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Non-valvular prostheses/device-related infective endocarditis: Study of diagnosis, management, and outcomes of surgery

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Abstract

Endocarditis caused by foreign hardware is not common, but its incidence is rising; it presents difficult management problems to clinicians. We evaluated our experience as a tertiary referral center focusing on the management and the outcome, including medical and surgical approaches. Focus on decision-making about timing and surgery techniques. This case series analytical descriptive study enrolled 60 patients with infective endocarditis caused by an inserted hardware retrospectively and prospectively between January 2016 and August 2023. The mean age was 24.2 years, including 26 males and 34 females. 42 patients (70%) were diabetics and 43 patients (72%) had underlying cardiac disease. The operation was done with a mean timing of 32 +/- 2.9 days after the diagnosis. Surgery was by either percutaneous extraction in 13 patients versus intra-cardiac intervention in 37 patients. Culture of surgical specimens showed MRSA, MSSA, and others in 72%, 12%, and 16% of cases, respectively. The mean postoperative ventilation time was 6.5 +/- 3.87 hours, and the mean ICU stay was 4 +/- 3.5 days. **Conclusion:** The clinician should be aware of any sign or symptom developed in a patient who previously underwent a hardware insertion, taking cultures before starting antibiotics and applying a management plan by heart team coordination.

Keywords: Endocarditis, Infective, endocardium, Non-Valvular Prostheses/Device.

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1.Introduction

Infective endocarditis is defined as a focus of infection in the endocardium of the heart; it is a feared disease across the field of cardiology. It is frequently acquired in the health care setting. Despite optimal care, the challenges, morbidities, and mortalities posed by infective endocarditis are significant [1-2]. The most common organisms for such pathology are the gram-positive cocci (ie, *Staphylococcus aureus* (*S. aureus*), *Coagulase Staphylococci (CoNS), enterococci, non-enterococcal streptococci)* [3]. The indications for surgery have been predominantly derived from observational studies that show benefit in patients with valve dysfunction causing heart failure, uncontrolled infection (defined as a para-valvular extension, abscess, or persistent bacteremia), or recurrent embolism [4]. The present study reviews the challenges posed by hardware-associated infective endocarditis and outlines strategies to limit its impact based upon our center experience in the field. The purpose of this study was to describe the causes, predisposing factors, management and outcome of endocarditis caused by a non valvular prosthesis, including both medical and surgical approaches. Focusing on the decision making about timing and techniques of surgeries, with follow up during the postoperative period in the hospital.

2. Methodology

The study enrolled up to 50 subjects assigned to cardiac surgery as a part of management of hardware-related infective endocarditis. The patients were recruited from Cairo University affiliated hospitals after an informed written consent has been taken, retrospectively and prospectively in the period from March 2022 to September 2023. Patients were selected according to the following criteria.

2.1: Inclusion criteria

Only patients with definite hardware-related IE using the modified Duke criteria for IE were included: All patients, with or without local signs of pocket infection, had valve vegetations in either valve or attached to the prosthesis and positive blood cultures and/or foreign body culture. The causative non-valvular foreign bodies include the following: Prosthetic intravascular devices: central or peripheral

intravenous catheters, chemotherapeutic and hyper-alimentation lines, rhythm control devices: pacemakers and defibrillators, cardiac or extra-cardiac prostheses used in congenital heart diseases such as atrial or ventricular septal defects closure devices or patches, patent ductus arteriosus closure devices or stents, hemodialysis catheters and dacron grafts.

2.2: Exclusion criteria

Patients with no definite criteria for IE, prosthetic cardiac valve endocarditis and combined other cardiothoracic surgery; such as coronary artery bypass graft surgery, cardiac or lung tumors surgeries.

3. Methods

All patients will be evaluated by the following parameters.

3.1: Patient assessment

3.1.1: Age and sex, **Clinical evaluation: Presenting symptoms**

Onset, time, duration: Fever, symptoms of systemic illness: fatigue, myalgia, anorexia, weight loss, back pain, nausea and vomiting, extremities: bony pain or arthralgia, hematuria, cardio-respiratory symptoms: dyspnea, cough dry or expectorant, neurological: disturbed consciousness and convulsion, ocular and surgical emergency: pneumothorax or acute limb ischemia.

3.2: History of present illness

Main symptoms which deteriorated, symptoms onset, course and duration, blood cultures withdrawn and the results, prior antibiotic use and route and duration and long-acting penicillin administration.

3.3: Relevant past history

Possible culprit procedure, known heart disease and hospitalization in last 3 months.

3.4: Underlying cardiac disease

Cardiac condition, prosthetic valve(s): excluded, congenital heart disease including congenital heart block and rheumatic heart disease.

3.5: Vitals

Heart rate, rhythm, blood pressure, respiratory rate and temperature.

3.6: Skin, nails and mucous membrane lesions

Osler's nodules, clubbing, splinter hemorrhage, drug eruption, Janeway lesions, gangrene, sub-conjunctival hemorrhage, pallor, needle puncture marks, mucous membrane petechiae, and jaundice.

3.7: Abdominal manifestations

Organomegaly, tenderness and rigidity.

3.8: Cardiovascular manifestations

Heart failure, new murmur and other murmurs.

3.9: Neurological manifestations

Paresis, hemiplegia, intra-cranial hemorrhage and conulsons and major arterial embolization**.**

3.1: Laboratory investigation

CBC: anemia, differential leucocytic count, kidney function tests Liver functions tests, coagulation profile, blood sugar test and IE tests ESR, CRP, pan cultures and antibiotic sensitivity. Blood cultured as follows: blood from patients suspected of having IE was cultured in 3 sets (each set equals 1 aerobic plus 1 anaerobic bottle).

3.10.1: Imaging **Trans-thoracic and trans-esophageal echocardiography** Cardiac CT is the adjunctive modality for delineating the anatomy, PET/CT and cardiac MRI may be used.

3.11: Management plans

Operative data are collected and photographed in the cardiothoracic operating theater of Kasr El-Aini school of medicine affiliated hospitals and they are summarized as follows: Type of operation (extra or intra cardiac), if extra-cardiac: percutaneous extraction of leads, skin pocket debridement and device removal, cardiopulmonary bypass time, total cross clamp time, valve replacement: type and size, area of debridment, surgical specimen, intra-operative complications: bleeding, failure to wean from bypass, iatrogenic injury, heart block, clinical state at the end of the operation, infusion supports, need of mechanical support: intra-aortic balloon or extra-corporeal membrane oxygenator (ECMO).

3.12: Operative procedure

The following cases are some examples of our documented operations, consisting of debridement of infected tissues either intra or extra cardiac, taking a surgical specimen and valve replacement if needed. For extra-cardiac lesions, those are some examples included in our study. Patient number (13) is a 9 years old female with history of tricuspid valve repair and pacemaker insertion at age of 6 years, then pacemaker replacement due to dysfunction 1 year later. The second pacemaker pocked developed pus discharge and echocardiography showed small vegetation related to the pacemaker wires. Surgery was done to replace the infected pacemaker device and wound debridement, and medical treatment continued for the infective endocarditis with follow up. Patient number (17) is a 25 years old male patient with hypothyroidism on replacement treatment. He had congenital complete heart block, and abdominal pacemacker device is inserted at age of 2 years. Then a left subclavian device VVI with one ventricular lead is inserted at age of 10. Transvenous right jugular temporary pacer implanted, TEE done showed multiple vegetations on two leads, infective endocarditis protocol started and operation done for leads extraction and battery replacement into the right subclavian region. For intra-cardiac lesions, steps were as follows: The patients were placed in supine position. All patients are approached via median sternotomy, followed by pericardiotomy (figure 1) and full heparinization is given. Arterial and venouse cannulation applied while taking care not to dislodge vegetations if any is suspected. (Figure 2). Going on bypass and if needed aortic cross clamping and cold cardioplegia (Del Nido) is given over 20 minutes. Then the affected intra-cardiac part is attacked for debridement, taking a surgical specimen and valve replacement if needed.

The following are some examples of intra-cardiac lesions: Patient number (29) is a 6 years old female admitted into hospital due to repeated pneumonia attacks, Central Venous Line (CVL) showed infected debris and echo showed large vegetation related to the atrial surface of tricuspid valve indicated for surgical debridement and tricuspid valve replacement (Figure 3).

Next, the heart chamber (aortotomy, right or left atriotomy) is closed, de-airing is done and if cross clamp is applied, it is removed allowing time for recirculation of blood into the coronaries. When heart rhythm was restored and the rate was satisfactory for age; weaning off bypass was gradually achieved after restoration of lung ventilation. If the cardiac output was satisfactory, venous cannulae were removed, and heparinization was reversed using protamine sulfate in a dose of (3-4 mg/Kg IV). Aortic de-cannulation was continued after re-infusing the remaining amount of patient's blood from the reservoir of the heart-lung machine. A temporary cardiac pacemaker was used to pace through the inserted epicardial leads as a backup in cases of postoperative heart block.

3.13: Postoperative care

Patients were transmitted to cardiac ICU, while ventilated and on inotropic support if needed.

All patients in ICU were fully monitored: invasive blood pressure monitoring, direct CVP measuring, continuous ECG monitoring, urine output hourly monitoring, fluid balance and chest tubes and surgical drains are monitored.

Hemodynamic stability is maintained by intra-venous fluid compensation of blood loss as mentored by chest tube drainage compensated by blood and plasma infusion, inotropic support and vasodilator to maintain hemodynamic stability, the latter are gradually weaned off, and discontinued after gradual weaning from artificial ventilation and extubating is done.

3.14: Further assessment

Cultures results and antibiotic sensitivity, Hospital morbidities or mortality and Hospital stay time.

4. Statistical analysis

Data collected will be computed, coded, verified and statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 25. Categorical variables will be described using frequency tables (as frequency and %), and quantitative variables will be described as mean, standard deviation and range (median and interquartile range will be used if variables are not normally distributed). Non-parametric Mann-Whitney test, will be used if data are not normally distributed. The odds ratio and corresponding 95% confidence intervals will be reported for covariates. Findings will be presented in tables and graphs as appropriate.

5. Results

Our study was carried out on 60 patients with different culprit interventions including: 16 patients with CVL, 13 patients with pacemaker insertion, 16 CKD patients with dialysis shunt or catheter, 4 patients with Dacron tube graft for aorta replacement, 1 case of PDA occluder device, 4 patients with ASD or VSD occluder device and 6 patients with ASD or VSD Dacron patch.

The study included 26 males representing 43.3% and 34 females representing 56.7% and the age ranges from 1 month to 78 years with mean 24.2 years. Demographic data are illustrated in tables (1). Symptoms and signs were variable including cardiovascular, neurological and embolic manifestations, but fever and chills were the most common symptoms. Table 2. Staphylococci represented more than third of cases either MSSA or MRSA, enterococci were dominant in cases of CVL and dialysis catheter infection. Other results or no growth also were detected.

10 patients were treated medically according to the guidelines listed before. Patients received both symptomatic treatment for fever, myalgia and treatment of complications as diuretics and cardiac supports for heart failure. Systemic illness was also addressed as treatment of hypertension, diabetes and renal failure. Treatment of the cause by antibiotics is started empirically after withdrawal of blood culture and skin swabs and adjusted according to the result of culture and sensitivity. Our study included 13 cases of percutaneous extraction of the hardware representing the source of infection in the form of pacemaker lead (in 6 cases) and CVL (in 7 cases). 37 cases needed intra-cardiac intervention detailed as follow:37 patients underwent intra-cardiac intervention. They included 25 cases of debridement of infected material with little or no valve repair was needed like tricuspid or mitral bad annuloplasty, 8 cases needed tricuspid replacement with tissue valve, 2 cases needed aortic valve replacement along with debridement of aortic root abscess, 2 cases with destructed mitral valve leaflets causing severe mitral regurge had mitral valve replacement. Cases needing cardioplegia and ischemic arrest were assessed in table 4.

6. Discussion

In this study**,** we analyzed a total of 60 patients of both genders and of all age groups suffering from infective endocarditis with a non-valvular prosthesis/device as source of infection, 10 patients were managed only medically and 50 patients needed surgical intervention as a part of management. The patients were recruited from Cairo University affiliated hospitals after an informed written consent had been taken. The data were retrospectively and prospectively collected in the period from January 2016 till August 2023.

Our demographic data of the patients included 60 patients with infective endocarditis caused by an inserted device or prosthesis, the study included all age groups ranging from 2 months old to 78 years old, with mean age of patients was 24.2 years. Both genders were included with 26 patients are male and 34 are females.16 patients with IEC originating from an inserted CVL, 13 cases of pacemaker leads, 10 patients with Dacron tube graft or Dacron patch infection, 16 patients with dialysis catheter infection, and 5 patients with ASD, VSD or PDA occlude device as source of infection.

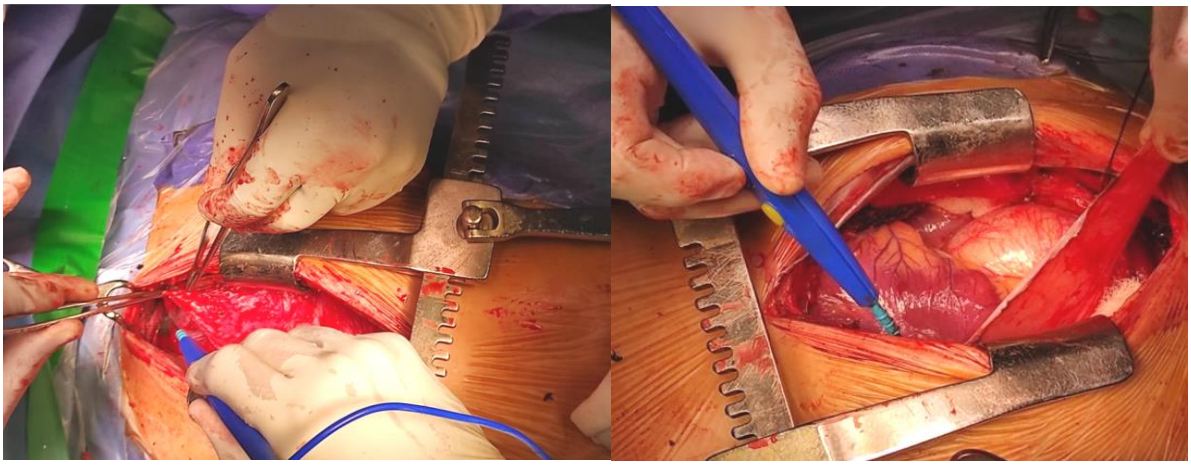

Figure 1: Median sternotomy then pericardiotomy

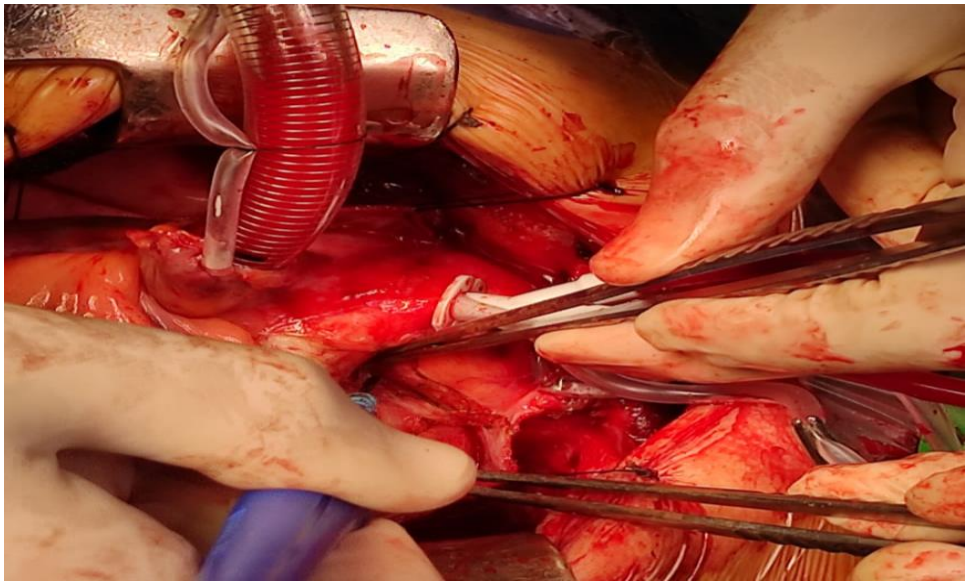

Figure 2: Aortic and cardioplegia cannulae insertion

Table (1): Demographic data

		Number	Percentage
Gender	**Male**	26	43.3%
	Female	34	56.7%
Age		From 0.08 to 78 years with mean of 24.22 years	

Table 2: Presence of symptoms and signs of systemic illness

symptoms and signs of systemic illness	Number	Percentage
Fever and chills	43	71.6%
Other	17	28.4%

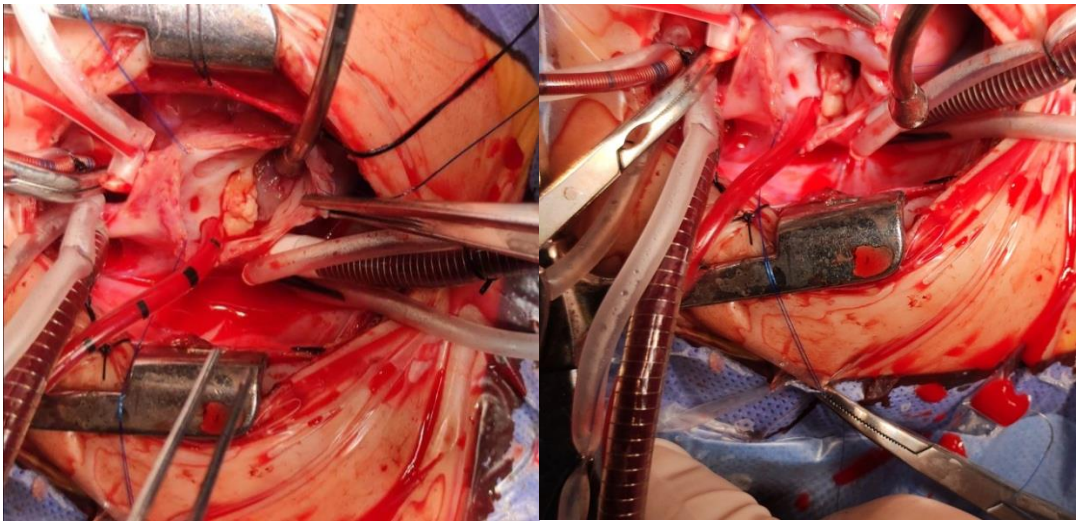

Figure 3: Right atriotomy showing tricuspid valve large vegetation.

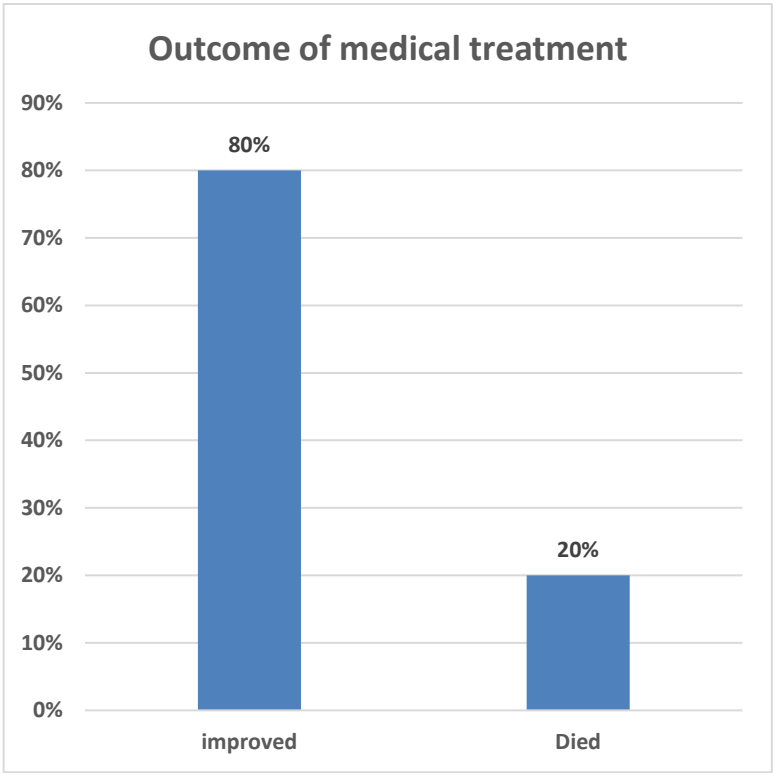

Figure 4: graph chart showing the end result of medical treatment

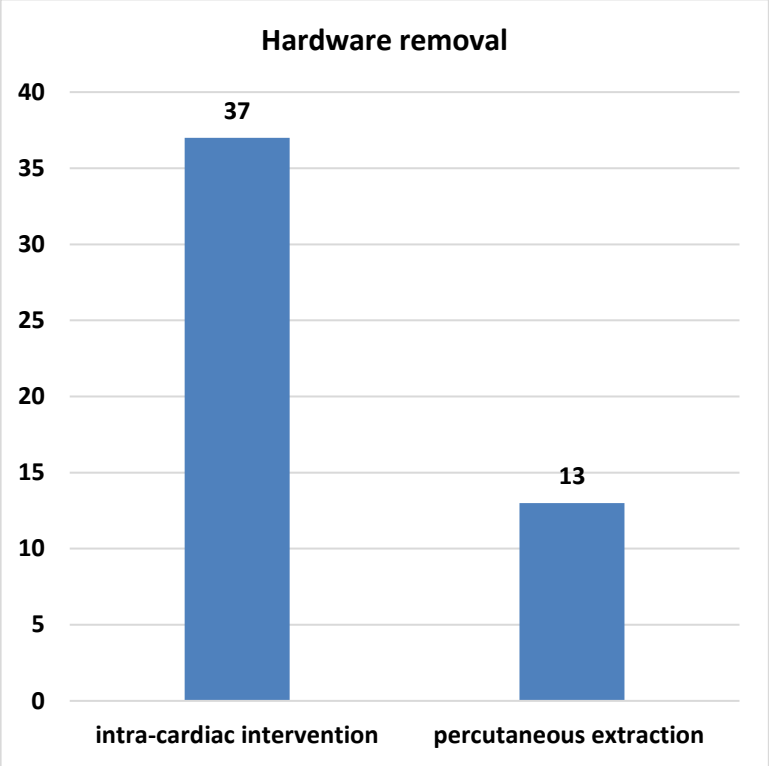

Figure 5: graph chart showing number of each type of surgery

Table 3: Patients' presentation according NYHA classification of heart failure

NYHA classification	Number	Percentage
Class I	14	23.3 %
Class II	27	45 %
Class III	12	20 %
Class IV	7	11.7%

Table 4: Bypass and ischemia times

	Bypass time (minutes)	Ischemia time (minutes)
Minimum	*65*	*50*
Maximum	*115*	95
Mean	76.1	*68.*1
Standard deviation (+/-)	14.03	12.43

Table 5: Culture results of surgical specimen

Cultures of surgical specimen		
Bacterial growth	**Number of cases**	**Percentage**
MRSA	36	72%
MSSA	6	12%
OTHERS	8	16%

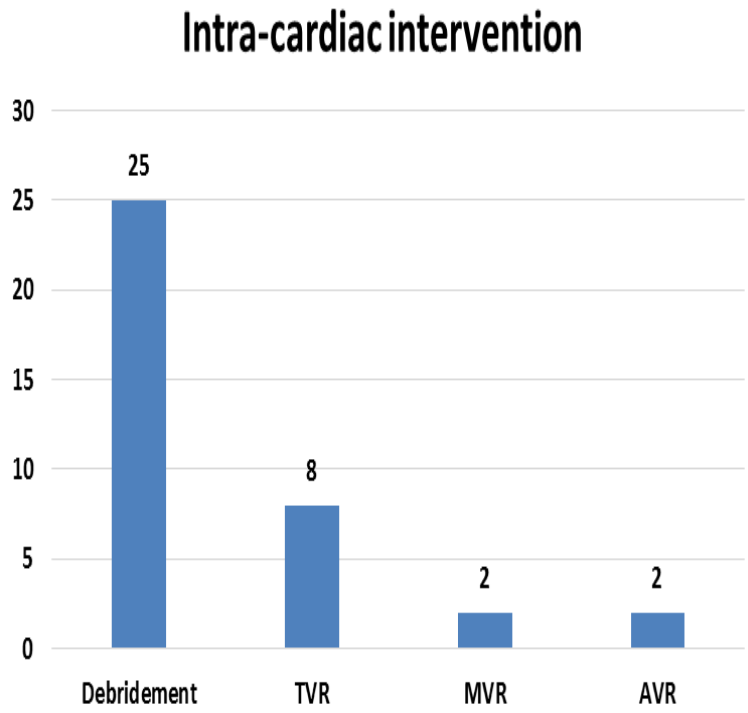

Figure 6: number of patients with intra-cardiac intervention

Table 6: Duration of mechanical ventilation till extubated

Duration of mechanical ventilation (hours)	
Extra-cardiac procedures	3 +/- 1.5 hours
Intra-cardiac intervention	8 +/- 4 hours

Table 7: Outcome of surgical management

Outcome	**Number of patients**	**Percentage**
improved	43	86%
Died	7	14%

About the timing of diagnosis, there is a significant delay between the symptoms of the disease and the diagnosis. Cacoub et al., [5] reported on 33 patients in whom device-related endocarditis was diagnosed, and in whom the delay from the onset of symptoms to evidence of the disease was, on average, 5 months ± (one to 27 months). Laguno et al., [5] reported an average delay of 17.5 months until the diagnosis in a series of seventeen patients. Victor et al., [6] reported an average delay of 2.6 months ± (range three days to 15 months) in a series of 23 patients.

Overall, based on these studies, the average reported delay in diagnosis was 5.5 months, versus 8.4 +/- 2.6 months in our study. Longer average timing of diagnosis in our study may be due to lower socio-economic state of the country and the less medical orientation, thus delay of seeking medical advice. In general, this relatively prolonged timing denotes that the type of infection is not easy to identify and the delay of diagnosis on itself is a predisposing factor to more complications of the disease. Based on one of the largest historical cohort focused on CIED-IE by Mestres CA et al, [7] a study done over 30 years and managed by a single IE team in a referral center since 1985, all cases have been evaluated with uniform medical and surgical management criteria. The medical and surgical approach is established that removing the entire hardware is mandatory with antibiotic coverage. [8, 9] Complete causative foreign body removal is the most important protective factor as has been shown. [9,10]. Other authors have also reported the increasing use of medical therapy to manage CIED-IE when device removal is not possible or has higher risk of complications like injury or embolization of vegetation. [11]

Antimicrobial therapy as per ESC guidelines 2023 for CDR-IE should be individualized and based on culture and susceptibility results if possible. We studied 10 patients managed medically following the ESC 2023 guidelines as follows: Vancomysin administered initially as empirical antibiotic coverage until microbiological results are known [12]. After blood cultures withdrawal, IV antibiotics were initiated. The duration of therapy was 4 – 6 weeks in most cases [13]. Then symptoms improved, fever subsided. Serail follow up TTE and/or TEE showed that the detected vegetation has been diminished then vanished. Patients with sustained positive blood cultures despite an appropriate antimicrobial therapy received parenteral therapy for at least 4 weeks [13-14]. Two encountered mortalities during medical treatment (20% of cases treated medically) due to septic shock in one patient who was presented after severe deterioration of his physical state, and hospital acquired pneumonia in the other old (76 years old) patient. And this is going in line with a computerized systemic literature search by PubMed, Scopus and Google Scholar from 2000 to august 2016 including 22,382 patients with infective endocarditis, the overall pooled mortality estimates during the short-term and long-term follow-up were 20% and 37% respectively [15].

Our study analyzed data of 50 patients who underwent an operative intervention to remove the underlying hardware plus or minus cardiac valve(s) repair or replacement. Average timing of surgical intervention was after 32 days of diagnosis and IV antibiotics. We operated on13 patients representing 26% by hardware extraction as an extra-cardiac procedure, 6 patients of them representing 12% underwent extraction of PM leads, and the other 7 patients representing 14% underwent extraction of CVL 37 patients (74%) needed intra-cardiac tackling of the infection and removal of the infected hardware; such as: dialysis shunt, dacron tube graft, PDA occluder, ASD occlusion device, VSD patch, then debridement of the surrounded infected tissues and replacement of the hardware if needed. 8 of them representing 16% needed TV replacement, 2 patients needed MVR and AVR in 2 patients. Intra-cardiac cases had an average bypass time of 76.1 minutes and average ischemia time of 68.1 minutes.

Mugge et al., [16] studied the management of PM leads IEC. They concluded that with the presence of large vegetations (10 mm or more), the PM system should be removed by opening the chest wall to avoid thromboembolic events. In patients with small vegetations (less than 10 mm), the lead is only removed by external traction [16, 17]. In our study, we reported 6 cases of pacemaker wire removal, with 1 case of pulmonary embolism at the time of external traction, and 3 cases of wires extraction in one session followed by TV replacement in another session. 2 cases needed no further intervention and improved. While in our study, we reported 16 cases of dialysis shunt removal, one of them was accompanied with MVR, 2 cases accompanied by TV replacement that went well. And following percutaneous ASD device closure, infective endocarditis is commonly considered to be an exceptional event as mentioned by Chessa M and Kutty et al., [18, 19] In a study by Pascal Amedro et al., [20] and review of a meta-analysis [21] and 2 FDA databases, [22] they identified twenty-one cases of infective endocarditis following atrial septal device closure representing about 0.8% [23] with mean age ranging from 2 to 20 years old. [19]. And this goes in line with our statistics denoting that 4 patients with ASD or VSD occlusion device-related endocarditis (8% of cases) are treated surgically, and their outcome was successful, but 1 (2% of cases)0 patient died after the operation from sepsis. Postoperative surgical outcome reflected the pre-operative state of cases which were mostly complicated and associated with co-morbidities aggravating morbidities and mortalities. Regarding the culture and sensitivity done from the surgical specimen, 84% of cases showed staphylococcal species either MSSA (12%) or MRSA (72%). Baddour LM et al., [24] also noted the predominance of staphylococcal infections cultured from the infected hardware. However, interestingly, they identified an increase of Enterococcus spp infections, probably due to aging and more frequent comorbidities. In their study of the device-related EC, Oh et al., [25] conducted a descriptive analysis and reported 4.8% of enterococcal infections from the whole database of 433 patients. In their study, Hee D. Jeon et al., [26] reported an overall in-hospital mortality rate of 33.8%, decreased to 31.7 % in patients undergoing surgery that but this was not statistically significant due to the small size sample [27]. During our post-operative follow up, 7 in-hospital mortalities occurred (14%), due to MOF complicating sepsis. Median length of stay in ICU and hospital of 14.3 ± 15.6 and 42.5 ± 27 days, respectively, in a total of 82 cases with IE studied by Hugues Georges at al. , [28] & Hauts de France endocarditis study group. Compared with our study that noted 14 ± 7 and 37 ± 11 days of ICU and hospital stay respectively.

7. Conclusions

After assessing our results, we concluded that there is a significant delay in diagnosing such infection – an average of 8.4 months from the clinical onset – which the clinician should be aware of any time a clinical sign or symptom develops in a patient who previously underwent any device insertion. The clinician must insist on taking cultures from any suspected site of infection related to the catheter, lines or device before antibiotic initiation. The most common pathogens are Staphylococcus species. The treatment may be medical treatment only or a combination of antibiotic treatment and surgical removal of the foreign body itself with or without intra-cardiac intervention according to the need.

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