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Mortality Predictors in Patients with Infective Endocarditis Undergoing Surgery

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ABSTRACT

Background: Infective endocarditis (IE) is considered a series disorder with high in-hospital mortality, so early detection and therapy can improve outcomes. Diagnosis relies upon consistent history and manifestations like persistent bacteremia, fungemia or active valvulitis. Surgical treatment in infective endocarditis is considered as a part of management rather than a consequence of medical treatment failure.

Objectives: To assess the risk factors influencing the early outcome of surgical intervention in patients with IE**.**

Patients and methods: This prospective cohort study was conducted on sixty patients diagnosed with infective endocarditis and underwent cardiac surgery. We tested preoperative, intraoperative and postoperative factors that may act as prospective predictors of mortality.

Results: Rheumatic heart was found to be the most common underlying fundamental issue among most of the cases. Mitral valve regurgitation was the frequent lesion found (61.7%). The mean EuroScore II in non-survivor group was 25.69 ± 8.13. The hospital mortality was 21.7% (13 patient), while the 6-month mortality was 12.8% (6 patients). Congestive heart failure, embolization, and periannular extension of infection are the most significant predictors of hospital mortality and 6 month mortality also.

Conclusion: Surgery for IE keeps on being challenging. EuroScore II was found to have a very good capability to anticipate mortality in IE surgery. Also favorable outcomes could be acquired with valve repair techniques even in cases of IE.

Keywords: Infective endocarditis, Predictors, Mortality, Risk factors, Surgery.

INTRODUCTION

Infective endocarditis (IE) is characterized by being an infection of the endocardial surface of the heart, which may incorporate at least one heart valve, the endocardium or a septal defect [(1)]. It has an annual incidence of 3–10/100,000 of the population with 30 days mortality reaches up to 30% [(2)]. The modified Duke criteria can be utilized to help diagnose IE. These criteria have 80% sensitivity. However, this is altogether lower in instances of prosthetic valve endocarditis or implantable electronic device infections. In this case clinical doubt, microbiological correlation and additional imaging may be required [(3)]. Heart failure as a consequence to valvular insufficiency, uncontrolled resistant infection, persistent bacteremia regardless proper antimicrobial treatment, infection with a fungus and presence of a risk of systemic embolization are the main surgical indication [(4)].

The aim of this work was to assess the risk factors affecting the early outcome of surgical intervention in patients with IE.

PATIENTS AND METHODS

This prospective cohort study was conducted on 60 patients who were admitted at Sheikh Zayed Specialized Hospital. They were diagnosed with definite IE and required cardiac surgery. Cases were selected during the study period from December 2017 to December 2019.

Ethical consent:

An approval of the study was obtained from Benha University Academic and Ethical committee. Every patient signed an informed written consent for acceptance of the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Case definition:

Case definition depended on definitive items meeting the modified Duke's criteria with assistance of special endocarditis team, which included demographic criteria, pathological criteria (presence of micro-organism in a vegetation), major clinical criteria (blood culture positive for endocarditis, echocardiographic evidence of endocardial involvement) and minor clinical criteria (predisposing heart disease, intravenous drug abuse, fever, vascular phenomena as major arterial emboli and mycotic aneurysm, immunologic phenomena as rheumatoid factor and microbiological evidence as serological evidence of active infection) [(5)].

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Inclusion criteria: Patients with endocarditis either influencing native or prosthetic valve including mitral, aortic, tricuspid or combined valves .

Exclusion criteria: Patients with persistent septic shock and failure of medical treatment, presence of neurological insult as profound coma or intracranial hemorrhage and presence of serious comorbidities as poor ejection fraction (EF < 30%) or mycotic aneurysm. The primary outcomes were hospital mortality and major adverse cardiac events (MACEs) including cerebrovascular events, HF, MI or cardiac death, late mortality and determination of the main factors associated with increased mortality.

All patients were subjected to the following:

Pre-operative assessment:

Including thorough history taking and clinical assessment, presence of co-morbidities such as (diabetes mellitus, COPD, renal failure, liver dysfunction, anemia and IV drug addiction), EuroScore, chest x-ray, echocardiographic description of the valve including shape and pathology, LV function, presence of pulmonary hypertension and associated congenital heart diseases, presence of abscesses, pseudo aneurysms or intracardiac fistulae, laboratory investigation especially erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and 3 consecutive blood cultures at least 1 hr. apart, presence of complications as embolization (e.g. cerebrovascular accidents, peripheral) and heart failure or pericardial effusion. Pre-operative medical treatment included empirical antibiotic including amoxicillin-clavulanate or vancomycin in case of penecilline allergy till the result of the blood culture appears, or up to 6 weeks in case of elective cases .

Operative assessment:

Including timing of surgery (emergency, urgent or elective), surgical procedure (valve replacement with mechanical or biological prosthesis, valve repair or combined replacement and repair and for which valve), first do or redo surgery, intraoperative findings with precise assessment of infected tissue including endocardial, valvular affection and size of vegetations with a special consideration given to periannular extension and aortic root involvement. In addition to, bypass time, cross clamp time, total operative time, method of cardioplegia, weaning from cardiopulmonary bypass, use of inotropes and culture & sensitivity from excised infected tissue.

Operative technique:

Under cover of appropriate antibiotics, patients were operated. Through median sternotomy approach, ascending aorta was cannulated directly while venous cannulation was either single, double staged or bicaval cannulation according to the case. Cardiopulmonary bypass was initiated with mild hypothermia, a combination of antegrade and/or retrograde cold blood cardioplegia was administered to achieve cardiac arrest. after careful observation for the extent of infection, resection of all infected tissue was done then either valve repair in case of sufficient leaflet tissue could be preserved or replacement in case of extended affection. If the infection was extending to the aortic annulus causing abscess, fistula or disruption, reconstruction via pericardial patch or even total replacement of the aortic root using a tube graft was done.

Postoperative assessment:

Including duration of mechanical ventilation, inotropic support, complications (re-exploration for bleeding, low cardiac output syndrome, neurological complications, arrhythmias, deep wound infection and mortality), ICU stays, laboratory work up including serial total leucocytic count & C-reactive protein, blood culture and sensitivity detecting residual infection and hospital stays.

Follow up:

Six months follow up by echocardiography for assessment of cardiac condition and detection of relapse.

Statistical Analysis

The collected data were tabulated and analyzed using SPSS version 23 software (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). Statistical analysis was done through: Descriptive: e.g. percentage (%), mean and standard deviation and analytical that included Student's t-test for comparison of means and Fisher's exact or Chi-Squared (χ^2) tests for comparison of categorical parameters. P value ≤ 0.05 was considered statistically significant.

RESULTS

In the current study, the frequent indications for surgery were congestive heart failure due to valve dysfunction in 38 (63.3%), large pieces of vegetations in 28 (46.6%) and uncontrolled infection was the reason for surgery in 23 patients. Staphylococcus aureus was the common identified organism in blood cultures (33.3%). Echocardiographic findings showed the type and site of IE, which was on native valves (61.7%) and prosthetic valves (38.3%). The most frequent affected valves were tricuspid valve (31.7%) and mitral valve alone (28.3%). Most vegetation showed severe mobility (45%) and mobile vegetation (30%). Periannular extension of infection presented mainly by abscess (10%) and pseudo aneurysm (10%) as shown in table (1).

Table (1): Indications of surgery in IE patients, echocardiographic findings, and periannular extension of infection

Indications	Patients	
	No.	**%**
CHF	38	63.3%
Large vegetation (>10mm)	28	46.6%
Uncontrolled infection	23	38.3%
Prosthetic valve dysfunction	23	38.3%
Recurrent emboli	10	16.6%
Abscess	10	16.6%
Identified microorganism		
Staphylococcus aureus	20	33.3%
Streptococcus viridians	7	11.7%
Streptococcus pneumonia	2	3.3%
Enterococcus faecalis	6	10%
Escherichia coli	7	11.7%
Klebsiella	6	10%
Brucella	5	8.3%
Aspergillus fumigatus	2	3.3%
Candida Albicans	3	5%
Polymicrobial	3	5%
Echocardiographic findings		
Type of IE		
Native valve	37	61.7%
Prosthetic valve	23	38.3%
Early PVE (< 1 year)	11	18.3%
Late PVE (> 1 year)	12	20%
Site		
Mitral valve	17	28.3%
Aortic valve	13	21.7%
Mitral and aortic valves	11	18.3%
Tricuspid valve	19	31.7%
Vegetations mobility		
Fixed vegetation	15	25%
Mobile Vegetation	18	30%
Severely mobile	27	45%
Periannular extension		
Abscess	10	16.7%
Pseudoaneurysm	10	16.7%
Fistula	2	3.3%
Paravalvular leak	13	21.7%

Table (2) showed that mitral valve involvement especially regurgitation was the frequent lesion found and replacement was done mostly by mechanical valves. The most reported causes of hospital mortality were congestive heart failure and systemic sepsis (6.7%), and major postoperative complications were found to be new renal impairment (13.3%), chest infection and respiratory failure (11.7%) followed by low cardiac output syndrome (10%).

Table (2): Showing operative procedures, types of implanted valves, causes of hospital mortality in IE patients and major postoperative complications and morbidities

Operative procedures	No.	%	Types of valves
Mitral valve involvement	**37**	**61.7%**	Mechanical (19)
MVR	24	64.9%	Bioprosthic (5)
MVR+TV repair	7	18.9%	Mechanical (7)
MV repair + TV repair	6	16.2%	Mechanical (6)
Aortic valve involvement	**16**	**26.7%**	Mechanical (10)
AVR	12	75%	Bioprosthic (2)
Aortic valve and root replacement	4	25%	Mechanical (2)
Double-valve involvement	**10**	**16.7%**	
DVR	4	40%	Mechanical (4)
DVR+ TV repair	4	40%	Mechanical (4)
Commando procedure	2	20%	Mechanical (2)
Tricuspid valve involvement	**19**	**31.7%**	
TVR	5	26.3%	Bioprosthic (5)
TV repair	12	63.2%	----------
TV repair with closure of VSD	2	10.5%	----------
Causes of hospital mortality			
Congestive heart failure	4	6.7%	
Systemic sepsis	4	6.7%	
Chest infection	1	1.7%	
Renal failure	1	1.7%	
Cerebral hemorrhage	1	1.7%	
Failure of weaning from CPB	1	1.7%	
Postoperative consequences			
Renal insults	8	13.3%	
Pulmonary infections	7	11.7%	
Low cardiac output	6	10%	
Fever	5	8.3%	
Re-exploration	4	6.7%	
Systemic sepsis	4	6.7%	
Novel CNS insult	2	3.3%	
Conductive aberration	2	3.3%	
Embolization (other than CNS)	2	3.3%	

EuroScore II significantly increased in non-survivor group. The noticed complications preoperatively were congestive heart failure developed in 38 patients (63.3%), embolization in 10 patients (16.7%). The sites of embolization were in the CNS (4 patients), upper/lower extremities (3 patients), spleen (1 patient), lung (1 patient), and kidney (1 patient). Most of patients did not need urgent or emergency surgery (Table 3).

Table (3): Preoperative predictive variables for hospital mortality

Items	Hospital mortality (n=13)		Hospital survival (n=47)		X^2	P- value
	No.	%	No.	%		
Underlying cardiac disease Prosthetic valve	9	69.2%	13	27.7%	7.58	0.006
EuroScore II (%)**,** Mean ± SD	25.69 ± 8.13		6.96 ± 3.76		t=11.99	< 0.0001
Echocardiographic predictors						
Type of IE	6	46.2%	32	68.1%	6.59	0.01
Native valve	6	46.2%	17	36.2%	5.33	0.02
Prosthetic valve	6	46.2%	4	8.5%	10.39	0.002
Periannular extension of infection	6	46.2%	4	8.5%	10.39	0.002
Abscess						
Laboratory predictors, Mean ± SD						
Serum creatinine (mg/dL)	3.17 ± 0.24		1.57 ± 0.64		t=8.9	<0.0001
CRP (mg/L)	103.31 ± 32.3		59.09 ± 21.56		t=5.8	<0.0001
Complications						
CHF	9	69.2%	29	61.7%	8.82	0.002
Embolization	3	23.1%	7	14.9%	4.78	0.024
Timing of surgery:						
Emergency	5	38.5%	6	12.8%	13.9	0.0009
Urgent	7	53.8%	10	21.3%		
Elective	1	7.7%	31	65.9%		
First do	5	38.5%	40	85.1%	11.8	0.0006
Redo	8	61.5%	7	14.9%		

X^2: chi-square, t: student t-test, SD: stander deviation, CRP: C-reactive protein, CHF: congestive heart failure, IE: infective endocarditis.

Bypass time, cross clamp time and total operative times were longer in non-survivor group. 54 patients (90%) were weaned safely from cardiopulmonary bypass, but the remaining 6 patients (10%) needed a second trial of going on bypass. Again 5 of those 6 patients were weaned successfully from this second trial but with the help of high doses of inotropic support, precisely adrenaline (> 0.15 ug/kg/min), noradrenaline (> 0.2 ug/kg/min) and dobutamine (>15 ug/kg/min.). While, unfortunately, the remaining patient died intraoperatively after failure of weaning from bypass in spite of using maximum doses of the previously mentioned inotropic supports. Forty-five patients (90%) needed intraoperative inotropic support. The most noticed complication was chest infection and respiratory failure (7 patients). Mechanical ventilation time ranged from 9 to 286 hours. This time was < 24 hours in 41 patients (68.3%), from 24 to 48 hours in 4 patients (6.7%) and > 48 hours in 15 patients (25%) as shown in table (4).

The in-hospital mortality was 13 patients (21.7%). 30 patients (50%) experienced one or more postoperative complication. Forty-nine patients (81.7%) were kept on inotropic support. Regarding ICU stay it ranged from 1 to 11 days (Table 4).

During six-month follow-up period, six patients died among hospital survivors (47 patients), yielding an overall 6 months mortality of 12.8%. Periannular extension of infection was the major postoperative echo finding that predicted mortality. Also elevated WBC count and serum creatinine as a marker of infection and sepsis were significant predictors for mortality. Congestive heart failure (CHF) and cardiogenic shock was the remarkable cause of death (Table 4).

Table (4): Showing operative predictive variables for hospital mortality, preoperative predictive variables for 6-month mortality, causes of 6 months mortality in IE patients regarding surviving group after six months of follow up (47 patients)

Items	Hospital mortality (n=13)		Hospital survival (n=47)		x^2	P value
	No.	%	No.	%		
Bypass time (min), Mean ± SD	134.62 ± 24.36		96.43 ± 23.83		t=5.09	<0.0001
Cross clamp time (min.), Mean ± SD	103.08 ± 21.27		70.8 ± 20.9		t=5.06	<0.0001
Total operative time (min)	284.62 ± 37.99		201.1 ± 41.11		t=6.6	<0.0001
Complications					*	
Postoperative fever	4	30.7%	1	2.1%	10.9	0.006
Low cardiac output syndrome New renal	4	30.8%	2	4.3%	7.95	0.02
impairment	4	30.8%	4	8.5 %	4.37	0.04
Chest infection and respiratory failure	6	46.2%	1	2.1%	19.15	0.0001
Systemic sepsis	4	23.1%	0	0	10.9	0.0009
Period of mechanical ventilation (hours), Mean ± SD	239.11 ± 55.9		10.08 ± 0.13		t=28.7	<0.0001
High inotropic support						
No	0	0	8	15%	9.46	0.009
< 48 hours	3	11.1%	26	57.5%		
> 48 hours	10	88.9%	13	27.5%		
Duration of ICU stay (days), Mean ± SD	9.55 ± 1.75		4 ± 3.10		t=6.2	<0.0001
	6-month mortality (n=6)		**6-month survival (n=41)**			
Echocardiographic predictors					*	
-Periannular extension of infection	3	50%	1	2.4%	15.2	<0.0001
- Abscess	2	33.3%	1	2.4%	8.4	0.004
Euro Score II (%)	15.33 ± 3.27		3.05 ± 0.63		t=22.7	<0.0001
Laboratory predictors						
WBC count (mean × 10^3 / µL)	19.83 ± 5.42		9.44 ± 2.37		8.28	<0.0001
Serum creatinine (mg/dL)	2.7 ± 0.81		1.01 ± 0.27		9.9	<0.0001
Causes of 6-month mortality	**Patients (n=6)**					
	No.		**%**			
CHF and cardiogenic shock	3		50%			
Relapse of IE	1		16.7%			
Renal failure	1		16.7%			
Undetermined	1		16.7%			

X^2: chi-square, t: student t-test, SD: stander deviation, ICU: intensive care unit, WBC: white blood cells, CHF: congestive heart failure, IE: infective endocarditis. *: Fischer exact test.

In univariable cox regression analysis for preoperative predictive variables for hospital mortality, each one unit increase in EuroScore, the hazard of mortality increased by 6.6%. Every one unit increase in creatinine was associated with 41.8% increase in mortality. Also the risk of death was 7.17% greater in patients with prosthetic valves than those without, and these effects were statistically significant (Table 5).

Table (5): Univariable cox regression analysis for preoperative predictive variables for hospital mortality

Variable	B	X_2	P value	Hazard ratio	95 % CI for	
					Lower	Upper
EuroScore	0.064	5.37	0.020	1.066	1.010	1.125
S. creatinine	1.645	6.32	0.012	5.180	1.437	18.668
Prosthetic valve	1.970	7.46	0.006	7.172	0.034	0.574
CRP	0.011	1.5	0.219	1.012	0.993	1.030
Emergency surgery		3.67	0.160			
Urgent surgery	2.037	3.59	0.058	7.665	0.933	62.964
Elective surgery	1.586	2.00	0.157	4.885	0.543	43.988
Cross clamp time	-.021-	0.99	0.321	0.979	0.938	1.021
Bypass time	-.021-	1.22	0.270	0.980	0.944	1.016
Total operative time	0.001	0.006	0.936	1.001	0.983	1.018
CHF	1.084	3.086	0.079	2.956	0.882	9.905
Embolism	1.135	3.36	.067	3.110	0.925	10.450
Inotropic support < 48Hrs		0.56	0.455			
Inotropic support > 48Hrs	6.875	.557	.455	967.518	.000	66697862432.253
Peri annular extension of infection	0.408-	0.269	0.604	0.665	0.142	3.109
Abscess	0.080	0.010	0.920	1.083	0.230	5.097

CI: confidence interval, CRP: C-reactive protein, CHF: congestive heart failure.

Multivariable cox regression analysis for preoperative predictive variables for hospital mortality showed that patients with prosthetic valves were 108.5 times more likely to receive a death sentence due to the disease or its complications as patients without. The overall model is highly significant (Table 6).

Table (6): Multivariable cox regression analysis for Preoperative predictive variables for hospital mortality

	B	X_2	P value	Hazard ratio	95% CI	
					Lower	Upper
Prosthetic valve	4.687	4.404	0.036	108.5	1.363	8637.9
EuroScore	0.178	1.880	0.170	1.195	0.926	1.542
S. creatinine	0.331	0.061	0.805	1.392	0.101	19.161
$X_{2(\text{overall model})}$	18.26(.000*)					

CI: confidence interval.

Univariable cox regression analysis for predictive variables for mortality after 6 months follow up showed that with each one unit increase in EuroScore, the hazard of mortality increased by 27.1%. Every one unit increase in creatinine was associated with 2 folds increase in mortality. Also, the risk of death is decreased by 82.3% in patient without an abscess than those with abscess. For each additional unit of WBCs, the hazard of death was increased by 20.4%, and these effects were statistically significant (Table 7).

Table (7): Univariable cox regression analysis for predictive variables for mortality after 6 months follow up

	B	X_2	P value	Hazard ratio	95.0% CI	
					Lower	Upper
EuroScore	0.240	4.885	0.027*	1.271	1.028	1.572
S. creatinine	0.998	4.362	0.037*	2.713	1.063	6.923
Abscess	1.729-	3.514	0.061	0.177	0.924	34.346
WBCs	0.186	4.686	0.030*	1.204	1.018	1.425

CI: confidence interval, WBCs: white blood cells.

In multivariable model after 6 months follow up showed that with each one unit increase in EuroScore, the hazard of mortality increased by 229.5%. The overall model was highly significant (Table 8). **Table (8):** Multivariable cox regression analysis for predictive variables for mortality after 6 months follow up

	B	Wald	P value	Hazard ratio	95 % CI	
					Lower	Upper
EuroScore	1.192	3.627	0.05*	3.295	0.966	11.242
S. creatinine	6.310-	2.992	0.084	0.002	0.000	2.316
WBCs	0.184	0.420	0.517	1.202	0.689	2.094
$X_{2(\text{overall score})}$	15.16(.002*)					

CI: confidence interval, WBCs: white blood cells.

DISCUSSION

Current published guidelines of the American Association for Thoracic Surgery (AATS) stated indications for surgical intervention in patients with IE detailing those with severe valvular affection, heart failure (HF), prosthetic valve endocarditis (PVE), large movable vegetations, frequent embolization, and constant septicemia regardless of satisfactory antibiotic treatment for at least 5 to 7 days with special consideration to those having paravalvular abscesses or fistulas [6]. In our study, severe valvular regurge with persistent heart failure (63.3%) was found to be the most common indication for surgical treatment for both NVE and PVE. **Rekik *et al.*** [7] found that the main indication for surgery was severe valvular dysfunction with congestive heart failure (CHF) (52.3%). In a similar study done by **Mahmoud *et al.*** [8], they reported that the common surgical indication was CHF (64%). Additionally, **Akca *et al.*** [9] announced in their study on 46 patients with IE that the main indication for early surgical intervention was HF.

Most identified organisms by blood culture were Staphylococcus aureus, Streptococcus viridians followed by Escherichia coli. In a similar study done by **Akca *et al.*** [9], the commonest found organism was Staphylococcus aureus. **Farag *et al.*** [10] reported that Streptococcus haemolyticus group B and Streptococcus viridians were frequently found.

In this study, EuroScore II had a good capability to anticipate either in-hospital mortality or six months mortality. This is similar to studies done by **Di Dedda *et al.*** [11] and **Borracci *et al.*** [12]. Also, regarding EuroScore II, it was ranging from 1.23 to 36.99%, with a mean value of 5.71% in a similar study done by **Mahmoud *et al.*** [8]. **Pivatto Junior *et al.*** [13] revealed in a study on 107 patients who underwent surgery for IE that the best predictor for mortality was accomplished by the PALSUSE score (1.01, 95% CI: 0.70-1.42; p = 0.919), followed by the EuroScore (1.3, 95% CI: 0.92-1.87; p = 0.123).

Also, prosthetic valve endocarditis (PVE) was a univariable indicator of in-hospital mortality. PVE is frequently complicated by peri-valvular extension of infection where it spreads beyond the attachments of its ring bringing about valve dehiscence in vast majority of cases, which increases the volume overload on the corresponding ventricle precipitating HF. PVE was found to be a significant risk predictor of mortality likewise in the other studies [8, 13, 14, 15].

Peri-annular extension of infection was an independent predictor of hospital mortality and six months mortality in the current study. **Musci *et al.*** [16] found that abscess formation is a significant risk factor for early mortality (≤ 30 days) in the univariable analysis. While **Mahmoud *et al.*** [8] revealed that periannular extension of infection in the form of abscess (16%); pseudoanurysm (16%), fistula (2%) and paravalvular leak (22%) were significant risk factors for early mortality. The fundamental reason for surgical intervention in such cases is debridement of the infected tissue and the limitation of infectious foci to prevent or treat HF and dissemination of the infection, and it also

diminishes the danger of embolism related morbidity and even mortality in the ideal clinical conditions [17].

In this study, the methodology we followed in treating renal impaired patients was by attempting to avoid fluid overload in congested patients with diseased kidneys by shortening the length of cardiopulmonary bypass (CPB) circuits and priming by colloids as plasma or packed RBCs as opposed to crystalloids, and keeping the mean blood pressure above 60 during CPB. **Rekik *et al.*** [7] stated that creatinine was strongly related to mortality. Also **Elmasry *et al.*** [18] found in a similar study on 50 patients that those who have preoperative elevated serum creatinine were significantly connected with hospital mortality. **Mahmoud *et al.*** [8] reported the same result.

In this study, CHF was a strong independent predictor of in hospital mortality. In serious cases of endocarditis, infection spread results in destruction of perivalvular tissue causing acute regurgitation in native valve endocarditis (NVE) or dehiscence and para-valvular leak in PVE, both causing volume overload on relating ventricle precipitating HF. Additionally, enormous vegetations obstructs blood outflow causing CHF. Associated myocarditis causes pump failure. HF is agreed to be a contributing component in the mortality of cases with IE as appeared in several studies [8, 18, 19].

High C-reactive protein (CRP) level and white blood cell count were univariate predictors of in-hospital mortality. It is a sign of active infection, which makes the tissues friable expanding operative technical difficulty. Similarly, high CRP values (≥100 mg/l) on admission significantly anticipated both short-term and 1-year mortality in **Heiro *et al.*** [20] study. 1n a study done by **Elmasry *et al.*** [18] patients out of 50 had preoperative CRP levels above 100 and related with hospital mortality. Also, CRP > 120 mg/l was an independent prognostic factor of 5-year mortality [21]. **Rostagno *et al.*** [22] found that patients with white blood cell (WBC) count extending beyond the ordinary range were at a significantly higher risk of death either at discharge or at 6 months while elevated WBC count did not foresee in-hospital or 1-year mortality in another study [20]. In terms of CRP, each 1 mg/ dL was found to increase the opportunity of death 1.034-fold [23].

On the other hand, regarding postoperative white cell count (WCC) and CRP course in 30-day survivors vs. 30-day non-survivors, there was no statistically significant contrasts between the two groups (p=0.788, 0.7 respectively) [24].

This study exhibited that emergency surgery was a powerful univariable predictor of hospital mortality and six-month mortality. Our methodology in surgical IE management was not to urge surgery until the patient was stabilized. So, the majority of our cases were managed on urgent bases. Nonetheless, the data analysis during follow-up period showed that six patients died during this period. This high hospital mortality might be contributed to inadequate patient preparation, anti-microbial treatment and infection control, failure of controlling patients risky co-morbidities preceding surgery as toxemia, CHF and pulmonary oedema, lack of time needed for arrangements to provide different blood products. Our results come in accordance with **Musci *et al.*** [16] who found also that emergency surgery was a powerful predictor of in hospital mortality.

It was found that redo surgery was a powerful univariable predictor of in-hospital mortality. In redo surgery, presence of PVE increases time required for valve excision expanding CPB time and subsequently the ischemic time. Likewise redo surgery was a powerful univariable predictor of in-hospital mortality in a study performed by **Elmasry *et al.*** [18]. Prolonged cardiopulmonary bypass time was a powerful univariable predictor of hospital mortality, which may be because of expanded time required for dissection and prosthetic valve extraction in cases with PVE. While, in cases with NVE there was increased time required for good debridement and valve repair. Also, the presence of friable tissues makes operations technically more troublesome due to difficult suturing increasing the ischemic time. This result coincides with the one got by **Mahmoud *et al.*** [8], **Elmasry *et al.*** [13], **Klieverik *et al.*** [25] and **Nayak *et al.*** [26] demonstrated that either bypass time or cross clamp time were powerful univariable predictors of either one month mortality or longer-term mortality. In a single center study, it was observed that redo surgery and prolonged duration of bypass time were a critical factor for hospital mortality in patients with IE who underwent cardiac surgery [27].

Postoperative fever was found as a good predictor of mortality and **Elmasry *et al.*** [18] and **Rostagno *et al.*** [23] are in agreement with our result.

Postoperative chest infection is a serious postoperative complication. In severe cases, this infection may advance to respiratory failure or systemic sepsis bringing about serious vasodilatation, hypotension and simultaneously diminished peripheral perfusion and low cardiac output syndrome which lead to various organ ischemia (e.g. renal ischemia and pulmonary ischemia). Presence of fever, pulmonary ischemia, and low cardiac output yield prolonged ventilation. At last, prolonged ventilation and high dosages of inotropic support prolongs the length of ICU stay. In **Mahmoud *et al.*** [8], **Elmasry *et al.*** [18], **Sheikh *et al.*** [28] and **Smith *et al.*** [29] studies, postoperative chest infection and systemic sepsis were good predictors of mortality. **Farag *et al.*** [10] studied 360 patients who underwent cardiac surgery for infective endocarditis and found that reasons for death were sepsis in 32 patients (8.9%), followed by multi-organ failure in 18 patients (5.0%). In a study by **Cresti *et al.*** [30], either septic shock or intractable bacteremia was an individual mortality predictor, adopting our results, where shock was significantly related to higher in-hospital mortality rates.

Presence of postoperative low COP expands mortality hazard because of diminished peripheral perfusion making various organs at ischemic risk

particularly the kidneys decreasing renal perfusion predisposing to renal impairment, which may advance to renal failure in severe cases. Also, low cardiac output increases the requirement for inotropic support, which prolongs the duration of ICU stay. Decreased peripheral perfusion predisposes to different organ infection. Along with related post-operative mechanical ventilation predisposes to chest infection, which thus prompts delayed period of mechanical ventilation, which in severe cases may advance to respiratory failure [(31)].

The presence of new renal impairment was a significant predictor of post-operative mortality. Pathogenic bacteria in IE can initiate an immune response, diminishing the glomerular filtration rate and causing retention of water and sodium. With the preexisting distorted cardiac function, systemic congestion, and inadequate renal perfusion brought about by the original heart illness, renal function can also deteriorate, leading to endless loop [(32)]. **Mahmoud *et al.* [(8)], Elmasry *et al.* [(18)], Sheikh *et al.* [(28)]** and **Smith *et al.* [(29)]** agree with that.

Also **Farag *et al.* [(10)],** in a comparable study found that 11 patients (3.8%) needed dialysis in non-survivor group while only 2 patients (3.1%) in survivor group needed dialysis.

Prolonged time of mechanical ventilation and employments of inotropic support for more than two days were an important factor for mortality in the current study. In concurrence with that, **Perrotta *et al.* [(33)]** reported that time of mechanical ventilation, inotropic support more than two days, and prolonged ICU stay were all noteworthy univariable predictors of in-hospital mortality. Also, **Mahmoud *et al.* [(8)]** reported significant longer periods of mechanical ventilation in non-survivor group and **Elmasry *et al.* [(18)]** agreed with that. EuroScore and serum creatinine were significant univariate predictors of mortality in postoperative period. Also, during 6 months follow up creatinine level, presence of abscess and elevated WBCs count were significant predictors of mortality. In a study on 88 patients with infective endocarditis, **Oliveira *et al.* [(24)]** showed in the univariate analysis that S. creatinine and creatinine clearance, EuroScore and CRP were significant predictors for mortality. While, in postoperative period, presence of complications was the significant mortality predictor. They demonstrated in multivariate analysis that creatinine clearance was a significant mortality predictor.

CONCLUSION

Surgery for IE keeps on being challenging and strongly related to higher mortality. Risk factors for in-hospital mortality were prosthetic valve IE, periannular extension of infection, high serum creatinine, CHF, embolization, emergency surgery, prolonged cardiopulmonary bypass time, the period of mechanical ventilation, inotropic support for > 48 hours, and ICU stay were the most remarkable predictors of hospital mortality. Risk factors for 6 months mortality were periannular extension of infection, abscess formation, high serum creatinine and WBCs count, and emergency surgery. Main causes of mortality after 6 months were CHF and relapse of IE. Euro SCORE II has a good discrimination capacity to anticipate both in-hospital and 6 months mortality in IE surgery.

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