Surgical aspects of valve replacement in carcinoid heart disease

Anders Albåge[1] and Marco Montibello[1]

[1]Uppsala University Hospital

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Abstract

Tricuspid and pulmonary valve replacement in patients with carcinoid heart disease (CaHD) reduces right heart failure and improves prognosis. The surgical literature is limited concerning technical aspects of valve replacement in CaHD. Although dedicated multidisciplinary care is required, optimization of surgical details is important and may lead to better postoperative outcomes in these frail patients.

Introduction

Carcinoid heart disease (CaHD) is a complication of neuroendocrine tumors (NETs), rare slow-growing malignancies which usually originate in the small intestine and metastasize to the liver. High levels of circulating serotonin and other vasoactive substances released by the tumors cause fibrosis and retraction of the tricuspid (TV) and pulmonary valves (PV), resulting in severe regurgitation and/or stenosis. This eventually leads to progressive right heart failure, often worsening the forecast of the patient further (11Hayes AR, Davar J, Caplin ME. Carcinoid Heart Disease: A Review. Endocrinol Metab Clin North Am. 2018;47(3):671-682.). Valve surgery in CaHD patients has been shown to reduce right heart failure, increase functional capacity, allow for more aggressive oncological treatment and improve long-term prognosis. Several smaller case series of 19-32 patients have been reported (22Bhattacharyya S, Raja SG, Toumpanakis C et al. Outcomes, risks and complications of cardiac surgery for carcinoid heart disease. Eur J Cardiothorac Surg. 2011;40:168-172.,33Mokhles P, van Herwerden LA, de Jong PL et al. Carcinoid heart disease: outcomes after surgical valve replacement. Eur J Cardiothorac Surg. 2012;41(6):1278-83.,44Edwards NC, Yuan M, Nolan O et al. Effect of Valvular Surgery in Carcinoid Heart Disease: An Observational Cohort Study. J Clin Endocrinol Metab. 2016;101(1):183-90.), with acceptable results given the oncological prognosis involved. Nguyen et al reported on 240 CaHD patients, who had valve surgery over the course of 30 years (55Nguyen A, Schaff HV, Abel MD et al. Improving outcome of valve replacement for carcinoid heart disease. J Thorac Cardiovasc Surg. 2019;158(1):99-107.,66Ayala AR, Salerno TA. Commentary: Dance with me to the end of love: Serotonin and the carcinoid heart. J Thorac Cardiovasc Surg. 2019;158(1):108-109.). Thirty-day mortality was 5%, while 2-year survival was 60%. Functional results were greatly improved postoperatively and most patients died from progressive tumor burden. Despite prevalent outcome reporting, there is a shortage in the surgical literature concerning the technical aspects and optimization of surgical details in these rare patients. Furthermore, replacement of the TV or PV is uncommon in routine adult cardiac surgery practice. The focus of the current report is not to report patient outcomes, but to describe some of the surgical technical issues concerning valve replacement in CaHD, based on our recent experience of 17 cases in the past 4 years (Table 1).

Pre- and perioperative considerations

Indications for valve surgery in CaHD patients are outlined in guidelines (11Davar J, Connolly HM, Caplin ME et al. Diagnosing and Managing Carcinoid Heart Disease in Patients With Neuroendocrine Tumors: An Expert Statement. J Am Coll Cardiol. 2017;69(10):1288-1304.) and include progressive right heart

failure with echocardiographical findings of moderate to severe insufficiency of the right-sided valves. The TV is always involved in surgical candidates and is usually severely regurgitant, while the PV is often affected, showing a combination of stenosis and regurgitation. The decision for valve replacement should be based on a multidisciplinary evaluation of general operability in relation to oncological status and cardiac function. Timing of surgery with preoperative optimization of nutritional status and somatostatin analog treatment for carcinoid hormonal activity is essential. Studies indicate that earlier intervention rather than late improves outcomes (7). Valve surgery always involves tricuspid valve replacement (TVR) and most often pulmonary valve replacement (PVR). In our experience, the PV pathology is often underestimated on echocardiography, and a larger regurgitation may be unmasked by a higher forward flow after TVR, if leaving the PV untreated. Also, an uncorrected significant pulmonary regurgitation after TVR may lead to progressive right heart dilatation and poorer results (22Connolly HM, Schaff HV, Mullany CJ et al. Carcinoid heart disease: impact of pulmonary valve replacement in right ventricular function and remodeling. Circulation. 2002;106(12 Suppl 1):I51-I56.). Thus, a low threshold is recommended for replacing the PV. The aortic or mitral valves may also be involved in 10-15% of cases with CaHD. A previous report has shown that surgery of the left-sided valves is not a factor for worse results and should be performed concomitantly with right-sided valve surgery if indicated (5).

A particular risk with CaHD patients is the occurrence of a carcinoid crisis during surgery. Anesthesia, surgery or drugs may trigger release of vasoactive hormones, causing potentially life-threatening circulatory instability with severe hypotension and flushing (33Castillo J, Silvay G, Weiner M. Anesthetic Management of Patients With Carcinoid Syndrome and Carcinoid Heart Disease: The Mount Sinai Algorithm. J Cardiothorac Vasc Anesth. 2018;32(2):1023-1031.). Routine therapy to counter this complication is infusion of short-acting octreotide, started prior to surgery (in some cases 24 hours), continued perioperatively and for several days postoperatively. Furthermore**,** intraoperative protection of right ventricular (RV) function is key. The RV is dilated in most surgical candidates, and surgery should be performed before significant RV dysfunction develops. CaHD patients are at increased risk of bleeding during surgery, due to their oncological status, severe preoperative venous stasis and reduced liver function. Increased attention to bleeding control is important, regarding surgical technique, use of autologous blood recovery systems and optimization of postoperative coagulation using point-of-care techniques.

Operative techniques

Both mechanical and bioprosthetic valves have been used for the right-sided valve replacements in CaHD. However, in recent reports, bioprostheses seem to be preferred, as life-expectancy is limited in these patients and warfarin therapy may not be well managed (5).

Aortic cannulation is performed in standard fashion, although inserting the cannula more to the right side of the ascending aorta will improve exposure of the PV. Both venae cavae are snared after separate venous cannulation and commencing CPB. Triple lines for pump suction are utilized and CO_2 wound irrigation is started. Basically, both right-sided valves can be replaced on CPB using no or intermittent aortic cross-clamping. In our view, cardioplegic arrest provides better visualization and detailed evaluation of the diseased valves, and more accurate placement of valve sutures. Before starting CPB, the planned incision on the anterior surface of the PA is marked by a felt pen. The order of valve replacement is by surgeon preference, but we generally begin with the PV. We use only antegrade cold blood cardioplegia, every 20 minutes and in large amounts, for optimal protection of the RV. Retrograde cardioplegia may be insufficient in this respect.

Pulmonary valve

An incision is made in the proximal PA and extended backwards across the PV and 3-4 cm into the right ventricular outflow tract (RVOT)(Fig 1A). The PV is exposed by stay-sutures, evaluated and the fibrotic cusps are excised (Fig 1B). A bioprosthetic valve of appropriate size is measured. Pledgeted matress sutures are placed in the annulus, matching the commissures of the prosthesis with the native annular shape (Fig 1C). Approximately one-fourth of the prosthesis is left unanchored with one commissure pointing anteriorly (fig 1D), to enhance RVOT and PA dimensions, as the inserted prosthesis will be seated in a slightly different

angle than the native PV. A wide bovine pericardial patch is attached with a running polypropylene suture, starting from the PA corner and continued proximally on both sides. The remaining part of the prosthetic valve is anchored to the patch horizontally, either with a running suture or with additional pledgeted sutures from the sewing ring through the patch. Lastly, the remainder of the patch is sutured to the RVOT incision (Fig 1E,F).

Tricuspid valve

After opening the right atrium (RA), a methodical inspection for and closure of a persistent foramen ovale (PFO) should be performed. The TV is generally fibrotic with retracted non-mobile leaflets and a narrowing of the valve opening. A prosthetic valve of the largest possible size should be implanted. Some authors advocate resection of the anterior and posterior leaflets, while leaving the septal leaflet intact with chords. We routinely keep all leaflets, making multiple incisions from the free edge to the annular plane and leaving the chordal attachments intact to preserve tricuspid annular and RV synchrony (Fig 2A,B,C). This technique widens the valve sufficiently and allows for an adequately sized prosthesis. Occasionally, a thickened chord clearly retracting the valve may have to be cut. We use atrially pledgeted sutures for anchoring the valve, passing the needles through the annulus and the body of the leaflets (Fig 2D). Caution is advised, as the annulus is frail, and deep bites in the posterior leaflet area may compromise the right coronary artery. We prefer pericardial bioprosthetic valves with a softer sewing ring, which fit better and can be tied in more gently without ripping the annular tissue. The valve should be oriented with one commissure towards the corner of the native anteroseptal commissure and another valve commissure towards the posteroseptal commissure.

Aortic and mitral valves

In very few CaHD patients, the aortic or mitral valves are severely regurgitant in addition to the dysfunctional right-sided valves and must be addressed with standard bioprosthetic AVR and/or MVR concomitantly. Repair of the mitral and aortic valves have also been reported. In our experience, carefully selected patients can tolerate and benefit even from quadruple valve replacement (11Albåge A, Alström U, Forsblad J, Welin S. Quadruple Bioprosthetic Valve Replacement in a Patient With Severe Carcinoid Heart Disease. JACC: Case Reports Vol 2, Issue 2, Feb 2020. DOI: 10.1016/j.jaccas.2019.11.030).

Postoperative course

Due to the risk of complete heart block after TVR, we routinely place permanent epicardial pacing wires on the RV and sometimes on the RA. The electrodes are placed in a subclavicular pocket on either side. In our experience, the majority of patients will not need a permanent pacemaker, but if so it may be connected in a separate procedure a few days postoperatively. CaHD patients undergoing valve surgery have a slower recovery and normally require prolonged intensive care to monitor cardiac and renal function, control of infection and carcinoid activity. Intravenous octreotide therapy is usually continued for 3 days postoperatively in collaboration with endocrine oncologists. For anticoagulation, we routinely use low-molecular weight Heparin for 3 months, and then switch to aspirin.

Conclusion

TVR and PVR are the most common procedures in surgery for CaHD. Although these patients are best cared for by a dedicated multidisciplinary team, optimization of surgical details is important and may lead to improved postoperative outcomes.

Figure legends

Figure 1A : Longitudinal incision from the distal PA to the RVOT.

Figure 1B : Exposed PV showing fibrotic cusps.

Figure 1C : Implantation of pulmonary bioprosthesis (Carpentier-Edwards Magna Ease), conforming to the natural PV commissures.

Figure 1D : Anterior portion of the bioprosthesis left unanchored.

Figure 1E+F : Enhancement of PA and RVOT with bovine pericardial patch (Fig 1A + 1D same patient, fig 1B + 1C different patients).

Figure 2A+B+C : Opened RA showing a fibrotic retracted TV. Multiple incisions are made from the free edge to the annulus respecting chordal attachments (suggested black lines fig 2A, performed in different patient fig 2B, illustration fig 2C).

Figure 2D : Implantation of a tricuspid bioprosthesis (Carpentier-Edwards Perimount Plus).

M+F		11+6
Mean age		**64.2**
Type of valve surgery	**TVR only**	**2**
	TVR+PVR	**12**
	TVR+PVR+AVrep	**1**
	TVR+PVR+AVR+MVR	**2**
Additional surgery	**CABG**	**1**
	PFO closure	**2**

Table 1: Patients undergoing valve surgery for CaHD 2016-2020.AVR – aortic valve replacement, AVrep – aortic valve repair, MVR – mitral valve replacement.

Author contributions

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References