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Factors predicting clinical outcome during hospitalization after pericardiocentesis in Sanglah General Hospital, Bali, Indonesia

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ABSTRACT

Background: Even though pericardiocentesis is a routine life-saving procedure for massive pericardial effusion, there is scarce data regarding risk factors predicting the outcome in patients undergoing pericardiocentesis. This study aimed to investigate the role of various clinical, demographic, and laboratory risk factors as a predictor of in-hospital mortality and Major Adverse Cardiac Events (MACE) in patients undergoing pericardiocentesis at Sanglah General Hospital, Bali, Indonesia.
Methods: Prospective cohort study with consecutive sampling was conducted in patients undergoing pericardiocentesis in Sanglah General Hospital, Bali, Indonesia, from May 2017 until September 2021. Risk factors and blood samples were observed and measured at the first admission. MACE and in-hospital mortality were observed during hospitalization. Data were analyzed using SPSS version 23 for Windows.
Results: Twenty-seven patients were involved in this study. Malignant etiology was associated with increased risk of in-hospital mortality with HR 13.459 (95%CI: 1.378-131.49). Respiratory Failure during admission was associated with increased risk of mortality with HR 5.99 (95% CI: 1.355-26.55) and increased risk of persistent pericardial effusion HR 5.72 (95% CI: 1.570-20.800).
Conclusion: Malignant etiology and respiratory Failure are independent predictors of in-hospital mortality in patients undergoing pericardiocentesis in Sanglah General Hospital. Respiratory Failure was associated with an increased risk of persistent pericardial effusion.

Keywords: Pericardiocentesis, In-Hospital Mortality, MACE.
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INTRODUCTION

Pericardiocentesis is a life-saving procedure in hemodynamically impaired cardiac tamponade. It is a class I recommendation for moderate to severe pericardial effusion unresponsive to medical therapy or suspected of bacterial or malignancy as an etiology.[1] The procedure involves direct access to the pericardium through an 18 G needle using an apical, subcostal, or parasternal approach followed by subsequent insertion of a catheter inside the pericardium.[1] In a study involving cancer patients undergoing pericardiocentesis, the procedure's success rate was 99%, with no procedure-related mortality. Meanwhile, the study also showed an 18% mortality in 1 month after the procedure in all patients.[2,3]

The clinical outcome after pericardiocentesis is still unclear. The worst clinical outcome was observed in patients with neoplastic etiology. Meanwhile, patients with idiopathic/viral causes had better outcomes. Higher procedure volumes were associated with a lower mortality rate. In addition, an older patient, hemodynamically unstable, respiratory failure, and need for ventilation were associated with a higher mortality rate after pericardiocentesis. Patients with a history of pericardial disease, thyroid abnormality, pericarditis/pleural effusion and heart failure were associated with lower mortality.[3,4]

Even though pericardiocentesis has become a routine procedure for moderate to severe pericardial effusion, no local or national studies have evaluated the in-hospital clinical outcomes after pericardiocentesis. Based on those mentioned above, this study aims to identify factors predicting the in-hospital clinical outcome in patients undergoing pericardiocentesis at Sanglah General Hospital, Bali, Indonesia

METHODS

This is an observational single-center prospective cohort study of consecutive patients undergoing pericardiocentesis in Sanglah General Hospital, Bali, Indonesia, from May 2017 until October 2020, to investigate factors predicting in-hospital mortality and Major Adverse Cardiovascular Events (MACE). Patients undergoing pericardiocentesis were observed for mortality and development

of MACE during hospitalization, which included: heart failure (HF), cardiogenic shock, lethal arrhythmia (ventricular arrhythmia or atrioventricular block causing hemodynamic imbalance, and death from a cardiovascular cause. Written informed consent was provided before the procedure. Pericardiocentesis was conducted in the cath lab using C-arm guiding/echocardiography. Local anesthesia was provided with lidocaine. A subxiphoid approach was performed using an 18 G needle and 10cc spuit followed by sheet insertion and echocardiography or fluoroscopy confirmation. A pigtail catheter was inserted to drain pericardial fluid and samples for pericardial fluid analysis were subsequently obtained. Blood samples were obtained from the peripheral vein at the initial admission. Patients were observed for Heart Failure (HF) developments, cardiogenic shock, lethal arrhythmias, persistent effusion, and death from a cardiovascular cause. Data were obtained from patient history, physical, and laboratory examination. Exclusion criteria were patients who declined standard treatment post pericardiocentesis

Malignancy etiology was defined by observing malignant cells in pericardial fluid cytology analysis or history of previous Malignancy. Infection etiology was defined by low pericardial fluid glucose and findings of bacteria from gram staining/culture, fungi from KOH staining or adenosine deaminase examination, or positive gene expert showing tuberculosis infection. Hemodynamic instability was defined as hypotension (systolic pressure < 90 mmHg) and associated with signs of hypoperfusion and tachycardia. Respiratory Failure was defined as respiratory rate > 35 times/minute related to respiratory muscle retraction, oxygen saturation < 70%, blood gas analysis showing partial arterial oxygen pressure < 50 mmHg and partial CO2 arterial pressure > 50 mmHg. This study's clinical comorbid analyzed included pericardial disease, thyroid abnormality, pleuritis/ pleural effusion, congestive heart failure, coronary artery disease, diabetes mellitus and anemia.

Several laboratory examinations were included in the analysis. The ratio of Lactate Dehydrogenase (LDH) was defined as the ratio of LDH taken from peripheral vein upon admission against LDH value of pericardial fluid with a cut-off value of 0,6. Albumin gradient was defined as serum albumin level subtracted against pericardial albumin level with a cut-off value of 12 g/L. The ratio of pericardial glucose has obtained the ratio of glucose taken from pericardial fluid to glucose taken in the peripheral vein upon admission. Pericardial pH was defined as the pH level of pericardial fluid with a cut of point of 7.3. Upon admission, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were taken from the peripheral vein.

Study characteristics of participants were described using univariate analysis. Data were presented using a table and divided into clinical and laboratory characteristics. Numerical and categorical data were presented by mean ± standard deviation and percentage and frequency distribution. The association between risk factors and MACE occurrence was analyzed using the multivariate Cox Proportional Hazard model to obtain its Hazard ratios (HR) with 95% CI and p-value. Statistical significance was assumed if the null hypothesis could be rejected at the level of p = 0.05. Analyses were performed using SPSS software version 23 for Windows.

RESULTS

A total of 27 patients with pericardiocentesis were included in the study. The mean age of participants was 47 ± 15 years, of whom 60% were male. Most patients presented with shortness of breath (93%), cough (75%), and weakness (32%). Patients were admitted with an average systolic blood pressure of 113.2 mmHg and an average pulse of 10 5x/ minutes. As many as 18% of patients had a previous history of heart failure, 10% had a history of pericardial disease, 14 % had a history of coronary artery disease and 3 % had a history of diabetes mellitus. Other clinical, demographic and laboratory characteristics are presented in Table 1. Among 27 patients included in the study, 19 (67%) patients died during hospitalization. During observation, as many as 22 (78%) patients experienced persistent pericardial effusion, 4 (14%) patients experienced acute heart failure, 10 (35%) patients experienced cardiogenic shock, and 5 (17%) patients had malignant arrhythmia (Table 1).

Bivariate analysis on clinical and etiology variables against mortality and MACE are shown in Table 2. Respiratory failure was associated with increased risk of mortality (HR 6.8 P = 0.009), Persistent effusion (HR 8.8 P = 0.003), and cardiogenic shock (HR 13.9 P = 0.000). Patients with a history of DM were associated with a higher risk of heart failure (HR 8.1 P = 0.004) and malignant arrhythmia (HR 5.6 P = 0.017). Figure 1. Shows In-hospital survival difference between malignancy and non-malignancy groups as presented by Kaplan–Meier curve. Patients with malignant etiology had higher risk of mortality (HR 7.5 P = 0.006) and persistent pericardial effusion (HR 4.4 P = 0.035). Bivariate analyses of laboratory variables on mortality and MACE are shown in Table 3. Abnormal CRP was associated with a higher risk of malignant arrhythmia (HR 6.4 P =0.011).

Malignant etiology was associated with increased mortality risk after multivariate analysis (Adjusted HR 13.4; 95%CI: 1.37-131.4). Meanwhile, respiratory Failure was associated with increased risk of mortality (Adjusted HR 5.9; 95%CI: 1.3-26.5) and persistent pericardial effusion (Adjusted HR 5.7; 95%CI: 1.5 -20.8), as shown in Table 4.

DISCUSSION

Pericardiocentesis is the principal therapeutic procedure for the initial management and diagnosis of severe symptomatic pericardial effusion.[5,6] This study aims to identify risk factors predicting the outcomes of patients undergoing pericardiocentesis in Sanglah General Hospital. Most patients in this study were male (60%) and presented with shortness of breath (93%), cough (75%), and weakness (32%). The average blood pressure and heart rate among the included patients were 112.5 mmHg and 103 x/minutes, respectively. Around 18% of patients had a previous history of heart failure, 10 % had a history of pericardial disease, 14% had a history of coronary artery disease and 3% had

Table 1. Demographic and Clinical characteristic.

Variable	Mean	SD	N (%)
Age (Year)	47.5	14.6	
Male (%)			16 (60)
Symptoms (%)			
Palpitation			4 (1)
Shortness of breath			93 (26)
Nausea			7 (2)
Weakness			32 (9)
Pregnancy			4 (1)
Cough			75 (21)
Chest pain			21 (6)
Unstable Hemodynamic (%)			14 (4)
Respiratory Failure (%)			25 (7)
Systolic Blood Pressure (mmHg)	113.2	18.1	
Pulse rate (times/minutes)	105	18.2	
History of pericardial effusion (%)			10 (3)
History of heart failure (%)			18 (5)
History of coronary artery disease (%)			14 (4)
History of Diabetes Mellitus (%)			3 (1)
LVEF %	67.9	9.4	
WBC (10^3/µL)	13.9	7.5	
Hb (g/dL)	11.7	2.1	
HCT (%)	36.3	6.3	
PLT (10^3/µL)	308.2	172	
BUN (mg/dL)	30.6	26.7	
SC (mg/dL)	1.33	1.24	
Na (mmol/L)	128	9.1	
K (mmol/L)	3.8	0.68	
pH	7.40	0.11	
Glucose serum (mg/dL)	120	29.3	
SGOT (U/L)	226	658	
SGPT (U/L)	134	198	
GFR (ml/minutes/1.73 m^2)	89.6	45.9	

SD: Standard Deviation; LVEF: Left Ventricle Ejection Fraction; WBC: White Blood Cells; Hb: Hemoglobin; HCT: Hematocrit; PLT: Platelet; BUN: Blood Urea Nitrogen; SC: Serum Creatinine; SGOT: Serum Glutamic Oxaloacetic Transaminase; SGPT: Serum Glutamic Pyruvic Transaminase; GFR: Glomerular Filtration Rate

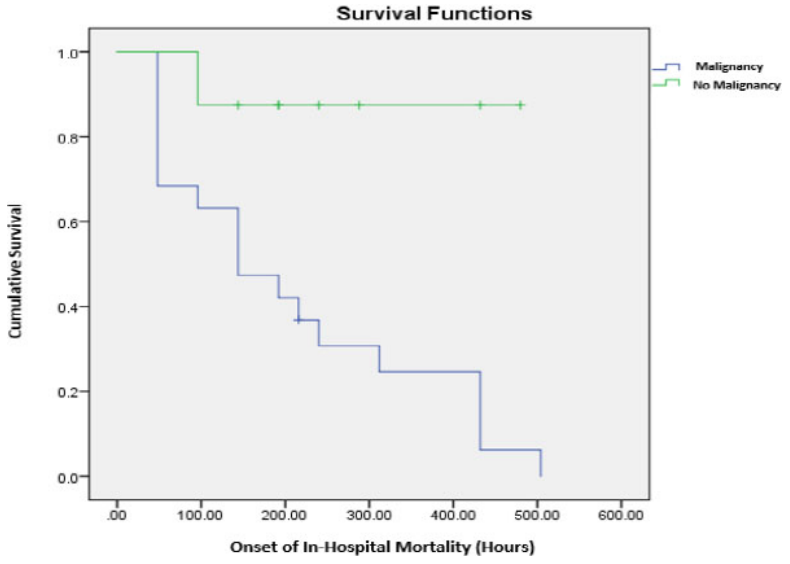

Figure 1. Kaplan–Meier survival analysis in In-hospital Mortality on Malignancy and Non-Malignancy group.

a history of diabetes. A Majority of the patients experienced persistent pericardial effusion (78%). Meanwhile, 4 patients had acute heart failure (14%), 10 (35%) had a cardiogenic shock, and 5 (17%) had malignant arrhythmias. This finding is consistent with a study reported by Gibbs CR et al., showing most patients undergoing pericardiocentesis presented with breathlessness (90%), chest pain (74%), and cough (70%).[7]

Several risk factors were shown to predict mortality and MACE among patients undergoing pericardiocentesis in this study. Based on bivariate analysis, respiratory Failure was associated with 6.8 times increased risk of mortality and an 8.8 times higher risk of persistent pericardial effusion compared to patients without respiratory Failure. Patients with DM had an 8.1 times higher risk of heart failure and 5.6 times higher risk of malignant arrhythmia. Malignant etiology was shown to increase the risk of mortality by 7.5 times and the risk of persistent pericardial effusion by 4.4 times compared to other causes of pericardial effusion. Meanwhile, an abnormal value of CRP was associated with a 6.4 times increased risk of malignant arrhythmia. Meanwhile, patients with abnormal LED, LDH and LDH ratios did not significantly correlate with mortality or MACE. After adjusting for compounding variables, multivariate analysis showed that patients with malignant etiology had a 13.4 increased mortality risk. Respiratory Failure was associated with a 5.9 increased risk of mortality and 5.7 times increased risk of persistent pericardial effusion. This result is consistent with a previous study reported by Strobbe A et al., showing worse survival in patients with known Malignancy than Malignancy free pericardial effusion (HR 5.40; 95% CI, 3.53-8.26). The study also showed worse survival in patients with pericardial Malignancy compared to patients without pericardial Malignancy (HR: 3.01; 95% CI, 1.66-5.45; P <0.001).[7] Malignancy related pericardial effusion could be explained by metastatic or direct invasion of non-cardiac tumor into the pericardium, often resulting in hemopericardium. Effusion could also be secondary to mediastinal lymph node involvement or paraneoplastic.[8,9]

Table 2. Bivariate analysis on clinical and etiologic variables against mortality and MACE.

Variable	Outcome	HR	p
Age > 65 years	Mortality	0.655	0.418
	Persistent Effusion	0.260	0.610
	Heart Failure	0.433	0.510
	Cardiogenic Shock	0.077	0.782
Male	Malignant Arrhythmia	0.374	0.541
	Mortality	1.781	0.182
	Persistent Effusion	0.717	0.397
	Heart Failure	2.204	0.138
	Cardiogenic Shock	0.308	0.579
	Malignant Arrhythmia	1.363	0.243
Unstable Hemodynamic	Mortality	0.083	0.773
	Persistent Effusion	0.003	0.958
	Heart Failure	3.168	0.750
	Cardiogenic Shock	1.168	0.280
	Malignant Arrhythmia	0.122	0.727
Respiratory Failure	Mortality	6.874	0.009*
	Persistent Effusion	8.859	0.003*
	Heart Failure	3.800	0.051
	Cardiogenic Shock	13.884	0.000*
	Malignant Arrhythmia	3.095	0.079
History of Pericardial Effusion	Mortality	0.486	0.486
	Persistent Effusion	0.171	0.680
	Heart Failure	0.368	0.544
	Cardiogenic Shock	2.327	0.127
	Malignant Arrhythmia	0.668	0.414
History of Heart Failure	Mortality	0.178	0.673
	Persistent Effusion	0.483	0.478
	Heart Failure	0.66	0.798
	Cardiogenic Shock	0.034	0.854
	Malignant Arrhythmia	0.946	0.331
History of CAD	Mortality	0.210	0.647
	Persistent Effusion	0.581	0.446
	Heart Failure	0.869	0.351
	Cardiogenic Shock	0.172	0.679
	Malignant Arrhythmia	2.312	0.128
History of DM	Mortality	0.576	0.448
	Persistent Effusion	0.576	0.448
	Heart Failure	8.145	0.004*
	Cardiogenic Shock	1.417	0.234
	Malignant Arrhythmia	5.687	0.017*
Pericardial Effusion Aetiology	Mortality	7.575	0.006*
	Persistent Effusion	4.449	0.035*
	Heart Failure	0.057	0.811
	Cardiogenic Shock	1.825	0.177
	Malignant Arrhythmia	1.436	0.231
Malignancy	Mortality	2.477	0.116
	Persistent Effusion	1.778	0.182
	Heart Failure	0.409	0.523
	Cardiogenic Shock	2.470	0.116
	Malignant Arrhythmia	0.816	0.366
Bacterial Infection	Mortality	1.335	0.248
	Persistent Effusion	1.961	0.161

Furthermore, malignancy related pericardial effusion could also be related to specific cancer treatments such as mediastinal radiation, certain chemotherapy agents, opportunistic infections, and post thoracic surgery complications. The primary solid tumor of the pericardium is very rare and heralds a poor prognosis.[9,10]

This study uses a cohort design to analyze the risk factors affecting the clinical outcome in patients undergoing pericardiocentesis. It has shown a significant relationship between malignant etiology and mortality. In addition, this study confirms the relationship between respiratory Failure and the occurrence of mortality and persistent pericardial effusion. This study is prospective, so it has some advantages over retrospective study where important data on risk factors, confounding factors, mortality and MACE can be used more extensively.

This study had several limitations. The sample selection was conducted using consecutive sampling. In addition, the study is single-center-based. The study period was fulfilled within a relatively short period, so we could not address the long -effects of the risk factors.

CONCLUSION

Malignant etiology and respiratory Failure upon admission are associated with increased mortality risk in patients undergoing pericardiocentesis at Sanglah General Hospital. Respiratory Failure is associated with an increased risk of persistent pericardial effusion. Further research with longer observation time and more sample size is necessary to obtain more representative results to assess the long-term effects of various risk factors in predicting the prognosis of patients undergoing pericardiocentesis.

CONFLICT OF INTEREST

There is no competing interest regarding the manuscript.

ETHICS CONSIDERATION

Ethics approval has been obtained from the Ethics Committee, Faculty of Medicine, Universitas Udayana, Sanglah

Variable	Outcome	HR	p
	Heart Failure	1.154	0.283
	Cardiogenic Shock	0.046	0.830
TB Infection	Malignant Arrhythmia	1.225	0.268
	Mortality	0.841	0.359
	Persistent Effusion	0.091	0.763
	Heart Failure	0.180	0.672
	Cardiogenic Shock	0.300	0.584
	Malignant Arrhythmia	3.239	0.072
Idiopathic Autoimmune	Mortality	2.585	0.108
	Persistent Effusion	1.307	0.253
	Heart Failure	0.058	0.809
	Cardiogenic Shock	0.882	0.348
	Malignant Arrhythmia	0.006	0.937

HR: Hazard Ratio; CAD: Coronary Artery Disease; DM: Diabetes Mellitus; TB: Tuberculosis; Statistically significant if p-value less than 0.05

Table 3. Bivariate analysis on laboratory variables against mortality and MACE.

Variable	Outcome	HR	p
Abnormal CRP	Mortality	0.336	0.562
	Persistent Effusion	0.577	0.447
	Heart Failure	0.006	0.938
	Cardiogenic Shock	0.436	0.509
	Malignant Arrhythmia	6.414	0.011*
Abnormal ESR	Mortality	0.928	0.335
	Persistent Effusion	3.733	0.053
	Heart Failure	0.561	0.454
	Cardiogenic Shock	1.813	0.178
	Malignant Arrhythmia	0.331	0.565
LDH Ratio	Mortality	0.384	0.536
	Persistent Effusion	0.102	0.749
	Heart Failure	1.512	0.219
	Cardiogenic Shock	0.277	0.599
	Malignant Arrhythmia	0.548	0.459

HR: Hazard Ratio; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; LDH: Lactate Dehydrogenase; *Statistically significant if p-value less than 0.05.

Table 4. Multivariate analysis of variable against mortality and MACE.

Outcome	Variable	HR	95% CI
Mortality	Malignancy	13.459	1.378-131.49
	Respiratory Failure	5.999	1.355-26.55
Persisten Pericardial Effusion	Respiratory Failure	5.724	1.573-20.825

HR: Hazard Ratio; CI: Confidence Interval

General Hospital, Bali, Indonesia prior to the study being conducted.

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AUTHOR CONTRIBUTION

All authors contribute to the study from the conceptual framework, data acquisition, data analysis, until reporting the study results through publication.

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