Original Article

Prognosis of Malignant Pericardial Effusion Patients after Pleuro-pericardial Window Surgery in Urban Population

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Objective: Malignant pericardial effusion (MPE) is uncommon in advance stage cancer. However, it could cause a life-threatening condition such as cardiac tamponade. Surgical drainage is routinely recommended as a rapid and effective treatment in this disease. This study aims to investigate an overall outcome after pleuro-pericardial window surgery in MPE patients.

Materials and Methods: From 2007 to 2017, 32 MPE patients who underwent pleuro-pericardial window were enrolled. Benign pericardial disease or patients who receive only pericardiocentesis or pericardial sclerosing agent were excluded. Baseline clinical data such as sex, primary cancer, complication rate and result of pathological from pericardial biopsy were collected, retrospectively. Overall survival (OS) was analyzed by the Kaplan-Meier method and log-rank test.

Results: There were 18 male patients with mean age of 55 years old. The majority of primary cancers was lung cancer, followed by breast cancer. Mean overall survival was 3.7 months. There was no recurrence. Overall survival at 30-day mortality, 3 months and 1 year were 75%, 59% and 19%, respectively. In subgroup analysis, there was no difference in overall survival between lung cancer and non-lung cancer group (p = 0.650).

Conclusion: Pleuro-pericardial window is a safe and effective procedure with low recurrence rate. However, decision-making should be made individually for each patient.

Keywords: Pericardial window, Malignant pericardial effusion, Cancer

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Malignant pericardial effusion (MPE) is an abnormal accumulation of fluid in the pericardial space, which is caused by metastatic disease[1]. MPE appears up to 15 to 20% of patients with advanced-stage cancer and usually affects patient survival[2-6]. Lung cancer is the most common primary tumor that associates with MPE, followed by breast cancer[7-9]. These two cancers combined make up 50 to 65% of all MPE[9].

Clinical manifestations of MPE may range from asymptomatic to life-threatening condition such as cardiac tamponade. The most common presenting symptom is dyspnea, which occurs in more than half the cases[10]. Despite advances in cancer treatment nowadays, the treatment of MPE remains palliative. The choice of treatment depends on several factors, including cancer stage, patient's prognosis from the underlying malignancy, the cardiovascular and medical status of the patient, and local hospital expertise. Several palliative procedures such as pericardiocentesis, surgical drainage (pericardiostomy or pericardial window operation) and pericardial instillation of anti-cancer drugs have been widely used for MPE treatment[9-11]. However, the question that arises here is: which one is the most effective treatment modality for MPE, especially in patients with recurrent pericardial effusion?

According to Thailand cancer statistics, lung cancer is the most common cancer among men and breast cancer is the leading cancer among women living in the Bangkok Metropolitan area[12]. The occurrence is likely due to smoking behavior and westernization of dietary habits and lifestyle patterns among Bangkokians. The increased rates of lung and breast cancers would affect the number of patients complicated by MPE and subsequent quality of life. Although surgical palliation could help relieve dyspnea symptoms by drainage of pericardial effusion, it seems that the life expectancy of these patients is still limited, and prognostic factors reported were sometimes inconsistent. The aim of this study was to investigate the outcomes of MPE patients after pleuro-pericardial window surgery among urban population in Bangkok. A further aim was to compare the prognosis of patients between lung cancer and non-lung cancer groups.

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Materials and Methods

Study population

A retrospective single-center observational study using database of all consecutive MPE patients who underwent pleuro-pericardial window operation in

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Department of Surgery, Faculty of Medicine Vajira hospital, Navamindradhiraj university between 2007 and 2018 was performed. The exclusion criteria were: 1) patients who underwent pericardiocentesis alone; 2) patients who received sclerotherapy along with pericardiocentesis; and 3) patients who were diagnosed as having benign pericardial disease. This study was approved by the Vajira Institutional Review Board (approval number 038/62) and was performed in accordance with the Declaration of Helsinki.

Surgical technique

All patients were operated under general anesthesia with endotracheal intubation. The pericardium was exposed beneath the left nipple, and the chest was entered through the 5th intercostal interspace with anterior mini-thoracotomy incision of 4 to 5 cm. After identification of the phrenic nerve, an anterolateral pericardial window of 2 to 3 cm was opened over the left ventricle. If the tamponade occurred as a result of posterior fluid collection, a posterior pericardial window below the phrenic nerve was created. Surgical pericardial fluid and the excised pericardium tissue were routinely sent for pathologic examination. A single chest tube drainage (No. 28 F) was placed via a separate incision. The drain was typically placed for 48 to 72 h postoperatively. It was removed when the drainage amount was less than 100 mL over a 24 h period. No patients received any sclerosing agents.

Data collection

The data collected were age, gender, cause of pericardial effusion, results of pericardial fluid cytology and pericardial biopsy, postoperative complications including cardiac arrhythmia and pneumonia, survival status at 30 days, 3 months and 1 year, overall length of survival. Survival status was classified as survival or death. Overall length of survival was the interval between the dates of operation and death or of last outpatient clinic.

Statistical analysis

All statistical analyses were performed using SPSS software version 22.0 for Windows (IBM corporation, Armonk, NY, USA). Categorized variables are presented as number with percentage. Continuous variables are depicted as mean with standard deviation. Overall survival was determined with the Kaplan-Meier method. The difference between survival curves of the lung cancer and non-lung cancer groups was analysed using the log-rank test. A value of $p<0.05$ was considered statistically significant.

Results

During the period of study, there were 32 patients who met the inclusion criteria: 17 (53.1%) were male and 15 (46.9%) were female. Their mean age was 55 years (range 33 to 80 years). Primary malignancy was from the lung in most patients (n = 25), followed by the breast (n = 3). The underlying cause of pericardial effusion was confirmed in most cases: cytological studies from pericardial effusion were positive for malignant cells in 28 cases (87.5%) whereas pathologic studies from pericardial biopsy were positive in only 15 patients (56.3%). Details of patient characteristics are presented in Table 1.

Four patients (12.5%) had surgical complications, which included cardiac arrhythmia (n = 3) and pneumonia (n = 2). There was three (9.4%) in-hospital death. The causes of death in two patients were pneumonia with sepsis and in the other was from advanced disease. Overall survival at 30-day mortality, 3 months and 1 year were 75%, 59% and 19%, respectively (Figure 1). The median survival of patients was 3.7 months.

In subgroup analysis, there was no difference in overall survival between the lung cancer and non-lung cancer groups (p = 0.650) (Figure 2). Further analysis also demonstrated that MPE patients with a positive result of pericardial biopsy had no difference in overall survival compared with those with negative pericardial biopsy (p =

Table 1. Patient characteristics

Characteristic	Total (n = 32)
Age (years), mean (range)	55 (33 to 80)
Sex, n (%)	
Male	17 (53.1)
Female	15 (46.9)
Cause of pericardial effusion, n (%)	
Lung cancer	25 (78.1)
Breast cancer	3 (9.4)
Head and neck cancer	1 (3.1)
Other	3 (9.4)
Positive pericardial fluid cytology, n (%)	28 (87.5)
Positive pericardial biopsy, n (%)	18 (56.2)
Postoperative complication, n (%)	
Cardiac arrhythmia	3 (9.4)
Pneumonia	2 (6.2)
30-day mortality rate, n (%)	8 (25.0)

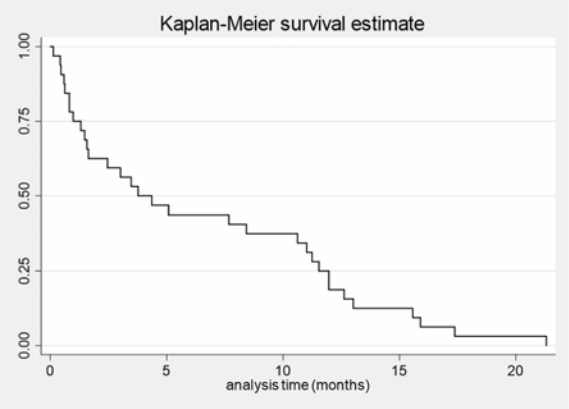

Figure 1. Overall survival of the study population.

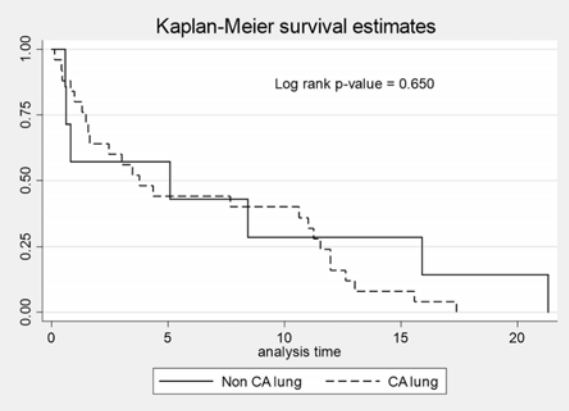

Figure 2. Survival curves of the lung cancer and non-lung cancer groups.

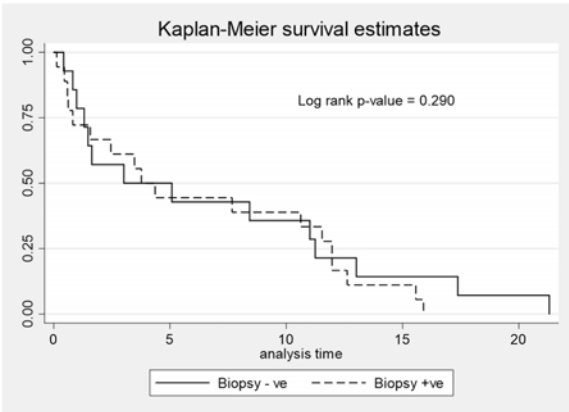

Figure 3. Survival curves of positive and negative pericardial biopsy.

0.290) (Figure 3).

Discussion

Pericardial effusion is uncommon in cancer patients. The mechanisms of MPE formation is caused by tumor metastasis to pericardium causing an obstruction of lymphatic drainage[13]. Nevertheless, the present study found that pericardial biopsy results were positive for malignant cells in only 56.2% of patients. In our cohort, lung and breast cancers were identified as the two most frequent underlying malignant diseases, accounting for 85% of the study population. The distribution of primary malignant disease seen in our series was consistent with other published reports[9,14,15].

The main purpose of MPE management was to relief of acute symptoms and hemodynamic effects. At the same time, collected pericardial fluid and tissue sample for pathologic diagnosis could be applied. The ideal treatment means should also prevent fluid re-accumulation within the pericardium. Currently, there are many treatment options for MPE. Nevertheless, no method is recommended as the best one. With respect to pericardiocentesis, it is a less invasive procedure with a low complication rate, so it is commonly used as a prompt treatment for acute dyspnea. However, its major disadvantage is its high recurrence rates[5,16,17]. One study reported a recurrence rate of 33% in patients who received an echo-guided percutaneous pericardial drainage[16]. Other series by Mayo clinic team found that 22% of MPE patients who were primarily treated with pericardiocentesis needed a second management for recurrent pericardial effusion[6].

In contrast to pericardiocentesis, surgical drainage by pericardiostomy or pericardial window operation could provide a definitive management by allowing the effusion to continuously drain to the pleural cavity[5]. This procedure has been reported to have a much lower recurrence rate of pericardial effusion than the pericardiocentesis. Celik et al who underwent a pleuro-pericardial window in 48 MPE patients found only 2.1% of recurrence rate[18]. Another study by Liberman et al showed a similar result with 3.7% of recurrence[19]. In line with both studies, our study which conducted on 32 patients did not find any recurrence of MPE. Despite its benefit, one should be cautious when performing this operation in patients with advanced-stage cancer because the operation may be related to high morbidity and mortality. Olsen et al created a pericardial window in 28 patients with large malignant pericardial effusions and reported a 21% rate of postoperative mortality[20]. The present study observed a 9.4% mortality rate along with 9.4% cardiac arrhythmia and 6.2% pneumonia after the procedure. The difference in the results between the study of Olsen et al and the present study might lie on the dissimilarity in several factors, including sample size, degree of pericardial effusions, type and stage of primary cancers and patient status.

Regarding the prognosis after palliative surgery for MPE, it is generally poor with reported median overall survival ranging from 4 to 6 months and 1-year survival rates, varying from 13.8% to 20% in other studies[21-23]. The present study which conducted on patients undergoing a pleuro-pericardial window revealed a median survival of 3.7 months and a 19% 1-year survival, which fell within the ranges of previous reports. Findings of other studies showed that MPE caused by lung cancer had a significantly poorer outcome, with 1-year overall survival of 10.5%, compared to non-lung cancer that caused MPE[24,25]. On the contrary, our results found no difference in overall survival rates between lung cancer and non-lung cancer groups. Nevertheless, the number of patients with non-lung cancer was quite limited, which might affect the significance of statistical analysis.

The present study has several limitations. First, it was a retrospective, single-institutional, and database-oriented study. Second, the number of patients was limited, so it might have inadequate strength to determine significant prognostic factors for patient survival. Furthermore, this study focused only on the survival of patients. Therefore,

other outcomes including psychological aspects and quality of life after the treatment were not explored. These data are also important when dealing with patients complicated by advanced-stage cancer as well as their family members. More research is needed to evaluate these issues.

Conclusion

MPE patients had a poor prognosis. The choice of palliative treatment should be made individually for each patient. Pleuro-pericardial window surgery should be considered to be a preferred treatment method, especially in patients with long-term survival expectancy, because of its low recurrence rate.

What is already known on this topic?

MPE is a common condition found in advanced-stage cancer. It can cause cardiac tamponade leading to mortality, if untreated. The treatment of MPE is only palliative, with the aim of reducing dyspnea symptoms. The prognosis of these patients is generally poor.

What this study adds?

MPE patients who underwent pleuro-pericardial window surgery did not have a better survival than patients undergoing other surgical palliation means reported in previous studies. Nevertheless, this surgical technique provides a lower recurrence rate of MPE, which might positively affect the quality of life of patients.

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Potential conflicts of interest

The authors declare no conflict of interest.

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