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EARLY RESULTS AFTER SURGICAL TREATMENT OF INFECTIVE ENDOCARDITIS

By

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ABSTRACT

Background: Infective endocarditis remains a major cause of morbidity and mortality worldwide. There are concerns related to the increased number of infections associatedwith virulent agents and medical procedures. **Objective:** The aim of this study was to reveiw the surgical experience in the cardiothoracic surgical department, National Heart Institute (NHI) regarding patients with native or prosthetic valve endocarditis and determining predictors of mortality. **Patients and Methods:** A prospective study of fifty consecutive patients diagnosed with definite infective endocarditis and underwent cardiac surgery from July 2014 till September 2015. We tested preoperative, intraoperative, and postoperative data as potential predictors of mortality. **Results:** Rheumatic heart disease was the most common underlying cardiac disease (n=28, 56%). Native valve endocarditis was present in 37 (74%) and prosthetic valve endocarditis in 13 (26%). Mean Euro SCORE II was 5.71%. The hospital mortality was 20%, while the 6-month mortality was 12.5%. Congestive heart failure, embolization, and periannular extension of infection are the most powerful predictors of hospital mortality. Periannular extension of infection is the most powerful predictor of 6-month mortality. **Conclusion:** Surgery for infective endocarditis continues to be challenging. EuroSCORE II has a good discrimination ability to predict in-hospital mortality in IE surgery. Satisfactory results can be obtained with valve repair in IE.

Keywords: Infective endocarditis, Surgery, Mortality, Predictors.

INTRODUCTION

Infective endocarditis (IE) is an endovascular infection and inflammation with vegetation formation, usually caused by infectious agents. Over the ensuing decades, developments in open-heart surgery and the evolution of cardiac-valvular prostheses have since made surgery for endocarditis part of the routine work of every cardiac surgical unit. Nevertheless, such surgery still poses unique challenges and carries substantial risk of morbidity and mortality. Furthermore, the indications, timing, and type of surgery remain controversial as there are few randomized trials to guide patient management **(Ozlem et al., 2013).**

IE is a disease that needs a multi-system approach for the following reasons: it is a systematic disease, but rather may present with very different aspects depending on the first organ involved, the underlying cardiac disease (if any), the microorganism involved, the presence or absence of complications and the patient's characteristics **(Lancellotti et al., 2013).**

The two primary objectives of surgery are total removal of infected tissues and reconstruction of cardiac morphology, including repair or replacement of the affected valve(s) **(De Kerchove et al., 2007).** When infection is confined to the valve cusps or leaflets, any method to repair or replacement may be used. However, valve repair is favoured whenever possible, particularly when IE affects the mitral or tricuspid valve. Perforations in a single valve cusp or leaflet may be repaired with an autologous glutaraldehyde-treated or bovine pericardial patch **(David et al., 2007).**

In complex cases with locally uncontrolled infection, total excision of infected and devitalized tissue should be done followed by valve replacement and repair of associated defects to secure valve fixation. Mechanical and biological prostheses have similar operative mortality. Therefore, the Task Force does not favour any specific valve substitute but recommends a tailored approach for each individual patient and clinical situation. The use of foreign material should be kept to a minimum **(Lopes et al., 2007).** Cardiac transplantation may be considered in extreme cases where repeated operative procedures have failed to eradicate persistent or recurrent PVE **(Kaiser et al., 2007).**

PATIENTS AND METHODS

1- Study design:

This prospective cohort study included 50 consecutive patients who were diagnosed with definite IE and required cardiac surgery. They were operated upon in the cardiothoracic surgical department, National Heart Institute (NHI), Giza, Egypt from July 2014 to September 2015. We tested preoperative, intra-operative, and post-operative data and followed up the patients prospectively for six months to detect relapse, re-infection, associated co-morbidities, mortality and outcome of surgical treatment of valve IE.

2- Selection criteria in this study:

Diagnosis was based on strict case definition fulfilling modified Duke's criteria in collaboration with the endocarditis team in our hospital.

Inclusion criteria: All native or prosthetic valve endocarditis patients with involvement of mitral, aortic or tricuspid valve either isolated or combined.

Exclusion criteria:

- Patients presented with irreversible septic shock with failed medical treatment.
- Patients with neurological insult as deep coma or intra-cranial haemorrahge.
- Patients with severe co-morbidities as mycotic aneurysm.
- Patients with Poor ejection fraction (EF<30%).

Data regarding demographics, preoperative clinical status, intra- and early postoperative course were collected prospectively. Operative mortality risk was assessed for every patient according to the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and a signed written informed consent was obtained from each patient before surgery.

Statistical Analysis:

SPSS (Statistical Package for the Social Sciences) version 20.0 was used for

data analysis. Data were expressed as mean ± SD or counts and percentages when appropriate. Univariate analysis was conducted using the Student's t-test for comparison of means and the Fisher's exact or chi-square tests for comparison of categoric parameters. Multivariate logistic regression analysis was used to depict variables that contribute independently to the event of mortality among our patients. A p value < 0.05 was considered statistically significant.

RESULTS

This prospective cohort study included 50 consecutive patients diagnosed with definite IE.

a) Indications of surgery:

The main indications for surgery were one or more of the following: Congestive heart failure due to valve dysfunction in 25 (50%), large vegetation (>10 mm in size) in 23 (46%), uncontrolled infection (blood cultures remain positive despite administration of culture specific antibiotic for >10 days) in 19 (38%), prosthetic valve dysfunction in 11 (22%), recuurent emboli in 8 (16%), abscess in 8 (16%) **(Table 1).**

Table (1): Indications of surgery in IE patients

Indications	Number of patients (%)
CHF	25 (50%)
Large vegetation	23 (46%)
Uncontrolled infection	19 (38%)
Prosthetic valve dysfunc-tion	11 (22%)
Recurrent emboli	8 (16%)
Abscess	8 (16%)

b) Timing of surgery:

Surgical treatment was performed on emergency (within 24 hour) in 5 patients (10%), on urgency bases (within a few days) in 25 patients (50%), and on elective bases (after at least 1 or 2 weeks of antibiotic therapy) in 20 patients (40%)

II- pre-operative data:

A) EuroSCORE II: Euro SCORE II ranged from 1.23 to 36.99%, with a mean value of 5.71%.

B) Echocardiographic findings (Tran-thoracic and transoesophageal): The findings of preoperative transthoracic and transoesophageal echocardio-graphy are summarized in **table (2).**

Table (2): Echocardiographic findings in IE patients.

Echocardiographic findings	Number of patients (%)
Type of IE • Native valve	 37 (74%)
•Prosthetic valve - Early PVE (< 1 year) - Late PVE (> 1 year)	13 (26%) 5 (10%) 8 (16%)
- Site of IE • Mitral valve alone • Aortic valve alone • Mitral and aortic valves • Tricuspid valve	 22 (44%) 13 (26%) 8 (16%) 7 (14%)
Vegetations • Visible vegetations • Vegetation size (mean mm) • Vegetation size > 10 mm • Severe mobility	 46 (92%) 13.9 23 (46%) 15 (30%)
Periannular extension of infec-tion • Abscess • Pseudoaneurysm • Fistula	8 (16%) 8 (16%) 1 (2%) 1 (2%)
Paravalvular leak	11 (22%)

C) Complications:

Preoperatively, congestive heart failure developed in 25 patients (50%). Embolization was evident in 18 patients (36%). The sites of embolization were the CNS (9 patients), upper/lower extremities (7 patients), spleen (4 patients), lung (4 patients), and kidney (2 patients). Renal impairment developed in 17 patients (34%) from which six patients were on dialiysis**.**

III - Intraoperative data:

All operative procedures and types of implanted valves are summarized in **table (3).**

Table (3): Operative procedures and types of implanted valves.

Operative procedures	**No. of patients (%)**	**Types of implanted valves**
• **Mitral valve involvement**	**22 (44%)**	Mechanical (9)
- MVR	11 (22%)	Bioprosthic (2)
-MVR + TV repair	3 (6%)	Mechanical (3)
-MVR + AVR + TV repair	2 (4%)	Mechanical (2)
-MV repair	5 (10%)	----------
-MV repair + TV repair	1 (2%)	----------
• **Aortic valve involvement**	**13 (26%)**	Mechanical (8)
-AVR	9 (18%)	Bioprosthic (1)
- Aortic valve and root replacement	2 (4%)	Homograft (2)
- AVR + SAM excision	1 (2%)	Mechanical (1)
- AVR + Open mitral valvotomy	1 (2%)	Mechanical (1)
• **Double-valve involvement**	**8 (16%)**	
- DVR	5 (10%)	Mechanical (5)
-DVR+ TV repair	2 (4%)	Mechanical (2)
-AVR + MV repair	1 (2%)	Mechanical (1)
• **Tricuspid valve involvement**	**7 (14%)**	
-TVR	5 (10%)	Bioprosthic (5)
- TV repair	1 (2%)	----------
-TV repair + Closure of VSD with Dacron patch	1 (2%)	----------

Ischemic time (aortic cross-clamp time) ranged from 28 to 191 minutes, with a mean value of 79.47 minutes. Cardio-pulmonary bypass time ranged from 40 to 253 minutes, with a mean value of 106.45 minutes.

Successful primary weaning from cardiopulmonary bypass was achieved in 45 patients (90%), while in the remaining 5 patients (10%) reinstitution of cardio-pulmonary bypass was needed. In 4 of these 5 patients, the weaning succeeded in

the second trial after administration of inotropic support at high doses including adrenaline and noradrenaline. The remaining patient died intraoperatively due to persistent low CO with failure to wean from CPB despite high inotropic support. Forty-five patients (90%) needed intraoperative inotropic support. Total operative time ranged from 110 to 360 minutes, with a mean value of 205.3 ± 63.4 minutes.

IV- Hospital mortality and morbidity:

The in-hospital mortality was 10 patients (20%). The causes of death were summarized in **Table (4).** Twenty-two patients (44%) experienced one or more postoperative complications **(Table 5).**

The period of mechanical ventilation ranged from 5 to 280 hours, with a mean value of 30.65 hours. The period of mechanical ventilation was < 24 hours in 34 patients (68%), 24 to 48 hours in 3 (6%), and > 48 hours in 12 (24%). Forty-three patients (86%) were kept on inotropic support (nineteen of them (38%) required inotropic support for more than 48 hours). The duration of ICU stay ranged from 2 to 12 days, with a mean value of 2.85 days.

Table (4): Causes of hospital mortality in IE patients

Causes of hospital mortality	Number of patients (%)
• **Congestive heart failure and cardiogenic shock**	3 (30%) 3 (30%)
• **Systemic sepsis**	1 (10%)
• **Chest infection and respiratory failure**	1 (10%)
• **Renal failure**	1 (10%)
• **Cerebral hemorrhage**	1 (10%)
• **Intraoperative persistent low CO with failure to wean from CPB**	

Table (5): Major postoperative complications and morbidities.

Complications	Number of patients (%)
• **Postoperative fever**	4 (8%)
• **Low cardiac output syndrome**	5 (10%)
• **Reexploration for bleeding**	3 (6%)
• **New neurologic insult**	2 (4%)
• **New renal impairment**	7 (14%)
• **Chest infection and respiratory failure**	6 (12%)
• **Systemic sepsis**	3 (6%)
• **Conduction abnormality**	2 (4%) 2 (4%)
• **Embolization (other than CNS)**	Nil
• **Recurrent endocarditis**	

Table (5): Major postoperative complications and morbidities

Complications	Number of patients (%)
• **Postoperative fever**	4 (8%)
• **Low cardiac output syndrome**	5 (10%)
• **Reexploration for bleeding**	3 (6%)
• **New neurologic insult**	2 (4%)
• **New renal impairment**	7 (14%)
• **Chest infection and respiratory failure**	6 (12%)
• **Systemic sepsis**	3 (6%)
• **Conduction abnormality**	2 (4%) 2 (4%)
• **Embolization (other than CNS)**	Nil
• **Recurrent endocarditis**	

▪ **Predictors of hospital mortality:**

A) Preoperative predictors:

Sixty-five preoperative variables were analyzed by univariate analysis to identify

significant predictors for hospital mortality. Only nine variables were found to have statistical significance as predictors of hospital mortality **(Table 6).**

Table (6): Preoperative predictive variables for hospital mortality

Groups / Parameters	Hospital mortality (n=10)	Hospital survival (n=40)	P-value
•Underlying cardiac disease			
-Prosthetic valve	5 (50%)	8 (20%)	**0.046**
• **EuroSCORE II** (mean %)	24.69	5.75	**< 0.001**
•Echocardiographic predictors			
-Type of IE			
Native valve	5 (50%)	32(80%)	**0.046**
Prosthetic valve	5 (50%)	8 (20%)	
-Periannular extension of infection	5 (50%)	3 (7.5%)	**0.005**
-Abscess	5 (50%)	3 (7.5%)	**0.005**
•Laboratory predictors			
-Serum creatinine (mean mg/dL)	2.7	1.27	**0.022**
-CRP (mean mg/L)	108.8	64.20	**0.016**
•Complications			
- CHF	9 (90%)	16(38%)	**0.011**
- Embolization	5 (50%)	11(26%)	**0.024**

B) Operative predictors:

Sixteen operative variables were analyzed by univariate analysis to identify significant predictors for hospital mortality. Only three variables were found to have statistical significance as predictors of hospital mortality **(Table 7).**

Table (7): Operative predictive variables for hospital mortality.

Groups / Parameters	Hospital mortality (n=10)	Hospital survival (n=40)	P-value
Timing of surgery			
Emergency	3 (30%)	2 (5%)	
Urgent	6 (60%)	19(47.5%)	**0.047**
Elective	1 (10%)	19(47.5%)	
First do	4 (40%)	33(82.5%)	**0.046**
Redo	6 (60%)	7 (17.5%)	
Bypass time (mean min)	156.1	110.58	**0.009**

C) Postoperative predictors:

Fourteen postoperative variables were analyzed by univariate analysis to identify significant predictors for hospital mortality. Only eight variables were found to have statistical significance as predictors of hospital mortality **(Table 8).**

Table (8): Postoperative predictive variables for hospital mortality

Parameters \ Groups	Hospital mortality (n=9) *	Hospital survival (n=40)	P-value
•Complications			
- Postoperative fever	3 (33.3%)	1 (2.5%)	**0.017**
- Low cardiac output syndrome	3 (33.3%)	2 (5%)	**0.037**
- New renal impairment	4 (44.4%)	3 (7.5%)	**0.016**
- Chest infection and respiratory failure	5 (55.5%)	1 (2.5%)	**0.0004**
-Systemic sepsis	3 (33.3%)	0	**0.005**
Period of mechanical ventilation (mean hours)	247.11	18.08	**< 0.0001**
• Inotropic support			
No	0	6 (15%)	
< 48 hours	1 (11.1%)	23(57.5%)	**0.004**
> 48 hours	8 (88.9%)	11(27.5%)	
Duration of ICU stay (mean days)	10.56	5	**< 0.0001**

* One patient who died intraoperatively was excluded from the analysis

V- Six-months follow-up data:

Five patients died during the follow-up period [12.5% among hospital survivors (40)], yielding an overall 6-month mortality of 30%. Causes of mortality were listed in **Table 9.**

Table (9): Causes of 6-month mortality in IE patients.

Causes of 6-month mortality	Number of patients (%)
• CHF and cardiogenic shock	2 (40%)
• Relapse of IE	1 (20%)
• Renal failure	1 (20%)
• Undetermined	1 (20%)

Regarding surviving group after six months of follow up (35 patients):

Two patients suffered permenant neurological disability, and 4 patients had dyspnea (NYHA FC III-IV). From the four dyspenic patients, one patient developed severe aortic paravalvular leak without endocarditis and underwent redo aortic valve replacement (AVR). Another two patients suffered a relapse. The offending microorganism was Staph. aureus in both cases. One of them had involvement of mechanical aortic prosthesis and died of sepsis before re-operation. The other patient had involve-

ment of mechanical mitral prosthesis. This patient underwent redo mitral valve replacement (MVR) with a mechanical prosthesis and survived.The other 29 patients had no detected comorbidity.

In the group of patients selected for valve repair strategy, none had recurrence of endocarditis, and at follow-up echocardiography did not show more than mild residual regurgitation.

▪ **Predictors of 6-month mortality:**

A) **Preoperative predictors:**

By univariate analysis, only five preoperative variables were found to have statistical significance as predictors of 6-month mortality **(Table 10).**

Table (10): Preoperative predictive variables for 6-month mortality.

Mortality / Parameters	6-month mortality (n=5)	6-month survival (n=35)	P-value
• **EuroSCORE II** (mean %)	16.3	4.24	**0.0005**
•Echocardiographic predictors			
- Periannular extension of infection	2 (40%)	1(2.9%)	**0.036**
- Abscess	2 (40%)	1(2.9%)	**0.036**
•Laboratory predictors			
- WBC count (mean × 10^3 / μL)	21.74	13.57	**0.033**
- Serum creatinine (mean mg/dL)	2.6	1.08	**0.005**

B) **Operative predictors:**

By univariate analysis, only one operative variable [emergency surgery (P=**0.049**)] was found to have statistical significance as a predictor of 6-month mortality.

C) **Postoperative predictors:**

By univariate analysis, all the post-operative variables were found to be insignificant predictors of 6-month mortality.

DISCUSSION

The ESC published guidelines on the prevention and treatment of IE in 2015 **(Gilbert et al., 2015),** including helpful recommendations concerning the indications for surgery. We followed these guidelines to detect the main indications for surgery.

In this study, we found that the most common findings leading to surgical treatment for both NVE and PVE was severe valvular regurgitation with intractable heart failure (50%). **Rekik et al. (2009)** in their retrospective study, the main indication for surgery was severe valvular dysfunction with congestive heart failure (52.3%).

Predictors of hospital mortality

I- Preoperative predictors of hospital mortality:

Euro SCORE II is an important risk stratification score valuable indetermining mortality risk in cardiac surgical operations. In this study, EuroSCORE II had a good discrimination ability to predict in-hospital mortality and six month mortality in IE surgery. This agreed with studies by **Di Dedda et al. (2013)** and **Borracci et al. (2014)** in which EuroSCORE II showed satisfactory prediction of mortality in patients undergoing heart valve surgery.

Prosthetic valve endocarditis (PVE) was a univariate predictor of in-hospital mortality. From ten patients died during hospital period, five had PVE. PVE is frequently complicated by peri-valvular extension of infection and in many of these cases, infection spreads behind the site of attachment of the valve prosthesis, resulting in valve dehiscence in most of cases. Dehiscence of prosthetic valve increases volume overload on corresponding ventricle precipitating heart failure. PVE was found a significant risk predictor of mortality also in the following studies: Similar results were obtained by **David et al. (2007)** and **Manne et al. (2012)**.

Peri-annular extension of infection was an idependent predictor of hospital mortality and six month mortality in the current study. Half of the dead patients had Peri-annular extension of infection out of total eight patients with peri-annular extension of infection preoperatively (5/8; 62.5%). **Musci et al. (2008)** found abscess formation a significant risk factor for early mortality (≤ 30 days) in the univariate analysis.

In the current study, seventeen patients had pre-operative renal impairment (s.creatnine > 1.3) of which six patients (35%) were on renal dialysis. From these six patients, only one patient (17%) died during hospital period from renal failure. High serum creatinine was a univariate predictor of hospital mortality and six month mortality.

In this study, the strategy we followed in treating renal impaired patients was trying to avoid fluid overload in congested patients with diseased kidneys. This was done by shortening the length of cardiopulmonary bypass (CPB) circuits and making priming by colloids as plasma or packed RBCs rather than crystalloids. Also, we managed to maintain mean blood pressure above 60 during CPB. **Rekik et al. (2009)** stated that creatinine was strongly associated with mortality.

In this study, CHF was a strong independent predictor of in-hospital mortality. It was found in 90% of the hospital mortality patients. In severe cases of endocarditis, infection spread results in destruction of peri-valvuler tissue causing acute regurgitation in native valve endocarditis (NVE) or dehiscence and para-valvuler leak in PVE, Both causing volume overload on corresponding ventricle precipitating heart failure. Also, large vegetations obstructs blood outflow causing congestive heart failure (CHF). Associated myocarditis causes pump failure. Heart failure is agreed as a contributing factor in the mortality of IE as shown in several studies. In a prospective WEB-based, nation-wide registration study conducted in Japan

(Ohara et al., 2013). Also, In a Spanish multicenter study involving the analysis of 257 patients with definite left-sided PVE **(L?pez et al., 2013).**

We found high C-reactive protein level a univariate predictor of in-hospital mortality. It is a sign of active infection which makes the tissues friable increasing operative technical difficulty. Similarly, high CRP values (≥100 mg/l) on admission significantly predicted both short-term and 1-year mortality in Heiro et al. study **(Heiro et al., 2007).** Also, C-reactive protein > 120 mg/L was an independent prognostic factor of 5-year mortality **(Bannay et al., 2011)**.

In the present study, systemic embolization was an independent predictor of in-hospital mortality. It was found in 50% of hospital mortality patients. We managed to maintain mean arterial blood pressure above 60 mmhg to maintain affected organ perfusion and prevent further complications of organ hypo-perfusion. Similarly, systemic embolic events were predictors of both in-hospital and one-year mortality in **Heiro et al. (2007)** study.

II- Operative predictors of hospital mortality:

This study showed that emergency surgery was a significant univariate predictor of hospital mortality and six month mortality. Our strategy in surgical IE treatment was not to rush surgery until patient is stabilized. So, majority of our patients were operated upon on urgent bases (50%). Five IE patients could not be stabilized. They all presented with CHF with hemodynamic instability despite high inotropic support. Two of them had NVE with new onset acute regurgitant lesions while other three had PVE with new onset sudden valve dehiscence and severe para-valvuler leak. These five patients were operated upon on emergency bases. Of these five IE patients, three patients (60%) had hospital mortality. This high hospital mortality may be contributed to deficient patient preparations, antibiotic therapy and infection control, failure of controlling patient risky co-morbidities prior to surgery as toxemia, CHF and pulmonary oedema, lack of time needed for preparations of different blood products. Our results go in line with other several studies as in **Musci et al. (2008)** study emergency surgery was a significant predictor of in-hospital mortality.

This study showed that redo surgery was a significant univariate predictor of in-hospital mortality. 50% of mortality patients had PVE with risky redo operations. In redo surgery, presence of PVE increases time needed for valve excision increasing CPB time and consequently the ischemic time. Similarly, redo surgery is a predictor of in-hospital mortality **(Sheikh et al., 2009)**.

This study showed that prolonged cardiopulmonary bypass time was a significant univariate predictor of hospital mortality. This prolonged CPB time may be contributed to increased time needed for dissection and prosthetic valve extraction in cases with PVE. While, in cases with NVE there is increased time needed for good debridement and valve repair. Also, the presence of friable tissues makes operations technically more difficult due to difficult suturing increasing the ischemic time. **Klieverik et al. (2009)** and **Nayak et al. (2011)** showed that bypass time and cross clamp time were significant univariate predictors

of 30-day mortality and long-term mortality.

III- Postoperative predictors of hospital mortality:

In this study, four patients suffered from post-operative fever. All started in the first postoperative day. Two patients had hectic fever and the other two patients had a continuous fever. Of those four patients, three died during the hospital period (75%). In agreement to our result, post-operative fever was found as a good predictor of mortality by **Rostagno et al. (2010).**

In this study, out of all six patients who had post-operative chest infection and respiratory failure, only one patient survived during the hospital period (mortality 84%). Post-operative atelectasis or pneumonia commonly causes post-operative chest infection which is associated with fever. In severe cases, this infection may progress to respiratory failure which is associated with prolonged ventilation, need to inotropic support and prolonged length of ICU stay. **Smith et al. (2007)** and **Sheikh et al. (2009)** stated that postoperative pulmonary complications were good predictors of mortality.

Systemic sepsis was found a significant predictor of hospital mortality in this study. All the three patients who had systemic sepsis died during hospitalization (mortality 100%). Sepsis resulted in severe vasodilation, hypotension and concurrently decreased peripheral perfusion and low cardiac output syndrome which led to different organ ischemia (e.g. renal ischemia and pulmonary ischemia). Presence of fever, pulmonary ischemia, and low cardiac output leads to prolonged ventilation. Finally, prolonged ventilation and high doses of inotropic support prolongs the length of ICU stay. **Sheikh et al. (2009)** showed that postoperative sepsis was a good predictor of mortality.

In this study, five patients suffered from post-operative low cardiac output syndrome. Of these five patients, three died during the hospital period (60%). Presence of postoperative low COP increases mortality risk due to decreased peripheral perfusion making different organs at ischemic risk especially the kidneys decreasing renal perfusion predisposing to renal impairment which may progress to renal failure in severe cases. Also, low cardiac output increases the need for inotropic support which prolongs the duration of ICU stay. Decreased peripheral perfusion predisposes to different organ infection. Together with associated post-operative mechanical ventilation predisposes to chest infection which in turn leads to prolonged period of mechanical ventilation which in severe cases may progress to respiratory failure **(Conrad et al., 2016).**

Smith et al. (2007) stated 14% mortality due to low COP. **Sheikh et al. (2009)** retrospective study which analyzed the data of 104 patients and also found post-operative low cardiac output syndrome as an independent predictor of hospital mortality.

In the current study, we found that presence of new renal impairment was a significant predictor of post-operative mortality. Seven patients had post-operative new renal impairment (s.creatinine > 1.3gm/dl). Only two patients required hemodialysis. Four

patients (out of these seven patients; 57%) died during hospital period with only one patient died of renal failure after haemodialysis, while the other three patients died from low COP syndrome. Similarly to our results, **Smith et al. (2007)** stated renal complications as a predictor of in-hospital mortality. **Sheikh et al. (2009)** also stated postoperative renal failure as a predictor of mortality.

Prolonged period of mechanical ventilation was found as a significant predictor of hospital mortality in current study. In agreement with several studies, this study showed that period of mechanical ventilation, inotropic support > 48 hours, and duration of ICU stay were all significant univariate predictors of in-hospital mortality. **Perrotta et al. (2010)** showed that prolonged intubation was an independent predictor of hospital mortality.

This study showed that presence of inotropic support for more than two days was a significant predictor of post-operative mortality. In this study, only six patients did not need inotropic support. From twenty four patients needed inotropic support for less than two days, only one patient died. From Seventeen patients needed inotropic support for more than two days, Six patients died (35%) during hospital period. These six patients who died, three had alpha medication and the other three had beta inotropic support. In agreement with several studies, this study showed that inotropic support > 48 hours was significant univariate predictor of in-hospital mortality. **Perrotta et al. (2010)** stated that prolonged inotropic support was univariate predictor of early mortality.

The current work detected that the prolonged duration of ICU stay was a significant predictor of post-operative mortality. Similarly, **Konstantinos et al. (2016)** found that longer stay in intensive care unit was an independent predictor for long-term mortality.

Effect of Valve repair on early outcome

Valve repair, in particular in patients with mitral valve endocarditis, is considered a valuable therapeutic option when technically feasible. Conservative surgery decreases the risks related to prolonged anticoagulation and the unfavourable left ventricular geometric changes associated with valve replacement **(Feringa et al., 2007).** Also, valve repair decreased risk of re-infection and re-operation. In our study, among patients undergoing NVE reparative surgery (n=8), only one mortality was recorded during the follow-up. All other patients remained free from reoperation and recurrent endocarditis until the end of follow-up.

The validity of comparing mitral valve repair with mitral valve replacement may be questioned because the valve replacement is often reserved for the sickest patients in whom mitral valve repair cannot be performed. Therefore, it would not be surprising that postoperative results would be worse for these patients. It was observed that mitral valve replacement is more frequently performed in the acute setting, in patients with heart failure, uncontrolled sepsis, and abscesses, or with endocarditis due to staphylococcus infection **(Gutierrez-Martin et al., 2010).**

Aortic valve repair is nearly exclusively limited to patients with aortic regurgita-

tion without a component of stenosis. Patients considered for repair are generally young who wish to avoid anticoagulation and would be expected to outlive a tissue valve should replacement be considered. In order to perform this operation, the cusps must be thin and flexible without calcifications. In case of IE, valve cusps are thickened with various vegetations attached. Most repairs result in downsizing the effective orifice area in order to increase coaptation with the available cusp area. There is a resultant increase in aortic valve gradient and this must be anticipated when evaluating patients preoperatively. The decision to repair an aortic valve is made by weighing the risk of repair failure versus the benefit of decreased risk of re-infection, re-operation and avoidance of oral anticoagulation therapy. Also, valve repair procedures are relatively time consuming, increasing ischemic time and CPB time with all its hazarads **(Konstantinos et al., 2016).**

Mayer et al. (2012) conclude that AV repair for active endocarditis seems to lead to better survival compared with replacement. Also, the use of large patches in combination with bicuspid anatomy results in increased risk of late failure.

Several reports on tricuspid valve (TV) reconstruction demonstrate that this treatment option offers good results with respect to hemodynamics and long-time survival. In study of **Gottardi et al. (2007)**, TV reconstruction was performed in 18 patients and TV replacement in 4 patients.

Predictors of 6-month mortality

I- Preoperative predictors of 6-month mortality:

By univariate analysis, only five preoperative variables were found to have statistical significance as predictors of 6-month mortality**.**

This study showed that high white blood cell count was a univariate predictor of 6-month mortality. Elevated white blood cell count is an indicator of presence of active infection. Similarly, **Rostagno et al. (2010)** found that patients with WBC count outside the normal range were at a significantly greater risk of death at both discharge and 6 months while elevated WBC count did not predict in-hospital or 1-year mortality **(Heiro et al., 2007)**.

II- Operative predictors of 6-month mortality:

Only one operative variable (emergency surgery) was found to have statistical significance as a predictor of 6-month mortality**.**

III - Postoperative predictors of 6-month mortality:

All the postoperative variables were found to be insignificant predictors of 6-month mortality**.** However, the data analysis during follow-up period showed that five patients died during this period, yielding an overall 6-month mortality of 30%.

An increased rate of relapse may be due to inadequate antibiotic treatment, resistant microorganisms, polymicrobial infection, empirical antimicrobial therapy for bacterial culture negative endocarditis, peri-annular extension, PVE, persistent

metastatic foci of infection (abscesses), resistance to conventional antibiotic regimens, positive valve culture, persistence of fever at the seventh postoperative day and chronic dialysis. Also, recurrence of infection occurred in the study of **Sheikh et al. (2009)**.

The undetermined cause of death during follow up period could be due to defective contact with the patient, death occurred in local hospital with defective registry or that death occurred due to non-cardiac cause.

CONCLUSION

Surgery for IE continues to be challenging and to be associated with high mortality. Risk factors for in-hospital mortality were: prosthetic valve IE, periannular extension of infection (especially abscesses), high serum creatinine, congestive heart failure, embolization, emergency surgery, prolonged cardiopulmonary bypass time, period of mechanical ventilation, inotropic support for >48 hours, and ICU stay, postoperative complications (fever, low cardiac output syndrome, new renal impairment, systemic sepsis, chest infection and respiratory failure). Congestive heart failure, embolization, and periannular extension of infection were the most powerful predictors of hospital mortality. Risk factors for 6-month mortality were periannular extension of infection (especially abscesses), high serum creatinine, and emergency surgery. Periannular extension of infection was the most powerful predictor of 6-month mortality. EuroSCORE II has a good discrimination ability to predict both in-hospital and 6-month mortality in IE surgery. Satisfactory results can be obtained with valve repair in IE.

REFERENCES

1. **Bannay A, Hoen B, Duval X, Obadia JF, Selton-Suty C and Le Moing V (2011):** The impact of valve surgery on short- and long-term mortality in left-sided infective endocarditis: do differences in methodological approaches explain previous conflicting results. Eur Heart J., 32(16):2003-15.

2. **Borracci RA, Rubio M, Celano L, Ingino CA, Allende NG and Ahuad Guerrero RA (2014):** Prospective validation of Euro SCOREII in patients undergoing cardiac surgery in Argentinean centres. Interact Cardio vasc Thorac Surg, 10.1093.

3. **Conrad L. E, Mary E. M, Eric L. W and John M. C. (2016):** Pathophysiology of Post-Operative Low Cardiac Output Syndrome. Current Vascular Pharmacology, 14: 14-23.

4. **David TE, Regesta T, Gavra G, Armstrong S and Maganti MD (2007):** Surgical treatment of paravalvular abscess: long-term results. Eur J Cardiothorac Surg., 31:43–48.

5. **De Kerchove L, Vanoverschelde JL, Poncelet A, Glineur D, Rubay J, Zech F, Noirhomme P, El Khoury G (2007):** Reconstructive surgery in active mitral valve endocarditis: feasibility, safety and durability. Eur J Cardiothorac Surg., 31:592–599.

6. **Di Dedda U, Pelissero G, Agnelli B, De Vincentiis C, Castelvecchio S and Ranucci M (2013):** Accuracy, calibration and clinical performance of the new EuroSCORE II risk stratification system. Eur J Cardiothorac Surg., 43(1):27-32.

7. **Feringa HH, Shaw LJ, Poldermans D, Hoeks S, van der Wall EE and Dion RA (2007):** Mitral valve repair and replacement in endocarditis: a systematic review of literature. Ann Thorac Surg., 83(2):564 –70.

8. **Gilbert H, Bruno H, Pilar T, Franck T, Bernard P, Isidre V, Philippe M, Manuel de Jesus A, Ulf T, John L, Maria L, Ludwig M, Christoph K. N, Petros N, Anton M and Jose**

L Z (2015): Guidelines on the prevention, diagnosis, and treatment of infective endocarditis. European Heart Journal, 30: 2369–2413.

9. **Gottardi R, Bialy J, Devyatko E, Tschernich H, Czerny M and Wolner E (2007):** Midterm follow-up of tricuspid valve reconstruction due to active infective endocarditis. Ann Thorac Surg., 84(6):1943-8.

10. **Gutierrez-Martin MA, Galvez-Aceval J and Araji OA (2010):** Indications for surgery and operative techniques in infective endocarditis in the present day. Infect Disord Drug Targets, 10(1):32-46.

11. **Heiro M, Helenius H, Hurme S, Savunen T, Engblom E and Nikoskelainen J (2007):** Short-term and one-year outcome of infective endocarditis in adult patients treated in a Finnish teaching hospital during 1980–2004. BMC Infect Dis., 7:78.

12. **Kaiser SP, Melby SJ, Zierer A, Schuessler RB, Moon MR, Moazami N, Pasque MK, Huddleston C, Damiano RJ Jr and Lawton JS (2007):** Long-term outcomes in valve replacement surgery for infective endocarditis. Ann Thorac Surg., 83:30–35.

13. **Klieverik LM, Yacoub MH, Edwards S, Bekkers JA, Roos-Hesselink JW and Kappetein AP (2009):** Surgical treatment of active native aortic valve endocarditis with allografts and mechanical prostheses. Ann Thorac Surg., 88(6):1814-21.

14. **Konstantinos D B, Antonios A. P and Harisios B (2016):** Floppy mitral valve (FMV) e mitral valve prolapse (MVP) - mitral valvular regurgitation and FMV /MVP syndrome. Hellenic Journal of Cardiology, 57, 73-85.

15. **Lancellotti P, Rosenhek R, Pibarot P, Iung B, Otto CM, Tornos P, Donal E,Prendergast B, Magne J, La Canna G, Pierard LA and Maurer G (2013):** ESC Working Group on Valvular Heart Disease position paper—heart valve clinics: organization, structure, and experiences. Eur Heart J., 34:1597–1606.

16. **Lopes S, Calvinho P, de Oliveira F and Antunes M (2007):** Allograft aortic root replacement in complex prosthetic endocarditis. Eur J Cardiothorac Surg., 32:126–130; discussion 131–132.

17. **L?pez J, Sevilla T, Vilacosta I, Garc?a H, Sarri? C and Pozo E (2013):** Clinical significance of congestive heart failure in prosthetic valve endocarditis. A multicenter study with 257 patients. Rev Esp Cardiol., 66(5):384-90.

18. **Manne MB, Shrestha NK, Lytle BW, Nowicki ER, Blackstone E and Gordon SM (2012):** Outcomes after surgical treatment of native and prosthetic valve infective endocarditis. Ann Thorac Surg., 93(2):489-93.

19. **Mayer K, Aicher D, Feldner S, Kunihara T and Sch?fers HJ (2012):** Repair versus replacement of the aortic valve in active infective endocarditis. Eur J Cardiothorac Surg., 42(1):122-7.

20. **Musci M, Siniawski H, Pasic M, Weng Y, Loforte A and Kosky S (2008):** Surgical therapy in patients with active infective endocarditis: seven-year single centre experience in a subgroup of 255 patients treated with the Shelhigh stentless bioprosthesis. Eur J Cardiothorac Surg., 34(2):410-7.

21. **Nayak A, Mundy J, Wood A, Griffin R, Pinto N and Peters P (2011):** Surgical management and mid-term outcomes of 108 patients with infective endocarditis. Heart Lung Circ., 20(8):532-7.

22. **Ohara T, Nakatani S, Kokubo Y, Yamamoto H, Mitsutake K and Hanai S (2013):** Clinical predictors of in-hospital death and early surgery for infective endocarditis: Results of CArdiac Disease REgistration (CADRE), a nation-wide survey in Japan. Int J Cardio., 167(6):2688-94.

23. **Ozlem S, Steve W. W. K, Dorothea T, Inmaculada T-C, Maximiliano ? -F, Yongping W, Aifeng W and Nicholas K (2013):** Recent Advances in Infective Endocarditis. InTech, 5:85-105.

24. **Perrotta S, Aljassim O, Jeppsson A, Bech-Hanssen O and Svensson G (2010):** Survival and quality of life after aortic root replacement

with homografts in acute endocarditis. Ann Thorac Surg., 90(6):1862-7.

25. **Rekik S, Trabelsi I, Maaloul I, Hentati M, Hammami A and Frikha I (2009):** Short- and long-term outcomes of surgery for active infective endocarditis: a Tunisian experience. Interact Cardiovasc Thorac Surg., 9(2):241-5.

26. **Rostagno C, Rosso G, Puggelli F, Gelsomino S, Braconi L and Montesi GF (2010):** Active infective endocarditis : Clinical characteristics and factors related to hospital mortality. Cardiol J., 17(6):566-73.

27. **Sheikh AM, Elhenawy AM, Maganti M, Armstrong S, David TE and Feindel CM (2009):** Outcomes of surgical intervention for isolated active mitral valve endocarditis. J Thorac Cardiovasc Surg., 137(1):110-6.

28. **Smith JM, So RR and Engel AM (2007):** Clinical predictors of mortality from infective endocarditis. Int J Surg., 5(1):31-4.

النتائج المبكرة بعد التدخل الجراحي فى حالات إلتهاب الشغاف المعدى

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خلفية البحث : يعتبر التدخل الجراحى فى حالات إلتهاب الشغاف المعدي منقذا للحياة حيث يحتاج أكثر من نصف مرضى حالات إلتهاب الشغاف المعدي للتدخل الجراحى. يفضل القيام بالتدخل الجراحى خلال المرحلة الغير نشطة من المرض في حالات فشل العلاج الطبي للقضاء على العدوى، أو فشل القلب الأحتقانى، أو في حالات فشل الصمام الأصطناعى، أو في حالات وجود خراج، أو وجود تنبتات كبيرة متحركة على صمامات القلب، أو وجود عدوى فطرية.

الهدف من البحث: مراجعة التجربة الجراحية في قسم جراحة القلب والصدربالمعهد القومى للقلب للمرضى الذين يعانون من إلتهاب الشغاف المعدي فى صمامات القلب الطبيعية أو الاصطناعية وتحديد عوامل التكهن بأسباب الوفاه في المستشفى و خلال الستة أشهر الأولى بعد الجراحة.

المرضى وطرق البحث: تم تسجيل خمسين مريضا تم تشخيص إصابتهم بإلتهاب الشغاف المعدي بدقة. وقد خضع جميع هؤلاء المرضى لعملية جراحية فى صمامات القلب في هذه الدراسة. وقد اختبرنا جميع بيانات هؤلاء المرضى قبل الجراحة، أثناء العملية، وبعد العملية الجراحية لتحديد عوامل التكهن بأسباب الوفاه في المستشفى و خلال الستة أشهر الأولى بعد الجراحة.

النتائج : كان معدل الوفيات داخل المستشفى خلال هذه الدراسة ٢٠٪. بينما كان معدل وفيات خلال الستة أشهر الأولى بعد الجراحة ١٢٪ وحدث تكرار الإصابة بالمرض في ٤٪ من المرضى خلال المتابعة.

أثبتت هذه الدراسة أن **العوامل الرئيسية للتكهن بأسباب الوفيات في المستشفى تنقسم الى:** عوامل ما قبل اجراء الجراحة {وجود الصمام الاصطناعي، إمتداد العدوى لحلقة الصمام (خاصة فى حالة وجود خراج)، إرتفاع نسبة الكرياتينين في الدم، وكذلك إرتفاع نسبة بروتين سي التفاعلي، وفشل القلب الاحتقاني، والإنسداد} و عوامل جراحية { اجراء الجراحة بصورة طارئة، إجراء الجراحة للمرة الثانية، وطول الوقت على ماكينة القلب الصناعى} و عوامل ما بعد اجراء الجراحة {وجود مضاعفات بعد العملية الجراحية مثل (الحمى، ووجود فشل فى وظائف القلب، وجود قصور كلوي

جديد، وعدوى الصدر وفشل في الجهاز التنفسي)، طول المدة على جهاز التنفس الصناعى، وإعطاء أدوية لضعف عضلة القلب لأكثر من يومين بعد الجراحة ومدة الإقامة وحدة العناية المركزة}.

بينما أثبتت أن **العوامل الرئيسية للتكهن بأسباب الوفيات خلال الستة أشهر الأولى بعد الجراحة تنقسم الى:** عوامل ما قبل اجراء الجراحة { امتداد العدوى لحلقة الصمام (خاصة فى حالة وجود خراج)، إرتفاع عدد خلايا الدم البيضاء ، ارتفاع نسبة الكرياتينين في الدم} و عوامل جراحية { اجراء الجراحة بصورة طارئة}.

ارتبط اجراء إصلاح للصمام الطبيعى بدلا من استبداله بأخر اصطناعى بانخفاض معدل الوفيات، ومقاومة إعادة العدوى.

الإستنتاج: التعامل مع هذا المرض من قبل فريق متعدد التخصصات يخفض الوفيات بشكل كبير. وبالتالي، فان التحديات في التعامل مع هذا المرض تشمل تحسين استراتيجيات التشخيص للحد من التأخير فى بدء العلاج المناسب، وتحديد ما هو أفضل للمرضى.