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ORIGINAL ARTICLE

Best management of patients with malignant pericardial effusion: A comparative study between imaging-guided pericardiocentesis and surgical pericardial window

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ABSTRACT

Background: The clinical course of malignancies is frequently complicated by third spacing in body cavities, including pericardial effusion. What remains the optimal management for malignant pericardial effusion is a dilemma.

Aim: We aimed to compare 30-day outcomes of imaging-guided pericardiocentesis and surgical pericardial window in patients with malignant pericardial effusion.

Methods: A retrospective observational study was done at a tertiary care hospital. We reviewed hospital record files of 91 consecutive patients admitted with malignant pericardial effusion from January 2010 to December 2019 and requiring imaging-guided pericardiocentesis or pericardial window.

Results: A total of 71 patients were included in the final analysis. Most patients were male (68%). The mean age was 45 years. Hypertension was the most common comorbid condition. Lymphoma or leukemia (39%) was the most common cause of malignant pericardial effusion followed by lung cancer (28%). About 57.7% of patients underwent pericardiocentesis, and the remainder underwent surgical pericardial window (42.3%). The overall procedural success was 97.2%, and the overall mortality was 5.6%. The success rate was similar when pericardiocentesis was compared with the surgical pericardial window ($p = 0.22$). The length of hospital stay was higher in patients undergoing pericardial window ($p = 0.007$), whereas the re-accumulation rate was higher in the pericardiocentesis group (0% versus 34%, $p < 0.001$). Patients undergoing pericardial window had higher odds of major bleeding requiring transfusions.

Conclusion: There is a higher rate of recurrence following isolated pericardiocentesis but a comparable mortality difference between the two procedures. Complication rates can be reduced by improving surgical technique and peri-operative management. Meticulous surgical care, infection precautions, and good glycemic control in this immunocompromised subset can preserve the pericardial window as a better management option.

Relevance to Patients: Pericardial window is a promising and effective management option for patients with recurrent malignant pericardial effusion, but it comes at the cost of bleeding and infection. More extensive trials are needed to understand better the long-term outcomes of pericardial window or pericardiocentesis in patients with malignant effusion.

1. Introduction

Cardiac tamponade is a syndrome characterized by hemodynamic abnormalities resulting from an increase in pericardial pressure due to the accumulation of fluid [1], Myriads of causes of pericardial effusion, complicating into cardiac tamponade, have been reported in the literature. These may include idiopathic, viral pericarditis, iatrogenic injury or trauma,

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malignancy, uremia, collagen vascular disease, tuberculosis, post-myocardial infarction, aortic dissection, and bacterial infection [2]. In the 1930s, Beck described a diagnostic triad for cardiac tamponade, consisting of hypotension, raised central venous pressure, and muffled heart sounds [3]. The mechanism of tamponade includes raised pericardial pressure which leads to restriction of cardiac filling, reduction of stroke volume, and cardiac output [4,5].

Echocardiography is considered the primary imaging modality for the evaluation of pericardial effusion because of its high sensitivity and specificity, lack of ionizing radiation, and low cost [6]. The treatment of cardiac tamponade is based on clinical presentation and may involve percutaneous pericardiocentesis or surgical drainage [7]. Echocardiographic-guided pericardiocentesis has been demonstrated to be a safe and effective procedure that can be performed at the bedside [8].

A recent study in our region has reported malignancy as the most common cause of cardiac tamponade and pericardial effusion requiring pericardiocentesis [9]. However, patients with malignant pericardial effusion require repeat pericardiocentesis or a pericardiac window if they develop recurrent effusion. There is limited data on the prognostic implications of the choice of treatment for malignant pericardial effusion. In this study, we aim to compare 30-day outcomes of pericardiocentesis and surgical pericardiac window, in patients having malignant pericardial effusion.

2. Materials and Methods

It was a retrospective observational study done at Aga Khan University Hospital, Karachi, which is a 700-bedded multidisciplinary tertiary care hospital, located in the largest city of Pakistan. All adult patients (age more than 18 years) admitted with malignant pericardial effusion who underwent pericardiocentesis or surgical pericardial window from January 2010 to December 2019, were enrolled in the study.

We reviewed hospital record files of 91 patients, including both males and females, admitted with malignant pericardial effusion, who underwent pericardiocentesis or surgical pericardial window. 20 patients were excluded based on prior history of pericardiocentesis, surgical pericardial window, pericardiocentesis followed by a surgical pericardial window, or those who underwent pericardial window along with other cardiac surgery, and those with proven prior infection. A total of 71 patients were included in the final analysis (Figure 1).

The decision to proceed with either pericardiocentesis or pericardial window was done after a combined consultation of cardiology, cardiothoracic surgery, and primary oncologist. The selection was at the discretion of the primary physician, and no strict criteria were followed.

For all patients, demographic information including age and gender and symptoms on presentation were recorded after reviewing written medical records. Comorbid conditions were tabulated including diabetes mellitus, hypertension, coronary artery disease, chronic kidney disease, chronic liver disease, chronic obstructive pulmonary disease (COPD), and heart failure. Echocardiographic data were reviewed for the size of pericardial effusion, distribution of pericardial effusion, echocardiographic signs of tamponade, and EF.

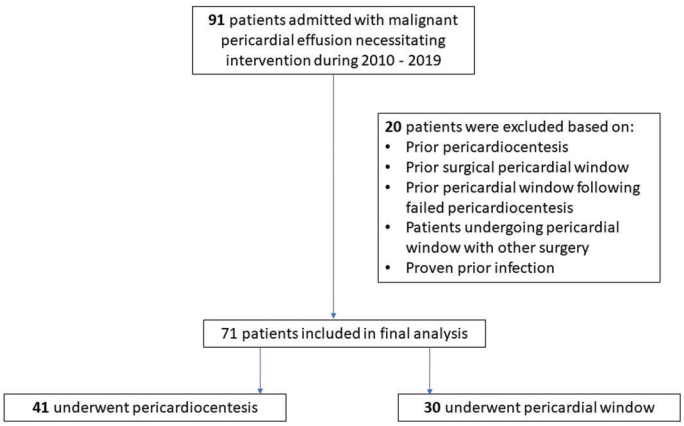

Figure 1. A flow diagram showing patient recruitment.

2.1. Procedure

After informed consent, pericardiocentesis or pericardial window was performed by a trained cardiologist or cardiothoracic surgeon. Details of the procedure including access site, anesthesia, imaging modality, and complications were recorded. Procedure success was defined as the successful drainage of pericardial fluids with the placement of a pericardial drain.

For pericardiocentesis, the subxiphoid approach was used in all patients. All patients underwent fluoroscopic-guided pericardiocentesis, along with echocardiographic guidance provided before, during, and after the procedure. The pericardial tube was retained for a minimum of 24 h in all patients.

For the pericardial window, a standard subxiphoid approach was used, under general anesthesia in all patients. With the patient in a supine position, a subxiphoid vertical skin incision was given, starting 1–2 cm above the xiphoid process to a length of 3–4 cm below the xiphoid process. After the excision of the subcutaneous fat and rectus sheath attachment, the xiphoid process was retracted, and a portion of the pericardium was grabbed using forceps and incised, creating a window.

2.2. In-hospital monitoring

All patients were followed during a hospital stay for hemodynamic instability, defined as a systolic blood pressure of <90 mmHg or requiring vasopressor support within the first 48 h following the procedure. Major bleed was defined as a decrease in hemoglobin of 2 g/dL or more or any blood transfusion within the 48 h following the procedure. Length of stay and in-hospital mortality were also recorded.

2.3. Follow-up

The follow-up of all patients was conducted by physical interviews or over a phone call until January 2020. Re-

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accumulation was defined as an increase in pericardial effusion size by one categorical variable (i.e., small to moderate) or an effusion requiring re-intervention. 30-day mortality was also recorded.

2.4. Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences version 23 (IBM Corp., Armonk, NY). To describe the characteristics of the patients admitted with malignant pericardial effusion, frequencies and proportions were reported for the categorical variables such as gender, presence of diabetes, COPD, coronary artery disease, and type of procedure performed. The normality assumption for continuous variables (age and ejection fraction) was checked by generating histograms superimposed with the normal curve. Since both age and EF variables appeared to be normally distributed, mean with standard deviation data were reported for these variables.

To compare 30-day outcomes of pericardiocentesis and surgical pericardial window in these patients, we used the Pearson's Chi-squared test or Fisher's exact test. The potential outcomes that were compared across two types of procedures were a procedural success, length of stay, re-accumulation within 30 days, in-hospital death, and complications. A univariable logistic regression analysis was undertaken to determine the association between the type of procedure (pericardiocentesis and surgical pericardial window) and the independent effect of each significant predictor on length of stay and complications.

We considered a $p < 0.05$ as significant for the final model. Finally, we conducted a multivariable logistic regression analysis to determine the association between the type of procedure and length of stay and any complications while adjusting for sociodemographic and clinical characteristics. We presented the results of regression analysis by unadjusted odds ratio (OR) and adjusted OR (aOR) with 95% confidence intervals.

2.5. Ethical considerations

The study was reviewed and approved by the ethical review committee of the Aga Khan University Hospital, Karachi, and was exempted from written informed consent (ERC number 2020-5733-15094).

3. Results

3.1. Sociodemographic and clinical characteristics of the patients with malignant pericardial effusion

The mean age of the patients was 45 years and 68% were males (Tables 1 and 2). About 39% were hypertensive and 16% of the patients were diabetic. Other comorbid conditions included coronary artery disease (1%), COPD (7%), and CKD (4%). The mean EF at the time of admission was 54.6% with a standard deviation of 5.4. The proportion of primary malignancy was as follows: 39.4% had lymphoma or leukemia, 28% had lung cancer, 11.3% had breast cancer, 4.2% had gastrointestinal cancers, and 2.8% had other cancers such as genitourinary, head and neck, gynecological, and thymoma each. Most patients (97%) presented with dyspnea and 3% had hypotension at the time of admission to the hospital.

Table 1. Sociodemographic and clinical characteristics of the patients with malignant pericardial effusion

Variable	N (%)
Age (mean ± SD)	45 ± 18.37
Gender	
Males	48 (68)
Females	23 (32)
Hypertension	28 (39)
Diabetes mellitus	11 (16)
Coronary artery disease	1 (1)
Chronic kidney disease	3 (4)
Chronic liver disease	0 (0)
COPD	5 (7)
Heart failure	1 (1)
Presenting symptom	
Dyspnea	69 (97)
Hypotension	2 (3)

Table 2. Clinical and echocardiographic characteristics of patients undergoing intervention for pericardial effusion

Type of malignancy	N (%)
Lung	20 (28)
Breast	8 (11.3)
Lymphoma/Leukemia	28 (39.4)
Thyroid	2 (2.8)
Gastrointestinal	3 (4.2)
Head and neck	2 (2.8)
Genitourinary	2 (2.8)
Gynecological	2 (2.8)
Thymoma	2 (2.8)
Others	2 (2.8)
Ejection fraction % (mean ± SD)	54.6 ± 5.4
Pericardial effusion size	
Medium	67 (94.4)
Large	4 (5.6)
Tamponade physiology	
Yes	98 (96.1)
No	4 (3.9)
Distribution of effusion	
Circumferential	46 (64.8)
Loculated	25 (35.2)
Indication of procedure	
Therapeutic	40 (56.3)
Diagnostic + Therapeutic	31 (43.7)

3.2. Type of procedure performed and proportion of patients experiencing adverse outcomes

The majority of patients underwent pericardiocentesis (57.7%) as compared to 42.3% of patients who underwent pericardial

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window. Nearly 97.2% of the patients with malignant pericardial effusion had procedural success and 59.2% had a complication-free procedure. Around 14.1% developed an infection and 26.8% experienced a major bleed that required blood transfusion. Overall, 19.7% developed re-accumulation within 30 days of the procedure. About 29.6% of the patients with malignant pericardial effusion stayed longer than 1 week. The overall in-hospital mortality was 5.6% (Table 3).

3.3. Comparison of 30-day outcomes of pericardiocentesis and surgical pericardial window

The procedural success was 100% in pericardial window versus 95% in pericardiocentesis, but this did not reach statistical significance ($p = 0.22$). The length of hospital stay (>7 days) was longer in patients undergoing pericardial window (47% vs. 17%, $p = 0.007$). The 30-day re-accumulation was significantly higher in patients undergoing pericardiocentesis (0% vs. 34%, $p \leq 0.001$). Patients undergoing pericardial window had greater number of complications ($p \leq 0.001$). This included major bleeding and infection. There was no significant difference in mortality ($p = 0.75$) (Table 4).

Table 3. Type of procedure performed and proportion of patients experiencing an adverse outcome

Variable	N (%)
Procedure performed	
Pericardiocentesis	41 (57.7)
Pericardial window	30 (42.3)
Procedural success	69 (97.2)
Complication	
None	42 (59.2)
Infection	10 (14.1)
Bleeding requiring transfusion	19 (26.8)
Re-accumulation within 30 days	14 (19.7)
Length of stay	
≤7 days	50 (70.4)
>7 days	21 (29.6)
In-hospital death	4 (5.6)

3.4. Association of procedure and clinical factors with complications and length of stay on bivariate analysis

Patients who underwent pericardial window were 82 times more likely to experience any complication and were 4.25 times more likely to stay longer in the hospital (>7 days) when compared with patients who underwent pericardiocentesis. Females were 2.6 times more likely to experience any complication. Patients with lung cancer had lesser complications (OR = 0.50) and a shorter hospital stay (OR = 0.50) than the rest of the malignancies. The odds of developing complications were higher in patients with breast cancer (OR = 10.5) (Table 5).

3.5. Association of procedure and clinical factors with complications and length of stay on multivariable analysis

After adjusting the results of multivariable analysis for gender, ejection fractions, and diabetes mellitus, it was found that patients who underwent a pericardial window were 224 (aOR = 223.98) times more likely to experience any complication and have a longer length of hospital stay (aOR = 5) when compared with patients who underwent pericardiocentesis. Female patients were more likely to have complications (aOR 8). Diabetes was also found to be a strong predictor of complications and longer stay (Table 6).

4. Discussion

Malignancy is one of the major causes for symptomatic pericardial effusion. Pericardial effusion frequently complicates the course of malignancy. Causes of pericardial effusion in patients with malignancy include direct metastatic pericardial deposit and acute pericarditis as a direct injury by cytotoxic agents or due to immune-mediated reactions [10,11].

Treatment of recurrent pericardial effusion is often challenging, especially when complete remission of the underlying cause is not possible. Pericardiocentesis is the standard treatment for acute management of symptomatic and/or hemodynamically significant pericardial effusion. However, recurrence is common following pericardiocentesis. Tsang *et al.* reported that echocardiography-guided pericardiocentesis is a safe and effective management

Table 4. Comparison of 30-day outcomes of pericardiocentesis and surgical pericardial window

Variable	Pericardiocentesis		Pericardial window		*p*-value
Outcomes	N	%	N	%	
Procedural success	39	95.1	30	100	0.22
Length of stay					
≤7 days	34	82.9	16	53.3	0.007
>7 days	7	17.1	14	46.7	
Re-accumulation in 30 days	14	34.1	0	0	<0.001
In-hospital death	2	4.9	2	6.7	0.75
Complications					
None	38	92.7	4	13.3	
Infection	3	7.3	7	23.3	
Bleeding requiring transfusion	0	0	19	63.3	<0.001

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Table 5. Association of procedure and clinical factors with complications and length of stay on bivariate analysis

Variables	Any complications		Longer hospital stay	
	OR	95% CI	OR	95% CI
Gender				
Males	1		1	
Females	2.60	0.94–7.21	1.06	0.36–3.14
Hypertension				
No	1		1	
Yes	0.70	0.26–1.87	0.69	0.238–2.007
Diabetes mellitus				
No	1		1	
Yes	1.25	0.34–4.56	0.20	0.02–1.67
COPD				
No	1		1	
Yes	0.96	0.15–6.16	0.58	0.06–5.47
Presenting symptom				
Hypotension	1		NA	
Dyspnea	0.68	0.04–11.38		
Malignancy				
Others	1		1	
Lung	0.50	0.12–2.12	0.50	0.11–2.32
Breast	10.50	1.02–108.58	0.67	0.10–4.58
Lymphoma/Leukemia	0.97	0.27–3.50	1.11	0.30–4.17
Ejection fraction	1.01	0.92–1.10	0.93	0.85–1.02

Table 6. Association of procedure and clinical factors with complications and length of stay on multivariable analysis

Variables	Any complications		Longer hospital stays	
	aOR	95% CI	aOR	95% CI
Procedure performed				
Pericardiocentesis	1			
Pericardial window	223.98	20.16–2489	5.11	1.62–16.11
Gender				
Males	1		1	
Females	8.67	0.91–82.73	1.24	0.36–4.35
Ejection fraction	1.06	0.90–1.26	0.94	0.84–1.05
Diabetes mellitus				
No	1		1	
Yes	3.24	0.28–37.57	6.76	0.71–64.55

aOR: adjusted odds ratio; CI: Confidence interval

option, but more than half of patients would develop recurrent effusion necessitating re-intervention [12]. Higher recurrence rate following isolated pericardiocentesis necessitates additional interventions such as prolonged-drainage catheter, instillation of sclerosing agents, or creating pericardial window surgically.

In a systemic review by Virk *et al.*, the pooled recurrence rate associated with isolated pericardiocentesis was 38%. In our study, the recurrence rate of this group was comparable at 34%. On the other hand, none of the patients undergoing pericardial window developed re-accumulation [13]. Horr *et al.* compared the outcomes of patients undergoing pericardiocentesis and pericardial window in 1281 patients. The in-hospital mortality did not differ between the two groups (p = 0.49). Pericardiocentesis was followed by higher recurrence rate (24% vs. 10%, $p < 0.0001$) [14]. These results are consistent with our data, whereby there was no statistically significant difference in mortality ($p = 0.75$) and re-accumulation rates were higher in the former group ($p < 0.001$).

Horr *et al.* reported greater percentage of major bleed in patients undergoing pericardial window (1% vs. 0%) but this did not reach statistical significance ($p = 0.16$) [14]. In contrast, our study reported that majority patients undergoing pericardial window had major bleeding requiring transfusion (63% vs. 0%, $p < 0.001$).

To date, no randomized trials have been conducted to compare surgical decompression and percutaneous approach. However, most retrospective studies have shown lower failure rate associated with surgical management in patients with malignancy pericardial effusion [15]. Outcomes are also driven by the type of malignancy (greatest with non-small cell lung cancer), positive cytology, and presence of concomitant pleural effusion [15]. In our study, female gender, diabetes, and breast cancer were associated with higher odds of developing any complication. Diabetes was also associated with longer length of hospital stay.

Malignancy is an immunocompromised state. The higher rate of infection in pericardial window group should be weighed against the need for recurrent hospitalizations and interventions in patients who undergo isolated pericardiocentesis. In addition, one could argue and weigh the length of hospital stay and the inherent risk of nosocomial infection against the higher recurrence rate necessitating recurrent intervention. Patient centered decision can help to decide the most appropriate strategy in any patients. Moreover, the expertise of treatment center can potentially alter the complication rates.

Pericardial window is a promising and effective management option for patients having recurrent malignant pericardial effusion but comes at a cost of complications such as bleeding and infection. There is a higher rate of recurrence following isolated pericardiocentesis but a comparable mortality difference between the two procedures. Complication rates can be reduced by improving surgical technique and peri-operative management. Meticulous surgical care, infection precautions, and good glycemic control in this immunocompromised subset can preserve the pericardial window as a better management option.

4.1. Limitations

This was a retrospective study conducted at a single center. There was a lack of long-term follow-up. A surgical window was chosen over pericardiocentesis, if the primary oncologist deemed it necessary, based on the disease status. This suggests the possibility of selection bias. The pericardial tube was retained for a minimum of 24 h in all patients; however, the exact period of the drainage was not recorded.

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Conflicts of Interest

The authors declare no conflict of interest.

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