The Egyptian Journal of Hospital Medicine (October 2022) Vol. 89 (2), Page 6080- 6084

Predictors of Mortality in Redo Aortic Valve Replacement for Prosthetic Aortic Valve Endocarditis

Hisham Mohamed El Batanony[1], Abdallah Samy Korany Gouda[1], Ahmed Hussein Gaafar[2], Hosam Fathy Ali*[2]
[1]Department of Cardio-Thoracic Surgery, Faculty of Medicine, Beni Suef University, Egypt
[2]Department of Cardio-Thoracic Surgery, Faculty of Medicine, Cairo University, Egypt
***Corresponding author:** Hosam Fathy Ali, **Mobile:** (+20) 01114567170; **Email:** amy.rh.209@gmail.com

ABSTRACT
Background: One of the most dreaded complications and a source of significant mortality after aortic valve surgery is prosthetic aortic valve endocarditis. Many studies were done to address the risk factors for hospital mortality and responsible for prolonged postoperative hospital stay.
Patients and Methods: Thirty patients underwent the study from September 2019 to March 2020 at Kasr Al-Aini University Hospitals, Cairo, and Beni Suef University Hospital, Egypt. Preoperative, operative, and postoperative data to determine the risk factors for hospital mortality were collected.
Result: The study included 16 (53.3%) males and 14 (46.7%) females. With mean age ±SD 38.5±7.7 years. The most prevalent isolated organism was staph aureus (30%) followed by coagulase negative staph (20%) then enterococcus fecalis and streptococcus bovis (13.3%). The hospital mortality was 26.7%. Pre-operative predictors of in-hospital mortality were CHF (p value 0.011), DM (p value 0.012), NYHA III&IV (p value 0.014), preoperative need to inotropic (p value 0.011), preoperative need to mechanical ventilation (p value 0.017), presence of aortic root abscess (p value 0.003). Intraoperative predictors of mortality were prolonged CPB time (p value 0.001), prolonged clamping time (p value <0.001). While postoperative predictors were low COP (p value 0.027) and postoperative sepsis (p value 0.029).
Conclusion: Once infective endocarditis suspected in patient has prosthetic valve combined management should be taken to minimize the perioperative complications and hence the operative mortality risk minimized.
Keywords: Prosthetic Valve, Aorta, Redo, Mortality, infective endocarditis.

INTRODUCTION

The increasing prevalence of valvular heart disease worldwide is a global clinical dilemma, where the demand for interventions is expected to hit 850,000 by 2050. Prosthetic heart valves have been used to address this problem and the two commonly used basic types are: surgically implanted mechanical heart valves (MHVs) and biological heart valves (BHVs) [(1)].

If a pathological heart valve is unrepairable, valve replacement is now performed with low morbidity and mortality. However, prosthetic valves are associated with some adverse effects, in particular infections, being a predisposing factor for the development of infective endocarditis (IE) [(2)].

One of the most dreaded complications and a source of significant mortality after valve surgery is prosthetic valve endocarditis (PVE). PVE is the infection of a surgically implanted prosthetic valve or repaired native valve with an annuloplasty ring, with an incidence of 3% to 6% over a patient's lifetime[(3)].

The prevalence of PVE grows steadily and the prognosis is worse than in cases of native valve endocarditis (NVE) due to the excavating destruction of periannular structures, which occurs in most cases (56% to 100%) lifetime [(4,5)]. Surgical therapy is essential for effective and successful treatment of IE and requires clear guidelines for the optimal treatment algorithm [(6)]. In each individual case, the risks and benefits of surgery need to be carefully weighed. Surgical intervention is most beneficial when patients present with complications of PVE, such as worsening heart failure, prosthetic valve dehiscence, worsening regurgitation or perivalvular leak, valvular obstruction and cardiac abscess formation[(7)].

Surgical treatment of prosthetic aortic valve endocarditis is particularly challenging due to destruction of the aortic root and the need for complex repairs[(8)]. Antimicrobial therapy for PVE should be guided by the susceptibility profile of the causative organism. Blood cultures should be drawn prior to administration of any empiric antibiotics. Specific antimicrobial regimens depending on the causative microorganisms have been published by the American Heart Association and European Society of Cardiology is the initial therapy for PVE should be initiated in a hospital setting under close observation, for any symptoms or signs suggestive of a worsening condition where surgical intervention should be considered[(9-11)].

The aim of this study is to detect the possible risk factors that may predict the occurrence of the hospital mortality in patients undergoing redo aortic valve replacement for prosthetic aortic valve endocarditis to pave the way towards decreasing the incidence rates of hospital mortality and their subsequent prolonged intensive care and hospital stay.

PATIENTS AND METHODS

Patients: Thirty cases underwent redo aortic valve replacement for prosthetic aortic valve endocarditis retrospectively reviewed and data analyzed at Kasr Al-Aini University Hospitals, Cairo, and Beni suef University Hospital, Egypt. In the period from September 2019 to March 2020.
Data collection: All patients were studied for age, sex, and detailed clinical examination with emphasis on the presence of comorbidity e.g. diabetes, CVS and associated medical diseases e.g. DM, renal failure. Echocardiography was performed to assess the Size of

Received: 28/9/2022
Accepted: 4/6/2022

vegetations, ejection fraction, left ventricular end diastole, left ventricular end systole and the presence of aortic root abscess. Blood culture & sensitivity was performed in all cases to detect the organism causing the sepsis. The total operative, total bypass and the ischemic times were recorded. The postoperative mortality and the causes of death were assessed and related to the risk factors.

Surgical technique:

In all cases, access to the heart was obtained through a median sternotomy. Cardiopulmonary bypass was instituted in a standard fashion with aortic and right atrial double stage cannulation. Cardiac manipulation before aortic cross-clamping was minimized to prevent peripheral embolization of vegetations. This was particularly important in patients with large, mobile, and friable vegetations. Surgeons prefer on pump arresting the heart Myocardial protection was achieved by intermittent cold blood antegrade cardioplegia solution, keeping the myocardial temperature at 10-15°C by local cooling with ice, accompanied by systemic cooling at 25-28°C.

Ethical approval:

The study was approved by the Ethics Board of Cairo University and Beni Suef University. An informed written consent was taken from every participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association(Ref) (Declaration of Helsinki) for studies involving humans.

Statistical Analysis

Data were presented as mean ± SD, numbers, and percentages as appropriate. Associations between categorical predictor variables and outcomes were analyzed using Pearson Chi-Square (χ^2) test for independence. Associations of continuous predictor variables were tested using t-test. Statistical analysis was performed using Microsoft® Office Excel 2010 and SPSS (Version 22, 2011). *P* value < 0.05 was considered statistically significant.

RESULTS

I- Patients' characteristics and preoperative data:

This retrospective study was conducted between September 2019 and March 2020 on 30 cases underwent redo aortic valve replacement for prosthetic aortic valve endocarditis for detection the mortality rate and its risk factors. The study included 16 (53.3%) males and 14 (46.7%) females. With age ranged from 23-53 years. The mean age ±SD was 38.5±7.7 years.

Preoperative assessment of the patients showed that 5 (16.7%) patients had COPD, 3 (10%) had neuro-dysfunction, 7 (23.3%) had Creatine more than 2, 5 (16.7%) had DM, 5 (16.7%) had congestive heart failure (CHF), 19 (63.3%) NYHA III and IV, 5 (16.7%) were in need to inotropes preoperatively and 2 (6.7%) were in need to preoperative mechanical ventilation.

The most prevalent isolated organism was Staph aureus in 9 (30%) patients followed by coagulase negative staph in 6 (20%) patients. then enterococcus fecalis and streptococcus bovis in 4 (13.3%) patients for each species. Proteus was isolated in 2 (6.7%) patients while e-coli, enterococcus viridans and candida were detected in one (3.3%) patient for each organism.

Echo was done for all patients to assess the vegetation size, ejection fraction, LVES, LVED, pulmonary artery pressure and the presence of aortic root abscess. Most patients (60%) had an ejection fraction more than 50%, there were (40%) had aortic root abscess and only (16.7%) had pulmonary hypertension. The mean LVED and LVES was 5.4±0.5 and 3.7±0.5, respectively. The mean vegetation size was 2.1±0.3 cm, it was ranging from 1.6 to 2.7 cm with median 2.1 cm.

Table (1): The echo parameters among the studies patients:

Echo parameters	Values No. =30 (%)
EF	
<30%	2 (6.7)
30%-50%	10 (33.3)
>50%	18 (60)
LVED	
Mean±SD	5.4±0.5
Range (min-max)	4.6-6.4
Median	5.3
LVEs	
Mean±SD	3.7±0.5
Range (min-max)	2.8-4.5
Median	3.8
Aortic root abscess	12 (40)
Pulmonary HTN	5 (16.7)

II- Intraoperative data:

The mean operative time was 290.5±28.7 minutes, the mean CPB time was 182.5±28.2 minutes and the mean clamping time was 106.8±21.7 minutes.

Table (2): Intraoperative circumstances among the studies patients:

Operation	Values No. =30 (%)
Timing	
Elective	14 (46.7)
Urgent	14 (46.7)
Emergency	2 (6.7)
Intraoperative time (minutes)	
Mean±SD	290.5±28.7
Range (min-max)	240-345
Median	290
CPB time (minutes)	
Mean±SD	182.5±28.2
Range (min-max)	135-240
Median	182.5
Clamping time (minutes)	
Mean±SD	106.8±21.7
Range (min-max)	80-155
Median	100

Postoperative data:

The ICU stay ranged from 3-10 days with median of 5 days and the mean was 5.4±1.7 days. during the ICU stay, 12 (40%) of the studied patients had low COP and most of them (76.7%) needed inotropes.

8 (26.7%) of the patients were on mechanical ventilation for less than 24 hours while 22 (73.3%) were ventilated for more than 24 hours. 20% of the studied patients underwent reoperation due to bleeding, 40% had low COP and 20% had RF, needed pacemaker and had sepsis.

Table (3): Postoperative complications among the studies patients:

Complications	Values No.=30 (%)
Reoperation due to bleeding	6 (20)
Low COP	12 (40)
Pneumonia	4 (13.3)
Stroke	2 (6.7)
RF	6 (20)
Pacemaker	6 (20)
Sepsis	6 (20)

The mortality rate during the study follows up period was (26.7%) and the most common cause of death was multi organ failure and low COP (50%) followed by sepsis (37.5%) then stroke (12.5%).

The mean hospital length of stay was 41.3±9.64 days and ranged from 4 days to 70 days with median 49.5 days.

Table (4): Operative outcome (mortality rate and hospital length of stay)

Postoperative	Values No. =30 (%)
Mortality	8 (26.7)
Cause of death (no=8)	
MOF & LCOP	4 (50)
Stroke	1 (12.5)
Sepsis	3 (37.5)
Hospital stay	
Mean±SD	41.3±9.64
Range (min-max)	4-70
Median	49.5

There were a statistically significant association between the occurrence of death and, CHF, DM, NYHA III&IV, preoperative need to inotropic, preoperative need to mechanical ventilation, presence of aortic root abscess, prolonged CPB time, prolonged clamping time, low COP and postoperative sepsis (P-value<0.05).

Table (5): Association between baseline, preoperative & postoperative risk factors and the occurrence of death:

Risk factors	Alive no. =22 (%)	Died no. =8 (%)	P-value
Age (Mean±SD) **(year)**	38.32±7.581	39.13±8.425	0.804
Sex no, (%):			
Males	12 (54.5)	4 (50)	0.825
Females	10 (45.5)	4 (50)	
Staphylococcal infection no, (%):	5 (22.7)	4 (50%)	0.540
COPD no, (%):	3 (13.6)	2 (25)	0.460
Neuro-dysfunction no, (%):	1 (4.5)	2 (25)	0.166
Create more than 2 no, (%):	5 (22.7)	2 (25)	0.812
DM no, (%):	2 (9.1)	**3 (37.5)**	**0.012 ** SS**
CHF no, (%):	1 (4.5)	**4 (50)**	**0.011* SS**
NYHA III and IV no, (%):	11 (50)	**8 (100)**	**0.014* SS**
Preop-need to inotropes no, (%):	1 (4.5)	**4 (50)**	**0.011* SS**
Prop-need to MV no, (%):	0 (0)	**2 (25)**	**0.017* SS**
Aortic root abscess no, (%):	5 (22.7)	**7 (87.5)**	**0.003* SS**
Vegetation size no, (%):	2.1±0.3	2.3±0.2	0.076
Timing no, (%):			
Elective	11 (50)	3 (37.5)	0.058
Urgent	11 (50)	3 (37.5)	
Emergency	0 (0)	2 (25)	
Intraoperative time (minutes) Mean±SD	280.9±24.8	316.9±21.7	0.157
CPB time (Mean±SD)	172.7±24.9	**209.4±17.4**	**0.001** SS**
Clamping time (Mean±SD)	98.6±15.8	**129.4±20.1**	**<0.001* * SS**
MV no, (%):	15 (68.2)	7 (87.5)	0.290
Need to inotropes no, (%):	15 (68.2)	8 (100)	0.068
Reoperation due to bleeding no, (%):	2 (25)	4 (18.2)	0.520
Low COP no, (%):	6 (27.3)	6 (75)	**0.027***
Pneumonia no, (%):	3 (13.6)	1 (12.5)	0.716
Stroke no, (%):	1(4.5)	1 (12.5)	0.469
RF no, (%):	4 (18.2)	2 (25)	0.520
Pacemaker no, (%):	5 (22.7)	1 (12.5)	0.536
Sepsis no, (%):	2 (9.1)	**4 (50)**	**0.029* SS**

DISCUSSION

Despite contemporary therapy, reoperation for aortic prosthetic valve endocarditis is still associated with relatively high perioperative mortality and limited long-term survival.**12** Mortality rates were relatively high (26.7%) in our study and the most common cause of death was multi organ failure and low COP (50%) followed by sepsis (37.5%) then stroke (12.5%). Our results are relatively compatible with those reported by **Leontyev *et al.*** [12] in a study of 152 IE patients, who found early mortality in 37 (24.3%). **Machado *et al.*** [13]**,** found a 30-day mortality of 17%, **Gatti *et al.*** [14]**,** reported an in-hospital mortality of 20.3%.

There was predominance of male gender (53.3%) with no statistical significance. This predominance may be explained by male sex predilection with intravenous recreational drug use. This was similar to other reported study done by **Leontyev *et al.***[12]. Our patient population has lower mean age of (38.5±7.7 year) compared to other series done for instance by **Leontyev *et al.*** [12]. This can be explained by increasing trend in the proportion of cases with rheumatic heart disease as a predisposing condition in our community but it is still not statistically significant as will.

DM was detected in 5 patients in our study and had a significant predictor of in hospital mortality (p value 0.012), as the presence of chronic illness suppresses the immune system against virulent organisms such as staph aureus & MRSA allowing spread of infection comparing to **Agca *et al.*** [15] that found that surgical mortality was significantly higher among diabetic patients (34%) than in non-diabetic (20%), and as in **Leontyev *et al.*** [12]**,** DM is a high-risk factor for mortality (P value 0.04).

Preoperative functional class according to the New York heart association (NYHA) classification in our study FC III, IV had the clinical presentation of 19 patients and has high significant value (p value 0.014) as predictor of early mortality as also descried by **Fang *et al.*** [16] a study included Seventy-four patients with prosthetic valve endocarditis, and by **Leontyev *et al.*** [12] (P value < 0.01).

Regarding renal impairment, 7 (23.3%) of our patients had renal impairment, no patients on regular dialysis, it showed no statistically significant association with mortality (P=0.53) compared to a study done by **Spies *et al.*** [17] and found that Mortality of infective endocarditis in patients with end-stage renal disease remains high and has been essentially unchanged during the past decade. If patients require valve replacement surgery, mortality is even higher reaching 70%.

Preoperative neurological condition in term of previous stroke, is not a risk factor that was statistically insignificant in our study (p value 0.166), like other studies of **Leontyev *et al.*** [12]**.**

The surgical treatment of root abscesses is a challenge, it is another risk factor in our study, patients having Aortic root abscess showed higher hospital mortality rate with statistical significance (p value 0.003). Likely founded by **Leontyev *et al.*** [12] (P value 0.02).

In our study, a trend toward a higher mortality with staphylococcal infection was noted, but statistical significance in the multivariate analysis was not reached, Unlike **John *et al.*** [18]**,** this study stated that the mortality rate associated with Staphylococcus aureus prosthetic valve endocarditis (PVE) remains high and significant.

Fungal infection is a fatal infection and occurred in one (3.3%) of our patients. the patient was died with un-resolving fulminant sepsis as **Lalani *et al.*** [19] that found in his study that was done on 490 surgically managed patients.

Left ventricular dysfunction was associated with higher hospital mortality but didn't reach statistical significance. This is also the same for LVEDD and LVESD which have no significant effect on the mortality rate. **Bortolotti *et al.*** [20]**,** in his series showed that E.F significantly influence hospital mortality rate but demonstrated no influence of ventricular dimension. In contrary others consider EF as a non-significant predictor for the hospital mortality. Low left ventricular ejection fraction (less than35%) and increased LVEDD more than 50 mm have been reported of significance in mortality by **Akay *et al.*** [21], According to **Maciejewski *et al.*** [22], and others operative mortality was significantly higher in those patients who were had impaired left ventricular function.

The indications of surgery in this series followed the European society of cardiology guidelines, including: Uncontrolled infection secondary to persistent sepsis, recurrent septic systemic embolization, and congestive heart failure not responding to maximum medical treatment. In this study sometimes more than one indication was present in the same patient[6].

Intraoperative factors are also related to lower survival, **Gatti at al.**[23], found associations between both extracorporeal circulation time and aortic clamping time in a study done on 138 patients in an Italian cardiac surgery center. These findings agree with our experience with p value 0.001 and p value <0.001 respectively. Ventilation time more than 24hr had no statically significant in hospital mortality (p value 0.290) like other study described by **Chu at al.** [24].

In our study a prolonged hospital stay was noticed (4-70 days) with a mean of 41.3±9.64 and median 49.5 days. This can be explained by the fact that patients were transferred after surgery to the cardiology department in our hospital till they finish their antimicrobial therapy to avoid patient incompliance to medical treatment and due to high cost of long-term antimicrobial therapy.

CONCLUSION

1. Once infective endocarditis suspected in patient has prosthetic valve combined management should be taken between cardiologist and cardiac surgery in specialized center to minimize progression of the functional class and the perioperative complications and hence the operative mortality risk minimized.
2. Preoperative Predictors of in-hospital mortality were; NHYA-FC, diabetes mellitus, aortic root abscess, bypass time, cross clamp time, develop of low COP and sepsis.
3. Despite our 26.7%% in-hospital mortality in this series, surgery for redo aortic valve replacement for prosthetic aortic valve endocarditis still can be performed with good surgical technique and good early & mid-term results.

Conflict of Interest: None
Funding source: None
Acknowledgment: None.

REFERENCES

1. **Li C (2019):** Bioprosthetic Heart Valves: Upgrading a 50-Year-Old Technology. Cardiovasc Med., 6:47. doi: 10.3389/fcvm.2019.00047.
2. **Thuny F, Grisoli D, Collart F *et al.* (2012):** Management of infective endocarditis: challenges and perspectives. Lancet, 379:965–975.
3. **Nataloni M, Pergolini M, Rescigno G *et al.* (2010):** Prosthetic valve endocarditis J Cardiovasc Med. (Hagerstown), 11: 869-883.
4. **Vincent L, Otto C (2018):** Infective endocarditis: Update on epidemiology, outcomes, and management. Curr Cardiol Rep., 20(10):86. doi:10.1007/ s11886-018-1043-2.
5. **Anguera I, Miro J, San Roman J *et al.* (2006):** Periannular complications in infective endocarditis involving prosthetic aortic valves. Am J Cardiol., 98(9):1261-8.
6. **Habib G, Lancellotti P, Antunes M *et al.* (2015):** 2015 ESC guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European society of cardiology (ESC). Endorsed by: European association for cardiothoracic surgery (EACTS), the European association of nuclear medicine (EANM). Eur Heart J., 36(44): 3075-128.
7. **Chirouze C, Alla F, Fowler V *et al.* (2015):** Impact of early valve surgery on outcome of Staphylococcus aureus prosthetic valve infective endocarditis: analysis in the International Collaboration of Endocarditis-Prospective Cohort Study. Clin Infect Dis., 60: 741-9.
8. **Cochrane A (2018):** Aortic valve prosthetic endocarditis remains a challenging problem. Heart Lung Circ., 27(3): 274–275.
9. **Baddour L, Wilson W, Bayer A *et al.* (2005):** Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: Endorsed by the Infectious Diseases Society of America. Circulation, 111(23): 394–434.
10. **Hoen B, Habib G, Tornos P *et al.* (2009):** Guidelines on the prevention, diagnosis, and treatment of infective endocarditis; Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. Eur Heart J., 30(19): 2369–2413.
11. **Thuny F, Grisoli D, Collart F *et al.* (2012):** Management of infective endocarditis: challenges and perspectives (review). Lancet, 379: 965–975.
12. **Leontyev S, Borger M, Modi P *et al.* (2011):** aortic valve surgery: Influence of prosthetic valve endocarditis on outcomes. J Thorac Cardiovasc Surg., 142(1):99-105.
13. **Machado M, Nakazone M, Murad-Júnior J *et al.* (2013):** Surgical treatment for infective endocarditis and hospital mortality in a Brazilian single-center. Rev Bras Cir Cardiovasc., 28(1):29-35.
14. **Gatti G, Benussi B, Gripshi F *et al.* (2017):** A risk factor analysis for in-hospital mortality after surgery for infective endocarditis and a proposal of a new predictive scoring system. Infection, 45(4): 413-23
15. **Agca F, Demircan N, Peker T *et al.* (2015):** Infective endocarditis: a tertiary referral center experience from Turkey. Int J Clin Exp Med., 8(8):13962–8.
16. **Yu V, Fang G, Keys T *et al.* (1994):** Prosthetic valve endocarditis: superiority of surgical valve replacement versus medical therapy only. Ann Thorac Surg., 58: 1073-107.
17. **Spies C, Madison J, Schatz I *et al.* (2004):** Infective endocarditis in patients with end-stage renal disease clinical presentation and outcome. Arch Intern Med., 164(1): 71-75.
18. **John M, Hibberd P, Karchmer A *et al.* (1998):** Staphylococcus aureus prosthetic valve endocarditis: optimal management and risk factors for death. Clin Infec Dis., 26(6): 1302–1309.
19. **Lalani T, Chu V, Park L *et al.* (2013):** In-hospital and 1-year mortality in patients undergoing early surgery for prosthetic valve endocarditis. JAMA Intern Med., 173:1495–504.
20. **Bortolotti U, Milano A, Mossuto E *et al.* (1994):** Early and late outcome after reoperation for prosthetic valve dysfunction: analysis of 549 patients during a 26-year period. J Heart Valve Dis., 3(1): 81 –7.
21. **Akay T, Gultekin B, Ozkan S *et al.* (2008):** Mitral valve replacements in redo patients with previous mitral valve procedures: mid-term results and risk factors for survival. J Card Surg., 23(5): 415–21.
22. **Maciejewski M, Piestrzeniewicz K, Bielecka-Dąbrowa A *et al.* ():** Redo surgery risk in patients with cardiac prosthetic valve dysfunction. Arch Med Sci., 7(2): 271 –7.
23. **Gatti G, Benussi B, Gripshi F *et al.* (2017):** A risk factor analysis for in-hospital mortality after surgery for infective endocarditis and a proposal of a new predictive scoring system. Infection, 45(4):413-23.
24. **Chu V, Cabell C, Benjamin D *et al.* (2004):** Early predictors of in-hospital death in infective endocarditis. Circulation, 109(14):1745-9.