International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)
Journal Home page: www.iscientific.org/Journal.html

Comparison of outcome between blood culture positive and negative infective endocarditis patients undergoing cardiac surgery

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Abstract

There have been reports of poor postoperative results following infective endocarditis (IE) surgery. It is still up for debate if the lack of positive cultures affects the prognosis. This study set out to assess the effect of negative cultures on the prognosis of IE patients who had undergone surgery. This was a retrospective research. From May 2022 to December 2022, 60 patients underwent cardiac surgery for infective endocarditis (IE). The patients are divided into two groups, one for individuals whose blood cultures are positive and another for those whose blood cultures are negative; each group contains 30 patients. Staphylococcus aureus (S. aureus) accounted for eleven infections (36.7%), Streptococcus spp. for Five (16.7%), E. faecalis for Four (13.3%), and other microbes for Ten (33.3%) of the blood culture positive endocarditis (BCPE) group in our investigation. Five patients (16.7%) experienced embolic events. Although it did not achieve statistical significance in multivariate analysis, the identification of microorganisms and increased CRP levels were shown to be substantially linked with intrahospital mortality in univariate studies. In regards to intrahospital mortality, intensive care unit (ICU) stay, or brief mortality, there are statistically insignificant variations between the groups of patients with blood culture-negative endocarditis BCNE and BCPE; nevertheless, the patients with BCBE had longer hospital stays. Although the BCPE group had higher levels of CRP, multivariate analysis did not reveal an independent correlation between CRP and death.

Keywords: Infective endocarditis, Blood culture negative, Blood culture positive.

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1. Introduction

Although the prevalence of infectious endocarditis (IE) is very low, the death rate is still significant (15–30%) and hasn't improved much over the past few decades despite advancements in diagnosis and treatment [1]. It is still difficult to diagnose IE. The modified Duke criteria is now the most often used diagnostic criteria, which include clinical, microbiological, and echocardiographic data [1]. Blood culture-negative infective endocarditis is mostly caused by fastidious or facultative intracellular microbes, fungal organisms, or non-infectious endocarditis (from lupus or Bechet disease), which accounts for up to 50% of cases [2]. According to some research, blood culture-negative endocarditis (BCNE) is linked to greater intra- and postoperative problems, a poorer prognosis, and a delayed diagnosis [2]. However, other research indicates that there is no distinction between blood culture-positive endocarditis (BCNE) and BCPE in terms of short-term mortality or intra- and postoperative outcomes. These publications point out that the clinical course is influenced more by other independent variables than by the discovery of microorganisms alone [3]. This study examined the postoperative course and short-term mortality of individuals with BCPE and BCNE having heart surgery.

2. Patients and Methods

Between May 2022 to December 2022 data of 60 cases with infective endocarditis underwent cardiac surgery at Beni suef university hospital and Kasr Al-Aini Hospitals. Prospectively and retrospectively reviewed and data analyzed.

2.1. Inclusion criteria

All patients undergoing cardiac surgery having a confirmed diagnosis of infective endocarditis documented by clinical examination and special investigations.

2.2. Exclusion criteria

Patients with severely impaired contractility (EF <30%), patients with chronic organ dysfunction and patients with massive neurological insult as deep coma or intra-cranial hemorrhage.

2.3. Methodology

Patients were examined for the primary variable items listed below:

2.3.1. Pre-operative variables studied

BMI, age, and sex A thorough physical examination is conducted, with special attention paid to neurological symptoms, heart murmurs, fever, and related medical conditions such diabetes, hypertension, and renal failure.

2.3.2. Echocardiography (TTE) to assess

The extent of the impacted leaves and vegetation, percentage of ejection, Systole and diastole of the left ventricle, Aortic root infection, Artificial paravalvular leak and artificial leaflet vegetations, or sewing rings.TEE is recommended in some patients to detect: Perivalvular extension of infection, Cardiac abscess and When TTE is inadequate as in obesity, chronic obstructive pulmonarydisease, chest-wall deformities or previous thoracic surgery.

Routine laboratory investigations including: CBC, CRP, hepato-renal functions and blood culture & sensitivity, Radiological investigations including: CXR, Pelviabdominal US, and others as needed, Timing of surgery (urgent, emergent or elective).

2.4. Intra-operative variables were studied

2.4.1. Anesthesia technique

Every patient will be under general anaesthesia. As long as the patient's critical functions are sufficiently supported, the choice of anaesthetic agent has been deemed to have minimal impact on the patient's result. Intraoperatively, ECG, invasive arterial blood pressure, nasopharyngeal temperature, urinary output and oximetric plethysmography were continuously monitored.

2.4.2. Surgical technique

In each case, a median sternotomy was used to get access to the heart. When there was just aortic valve affection and neither mitral nor tricuspid affliction, cardiopulmonary bypass was started in the conventional manner with aortic and right atrial double stage cannulation. Aorto bicaval cannulation was used to initiate cardiopulmonary bypass in cases with mitral or tricuspid affection. Minimise cardiac manipulation prior to aortic cross-clamping in order to avoid peripheral vegetation embolisation. This was especially crucial for patients whose vegetations were friable, big, and mobile. Myocardial preservation was obtained by using either cold crystalloid (Custdiol) or intermittent cold blood enriched antegrade cardioplegia solution. The myocardium was maintained at a temperature of 10-15°C by local chilling with ice and systemic cooling at 28°.

2.5. Operative data and parameters

A record was made of the following: Intraoperative findings with description of the pathological affection of theendocardium and size of vegetations, surgical procedure performed (replacement or repair of the affected valve)**,** aortic cross clamp time and Cardiopulmonary bypass time, use of inotropes and operative mortality and morbidity.

2.6. Post-operative variables will be studied

Throughout their hospital stay, every study participant was monitored closely by comprehensive clinical evaluation, standard laboratory testing, electrocardiogram, chest radiography, and transthoracic echocardiography. The following information was noted: The patients' heart rates: Heart rate and blood pressure, the length of mechanical breathing in hours, and inotropic support (whether inotropes were initiated intraoperatively and continued postoperatively or were needed postoperatively only), Incidence of major complications: Low cardiac output syndrome, neurologic dysfunction, new renal impairment**,** new hepatic impairment and Re- exploration for bleeding, ICU stay, Results of cultures for tissues excised intraoperatively, Postoperative fever, Results of postoperative transthoracic echocardiography to assess: function of the prosthetic valve and LV & RV function, Period of hospital stay and In-hospital mortality.

2.7. Statistical Data Analysis

SPSS for Windows, version 26, was used to tabulate, code, and analyse the data that were gathered. Categorical data were shown as percentages, while continuous variables were shown as mean values ± standard deviation (SD). The Fisher test and the chi-squared test were used to compare qualitative data between groups. When comparing groups of quantitative data, the independent sample t-test was employed. P-values less than 0.05 are going to be regarded as statistically significant.

3. Results

This study was conducted to analyze short term mortality and morbidity in patients with BCPE and BCNE undergoing cardiac surgery. The study included 2 groups: The first one with negative blood culture (BCNE) The second one with positive blood culture (BCPE). According to this table, there was no discernible difference in the examined groups' BMI, sex, or age (P-value>0.05) (table 1). The American Heart Association (AHA) 2020 guidelines, the European Society of Cardiology (ESC) 2015 guidelines, and the American Association for Thoracic Surgery (AATS) 2016 guidelines all included grounds for the necessity for cardiac surgery. This table showed that CHF is the main cause for surgery in BCNE patients (50%) of the cases and the second common cause in BCPE patients (36.7%). While uncontrolled infection is the most frequent cause for surgery in BCPE patients (53.3%) and the second one in the BCNE cases (table 2). This table showed that (56.7%) of each group underwent urgent surgery, (16.7%) and (20%) of the BCNE and BCPE patients respectively were indicated for emergent surgery, the rest of the patients underwent elective surgery (figure 1). There was no significant difference between the studied groups regarding the timing for surgery (P-value>0.05) (table 3). This table showed that there was insignificant difference between the studied groups regarding the cross-clamp time, Cardiopulmonary bypass time, and the total operative time (P-value>0.05) (table 4). Although this table showed that there was higher incidence of postoperative complications and longer duration of need for inotropic support in the BCPE patients, it doesn't report significant difference between the studied groups regarding the post operative complications (P-value>0.05) (table 5). This table showed that there was no significant difference between the studied groups regarding the ventilation period and ICU length of stay (P-value>0.05) but the hospital length of stay was significantly higher in the positive culture group (P-value=0.001) (table 6).

4. Discussion

Our study presents 60 cases of infective endocarditis underwent cardiac surgery in EL Kasr EL-Aini hospitals and Beni-suef university hospital. In our study there was predominance of male gender (73.3 %) in the BCNE group and (63.3%) in the BCPE group. This was similar to other reported series done by [4; 5; 6] which reported male /female ratio ranging mostly from 1.3: 1 to 3:1. Although the causes for this sex-specific difference are not fully understood, it can be explained by the higher rate of pre-disposing heart conditions in men [4; 7]. Our patient population has lower mean age. Mean (38.3±10.6) and (36.2±8.1) in the BCNE and BCPE respectively, compared to other series done for instance by Ursi et al., [8], this can be explained by high prevalence of rheumatic heart disease as a predisposing condition in our community. In this study 70% and 63.3% of the BCNE and BCPE patients respectively had rheumatic heart disease which is the most common predisposing factor in Egypt and developing countries [9]. In his study for clinical features and outcomes of IE Hussain et al., [10] found that 138 of 398 patients (34.7 %) had rheumatic heart disease. In our study preoperative embolic events (EE) were documented in (6.7%) of the patients with negative culture and (10%) of the positive culture patients. The sites of the EE were the lower limbs, the brain, the lung and the spleen, in his study to assess predictors of symptomatic embolism in infective endocarditis Hubert et al., [11] detected embolic events in 8.5 % of 1022 studied patients [11]. The study performed by Kissami et al., [12] reported embolic event in (33.3%) of the studied patients. In his study to compare BCPE and BCNE Kristians et al., [13] found that 29.82 and 27.96 of the BCPE and BCNE patients respectively had EE.30 % and 20 % of the BCNE patients and BCPE patients in our study underwent surgery in order to prevent occurrence of embolism. Through cultures, every etiological diagnosis of IE that underwent surgery was made. Neither molecular nor serological approaches revealed the presence of Coxiella burnetii endocarditis in the patients undergoing surgery. In our study the most common indication for surgery in the BCNE was CHF (50%) of the cases, while it was the second most common cause in the BCPE (36.7%). This in agreement with Katsouli, A., & Massad [14] in prospective study of 60 patients, CHF was the indication for surgery in 63% of the patients. Katsouli, A., & Massad [14], uncontrolled infection was the first indication for surgery in BCPE patients (53.3%).

Many cases have combined causes for surgery, such as HF due to valvular dysfunction with uncontrolled infection. Prevention of embolism due to the presence of large mobile vegetation was the indication of surgery in (30%) and (20%) of the BCNE and BCPE patients, respectively, as in Kumar et al., [15] that found in his, prospective study of 50 patients, (30%) had mobile vegetation and urgent surgery was needed in the patients with high risk for development of embolism, similar results reported by Ferrera et al., [16]. Throughout our work, we found that (16.7%) of the BCNE and (20%) of the BCPE patients needed emergent surgery, (56.7 %) of the two groups were indicated for urgent surgery, and the rest of the patients were planned for elective surgery. This study exhibited that emergency and urgency surgery were powerful predictors of mortality. The high mortality rate in the patients who underwent emergent or urgent surgery resembles an important predictor of mortality in the univariate and multivariate analysis; these results are in agreement with other studies that addressed the predictors of mortality in surgically treated IE patients [17]. The mean EF was 62.5±6.5 and 60.3±11.7 in the BCNE and BCPE patients respectively. In this study we excluded the patients with severely impaired contractility (EF <35%). The mean size of the vegetation was 15.4±6.7 and17.5±7.8 in the BCNE and BCPE patients respectively. we didn't find relationship between the mass size and the postoperative mortality or complications unlike what mentioned in [18]. Emil et al., [19] reported in his study for 1006 patients with left-sided IE (Large vegetations were present in 586 patients) that there were no differences between patients with large vegetations vs patients with small vegetations regarding the in hospital (14.8% vs 14.5% respectively) or 6 months mortality rates (18.1% vs 18% respectively). In this study it is clear that the blood cultures results have no effect on the intraoperative circumstances regarding the cross-clamp time, cardiopulmonary bypass time, weaning from the bypass and total operative time. Although these variables were slightly higher in the BCPE group but didn't indicate significant difference in the surgical course between the studied groups, in agreement with the study of Antonio Salsano [20]. However, we noticed that the Cross-clamp Time &CPB Time were longer in the patients who died (in the two groups), this was due to difficult weaning from CPB and the need for high doses of inotropic support. The predictive significance of BCNE is debatable based on the material that is currently accessible. Similar death rates and hospital stays were observed by Phua et al. (21) for patients with BCNE and BCPE. In contrast, BCNE was reported by Diez-Villanueva et al. (22) to be an independent predictor of postoperative heart failure and early death. Early postoperative mortality in our study was shown to be greater in BCPE patients (23.3%) compared to BCNE patients (13.3%), with BCPE patients having worse outcomes regarding postoperative, fever, re-exploration for bleeding, newly developed renal impairment, chest infection and respiratory failure and low cardiac output (CO) syndrome. The need for inotropic support for more than 48 hours was also higher in the BCPE group; the ventilation period was also higher in the positive culture endocarditis patients.

Table 1: Baseline characteristics of the groups under study

Characteristics	BCNE (no=30)	BCPE (no=30)	P-value
Age (mean±SD)	38.3±10.6	36.2±8.1	0.392
Sex			0.405
Male	22(73.3%)	19(63.3%)	
Female	8(26.7%)	11(36.7%)	
BMI (mean±SD)	26.6±2.5	26.1±2.5	0.425

Table 2: Major adverse sequalae requiring surgical intervention

Indications	BCNE (no=30)	BCPE (no=30)	P-value
CHF	15(50.0%)	11(36.7%)	0.297
Uncontrolled infection	13(43.3%)	16(53.3%)	0.605
Recurrent emboli	2(6.7%)	3(10.0%)	0.640 FET
Large vegetation >1.5mm	11(36.7%)	14(46.7%)	0.605
Prevention of embolism	9(30.0%)	6(20.0%)	0.371
Prosthetic valve dysfunction	2(6.7%)	2(6.7%)	>0.999 FET
Peri-annular abscess	0(0.0%)	2(6.7%)	0.999 FET

Table 3: Timing of surgery in IE patients depending on blood culture status

Timing for surgery	BCNE (no=30)	BCPE (no=30)	P-value
Emergent	5(16.7%)	6(20%)	0.924
Urgent	17(56.7%)	17(56.7%)	
Elective	8(26.7%)	7(23.3%)	

Table 4: Intraoperative data of the studied groups

Intra-operative	BCNE (no=30)	BCPE (no=30)	P-value
Cross clamp time(min) ± SD	76.9±17.7	78.4±24.8	0.798
Cardiopulmonary bypass(min), ± SD	106.2±21.6	107.4±27.6	0.852
Total operative time (min)	218±37.99	223±35.6	0.846

Table 5: Post-operative complication and need for inotropic support of the studied groups

Post-operative	BCNE (no=30)	BCPE (no=30)	P-value
Need to re-exploration	2(6.7%)	4(13.3%)	0.671 FET
Respiratory complications	2(6.7%)	5(16.7%)	0.424 FET
Renal complications	3(10.0%)	3(10.0%)	>0.999 FET
Hepatic complications	3(10.0%)	5(16.7%)	0.706 FET
New neurological insult	1(3.3%)	1(3.3%)	>0.999 FET
Post-operative fever	4(13.3%)	5(16.7%)	0.999 FET
Low CO syndrome	3(10.0%)	4(13.3%)	0.999 FET
Systemic sepsis	3(10.0%)	5(16.7%)	0.706 FET
High inotropic support			0.196
<48 hours	17(56.7%)	11(36.7%)	
>48 hours	8(26.7%)	15(50.0%)	
Not in need	5(16.7%)	4(13.3%)	

FET: Fisher exact test

Table 6: Post-operative hospital stay, and ICU stay, and ventilation time of the studied groups

Post-operative	BCNE (no=30)	BCPE (no=30)	P-value
Ventilation period(hours)	13.2±9.8	17.2±13.6	0.203
ICU length of stay (days)	4.7±3.2	5.7±2.7	0.234
Hospital length of stay (days)	(no=26) 26.6±4.7	(no=23) 31.3±4.4	0.001*

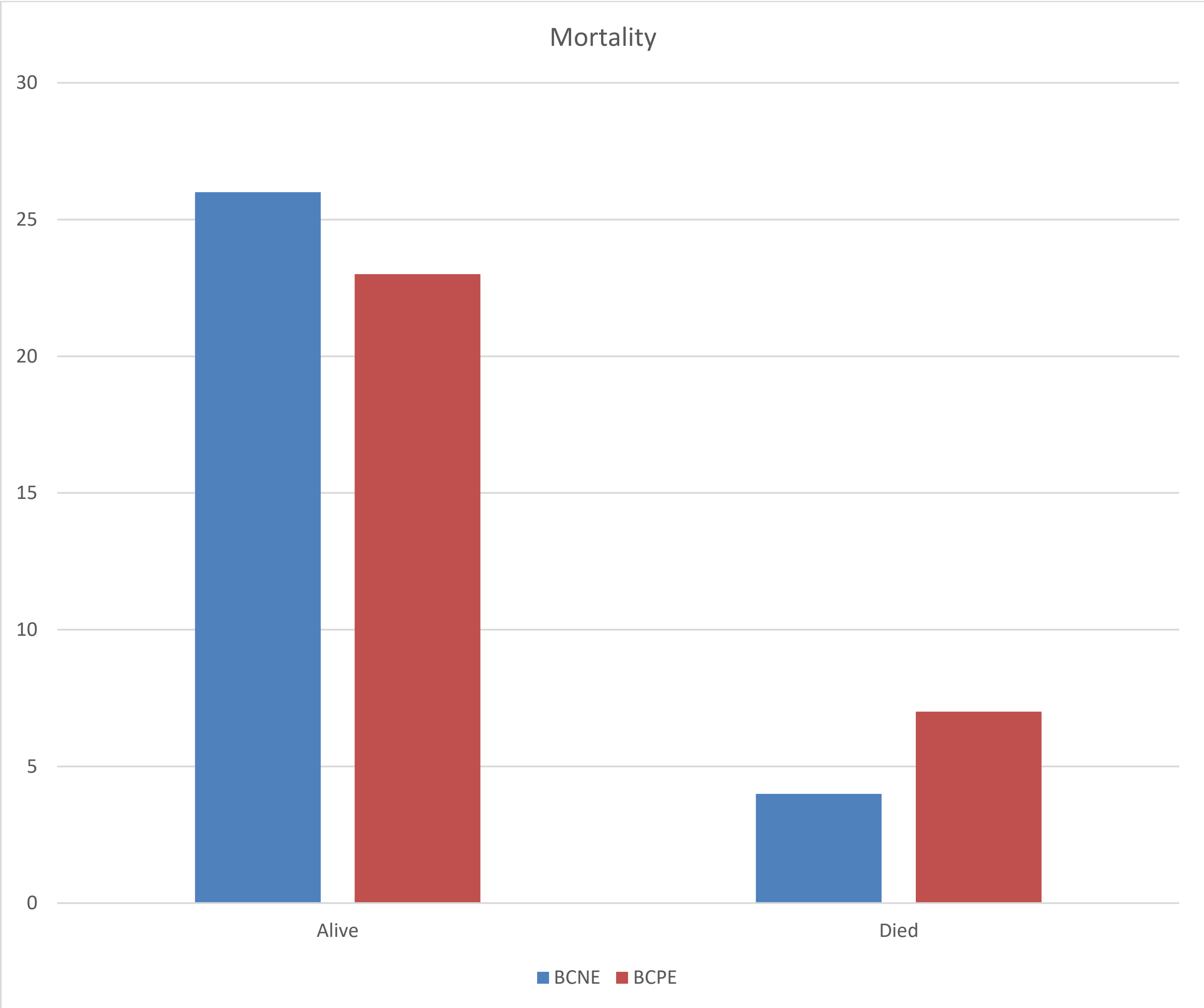

Figure 1: Comparison between the studied groups regarding the mortality

The average length of ICU stay was (4.7 ±3.2days and 5.7±2.7 days) in the BCNE and BCPE patients respectively, the ICU stay ranged from 3 to 17 days but yet no significant statistical difference. The higher average of ICU stay noticed in the BCPE patients can be explained by the occurrence of more postoperative complications and the need for inotropic support for more days compared to other studies which reported less duration of ICU stay for all the studied patients and equal period for both the culture negative and positive endocarditis [13, 20]. Prolonged postoperative hospital stay was noticed in the patients with BCPE (23 to 39) days with a mean of 31.3±4.4 days compared to (19 to 38) days with a mean of 26.6±4.7 days in the BCNE patients. This prolonged stay can be explained by the higher incidence of postoperative complications, which need hospital admission, the continuation of parenteral antibiotic treatment and close follow-up in the BCPE cases. In contrast to other studies that consider BCNE to have much worse outcomes regarding postoperative mortality and complications [20,21, 22]. Our study demonstrated that there was no statistical difference between the BCNE and BCPE regarding the postoperative outcome; on the contrary, BCPE had a higher rate of mortality and complications, which may be statistically significant in a bigger sample size.

5. Conclusion

Regarding in-hospital mortality, ICU stay, and postoperative complications, there are statistically insignificant differences between the BCPE and BCNE groups. But the BCPE patients have a statistically significant longer hospital stay duration.

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