Surgical Complications

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Contents

Abstract

Surgical complications following heart transplantation include a wide variety of clinical scenarios that can occur intraoperatively, early after surgery or even years following transplantation. An increasing number of patients are at risk of surgical injuries and bleeding complications as more patients are currently being bridged to transplantation with durable mechanical support devices and therefore have a history of prior sternotomies and are anticoagulated. CT imaging of the

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L. Bogar, A. Stempien-Otero (eds.), *Contemporary Heart Transplantation*, Organ and Tissue Transplantation,
https://doi.org/10.1007/978-3-319-58054-8_14

chest, optimal anticoagulation reversal, careful operative planning, and meticulous surgical technique are very important tools to prevent catastrophic complications or life-threatening bleeding. Primary and secondary graft dysfunction is common after heart transplantation and one of the most important causes of death within the first year. Although the initial therapeutic strategies include inotropes, vasopressors, and pulmonary vasodilators, many patients require temporary mechanical support to rest the heart and allow graft recovery. Other less common acute and chronic complications are also discussed in this chapter including aortic complications, heart oversizing, wound infections, pericardial effusions, constrictive pericarditis, and tricuspid regurgitation.

Keywords
Heart transplantation · Surgical complications · Redo sternotomy · Reentry injury · Primary graft dysfunction · Perioperative bleeding · Wound infections · Pericardial effusion · Constrictive pericarditis · Tricuspid regurgitation

Introduction

Heart transplantation represents the gold standard therapy for advanced heart failure. However the availability of suitable donors is limited, and unfortunately only a minority of patients eligible for heart transplantation will benefit from this procedure. Prevention and management of complications are of paramount importance to maximize outcomes. Surgical complications during or early after the procedure contribute to a significant proportion of early deaths. Some of them represent classic surgical complications such as surgical injuries, bleeding, and wound infections. Other complications are specifically related to the transplanted organ such as heart oversizing and valvular problems. Primary graft dysfunction represents one of the most feared complications and accounts for a significant proportion of early deaths after transplantation. Although graft dysfunction is not strictly a surgical complication, it will be discussed in this section as it usually manifests intraoperatively, and it is often treated with temporary mechanical support devices.

Since the first heart transplant performed by Christiaan Barnard in South Africa in 1967, the baseline characteristics of heart transplant recipients have changed dramatically. The relatively stable low number of donor hearts available worldwide and the high patient mortality on the heart transplant waiting list have resulted in the increasing use of durable mechanical circulatory support as a bridge to transplantation. Currently a significant proportion of heart transplant recipients have a history of previous cardiac surgical procedures, and at least half of them are being supported by some form of mechanical circulatory support at the time of transplantation (Lund et al. 2017). Furthermore, many patients have a history of more than one sternotomy, and most of them are receiving some form of anticoagulation therapy. As a result, the overall duration, complexity, and logistics of heart transplant surgical procedures have significantly increased which may be associated with a higher incidence of surgical complications.

As a reoperative sternotomy is necessary in more than 50% of current heart transplant recipients, careful preoperative evaluation and operative planning are of paramount importance to avoid catastrophic reentry injuries. Also, patients undergoing heart transplantation who are anticoagulated and require a redo sternotomy present a higher risk of significant perioperative bleeding due to more complex, time-consuming operations and coagulopathy.

Graft dysfunction is the most common early complication of heart transplantation and is associated with significant morbidity and mortality (Kobashigawa et al. 2014). Although milder forms of graft dysfunction frequently respond to pharmacologic management, the early institution of temporary mechanical circulatory support is often required. However, the use of this supportive technology prolongs operative times, increases the management complexity of these patients, and also is associated with a specific set of complications.

Tricuspid regurgitation is the most common valvular problem following heart transplantation and is associated with worse long-term outcomes (Wong et al. 2008). Although most patients respond to medical therapy, selected patients require valve repair or replacement to prevent symptomatic right ventricular failure and decreased long-term survival.

Less common but not less important surgical complications of heart transplantation such as aortic complications, heart oversizing, wound healing problems, pericardial effusions, and constrictive pericarditis will also be discussed in this chapter.

Reentry Injury

Although the risk of reentry injury during a redo sternotomy in general cardiac surgery is low, this complication can occasionally be catastrophic. Furthermore, patients with reentry injuries during redo sternotomy have increased morbidity and mortality secondary to bleeding, prolonged cardiopulmonary pump time, and increased blood product transfusion requirements (Imran Hamid et al. 2015). In heart transplant recipients, this complication can be particularly deleterious to the allograft, as increased bleeding and transfusion requirement are associated with RV failure, graft dysfunction, and potentially increased incidence of rejection (Kedziora et al. 2016).

Due to the shortage of donor hearts, an increasing number of patients are being bridged to heart transplantation with the use of durable mechanical circulatory support devices. Therefore the proportion of transplant recipients with a history of previous sternotomy continues to increase (Lund et al. 2017). Currently more than 50% of overall heart transplant recipients have a history of prior cardiac surgery. The use of different commercial biomaterials to reconstruct the anterior pericardium during previous cardiac procedures such as durable ventricular assist device insertion can ameliorate the development of adhesions between mediastinal structures and the posterior table of the sternum and minimize the risk. However reentry injuries can still occur during a redo sternotomy in these patients.

Preoperative planning is the best strategy to prevent this potentially catastrophic complication. Many centers have successfully adopted reoperative sternotomy protocols that include a preoperative 256-slice computed tomography (CT) scan of the chest to investigate the presence of potentially dangerous sternal adhesions (LaPar et al. 2013). Furthermore, careful evaluation of chest CT imaging has become standard of care at many transplant programs, as this imaging study has been incorporated to the heart transplant workup in patients with a history of previous heart surgery. Reoperative CTs are invaluable to safely plan reentry to the chest in patients with a history of multiple sternotomies, patent coronary grafts, patients with a history of high-dose radiation to the mediastinum, or a combination of these. Occasionally reoperative CT scan imaging can identify patients that may present excessively high-risk features for a redo sternotomy (i.e., aortic adhesions to the midline of the sternum) and therefore may be considered ineligible for heart transplantation. In these challenging patients, the final decision regarding patient eligibility for heart transplantation often relies on the surgical judgment of experienced transplant surgeons after carefully evaluating reoperative CT imaging and assessing the risk of potential catastrophic complications of a redo sternotomy.

High-risk features for reentry injury include adhesions between posterior table of the sternum and important mediastinal structures including the innominate vein, ascending aorta, pulmonary artery, right atrium, previous patent coronary grafts, free wall of the right ventricle, left ventricular assist device outflow graft, etc. A safe logistic approach prior to redo sternotomy in these patients includes either percutaneous or open wire cannulation of the femoral vessels under transesophageal echocardiography or fluoroscopic guidance in preparation for potential emergent groin cannulation if an injury occurs. In patients with extremely high-risk features on preoperative chest CT imaging, establishing cardiopulmonary bypass via femoral or axillary arterial

and femoral venous cannulation prior to redo sternotomy can represent the safest strategy.

If an injury unfortunately occurs, immediate institution of cardiopulmonary bypass may become the only viable strategy to maintain hemodynamic stability. In extreme cases deep hypothermic circulatory arrest may be necessary to control bleeding and repair the injury. As the entire mediastinal dissection is performed on a heparinized patient on cardiopulmonary bypass in these challenging cases, intraoperative and postoperative bleeding can become a significant problem. Experienced surgical teams can still achieve good outcomes in these circumstances by following meticulous surgical technique, minimizing cardiopulmonary bypass times, and appropriately correcting coagulopathy with the use of blood products. Avoiding right ventricular dilatation from excessive perioperative blood product administration is of paramount importance to prevent right ventricular dysfunction.

Primary Graft Dysfunction

Although graft dysfunction is very common after heart transplantation and is associated with significant morbidity and mortality, most major cardiac transplant centers have historically used different definitions and parameters of cardiac dysfunction. Single center studies have reported an incidence between 2.3% and 28.2% (Russo et al. 2010; D'Alessandro et al. 2010; Segovia et al. 2011). The consensus conference on primary graft dysfunction after cardiac transplantation took place during the 33rd Annual International Society of Heart and Lung Transplant meeting in 2013. Several specialists of 45 international transplant programs sought to unify diagnostic criteria and therapeutic strategies (Kobashigawa et al. 2014).

Graft dysfunction is associated with significantly increased 30-day and 1-year mortality. It remains the main cause of early death accounting for nearly 40% of the deaths in the first 30 days after the procedure and 18% at 1 year (Lund et al. 2017). Graft dysfunction is classified as primary and secondary graft dysfunction. Primary graft dysfunction must be diagnosed within 24 h of completion of surgery and very frequently starts in the operating room. Primary graft dysfunction is not associated with a discernible cause. Risk factors for the development of primary graft dysfunction include donor, recipient, and surgical procedural risk factors. The most consistently identified donor risk factors for primary graft dysfunction include donor age (Russo et al. 2010), cardiac dysfunction on echocardiography, female donor to male recipient (Hong et al. 2011), and cause of brain death (Iyer et al. 2011). Important recipient risk factors are age (Segovia et al. 2011), high pulmonary vascular resistance, and more severe pretransplant condition, including bridging to transplant with inotropes, mechanical circulatory support, and/or mechanical ventilation (Russo et al. 2010; Hong et al. 2011; Young et al. 2001). Significant procedural factors include ischemic time longer than 4 h (Russo et al. 2010; Marasco et al. 2012), suboptimal logistics of graft procurement, and donor-to-recipient weight mismatch.

Some of the associations between primary graft dysfunction and the risk factors previously mentioned are poorly understood. For example, our understanding of the increased risk of primary graft dysfunction in patients bridged with mechanical support devices remains obscure. Longer cardiopulmonary bypass times and tissue trauma during complex reoperations may lead to a greater inflammatory response in these patients. Also, increased graft ischemia due to longer explant times of the native heart may be implicated in graft dysfunction in some cases. The transition from continuous flow physiology to pulsatile physiology after transplantation may also play a role. More recently the preoperative use of amiodarone in patients awaiting heart transplantation has gained attention as some studies have shown a potential relationship (Wright et al. 2017). However this topic remains controversial. The development of more effective donor heart preservation strategies is an area of active research and may lead to procedures that reduce the incidence of primary graft dysfunction in the future. There is also evidence that additional blood cardioplegia administration may protect donor hearts (Wagner et al. 2013). Although the

etiology of primary graft dysfunction remains unknown in many cases, a recent validation study has suggested that the allocation of risky donors to risky recipients amplifies the risk of primary graft dysfunction (Sabatino et al. 2017).

Primary graft dysfunction is further classified as primary graft dysfunction – left ventricle (includes left and biventricular dysfunction) – and primary graft failure, right ventricle (includes right ventricular dysfunction alone). As shown in Table 1, primary graft failure – left ventricle – has been graded as mild, moderate, and severe based on hemodynamic variables, echocardiographic parameters, level of inotropic support, and the need for mechanical circulatory support (Kobashigawa et al. 2014).

Primary graft dysfunction is initially treated with low-dose inotropes and pulmonary vasodilators such as nitric oxide or inhaled epoprostenol. Allowing additional reperfusion time on cardiopulmonary bypass maybe helpful in some cases, but the negative consequences of a prolonged cardiopulmonary bypass time need to be considered. When climbing doses of inotropes are not sufficient to support the newly transplanted heart, the use of temporary mechanical circulatory support becomes necessary. Furthermore, the early institution of mechanical circulatory support may minimize the deleterious consequences of a very prolonged cardiopulmonary bypass time and the secondary negative effects of high-dose vasoactive drugs on end-organ function such as kidneys and liver. Although intra-aortic balloon pumps have been routinely used as first-line short-term devices, more robust forms of support are currently preferred such as extracorporeal membrane oxygenation (ECMO) or temporary ventricular assist devices. Venoarterial ECMO has become a preferred strategy to support patients with primary graft dysfunction over left, right, or biventricular assist devices at many transplant centers (Kobashigawa et al. 2014). ECMO provides biventricular support in addition to pulmonary support in patients with severe pulmonary edema and hypoxemia. Although additional studies are needed, the success rate of venoarterial ECMO to treat primary graft dysfunction approaches 50% (D'Alessandro et al. 2010). Central venoarterial

Table 1 Definition of severity scale for primary graft dysfunction (PGD) (from Kobashigawa J et al.)

PGD-left ventricle (PGD-LV)	Mild PGD-LV: one of the following criteria must be met	LVEF r 40% by echocardiography, or hemodynamics with RAP 4 15 mm Hg, PCWP 4 20 mm Hg, CI o 2.0 L/min/m^2 (lasting more than 1 h) requiring low-dose inotropes
	Moderate PGD-LV: Must meet one criterion from I and another criterion from II	I. One criteria from the following: Left ventricular ejection fraction r 40%, or hemodynamic compromise with RAP 4 15 mm Hg, PCWP 4 20 mm Hg, CI o 2.0 L/min/m^2, hypotension with MAP o 70 mm Hg (lasting more than 1 h) II. One criteria from the following: i. High-dose inotropes – Inotrope score 4 10[a] ii. Newly placed IABP (regardless of inotropes)
	Severe PGD-LV	Dependence on left or biventricular mechanical support including ECMO, LVAD, BiVAD, or percutaneous LVAD. Excludes requirement for IABP
PGD-right ventricle (PGD-RV)	Diagnosis requires either both i and ii or iii alone	i. Hemodynamics with RAP 4 15 mm Hg, PCWP o 15 mm Hg, CI o 2.0 L/min/m^2 ii. TPG o15 mm Hg and/or pulmonary artery systolic pressure o 50 mm Hg, or iii. Need for RVAD

BiVAD, biventricular assist device; CI, cardiac index; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RVAD, right ventricular assist device; TPG, transpulmonary pressure gradient

[a]Inotrope score 1/4 dopamine (%1) þ dobutamine (%1) þ amrinone (%1) þ milrinone (%15) þ epinephrine (%100) þ norepinephrine (%100)67 with each drug dosed in μg/kg/min

ECMO is established cannulating the aorta and the right atrium, with cannulae exiting the mediastinum through the upper abdominal wall to allow for chest closure. Peripheral venoarterial ECMO requires femoral arterial and venous cannulation and also allows for chest closure. A separate catheter should be used for distal limb perfusion in most patients to prevent limb ischemia. The main advantage of peripheral cannulation is the ability to eventually explant ECMO without reopening the chest. The main disadvantage is related to the increased risk of vascular injury and limb ischemia. As venoarterial ECMO does not directly unload the left ventricle, from a physiologic standpoint, it may not represent the best strategy for LV recovery particularly in patients with severe LV dysfunction. The concomitant afterload increment that occurs following initiation of ECMO support in cardiogenic shock patients shifts the left ventricular pressure-volume loops to the right (Fig. 1). This leads to increased left ventricular wall stress and may impact the chances of left ventricular recovery. Patients with profound left ventricular dysfunction and minimal or no ejection represent a particularly challenging problem as they are also at risk of thrombus formation secondary to blood stasis in the left-sided chambers. The addition of a left ventricular unloading device may be necessary in these patients to prevent thrombosis of the left-sided chambers and maximize the chances of recovery. The least invasive strategy to accomplish this goal is the insertion of a percutaneous left ventricular assist device while on ECMO. Conversion to surgical temporary left ventricular or biventricular support devices is an alternative option but is associated with more surgical trauma and potentially higher bleeding risk. Less invasive left ventricular assist devices placed percutaneously or via axillary arterial cannulation represent alternative options. Left ventricular assist devices directly unload the left ventricle and shift the pressure-volume loops to the left, decreasing wall stress and maximizing the chances of recovery. Further studies are needed to define the optimal device that provides to the best chances of recovery with minimal adverse events. Retransplantation may be an option for selected patients with severe early primary graft dysfunction not responsive to the previously described therapeutic strategies.

Secondary Graft Dysfunction

Secondary graft dysfunction has a discernible cause such as hyperacute rejection, pulmonary hypertension, or known surgical complications such as uncontrolled bleeding requiring massive blood transfusions that overdistends a vulnerable right ventricle (Kobashigawa et al. 2014). Additional etiologies of secondary graft dysfunction

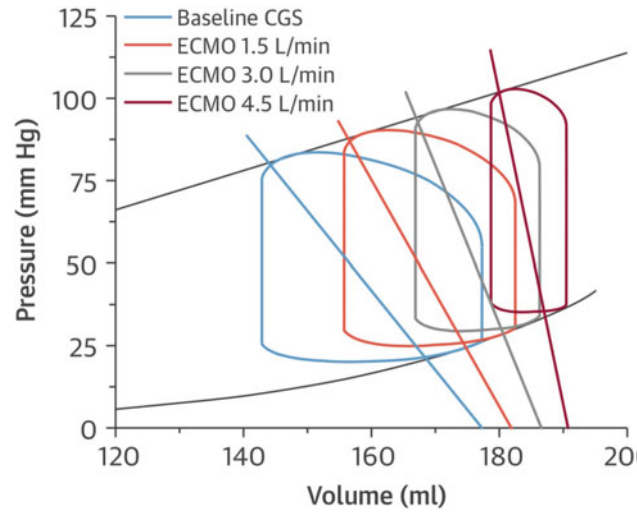

Fig. 1 Pressure-volume loops for ECMO in patients with cardiogenic shock. (Burkhoff et al. 2015)

include unrecognized coronary artery disease, anastomosis narrowing or kinking, etc.

The diagnosis of isolated right ventricular dysfunction secondary to pulmonary hypertension is supported by a postoperative pulmonary gradient ≥15 mm Hg associated with a low cardiac output (Sabatino et al. 2017). A well-demonstrated preoperative recipient risk parameter that increases the occurrence of right ventricular dysfunction is a pulmonary vascular resistance of more than 4 Woods units. Patients with elevated pulmonary vascular resistance are not eligible for heart transplantation. Preoperative identification of pulmonary hypertension is key to prevent this serious complication. Left ventricular assist devices and inotropes are used to reduce pulmonary vascular resistance and allow transplantation. In borderline cases, evaluation of responsiveness of the pulmonary vasculature to pulmonary vasodilators and optimization of heart failure treatment with inotropes and systemic vasodilators are mandatory. The recent trend toward a decrease incidence of secondary graft dysfunction may be related to improved patient selection and improved pretransplant pulmonary hypertension management (Sabatino et al. 2017).

Low cardiac output in the presence of elevated central venous pressure is the hemodynamic manifestation of right ventricular failure. Poor contractility and right ventricular dilatation can be easily observed in the operative field during surgery or assessed intraoperatively with the use of transesophageal echocardiography. Transthoracic or transesophageal echocardiography is essential to asses right ventricular function postoperatively. In cases of isolated right ventricular dysfunction, the left ventricle is underfilled and usually contracts vigorously in response to the inotropes used to treat right ventricular failure. Severe tricuspid regurgitation secondary to dilatation of the tricuspid valve annulus is often also seen on transesophageal echocardiography.

When severe right ventricular failure occurs intraoperatively, the surgeon must rule out mechanical problems at the level of the pulmonary artery anastomosis (kinking, anastomotic stenosis, etc.). Therapeutic strategies to treat right ventricular failure include preload optimization (CVP <15 mm Hg), improved contractility with the use of increasing doses of inotropes, afterload reduction with the use of pulmonary vasodilators, and chronotropic optimization (pharmacologic with β agonists or pacing). Because the right ventricle is very sensitive to systemic hypotension, it is critical to maintain an adequate systemic arterial blood pressure to ensure adequate ventricular perfusion. As the vasoconstrictors used to increase arterial blood pressure may also increase pulmonary vascular resistance, achieving a proper balance between pulmonary and systemic vascular resistances can be difficult. Adequate oxygenation and ventilation must also be assured to avoid the pulmonary vasoconstricting effects of hypoxia and hypercarbia. If these therapeutic maneuvers fail, the use of temporary mechanical circulatory support may be necessary including isolated right ventricular assist devices or venoarterial extracorporeal membrane oxygenation. The use of a newly approved percutaneous temporary right heart pump system may represent the least invasive strategy to support a failing right ventricle.

Hyperacute rejection is mediated by preformed recipient antibodies against donor graft causing widespread hemorrhage and thrombosis within the allograft (Kaczorowski et al. 2013). Because of comprehensive preoperative screening, hyperacute rejection is fortunately a rare complication. Besides graft failure, gross signs of rejection include dusky discoloration, edema, and petechiae (Kaczorowski et al. 2013; Kennel et al. 2012). Diagnosis should be confirmed with intraoperative endomyocardial biopsy (Costanzo et al. 2010). Treatment should be initiated as soon as diagnosis is made. Treatment options include high-dose corticosteroid, plasmapheresis, IVIG, immunosuppressive therapy, inotropes, and vasopressors (Costanzo et al. 2010). Ventricular assist devices and venoarterial ECMO can help provide support during immunotherapy (Kaczorowski et al. 2013). Urgent re-retransplantation may be needed but is associated with high mortality (Costanzo et al. 2010).

Right ventricular dysfunction associated with perioperative bleeding and massive transfusion of blood products is also treated with optimization of

preload, inotropic support, and pulmonary vasodilators. However, rapid control of surgical bleeding and/or correction of coagulopathy is of paramount importance to prevent further right ventricular dilatation, tricuspid regurgitation, worsening dysfunction, and elevated central venous pressure. Once bleeding is controlled, aggressive diuresis, ultrafiltration, or even dialysis may be necessary in some patients to normalize right ventricular preload and relieve venous hypertension that can lead to worsening renal and liver function.

Perioperative Bleeding

In addition to primary graft failure, perioperative bleeding is one of the most common complications after heart transplantation (Kim et al. 2013). Not surprisingly, postoperative bleeding after cardiac surgery is associated with increased morbidity and mortality (Kedziora et al. 2016). As the number of heart transplant patients with a history of previous cardiac surgery is increasing (Lund et al. 2017), the number of reoperative sternotomies associated with this procedure is growing. Furthermore, as many patients are bridged to transplant with a durable left ventricular assist device requiring anticoagulation, the incidence of perioperative coagulopathy is higher. Minimally invasive LVAD insertion techniques, which may result in lower perioperative bleeding at the time of transplantation, have not been widely adopted but hold promise.

Although there are no universal recommendations to guide the reversal of a prolonged INR before redo sternotomy, most centers follow institutional guidelines to achieve this goal. The administration of fresh frozen plasma (FFP) has been historically the only strategy to reverse warfarin in LVAD patients. However, this may be problematic in heart transplantation as it can lead to volume overload when the administration of several units of FFP is necessary. The use of concentrated coagulation factors, such as prothrombin complex concentrate (PCC), has recently become commercially available and is gaining popularity. Low-volume concentrated factors along with vitamin K are very effective and rapidly reverse the effects of warfarin with low side effects (Fig. 2).

Perioperative bleeding represents a significant problem in heart transplantation as it may contribute to exacerbation of primary graft failure and increase rejection rates (Kedziora et al. 2016; Jahangirifard et al. 2017). Postoperative bleeding can be surgical or secondary to coagulopathy. In a study including over 1,400 patients undergoing on-pump cardiac surgery, Kristensen et al. found that 7% of patients underwent at least one reoperation within 24 h due to excessive bleeding. Approximately 56%

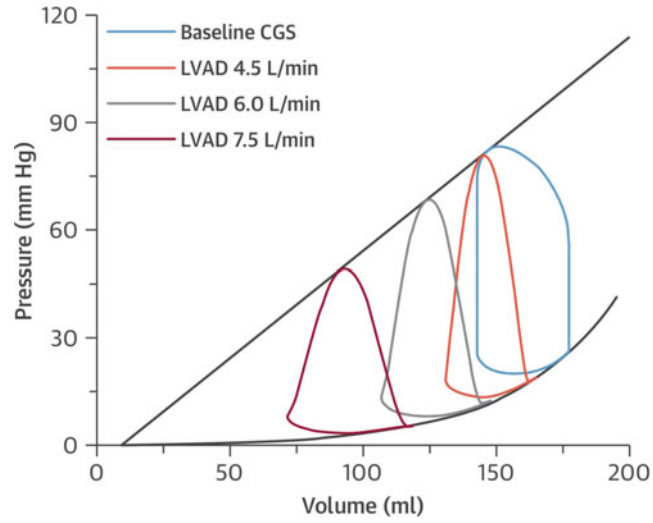

Fig. 2 Pressure-volume loops for LVAD in patients in cardiogenic shock. (Burkhoff et al. 2015)

of those patients had surgical bleeding that required clips or sutures, and 42% had coagulopathic bleeding or diffused oozing. Prolonged cardiopulmonary bypass times can induce coagulopathy by causing decrease in coagulation factors and platelets and activate fibrinolysis (Jahangirifard et al. 2017). Furthermore, intraoperative heparin use, hypothermia, and inflammatory cascade all contribute to abnormal hemostasis (Jahangirifard et al. 2017).

Some of the risk factors contributing to postoperative bleeding after general cardiac surgery include older recipient age, low body mass index, prolonged on-pump times, low ejection fraction, procedures other than CABG, elevated preoperative creatinine, and high EuroSCORE (Kristensen et al. 2012). The first postoperative hemoglobin after heart transplant can be predictive of excessive blood loss as a low level has been shown to correlate with higher chest tube output, need for re-exploration, and higher transfusions rates (Kedziora et al. 2016).

To prevent postoperative bleeding in heart transplant recipients, the International Society for Heart and Lung Transplantation (Costanzo et al. 2010) recommends that active clotting time be checked at multiple points during surgery to monitor level of heparin activity. Thromboelastography may be used during or after transplant to monitor hemostasis. FFP, platelets, and fibrinogen should be transfused based on measured levels. Recombinant factor VIIa may also be used in cases of intractable or excessive bleeding. Tranexamic acid and epsilon-aminocaproic acid can be used before cardiopulmonary bypass to reduce risk of bleeding in selected patients. Intraoperative use of fibrinogen after termination of bypass pump and heparin reversal may help reduce postoperative bleeding but may enhance postoperative acute kidney injury (Jahangirifard et al. 2017). Few studies have investigated postoperative bleeding in heart transplant recipients. Therefore, most recommendations are extrapolated from general cardiac surgery literature (Costanzo et al. 2010). Further studies are needed to improve prevention and management of postoperative bleeding after heart transplantation. Meticulous surgical technique, short cardiopulmonary bypass times, and properly correction of medical coagulopathy play a major role.

In patients that demonstrate excessive bleeding following surgery which cannot be obviously explain by medical coagulopathy, early return to the operating for an exploration is mandatory to minimize the amount of bleeding and prevent development of right ventricular failure secondary to massive administration of blood products. Patients bridged with extracorporeal membrane oxygenation may be more susceptible of bleeding and require especial attention. Also, patients who require temporary mechanical support for the treatment of primary graft dysfunction are at increased risk of postoperative bleeding. Mediastinal exploration for bleeding should be undertaken persistent high chest tube output (400 mL/hr. for 1 h, $>$ 300 mL/hr. for 3 h, and 200 mL/hr. for 4 h), any circulatory instability associated with bleeding, or radiographic or echocardiographic evidence of retained thrombus (Costanzo et al. 2010).

Tricuspid Regurgitation

Tricuspid valve regurgitation (TVR) is the most common valvular complication following orthotopic heart transplantation and affects up to 84% of the patients (Wong et al. 2008). The use of bicaval implantation technique and the construction of tension free anastomosis are important to reduce the risk of TVR in the cardiac allograft (Davies et al. 2010; Aziz et al. 1999). While concomitant tricuspid annuloplasty during heart transplantation has been proposed to decrease the incidence of TVR (Jeevanandam et al. 2006), this adjunct procedure is not currently widely accepted by the transplant community. Most patients with tricuspid valve regurgitation develop only mild to moderate regurgitation. In severe forms, however, tricuspid regurgitation can lead to right-sided failure symptoms including lower extremity edema, hepatorenal dysfunction, ascites, and dyspnea. The decision to surgically correct TVR can be very difficult, as

certain clinical scenarios have high risk of failure. Functional etiologies of tricuspid regurgitation associated with high pulmonary vascular resistance must be carefully evaluated. As it typically occurs with the native heart, anatomic etiologies have the greatest chances of success compared to functional etiologies. While repair techniques have been successfully described, there is an emerging body of evidence to support replacement as the more durable option (Raghavan et al. 2006). As mechanical valves are impractical in the heart transplant patient, biologic valves are preferred as they allow continued access to the right ventricle for biopsies. Furthermore, durability is acceptable in the low pressure system of the right-sided heart chambers.

Aortic Complications

Aortic complications can occur in 1–2% of patients receiving heart transplantation (Vigano et al.). The incidences may be higher in patients with aortic risk factors such as Marfan syndrome (Audenaert et al. 2015). Acute aortic ruptures can occur early after transplantation due to weakness of aortic tissue, technical errors, or severe hypertension (Vigano et al. 1999). The difference in compliance between donor and recipient aortic tissue may create excess tension on the suture line and subsequent predisposition to rupture or dissection. A double layer of non-absorbable suture technique is advocated by many surgeons. Atherosclerosis and hypertension are also additional risk factors. Preoperative CT of the chest and intraoperative epiaortic ultrasound can facilitate evaluation of aortic atherosclerosis and calcifications that can predispose to aortic complications. Additionally, mediastinitis and infection can lead to the development of mycotic pseudoaneurysm at the aortic anastomosis. In such cases, antibiotics and early surgical intervention are key to successful treatment. Both Dacron and homograft have been successfully used for aortic replacement and reconstruction in these challenging cases (Patane et al. 2009).

Heart Oversizing

Proper donor-to-recipient organ size matching represents a critical aspect of heart transplantation. It has been suggested that heart undersizing is associated with worse outcomes in nonobese recipients (Bergenfeldt et al. 2017). Although heart oversizing has not been associated with worse outcomes, extreme cases of oversizing can lead to the inability to properly close the sternum. Female recipients who receive male hearts and recipients with non-dilated hearts are at particular risk. Forcing sternal closure in these cases can have deleterious hemodynamic consequences secondary to right ventricular compression and dysfunction. However, leaving the chest open for a prolonged period of time hoping for a successful delayed sternal closure can increase the risk of mediastinal infections. Early consultation with plastic surgery is recommended in these difficult cases. The plastic surgeon armamentarium includes a variety of surgical options including pectoralis, omental, rectus abdominis, latissimus dorsi, as well as skin and subcutaneous flap closures. A sternectomy may be necessary in some of these cases. It is very important to avoid this problem by selecting an appropriate size heart following the recommended guidelines (Costanzo et al. 2010).

Wound Complications

Surgical wound infections (SWI) are an important source of morbidity and mortality after heart transplantation. These complications can often lead to life-threatening events such as sternal dehiscence and mycotic aneurysm formation of the aorta. The incidence of SWI after heart transplant has been reported in 8–15% of patients and is higher than after other types of cardiac surgery procedures (Zuckermann et al. 2011). Data on risk factors for SWI are limited and controversial due to small study sizes. However, some potential risk factors identified include age, body mass index, diabetes mellitus, immunosuppressive regimens (i.e., sirolimus vs. mycophenolate mofetil), prolonged cardiopulmonary bypass time,

reoperation, and pretransplant use of ventricular assist devices (Zuckermann et al. 2011). The most commonly isolated organisms are Gram-positive organisms, such as methicillin-resistant *Staphylococcus aureus*. Infections that demonstrated mixed organisms can also occur. In rare instances infection with Gram-negative organisms (i.e., *E. coli*, *Acinetobacter*) and fungal organisms (i.e., *Aspergillus*) has been reported as well (George et al. 2006).

The diagnosis of surgical wound infections after heart transplant requires high clinical suspicion. The typical signs of infection such as fever and leukocytosis may be absent due to immunosuppression. In two retrospective review studies (Senechal et al. 2004; Filsoufi et al. 2007), fever and leukocytosis were present in only 30 and 40% of patients with deep sternal wound infections and mediastinitis. Sternal pain out of proportion was the most common presentation (Senechal et al. 2004). Local signs of wound infection such as purulent drainage or erythema were present in only 33 to 40% of cases. Most patients present with more than one clinical signs. Computed tomography of the chest demonstrating mediastinal air or fluid collection can be supportive of this diagnosis.

Successful treatment of sternal wound infections requires early and aggressive surgical management in addition to antimicrobials. Several surgical management options have been described to successfully treat mediastinitis following heart transplantation. These include early debridement with substernal irrigation and primary closure (Abid et al. 2003), sternal debridement and closed-chest drainage (Senechal et al. 2004), as well as open debridement with vacuum-assisted drainage (Filsoufi et al. 2007). Muscle or omental flaps may also be used to help close dead space after debridement (Carrier et al. 2001).

Pericardial Effusion

Pericardial effusions not secondary to bleeding are commonly observed after heart transplantation, occurring in 20–36% of patients receiving heart transplant (Quin et al. 2002; Urbanowicz et al. 2015). There is no clear etiologic explanation for its occurrence. One proposed theory is that pericardial effusions represent an immune-related process. Several studies have suggested that pericardial effusions are associated with higher incidence of acute rejection episodes with more severe histologic grading (Ciliberto et al. 1995). A positive recipient-donor weight mismatch and absence of previous cardiac surgery have also been observed to contribute to development of large pericardial effusions (Hauptman et al. 1994). This is thought to be due to relatively well-preserved pericardium and large recipient-donor weight mismatch providing favorable anatomy for exudation of fluid into the pericardial space (Hauptman et al. 1994). Other risk factors identified include prolonged donor ischemia time (Al-Dadah et al. 2007), intraoperative aminocaproic acid use (Quin et al. 2002), postoperative immunosuppression with mTORi (Bouzas-Mosquera et al. 2008), and worse preoperative clinical condition (Urbanowicz et al. 2015). Rare cases of pericardial effusion due to lymph leak (chylopericardium) have also been reported (Wierzbicki et al. 2016).

While the clinical course is generally benign, significant large pericardial effusions causing cardiac tamponade can occur. Therefore, close early postoperative monitoring is recommended. Transthoracic echocardiography is generally the modality of choice (Costanzo et al. 2010). Most effusions will resolve within 3 months and are not associated with adverse clinical outcomes (Al-Dadah et al. 2007). Therefore, pericardial effusions not causing hemodynamic instability do not require intervention unless an infectious etiology is suspected (Costanzo et al. 2010). Patients with echocardiographic evidence of tamponade or hemodynamic instability can be successfully treated with percutaneous or surgical drainage (Costanzo et al. 2010). Those with recurrent symptomatic effusion or failing pericardiocentesis may be treated with subxiphoid pericardial window or pericardiectomy (Hauptman et al. 1994). A pericardial soft drain can help reduce pericardial effusions, but the duration of drainage should be balanced against the potential risks for wound infection and length of hospital stay (Kim et al. 2016).

Constrictive Pericarditis

Although constrictive pericarditis is usually considered a particularly rare complication following heart transplantation, some series report a higher incidence than constrictive pericarditis following general heart surgery (Carrier et al. 1994). Among the risk factors associated with this increased incidence, we can list recurrent pericardial effusions from traumatic right ventricular biopsies, mediastinal infections, and increased inflammation after multiple sternotomies. Recurrent episodes of rejection have also been linked to an increased risk of constrictive pericarditis. Constrictive pericarditis is characterized physiologically by impaired ventricular diastolic filling due to a fixed pericardial volume resulting in the classic dip-and-plateau pattern observed on intracardiac pressure tracings (Kumar et al. 2008). Elevation of central venous pressures and Kussmaul sign is frequently seen on physical examination. Clinically patients demonstrate symptoms of right-sided heart failure, including peripheral edema and liver and bowel congestion, leading to ascites and early satiety. Pleural effusions can present later during progression of the disease. The definitive treatment of chronic pericardial constriction is surgical pericardiectomy. This is a significant surgical procedure associated with considerable morbidity and a mortality greater than 6% (Bertog et al. 2004). Because of the high operative risk, most patients undergo multiple diagnostic procedures to ensure a correct diagnosis.

Conclusions

With the introduction of durable mechanical circulatory support, the landscape of the heart transplant recipient population has changed significantly since the early heart transplants were performed 50 years ago. As the use of circulatory support devices as a bridge to transplantation continues to grow, an increasing number of patients are brought to the operating room with a history of multiple cardiac surgical procedures. Furthermore, most of these patients are anticoagulated with warfarin. The rapidly evolving characteristics of this patient population result in longer and more complex surgical procedures, higher risk of reentry injuries, longer cardiopulmonary bypass times, greater probability of coagulopathy and bleeding, higher incidence of primary graft failure, increased exposure to wound healing problems, pericardial effusions, etc. The skills and experience of the surgical team is key to prevent and treat these surgical complications that can be associated with high morbidity and mortality in this complex patient population.

Despite the increasing technical and management challenges posed by this unique patient population during surgery, outcomes after heart transplantation have continued to improve over the last two decades thanks to improved early survival. This is likely secondary to improved recognition and management of primary graft dysfunction in the operating room and early ICU course (Kobashigawa et al. 2014). The diagnosis of primary graft dysfunction was historically associated with very poor prognosis before temporary mechanical support was adopted as a lifesaving strategy. Recent studies have found that more than 50% of primary graft failure patients supported with extracorporeal membrane oxygenation or ventricular assist devices demonstrate recovery. Current and future percutaneous or minimally invasive ventricular assist devices may improve chances of graft recovery with less adverse events. The expertise and clinical judgment of the transplant team play a significant role in the successful management of surgical complications following heart transplantation.

Cross-References

- ▶ Cardiac Allograft Rejection
- ▶ Donor Operation and Organ Preservation
- ▶ Matching Donor to Recipient

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