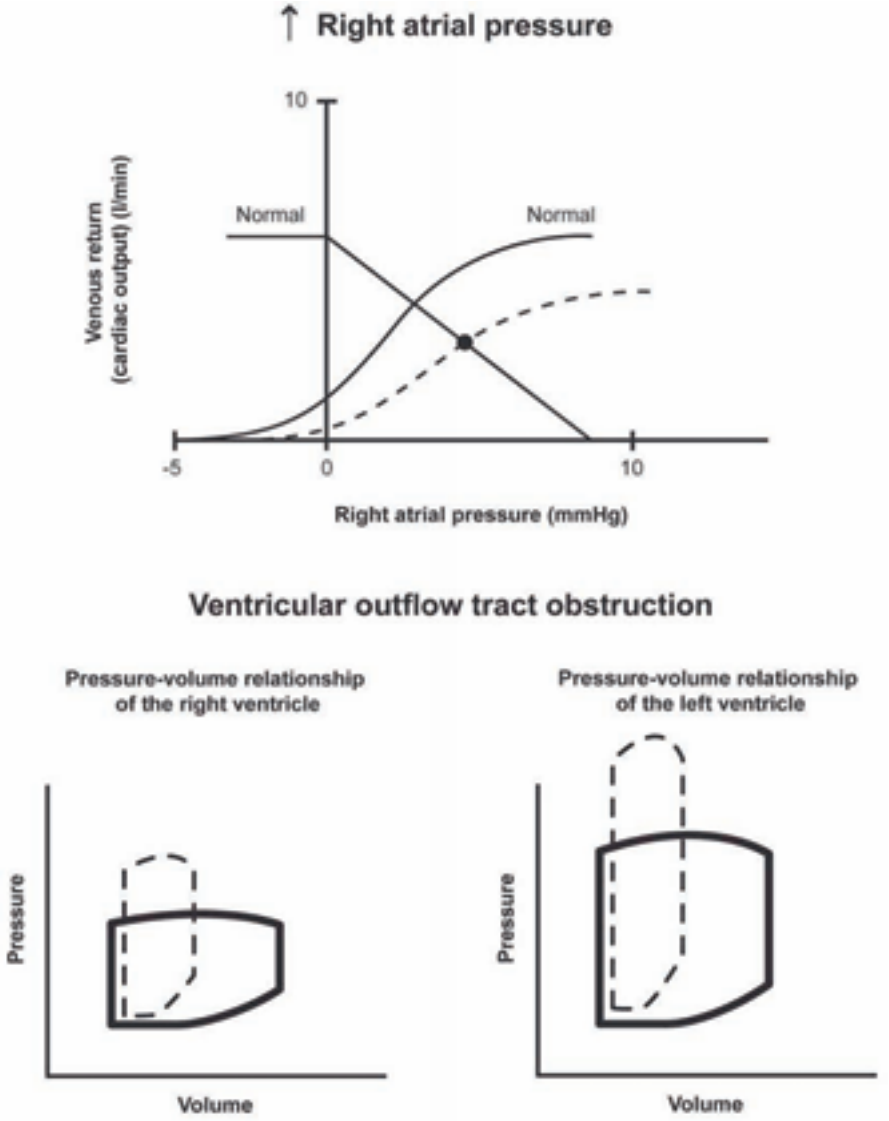

Figure 29 Ventricular outflow tract obstruction

Ventricular outflow tract obstruction of the right or left ventricle will be associated with a reduced venous return and cardiac output. The right atrial pressure will increase along the axis of the venous return curve. In that situation, the filling pressure will increase significantly and the ventricular stroke volume will be reduced.

Two types of LVOTO can be clinically present: one is dynamic and the other will have underlying structural anatomical abnormalities such as those observed in hypertrophic obstructive cardiomyopathy or extrinsic mechanical compression. In the dynamic form,

tachycardia and preload reduction will predispose to LVOTO. The dynamic form has been observed in aortic valve replacement, in mitral valve repair and in the critically ill patient (Figure 28).

In aortic stenosis, abnormal systolic intraventricular flow velocities can be observed reaching 14% and are aggravated with inotropes and vasodilators. [214] Aortic valve replacement for aortic stenosis in a patient with pre-existing left ventricular hypertrophy can cause significant SAM in the postoperative period. This results from the acute reduction in afterload, which allows increased left ventricular ejection in a small left ventricular outflow tract, thereby producing subvalvular stenosis or mid-ventricular obstruction. [12] This is usually transient and responds well to volume loading and cessation of inotropic drugs. However, in certain cases, surgical correction may be required (Figure 30). [215]

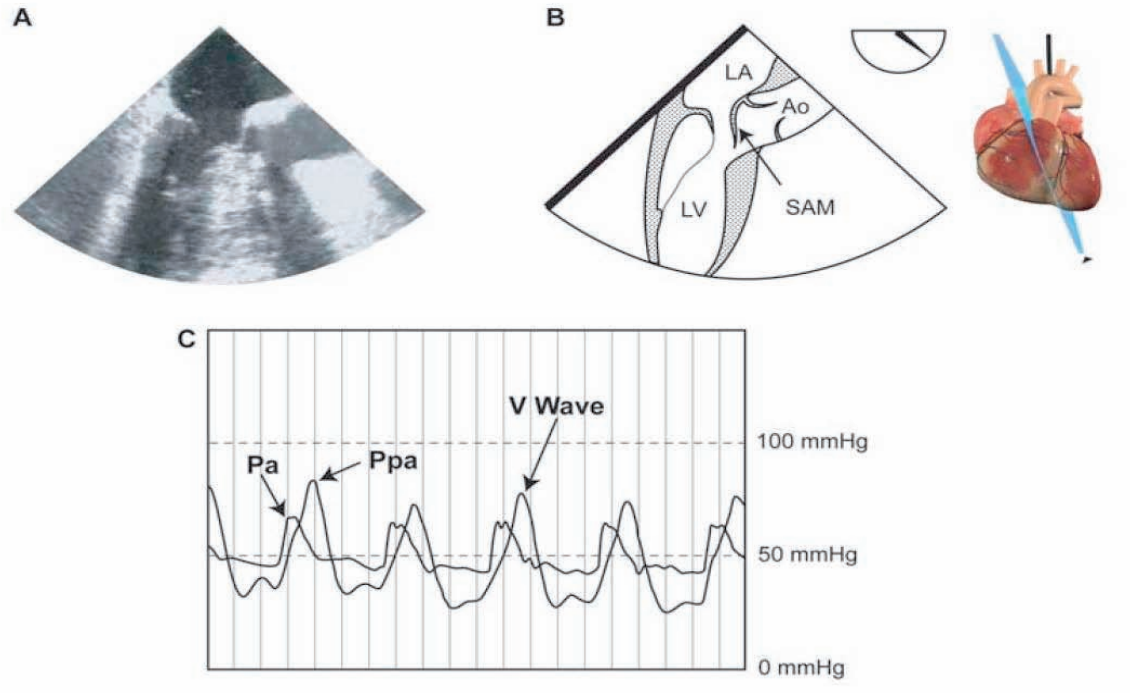

Figure 30 Left ventricular outflow tract obstruction (LVOTO).

A 53-year-old man with LVOTO after aortic valve replacement. (A,B) The mid-esophageal long-axis view showed the LVOTO secondary to left ventricular septal hypertrophy. (C)

Systemic hypotension was associated with the appearance of a giant "V" wave on the wedged pulmonary artery pressure (Ppa); tracing occurred as the patient was weaned from cardiopulmonary bypass. The "V" wave was secondary to mitral regurgitation from abnormal systolic anterior motion (SAM). This patient did not respond to medical therapy and underwent mitral valve replacement (Ao, aorta; LA, left atrium; LV, left ventricle; Pa, arterial pressure). (With permission of Denault *et al.* [12])

Systolic anterior motion can also occur after MV repair for prolapse. This complication must be specifically looked for while in the operating room after surgery. The incidence of LVOTO after mitral valve repair varies from 2% to 14% [216] and is more frequent with myxomatous changes involving both leaflets. The underlying mechanisms include the anterior displacement of the coaptation point, as well as a longer and redundant posterior leaflet (with or without a more acute mitro-aortic angle), causing the mitral valve apparatus to be displaced toward the LVOT and be dragged by the outflow, provoking a typical SAM and subsequent subvalvular obstruction. Preoperatively, a longer posterior leaflet compared to the anterior leaflet (anterior/posterior length ratio ≤ 1.3) and a shorter distance (≤ 2.5 cm) between the coaptation point and the septum are predictors of SAM development post-repair (Figure 31). [212] For some patients, the problem can be alleviated by increasing LV filling or reducing inotropic support. However, other patients require mitral valve replacement or subsequent repair. The sliding technique has been developed to decrease the incidence of this complication by reducing the posterior leaflet redundancy. [217]

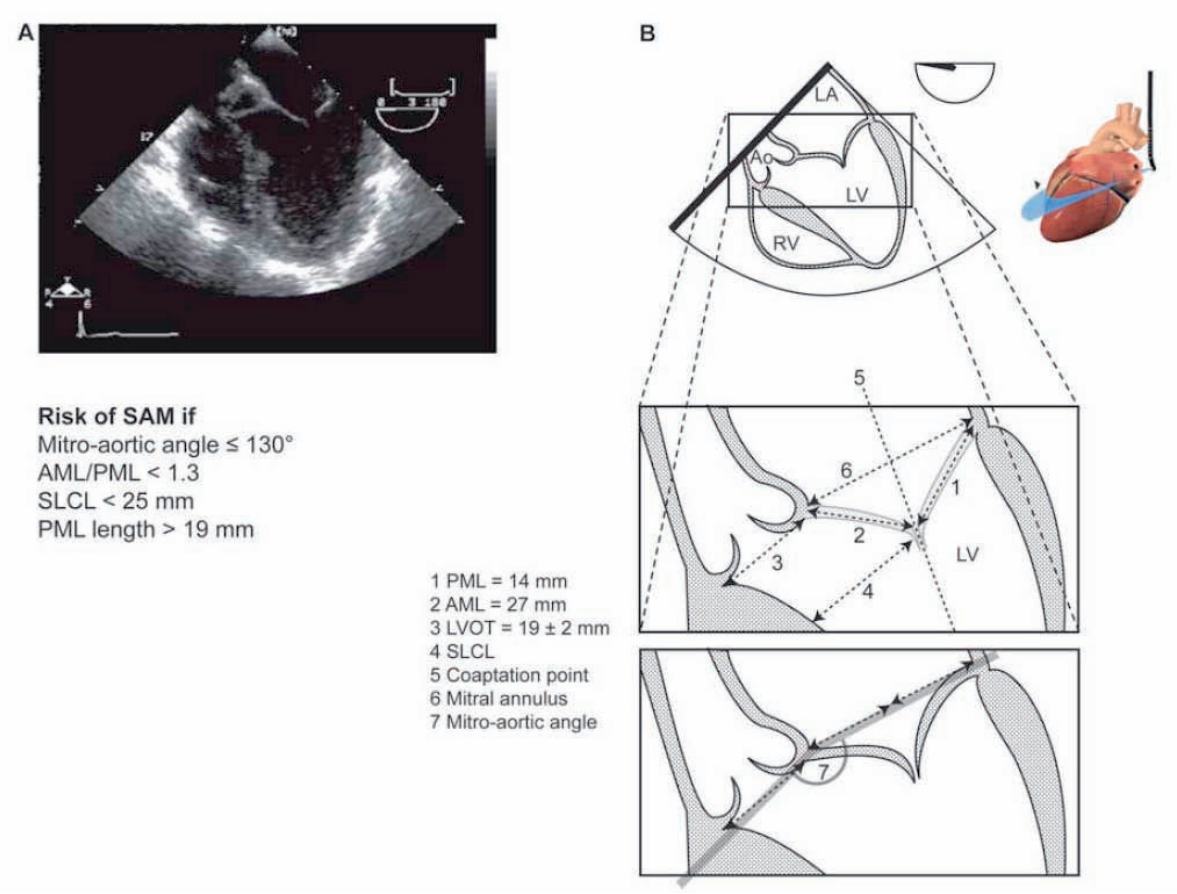

Figure 31 Risk factors of systolic anterior motion (SAM)

(A,B) Measurements to assess the risk for postoperative systolic anterior motion (SAM) after septal resection from a mid-esophageal four-chamber view (AML, anterior leaflet length; Ao, aorta; LA, left atrium; LV, left ventricle; PML, posterior leaflet length; RA, right atrium; RV, right ventricle; SAM, systolic anterior motion; SLCL, septal to leaflet coaptation length). (Adapted with permission of Denault *et al.* [12])

Finally, when using TEE in a series of 61 adults with unexplained hypotension for more than one hour in the intensive care unit, Heidenreich *et al.* [218] observed that LVOTO was present in 3% of patients.

Among the mechanical or extrinsic etiology of LVOTO, in some patients, right ventricular failure can predispose to LVOTO, as previously discussed (Figure 27). In this situation, right ventricular dilatation will reduce the filling of the left ventricle, thus leading

to LVOTO. This is a very difficult situation to manage, as right ventricular dysfunction is associated with poor outcome in numerous scenarios. Inotropic therapy to improve right ventricular function may worsen LVOTO. In such a situation, to improve right ventricular function, we have been using inhaled pulmonary vasodilators, such as prostacyclin or nitric oxide, with good results. [18] Finally, we have also observed extrinsic cardiac obstruction leading to LVOTO in cases such as regional tamponade after cardiac surgery. [12] In these situations, LVOTO will resolve as soon as the underlying cause is removed.

3.1.2.6 Right ventricular outflow tract obstruction

Right ventricular outflow tract obstruction (RVOTO), which can also be due to extrinsic [219-221] or intrinsic causes, [222-224] can also result in hemodynamic instability. According to time-honoured hemodynamic criteria, RVOTO is defined as "significant" when the peak right ventricular to pulmonary artery systolic gradient exceeds 25 mmHg. [225-227] Furthermore, when observed via TEE, significant RVOTO is defined as "fixed" if there is no change in RV outflow tract (RVOT) dimensions during the cardiac cycle with an anatomic substrate for obstruction, and as "dynamic" if RVOT dimensions increase appreciably in diastole. Dynamic RVOTO has been observed in hypertrophic cardiomyopathy [228] and after lung transplantation, [229;230] but it has rarely been described during cardiac surgery. [231]

3.1.2.7 Patient-prosthesis mismatch (PPM)

The indexed effective orifice area for each prosthesis is derived from normal reference values of effective orifice area published in the literature divided by the patient's BSA, as previously described and validated. [120;123;232] Aortic PPM is defined as not clinically significant if the indexed effective orifice area is > 0.85 cm^2/m^2, as moderate if it is > 0.65 cm^2/m^2 and ≤ 0.85 cm^2/m^2, and as severe if it is ≤ 0.65 cm^2/m^2. Mitral PPM is defined as not clinically significant (i.e. mild or no PPM) if the indexed effective orifice area is > 1.2 cm^2/m^2, as moderate if it is > 0.9 cm^2/m^2 and ≤ 1.2 cm^2/m^2, and as severe if it is ≤ 0.9 cm^2/m^2. [128] Moderate to severe aortic or mitral PPM can lead to increased LVEDP, filling

abnormalities (Figure 23), reduced coronary flow reserve, [126] pulmonary hypertension and right ventricular failure (Figure 27). This might explain why patients with PPM show an increase in mortality; however, the link between difficult separation from CPB and PPM has not yet been described.

3.1.2.8 Embolism

Embolism can be directed in the right or the left-sided cardiac chambers. It can be caused by thrombus, air, carbon dioxide or other materials (Figure 7). Right-sided embolism rarely occurs during cardiac surgery but can lead to acute right ventricular failure (Figure 27). Pulmonary embolism secondary to venous thrombus originating from the lower extremity is unusual during cardiac surgery because of the use of heparin. However, after heparin reversal using protamine and with mobilization, patients with predisposing conditions could develop this complication. The presence of mobile thrombus in the right atrium, right ventricle or pulmonary artery is pathognomonic of this condition (Figure 32).

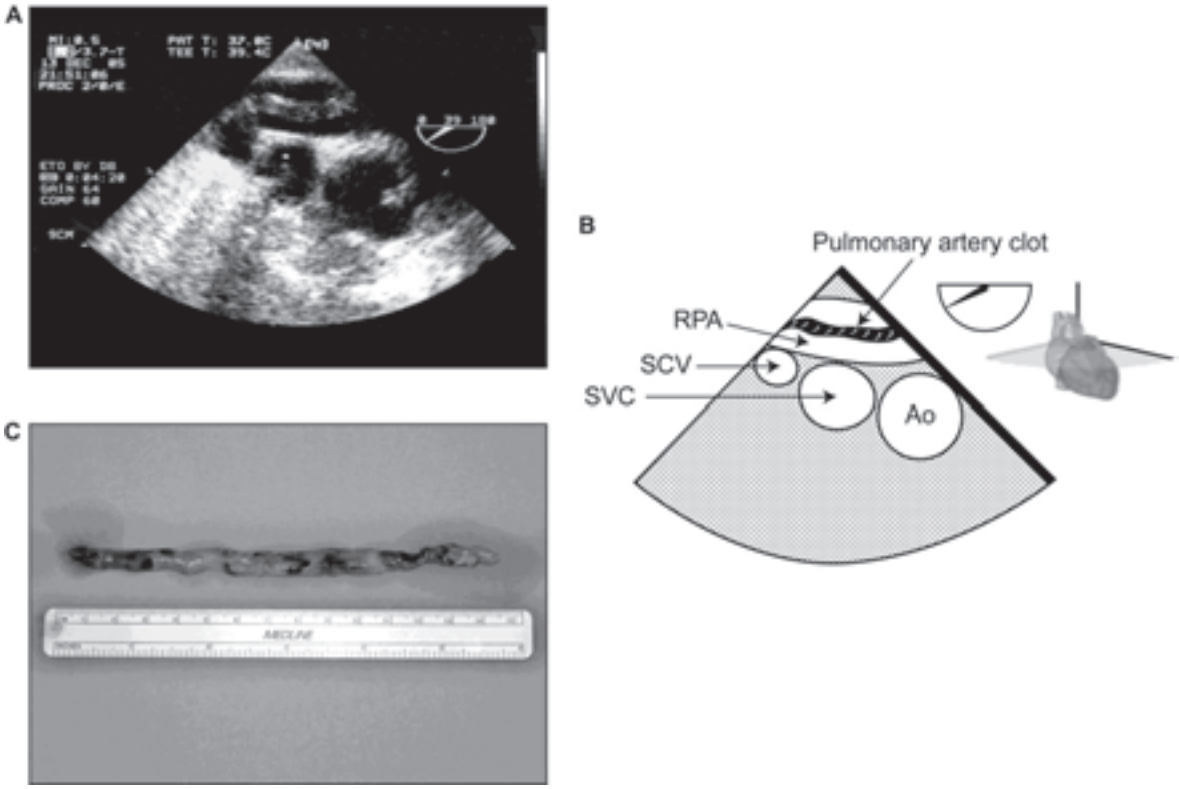

Figure 32 Pulmonary embolism immediately after coronary revascularization

This patient was hospitalized and waiting for more than a week before the procedure could take place. At the end of the procedure, while she was transferred in her bed, she became hemodynamically unstable. A transesophageal echocardiographic exam was immediately performed and showed the appearance of a clot in the right pulmonary artery (A-B). She was brought back to the operating room for urgent embolectomy and the clot was removed (C). She was discharged from the hospital in good condition. (Ao: aorta, RPA: right pulmonary artery, SCV: subclavian vein, SVC: superior vena cava) (Courtesy of Dr. David Bracco and Dr. Nicolas Noiseux).

Air embolism is frequently observed during cardiac surgery and usually has minimal or no consequence when present on the right-sided chambers, unless massive. In such a situation, the diagnosis is based on the appearance of an hyperechoic mobile signal in the right-sided chambers and pulmonary artery. Air will tend to accumulate in the most anterior portion of the right ventricle, i.e. the anterior leaflet of the pulmonic valve (Figure 33).

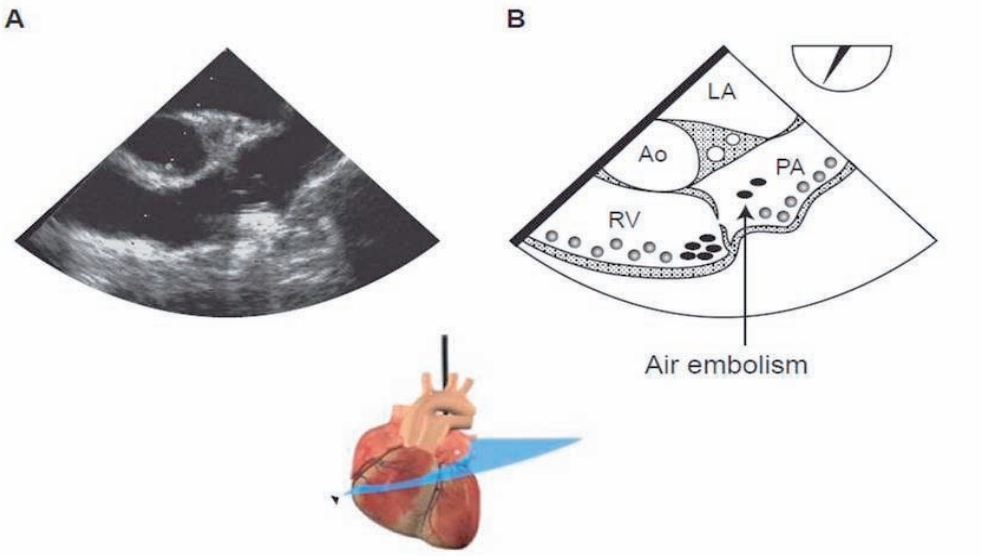

Figure 33 Air embolism

Air embolism in a 46-year-old woman hemodynamically unstable during spinal surgery in a ventral position. (A,B) She was turned back to a supine position and a mid-esophageal right ventricular outflow view revealed the residual presence of air bubbles on the most anterior aspect of the right ventricle (RV), pulmonary artery (PA) and on both sides of the anterior pulmonic valve (Ao, aorta; LA, left atrium). (Adapted with permission of Denault *et al.* [12])

The presence of air in the left-sided chambers is also common during valvular or open heart surgery. When present, it can lead to right ventricular dysfunction through air embolisation of the right coronary artery. This explains why the de-airing process of the left-sided chambers is of significant importance in valvular surgery (Figure 34).

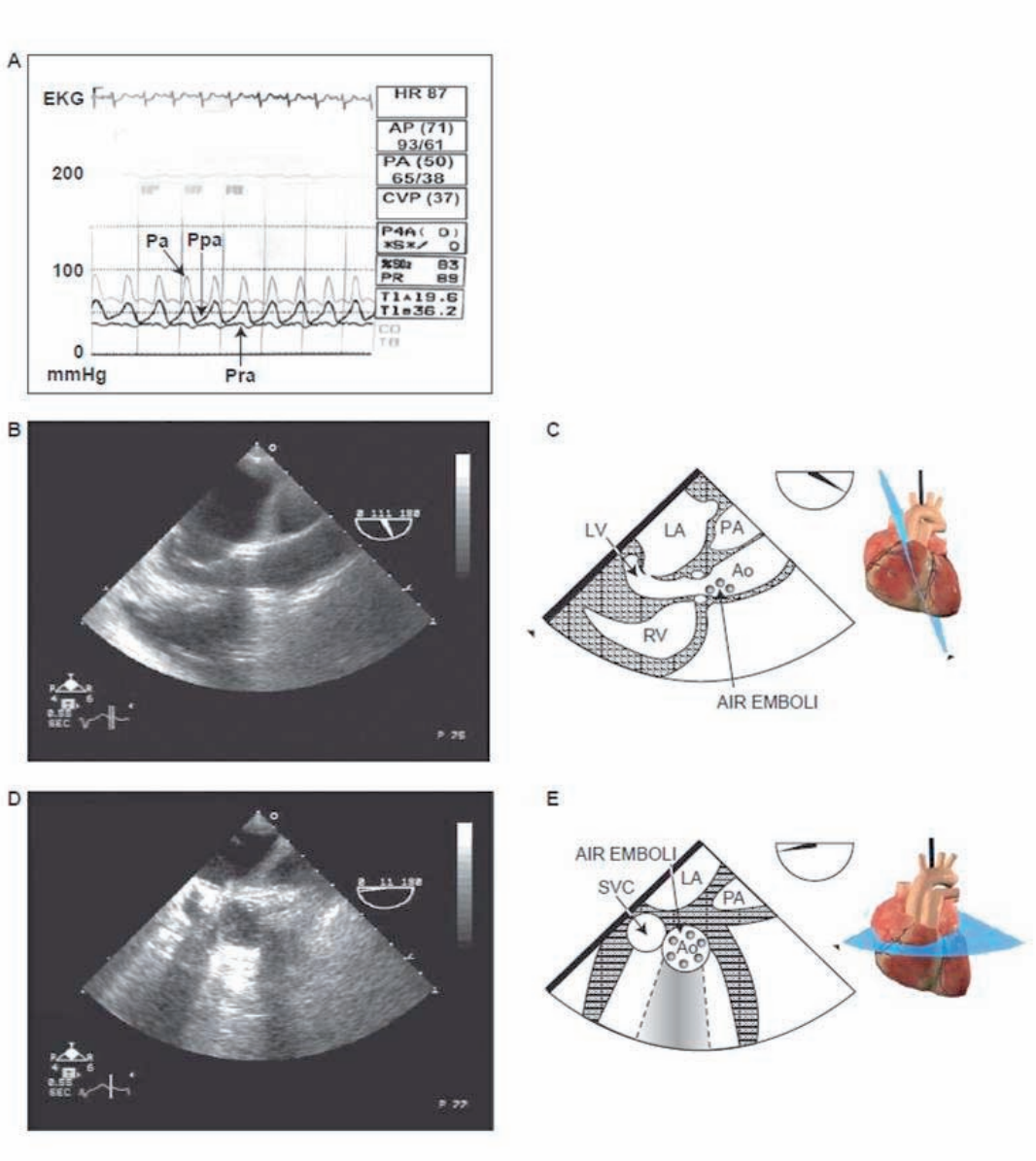

Figure 34 Air embolism

A 61-year-old woman underwent aortic valve replacement. She was easily weaned from cardiopulmonary bypass (CPB). As she was transferred onto the transportation bed, she developed acute pulmonary hypertension (A) followed by ventricular fibrillation. (B–E) She was resuscitated and a transesophageal echocardiographic exam was performed. A mid-esophageal aortic valve long-axis and short-axis view revealed strong echogenic material close to the prosthetic valve, consistent with air emboli dislodged during mobilization of the patient (Ao, aorta; EKG, electrocardiogram; LA, left atrium; LV, left ventricle; Pa, arterial pressure; PA, pulmonary artery; Ppa, pulmonary artery pressure; Pra,

right atrial pressure; RV, right ventricle; SVC, superior vena cava). (Adapted with permission of Denault *et al.* [12])

Carbon dioxide used during saphenectomy can also inadvertently be directed into the systemic circulation. Carbon dioxide embolism should be suspected when an increase in end-tidal carbon dioxide is followed by a decrease in cardiac output and hypotension. TEE is the most sensitive method to detect gas embolism [233] (Figure 35). We have observed such cases on two occasions. [28;234] Acute right ventricular failure requiring emergency CPB was the consequence of the first case. However, in the second case, the use of inhaled prostacyclin prevented us from using CPB. [28]

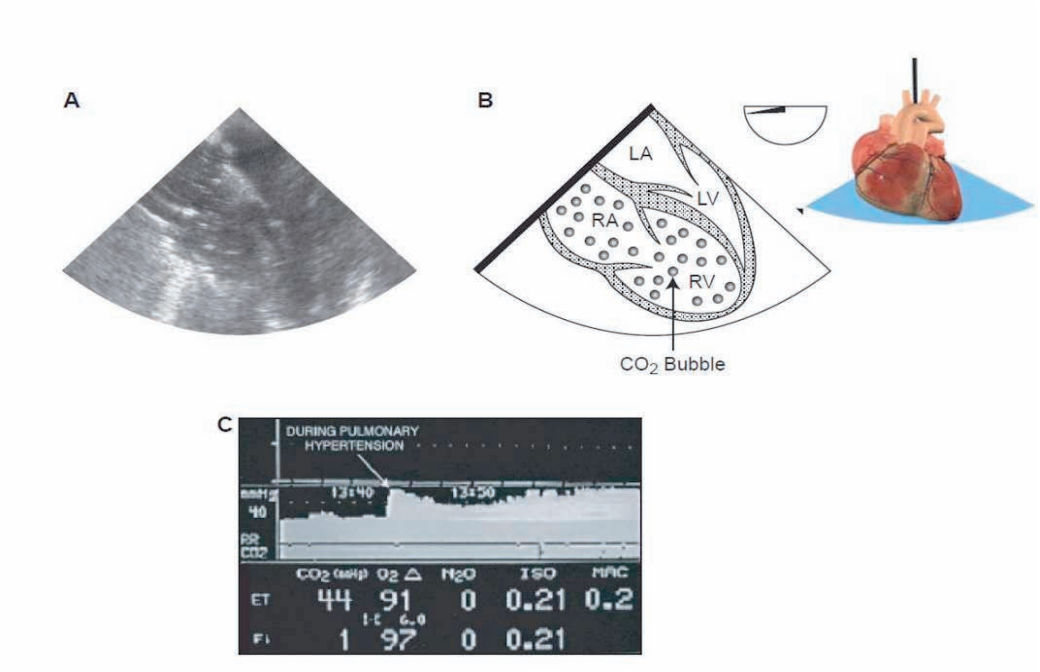

Figure 35 Carbon dioxide (CO_2) embolism

Mid-esophageal four-chamber view showing CO_2 embolism in a 69-year-old man undergoing laparoscopic saphenectomy who suddenly became hemodynamically unstable. (A, B) A mid-esophageal four-chamber view showed the appearance of bubbles in the right atrium (RA) and right ventricle (RV) originating from the inferior vena cava. This was associated with right cardiac chamber dilatation. (C) The hemodynamic instability coincided with an abrupt rise in end-tidal CO_2 (LA, left atrium; LV, left ventricle). (Adapted from Martineau *et al.* [28])

3.1.2.9 Hypoxemia and hypercapnia

Both hypoxemia and hypercapnia will lead to pulmonary vasoconstriction, pulmonary hypertension and increased right atrial pressure. This is consistent with the rationale for the Airway-Breathing-Circulation (ABC) method in resuscitation. Airway management and breathing remain the two initial and essential steps in the management of any hemodynamically unstable patient. The effect of hypoxemia is illustrated in Figure 36.

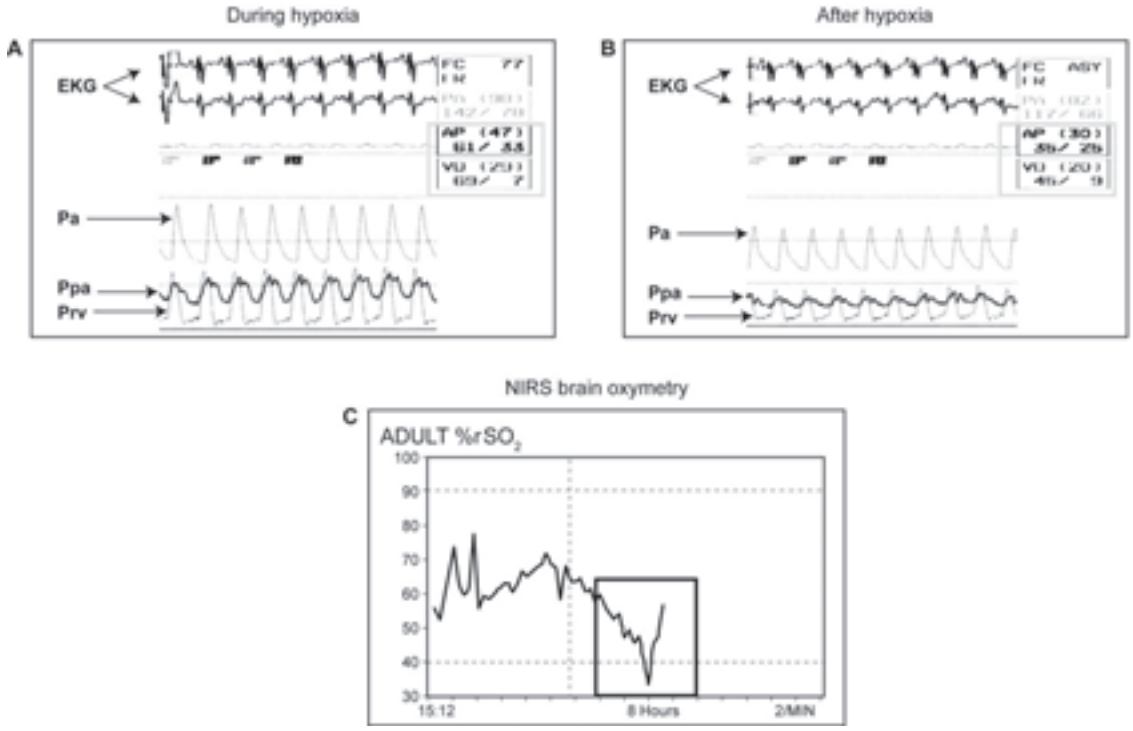

Figure 36 Hemodynamic effect of hypoxemia

Severe hypoxemia in a 48-year-old man observed after coronary revascularization. (A) During the hypoxic episode, the pulmonary artery pressure increased to 61/33 mmHg. (B) Using positive end-expiratory pressure, the hypoxic episode was corrected and the pulmonary artery pressure decreased to 35/25 mmHg. (C) Using near-infrared spectroscopy, the hypoxemia was associated with a reversible reduction in the brain oximetry signal.

Hemodynamic instability through hypoxemia will lead to right ventricular failure and its consequences on left ventricular function (Figure 27). During cardiac surgery, hypoxemia can result from a ventilation-perfusion mismatch or through a right to left shunt. In the latter case, the shunt is typically through a patent foramen ovale. (PFO or "*Trou de Botal*") present in 20% of the adult population (Figure 37).

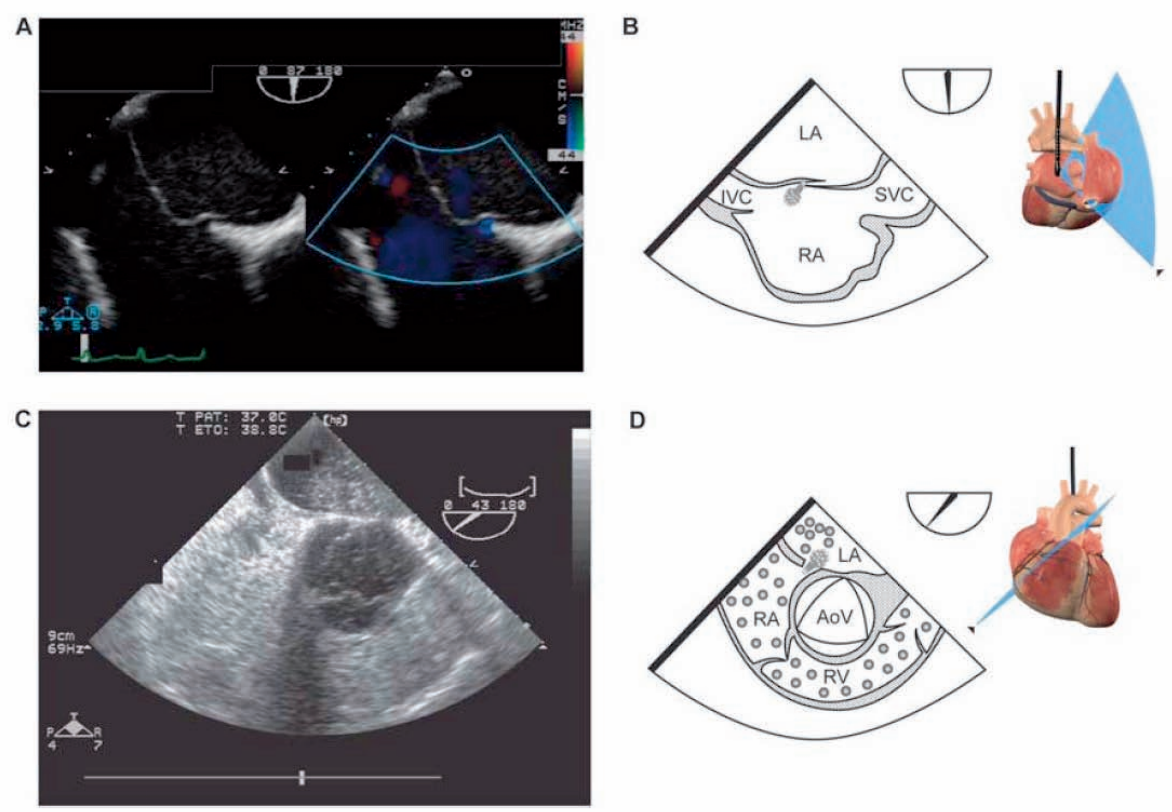

Figure 37 Patent foramen ovale (PFO)

(A,B) A PFO demonstrated by color flow Doppler in a mid-esophageal bicaval view. (C,D) Opacification of the right-sided cardiac chambers by intravenous injection of agitated normal saline. During the release phase of the Valsalva maneuver, microbubbles are seen crossing to the left atrium (LA) through a PFO. (With permission of Denault *et al.* [12])

A PFO has a normal amount of tissue when the septum primum is complete, but it does not fuse with the septum secundum to obliterate the foramen ovale. A right to left shunt can be elicited with a Valsalva maneuver. Patency of the foramen ovale can be

anatomically demonstrated with a probe. It usually has no consequences unless it is responsible for a cerebrovascular accident through paradoxical emboli (Figure 38). Some authors, however, suggest that it should be closed if found in a patient in whom a cardiac surgical procedure is performed, [235] but recent evidence suggest no survival benefit. [236] The presence of a PFO may alter the method of venous cannulation in the case of left-sided valve surgery or the need for cardioplegia in right-sided valve surgery. In cases where the patient is at a high risk of hypoxemia post-bypass, such as LVAD insertion and heart transplant, closure of the PFO is warranted.

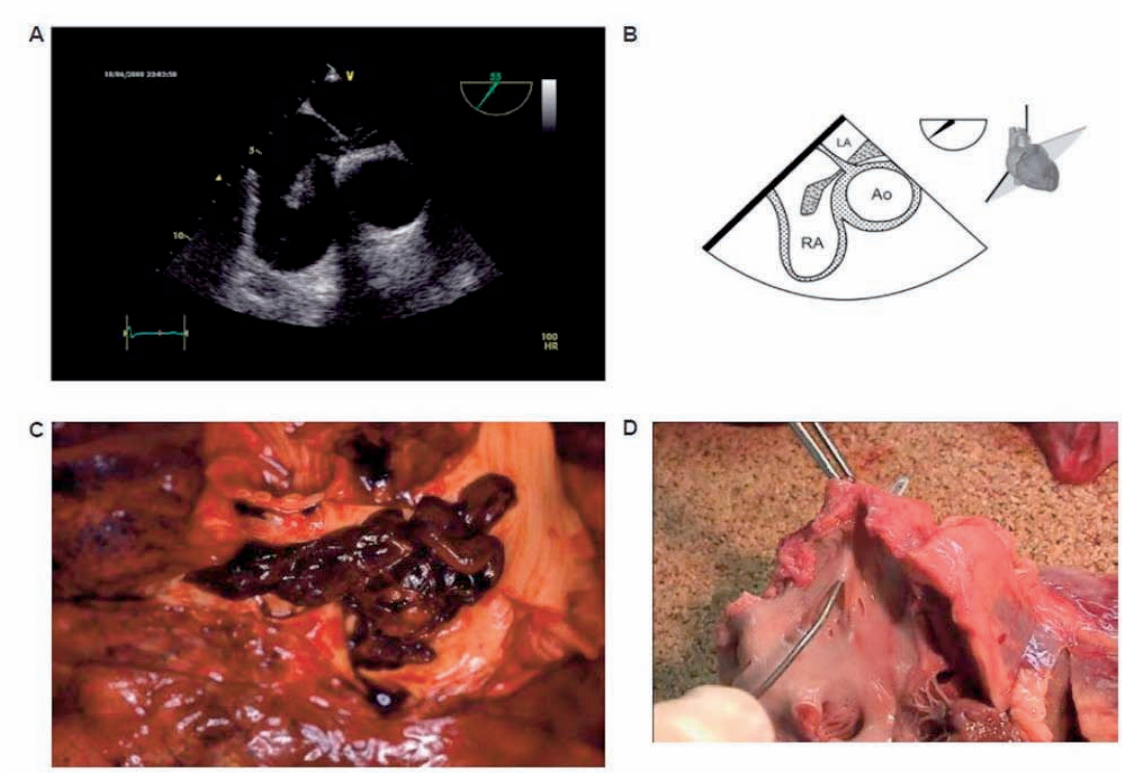

Figure 38 Paradoxical pulmonary embolism

Paradoxical pulmonary embolism in a 48-year-old man who presented with acute hypotension. (A,B) Mid-esophageal view at 55° showing a thrombus across the patent foramen ovale. (C) Intraoperative aspect of the pulmonary emboli. (D) Autopsy finding of a patent foramen ovale in a patient who died of refractory hypoxemia. (Courtesy of Dr. Michel Pellerin and Dr. Tack Ki Leung) (With permission of Denault *et al.* [12])

Hypercapnia also results in pulmonary vasoconstriction and pulmonary hypertension. The hemodynamic and echocardiographic consequences are the same as those of hypoxemia. [237;238] The effect of hypercapnia can easily be demonstrated during organ donation. In the determination of cardiac death, it is essential to demonstrate the absence of any spontaneous breathing during 10 minutes of apnea. In such a situation, the hemodynamic and echocardiographic effects of hypercapnia can be appreciated (Figure 39). Interestingly, changes in the dimension of the right atrium precede the increase in right atrial pressure (Figure 40). This is most likely secondary to the normal reduced compliance of the right atrial cavity.

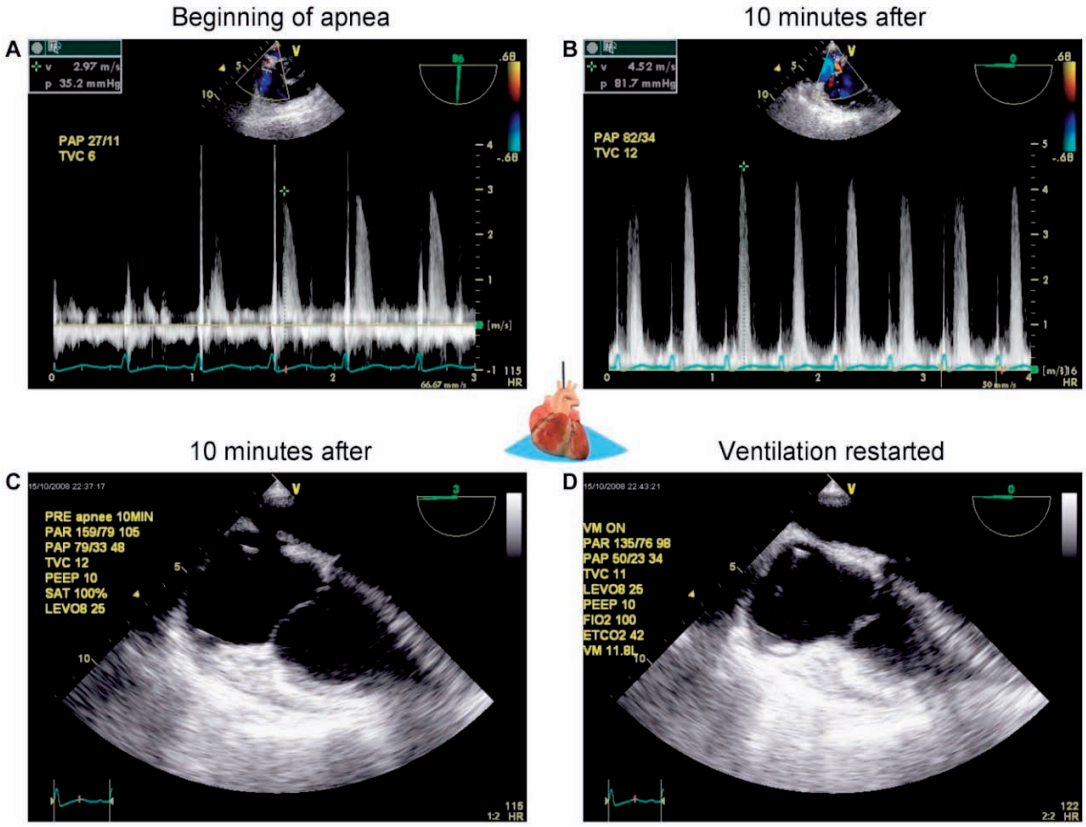

Figure 39 Hypercapnia and cardiac function

(A) Tricuspid regurgitation continuous-wave Doppler signal before the apnea testing. The peak presssure gradient is 35.2 mmHg. The pulmonary artery pressure and right atrial pressure were 27/11 and 6 mmHg. (B) After 10 minutes of apnea, the peak pressure gradient increased up to 81.7 mmHg. The pulmonary artery pressure and right atrial

pressure were 82/43 and 12 mmHg. (C) At about the same time, right ventricular and atrial dilatation were present. (D) The right-sided dilatation were reversed once mechanical ventilation was resumed.

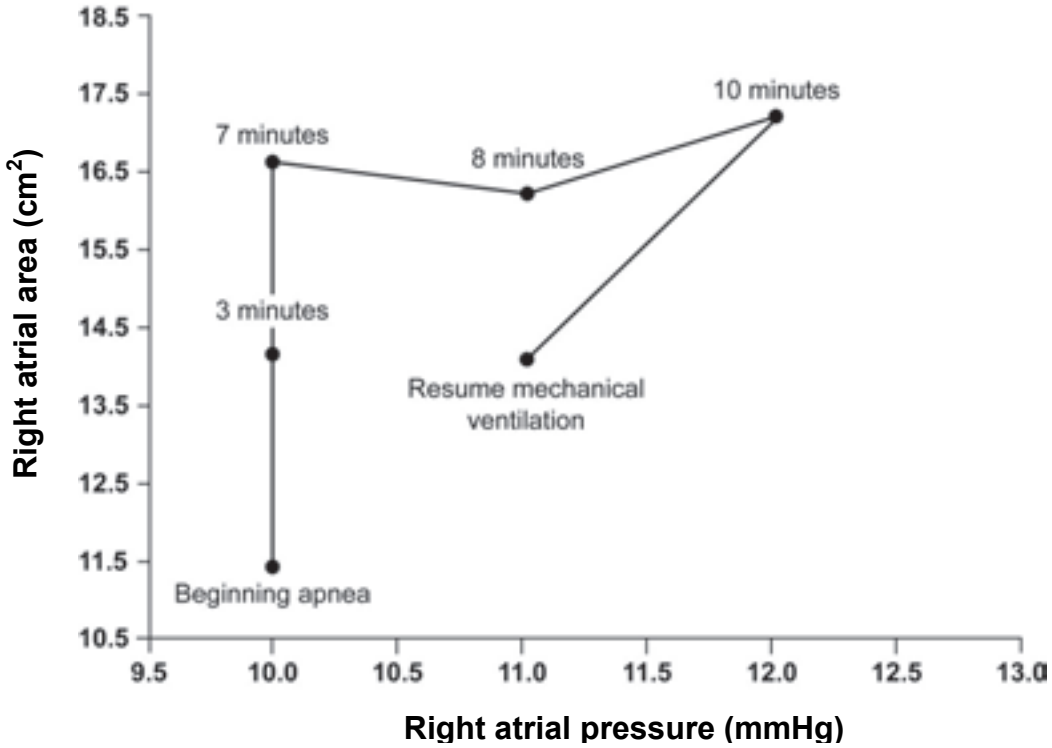

Figure 40 Hypercapnia and right atrial dimension and pressure

Relation between the right atrial area and the right atrial pressure (Pra) during apnea testing in organ donation. Initially, the right atrial area increases in size, but at 7 minutes only, the Pra starts to rise, reaching maximal value at 10 minutes. A reduction in right atrial area and Pra was observed when mechanical ventilation was resumed.

In summary, several conditions will contribute to the increase in right atrial pressure. The use of TEE is essential in the diagnosis and treatment of these various conditions. If there is no evidence of altered Pms or Pra, then the next step is to rule out any increase in resistance to venous return.

3.1.3 Increased resistance to venous return

There are two mechanisms of increased resistance to venous return: the first is the extrinsic compression of the circulatory system, or compartment syndrome, and the second is the intrinsic partial or complete occlusion of the extracardiac large vessels, or vena cava syndrome.

The resistance to venous return will be significantly impeded in situations in which pericardial, mediastinal, thoracic or abdominal pressure will increase, such as during an abdominal compartment syndrome. [148;239] In these situations, an upward shift of the pressure-volume curve will be observed. The right and left ventricular pressure will be high (from the outside compression) and volume normal or low (Figure 41).

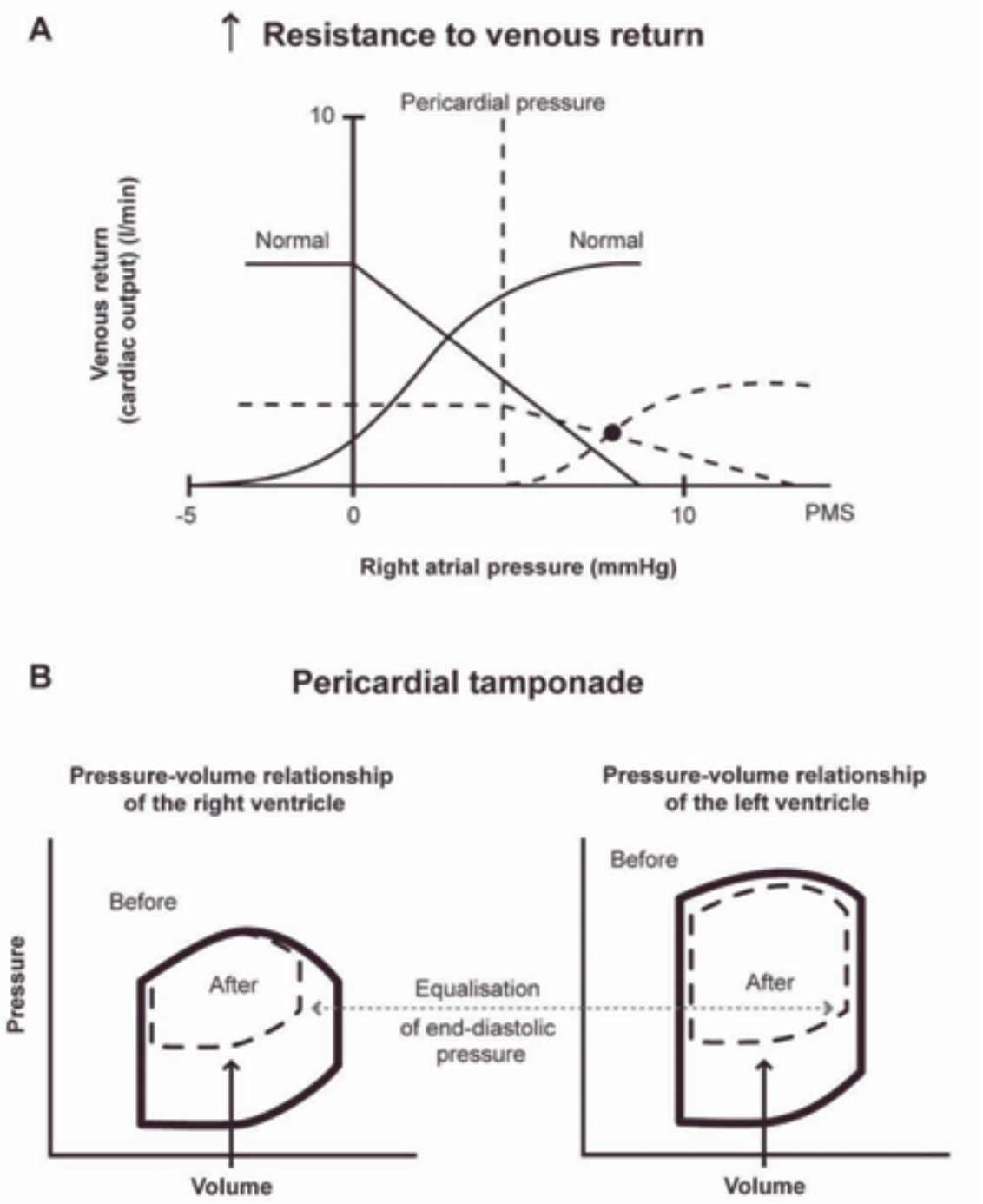

Figure 41 Mechanism of increased resistance to venous return during tamponade

In tamponade, venous return and cardiac output are reduced. Right atrial pressure is increased. This is secondary to the rise in pericardial pressure. In addition, venous return will now be limited not by subatmospheric pressure but by the pericardial pressure. As a

result, venous return is now equal to the difference between Pms and the pericardial pressure divided by the resistance to venous return. The venous return slope is reduced from an increase in the resistance to venous return. A normal compensatory increase in mean systemic pressure (Pms) will also be observed secondary to the activation of the autonomic nervous system. (B) Biventricular pressure-volume relationships in pericardial tamponade. The increase in pericardial pressure will be transmitted to both ventricles. As a consequence, an upward shift of the horizontal part of the pressure-volume relationship will be observed. This is typically associated with the equalization of end-diastolic pressures. As pericardial pressure increases and tamponade develops, biventricular volumes will be further reduced. Consequently, left ventricular pressure and systemic pressure will be reduced. (With permission of Durand *et al.* [240])

These conditions are difficult to diagnose without echocardiography and extracardiac pressure or intra-abdominal monitoring. [27] However, as the chest and pericardium are opened at the end of cardiac surgery, their contribution to hemodynamic instability is minimal and can be neglected. However, their contribution will appear as soon as the chest is closed. The causes of increased Rvr are pericardial (cardiac tamponade), mediastinal (after CPB), pleural (hemothorax and pneumothorax) and abdominal compartment syndromes.

In the classical presentation of cardiac tamponade, fluid accumulates across the pericardium. The right atrium, having the lowest pressure, will be the first cardiac chamber to collapse in diastole, followed by the right ventricle and left atrium in diastole. This can be easily diagnosed using transthoracic or transesophageal echocardiography (Figure 42).

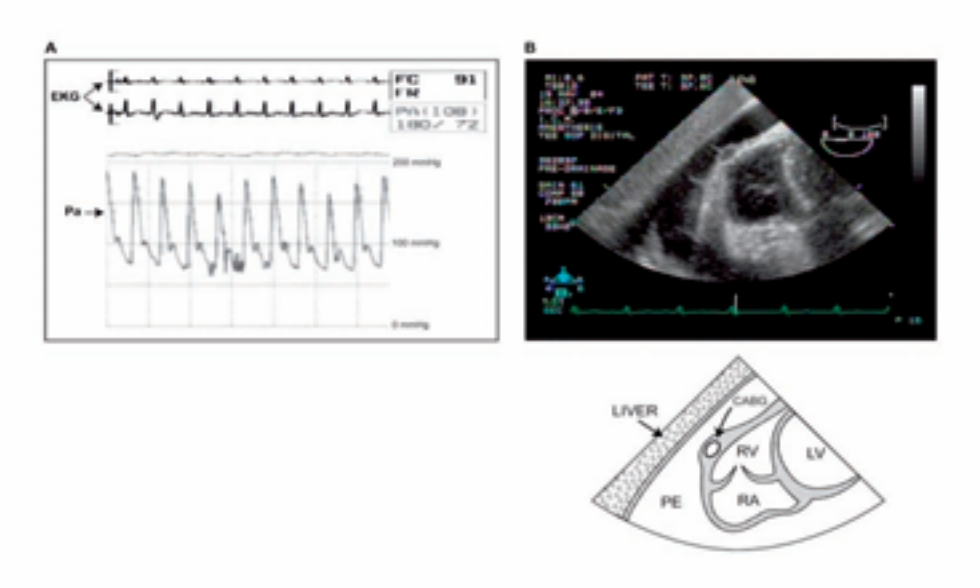

Figure 42 Classical tamponade.

Classical tamponade diagnosed using transesophageal echocardiography in a patient, developing after surgical coronary revascularization from a deep transgastric view. (A) The arterial pressure (Pa) waveform shows the typical respiratory variation of pulsus paradoxus. The patient was on significant high doses of noradrenaline. (B) The intermittent compression of the right atrium (RA) can be visualized (CABG, coronary artery bypass graft; LV, left ventricle; PE, pericardial effusion). (With permission of Durand *et al.* [240])

After cardiac surgery, however, localized tamponade can occur with the regional compression of any of the cardiac chambers. In such a situation, transesophageal echocardiography is mandatory to rule out regional tamponade (Figure 43). As tamponade progresses and shock worsens, coronary perfusion pressure is compromised, leading to additional myocardial dysfunction. [241]

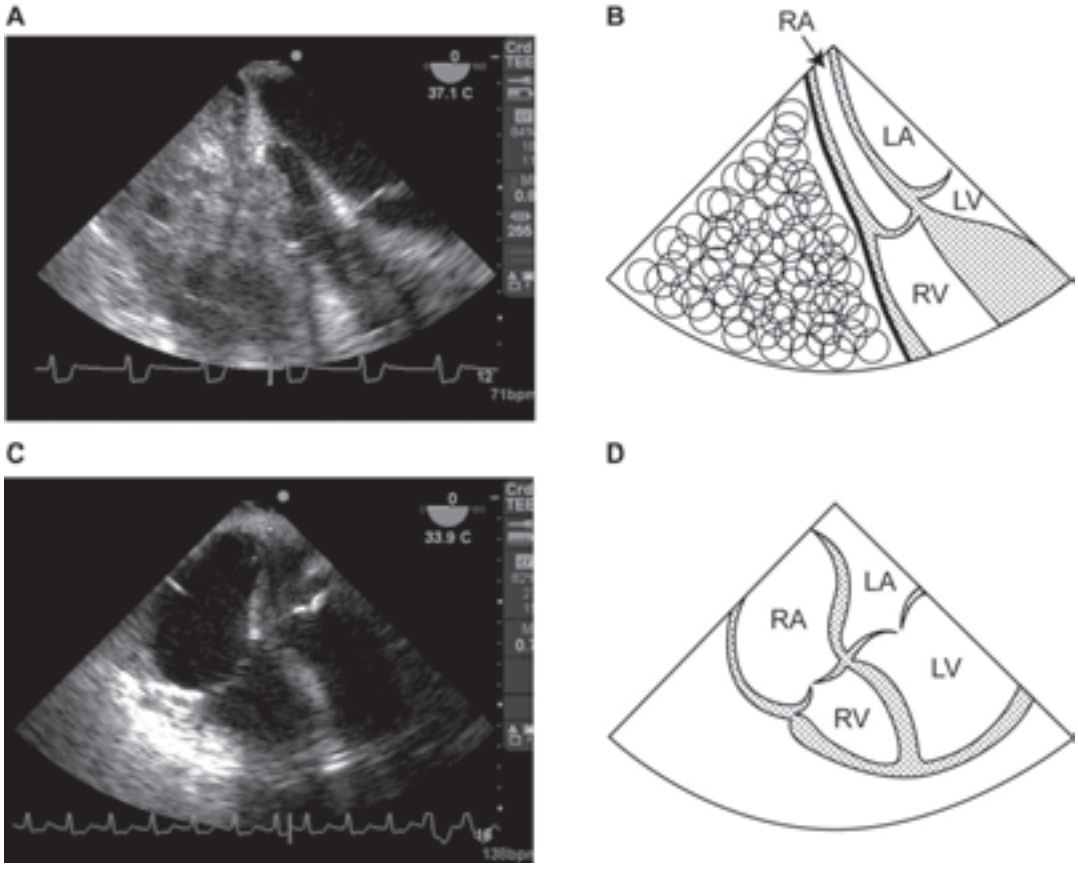

Figure 43 Regional tamponade.

Transesophageal echocardiography from a mid-esophageal view showing a large clot compressing the right atrium (RA) and right ventricle (RV) before (A,B) and after (C,D) removal . (LA: left atrium, LV: left ventricle) (With permission of Durand *et al.* [240])

The other mechanism of increased Rvr is any pleural pathology that would increase the extrinsic cardiac pressure. This can be a hemothorax or a pneumothorax. The former can be diagnosed using echocardiography (**Erreur ! Source du renvoi introuvable.**); however, the latter is more difficult to diagnose, as ultrasound does not penetrate air. Nevertheless, specific echocardiography signs of pneumothorax have been described using chest ultrasound [242] and could perhaps be used together with transthoracic echocardiography at the bedside. Just as with tamponade, the consequence of the pneumothorax is the compression of the cardiac cavity with the lowest pressure. If the

pneumothorax is anterior to the left side, the RVOT will be compressed specifically during diastole (Figure 44) We observed and reported this condition after lung transplantation. [27]

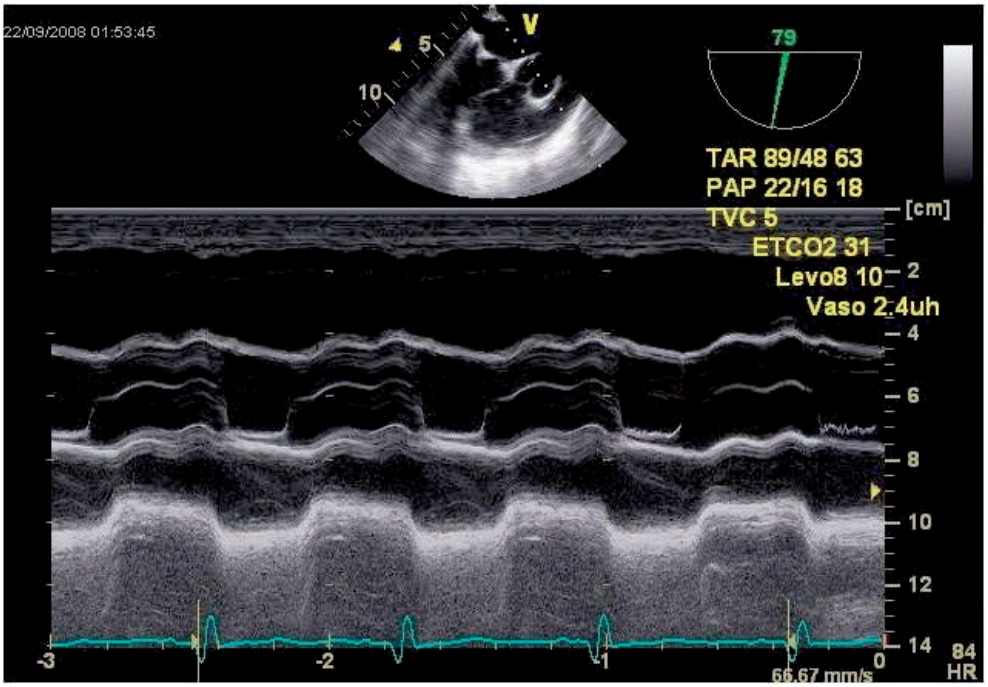

Figure 44 Hemodynamic consequence of a pneumothorax

A 19-year-old hemodynamically unstable man with chest contusion was admitted for organ donation. Using a mid-esophageal view of the right ventricular outflow tract (RVOT), a diastolic obstruction of the RVOT was observed using M-mode. The obstruction was secondary to an anterior left pneumothorax compressing the RVOT.

In complex and long procedures, it has been noted in some patients that the closure of the sternum produces hemodynamic instability that is reversible when the chest is reopened. The mechanism is secondary to extrinsic compression of the cardiac structures (Figure 45).

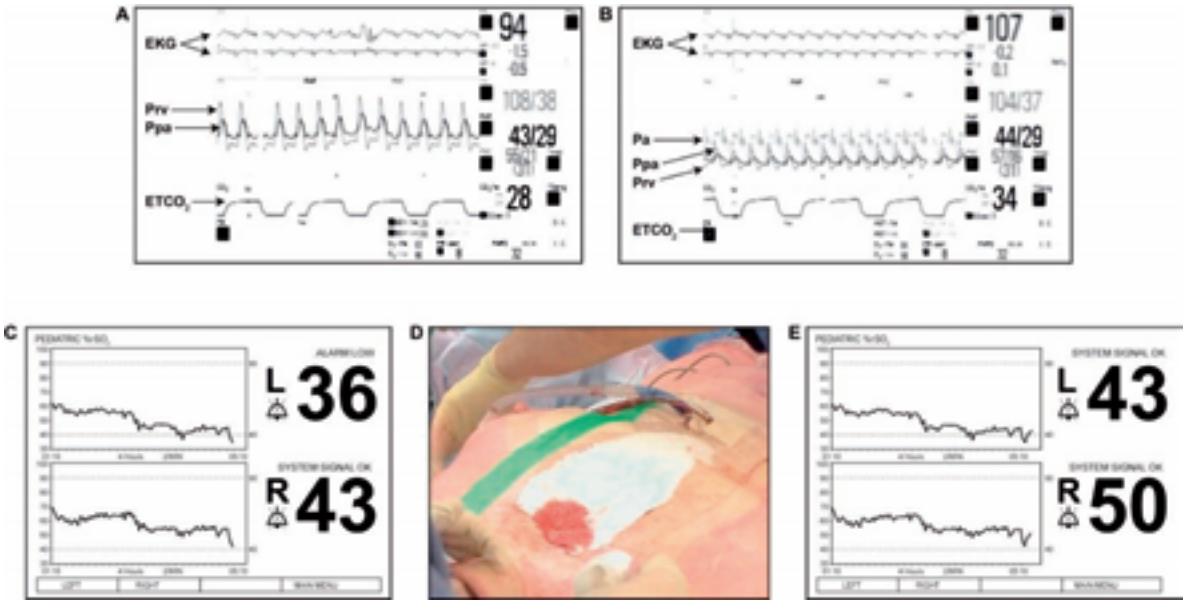

Figure 45 Mediastinal tamponade

A 62-year-old woman was admitted for urgent revascularization after failure of coronary angioplasty. She was intubated and on vasoactive agents before the surgery. (A) Her hemodynamic waveforms are shown before. As the chest was closed, she became more hemodynamically unstable with increased vasoactive requirements. This was associated with equalization of the right ventricular and diastolic pulmonary artery pressures (B). In addition, profound bilateral brain desaturation was observed using near-infrared spectroscopy (NIRS) (C). It was then decided to reopen the chest (D) and to transfer the patient to the intensive care unit with a sterile dressing on the mediastinum. The reopening of the chest was associated with an improved hemodynamic condition and improved NIRS values (E).

The last mechanism of extrinsic compression is the abdominal compartment syndrome (ACS) and, unfortunately, it is still poorly recognized and diagnosed in cardiac surgery. Abdominal compartment syndrome is defined as a sustained abdominal pressure > 20 mmHg with evidence of organ dysfunction relieved by abdominal decompression. [239] The term intra-abdominal hypertension (IAH) is used to describe abdominal pressures ranging from 12 to 20 mmHg. An increased pressure in a non-expendable compartment reduces capillary bed perfusion and promotes bacterial translocation, which is then followed by the activation of inflammatory cytokines. [136] The latter causes leakage through vascular walls and edema, which further contributes to the rise in intra-abdominal

pressure. The reduction in the abdominal perfusion pressure (APP) defined as the difference between mean arterial pressure (MAP) and intra-abdominal pressure (IAP) leads to organ ischemia. The associated rise in abdominal pressure increases the resistance to venous return (Figure 41). This will reduce venous return and lead to low cardiac output and shock. [243] Furthermore, as the IAP increases, the diaphragm is pushed cephalad which reduces thoracic or the extrapulmonary compliance. The consequences of this condition include a reduced glomerular filtration, an oligoanuric state, hepatic dysfunction and intestinal ischemia. The acute compartment syndrome has been shown to be an independent risk factor for mortality in the intensive care unit. [244] The risk factors of ACS are summarized in Table 13 and can be divided in three categories: diminished wall compliance, increased intra-abdominal content and capillary leak. [244;245]

From Table 13, it appears that several of these risk factors can be present during cardiac surgery. Clinical manifestations are non-specific and include decreased urine output, high ventilatory pressures and a tense abdomen. Monitoring the intravesical pressure is essential to establishing the diagnosis. In patients with intra-abdominal hypertension and acute compartment syndrome, the abdominal perfusion pressure should be maintained above 50-60 mmHg. [148] Treatment should be directed towards the management of the underlying cause. Specific goals should be to improve abdominal wall compliance, reduce abdominal fluid and/or air and to correct the positive fluid balance. The most definitive intervention is decompression laparotomy with temporary abdominal closure. [246] However, this approach is not without risks and is not always curative. [247] The use of diuretics, paracentesis, nasogastric tubes (Figure 46) and dialysis can be very effective.

Table 13 Abdominal compartment syndrome

1) Diminished wall compliance

Abdominal surgery
Acute respiratory distress syndrome
Major burns/trauma
Mechanical ventilation
Prone position
Obesity (body mass index > 30 kg/m²)

2) Intra-abdominal content

Liver dysfunction (ascitis)
Hemo-/pneumoperitoineum
Increasing intraluminal fluid content (Ex. contrast enema)
Ileus/gastroparesis
Acute colonic pseudo-obstruction; colonic dilatation (Ogilvie syndrome)
Tumor

3) Capillary leak/resuscitation

Massive resuscitation
Polytransfusion (> 10 blood units/24 h)
Acidosis (pH < 7.2)
Sepsis
Hypothermia (< 33^{o} C)
Hypotension
Coagulopathy
Major burns/trauma
Emergency laparotomy

(With permission of Deslauriers *et al.* [158])

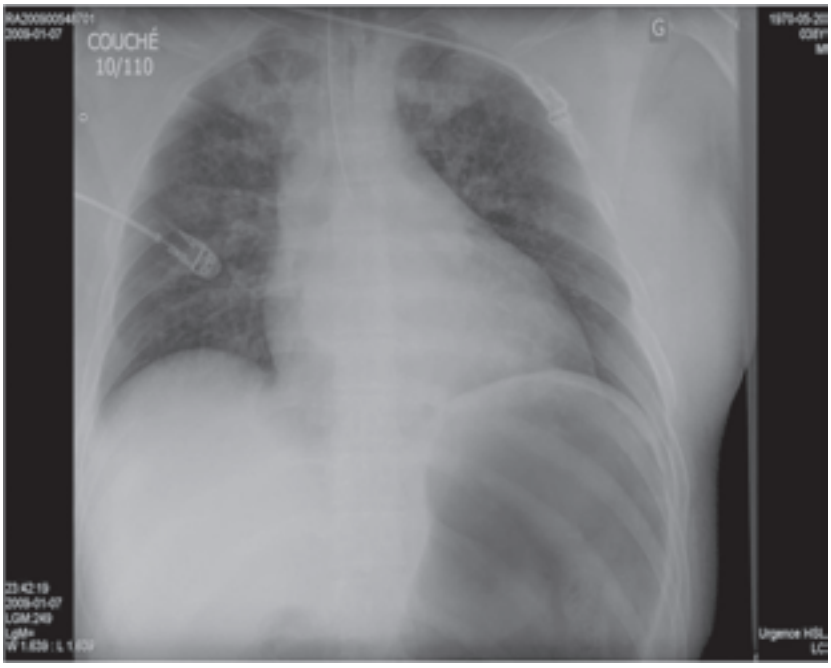

Figure 46 Acute abdominal compartment syndrome after induction of anesthesia.

A 65-year-old woman difficult to intubate and ventilate was hemodynamically unstable after the induction of general anesthesia. A chest radiograph demonstrates a distended stomach. A nasogastric tube was inserted and the vasoactive support stopped.

The second mechanism of increased resistance to venous return is the vena cava syndrome, which results in the intrinsic obstruction of the large vessels. In such a situation, a significant hemodynamic instability will be present with a normal or reduced cardiac volume similar to a reduction in Pms. This has been observed following the removal of the inferior vena cava cannula and accidental partial closure of the inferior vena cava (Figure 47). We have seen it also during a Fontan procedure during which the anastomosis to the inferior vena cava was partially obstructed (Figure 48).

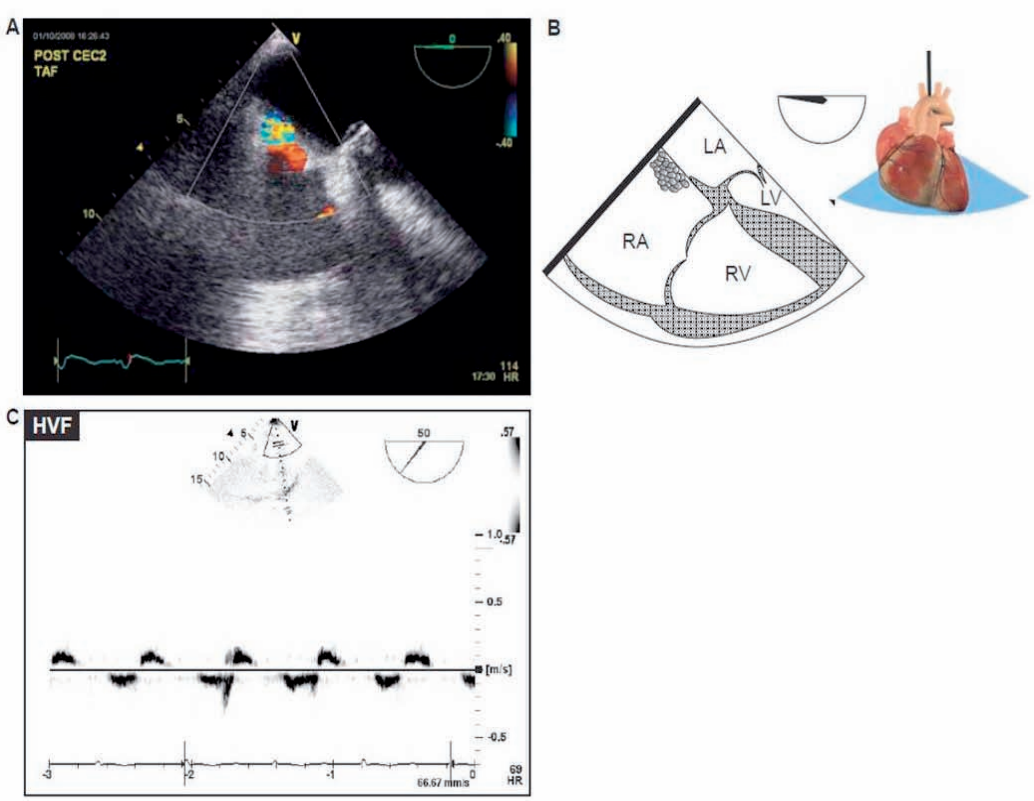

Figure 47 Partially occluded inferior vena cava (IVC)

(A,B) Mid-esophageal right ventricular view in a patient after aortic valve replacement. A turbulent flow was observed at the entrance of the IVC. It was secondary to a partial obstruction of the IVC at the site of cannulation. (C) Significantly reduced hepatic venous flow (HVF) with systolic reversal was present.

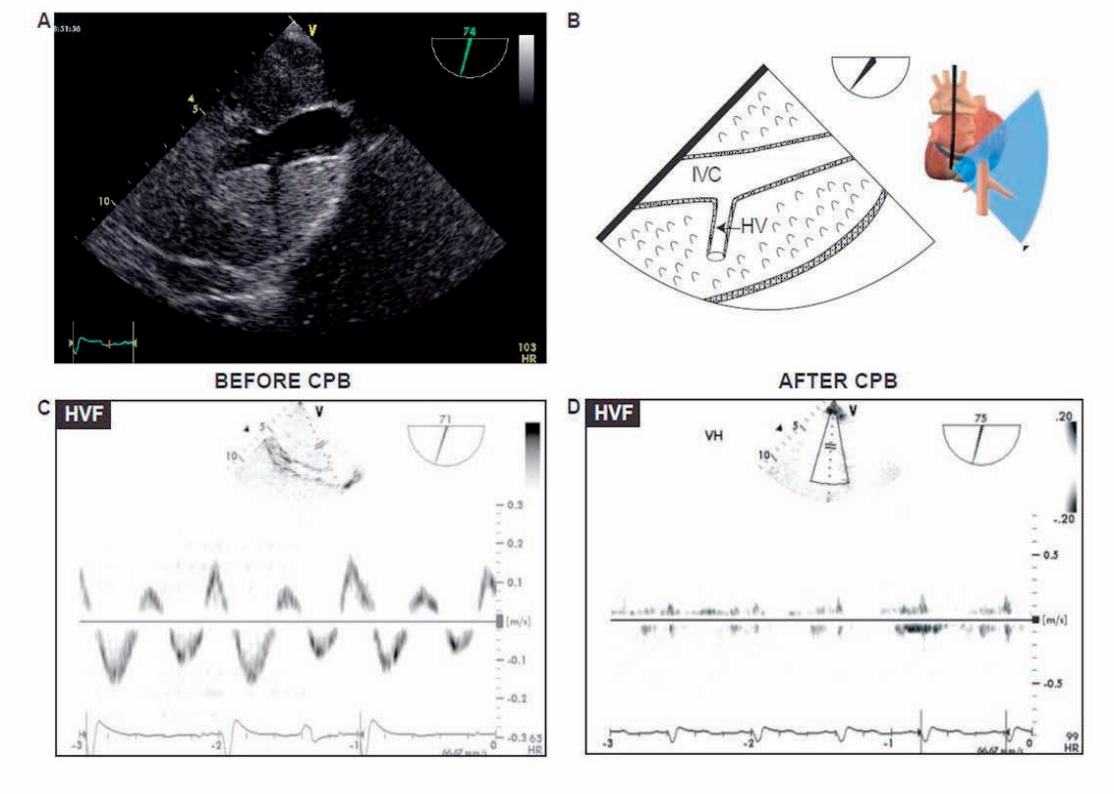

Figure 48 Inferior vena cava (IVC) occlusion during Fontan procedure

(A,B) Transgastric view showing a dilated IVC following a Fontan procedure. The occlusion was secondary to a partial occlusion at the level of the graft anastolosis to the IVC. (C,D) Hepatic venous flow (HVF) before and after cardiopulmonary bypass (CPB). The HVF is almost absent after CPB.

A misplaced intra-aortic balloon catheter in the inferior vena cava will also contribute to hemodynamic instability, particularly during diastole when it is inflated (Figure 49). All these conditions can be suspected or diagnosed with the use of TEE.

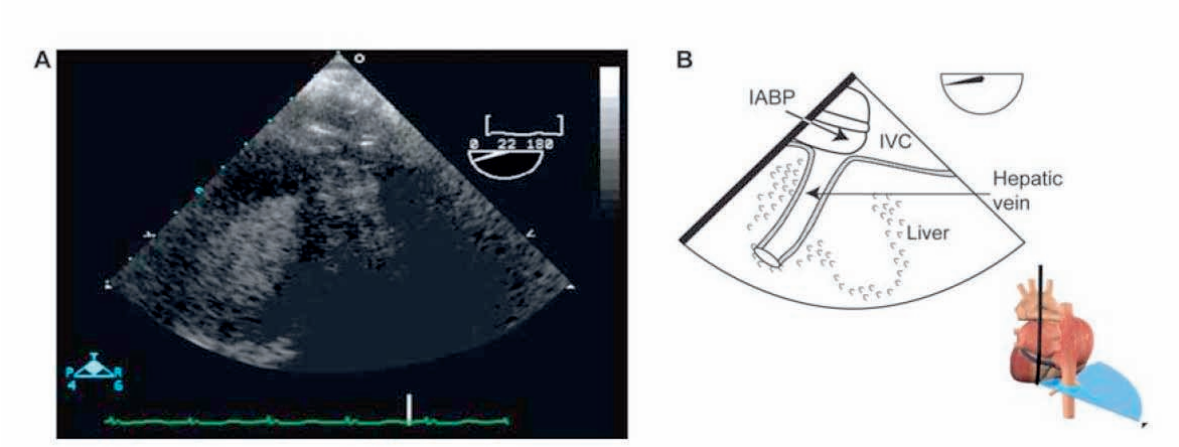

Figure 49 Intra-aortic balloon pump (IABP) catheter in the inferior vena cava (IVC).

(A,B) Emergency positioning of the IABP in the operating room after cardiopulmonary bypass. The IABP was not in the aorta but in the IVC. (With permission of Denault *et al.* [13])

The superior vena cava can also be obstructed during cardiac surgery. Typically, it is caused by a misplaced or obstructing superior vena cava venous cannula. Although this is not typically associated with hemodynamic instability, it can lead to brain hypoperfusion by reducing the cerebral perfusion pressure. Pressure monitoring of the internal jugular pressure and infrared spectroscopy are modalities useful in such diagnoses (Figure 50).

In summary, the resistance to venous return, either through the extrinsic compression of the cardiac chambers or great vessels (compartment syndrome) or through a partial or complete vascular occlusion (vena cava syndrome), is an important factor that needs to be diagnosed during cardiac surgery as a potential mechanism of hemodynamic instability and difficult separation from CPB.

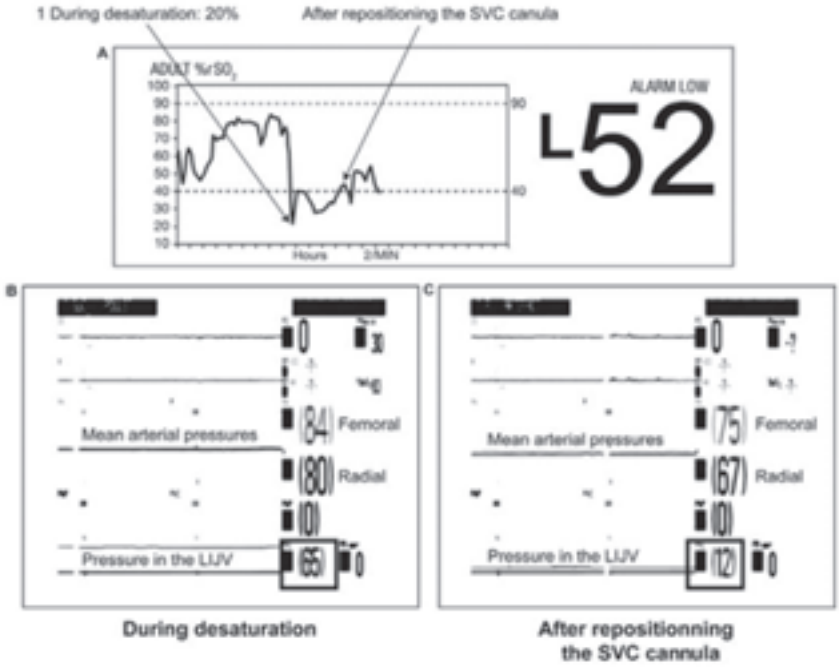

Figure 50 Brain desaturation during cardiac transplantation.

(A) A reduction down to 43% in brain saturation was observed during cardiac transplantation. (B) Despite adequate mean arterial pressure (from radial and femoral transducers) during cardiopulmonary bypass, the desaturation was associated with an increase in the left internal jugular vein (LIJV) pressure of 65 mmHg. At that point, the cardiothoracic surgeon decided to reposition the superior vena cava (SVC) cannula that was occluding cerebral venous return. The brain oximetry value increased. (C) The LIJV pressure decreased to 12 mmHg. (With permission of Denault *et al.* [130])

3.1.4 Combined mechanism

Finally, combinations of causes of difficult separation from CPB are the rule rather than the exception. [19] For instance, RV systolic failure will lead to LV diastolic dysfunction through septal interaction (Figure 27). In these conditions, the hemodynamic values will be the result of two different conditions, and only echocardiography can enable the diagnosis of these two separate entities, as previously shown. [19] Severe shock state independently of their cause, when persisting, can lead to vasodilatory shock. [137]

In our experience, the majority of these diagnoses can be made via the combination of both hemodynamic and echocardiographic modalities. These conditions require a specific treatment. [44] For instance, inotropes are indicated in the presence of left or right ventricular systolic dysfunction, but contra-indicated in the presence of outflow tract obstruction. [38] In both conditions, the hemodynamic characteristics will be the same: reduced venous return and elevated filling pressure. However, the treatment is completely the opposite: inotropic therapy is indicated with systolic dysfunction, but inotropic withdrawal is the therapy for any outflow tract obstruction.

Conditions associated with increased right atrial pressure are particularly important to differentiate using TEE. Each condition has a different therapeutic implication, as shown in Table 14. This is one of the reasons why the use of TEE is considered a type 1 indication in the presence of hemodynamic instability. [248] Echocardiography is therefore an essential tool in any research dealing with complex hemodynamic conditions. A systematic approach in the diagnosis and treatment of hemodynamic instability should be proposed in cardiac surgery. This approach should be based on the concept of venous return and uses combined and simultaneous TEE and hemodynamic monitoring to estimate biventricular pressure volume relationships.

Figure 51 summarizes the mechanisms of hemodynamic instability resulting from reduced Pms, increased Pra and Rvr. Relevant hemodynamic and echocardiographic measurements performed during cardiac surgery are summarized in Table 15.

Table 14 Mechanisms of hemodynamic instability and therapeutic implication

Etiology	**Timing**	**Possible mechanism**	**Therapeutic implication**	**Pharmacological treatment of hemodynamic instability after CPB**				
			Surgical consideration	Fluid therapy	Inotropes[1]	Vasodilators[2]	Vasopressors[3]	Other
LV systolic dysfunction	Before CPB	Coronary artery disease	Coronary revascularization					
		Natural evolution of U/L disease	No indication for revascularization					
	During CPB	Poor myocardial protection?	Retrograde cardioplegia position adequate?					
	After CPB	Air embolism	LV de-airing					
		Coronary ostium obstruction from the prosthesis	Coronary revascularization and LVAD if severe	+	++	+	+	
LV diastolic dysfunction	Before CPB	Coronary artery disease or natural evolution	Coronary revascularization					
	After CPB	Poor myocardial protection?	If associated with new systolic dysfunction, revascularization might be considered	+	-	+/-	+/-	Some benefit from beta-blockade
LV outflow tract obstruction	Before CPB	LV hypertrophy	LV outflow tract enlargement					
	After CPB	LV hypertrophy, edema and inotropes	May lead to return on CPB and MVR if associated with SAM	+	-	-	+	Some benefit from beta-blockade
Pulmonary hypertension	Before CPB	Post-capillary from increased LVEDP	Rule out absence of correctable mitral regurgitation					
	After CPB	Valve dysfunction of pulmonary reperfusion syndrome	Return of CPB if dysfunctional prosthesis	+	+	+	+	Inhaled agents may be considered
RV systolic dysfunction	Before CPB	Coronary artery disease or consequence of PHT						Preemptive inhaled agents may be considered
	After CPB	Poor myocardial protection or consequence of PH	Coronary revascularization and RVAD if severe	+	+	+	+	Inhaled agents may be considered
		Associated with septal shift		-	+	++	++	
RV diastolic dysfunction	Before CPB	Consequence of PH						

Etiology	Timing	Possible mechanism	Therapeutic implication Surgical consideration	Pharmacological treatment of hemodynamic instability after CPB Fluid therapy	Inotropes[1]	Vasodilators[2]	Vasopressors[3]	Other
	After CPB	Poor myocardial protection or consequence of PH		+/-	-	+/-	+/-	Treatment of PH may improve
RV outflow tract obstruction	Before CPB	LV septal hypertrophy						
	After CPB	LV hypertrophy, edema and inotropes		+	-	-	+	Some benefit from beta-blockade
Patient-prosthesis mismatch	Before CPB	Small aortic root	Aortic root enlargement, homograft					
	After CPB	Small prosthetic area in relation with body surface area		+	-	-	+/-	Some benefit from beta-blockade

CPB: cardiopulmonary bypass, LV: left ventricle, LVAD: left ventricular assist device, LVEDP: left ventricular end-diastolic pressure, MVR: mitral valve replacement, PH: pulmonary hypertension, RV: right ventricle, RVAD: right ventricular assist device, SAM: systolic anterior motion, U/L: underlying

1 Inotropes: adrenaline, milrinone, isoproterenol, ephedrine

2 Vasodilators: nitroglycerin, nitroprusside, milrinone

3 Vasopressors: phenylephrine, noradrenaline, vasopressin, methylene blue

Inhaled agents specific to pulmonary vessels (inhaled prostacyclin, inhaled milrinone, nitric oxide)

+ Indicated; - Counter-indicated; +/- Benefit is unclear

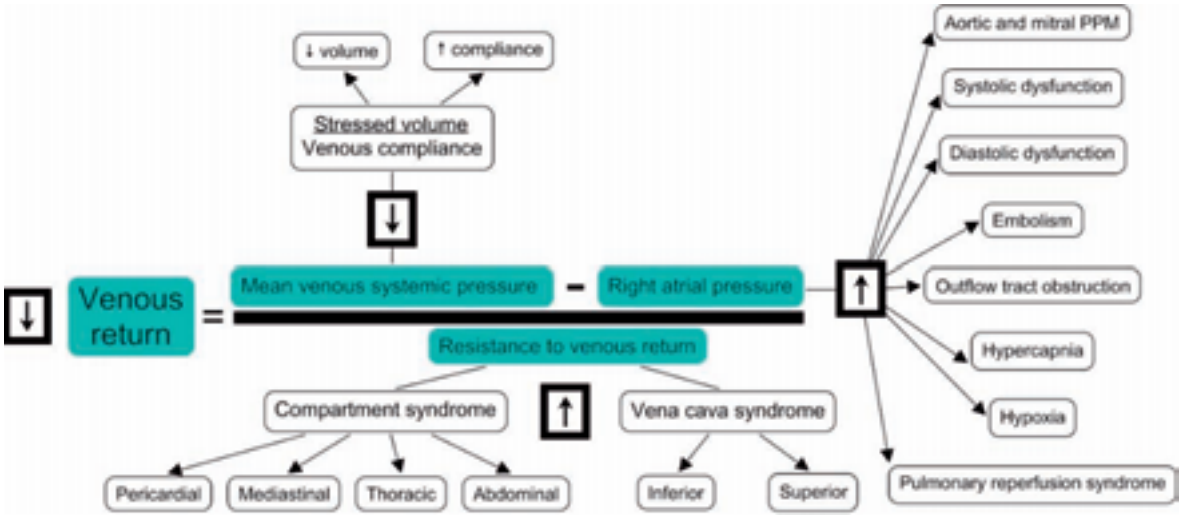

Figure 51 Mechanism of hemodynamic instability in cardiac surgery

(PPM, patient-prosthesis mismatch)

Table 15 Summary of the hemodynamic and echocardiographic measurements

Etiology	Measurement	Timing			Echocardiographic assessment
		Before CPB	During CPB	After CPB	
LV systolic dysfunction	LV hypertrophy	X			LVH based on LV mass
	LV dilatation	X		X	45 mm systole and 55 mm diastole
	LA dilatation	X		X	Maximum transverse diameter
	Regional wall motion abnormalities	X		X	1 = normal, 2 = hypokinetic, 3 = akinetic, 4 = dyskinetic
	Regional wall motion score index	X		X	Total score divided by the number of segments
	Left ventricular ejection fraction	X		X	Simson's rule using a 2- and 4-chamber view
	Left ventricular fractional area change	X		X	Transgastric view in diastole and systole
	Other: air embolism, floating plaques	X		X	Continuous 2D monitoring
LV diastolic dysfunction					Classified according to an algorithm using:
	Transmitral flow	X		X	Pulsed-wave Doppler at the tip of mitral valve
	Pulmonary venous flow	X		X	Pulsed-wave Doppler 1 cm within pulmonary vein
	Mitral annular velocities	X		X	Tissue Doppler on lateral wall

Etiology	Measurement	Timing			Echocardiographic assessment
		Before CPB	During CPB	After CPB	
	Propagation velocities	X		X	Color M-Mode mid-esophageal 120º
LV outflow tract obstruction	LV outflow tract measurements	X			Measured in the ME 5 chamber
	Color Doppler in the LVOT	X		X	Color Doppler mid-esophageal 120º
	LV septal wall measurement	X			Mid-esophageal 120º
	Pressure gradient measurement across the LVOT				Mid-esophageal 120º: normally less than 4 mmHg
	Brockenborough Braunwald phenomenon	X		X	A reduced arterial pressure after a premature ventricular complex is almost pathognomonic
Pulmonary hypertension	Using the pulmonary artery catheter	X		X	Mild PHT: PAPS > 30 mmHg, MPAP > 25 mmHg and MAP/MPAP 33-50% Severe PHT: SPAP > 50 mmHg, MPAP > 30 mmHg and MAP/MPAP > 50%
RV systolic dysfunction	2D Measurement of the RA and RV	X		X	Mid-esophageal 4-chamber view
	Fractional area change	X		X	Mid-esophageal 4-chamber view
	RV myocardial performance index	X			Using CW across TV valve and deep TG view for ET

Etiology	Measurement	Timing			Echocardiographic assessment
		Before CPB	During CPB	After CPB	
	Septal shift	X		X	Eccentricity index will be used
	Tricuspid annular plane systolic excursion	X		X	Measured using anatomic M-mode
RV diastolic dysfunction					Classified according to an algorithm using:
	Transtricuspid flow	X		X	Pulsed-wave Doppler at the tip of tricuspid valve
	Hepatic venous flow	X		X	Pulsed-wave Doppler 1 cm within hepatic vein
	Tricuspid annular velocities	X		X	Tissue Doppler on inferior wall
RV outflow tract obstruction	Using the paceport of the pulmonary artery catheter	X		X	Dedicated transducer for RV measurement
	2D view of the RV inflow-outflow	X		X	Mid-esophageal 40º to 70º view
	Deep transgastric view of the RV inflow-outflow	X		X	Deep transgastric view
	Measurement of the pressure gradient across the TV	X		X	A pressure gradient superior to the systolic pulmonary artery pressure will be observed
Patient-prosthesis mismatch	Measurement of the aortic annulus	X			Mid-esophageal 120º
	Table consultation of the EOA of the inserted prosthesis	X			Table used to obtain values for each type of valve
	Pressure-gradient across the LVOT	X		X	Deep transgastric view

Etiology	Measurement	Timing			Echocardiographic assessment
		Before CPB	During CPB	After CPB	
	Measurement of the aortic valve area	X		X	Using the continuity equation
Other measurements and observations:	Confirmation of the absence of any paravalvular leaks			X	Mid-esophageal 120º
	Confirmation of the position of the retrograde cardioplegia		X		Confirm presence in the coronary sinus
	Confirmation of the position of the inferior vena cava cannula		X		Confirm presence in the inferior vena cava
	Confirmation of the position of the aortic cannula	X	X		Confirm adequate position and good flow
	Confirmation of the position of any LVAD, RVAD or IABP		X	X	Confirm adequate position and good flow
	Severity of aortic atheromatosis	X			Classified using grade 1 to 5
	Ruling out aortic dissection	X	X	X	Confirm adequate position and good flow
	Ruling out inferior vena cava obstruction			X	Low-esophageal view 0°
	Ruling out free pleural or peritoneal fluid			X	Mid-esophageal, low-esophageal and transgastric views

Legends: AVR: aortic valve replacement, 2D: two-dimensional, CPB: cardiopulmonary bypass, IABP: intra-aortic balloon pump, LV: left ventricle, LVAD: left ventricular assist device, LVEDP: left ventricular end-diastolic pressure, LVOT: left ventricular outflow tract, ME: mid-esophageal, PHT: pulmonary hypertension, RA: right atrium, RV: right ventricle, RVAD: right ventricular assist device.

3.2 Research and development since the beginning of the PhD in 2006 at the MHI

Several of the determinants of venous return were studied over the last four years. They will be discussed in this section.

3.2.1 Studies on alternative measurement of venous return and cardiac output

Venous return and cardiac output can be measured using several techniques. In the operating room, we commonly use the pulmonary artery catheter to obtain thermodilution-derived cardiac output. In addition, the use of Doppler echocardiography allows us to calculate cardiac output. [12] The limitation of these two methods is that they are invasive and provide intermittent measurements only. An alternative to this technique would be near-infrared spectroscopy (NIRS).

Near-infrared spectroscopy (NIRS) is a technique that was first developed in the 70s [249;250] and that can be used as a non-invasive and continuous monitor of the balance between cerebral oxygen delivery and consumption. [135] Several different specialties such as neurology, [251] neurosurgery, [252] traumatology, [253] vascular surgery, [254] and adult [135] and pediatric cardiac surgery [255] have been using this monitor to measure brain and tissue perfusion. [129] In fact, some randomized controlled trials have recently shown the usefulness of this monitor to predict negative outcomes in non-cardiac [133] and cardiac surgery. [134] Several factors can affect oxygen delivery to the brain such as cardiac output, hemoglobin concentration, arterial oxygen saturation and partial pressure of oxygen. However, in an awake patient, the major determinants of baseline brain oximetric signals are not clearly described. Few studies have reported the relationship between cerebral oximetry values (ScO_2) and cardiac function. [249;250] As cardiac performance is reduced, increased brain oxygen extraction and lower ScO_2 values can be observed. [249] In addition, ScO_2 has been shown to correlate with the presence of left ventricular dysfunction in patients with valvular disease during exercice testing. [250] However, ScO_2 has never been compared with both hemodynamic and echocardiographic assessments of

the cardiac function in patients undergoing cardiac surgery. Our hypothesis was that the baseline mean ScO_2 value measured before surgery is determined by cardiac function and correlates with hemodynamic and echocardiographic parameters.

In order to test our hypothesis, we performed a retrospective analysis of patients undergoing cardiac surgery with bilateral recording of their baseline cerebral brain oxygen saturation (ScO_2) using the INVOS 4100 (Somanetics, Troy, MI, USA). [47] A pulmonary artery catheter was used to obtain their hemodynamic profile. Left ventricular systolic and diastolic function were evaluated by TEE, after induction of anesthesia, using standard criteria. A model was developed to predict ScO_2. A total of 99 patients met the inclusion criteria. There were significant correlations between mean ScO_2 values and central venous pressure (CVP) ($r = -0.31$, $p = 0.0022$), pulmonary capillary wedge pressure (PCWP) ($r = -0.25$, $p = 0.0129$), mean pulmonary artery pressure (MPAP) ($r = -0.24$, $p = 0.0186$), mean arterial pressure/mean pulmonary artery pressure ratio (MAP/MPAP) ($r = 0.33$, $p = 0.0011$), LV fractional area change (< 35, 35-50, ≥ 50, $p = 0.0002$), regional wall motion score index ($r = -0.27$, $p = 0.0062$) and diastolic function ($p = 0.0060$). Mean ScO_2 presented the highest area under the receiver operating curve (ROC) (0.74; CI 0.64-0.84) to identify LV systolic dysfunction. A model predicting baseline ScO_2 was created based on LV systolic echocardiographic variables, CVP, gender, mitral valve surgery and the use of beta-blocker ($r^2 = 0.42$, $p < .001$). Baseline ScO_2 values were related to cardiac function and superior to hemodynamic parameters at predicting left ventricular dysfunction. Our observations are summarized in Figure 52.

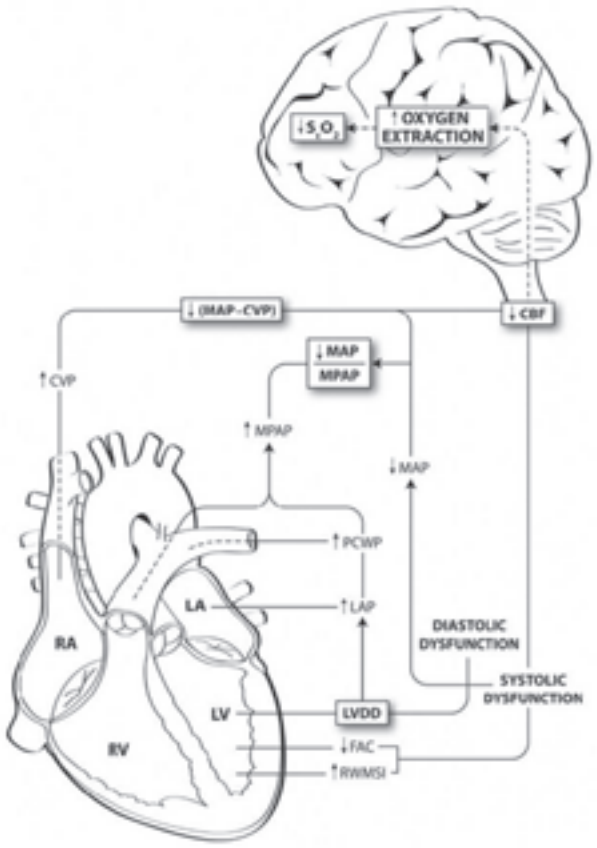

Figure 52 Brain-heart interaction

Relationship between reduced cerebral oxygen saturation (ScO_2) and cardiac systolic/diastolic function. As systolic cardiac function is reduced through a reduction in the left ventricular fractional area change (FAC) or an increase in the regional wall motion score index (RWMSI), the mean arterial pressure (MAP) will be reduced. Cardiac performance can also result from left ventricular diastolic dysfunction (LVDD), which can be present with or without systolic dysfunction. In this case, the left atrial pressure (LAP), pulmonary capillary wedge pressure (PCWP) and consequently the mean pulmonary arterial pressure (MPAP) will increase, the MAP/MPAP ratio decrease and this may lead to an increase of the central venous pressure (CVP). As the CVP is used to estimate the intra-cranial pressure, the cerebral perfusion pressure (MAP-CVP) will be reduced. The result will be a reduction in cerebral blood flow (CBF). This will lead to an increase in the oxygen extraction of the brain. This explains why a reduced cardiac function is associated with reduced ScO_2. (LA: left atrium; LV: left ventricle; RA: right atrium; RV: right ventricle). (With permission of Paquet *et al.* [47])

3.2.2 Studies on causes of increased Pra

Over the last 4 years we performed studies on systolic and diastolic dysfunction and documented the prevalence of RVOTO.

3.2.2.1 Left ventricular systolic and diastolic function

To support our hypothesis on the role of left ventricular systolic dysfunction as a predictor of outcome in cardiac surgery, we performed an observational study that included 3024 adult patients who underwent cardiac operations at the Montreal Heart Institute (MHI) from 1996 to 2000 (61% of the population operated in that period) and in whom left ventricular ejection fraction and other variables were measured prior to the cardiac surgery. [11] Left ventricular ejection fraction was the last measured value reported prior to surgery by left ventriculography, [256] echocardiography [257] or nuclear medicine. [258] The lowest value was selected. Surgical procedures were categorized as coronary revascularization, valvular, complex valve, re-operations and various. The complex operations were either multivalvular or valvular with or without coronary revascularization. Include also were ascending thoracic aorta operation and surgery for complications of myocardial infarction. Off-pump cardiac surgery and surgery of the descending aorta or patent ductus arteriosus were excluded. The primary outcome in this study was hospital mortality. Patients undergoing coronary revascularization were further stratified according to abnormal LV. Those left ventricular ejection fraction values were based on previous studies which identified them as cut-offs associated with increased mortality and morbidity. [8;100;259] Only variables with p values < 0.25 in univariate analysis were considered potential predictors of the primary outcome for multivariate analysis. Variable clustering was employed to further reduce the number of redundant variables before building a multivariate model. Then, stepwise multiple logistic regression analysis was undertaken to determine the independent predictors of death. P values < 0.05 were considered to be statistically significant. A total of 3024 patients were taken into account in the study. There were 99 deaths (3.3%). Of the 35 variables subjected to univariate analysis, 23 demonstrated a significant association with the occurrence of death. Stepwise

multiple logistic regressions identified eight variables to be independent predictors of death after cardiac surgery. These included age, weight, hypertension, treated diabetes, reoperation, left ventricular end-diastolic pressure, left ventricular ejection fraction and duration of CPB. Therefore, for a relative reduction of 10% of left ventricular ejection fraction, the risk of death increases by 32% (14-53%). A total 57% of deaths were attributed to hemodynamic instability. Postoperatively, 6% of those who died required vasopressors and 17% required an intra-aortic balloon pump (IABP) to be weaned, compared with 1% and 4% in the survivors group, respectively ($p < 0.0001$).

As mentioned previously, Salem *et al.* conducted an observational study to determine the relationship between preoperative left ventricular end-diastolic pressure and mortality following cardiac surgery. [11] The hypothesis was that an elevated left ventricular end-diastolic pressure, with or without preserved left ventricular systolic function, is associated with a poor outcome after cardiac surgery. As shown in Table 16, left ventricular end-diastolic pressure was found to be an independent predictor of mortality. For a relative increase in 5 mmHg of left ventricular end-diastolic pressure, the risk of mortality increases by 19% (5-35%).

Table 16 Multivariate analysis for mortality

Predictors	***P***	**Units**	**Odds ratio**	**95% CI**
Age	< 0.0001	20	4.255	2.461, 7.355
Weight, kg	0.0403	-10	1.190	1.008, 1.404
LVEDP	0.0062	5	1.195	1.052, 1.357
LVEF	0.0002	-10	1.326	1.145, 1.535
CPB length, min	< 0.0001	30	1.813	1.608, 2.044
Reoperation	< 0.0001	--	2.669	1.636, 4.354
Hypertension	0.0211	--	1.687	1.082, 2.632
Treated diabetes	0.0277	--	1.759	1.064, 2.906

CI indicates confidence interval; LVEDP, left ventricular end-diastolic pressure; LVEF, left ventricular ejection fraction; CPB, cardiopulmonary bypass. (From Salem *et al.* [11])

Furthermore, in patients undergoing coronary revascularization ($n = 2445$), the mortality in patients with left ventricular ejection fraction < 30% was higher in those with elevated left ventricular end-diastolic pressure > 19 mmHg (12%) compared to those with left ventricular end-diastolic pressure ≤ 19 mmHg (0%) (Table 17).

Table 17 Mortality in patients undergoing coronary artery bypass grafting

	LVEDP > 19mmHg LVEF ≤ 30%	**LVEDP > 19mmHg LVEF > 30%**	**LVEDP ≤ 19mmHg LVEF ≤ 30%**	**LVEDP ≤ 19mmHg LVEF > 30%**
No	75 (88%)	1244 (97%)	30 (100%)	1033 (98%)
Yes	10 (12%)*	35 (3%)	0 (0%)	18 (2%)
Total	85	1279	30	1051

LVEDP, left ventricular end-diastolic pressure; LVEF, left ventricular ejection fraction * $P < 0.0001$ compared with patients with LVEDP ≤ 19 and LVEF < 30 (From Salem *et al.* [11])

A similar trend was observed in non-coronary revascularization patients ($n = 895$), but it was not statistically significant (Table 18). The definition of diastolic dysfunction can be applied to patients with or without LV systolic dysfunction who have filling abnormalities. In summary, these observations support the link between mortality and both left ventricular systolic and diastolic dysfunction.

Table 18 Mortality in patients undergoing non-coronary artery bypass grafting

	LVEDP ≥ 19mmHg LVEF ≤ 30%	**LVEDP ≥ 19mmHg LVEF > 30%**	**LVEDP < 19mmHg LVEF ≤ 30%**	**LVEDP < 19mmHg LVEF > 30%**
No	41 (89%)	292 (94%)	26 (93%)	480 (96%)
Yes	5 (11%)	19 (6%)	2 (7%)	20 (4%)
Total	46	311	28	500

LVEDP, left ventricular end-diastolic pressure; LVEF, left ventricular ejection fraction. (From Salem *et al.* [11])

3.2.2.2 Right ventricular systolic and diastolic function

To further assess the value of right ventricular function in relation to other validated risk factors in open valvular heart surgery, we published our experience with 50 consecutive patients undergoing valvular surgery. [46] In our study we confirmed that, in patients with a right ventricular myocardial performance index (RVMPI) above 50% ($n = 20$), the number of patients with difficult separation from CPB (16/20 (80%) *vs.* 6/30 (20%), $p < 0.0001$) and the endpoint of mortality of postoperative heart failure (14/20 (74%) *vs.* 3/30 (10%), $p < 0.0001$) were significantly higher. On a multivariate analysis, among all other demographic, hemodynamic and echocardiographic variables, the RVMPI was the only independent predictor of heart failure and mortality (OR: 25.20, 95% CI 5.24-121.15, $p < 0.0001$).

3.2.2.3 Right ventricular outflow tract obstruction

The prevalence of RVOTO was retrospectively studied in 670 consecutive patients undergoing cardiac surgery. [38] Significant RVOTO was diagnosed if the right ventricular systolic to pulmonary artery peak gradient was over 25 mmHg. The diagnosis was based on the measurement of the right ventricular and pulmonary artery systolic pressures through the paceport and distal opening of the pulmonary artery catheter. To further validate the prevalence and the importance of RVOTO, 130 patients were prospectively studied over a 12-month period. In the retrospective cohort, 6 patients (1%) undergoing various types of cardiac surgical procedures were found to have significant dynamic obstruction with a mean gradient of 31 ± 4 mmHg (26 to 35 mmHg). In the prospective study, significant dynamic obstruction was identified in 5 patients (4%) (average peak: 37 ± 15 mmHg; range: 27 to 60 mmHg). The typical transesophageal echocardiography finding was end-systolic obliteration of the RVOT (Figure 53).

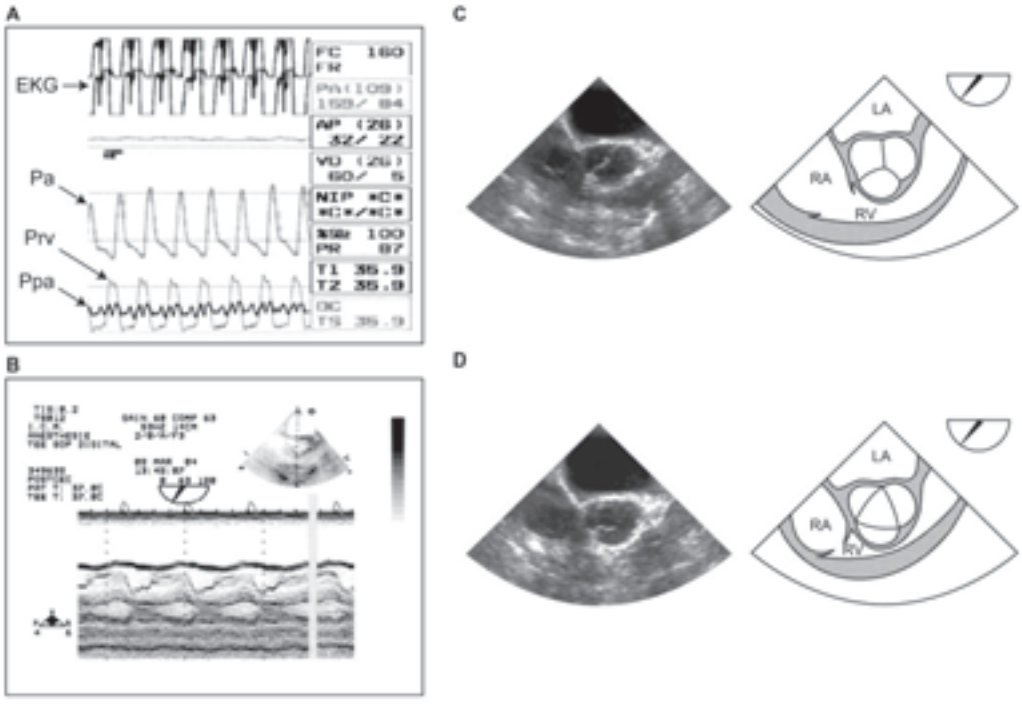

Figure 53 Dynamic right ventricular outflow tract (RVOT) obstruction

Septal myomectomy and aortic surgery in a 68-year-old man complicated by dynamic RVOT obstruction appearing during weaning from cardiopulmonary bypass. (A) The systolic gradient between the right ventricle and the pulmonary artery was 28 mmHg. (B,C,D) M-mode view from a mid-oesophageal right ventricular inflow-outflow view at 63º. Note the dynamic obstruction of the right ventricular outflow in systole in this (LA, left atrium; Pa, arterial pressure; Ppa, pulmonary artery pressure; Prv, right ventricular pressure; RA, right atrium; RV, right ventricle). (With permission of Denault *et al.* [38])

In patients with significant dynamic RVOTO, hemodynamic instability was present in 10/11 patients (91%). Therefore, RVOTO is easily diagnosed using the paceport of the pulmonary artery catheter (Figure 54) and should be considered a potential cause of hemodynamic instability, especially when TEE shows systolic right ventricular cavity obliteration.

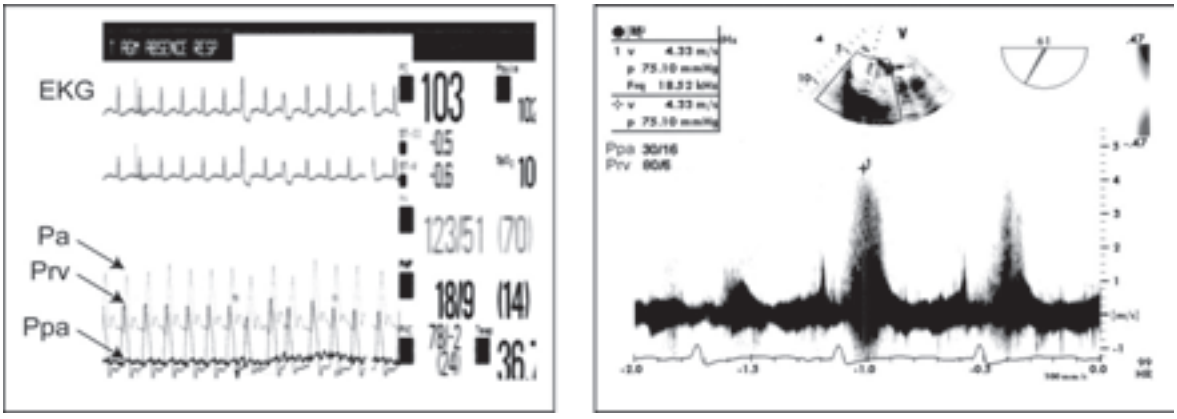

Figure 54 Hemodynamic and Doppler findings in dynamic RVOT obstruction

A 68-year-old man underwent aortic valve replacement. He became hemodynamically unstable with right ventricular dysfunction and was put back on cardiopulmonary bypass. Inotropes were initiated. On the second weaning attempt, he developed severe right ventricular outflow tract (RVOT) obstruction confirmed with the paceport of the pulmonary artery catheter and through continuous-wave Doppler interrogation of the tricuspid regurgitant flow in a mid-oesophageal ventricular inflow-outflow view at 61º. The measured pressure gradient of the tricuspid regurgitant flow was 75 mmHg (with a right ventricular systolic pressure of 80 mmHg) and the pulmonary artery pressure (Ppa) was 30/16 mmHg during the echocardiographic measurement. (EKG, electrocardiogram; Pa, arterial pressure; Prv, right ventricular pressure). (With permission of Denault *et al.* [38])

In summary, the mechanism of hemodynamic instability is complex but can be understood through a specific approach based on hemodynamic and echocardiographic variables. Therefore, such measures are essential to the evaluation of hemodynamic instability in cardiac surgery. So far, no studies have measured hemodynamic and echocardiographic variables in consecutive patients undergoing valvular surgery and determined the mechanism of difficult separation from CPB. The mechanism of difficult separation from CPB is important to understand if the next step is to prevent it.

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Abbreviations

2D	two-dimensional
A dur	duration of mitral inflow A-wave
A	peak late or atrial diastolic flow velocity
ABC	Airway-Breathing-Circulation
AC	aortic occlusion
ACC/AHA	American College of Cardiology and American Heart Association
ACE	angiotensin converting enzyme
ACS	abdominal compartment syndrome
Am	atrial mitral annular velocity
AML	anterior mitral leaflet length
AMP	adenosine monophosphate
ANCOVA	analysis of covariance
ANOVA	analysis of variance
Ao	aorta
AoV	aortic valve
AP	arterial pressure
APP	abdominal perfusion pressure
AR	aortic regurgitation
AR	atrial reversal
ASD	atrial septal defect
At	atrial tricuspid annular velocity
AVR	aortic valve replacement
BART	Blood Conservation Using Antifibrinolytics in a Randomized Trial
BMI	body mass index
BP	blood pressure
BSA	body surface area

CABG	coronary artery bypass grafting
CAD	coronary artery disease
CARE	Cardiac Anesthesia Risk Evaluation
CASS	Coronary Artery Surgery Study
CBF	cerebral blood flow
CHF	congestive heart failure
CI	cardiac index
CI	confidence interval
CK	creatinine kinase
CO	cardiac output
COPD	chronic obstructive pulmonary disease
CPB	cardiopulmonary bypass
CTICU	cardiothoracic intensive care unit
CVD	cerebrovascular disease
CVP	central venous pressure
D	diastolic
DAP	diastolic arterial pressure
DPAP	diastolic pulmonary arterial pressure
DSB	difficult separation from bypass
DT	deceleration time
E	early
ECMO	extra-corporeal membrane oxygenator
EDA	end-diastolic area
EDV	end-diastolic volume
EF	ejection fraction
EKG	electrocardiogram
Em	early mitral annular velocity
EOA	effective orifice area
ESA	end-systolic area

ESV	end-systolic volume
Et	early tricuspid annular velocity
ET	ejection time
FAC	fractional area change
Fem	Femoral
FRC	functional residual capacity
Gd	gradient
GEE	generalized estimating equation
HR	heart rate
HVF	hepatic venous flow
IABP	intra-aortic balloon pump
IAH	intra-abdominal hypertension
IAP	intra-abdominal pressure
ICU	intensive care unit
iEOA	indexed effective orifice area
IL	interleukin
iMil	Inhaled milrinone
iNO	inhaled nitric oxide
$iPGI_2$	inhaled prostacyclin
IU	international unit;
IV	intravenous
IVC	interior vena cava
IVCT	isovolumic contraction time
IVRT	isovolumic relaxation time
LA	left atrium
LAA	left atrial appendage
LADt	left atrial transverse dimension
LAP	left atrial pressure
LCOS	low cardiac output syndrome

LHV	left hepatic vein
LIJV	left internal jugular vein
LIMA	left internal mammary artery
LOF	low output failure
LUPV	left upper pulmonary vein
LV	left ventricle or left ventricular
LVAD	left ventricular assist device
LVDD	left ventricular diastolic dysfunction
LVEDA	left ventricular end-diastolic area
LVEDP	left ventricular end-diastolic pressure
LVEF	left ventricular ejection fraction
LVESA	left ventricular end-systolic area
LVFAC	left ventricular fractional area change
LVOT	left ventricular outflow tract
LVOTO	left ventricular outflow tract obstruction
LVWMSI	left ventricular wall motion score index
MAP	mean arterial pressure
MAV	mitral annular velocity
MHI	Montreal Heart Institute
MI	myocardial infarction
MPAP	mean pulmonary artery pressure
MPI	myocardial performance index
MR	mitral regurgitation
MV	mitral valve
MVO_2	mixed venous oxygen
MVR	mitral valve replacement
NIH	National Institute of Health
NIRS	near-infrared spectroscopy
NO	nitric oxide

NTG	nitroglycerin
NTP	nitroprusside
NYHA	New York Heart Association
OM	obtuse marginal
OR	odds ratio
OR	operating room
Pa	arterial pressure
PA	pulmonary artery
PAC	pulmonary artery catheter
Paf	femoral arterial pressure
PAF	platelet activating factor
PAP	pulmonary artery pressure
Par	radial arterial pressure
PCWP	pulmonary capillary wedge pressure
PEEP	positive end-expiratory pressure
PFO	patent foramen ovale
PGE_1	prostaglandin E_1
PGI_2	prostacyclin
PH	pulmonary hypertension
PML	posterior mitral leaflet length
Pms	mean systemic pressure
PMV	prosthetic mitral valve
PN	pseudonormal
Ppa	pulmonary artery pressure
PPM	patient-prosthesis mismatch
Pra	right atrial pressure
Prv	right ventricular pressure
PVF	pulmonary venous flow
PVR	pulmonary vascular resistance

PVRI	indexed pulmonary vascular resistance
PW	pulsed-wave
QHLI	Quebec Heart and Lung Institute
Ra	arterial resistance
RA	relaxation abnormality
RA	right atrium
Rad	Radial
RADt	right atrial transverse diameter
RBC	red blood cell;
RCA	right coronary artery
RCT	randomized controlled trial
ROC	receiver operating characteristics
RPA	right pulmonary artery
Rrv	resistance to venous return
RV	residual volume
RV	right ventricle or right ventricular
RVAD	right ventricular assist device
RVDD	right ventricular diastolic dysfunction
RVED	right ventricular end-diastolic volume
RVEDA	right ventricular end-diastolic area
RVEF	right ventricular ejection fraction
RVES	right ventricular end-systolic volume
RVESA	right ventricular end-systolic area
RVFAC	right ventricular fractional area change,
RVMPI	right ventricular myocardial performance index
RVOT	right ventricular outflow tract
RVOTO	right ventricular outflow tract obstruction
Rvr	resistance to venous return
RWMA	regional wall motion abnormalities

RWMSI	regional wall motion score index
S	systolic
SAM	systolic anterior motion
SAP	systemic arterial pressure
ScO_2	cerebral oxygen saturation
SCV	subclavian vein
SD	standard deviation;
SE	standard error
Sec	seconds
SLCL	septal to leaflet coaptation length
Sm	systolic mitral annular velocity
SPAP	systolic pulmonary artery pressure
St	systolic tricuspid annular velocity
STS	Society of Thoracic Surgeons
SV	stroke volume
SVC	superior vena cava
SVR	systemic vascular resistance
SVRI	indexed systemic vascular resistance
TAPSE	tricuspid annular plane systolic excursion
TAV	tricuspid annular velocity
TD	thermodilution
TDI	tissue Doppler imaging
TEE	transesophageal echocardiography
TLC	total lung capacity
TMF	transmitral flow
TNF	tumor necrosis factor
TO_2	oxygen transport
TTF	transtricuspid flow
TV	tricuspid valve

UK	United Kingdom
USA	United States of America
VAD	ventricular assist device
Vp	velocity of propagation
VR	venous return