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Case Series

Internal Medicine Section

Role of Early Mitral Valve Surgery in Acute Infective Endocarditis: A Case Series and Review of Literature

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ABSTRACT

Infective Endocarditis (IE) is a serious cardiac infection diagnosed with syndromic approach based on clinical, immunological, sonographic, and microbiological findings. It is highly suspected in patients with pre-existing heart disease who have bacteremia in absence of other obvious source. Due to its non-specific symptoms and delayed diagnosis causes severe septicemia, multiple organ failure, and high mortality. This case series describes three critically ill patients who were diagnosed with active IE upon admission to the Intensive Care Unit (ICU). All three patients were admitted in critical condition and were newly diagnosed with IE. They were initially stabilised with appropriate antibiotics. However, during their ICU stay, after two weeks, they experienced recurrent arrhythmias and severe Mitral Regurgitation (MR), complicating recurrent pulmonary oedema that hindered weaning from mechanical ventilation. Therefore, it was decided to perform Mitral Valve (MV) correction surgery during the acute phase of endocarditis (2 weeks after starting antibiotics). Unfortunately, all patients had in-hospital mortality. Intraoperative findings revealed extensive vegetation on the Anterior and Posterior Mitral Leaflet (AML and PML) with extension to the chordae. The high mortality was attributed to their critical pre-operative condition, septic shock, and cerebral embolism. Guidelines and task force management clearly state that early surgery plays a definitive role in acute endocarditis with complications. However, identifying the appropriate candidates for early surgery is challenging due to the associated high mortality. A database search on MV surgery in acute IE, comparing repair and replacement, has concluded that repair is safe and associated with better survival than replacement.

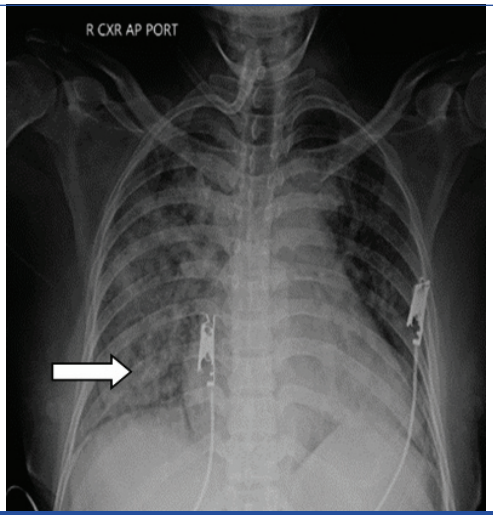
Keywords: Anti-bacterial agents, Arrhythmias, Bacterial endocarditis, Cardiac embolism, Intensive care units, Sepsis

CASE SERIES

Case 1

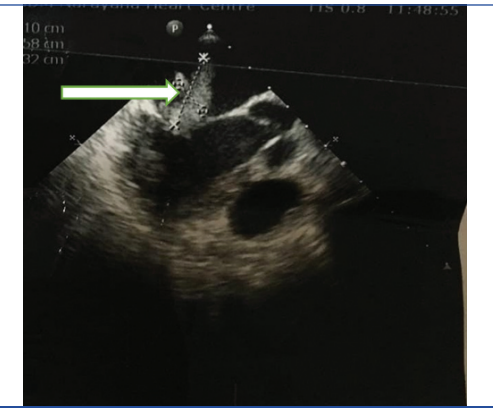
A 50-year-old female patient presented with a history of paroxysmal nocturnal dyspnoea and breathlessness for the past 15 days. She was apparently fine 15 days ago and visited the outpatient department with the aforementioned symptoms. She had a known case of hypertension and end-stage renal disease, requiring haemodialysis for the last three months.

Her dialysis access consisted of a right internal jugular tunnel catheter in-situ, arteriovenous fistula. Physical examination revealed pallor, icterus, and pedal oedema. Bilateral rhonchi were noted. She was diagnosed with an infected permacath with sepsis and congestive cardiac failure. To maintain saturation, she required 4L of oxygen through a facemask. A two Dimensional (2D) echocardiogram showed a large vegetation in the anterior mitral leaflet. Appropriate antibiotics (Injection (Inj.) Vancomycin, Inj. Ceftazidime, and Inj. Amikacin) were initiated, and the tunnel catheter was removed. Chest X-ray (CXR) revealed features of pulmonary oedema [Table/Fig-1].



[Table/Fig-1]: Chest x-ray Shows bilateral parenchymal infiltration (perihilar) suggestive of pulmonary odema.

On the first day of ICU admission, the patient was in shock. Blood culture and sensitivity reported the growth of *Enterococcus species* and Methicillin-Resistant *Staphylococcus Aureus* (MRSA). On the fourth day, there was worsening hypoxia necessitating mechanical ventilation. During her further hospital course, new-onset hypoxia (pulmonary oedema) with ventricular bigeminy rhythm/multiple ectopic beats interrupted weaning. Her cardiac enzymes were elevated (Troponin 78 ng/mL, pro-Brain Natriuretic Peptides (BNP) 35,000 ng/mL, myoglobin 1960 ng/mL). On day 10 of ICU stay, transthoracic echocardiography and Transesophageal Echocardiography (TEE) confirmed persistent large vegetation on AML tip and severe MR [Table/Fig-2].



[Table/Fig-2]: Trans-thoracic Echocardiography (TEE) showing large vegetation on AML tip.

On the 13th day, the patient's general condition worsened, and the CXR showed worsening bilateral lung infiltrates. She experienced

arrhythmias (ventricular tachycardia/ventricular fibrillation) and required Cardiopulmonary Resuscitation (CPR) for eight minutes with a defibrillator shock for VF rhythm. Post-return of Spontaneous Circulation (ROSC), the patient was conscious and obeying commands.

On the 14th day, after confirming normal coronaries, she underwent MV repair or replacement surgery depending on intraoperative findings how amenable is the valve reconstructive surgery. Intraoperative findings revealed a healthy aorta, dilated pulmonary artery, firm and dilated right atrium and ventricle, and a small left atrium. Vegetation measuring 25×10 mm was observed over the Anterior Mitral Leaflet (AML) body, and a 10×10 cm vegetation was noted over the PML noted. Subvalvular apparatus was destroyed, resulting in severe Mitral Regurgitation (MR). The decision was made to perform MV replacement with a bicor bio prosthesis. Post-operative Transesophageal Echocardiography (TEE) showed satisfactory MV function.

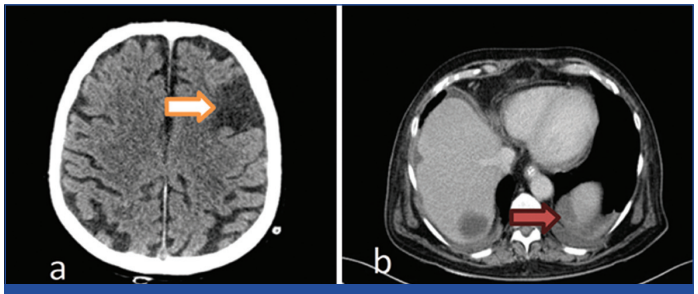
On the 18th day, she was gradually weaned off and extubated, but she was re-intubated on the same day due to worsening respiratory distress and haemodynamics. She had a prolonged ICU stay with hospital-acquired infection, severe sepsis, and septic shock. On the 39th day, she was successfully weaned off the ventilator, and her pulmonary infiltrates showed improvement. However, five days later, she had increased Tracheostomy Tube (TT) secretions and increased Work Of Breathing (WOB). TT cultures were positive for *Klebsiella* and *Pseudomonas*, while blood culture was positive for Methicillin-Resistant *Staphylococcus Aureus* (MRSA). Appropriate sensitive antibiotics were started.

A follow-up Transthoracic Echocardiography (TTE) did not show the recurrence of endocarditis or any regurgitation. On the 52nd day, the patient developed worsened hypotension and rising lactate values. Screening echo revealed the presence of pericardial effusion with septations. Left intercostal drainage and pericardial drain were placed, and 300-400 mL of fluid was drained. Blood and blood products were transfused to optimise the coagulation parameters. Due to the prolonged ICU stay and hospital-acquired multidrug-resistant infection, she succumbed to the illness and was pronounced dead on the 68th day of hospital stay.

Case 2

A 71-year-old male patient with no co-morbidities presented with fever, cough and expectoration since four days, and complained of gradually worsening breathlessness for 15 days. On arrival, he was in an altered sensorium and in a hypoxic state, requiring endotracheal intubation.

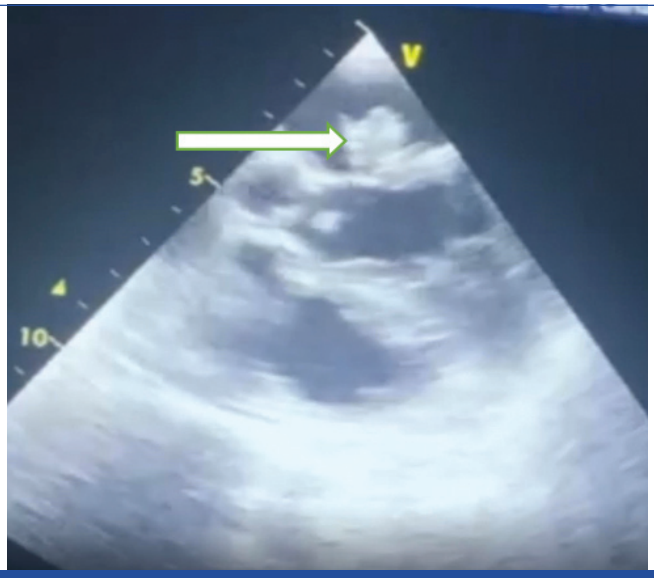
Further work-up revealed bilateral pneumonia and Acute Respiratory Distress Syndrome (ARDS). Computed Tomography (CT) brain confirmed bilateral multi-infarcts [Table/Fig-3a], and CT abdomen [Table/Fig-3b] showed a splenic infarct with developing abscess [Table/Fig-3b].



[Table/Fig-3]: a) Day 6 CT brain- arrow depicts Ill-defined hypodense in left frontal and fronto parietal region suggestive of subacute infarct; b) CT Abdomen contrast an ill-defined non-enhancing hypodense area in superior pole (arrow) of the spleen.

A 2D echocardiogram showed vegetation on the Anterior Mitral Leaflet (AML) and Posterior Mitral Leaflet (PML) with severe Mitral Regurgitation (MR). The patient was in shock and required vasopressors. Appropriate antibiotics (ceftriaxone, gentamicin, vancomycin) were administered, and blood cultures showed streptococcal infection. He received 14 days of antibiotics and showed improvement in shock and severe sepsis.

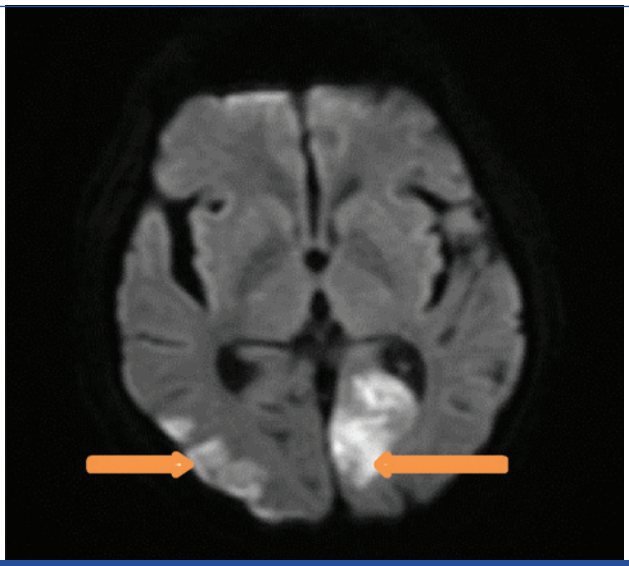
Due to the severe MR, the patient could not be weaned from mechanical ventilation and experienced recurrent pulmonary oedema. Follow-up 2D echo showed [Table/Fig-4] there was an increasing size of the vegetation. Hence, he was taken up for MVR of D14 (coronary angiogram was normal). Intraoperative findings revealed extensive vegetations on the AML and PML with extension to the chordae. MV replacement was done with TTK Chitra MV prosthesis, size 27. On the third postoperative day, he experienced sudden arrhythmias VT/VF and could not be revived.



[Table/Fig-4]: Trans oesophageal echocardiogram (TEE) shows mitral valve mobile vegetation.

Case 3

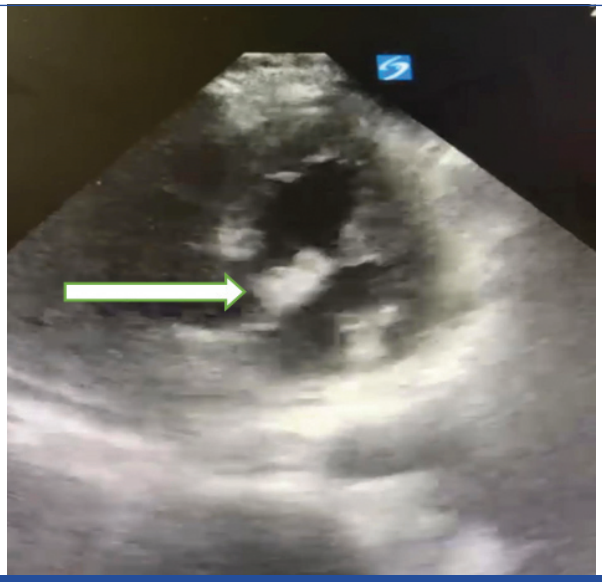
A 68-year-old male patient, known to have diabetes, hypertension, and chronic renal disease on maintenance haemodialysis for the past four months, presented to the emergency department with a history of irrelevant speech and breathlessness. MRI Brain [Table/Fig-5] revealed an ischemic stroke.



[Table/Fig-5]: Day 2 MRI brain Diffusion weighted imaging (DWI) images shows acute infract (arrow) in bilateral temporo-occipital region.

Upon arrival, he was intubated due to respiratory distress and required vasopressors to support his haemodynamics. A 2D echocardiogram showed vegetation attached to the Anterior Mitral Leaflet (AML) with adequate left ventricular function [Table/Fig-6] and severe Mitral Regurgitation (MR). Blood culture and haemodialysis

line cultures were positive for enterococci. Hence, treated with antibiotics including meropenem, gentamicin, and teicoplanin. On the fourth day, he was successfully disconnected from artificial ventilation but experienced intermittent episodes of respiratory distress, requiring non-invasive ventilation. Daily haemodialysis was performed to remove fluids. Due to recurrent respiratory distress and persistent sepsis (high WBC count, thrombocytopenia with a platelet count of 61,000/cumm, high procalcitonin, and CRP) MV replacement done on day 21 of hospital stay. Unfortunately, on the fourth day postoperatively, he developed worsening shock and was pronounced dead.



[Table/Fig-6]: A 2D echocardiogram shows mobile mitral valve vegetations.

DISCUSSION

Infective Endocarditis (IE) is a serious, life-threatening disease with adverse complications [1]. A systematic review of IE epidemiology from the GBD 2010 (Global Burden of Disease, Injuries, and Risk Factors) study estimated the crude incidence of native valve disease, as reported from 10 countries (USA, Australia, Africa, Europe), ranged from 1.5 to 11.6 cases per 100,000 people. In-hospital mortality of native valve IE is 22%, while the 5-year mortality rate is 40%. The systematic review aimed to assess epidemiology in various regions of the world. However, due to lack of information from low and middle-income regions, improved surveillance is required to assess the global burden [2]. According to the results of the Global Burden of Disease IE Study 2019, the incidence of IE has increased 2.5 times from 1990 to 2019, and there has been a sharp rise in deaths over the past 30 years, from 28,750 in 1990 to 66,320 in 2019 [1].

Choudhury R et al., conducted a retrospective analysis of 186 patients with 190 episodes of IE over a 10-year duration. Rheumatic heart disease was the most frequent (42%) underlying cardiac condition [3]. Garg N et al., also confirmed similar findings in their study of 192 patients, with 46% of cases attributed to rheumatic aetiology. The overall in-hospital mortality rate was 25%, and higher neurological complications were observed in patients who died compared to those who recovered [4]. Gupta A et al., reported similar findings in their study of 61 patients with IE, with 38% of cases attributed to rheumatic aetiology. Congestive heart failure was the most common complication (47%), followed by sepsis (21%) [5].

The evolving epidemiological profile and diverse nature continue to pose diagnostic challenges. The diagnosis is defined by the Dukes or modified Dukes criteria, which include microbiological, echocardiographic, fever, vascular phenomena, and immunologic phenomena [6].

The Euro Heart Survey of 2005 described the characteristics, treatment, and outcomes of active IE in Europe. The study included 159 patients, out of which 118 patients had heart failure (55%), embolism (31%), and fever more than 38 degrees Celsius (89%). Surgery was performed in over 50% of patients, with 12.5% undergoing surgery within the first 24 hours, 75% during the initial hospitalisation, and 12.5% electively. The reasons for surgery (native valve, n=62) were heart failure (58%), persistent sepsis (39%), followed by embolism (18%) [7].

In an Indian scenario, the clinical presentation and complications were not significantly different from those in the West or the developing world. However, there was a lower incidence of stroke compared to the Western report [7].

Surgery is indicated in patients with IE and heart failure caused by severe Mitral Regurgitation (MR), intra-cardiac fistula, or valve obstruction. Surgery may also be considered in patients without heart failure but with echocardiographic signs of elevated end-diastolic pressure, high left atrial pressure, or moderate to severe pulmonary hypertension [7]. According to the European Society of Cardiology (ESC) guidelines, surgery must be performed on an emergency basis regardless of the infection status when patients experience persistent pulmonary oedema or cardiogenic shock despite medical therapy. In cases of uncontrolled infection, indications for surgery include persistent fever (more than 10 days), perivalvular complications (such as abscess formation, pseudoaneurysm, and fistula), and persistent positive culture for several days (more than 7 to 10 days) despite appropriate antibiotic treatment. Perivalvular extension should be suspected in cases with persistent unexplained fever or new atrioventricular block, which warrants Transesophageal Echocardiography (TEE) as the preferred diagnostic technique for perivalvular complications. The ESC recommends surgery for organisms that are difficult to treat, for example, MRSA or vancomycin-resistant enterococci, as well as gram-negative bacteria [8].

Embolic events are life-threatening complications, with an overall incidence of 20-50%. The brain and spleen are the most common sites for embolism in left-sided IE. The crucial part of predicting the risk of embolism in an individual remains challenging. The size (>10 mm), mobility of vegetation, and location of vegetation on the MV on echocardiography play a key role in predicting embolic events [9]. Surgery undertaken for the prevention of embolism should be performed very early, within the first few days of antibiotic therapy [9].

To summarise, heart failure complicating IE requires emergency surgery (within 24 hours, level of evidence class 1B), regardless of the duration of antibiotic treatment. Uncontrolled infection with a high risk of embolism require urgent surgery (within a few days, level of evidence 1B) [8].

In the European Heart Survey, the commonly performed surgical techniques for left-sided single valve IE were valve replacement with mechanical prosthesis (63% of 118 patients), bioprosthesis in 21%, and valve repair in 11% [7]. Surgical methods should be tailored to the individual patient and the clinical scenario. Valve repair is favoured in perforations, especially in mitral or tricuspid valve involvement, when the disease is confined to leaflet or valve cusps, although replacement can also be used. In cases of locally uncontrolled infection, valve replacement is performed after total excision of infected and devitalised tissue, with minimal use of foreign material. In the case of abscess, small ones can be closed directly, while large ones should be drained into the pericardium or circulation [8].

Guidelines and task force management clearly state the definitive role of early surgery in acute endocarditis with complications (heart failure, prevention of embolism, and uncontrolled infections). However, identifying the right patient for early surgery is difficult due to the associated high mortality. [Table/Fig-7] shows the findings of studies involving acute IE and MV surgery from January 2012

Author/year	Place of study	Total number of patients	MVR	MV repair	Recurrence of IE MV repair Vs MVR	Out come	Study conclusion
Kerchove L et al., 2012 [10]	Belgium	137	28	109	1 patient in MV repair group	17%	Repair-oriented surgical approach achieves a repair rate of 80% with acceptable morbidity and good long-term results.
Gelsomino S et al., 2012 [11]	Italy	379	165	214	No difference	23 repair vs 20% in replacement group	Emergency MV surgery presence of septic shock post 4 times higher risk of death. 18 years follow-up is better with MV repair.
Chang HW et al., 2014 [12]	-	17	6	11	-	3 vs 0	MV repair showed successful clinical outcomes. Valve replacement was performed in some patients with a repair-favourable pathology.
Wang T et al., 2014 [13]	New Zealand	60	35	25	No difference	Repair group tended to have better 5-year survival estimates (91.6% vs 70.0%, p=0.08)	Valve replacement patients were older (p=0.029), had a higher prevalence of intracardiac abscess (p=0.035), worse renal function (p=0.013), and longer operation times (p<0.001).
Miura T et al., 2014 [14]	Japan	57	21	36	-	8 in repair vs 9 in replacement group	MV repair is appropriate to prevent postoperative cardiac-related events.
Lee SJ et al., 2015 [15]	south Korea	27	0	27	-	1 out of 27 mortality. 5-year survival 96.3%	Mitral annuloplasty by lifting mitral annuloplasty with a strip with or without posterior leaflet augmentation.
Toyoda N et al., 2017 [16]	New York	1970	367	1603	4.7 vs 9.5	68.8 vs 53.5% survival at 12 years	Favours MV repair.
Tomsic A et al., 2018 [17]	Netherlands	83	32	51	Nil	13% early mortality	Favours MV repair in all possible scenario.
Solari S et al., 2019 [18]	Belgium	192	37	155	-	12.7% (n=29) repair vs replacement 11.6% vs 29.7%, p=0.006	The patients who received MV replacement. the higher mortality rate observed in the MVR group in up to 6 months post operatively. MVR group were older and in worse clinical conditions than patients who had MV repair.
Elgabry M et al., 2019 [19]	Germany	35	0	35	2 of 35	11% (all-cause mortality) (4/35)	Repair feasible in acute endocarditis and better outcome.
Tepsuwan T et al., 2019 [20]	Thailand	114	76	38	0 vs 4	Repair group tended to have better 5-year survival estimates (91.6% vs 70.0%, p=0.08).	MVR group were more critical.
Cuerpo GP et al., 2019 [21]	Spain	437	369	68	7.1% vs 3.7%; p=ns	One-year mortality 3.7% vs 2.9%.	National wide registry, Mortality in the repair group was inferior to that in the replacement group.
Defauw RJ et al., 2020 [22]	Netherland	149	52	97	6 vs 5	14 in repair vs 9 in replacement group	Focusing on early surgery as part of a comprehensive approach to endocarditis could improve late results by allowing durable repair. For durable repair timing of surgery, radical dissection, early surgery is important. due to unpredictable extension of disease should be reserved for experienced surgeon has to considered.
Roberts WC et al., 2022 [23]	Japan	37	37	0	-	5/37 mortality in repair group	Retrospective observation in MV repair technique. Describes clinical and morphological pattern of the infected valve.

[Table/Fig-7]: Details of studies involving acute IE and MV surgery from January 2012 to March 2022 [10-23].

to March 2022 [10-23]. It's important to note that some of these studies discussed only MV repair, accounting for the larger study population undergoing repair.

In a retrospective study by Gelsomino S et al., from Italy, 379 patients with acute MV endocarditis, with or without shock, were examined. The existing diagnostic difficulty in differentiating the type of shock, in multivariate logistic regression analysis, shows that septic shock is an independent predictor of mortality, with 3.8 times higher mortality than cardiogenic shock [11].

In active native MV endocarditis, consensus guidelines support surgical treatment with repair rather than replacement. Similar findings were observed by Toyoda N et al., who analysed 1,970 patients. Although 367 patients were in the repair group and 1,603 patients underwent replacement, there was an increasing trend towards the repair group, with better twelve-year survival and a lower recurrence rate in the repair group [16].

Tepsuwan T et al., conducted a retrospective study involving 114 patients and concluded that MV repair surgery has a better 5-year survival rate than MV replacement (91.6% vs. 70%, p=0.08) [20]. Two retrospective studies involving 149 and 192 patients respectively concluded that an early and repair-oriented surgical approach results in good long-term durability of the repair and a very low recurrence rate of IE [18,22]. In a Spanish registry involving 437 patients, MV repair was deemed an attractive option for acute IE, and at one year, the replacement group had a higher mortality rate (3.7% vs. 2.9%) [23].

Although retrospective studies favour MV repair, our search criteria identified case reports with rare IE, the majority of which involved MV replacement. Indications for MV replacement include delayed diagnosis, degenerative valve, destroyed valve, mycotic aneurysm, and embolic events in IE and rare IE. The timing of surgery varied in the retrospective data and was around 1-2 weeks [9,10,15,17,18,20-23].

CONCLUSION(S)

Due to the complexity of the disease and the varied clinical presentation, the primary objectives of surgery in endocarditis are source control and reconstruction of the valve. Based on early diagnosis and early surgery, observations in the present study favour MV repair surgeries in acute endocarditis. Although MV repair shows less morbidity and mortality compared to MV replacement, the surgical procedure and technique should be tailored to individual patients and the local invasion of the disease.

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