

Research Article

Pericardial window operation for malignant pericardial effusion may have worse outcomes for lung cancer than the other cancers

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Abstract

Background

Malignant pericardial effusion (MPE) compromises cardiac function in cancer patients and pericardial window operation provides pericardial decompression and histology sampling. We seemed to observe worse outcomes of lung cancer with MPE. Using electronic medical records from hospital information system, we analyzed the data to test the hypothesis that MPE with lung cancer has worse clinical outcomes than other cancers.

New information

From 08/2005 to 11/2015, 52 cases of pericardial window with MPE (30 cases of lung cancer) were retrieved and analyzed. Comparing to non-lung cancer, hospital mortality and length of stay did not differ significantly, but lung cancer cases had worse overall survival and Kaplan-Meier survival. Percutaneous pericardiocentesis with prolonged drainage may be a good non-inferior alternative. Readiness for paradoxical hemodynamic instability (PHI), occurring in 10% pericardial window cases, should never be overlooked.

Keywords

pericardial window, malignant pericardial effusion (MPE), lung cancer

Introduction

From our experience of pericardial window operations for malignant pericardial effusion (MPE), we seemed to observe the worse outcomes of lung cancer in comparison to other cancers. With this hypothesis, we retrieve data from our hospital information system (HIS) for analysis.

Materials and Methods

The retrospective study collected patient data from electronic hospital information system (HIS) from the earliest date available to the date of data retrieval, which were from 08/19/2005 to 11/06/2015. HIS stored the diagnoses as ICD-9 codes and procedures as National Health Insurance (NHI) billing codes. The included patients all received pericardial window operation for malignant pericardial effusion (MPE). Lung cancer cases were compared with non-lung cancer cases for baseline characteristics and outcomes. Institutional review board (IRB) approved the HIS data retrieval and the waiver of consent.

Cohort definitions

The study cohort included all the patients with malignant pericardial effusion (MPE) with pericardial window operations. They all had discharge diagnoses whose ICD-9 ranged from 140 to 239. Pericardial window operation was defined as the procedure NHI billing code that was 68001B, 68002B, or 68003B. Lung cancer cases were defined as the discharge diagnosis with the ICD-9 main code of 162.

Outcome definitions

The study outcomes included hospital length of stay, hospital mortality, overall mortality, overall length of survival and Kaplan-Meier survival. Dates of operation, of hospital discharge, of death, and of last outpatient clinic were collected. Hospital length of stay was the interval between dates hospital discharge and operation. Survival status at hospital discharge defined hospital mortality, and that at last outpatient clinic defined overall mortality. Overall length of survival was the interval between the dates of operation and death or of last outpatient clinic.

Statistical methods

We defined data specification and sent the request to hospital information technology (IT) team. With the IRB approval, hospital IT team used SQL to retrieve the specified data.

Stata/MP 13.1 for Mac was used for statistical analyses and graphing. Non-parametric methods were preferred since normality robustness was unknown. Scale variables were summarized as median +- interquartile range (IQR). Their two-groups comparisons were made with Mann-Whitney U test. Nominal variables were summarized as count and percentage and compared with Fisher's exact test. Survival analysis was done with Kaplan-Meier method. Kaplan-Meier survival curves were compared with log-rank test. Statistical significance was defined as p-values less than 0.05.

Data resources

With the above definitions and criteria, all cases with the discharge diagnosis of cancer (ICD-9 = 140~239) and with the procedure of pericardial window (NHI code = 68001B, 68002B, or 68003B) were retrieved for the variables that included medical record number, birthday, gender, discharge diagnoses, procedure codes, date of operation, date of discharge, discharge survival status, and date of last outpatient clinic (if survived to discharge). Lung cancer cases were flagged if the discharge diagnosis had the ICD-9 main code of 162.

With IRB approval, the data, confidential and saved in a password-protected computer, were not de-identified since further information might be sought from paper medical record for future research. The raw and processed datasets were only available to the authors of the study and statistical work was exclusively done by the author RJC without any outsourcing to external biostatisticians.

Results

Our HIS retrieved all the 52 cases of pericardial window operations for malignant pericardial effusion (MPE) from 08/19/2005 to 11/06/2015. Among them, there were 30 cases of lung cancer. The retrospective follow-up time was approximately ten years. The cases of lung and non-lung cancers had similar age and gender distributions (Table 1).

For hospital death rate, the lung cancer's was 20% and the non-lung cancer's was 13.6%, not statistically different ($p=0.717$, by Fisher's exact test). For hospital length of stay, the lung cancer's was 10 days (median) and the non-lung cancer's was 8.5 days, not statistically different ($p=0.3779$, by Mann-Whitney U test) (Table 1). For Kaplan-Meier curves on hospital mortality, the lung cancer and the non-lung cancer cases did not differ significantly ($p=0.9736$, by log-rank test) (Fig. 1). Thus, the two groups had similar in-hospital outcomes (hospital death, hospital length of stay, and Kaplan-Meier hospital survival).

Table 1.

Cohort characteristics and clinical outcomes of malignant pericardial effusion with pericardial window

	Lung cancer		Non-lung cancer		p-value
N	30		22		
Sex (M:F)	21:9		11:11		0.162
Age	63.0	+15.8	60.9	+14.9	0.2911
Hospital death	6	(20%)	3	(13.6%)	0.717
Overall death	24	(80%)	6	(27.3%)	<0.0001
Hospital stay (day)	10	+8	8.5	+10	0.3779
Overall survival (day)	83	+549	1427	+3102	0.0014
Scale variables as median +- IQR					
Categorical variables as count (percentage)					

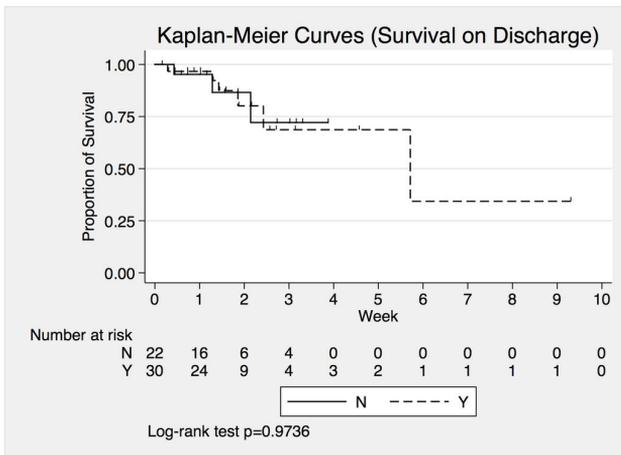


Figure 1.

Kaplan-Meier Curves for Survival at Discharge, by Lung Cancer Status

Over the ten-year follow-up, however, the lung cancer cases had significantly better outcomes than the non-lung cancer cases. For overall mortality, the lung cancer's was 80% and the non-lung cancer's was 27.3% ($p < 0.0001$, by Fisher's exact test) (Table 1). For Kaplan-Meier curves on overall mortality, the lung cancer cases had worse survival than the non-lung cancer cases ($p = 0.0002$, by log-rank test) (Fig. 2). After two years postoperatively, the Kaplan-Meier survival of the non-lung cancer cases was approximately 75% but that of the lung cancer cases was less than 25% (Fig. 2).

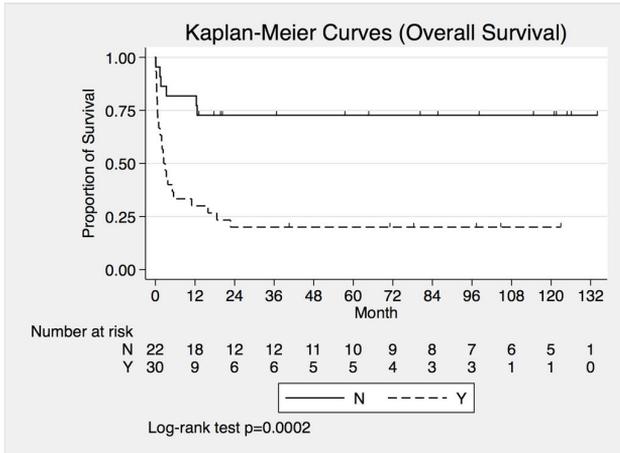


Figure 2.

Kaplan-Meier Curves for Overall Survival, by Lung Cancer Status

Therefore, for the cases of pericardial window for malignant pericardial effusion, compared to non-lung cancer cases, our data showed that lung cancer cases had similar hospital death and hospital length of stay, but had significantly worse overall survival during the ten-year follow-up.

Discussion

Pericardial window operation for MPE had better outcomes in non-lung cancer than in lung cancer patients, in terms of overall mortality and Kaplan-Meier survival, although the hospital death and hospital length of stay might not differ significantly (Table 1, Fig. 2). Our findings were compatible with some prior studies (Celik et al. 2012, Cullinane et al. 2004, Rousseau-Bussac et al. 2014, Tsang et al. 2000, Apodaca-Cruz et al. 2010).

In the patients with MPE, lung cancer is the most common malignancy, approximately 40% of all MPE (Celik et al. 2012, Gumrukcuoglu et al. 2011, Olsen et al. 1990, Patel et al. 2013, Tsang et al. 2000, Wagner et al. 2011). Provided with the heterogeneity of lung cancer in terms of their histology-specific prognosis, lung cancer-related MPE needs additional considerations for the surgical management.

Lung cancer has the worst outcomes in patients with MPE (Tsang et al. 2000, Celik et al. 2012, Cullinane et al. 2004, Apodaca-Cruz et al. 2010, Rousseau-Bussac et al. 2014). Male sex, positive effusion cytology for malignancy, lung cancer, and tamponade or hemodynamic collapse are independently associated with poor survival for MPE (Tsang et al. 2000). For MPE with left minithoracotomy pericardial window, the risk factors for unfavorable survival include age over 55 years and lung cancer, but interestingly, does not include left ventricular ejection fraction under 55% (Celik et al. 2012).

One of the most devastating complications following pericardial window is paradoxical hemodynamic instability (PHI), a poorly understood phenomenon, with incidence as high as 10%, and presenting as mysterious shock after pericardial drainage (Wagner et al. 2011). Dr. Wagner and his team performed vigorous analyses trying to identify the risk factors that predicted PHI. They found that the possible factors might include tamponade, positive cytology/pathology, and more drainage volume, but however, not include cancer types or echocardiographic findings of left or right ventricular dysfunction (Wagner et al. 2011). Surprisingly, lung cancer did not have more PHI (10.26%) than the other cancers (10.89%), $p=0.546$ (Wagner et al. 2011). We may infer that PHI may not be the reason why lung cancer has worse outcomes in MPE. Further research is needed to identify the predictors for PHI in MPE in the surgical practice.

Pericardial window is effective and safe for managing MPE (Celik et al. 2012, Cullinane et al. 2004, Olsen et al. 1990, Rousseau-Bussac et al. 2014, Tsang et al. 2000). Nevertheless, echo-guided percutaneous pericardial drainage or pericardiocentesis may work with comparable or non-inferior efficacy (Apodaca-Cruz et al. 2010, Gumrukcuoglu et al. 2011, Patel et al. 2013, Tsang et al. 2000). Given the unfavorable outcomes of lung cancer in MPE in comparison to the other cancers, should we prefer the percutaneous to surgical approach? Since the MPE prognosis is multi-factorial, the superiority of percutaneous versus surgical approach is still controversial. The decision should be made individually for each patient.

Clinical perspectives

Lung cancer with MPE should be managed carefully since the patients have worse outcomes than other cancer patients. Percutaneous drainage may be preferred to surgical window because it is non-inferior for outcomes and less invasive. Paradoxical hemodynamic instability may occur in 10% of MPE patients with pericardial window, similarly for both lung and non-lung cancers, and it is not predicable by preoperative cardiac function. Precautious measures for unexpected postoperative shock should always be made, such as thorough preoperative doctor-patient communication, vigorous anesthesiologist monitoring, and routine postoperative intensive care unit, even when the case appears to be low risk.

Limitations and Pitfalls

The study was retrospective, single-institutional, and database-oriented. Intrinsic pitfalls existed as non-randomization, non-blindness, selection bias from referral, information bias from missing value, etc. Data confirmation of the electronic records by paper records was not done in this study and should be done in further studies. More detailed data for more analyses and inference might be obtained from paper records as well, such as effusion drainage volume, effusion cytology, pericardium pathology, lung cancer histology, more detailed cancer diagnoses, pericardial window surgical approach, preoperative echocardiography data, presence of paradoxical hemodynamic instability (PHI), etc.

Conclusions

Pericardial window for malignant pericardial effusion (MPE) with lung cancer may have worse overall survival but similar hospital survival and length of stay. Percutaneous pericardiocentesis or prolonged drainage is a good alternative. Paradoxical hemodynamic instability (PHI) may occur in 10% cases, regardless cancer type or cardiac function. Preparedness for postoperative unexpected shock should be done.

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Ethics and security

Taipei Tzuchi Hospital's Institutional review board approval No. 04-X22-043

Author contributions

Motivation: Chen RJ, Shen TC; Study design: Chen RJ; Patient sources: Chen RJ, Shen TC, Tsai KT, Hu CY; Data management & biostatistics: Chen RJ; Manuscript writing: Chen RJ; Supervision & advice: Shen TC, Tsai KT.

Conflicts of interest

None

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Supplementary materials

Suppl. material 1: Raw Statistical Output by Stata/MP 13.1

Authors: Robert J. Chen, MD, MPH

Data type: Raw Statistical Results

Brief description: Detailed statistical output by Stata/MP 13.1

Filename: pwin.html - [Download file](#) (44.15 kb)

Suppl. material 2: Stata/MP 13.1 program

Authors: Robert J. Chen, MD, MPH

Data type: Stata 13.1 program *.do

Brief description: Stata/MP 13.1 program *.do (including self-made macros (sharable upon request))

Filename: pwin.do - [Download file](#) (1.64 kb)