Chapter

Surgery for Tricuspid Valve Endocarditis in the Current Era

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Abstract

Tricuspid valve endocarditis (TVE) continues to be on the rise and has been mostly attributed to the growing epidemic of intravenous drug abuse (IVDA). Other risk factors include long-term indwelling central venous catheters and implantable cardiac devices. While medical management continues to be the first line therapy, surgery is indicated when medical management fails, and in the presence of hemodynamic deterioration, recurrent septic pulmonary embolization and/or persistent sepsis. Tricuspid valve (TV) excision once was the main surgical strategy, but other options include TV repair/reconstruction and replacement. Remaining challenges include management of drug-induced endocarditis and the best strategy for recurrent infection.

Keywords: endocarditis, tricuspid valve endocarditis, intravenous drug abuse, implantable cardiac devices

1. Introduction

Infective endocarditis remains a serious disease that is associated with significant morbidity and mortality. The overall incidence is relatively low, about 5/100,000 person-years [1]. In the current era, aggressive medical therapy and earlier surgical interventions with few exceptional circumstances have been the goal. Recent literature shows relatively stable mortality rates, despite the improvement in diagnostic and therapeutic tools including medical therapy and surgical techniques [2]. Isolated TVE overall is less common in comparison to left sided endocarditis. In a study of 801 adult patients with endocarditis, tricuspid or multivalvular involvement was present in 31.2% and this was a significant risk factor of early mortality on multivariate analysis [3]. The incidence of TVE is increasing, mostly related to the growing epidemic of drug abuse. In the report by Seratnahaei et al., the incidence of tricuspid endocarditis increased from 6% between 1999 and 2000 to 36% between 2009 and 2010 [4].

2. Epidemiology

Right-sided endocarditis occurs at lower incidence in comparison to left-sided infection due to the less common pathology that involves the right heart in addition to the lower pressures and decrease oxygen content in comparison to the left side of the heart [5].

Right-sided endocarditis represents 5–10% of infective endocarditis cases [6], and TVE constitutes the majority of these cases. Of all surgeries for endocarditis in North America, 4.1% involves TVE [7].

3. Natural history

Isolated TVE has been reported to have a favorable prognosis and good response to medical therapy with few exceptions. Ginzton and colleagues studied 16 patients (12 had history of IVDA) with TVE to define echocardiographic criteria to help identifying those at risk for complications or need for TV surgery [8]. The authors concluded that TV vegetations tend to resolve with time, however, those with persistent infection, cardiomegaly and right heart failure are at increased risk, and no M mode or two-dimensional echocardiographic feature is a predictor of outcome.

This tendency for TV vegetations to resolve overtime is different from left-sided endocarditis which tend to persist. This could be related to bacteriological cure or silent embolization to the lung overtime.

4. Risk factors

- *Intravenous Drug Abuse (IVDA)*
  - This is the most common predisposing factor for right sided endocarditis and it ranges between 2 and 5% per year.
  - Approximately 15 opioid overdose deaths and 5 heroin overdose death per 100,000 population reported in 2016, in comparison to 6 opioid overdose deaths and one heroin overdose death per 100,000 population in 2010, according to the Centers for Disease Control data [9]. This growing epidemic of drug abuse constitutes a major risk factor for TVE. In an analysis of the Society of Thoracic Surgeons national database, isolated TV operations were performed in 1613 patients with intravenous drug-associated TV endocarditis between 2011 to 2016 [10].
  - Structural abnormalities of the TV have been noticed in those with chronic use of injected drugs. These abnormalities have been visualized by echocardiography and include leaflet thickening, and/or prolapse with or without regurgitation [11].
- *Long-term Indwelling Catheters*
  - One of the most common complications of long-term indwelling central venous catheters that are used for long-term hemodialysis or long-term delivery of medications such as chemotherapy has been infection [12]. The incidence of this type of infection is increasing and is parallel to the increase use of indwelling central venous catheters. In the United Sates, it is estimated that about 35,000 cases of catheter-related *Staphylococcus aureus* infection are reported each year with 6% of them developing into endocarditis [13].
- *Implantable Cardiac Devices*
  - This is a severe type of infection that is seen in patients with permanent pacemakers and defibrillators, and its incidence has been on the rise due to the increase use of these devices. In a prospective study of 2760 patients by Athan et al. [14], the incidence of cardiac device-related infection was 6.4%. Coexisting valvular involvement was present in 37.3%, of which 24.3% was TVE.

- The risk of infection after pacemaker implantation is 0.5–1% in the first year after implantation and with the increase complexity of the implanted device, and the need for device replacement or revision procedures, it increases further [15].

- *Congenital Heart Defects*

  - Patients with ventricular septal defect (VSD) and left-to-right shunts are at risk of endocarditis. TV involvement occurs secondary to the jet lesion against the anterior or the septal leaflets of the TV. Current guidelines do not recommend endocarditis prophylaxis anymore in those with acyanotic heart defects due to the low risk of its occurrence in this population [16].

  - Endocarditis in the presence of atrial septal defects is extremely rare due to the slow velocity of the shunt flow, and only few reported cases exist in the literature. An explanation of such occurrence could be related to the development of tricuspid regurgitation secondary to right ventricular volume overload which increases the risk of TV involvement [17].

5. Microbiology

The most predominant organism is *Staphylococcus aureus* (60–90%). In IVDA, there has been an increase in methicillin-resistance and polymicrobial infection [18]. Coagulase-negative Staphylococcus infection occurs more frequently in the presence of prosthetic valves and indwelling central catheters. Although infection with Streptococci can occur (<10%), it remains higher in left-sided endocarditis [19]. There is also increase in infection with Pseudomonas and other gram-negative bacteria. Fungal infection is not uncommon and has been associated with high mortality especially in immunocompromised patients and those with intracardiac devices [20].

6. Clinical presentations

Clinical presentation may vary depending on degree of involvement/destruction of the tricuspid valve and presence or absence of complications. The most common presentation has been persistent fever, chills, anorexia, fatigue, cough, dyspnea, dizziness, cardiac murmur, and varying degrees of heart failure. Septic shock may occur in severe cases.

7. Complications of tricuspid endocarditis

The most common complications are related to valvular destruction with subsequent varying degrees of tricuspid regurgitation. Large vegetations can lead to valvular obstruction or recurrent septic pulmonary embolization (**Figure 1(A)**) and hemoptysis or pulmonary abscesses (**Figure 1(B)**). This repeat pulmonary embolization can result in elevation of the right-sided pressures, which in the presence of atrial level shunting, can lead to systemic embolization as well [21]. In severe cases, abscess formation is not uncommon [22], so as varying degrees of atrioventricular block. Acute diffuse glomerulonephritis secondary to immune complex formation and complement C3 deposition in the renal glomeruli resulting in acute renal failure

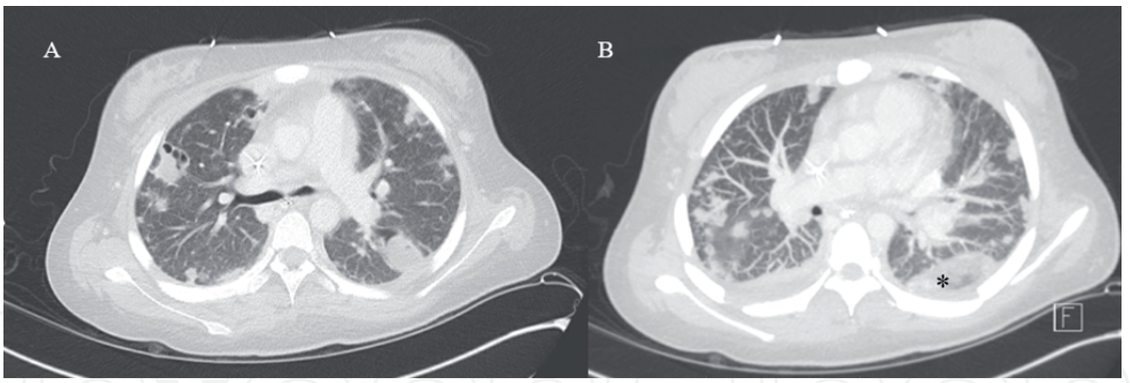

Figure 1.
(A and B). Preoperative computed tomography scan in a patient with isolated tricuspid valve endocarditis secondary to intravenous drug use showing: (A) multiple bilateral septic pulmonary emboli with cavitation. Notice in (B), the development of necrotic changes with possible abscess (asterisk) formation in the left lung.

has been reported with *Staphylococcus aureus* [23]. When sepsis is uncontrolled, this can lead to right heart failure, septic shock, and multiorgan failure.

Acquired VSD can occur after an episode of endocarditis. Gerbode described in 1958 [24] an acquired form of left ventricular-to-right atrial shunting with successful repair. Acquired Gerbode defect is a type of paramembranous VSD that is associated with left ventricular-to-right atrial shunting which can occur above (Type I), below (Type II) or both sides (Type III) of the septal leaflet of the TV [25].

8. Diagnosis

Diagnosis depends on high index of suspicion and by identifying the patient's risk factors and the occurrence of the usual manifestation of infection such as persistent fever and other signs of bacteremia. Echocardiography remains the most appropriate initial test in these patients. Both transthoracic and transesophageal modalities are important to confirm the diagnosis, identify the presence of vegetations (**Figure 2**; **Video 1**—https://bit.ly/3mDCQxK), evaluate the degree of TV destruction/regurgitation (**Video 2**—https://bit.ly/3mDCQxK), rule out any intra-cardiac shunts and evaluate the left side of the heart for any evidence of multivalvular involvement.

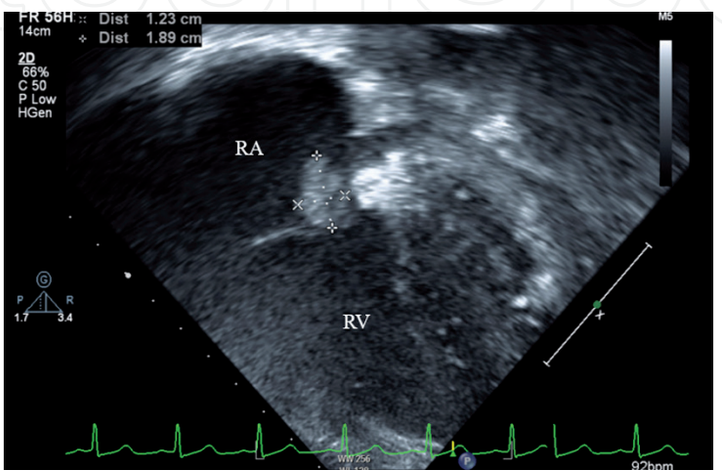

Figure 2.
A large tricuspid valve vegetation (1.9 × 1.2 mm) is shown on preoperative transthoracic echocardiography. RA: Right atrium; RV: Right ventricle.

Computed tomography (CT) scan is indicated to evaluate the lung parenchyma and vasculature. Due to the difficulty in diagnosing septic pulmonary emboli, we obtain chest CT scan routinely as this may change the timing of intervention. Other relevant tests depend on presence of other systemic manifestations of infection/embolization may include other cross-sectional imaging, brain imaging etc.

It is important to know that it is difficult to apply the Duke's criteria [26] to diagnose TVE due to: (1) the unique anatomy of the structures in the right side of the heart which could simulate vegetations, (2) embolization if occurred is pulmonary rather than systemic which is difficult to diagnose until it evolves into pulmonary infarcts or abscesses, and (3) many of the radiologic findings can be mistaken for pneumonia.

9. Treatment

- *Medical Treatment*

  In general, right-sided endocarditis resolves with medical treatment in the majority of cases (70–85%).

- *Surgical Treatment*

  Although antibiotics remained the first line treatment for TVE, several patients may fail this line of therapy and require surgical interventions. In addition, those who have residual TV regurgitation will need either early or late reconstruction or replacement of the TV.

  ○ Indications for Surgical Intervention

The following constitutes reasonable indications for surgical intervention [27]:

1. Right heart failure secondary to severe tricuspid regurgitation with poor response to medical therapy.

2. Persistent bacteremia/sepsis (> 7 days) with poor response to antibiotics which sometimes occurs in the presence of a highly virulent bacteria (*Staphylococcus aureus*, and Pseudomonas bacteremia), and infection with organisms that are difficult to eradicate such as fungi.

3. Recurrent septic pulmonary embolism with or without right heart failure.

4. Large TV vegetations (>20 mm) with or without right heart failure.

5. Abscess (more common in the presence of a prosthesis)

   ○ Timing of Surgery

While the exact timing of surgery remains unclear in many of these scenarios, it should be a team approach in decision with input from the cardiologist, cardiac surgeon, and the infectious disease specialist. In absence of urgent/emergent surgical indications (persistent sepsis, recurrent septic embolization, and heart failure), surgery is usually done on elective basis after a good duration of antibiotic therapy and appearance of negative blood cultures. This increases the chance of successful valve repair and minimize risk of recurrent infection. Decision is a bit more complicated in IVDA and in those with recurrent endocarditis.

Other factors that may affect the timing include: (1) the presence of infected intracardiac devices, (2) the causative organism (fungal may not respond to medical therapy), and (3) the presence of concomitant left-sided infection.

- **Surgical Options**

The principles of surgical treatment for isolated TVE follows the same principles in endocarditis cases which include thorough debridement, vegetation removal (**Figure 3**), and excision of all infected non-viable tissues. The preference after that will be to minimize the use of prosthetic materials especially in patients with history of IVDA and to attempt TV repair if possible.

- *Tricuspid Valvectomy*

Excision of the TV has been proposed for those with massive valvular destruction and concerns with compliance to therapy, continued IVDA, and increased risk with repeat operations for infected prosthetic TV [28]. In the presence of low-normal pulmonary vascular resistance, this option may work as a temporary measure till sepsis is controlled.

The downside of this approach is right heart failure with development of ascites, peripheral edema and low cardiac output and this should be considered as a bridge for valve replacement once infection is cleared.

- *Tricuspid Valve Repair*

TV repair should be strongly considered especially in IVDA cases to minimize the use of prosthetic materials and prosthesis that can lead to recurrent infection. The technique of valve reconstruction depends on the degree of valvular destruction:

1. **Direct Suturing:** suitable for small defects that is limited to one or two leaflets.

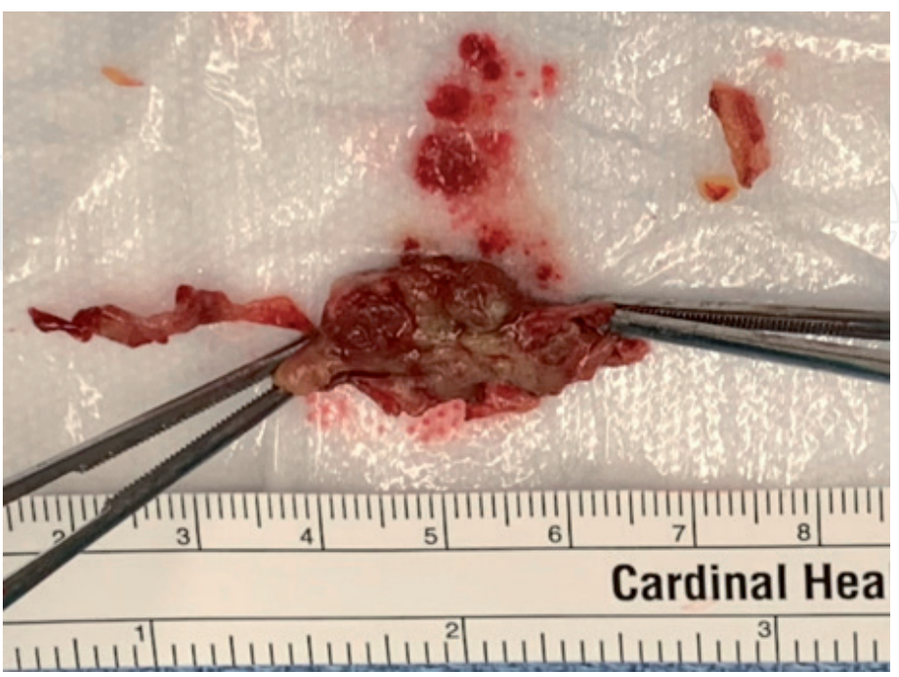

Figure 3.
Intraoperative photo showing a large, excised vegetation from the posterior leaflet of the tricuspid valve. This was performed in a 16-year-old who presented with isolated tricuspid valve endocarditis secondary to intravenous drug abuse and underwent successful tricuspid valve repair after excision of the vegetations.

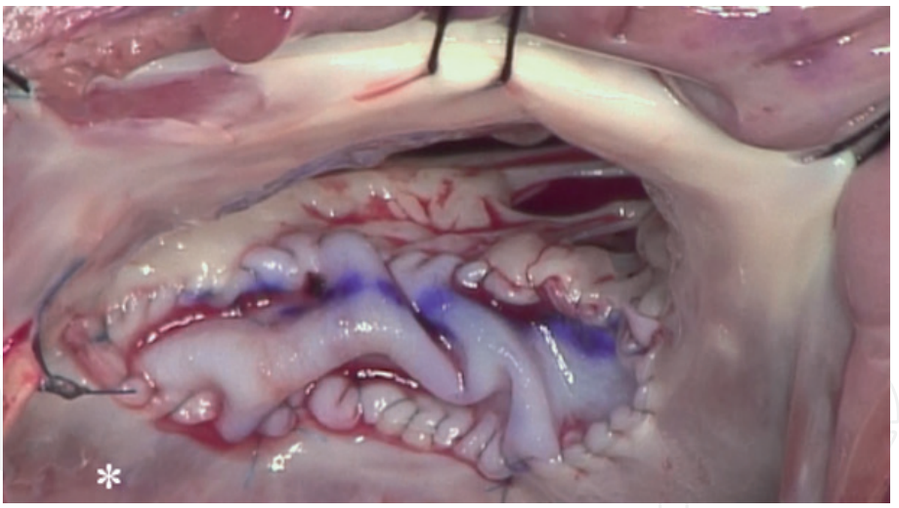

Figure 4.
Intraoperative photo showing a bovine pericardial patch that is used to augment the septal leaflet of the tricuspid valve and improve coaptation in a patient who presented with severe tricuspid valve regurgitation and history of endocarditis. Notice that augmentation should be done in the belly of the leaflet and not at the free leading edge. Also notice the area of the atrioventricular node (asterisk).

2. **Patch Repair** (**Figure 4**): our preference has been to use autologous pericardium or bovine pericardium to repair larger defects in the leaflet after excision of the vegetation and debridement of infected tissues.

3. **Leaflet Replacement:** a complete replacement of one leaflet can be performed using a variety of materials such as autologous or bovine pericardium. Multiple artificial chordae (neo-chordae) may be needed to join the newly formed leaflet with the papillary muscles of the TV and prevent prolapse.

4. **Bicuspidization of the TV:** this is suitable more when infection is localized to the posterior leaflet which can be excised, and both the anterior and septal leaflets are mobilized to form a bicuspid valve.

5. **Annuloplasty:** annuloplasty maneuvers are needed when the tricuspid annulus is dilated to support the repair and minimize recurrence of regurgitation. This varies from suture annuloplasty (Kay's or De Vega's) to a ring annuloplasty (**Figure 5(A)** and **(B)**). Several studies reported that ring annuloplasty is superior to suture annuloplasty in terms of recurrence of regurgitation [29].

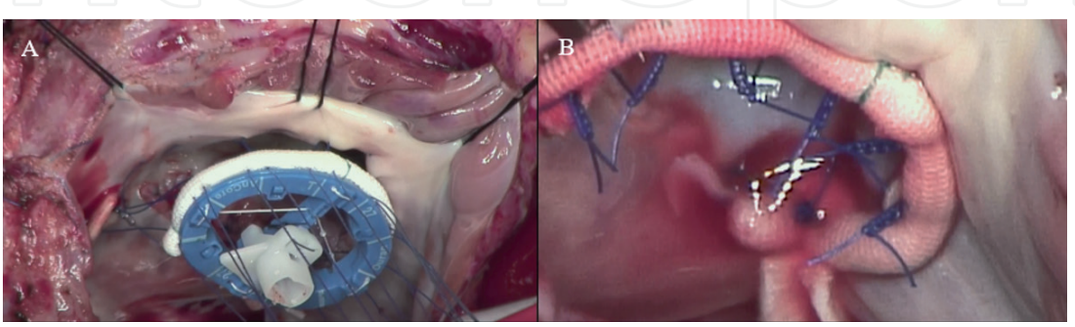

Figure 5.
(A and B). Intraoperative photos showing the technique of tricuspid valve ring annuloplasty. We prefer to use non-pledgeted prolene sutures in a horizontal mattress fashion (A) to secure the ring due to the fragility of the right atrioventricular junction. It is important to secure the ring from the anteroseptal to posteroseptal commissures. The last stitch (pledgeted) is placed within the mouth of the coronary sinus which is critical to reduce the length of the inferior annulus as most of the recurrence of regurgitation occurs due to re-dilation of the tricuspid annulus in this area.

- *Tricuspid Valve Replacement*

While TV repair is preferred, TV replacement remains the most commonly performed procedure [30]. Bioprostheses have been the first choice but mechanical prostheses have been also used in these cases. In a study by Cho et al., there was no difference in long-term valve-related complications such as thromboembolic or bleeding events between mechanical and biological prostheses [31].

Total autologous reconstruction of the TV using autologous/bovine pericardium or extracellular matrix reconstruct has been reported in some case reports to avoid the use of the prosthetic materials in the setting of infection [32]. We do not know the long-term outcome of such maneuvers.

- *Special Circumstances*

- **Isolated TV Vegetations without Valvular Destruction**

In some unique scenarios, large vegetations have been identified on the tricuspid valve without any evidence of valvular destruction or in some patients where the risk of surgery is quite high. Percutaneous aspiration of these large vegetations has been performed as an alternative to surgery [33]. The AngioVac system (AngioDynamics, Latham, NY) was approved in 2014 by the US Food and Drug Administration for removal of intravascular materials such as thrombi and emboli.

This system consists of two percutaneous venous cannulae (reinfusing/drainage) that are connected to an extracorporeal circuit pump head and bubble trap. Thrombotic materials/vegetations are aspirated when the pump is started and then the blood is circulated through a filter prior to returning to the patient. In a study by George et al., the authors reported the outcomes of percutaneous aspiration in 33 patients with large vegetations. Most of these patients (91%) were discharged home with reduced vegetations size in two-thirds [34]. This seems to be a reasonable option especially in those with prohibitive risk of surgery and in those with recurrent infection especially IVDA.

The obvious risks associated with percutaneous aspiration includes pulmonary embolization and vascular access complications.

- **Prosthetic Tricuspid Valve Endocarditis**

In the presence of TV prosthesis, infection will be difficult to eradicate without removal of the prosthesis. This subgroup of patients may require early and aggressive surgical eradication of infection to minimize in-hospital mortality and morbidities. There is a higher risk of heart block in this subgroup of patients.

- **Management of Implantable Cardiac Devices/Indwelling Catheters**

All infected leads and devices have to be removed. Hospital mortality is less when infected devices are identified earlier and removed promptly. Extraction of these devices by interventional cardiologist/electrophysiologist is preferred if possible, over the surgical extraction due to higher success and lower complication rates. One option, in less severe cases, is to remove these infected leads/devices, use temporary leads for pacemaker-dependent patients and continue antibiotic therapy and reevaluate the TV later, if repair or replacement is needed.

In severe cases that require urgent surgery, TV repair/replacement with concomitant extraction of the infected leads/devices is a better approach. Temporary

pacemaker leads can be used with subsequent endovenous implantation of a new permanent system once infection is cleared is a reasonable approach.

Other options for pacemaker-dependent patients is to use leadless pacemakers or trans-coronary sinus approach to avoid placing the lead through a freshly repaired TV or replaced tricuspid prosthesis. We have used epicardial permanent pacemaker system as well in some of these complex cases with limited vascular access.

This is a team decision that should be discussed thoroughly between the electrophysiologist, cardiologists, cardiac surgeon, and the patient.

- **Concomitant Left Sided Disease (Multi-valvular Endocarditis)**

Those with left sided involvement have worse outcomes in comparison with isolated TVE. These patients will require early surgical intervention to decrease mortality and improve outcomes. In a study by Musci and colleagues, 30-day survival was 96.2% for isolated right sided involvement in comparison to 72% for combined right and left-sided endocarditis [35].

- **Mycotic Aneurysms**

Mycotic aneurysms involving the pulmonary vasculature are less common and small number of cases have been reported in the literature [36]. Staphylococcus and streptococcus species are the most common organisms involved in developing these aneurysms, but it can also occur in the settings of mycobacterial or fungal infections. Clinical manifestations are usually related to the underlying endocarditis and manifestations specific to these mycotic aneurysms are rare except when rupture occurs which can lead to catastrophic hemoptysis.

Computed tomography scan is the most reliable for detection of these aneurysms. Due to the high mortality associated with rupture of these aneurysms, transcatheter embolization is recommended, although successful antibiotic therapy have been documented in those with small aneurysms that are stable [37].

- **Concomitant Pulmonary Emboli**

In patients with TV endocarditis and large vegetations, the search for evidence of pulmonary embolization is necessary especially in the presence of hemodynamic instability or acute new pulmonary manifestations. Concomitant pulmonary embolectomy at the time of TV surgery may be considered in patients with large bilateral/unilateral emboli especially if they are accessible. We have performed a retrograde pulmonary embolectomy in a recent case of TVE in an IVDA with CT evidence of bilateral pulmonary septic emboli. This technique is valuable in the presence of emboli in the distal pulmonary arterial bed that may not be accessible with the traditional pulmonary embolectomy technique [38].

- **Recurrent Endocarditis**

The highest risk of recurrence occurs among those with IVDA [39]. In a study by Huang and colleagues, the authors followed 87 patients who survived their first episode of endocarditis and up to 25% of these patients experienced recurrence of infection within a year of the first episode [40]. Outcomes of repeat operation in this population has been poor with increased mortality. In another study by Jeganathan and colleagues, 68 patients underwent repeat TV operations with early mortality of 13.2% and higher incidence of postoperative bleeding, low cardiac

output syndrome, renal failure, and stroke [41]. A debate continues regarding offering IVDA patients and those who are noncompliant, repeat surgery when infection recurs.

10. Prognosis

The majority of TVE respond to medical therapy but is associated with higher risk of recurrence, specifically in IVDA.

The overall prognosis of isolated TV endocarditis is better than left-sided and multivalvular infection. This may be due to younger age of patients, less occurrence of systemic embolization or development of drug-resistance, in addition to the fewer significant hemodynamic derangements that may occur from tricuspid regurgitation in contrast to aortic and/or mitral involvement.

The following have been associated with poor prognosis according to several reports: (1) persistent sepsis with failure to respond to medical therapy, (2) development of right heart failure, (3) fungal infection, (4) recurrent pulmonary embolization, (5) septic shock, and (6) multivalvular involvement.

11. Surgical outcomes

The estimated operative mortality for surgery for TVE is between 6 and 10% [42]. Excision of the TV has been associated with high morbidity due to right heart failure [43], and TV replacement has been associated with increased risk of recurrent infection and need for permanent pacemaker.

Yanagawa and colleagues reported the outcome sin 1165 patients who underwent surgery for TVE. The indications were recurrent pulmonary embolization, right heart failure, persistent sepsis and concomitant left-sided infection. TV repair was possible in 2/3 of these patients and the majority underwent TV replacement with a bioprosthesis. The authors concluded that both TV repair and replacement have good long-term survival, but repair is associated with less risk of need for pacemaker, recurrence of infection and reoperation [44].

Di Mauro et al. reported the surgical outcomes of isolated TVE in 157 patients (IVDA was present in 38%) of a multicenter registry. Repair was performed in 49%, while replacement with a bioprosthesis was the main procedure in 46% and a mechanical prosthesis was used in 5%. Early mortality was 11% with no difference between repair or replacement. The authors identified the following factors as predictors of poor outcomes: older age, IVDA, fungal endocarditis, repeat operation, the use of a prosthesis, and the presence of intracardiac devices [45].

In a recent systemic review and metanalysis of 752 patients with TVE by Luc and colleagues, tricuspid valvectomy was performed in 14%, while 86% underwent TV replacement. There was more prolonged duration of mechanical ventilation in the valvectomy group, but there was no significant difference in early mortality, right heart failure and recurrence of endocarditis between the two groups. The authors concluded that tricuspid valvectomy is an acceptable initial therapy in those with IVDA to help identify those who will self-select as candidates for later valve replacement [46].

12. Conclusions

TVE has several features that are unique in comparison to left-sided infection. These include the different population demographics, etiology of infection,

response to medical therapy and prognosis. High index of suspicion and use of appropriate imaging modalities facilitate early diagnosis and early initiation of appropriate therapy. Surgery remains indicated in those with failure to respond to medical therapy and in the presence of complications. The same principle of surgery for endocarditis apply which are adequate and thorough debridement of all infected materials and excision of all vegetations. Extraction of all associated infected cardiac devices is critical to ensure complete eradication of all sources of infection. Excision of the TV is associated with higher morbidity due to ongoing right heart failure, and TV repair is preferred over replacement if feasible. Debate remains ongoing in regard to offering surgery for those with recurrent infection and specifically IVDA.

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