ORIGINAL ARTICLE

Surgical management of the tricuspid valve endocarditis

Felipe G. Rendón-Elías, MD[a], Gustavo A. de la Cerda-Belmont, MD[a], Gabriel Anaya-Medina, MD[a], Carlos M. Salas-Ríos,MD[a], Marely Hernández-Sánchez, MD[a], Vicente Fuentes-Puga, MD[b], Rosemberg Albores-Figueroa, MD[b], María Goretti-Cépeda, MD[b], and Luis H. Gómez-Danés, MD[a]

[a]Department of Thoracic and Cardiovascular Surgery, [b]Department of Cardiovascular Anesthesia. Hospital Universitario ¨ Dr. José Eleuterio González ¨ Monterrey, Nuevo León, MÉXICO.

Objective. **To evaluate the surgical management of tricuspid valve infective endocarditis and its complications, from 2000 to 2019 in a Mexican tertiary center.** ***Methods.*** **Details of 22 consecutive patients operated upon for tricuspid valve infective endocarditis from September 2000 to December 2019 were analyzed.** ***Results.*** **Two (9%) patient died at the hospital. Follow-up was complete in all patients. There were no late deaths, 3 and 22 months after hospital discharge. The follow-up extended from 2 to 72 months and the overall survival was 95% and no cases of recurrent endocarditis.** ***Conclusion.*** **An early diagnosis and indication of surgical treatment prior to complication onset and generalized sepsis is the key to improve prognosis.**

Key words: **Endocarditis; Infection; Tricuspid valve, endocarditis; Tricuspid valve, regurgitation.**

Objetivo. **Evaluar el manejo quirúrgico de la endocarditis infecciosa de la válvula tricúspide y sus complicaciones, de 2000 a 2019 en un centro terciario mexicano.** ***Métodos.*** **Se analizaron detalles de 22 pacientes consecutivos operados por endocarditis infecciosa de la válvula tricúspide desde septiembre de 2000 hasta diciembre de 2019.** ***Resultados.*** **Dos (9%) pacientes murieron en el hospital. El seguimiento fue completo en todos los pacientes. No hubo muertes tardías, 3 y 22 meses después del alta hospitalaria. El seguimiento se extendió de 2 a 72 meses y la supervivencia general fue del 95% y no hubo casos de endocarditis recurrente.** ***Conclusión.*** **Un diagnóstico temprano e indicación de tratamiento quirúrgico antes de la aparición de complicaciones y sepsis generalizada es la clave para mejorar el pronóstico.**

Palabras clave**: Endocarditis; Infección; Válvula tricúspide, endocarditis; Válvula tricúspide, insuficiencia.**

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Infective endocarditis (IE) is more frequent on the left side of the heart. Right-sided IE (RSIE) is relatively rare, encompassing only 5–10% of IE cases [1,2]. The vast majority of RSIE cases involve the tricuspid valve (TV), with pulmonic valve involvement accounting for less than 10% of all right- sided cases [2]. In the last years, we have seen a steady improvement in the management strategies among patients with IE, greatly in part due the participation of a multidisciplinary team but despite all diagnostic and therapeutic advances. IE still shows a high risk of mortality and morbidity, and remains as a challenge to cardiac surgeons. Most tricuspid valve infective endocarditis (TVIE) cases are treated medically, whereas only 4.1% of all IE surgeries in North America are for TVIE [3].

The purpose of our study is to describe our experience in the last nineteen years of surgical treatment of TVIE.

Corresponding author: Dr. Felipe Gerardo Rendón Elías
email: drfrendon@gmail.com

MATERIAL

In a systematic retrospective review of clinical records, we analyzed data on 132 patients who underwent surgery for IE from September 2000 to December 2019, selecting just the patients with TVIE. All patients were reviewed at a peer review meeting for a decision-making process treatment.

The diagnosis of IE was based on the modified Duke criteria; these criteria are based on pathological, clinical, and echocardiographic findings [4]. The indications for surgery in native and prosthetic TVIE were categorized into three groups according to the clinical consequence of IE: a) hemodynamic instability b) sepsis and c) embolic events.

Hospital records were reviewed for patient's demographic characteristic, preoperative status and co-morbidities, intraoperative variables, and postoperative course. Surgery was considered urgent if the patient was treated with IV antibiotics until completion of assessment. Emergent operation was defined as the condition that prompted immediate operation within 24 hours from diagnosis. The follow-up time was cal-

culated as the period from diagnosis to last contact or death. For definitions of mortality and morbidity, standard guidelines were used [5]. An early event was defined as any event within the first 30 postoperative days or during the entire hospital stay.

Operative management

All patients were operated on using a standard cardiopulmonary bypass technique with mild to moderate hypothermia (28-320C). Myocardial protection was achieved with anterograde cold blood cardioplegia and warm blood hyperkalemic reperfusion and, for the last 5 years, with Del Nido cardioplegia. The surgical protocol for treatment was based on elimination of infection foci and correcting the hemodynamic condition. If the infection was limited to the leaflets of the valve, and there were no indications for valve replacement, simple valve repair using simple monofilament sutures or reinforced with pledgets or pericardial patch were used; in case that the valve repair was not possible we did TV replacement with biological prothesis valve. If the infection had extended into annulus and adjoining structures, it was repaired with either fresh autologous pericardium or glutaraldehyde-fixed bovine pericardium.

Patients received IV antibiotic therapy for a total 6 weeks, or in selected cases, for longer. No patient was kept on antibiotics permanently.

Table 1. Demographic, clinical and risk factors characteristics

VARIABLE	n (%)
Number of cases (n)	22
Age (years)	
Mean	32
Range	8-62
Gender	
Male	15 (69)
Female	07 (31)
Cardiac risk factors	04 (18)
Atrial septal defect	03
Ventricular septal defect	01
Non-cardiac risk factors	16 (72)
Central IV lines	03
Hemodialysis	08
Intravenous drug use	5
No risk factors	2 (9)
NYHA	
I	1 (4)
II	9 (41)
III	7 (32)
IV	5 (23)
Clinical presentation	
Fever	4 (18)
Embolic events	11 (50)
Sepsis	4 (18)
Heart failure	3 (14)
Surgical indication	
Hemodynamic instability	1 (04)
Echocardiographic finding	3 (14)
Uncontrolled infection	7 (32)
Embolic events	11(50)

RESULTS

Demographic, clinical and risk factors characteristics are summarized in **Table 1.** From one hundred and thirty-two patients that were operated on because of IE, just twenty-two patients correspond to patients underwent surgery for TVIE (16%), who were enrolled in the study. Patient's mean age was 38 years, ranging from 8-62 years. There was only one pediatric patient. According to the New York Heart Association functional class classification, most of patients were in class II and III (73%). Potential risk factors for the development of endocarditis varied widely. Most patients had non-cardiac risk (72%), but 18% had cardiac risk factors and only 9% had no risk. From the patients with no cardiac risk, the most common risk was the presence of catheter for hemodialysis, IV drug use and central IV lines. From the cardiac risk, the atrial septal defect was the most frequent one.

The most common clinical findings were preoperative signs and symptoms of embolic events (50%), sepsis (18%) and fever (18%) (**Fig. 1**).

All patients underwent at least one preoperative echocardiographic evaluation. Transthoracic echocardiography (TTE) (**Fig. 2**) was undertaken in all the patients and transesophageal echocardiography (TEE) in 16 patients. Echocardiographic findings were acute valve incompetence, evidence of vegetation (most common) abscess, and paravalvular leak. Complementary studies included, magnetic resonance and computerized tomography in other 11 patients. None patient required coronary angiography. Main indication for surgery were embolic events and uncontrolled infection (82%). Other reasons for surgery for the rest of the patients were hemodynamic instability (4%), and echocardiographic findings (14%).

The site of involvement was determined by echocardiographic and confirmed at surgery (**Fig. 2**). The infective process involved the native valve in 22 patients (100%). Out of them, 21 (95%) had positive blood cultures; gram-positive cocci were the most common pathogens. **Table 2** summarizes the blood culture results.

Table 2. Microorganism in tricuspid valve

PATHOGEN AGENT	n (%)
Staphylococcus aureus	14 (6)
Staphylococcus epidermidis	3 (14)
Streptococcus viridans	2 (9)
Candida albicans	2(9)
Culture-negative	1 (5)

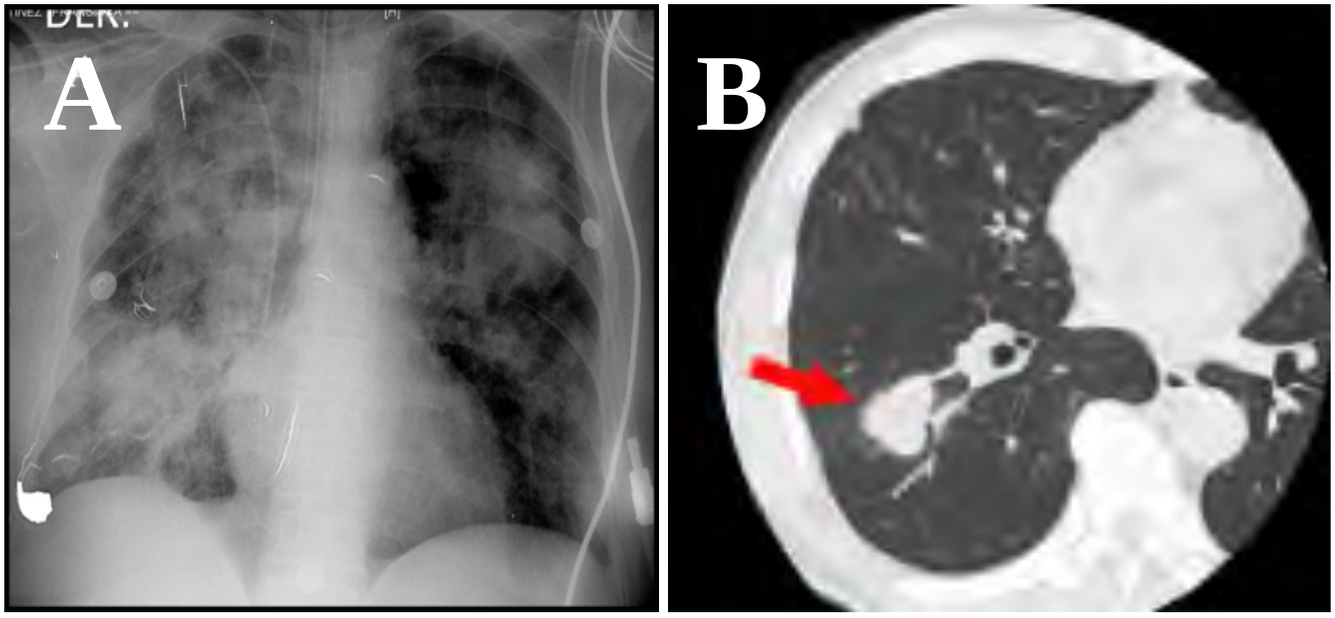

Figure 1. Thirty-two-year-old patient with the diagnosis of tricuspid valve endocarditis presenting a multiple focus pneumonia in a chest x-ray (A) and pulmonary infarct in the CT scan (B).

Most procedures were performed in an urgent basis (86%). The mean interval from diagnosis to surgery was 3-20 days (median, 9 days). The surgical procedure in 20 of the patients included valve replacement with biological prothesis and just two tricuspid valve repairs. In 3 patients, surgical treatment included correction of atrial septal defect, and other patient required correction of ventricular septal defect (**Table 3**).

The mean length of stay in the intensive care unit was 4 days (range 3-18 days) and the mean hospital stay was 23 days (range 12-43 days). All patients were treated with intravenous antibiotics for a mean period of 42 days.

The hospital mortality was 9%, corresponding to 2 patients with high-risk factors, such as intravenous drug abusers and urgent operation. They had staphylococcal endocarditis, and succumbed to sepsis and multiorgan failure, during the first postoperative week. Morbidity was 54% (12 patients). Four patients developed low cardiac output syndrome, five patients with pneumonia, and three with acute renal failure. The postoperative data are showed in **Table 4.**

DISCUSSION

Since the first modern clinical description of IE by Osler [4], the profile of the disease has continuously evolved. It has been described in different epidemiological studies all around the world [5,6]. Unlike others countries, in Mexico, the profile of IE has not changed too much in the last five decades [7]. Although in Mexico there is no national epidemiologic study about IE, the incidence of IE is calculated to be between one to six cases per 100,000 patient/year (personal communication from The National Institute of Statistic, Geography and Informatics, Mexico).

RSIE accounts for only 5–10% of all cases of IE [8,9]. However, an increase in the incidence of RSIE has recently been reported, primarily attributable to the global rise in number of intravenous drug use (IVDU), along with an increased number of patients with cardiac implantable electronic devices (CIED) and a rising number of central venous catheters in clinical care [10-12]. The large majority of RSIE cases involve theTV, with pulmonary valve involvement accounting for less than 10% of all right- sided cases [2]. Seratnahaei et al. reported that the incidence of TVEI was 6% between 1999 and 2000, and it markedly increased up to 36% between 2009 and 2010, and also reported history of intravenous drug use

Figure 2. Transthoracic echocardiographic showing a vegetation in the anterior leaflet of the tricuspid valve.

Table 3. Operative data

VARIABLE	n (%)
Surgical procedure	
Elective	**03 (14)**
Urgent	**17 (77)**
Emergent	**02 (9)**
Cardiopulmonary bypass time (min)	
Mean	**118**
Range	**75-132**
Aortic cross-clamping time (min)	
Mean	**62**
Range	**40-87**
Valve procedures	**18**
Tricuspide valve replacement	**14**
Tricuspid valve repair	**04**
Additional procedures	**04**
Atrial septal defect closure	**03**
Ventricular septal defect closure	**01**

increased from 15 to 40% [13]. In the study of Murdoch et al., current intravenous drug use was found in 16% of the cohort of North America, chronic intravenous access in 25%, implantable cardiac devices in 12%, and congenital heart disease in 25% [2]. Moss et al. reported that 41% of injection drug users with bacteremia had the evidence of IE [14]. Athan et al. performed a prospective cohort study which described a 6.4% incidence of cardiac device-related IE among 2,760 patients. There was coexisting valve involvement in 37.3% patients and predominantly TV infection (24.3%) [15].

Table 3. Postoperative data

VARIABLE	n (5)
Time interval from diagnosis to operation (days)	
Mean	**09**
Range	**03-20**
Length of stay in Intensive Care Unit (days)	
Mean	**04**
Range	**03-18**
In-hospital stay	
Mean	**23**
Range	**12-43**
Operative mortality	**02 (9)**
Cause of early deaths	
Sepsis	**02 (9)**
Postoperative complications	**12 (54)**
Low cardiac output	**04**
Pneumonia	**05**
Renal failure	**03**

In our institution, the incidence of IE is from 8 to 19 cases per year, and just 30% require surgical therapy. Out of them, only 16 % correspond to TVEI. In our study, like in other previous reports [16,17], the incidence is higher in men than in women (3:1), but the average age group affected is in the third decade, different than patients with left-sided IE, where the age group most affected is after the fifties (mean 46-64 years). This difference could be due to the high prevalence of congenital cardiac diseases, increasing group of IVDU and the most frequent use of central venous catheters and CIED as described above. Lately, all of them are major risk factors for IE in México.

The current most common risk factors for TVIE are IVDU, CIED, and indwelling venous access lines implanted (hemodialysis, parenteral nutrition and chemotherapy), which represent similar risk factors herein in our report. Infection resulting from IVDU constitutes approximately 30–40% of all TVIE cases [1,18,19]. The IE presentation is by TV lesions in 50–65% of IVDU, and the prevalence of IE in IVDUs is about 2 to 5% per year [20-22]. There is no single hypothesis to explain why RSIE occurs most commonly in IVDU. The various hypotheses to explain this phenomenon include differences in effects of injected substances on valves and valve endothelium, different infecting organisms, a higher bacterial load and immunologic changes associated with IVDU. It is assumed that there is a dynamic combination of host, environmental, immunological and microbial factors acting in full-concert to cause predominantly RSIE in this population, with specific factors contributing relatively more or less in any individual patient [21]. Once the valve has been infected and damaged or replaced, repeated episodes of IE occur ever more frequently in IVDUs, with reinfection of up to 28% [22]. One study reported a long-term cumulative incidence of reoperation of 20% in IVDU, as opposed to less than 5% in non-users [19]. The cumulative incidence of death was similar between the two groups approximately 20%. This is echoed by other papers that found no difference in survival between users and non-users [23,24]. IVDUs patients are more likely to be younger, and their very high likelihood of continued drug use is a serious clinical challenge. However, it has become clear that from a survival standpoint, IVDU itself is not a contraindication for surgery [21]. A multidisciplinary approach to these patients is required, with drug rehabilitation and long-term cessation of drug use essential in preventing reinfection [1,20].

CIED lead infection is an increasingly important cause of TVIE. CIED infection should be considered separate from TVIE in that the majority of CIED infections are localized to the device pocket and leads and do not involve the TV. This distinction is sometimes confused in the literature [25,26]. IE should be considered CIED related only if there is evidence of valve vegetations and/ or tricuspid insufficiency, in concert with positive blood cultures. Lead echo-densities are very common and indistinguishable from IE vegetations, but usually they are not infectious vegetations [27]. On the other hand, CIED-related IE should always be suspected and considered in cases of CIED infection.

Chronic IV access infections account for approximately 10% of all IE, 8% of which occur in hemodialysis patients [13]. This study, however, had an over representation of North American patients, who accounted for 60% of the study cohort. A smaller North American study demonstrated

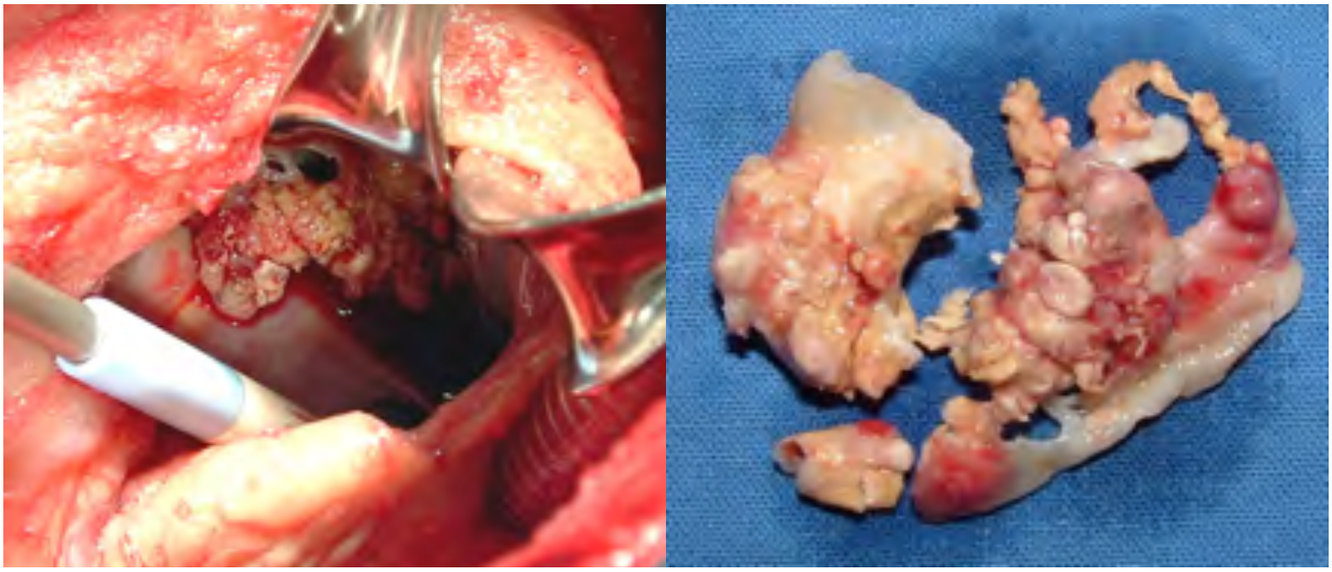

Figure 3. Twenty-four year-old patient with history of intravenous use drugs presenting tricuspid valve endocarditis and pericarditis.

that approximately 20% of hemodialysis-related IE involved the TV [28]. Dialysis patients often have a greater burden of comorbidities, including diabetes, hypertension and atrial fibrillation, besides their end-stage renal disease. The most common microbes are S. aureus and Enterococcus spp. There is a lack of literature about patients with IE due to chronic IV access, especially focusing on surgical management. TVIE specific discussion is even less common, so it is difficult to get guidance from these small sample sets besides recognizing the overall poor health of these patients.

Staph. aureus is the predominant causative microorganism for TVIE, occurring in 60–90% of cases in some studies, irrespective of associated risk factors [1,2,21,22]. 1Pseudomonas aeruginosa, other gram-negative microorganisms, fungi, enterococci, streptococci and polymicrobial infections occur less frequently. These pathogens are rare and vary by source of infection. However, coagulase-negative staphylococci are more common and represent 25% of CIED-related infections. Staph. aureus IE is associated with the highest morbidity/mortality, and the proportion of Staph. aureus cases with methicillin resistance is increasing [11]. Also, Staph. aureus is associated with a larger number of comorbid factors, including hemodialysis, CIED, IVDU and advanced age [11]. HIV infection is another comorbidity associated with IVDU and IE, and its prevalence varies drastically according to region. However, it seems to there be a little impact of HIV infection on the occurrence of IE if CD4 counts are above 200 cells/μL [20]. Two studies have also noted a very high prevalence of hepatitis C in patients with IVDU and RSIE [28,29]. Approximately 10% to 20% of patients have negative blood culture findings at presentation, leading to diagnostic uncertainty. Negative results on blood cultures may occur due to previous antibiotic use, infection with fastidious intracellular organisms or fungi, or an alternative diagnosis. The incidence of blood culture–negative IE may drop with increasing use of newer blood culture techniques, which allow direct identification of bacterial species by mass spectroscopy and are significantly faster than standard culture methods. The list of microorganisms causing IE reported in our analysis included: Staph epidermidis, S viridans, Candida Albincans but the Staph aureus was the most frequent causative organism and there was just one negative blood culture (5%) like in other reports.

The clinical presentation of TVIE is frequently neglected and notoriously diverse, ranging from acute sepsis to an indolent low-grade febrile illness. Clinical suspicion should be highly emphasized until diagnostic definition. The usual manifestations of TVIE are persistent fever and bacteremia. Multiple septic pulmonary emboli cause chest pain, cough and occasionally hemoptysis. Systemic emboli are rare manifestations of TVIE and, when noted, should be considered evidence of either left- sided involvement or paradoxical embolism [1]. Right heart failure is rare and caused by increased pulmonary pressure combined with severe TR or TV obstruction from huge vegetations. Pulmonary septic emboli cause pulmonary infarcts and pulmonary abscesses and may be complicated by pneumothorax and empyema [30-34].

Application of the criteria reported in the literature allows an approach with excellent sensitivity and specificity for the diagnosis of IE [35]. Although the gold standard for diagnosing IE remains as the modified Duke Criteria [3], these criteria have a lower sensitivity for patients with prosthetic valve endocarditis or CIED [34-35], thus these criteria may be difficult to determine in TVIE because of firstly, the right heart has many echocardiographically anomalous anatomic features that may be difficult to distinguish from vegetations; second, septic emboli are pulmonary, as opposed to systemic, and clinically less obvious until they cause pulmonary infarcts and abscesses; third, early pulmonary radiographic findings may be mistaken for pneumonia. Then, definitive cardiac imaging and microbiology are therefore of integral importance in making the diagnosis and also inform risk stratification, direct management, identify complications, and assist with monitoring therapy. Key advances have been made in recent years in reaching a definitive diagnosis in patients who

fall into the "possible" group according to the Duke criteria. Echocardiography remains the cornerstone of imaging and is rapid, straightforward, and, in many cases, diagnostic [1]. TTE is the recommended initial modality of choice for both native and prosthetic valve IE and has a sensitivity of 50% to 90% and a specificity of 90%. TEE is indicated when TTE is positive or nondiagnostic, when complications are suspected, or when intracardiac device leads are present. For suspected native valve endocarditis, TEE has a sensitivity of 90% to 100% and a specificity of 90% for detection of vegetations, and it is superior to TTE for detection of complications, such as perforations, abscesses, and fistulae. In prosthetic valve endocarditis, a recent meta-analysis reported a pooled sensitivity of only 86% (95% confidence interval: 77% to 92%) for TEE in making the diagnosis and other imaging modalities are emerging to help make or exclude the diagnosis in cases in which TEE is useless [37]. Even when abnormalities are detected, it can be difficult to make a clear difference between nodules and small vegetations or distinguish signs of infection from post-operative changes.

Cardiac computed tomography (CT) scanning is the key adjunctive modality for use when the anatomy is not clearly delineated according to echocardiography, and it now has a Class II, Level of Evidence: B recommendation for use in IE in the 2014 ACC/AHA valvular heart disease guidelines [34]. Cardiac CT is equivalent (and likely superior) to TEE for demonstrating paravalvular anatomy and complications (e.g., paravalvular abscesses or mycotic aneurysms) and is subject to fewer prosthetic valve artifacts than echocardiography [38-40]. This approach may help with planning surgical strategy, and concurrent CT angiography allows exclusion of significant coronary disease in younger patients. Detection of paravalvular lesions by using CT imaging is now a major diagnostic criterion in the 2015 ESC guidelines on IE [1].

Combining CT imaging with metabolic imaging by 18-fluorodeoxyglucose positron emission tomography (18FDG-PET) or leukocyte scintigraphy (radiolabeled leukocyte single-photon emission computed tomography [SPECT]) to show regions of metabolic activity or inflammation, respectively, is a promising approach in patients who, according to the Duke criteria, have "possible" IE or suspected CI. Several studies have now investigated the sensitivity and specificity of PET/CT or SPECT/CT imaging in this setting. In a cohort of 72 patients with suspected PVE, 18FDG PET/CT imaging had an overall sensitivity of 73% and a specificity of 80% [41]. The addition of "abnormal prosthetic valve 18FDG-PET signal" as a diagnostic criterion increased the sensitivity of the modified Duke criteria from 70% to 95%, reducing the number of patients with "possible IE" from 56% to 32%. In a Spanish cohort of patients with suspected PVE or CDI, 18FDG-PET/CT (angiography) demonstrated an overall sensitivity and specificity of 87% and 90%, respectively, and increased the sensitivity of the modified Duke criteria from 51% to 91% [42]. Use of PET/CT imaging allowed reclassification of 90% of cases (35 of 39) with "possible" IE and provided a conclusive diagnosis in 95% of cases overall. For leukocyte scintigraphy with SPECT/CT imaging, a sensitivity of 90% and a specificity of 100% have also been reported [43]. When directly compared in a cohort with suspected PVE and inconclusive echocardiography findings, 18FDG-PET/CT imaging had higher sensitivity than SPECT/CT imaging, but SPECT demonstrated higher specificity [44]. The significance of abnormal 18FDG-PET/SPECT imaging has been recognized in the 2015 ESC guidelines; a positive signal at the site of a prosthetic valve (if implanted >3 months previously) is now regarded as a major diagnostic criterion for PVE.

Routine cross-sectional imaging of the brain, chest, spine, and viscera can be diagnostic and can change management. Imaging cohort studies suggest that patients with IE have a high incidence of subclinical complications, such as embolism, hemorrhage, or abscess. Multimodality assessment by cross-sectional imaging, cardiac CT, and 18FDG-PET or SPECT has the potential to improve diagnosis and detection of complications in patients with suspected IE. We see CT and 18FDG-PET/CT becoming widely used for diagnosis in the "Duke possible" subgroup of patients and for CIED. There are drawbacks, metabolic imaging cannot accurately discriminate between sterile inflammation and infection, and it is therefore of limited use in the early post-operative period. Finally, identifying which patient groups derive the most clinical benefit from advanced imaging remains to be established.

Management of patients with TVIE and in general any patient with IE is both a clinical and logistical challenge. Delivery of optimal care requires an administrative infrastructure and the involvement of multiple hospital specialists (cardiologists, surgeons, infectious disease physicians, microbiologists, nephrologists, neurologists, and radiologists). Optimizing service delivery and early decision making have the potential to improve clinical outcomes, leading to calls for formation of "IE teams," modeled on the heart team approach to coronary and heart valve disease [45]. Introduction of a formalized multidisciplinary team approach in Italy, defined by initial evaluation within 12 h, early surgery (within 48 h) if indicated, and weekly review, led to a reduction in in-hospital (28% vs. 13%; p=0.02) and 3-year (34% vs. 16%; p= 0.0007) mortality, despite patients being older and having more comorbidities [46]. Similarly, a French multidisciplinary team approach to standardizing care, including antibiotic protocols and indications for surgery, reduced 1-year mortality from 18.5% to 8.2% [46]. Centralized care concentrated in tertiary centers with advanced diagnostic imaging, surgical expertise, has a very important role in complex cases and may be beneficial but exists arguments against this model such as delays during transfer and loss of local expertise.

Before the discovery of penicillin, IE was an untreatable disease. Effective microbial clearance requires bactericidal antibiotic regimens. Detailed empirical and organism-specific antibiotic protocols are beyond the scope of the present review but are provided in the latest AHA and ESC guidelines [1,47]. The importance of balancing efficacy of treatment with the overall risk and toxicity of prolonged in-patient therapy is increasingly recognized. Emerging evidence supports short-course or stepped-down antibiotic treatment in selected groups. A 2-week course of penicillin monotherapy or penicillin-aminoglycoside in combination is effective for uncomplicated methicillin-sensitive S. aureus right-sided IE [48]. There are increasing data to suggest that the use of aminoglycosides may be causing harm without clear clinical benefit. In 2006, one RCT of daptomycin compared with conventional therapy (penicillin or vancomycin with initial gentamicin) for S aureus bacteremia or right-sided endocarditis, daptomycin was shown to be non-inferior. Importantly, renal dysfunction occurred in 11% of those treated with daptomycin compared with 26% of the conventional therapy arm [49,50]. Aminoglycosides have now been removed from the ESC and AHA

guidelines for the treatment of methicillin-sensitive S aureus or methicillin-resistant S aureus NVE. Further research is needed to determine whether additional patient groups may be suitable for shortened courses of antibiotic therapy. For example, in patients who have undergone successful surgery and have negative valve culture findings suggesting successful microbial elimination (after initially positive blood culture results), it may be safe to stop antibiotics after 2 weeks [51-52]. However, current AHA guidelines suggest that the remaining duration of antibiotics should be given (including administration before surgery), but this suggestion is Level C evidence [47].

Reduction of in-hospital stay may also be achieved through an early switch to regimens of oral antibiotics with good bioavailability. In IV drug users, there are RCT data supporting the safety and efficacy of oral ciprofloxacin and rifampicin for uncomplicated methicillin-sensitive S aureus NVE, although increasing rates of fluoroquinolone resistance limit applicability [53]. The POET (Partial Oral Treatment of Endocarditis) trial is an ongoing Danish multicenter study designed to address whether step-down to oral treatment is safe after the first 10 days of IV antibiotics in staphylococcal, streptococcal, or enterococcal NVE. Four hundred patients will be randomized to receive 4 to 6 weeks of IV treatment, compared with step-down to oral therapy after a minimum of 10 days, with a primary endpoint of all- cause mortality, unplanned cardiac surgery, embolism, or relapse of positive blood culture findings [54].

Early hospital discharge is frequently facilitated by the use of outpatient parenteral antibiotic therapy (OPAT). OPAT can be initiated in specific patients after completion of the first 2 weeks of treatment, after which the risk of complications is reduced. OPAT is contraindicated in patients with heart failure, complex infection, high risk of embolism, neurological complications, or renal impairment [55-57]. The risk of tolerance, combined with relatively slow bactericidal antibiotic effects, underlies the requirement for 4 to 6 weeks of parenteral antibiotic in the protocol of our institution but these is slowly changing.

Currently the indications for surgery in RSIE are still not well defined, but should be considered in the presence of any of the following criteria: a) TV vegetations >20 mm and recurrent septic pulmonary emboli with or without concomitant right heart failure; b) IE caused by microorganisms that are difficult to eradicate (e.g., fungi) or bacteremia for at least 7 days (e.g., S. aureus, P. aeruginosa) despite adequate antimicrobial therapy; and c) Right heart failure secondary to severe TR with poor response to diuretic therapy [1,34].

Timing of surgery in RSIE is less clear than in left-sided IE. Earlier intervention prevents further septic pulmonary embolism and further destruction of TV leaflet tissue, increasing the likelihood of good repair. Early operation for TVIE should be considered in the presence of any of the following: concomitant left- sided IE, atrial septal defect, infected indwelling catheters or pacing leads and prosthetic valve endocarditis [58]. Patients with RSIE have often suffered from septic pulmonary emboli, multiple pulmonary infarcts and abscesses, resulting in elevated pulmonary pressure and increased vascular resistance. This reduces their tolerance to severe tricuspid regurgitation. Although pulmonary issues may be an argument to postpone operating, large or huge vegetations that increase the risk of additional emboli make the argument for surgical intervention more compelling—the decision regarding when to operate must be based on clinical judgment.

The principles of surgery for TVIE include radical debridement of vegetations, infected tissue and valve repair whenever possible. If the valve is largely destroyed and non-repairable, and if the pulmonary pressures and vascular resistance are elevated, replacement is necessary [1,22,58]. If pulmonary vascular resistance is low-normal, excising the valve without replacement may work as a temporary solution [1,22]. In IVDUs patients, who are most likely young and non-compliant, valve replacement is associated with a higher risk of recurrent infection and reoperation [59].

Fortunately, TV repair can be accomplished in most cases, even those with extensive valve destruction, using a variety of techniques [59-62]. These include autologous pericardial patch augmentation of the destroyed leaflets, implantation of an annuloplasty ring and expanded polytetrafluoroethylene neo-chords, used as necessary. Contrary to the assumption that implantation of prosthetic annuloplasty rings should be avoided in IE, especially in IVDU patients, risk of reinfection with their use is very low [58].

Whilst the choice of prosthesis for TV replacement remains controversial, long-term survival is similar regardless of prosthesis type used in many series [60-64]. However, if valve replacement becomes necessary in TVIE, a bioprosthesis is preferable over a mechanical one, which requires lifelong anticoagulation in patients in whom IVDU is predominant and non-compliance is a major issue. If a mechanical valve is implanted, access to the right ventricle for pacer leads and pulmonary catheters is also lost.

Complete excision of the TV without prosthetic replacement was first described by Arbulu et al. [25]. They reported 64% survival among 53 IVDUs patients, 22 years after valvulectomy. However, in up to a third of patients it will cause ascites, peripheral edema and low cardiac output due to right ventricular dysfunction within 6–9 months. Surprisingly, valvulectomy accounted for 7.2% of operations performed for TVIE in North America [3]. TV excision for IE should be limited to extreme cases only, and only if pulmonary artery pressure and vascular resistance are not elevated. Subsequent valve replacement should be considered once the infection is resolved.

Injury to the conduction system is a major concern with TV surgery, and the risk is higher with replacement than repair patients [3,58]. TV replacement resulted in significantly more heart block (16%) than did repair (3%, P<0.0001) in 910 operations reported in North America for TVIE from the Society of Thoracic Surgeons database [3]. This prevalence of heart block may be higher than it need be: the atrio-ventricular node is localized between the coronary sinus and the membranous septum, and the bundle dives down under the atrial portion of membranous septum in the corner between the membranous septum and the tricuspid anulus where deep suture bites will cause heart block.

Placement of a CIED may be necessary after surgery due to previous or new heart block, but a CIED is an important additional risk factor for reinfection. There is no clear recom-

mendation concerning the optimal timing of CIED implantation reimplantation. Factors such as persistent bacteremia and pacemaker/CIED dependency should be considered, with the decision individualized to each patient. Placement of permanent endocardial leads across a bioprosthesis may result in regurgitation and is likely to reduce prosthesis durability by causing leaflet fibrosis and retraction. Epicardial leads placed at the time of surgery may prevent these issues and may also have a lower risk of becoming infected. Epicardial lead placement at the time of surgery should be considered when there is heart block that is not resolved in the operating room, or high suspicion of damage to the conduction system and likely need for permanent pacing. Epicardial leads have a higher threshold and drain pacemaker batteries faster.

In our case series we performed TV replacement in the majority of the patients because almost all the patient had an unrepairable valve (**Fig. 3.**), maybe due of presence of very destructive bacterias, the time of the diagnosis and also, we preferred a replacement in some patients because of socioeconomic disadvantages. Despite the 81% of the cases were TV replacement, we had no case for heart block. Before the date of this report, in the late nineties, we tried in IVUD excision of the valve with bad outcome, so we never made this procedure again.

TVIE has an in-hospital mortality of less than 10% and long-term mortality of less than 15% [1,2,19,34]. Continuing IVDU is a significant risk factor for IE recurrence and death. Staph aureus infection is another independent predictor of poor outcomes [1,22,62], as is hemodialysis [27], valve replacement (vs. repair) [58], vegetation >20 mm, fungal etiology and HIV infection with a CD4 count below 200 cells/μL [1]. Higher priority of surgery (emergency vs. urgent vs. elective) could be pointed to as an independent risk factor for early mortality as well [22].

In conclusion, an endocarditis team is necessary to get an appropriate diagnosis and management. If indicated the TVIE operations can be performed with low operative mortality and excellent survival. Large vegetations, septic pulmonary embolism and failed medical therapies are more important reasons to operate than severe TV regurgitation. Earlier surgical intervention will prevent further embolism and destruction of TV leaflet tissue, in addition to increasing the likelihood of TV repair.

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