

# World Journal of *Clinical Cases*

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## Contents

Thrice Monthly Volume 9 Number 30 October 26, 2021

## REVIEW

- 8953 Endothelial progenitor cells and coronary artery disease: Current concepts and future research directions  
*Xiao ST, Kuang CY*

## MINIREVIEWS

- 8967 Regulation of bone metabolism mediated by  $\beta$ -adrenergic receptor and its clinical application  
*Zhong XP, Xia WF*
- 8974 Tricuspid valve endocarditis: Cardiovascular imaging evaluation and management  
*Fava AM, Xu B*

## ORIGINAL ARTICLE

## Case Control Study

- 8985 Novel application of multispectral refraction topography in the observation of myopic control effect by orthokeratology lens in adolescents  
*Ni NJ, Ma FY, Wu XM, Liu X, Zhang HY, Yu YF, Guo MC, Zhu SY*

## Retrospective Cohort Study

- 8999 Uncertainty in illness and coping styles: Moderating and mediating effects of resilience in stroke patients  
*Han ZT, Zhang HM, Wang YM, Zhu SS, Wang DY*

## Retrospective Study

- 9011 Development and validation of a prognostic nomogram model for Chinese patients with primary small cell carcinoma of the esophagus  
*Zhang DY, Huang GR, Ku JW, Zhao XK, Song X, Xu RH, Han WL, Zhou FY, Wang R, Wei MX, Wang LD*
- 9023 Preliminary establishment of a spinal stability scoring system for multiple myeloma  
*Yao XC, Shi XJ, Xu ZY, Tan J, Wei YZ, Qi L, Zhou ZH, Du XR*
- 9038 Effect of intrauterine perfusion of granular leukocyte-colony stimulating factor on the outcome of frozen embryo transfer  
*Zhu YC, Sun YX, Shen XY, Jiang Y, Liu JY*
- 9050 "An integrated system, three separated responsibilities", a new fever clinic management model, in prevention and control of novel coronavirus pneumonia  
*Shen J, He Q, Shen T, Wu ZQ, Tan MM, Chen YL, Weng Q, Nie LM, Zhang HF, Zheng B, Zhang J*

**Clinical Trials Study**

- 9059** Single dose dexamethasone prophylaxis of postembolisation syndrome after chemoembolisation in hepatocellular carcinoma patient: A randomised, double-blind, placebo-controlled study  
*Sainamthip P, Kongphanich C, Prasongsook N, Chirapongsathorn S*

**Observational Study**

- 9070** Serum calcium, albumin, globulin and matrix metalloproteinase-9 levels in acute cerebral infarction patients  
*Zhong TT, Wang G, Wang XQ, Kong WD, Li XY, Xue Q, Zou YA*

**SYSTEMATIC REVIEWS**

- 9077** Neoadjuvant radiotherapy dose escalation for locally advanced rectal cancers in the new era of radiotherapy: A review of literature  
*Delishaj D, Fumagalli IC, Ursino S, Cristaudo A, Colangelo F, Stefanelli A, Alghisi A, De Nobili G, D'Amico R, Cocchi A, Ardizzoia A, Soatti CP*

**META-ANALYSIS**

- 9090** Clinical significance of breast cancer susceptibility gene 1 expression in resected non-small cell lung cancer: A meta-analysis  
*Gao Y, Luo XD, Yang XL, Tu D*

**CASE REPORT**

- 9101** Particular tumor of the pancreas: A case report  
*Zhu MH, Nie CF*
- 9108** Dynamic changes in the radiologic manifestation of a recurrent checkpoint inhibitor related pneumonitis in a non-small cell lung cancer patient: A case report  
*Tan PX, Huang W, Liu PP, Pan Y, Cui YH*
- 9114** Spontaneous rupture of a mucinous cystic neoplasm of the liver resulting in a huge biloma in a pregnant woman: A case report  
*Kośnik A, Stadnik A, Szczepankiewicz B, Patkowski W, Wójcicki M*
- 9122** Diagnosis and laparoscopic excision of accessory cavitated uterine mass in a young woman: A case report  
*Hu YL, Wang A, Chen J*
- 9129** Unusual cervical foreign body - a neglected thermometer for 5 years: A case report  
*Yang L, Li W*
- 9134** Long-term survival of a patient with pancreatic cancer and lung metastasis: A case report and review of literature  
*Yang WW, Yang L, Lu HZ, Sun YK*
- 9144** Synchronous diagnosis and treatment of acute myeloid leukemia and chronic lymphocytic leukemia: Two case reports  
*Chen RR, Zhu LX, Wang LL, Li XY, Sun JN, Xie MX, Zhu JJ, Zhou D, Li JH, Huang X, Xie WZ, Ye XJ*

- 9151** Conversion therapy of hepatic artery ligation combined with transcatheter arterial chemoembolization for treating liver cancer: A case report  
*Feng GY, Cheng Y, Xiong X, Shi ZR*
- 9159** Hemophagocytic lymphohistiocytosis secondary to composite lymphoma: Two case reports  
*Shen J, Wang JS, Xie JL, Nong L, Chen JN, Wang Z*
- 9168** Fatal visceral disseminated varicella-zoster virus infection in a renal transplant recipient: A case report  
*Wang D, Wang JQ, Tao XG*
- 9174** Choriocarcinoma misdiagnosed as cerebral hemangioma: A case report  
*Huang HQ, Gong FM, Yin RT, Lin XJ*
- 9182** Rapid progression of colonic mucinous adenocarcinoma with immunosuppressive condition: A case report and review of literature  
*Koseki Y, Kamimura K, Tanaka Y, Ohkoshi-Yamada M, Zhou Q, Matsumoto Y, Mizusawa T, Sato H, Sakamaki A, Umezu H, Yokoyama J, Terai S*
- 9192** Temporary pacemaker protected transjugular intrahepatic portosystemic shunt in a patient with acute variceal bleeding and bradyarrhythmia: A case report  
*Yao X, Li SH, Fu LR, Tang SH, Qin JP*
- 9198** Recurrent pyogenic liver abscess after pancreatoduodenectomy caused by common hepatic artery injury: A case report  
*Xie F, Wang J, Yang Q*
- 9205** Transient ventricular arrhythmia as a rare cause of dizziness during exercise: A case report  
*Gao LL, Wu CH*
- 9211** Successful management of infected right iliac pseudoaneurysm caused by penetration of migrated inferior vena cava filter: A case report  
*Weng CX, Wang SM, Wang TH, Zhao JC, Yuan D*
- 9218** Anterior abdominal abscess - a rare manifestation of severe acute pancreatitis: A case report  
*Jia YC, Ding YX, Mei WT, Xue ZG, Zheng Z, Qu YX, Li J, Cao F, Li F*
- 9228** Monteggia type-I equivalent fracture in a fourteen-month-old child: A case report  
*Li ML, Zhou WZ, Li LY, Li QW*
- 9236** Diagnosis and treatment of primary pulmonary enteric adenocarcinoma: Report of Six cases  
*Tu LF, Sheng LY, Zhou JY, Wang XF, Wang YH, Shen Q, Shen YH*
- 9244** Choroidal metastatic mucinous abscess caused by *Pseudomonas aeruginosa*: A case report  
*Li Z, Gao W, Tian YM, Xiao Y*
- 9255** Diagnosis and treatment of acute graft-versus-host disease after liver transplantation: Report of six cases  
*Tian M, Lyu Y, Wang B, Liu C, Yu L, Shi JH, Liu XM, Zhang XG, Guo K, Li Y, Hu LS*



- 9269** Hepatic portal venous gas without definite clinical manifestations of necrotizing enterocolitis in a 3-day-old full-term neonate: A case report  
*Yuan K, Chen QQ, Zhu YL, Luo F*
- 9276** Emergence of lesions outside of the basal ganglia and irreversible damage to the basal ganglia with severe  $\beta$ -ketothiolase deficiency: A case report  
*Guo J, Ren D, Guo ZJ, Yu J, Liu F, Zhao RX, Wang Y*
- 9285** Skeletal muscle metastasis with bone metaplasia from colon cancer: A case report and review of the literature  
*Guo Y, Wang S, Zhao ZY, Li JN, Shang A, Li DL, Wang M*
- 9295** Biopsy-confirmed fenofibrate-induced severe jaundice: A case report  
*Lee HY, Lee AR, Yoo JJ, Chin S, Kim SG, Kim YS*
- 9302** Missense mutation in *DYNC1H1* gene caused psychomotor developmental delay and muscle weakness: A case report  
*Ding FJ, Lyu GZ, Zhang VW, Jin H*
- 9310** Isolated hepatic tuberculosis associated with portal vein thrombosis and hepatitis B virus coinfection: A case report and review of the literature  
*Zheng SM, Lin N, Tang SH, Yang JY, Wang HQ, Luo SL, Zhang Y, Mu D*

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## Tricuspid valve endocarditis: Cardiovascular imaging evaluation and management

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### Abstract

Right-sided infective endocarditis is an increasingly recognized disease entity, with tricuspid valve being most frequently involved. Risk factors for tricuspid valve endocarditis (TVIE) include intravenous drug use, cardiac implantable electronic devices and indwelling catheters. *Staphylococcus aureus* is the predominant causative organism in TVIE. The diagnosis of infective endocarditis (IE) is based on clinical manifestations, blood cultures, and the presence of valvular vegetations detected by echocardiography. Complementary imaging is helpful when there is ongoing clinical suspicion for IE following initially negative echocardiography. Multislice computed tomography allows for assessment of extra-cardiac complications in TVIE, including pulmonary septic emboli. 18F-fluorodeoxyglucose positron emission tomography/computed tomography and radiolabelled white blood cell, single-photon emission computed tomography provide important clinical information concerning the presence of IE in right-sided prosthetic valves or cardiac implantable electronic devices. The aim of this review is to provide an update on TVIE, discussing the role of multimodality imaging in TVIE and the management of these patients.

**Key Words:** Tricuspid valve endocarditis; Multimodality imaging; Echocardiography; Computed tomography; Positron emission tomography/computed tomography

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**Core Tip:** Right-sided infective endocarditis (RSIE) is an increasingly important subtype of infective endocarditis (IE), although less published literature is available

States

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regarding RSIE compared to left-sided IE. Recently, with improvements in multimodality imaging, there is an increasing role for imaging in the evaluation and management of tricuspid valve endocarditis (TVIE). We review the role of cardiac imaging in diagnosis and evaluation of TVIE, and provide a concise update on the management of these patients.

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## INTRODUCTION

It has been reported that right-sided infective endocarditis (RSIE) makes up 5%-10% of all cases of infective endocarditis (IE)[1-3]. RSIE involves native or prosthetic valves, any intracardiac devices within the right heart, and more rarely non-functional embryonic remnants such as Eustachian valve or Chiari network that are present in the right atrium (RA)[4]. Among patients with RSIE, the tricuspid valve is involved in approximately 90% of cases[5]. Echocardiography is the technique of choice for the diagnosis of IE. Other imaging modalities such as computed tomography and nuclear imaging have also been shown to be particularly useful for the detection of acute infection, especially in those cases of prosthetic valve IE or cardiac implantable electronic device infection[6,7].

Many patients with tricuspid valve endocarditis (TVIE) can be successfully treated with antibiotics, with a smaller proportion of patients requiring surgical intervention. Compared to left-sided IE, less data is available guiding the indications and timing for surgery[8]. As the vast majority of RSIE cases involve the tricuspid valve, in this review, we focus on TVIE and the utility of multimodality imaging for the diagnosis and practical management.

## EPIDEMIOLOGY

In terms of risk factors for TVIE, it is strongly associated with intravenous drug use (IVDU), presence of a cardiac implantable electronic device (CIED) or other intravascular device, and presence of an underlying right-sided cardiac anomaly[9].

### *Injection drug users*

IVDU is the most common predisposing factor for TVIE, and is responsible for the increasing incidence of IE in developed countries, with an overall incidence of IE among IVDU patients ranging between 2% and 5% per year[10]. Repetitive use of injected drugs can lead to structural abnormalities of the TV detected by transthoracic echocardiography (TTE), such as focal thickening, valve prolapse, and regurgitation. These findings are likely the result of particles contaminating the illicit drugs being injected intravenously[10]. Among injection drug users presenting with fever, 13% will have echocardiographic evidence of IE and when concomitant bacteremia is present, up to 41% will show evidence of IE[10]. Blood cultures are positive in a high proportion of cases of right sided IE[9]. When culture negative right sided IE occurs, it is usually as a result of antibiotic use prior to the drawing of blood cultures[9].

### *Cardiac implantable electronic device infection*

IE related to CIED (CIED-IE) is an important subtype of RSIE that typically involves the device leads in the right heart, with frequent involvement of the adjacent tricuspid valve leaflets[11]. The infection can spread from an infected device pocket or through bacterial seeding[11]. With ageing population, its incidence has risen due to growing use of intra-cardiac devices[12].

The reported risk of infection is 0.5%-1% in the first year after implantation of a cardiac pacemaker, and rises with increasing complexity of the implanted device. For example, the infection rate for implantable cardioverter-defibrillator implantations is

1.7%, and even higher (2%) for cardiac resynchronization therapy implantations within 6 mo of hospital discharge. Compared with primary implantation, the risk of infection in the case of device replacement or revision procedures is between 2- and 4-fold higher[12].

### **Catheter-related blood stream infections**

TVIE resulting from peripheral venous lines is a relatively uncommon entity[1,6]. However, independent risk factors of TVIE have been shown include local cellulitis, use of infusion pumps, and insertion of a cannula in the lower extremity[12,13]. Dialysis patients often have a greater burden of co-morbidities, including diabetes, hypertension and atrial fibrillation, in addition to end-stage renal disease[11]. A total of 119 patients who underwent surgery to treat IE from a North American study showed that 16 patients were receiving chronic hemodialysis and approximately 20% of hemodialysis-related IE involved TV[11].

## **MICROBIOLOGY**

*Staphylococcus aureus* is the most common cause of TVIE, being responsible for up to 70% of cases[9,11]. *Streptococci* and *Enterococci* are the next most common pathogens, accounting for 5-30, and 2%-5% of cases, respectively[9]. Prosthetic valve IE and CIED-IE have a distinct distribution of causal microorganisms, as coagulase negative *Staphylococcal* infections are responsible for 25% of CIED-IE[14]. Fungi and gram-negative bacilli can also cause RSIE (less than 1% of cases)[9]. Increasing numbers of immunocompromised patients and the use of intravascular and intra-cardiac devices may be associated with a rise in fungal RSIE, associated with a high mortality[15]. In terms of fungal endocarditis, the in-hospital mortality is usually very high[16]. In a study of 78 patients with fungal endocarditis, 19 had isolated RSIE, and the overall mortality was 54%[16]. Infrequently, polymicrobial TVIE has been reported in a small number of TVIE cases[1,6].

## **DIAGNOSIS**

The accepted diagnostic criteria for IE are based on the modified Duke criteria[9]. The diagnosis is established based on clinical manifestations, blood cultures, and the presence of valvular vegetations detected by echocardiography[9].

## **IMAGING TECHNIQUES**

Echocardiography remains the first-line imaging modality for the evaluation of TVIE. However, there is emerging evidence for multimodality imaging in TVIE, potentially allowing better anatomical assessment with improved diagnosis in certain cases. A review of the relative strengths and weaknesses of the imaging modalities are shown in Table 1.

## **ECHOCARDIOGRAPHY**

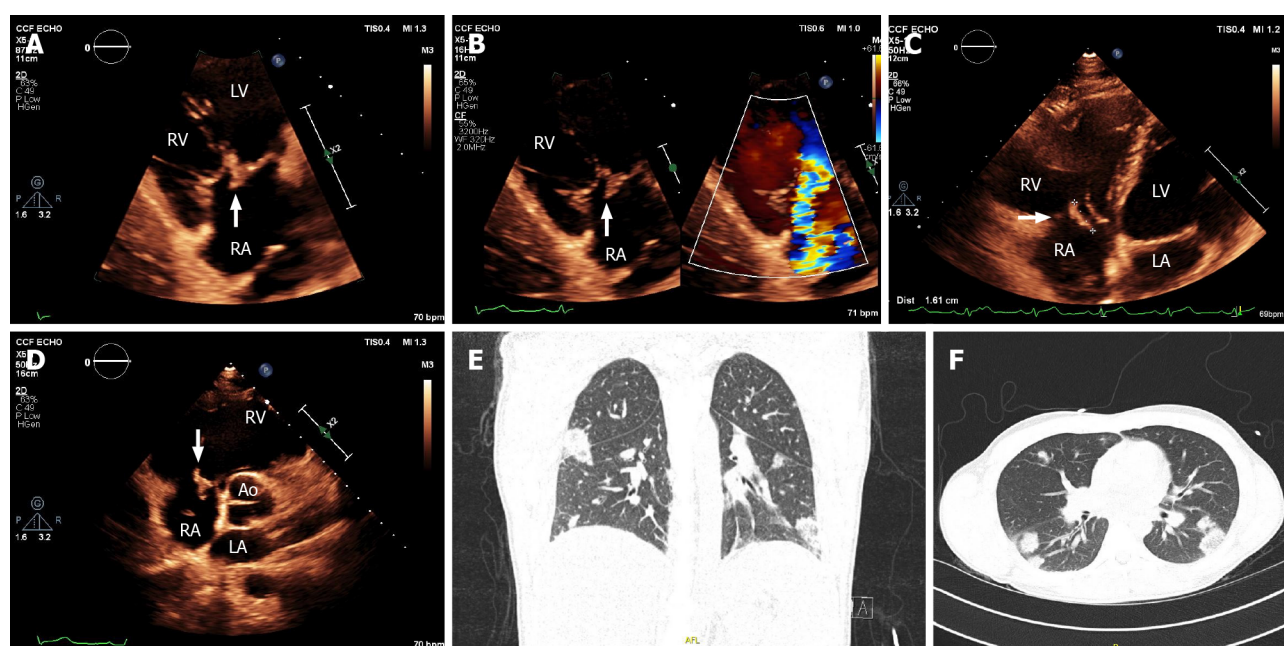
Echocardiography must be performed as soon as IE is suspected[1]. TTE is the recommended initial modality of choice[1]. Vegetations are detected by echocardiography as irregular shaped echodensities of variable size with independent oscillatory motion[6,11]. Tricuspid vegetations tend to be larger than left-sided lesions, partly due to lower pressure conditions (Figure 1). In native valve endocarditis, vegetations are typically found on the low-pressure surface, occurring usually on the atrial side of the atrioventricular valves[6]. TVIE lesions may cause valve stenosis, and valvular regurgitation secondary to leaflet/cusp perforation, subvalvular involvement with chordal rupture, or mal coaptation related to bulky vegetations[11]. TEE is indicated when TTE is non-diagnostic in cases of suspected complicated RSIE, prosthetic TVIE, or when intra-cardiac device leads are present. In addition, when an initial TEE is negative, but there is a high suspicion of IE, a repeat TEE is recommended[1,6]. Multiple non-standard views are essential and when available, multiplanar and 3D



**Table 1 Strengths and weakness of multimodality imaging techniques in evaluating tricuspid valve infective endocarditis**

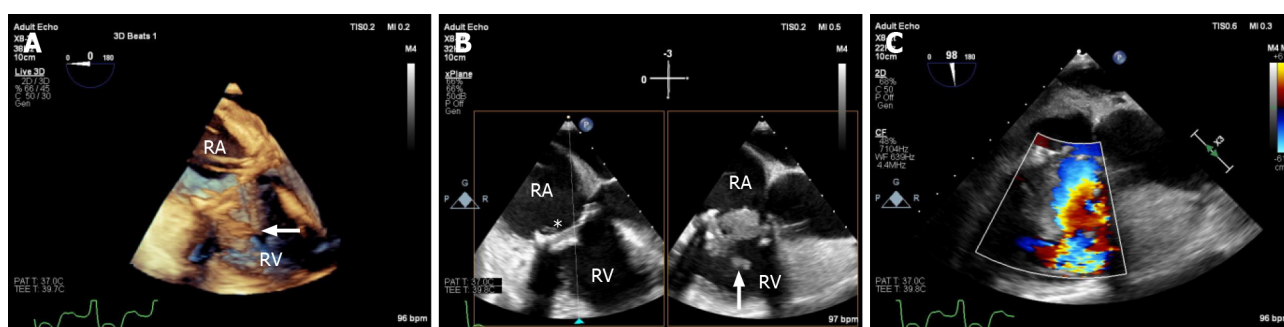
Imaging modality	Strengths	Weaknesses
Transthoracic echocardiography	Good assessment of vegetation and valvular function; Reproducible and low cost; Evaluation of the hemodynamic consequences	Limited sensitivity for vegetations attached to pacemaker leads and paravalvular complications; Limited ability to evaluate PVE
Transesophageal echocardiography	Better evaluation in PVE and CIED; Tricuspid valve function and PHT assessment; Detection of potential residual material after device extraction	Potential procedural complications for TEE; Limited differentiation between lead vegetation <i>vs</i> thrombus; Limited detection of peripheral complications
Multislice computed tomography	Can detect abscess/pseudoaneurysms; PVE extension and fistulas; Coronary artery preoperative assessment; Identifying pulmonary diseases as abscesses; Evidence of extracardiac involvement	Radiation exposure; Lead artifacts; Limited assessment in small vegetations contrast-induced nephrotoxicity
Magnetic resonance	Detection of extra-cardiac embolic lesions and systemic emboli	Claustrophobia; Cannot be performed for certain CIED
18F-FDG PET/CT	High sensitivity in PVE, generator/pocket and extracardiac or extravascular lead infection; Hypermetabolism + anatomic lesions (vegetations, leaflet thickening and perforation, fistulas); Better definition of the locoregional extension of the infection	Radiation exposure; Patient preparation (myocardial suppression); Visual interpretation. Non-standardized quantification analysis; False positive studies from inflammation or FDG uptake of the prosthetic materials
WBC-SPECT/CT	High specificity for pocket/generator or extravascular lead infection	Radiation exposure; Longer acquisition time; Lower spatial resolution

PVE: Prosthetic valve infection; CIED: Cardiac implantable electronic device; PHT: Pulmonary hypertension; TEE: Limited detection of peripheral complications; 18F-FDG PET/CT: 18F-fluorodeoxyglucose positron emission tomography/computed tomography; WBC-SPECT/CT: White blood cell-single photon emission computed tomography/computed tomography.

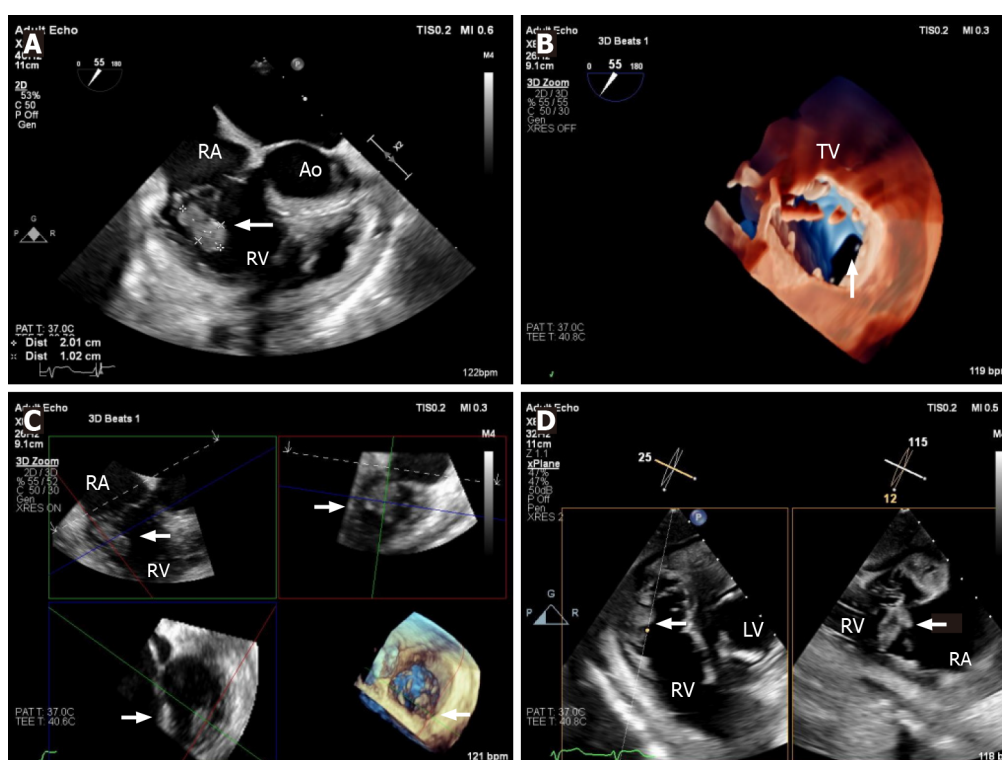


**Figure 1** Transthoracic echocardiography and computed tomography imaging assessment of native tricuspid valve endocarditis. A: Modified apical four-chambers view, focused on the tricuspid valve showing a vegetation attached on tricuspid valve (arrow); B: Color Doppler analysis showing severe tricuspid regurgitation caused by the vegetation; C: Sub-xiphoid view, measuring the vegetation as 1.6 cm; D: Short-axis view, showing the vegetation on the tricuspid valve prolapsing into the right atrium (arrow); E and F: Computed tomography lung demonstrating multiple areas of septic cavitations. RA: Right atrium; RV: Right ventricle; LA: Left atrium; LV: Left ventricle.

imaging should be used. In fact, a study with 203 patients with diagnosis of IE were analyzed with 2 d and 3D TEE and has shown that mayor diameter by 3D TEE had better embolic predictive performance than 2D TEE [AUC 0.76 (0.57-0.89) *vs* 0.71 (0.53-0.86);  $P = 0.611$ ]. The best cutoff points associated with embolic events during the infection were found to be 17 mm for RT 3D TEE and 15 mm for 2D TEE[7,17]. 3D TEE provides clear characterization of the vegetation, allowing precise determination of the size, allowing improved assessment for the risk of embolism in IE patients (Figures 2 and 3)[18]. It is important to mention that other than valvular vegetations, several other echocardiographic findings may qualify as major diagnostic criteria for IE, including abscess/pseudoaneurysm formation, fistulae, dehiscence of a prosthetic



**Figure 2** Transesophageal echocardiography of prosthetic tricuspid valve endocarditis. A: 3D view showing a prosthetic tricuspid valve with an attached mobile vegetation (arrow); B: 2D multi-plane view showing (arrow) a bulky lesion prolapsing across the tricuspid prosthesis (asterisk); C: Color Doppler interrogation confirms significant prosthetic tricuspid stenosis (transvalvular gradients: 37/21 mmHg at 98 beats per minute). RA: Right atrium; RV: Right ventricle.



**Figure 3** Transesophageal echocardiography in native tricuspid valve endocarditis. A: Mid-esophageal modified short-axis view showing a large vegetation attached to the native tricuspid valve (arrow); B: 3D transesophageal echocardiography imaging showing the vegetation to arise from posterior tricuspid leaflet; C: 3D multi-planar reconstruction on the vegetation, confirming the location on the posterior leaflet (arrow); D: Transgastric view, showing multi-planar assessment of the vegetation. RA: Right atrium; RV: Right ventricle; LA: Left atrium; LV: Left ventricle; TV: Tricuspid valve.

valve, perforation, and valve aneurysm[7,11]. In addition, when surgery is needed to manage RSIE, intraoperative TEE is mandatory; it provides the surgeon with a final anatomical evaluation of the extent of valvular and perivalvular damage[1,6,9,20].

## MULTISLICE COMPUTED TOMOGRAPHY

Multislice computed tomography (MSCT) should be considered when there is an absolute contraindication for TEE[21]. A gated CT study is recommended to reduce motion artifact. MSCT can be used to detect abscesses/pseudoaneurysms with a diagnostic accuracy similar to TEE, and it is excellent in evaluating the extent and consequences of any peri-valvular extension, including the anatomy of pseudoaneurysms, abscesses and fistulae (Figure 4)[22]. It should be noted, in RSIE, if cardiac CT is performed, meticulous attention must be paid to contrast timing, to maximize the ability to interrogate infective changes, such as vegetations. A recent study



**Figure 4 Multislice computed tomography with contrast.** Status post tricuspid valve repair. Lobulated pocket of free flowing blood/contrast interposed between the tricuspid annulus and the aortic annulus compatible with an abscess/fistula (arrow). Asterisk showing the tricuspid valve repair.

evaluated the associations between cardiac CT and TEE findings and adverse outcomes after IE surgery, including 155 patients who underwent both preoperative ECG-gated contrast-enhanced CT and TEE. Pseudoaneurysm or abscess detected on CT and fistula detected on CT were the only independent predictors of total mortality during follow-up, with hazards ratios (95%CI) of 3.82 (1.25-11.7),  $P < 0.001$  and 9.84 (1.89-51.0),  $P = 0.007$ , respectively[20,23].

It must be noted that in RSIE, the utility of cardiac CT also lies in evaluating extra-cardiac complications. Specifically, in TVIE, there are often associated pulmonary pathologies, and MSCT can be used to support IE diagnosis. TVIE may reveal on MSCT concomitant pulmonary findings, such as septic pulmonary emboli, parenchymal opacities, nodules, cavitation, abscesses, pleural effusions and infarcts[6]. Detailed multiplanar and 3D angiographic reconstructions allow identification and characterization of peripheral vascular complications of IE[24]. Additionally, dedicated coronary CT angiography may be used in select patients, to rule out coronary artery disease prior to cardiac surgery[25].

## NUCLEAR IMAGING

<sup>18</sup>F-fluorodeoxyglucose positron emission tomography/CT (<sup>18</sup>F-FDG PET/CT) and radiolabelled white blood cell-single photon emission computed tomography (WBC-SPECT/CT) provide added diagnostic value to the Duke criteria, when the infection is related to prosthetic valves or CIEDs. The use of these alternative imaging modalities is supported by current guidelines. The European Society of Cardiology diagnostic algorithm for IE stipulate findings on both MSCT and nuclear imaging modalities (FDG PET and leukocyte SPECT) as major criteria, in the context of prosthetic valve IE [1]. In addition, the American College of Cardiology in the Appropriate Use Criteria for Multimodality Imaging in Valvular Heart Disease guidelines recommend FDG PET as an appropriate imaging modality to use in suspected prosthetic valve endocarditis [21]. This imaging modality has the capability to demonstrate infective changes the whole device[26]. FDG PET/CT is useful in patients with evidence of pocket infection (local signs of inflammation at the generator pocket) and negative microbiological and echocardiographic examinations, and in patients with positive blood cultures but negative echocardiographic examinations[27]. FDG PET/CT is very specific when tracer uptake is visualized, but its sensitivity is lower[11], and a negative result does not completely exclude the presence of small vegetations[27]. A recent meta-analysis [28] found FDG PET/CT to be most useful in assessing prosthetic valve IE and CIED-IE, but is unlikely to be diagnostically useful in native valve IE, with a high sensitivity for prosthetic valve IE (86%) and CIED-IE (74%), but low sensitivity for native valve IE (31%). Of note, FDG PET/CT is not recommended to evaluate the surgical region of interest within 3 mo of surgery, as it can be associated with false positive results, due to post-operative inflammation[27]. Other pathological conditions that can mimic the pattern of focally increased FDG uptake include vasculitis, atherosclerotic plaque, foreign body reactions (such as surgical adhesive used to repair the aortic root), active thrombus, Libman-Sacks endocarditis, cardiac metastasis from a non-cardiac tumors or primary cardiac tumors[29].



Radiolabeled WBC SPECT/CT is reported to be more specific for the detection of IE and infectious foci than 18F-FDG PET/CT. However, compared with PET/CT, this modality requires blood handling for radiopharmaceutical preparation and is more time-consuming, with a slightly lower spatial resolution and photon detection efficiency[29].

## MAGNETIC RESONANCE IMAGING

Magnetic resonance (MR) can be used to quantify the extent of valvular regurgitation caused by IE. However, this imaging modality seems to be of most value in the identification of extra-cardiac systemic complications, such as cerebral, pulmonary, and intra-abdominal embolization[9]. MR is not associated with ionizing radiation, but has a lower spatial resolution and reduced availability[30]. MR angiography in the setting of potential mycotic aneurysms from septic embolism may be useful[31]. However, a study where the aim was to compare 12 patients with a total of 17 aneurysms demonstrated that the sensitivities of CT scanning and MR angiography were 94% and 86%, respectively, for the detection of intracranial non-infectious aneurysms 5 mm or larger, but only 57% and 35%, respectively, for aneurysms < 5 mm[31]. Thus, conventional angiography remains the gold standard, and should be performed when non-invasive techniques are abnormal[32].

## MANAGEMENT

Successful treatment of TVIE relies on microbial eradication with appropriate antimicrobials. Non-operative management of TVIE with antibiotics alone has been reported to clear the bacteremia in 70%-85% of cases[1]. However, medical treatment alone is not always effective, and surgical intervention may be warranted in select cases. Patients undergoing surgery for TVIE compared to left side IE presented with a higher rate of pulmonary septic emboli, more *Staphylococcus aureus* infections and larger vegetations[2]. The proportion of patients who are reported to undergo surgery for RSIE ranges from 5%-40%[33], with an operative mortality as high as 15% for patients with isolated TVIE[14].

Because surgery during the active phase of TVIE has considerable risk, it is important to provide accurate assessment of the extent of peri-valvular extension of IE, and to identify those patients who would not be expected to recover with medical therapy alone[34]. In other words, the decision for surgery should be based on the best possible understanding of the pathology, incorporating multimodality imaging findings.

Common indications for surgery in patients with TVIE include: (1) Right heart failure secondary to severe tricuspid regurgitation, valvar obstruction or fistula[6]; (2) Uncontrolled infection (persistent bacteremia for more than 7 d despite adequate antimicrobial therapy (*e.g., fungi; bacteremia* due to *S. aureus*, *P. aeruginosa*); or peri-valvular abscess and/or aneurysm[6]; and (3) European Society of Cardiology Guidelines suggest vegetation size of  $\geq 20$  mm as a potential indication for surgery[1,6,9].

The American Association for Thoracic Surgery guidelines recommend that once a surgical indication is evident, surgery should not be delayed[19]. In the event that multiple valves are infected, the indication for surgery is of tendicated by the left-sided IE[8].

The principles of surgery for TVIE include radical debridement of vegetations/infected tissue and valve repair whenever possible[19]. If valve replacement is performed, then an individualized choice of prosthesis taking into account of patient factors, is important[6]. A tricuspid valve prosthesis is associated with an increased risk of recurrent IE, particularly in patients who relapse into intravenous drug use[14].

Infections related to cardiac devices should be diagnosed early, and mandate the removal of the device and all implanted leads[8]. Special note is made of percutaneous removal for RSIE, as an alternative to surgery. The use of percutaneous aspiration devices is effective in removing large tricuspid valve vegetations in cases where the risk of tricuspid surgery is prohibitive[35]. Vacuum assisted devices (AngioVAC system, AngioDynamics, Latham, NY, United States) can be used for the removal of right sided intra-cardiac masses[35]. This percutaneous aspiration is composed of an extracorporeal circuit pump head and bubble trap, an outflow line and a reinfusion cannula[35]. The aspiration of vegetations immediately prior to, and during the lead extraction procedure may prevent septic embolization into the pulmonary circulation,

and may confer improved short- and long-term survival[36]. On the other hand, it is important to mention that percutaneous vacuum-assisted devices have its own potential risks, such as disruption of the vegetation leading to pulmonary embolization and vascular access complications, such as bleeding[37]. It should be noted that percutaneous therapies for tricuspid valve vegetation removal have relatively limited availability, and is dependent on the experience of the individual centers. Currently, there are no guideline recommendations about percutaneous therapies for tricuspid valve vegetation removal.

## ENDOCARDITIS TEAM MANAGEMENT

The European Society of Cardiology and American Heart Association guidelines recommend a team approach for optimizing the management of patients with infective endocarditis. IE is not a single-faceted disease, but rather a very complex disease with many different aspects and factors involved, depending on the type of bacteremia, patient factors, and underlying cardiac disease.

Patients with TVIE due to IVDU are associated with a high risk of recurrence. To reduce this risk, these patients undergo comprehensive treatment, including psychotherapy, medication-assisted treatment, in order to establish a safe environment for recovery.

## PROGNOSIS

TVIE is generally associated with better clinical outcomes than left-side IE[38]. There is less systemic embolization, less abscess formation, and less drug-resistant infection and thus is clinically better tolerated. A retrospective study of patients with IE ( $n = 215$ ), Stavi *et al*[39] reported that in-hospital mortality was lower among patients with right-sided IE compared with left-sided IE (2.6% *vs* 17%,  $P = 0.037$ ). Conservative medical management may be used in many patients. However, there are some factors associated with poor prognosis. A size vegetation length of  $> 20$  mm, increase in vegetation size despite antibiotic treatment, fungal etiology, recurrent septic pulmonary emboli, severe tricuspid regurgitation are the main predictors of early post-operative mortality[11].

## CONCLUSION

Imaging has a crucial role in the diagnosis and management of patient with TVIE. With increasing IVDU and intra-cardiac device implantations, the diagnostic suspicion of TVIE should be high in appropriate clinical scenarios. Echocardiography should be always performed when TVIE is suspected, complemented by TEE when TTE results are inconclusive. MSCT, FDG PET/CT, and WBC SPECT/CT may add value to improve the accuracy of IE diagnosis, where there is a high suspicion of infection and negative echocardiographic imaging, and/or in the presence of an intra-cardiac prosthesis or device. Multimodality imaging may lead to improved diagnosis and appropriate tailored treatment. Many patients with TVIE can be successfully treated with antibiotic therapy. Some patients with TVIE require surgical intervention, with tricuspid valve debridement and repair/replacement being accomplished in most cases. More data are required to establish the role of percutaneous aspiration devices in the management of TVIE and CIED-IE.

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