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# VATS pericardiotomy for patients with known malignancy and pericardial effusion: Survival and prognosis of positive cytology and metastatic involvement of the pericardium: A case control study

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ABSTRACT

*Background:* Pericardiotomy for cancer patients with effusion can alleviate symptoms, but with unclear effect on long term survival. Our experience with VATS technique has produced some long-term survivors.
*Methods:* A retrospective review of 62 VATS pericardiotomy for pericardial effusion in patients with known malignancy. Kaplan–Meier survival curves and Log-Rank tests were used for analysis.
*Results:* The mean age was 54.8 ± 14.3 years (ranging from 19 to 79). The mean hospital stay was 8.7 ± 5.5 days. The median survival was 6.75 months (range 1 month–10 years). Overall one-year survival was 44.2%, 3-year survival 17.6%, and 5-year survival 10% after drainage of pericardial effusion. The mean survival in cytology negative patients ($n = 21$) was 13.4 ± 0.98 months, compared to 4.89 ± 0.9 months in cytology positive patients ($n = 27$) ($p = 0.0175$). The 5-year survival in cytology negative patients was 19.6%, while none of the patients with positive cytology were alive after 36 months. The mean survival in patients with no evidence of metastatic disease on the pericardium ($n = 28$) was 12.8 ± 0.9 months, compared to patients with metastatic disease of the pericardium ($n = 22$) 4.66 ± 0.8 months ($p = 0.026$).
*Conclusions:* VATS Pericardiotomy can provide effective long-term drainage in patients with symptomatic pericardial effusion. Positive cytology and metastatic involvement of the pericardium are predictive of worse survival. Survival greater than 5 years can be expected in 19% and 17% of patients with negative fluid cytology and negative metastatic disease of the pericardium, respectively.
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## 1. Introduction

Symptomatic pericardial effusions in patients with a history of cancer may represent a terminal event. Approximately 20% of patients with advanced malignancies will develop cardiac or pericardial involvement. The poor performance status of many cancer patients may preclude aggressive surgical approaches such as median sternotomy or anterolateral

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thoracotomy. These patients may benefit from a minimally invasive video-assisted thoracoscopic surgery (VATS) pericardiotomy (pericardial window).[1–4]

Previous studies have reported a poor prognosis for cancer patients with symptomatic pericardial effusions, with median survivals of 3 months or less.[5–8] The mean survival depends upon the extent of disease and tumor type.[1–4] Although multiple methods of operative and non-operative drainage of pericardial effusions have been described, surgical pericardial window has the lowest reported recurrence rate ranging from 8% to 10%.[9] Pericardiocentesis alone for patients with a history of cancer has a recurrence rate of 90% over a 3 months period.[1,10]

Surgical approaches in the past included median sternotomy or anterolateral thoracotomy with their attendant morbidity. A thoracoscopic pericardial window has been shown to be an effective and safe procedure in management of the life-threatening hemodynamic effects of cardiac tamponade.[11–14] Thoracoscopy allows an excellent view of both the pleural cavity and pericardium and the precise selection of pericardiotomy sites.[14,15] We note that patients with negative cytology and negative pathological examination of the pericardium have the greatest likelihood of long term survival.

## 2. Methods

Sixty-two patients with a history of malignancy who underwent VATS pericardiectomy for symptomatic pericardial effusion between 1999 and 2004 were retrospectively analyzed. Fluid cytology as well as metastatic involvement of the pericardium, seen within the pathologic specimen, were used as independent variables to dichotomize the cohort into those with cytology-positive effusions and those with cytology-negative effusions, as well as with or without metastatic disease of the pericardium. Kaplan–Meier survival curves and Log-Rank List were used to analyze the data.

### 2.1. *Surgical technique*

The operative side was often chosen based upon associated pleural effusions in anticipation of ipsilateral pleurodesis. After induction of general anesthesia, a 10 mm port was placed in the fourth or fifth intercostal space (ICS) in the mid-axillary line. A second port was placed in the 6th ICS between the mid- or posterior-axillary lines. If a third port was needed, it was placed in the 7th ICS in the anterior-axillary line. The camera was introduced through one of the two posterior ports and the pleural space and surface of the pericardium were inspected. In instances where the pericardium was markedly distended with fluid, it was often aspirated with a needle. Decompression of the pericardium allowed for easier grasping and manipulation of the pericardium. The pericardium was grasped with an Allis clamp placed through the anterior port, and was incised with either an electrocautery hook or thoracoscopic scissors placed through one of the posterior ports. After the initial incision in the pericardium, the heart was inspected underneath in order to insure that it was away from the cautery and sharp instruments. A window was created approximately 3 cm in diameter. With a right sided approach, the window was created anterior to the phrenic nerve, while with the left sided approach, the window was placed anteriorly, posteriorly, or in both locations (Fig. 1). A pericardial drain was placed via the window in a dependant fashion and a second drain was left in the pleural space. Intraoperative talc pleurodesis was performed in the presence of a moderate or large pleural effusion. Each drain was removed when the drainage was equal or less than 100–200cc/24 h, usually after 48 h.

## 3. Results

Sixty-two patients met criteria of having a symptomatic pericardial effusion requiring intervention and a history of malignancy. The study was approved by the Institutional Review Board at Brigham and Women's Hospital/Dana Farber Institute. There were 34 men (54.8%) and 28 women (45%). The mean age was $54.8 \pm 14.3$ years (ranging from 19 to 79). The most common histology of the primary malignancy was either small cell or non-small cell lung cancer (32/62, 51.6%). Other histologies included breast adenocarcinoma ($n = 8$; 12.9%), esophageal adenocarcinoma ($n = 5$; 8%) non-Hodgkin's lymphomas ($n = 5$; 8%), leukemia ($n = 3$; 4.8%) and 10 other cases (16%) listed in Table 1. There were no perioperative deaths within 30 days of the operative procedure. Ventilation support was required beyond the day of surgery in 1 patient, who was extubated 48 h after surgery. Mean hospital stay was $8.7 \pm 5.5$ days.

Overall median survival was 6.76 months, (range 1 month–10 years). For the entire group, one-year survival was 44.2%, three-year survival was 17.6%, and five-year survival was 10% (Fig. 2). Mean survival for female patients was 11.6 months, compared to 4.8 months for men; this did not reach statistical significance in this small cohort. There was no difference in survival when patients were dichotomized for age at 65 years ($p = 0.4$).

Pericardial fluid and the pericardium were examined for cytologic and pathologic evidence of malignant cells, respectively. The cytologic evaluation of pericardial fluid was performed in 48 of 62 patients (77.4%) and histologic evaluation of metastatic disease of the pericardium in 50 of 62 patients (80.6%). The mean survival in cytology negative patients ($n = 21$) was $13.4 \pm 0.98$ months, compared to cytology positive patients ($n = 27$) $4.89 \pm 0.9$ months ($p = 0.0175$) (Fig. 3). The 5-year survival in cytology negative patients was 19.6%, while none of the patients with metatstatic disease of the pericardium were alive after 36 months. The mean survival in patients with malignant disease of the pericardium ($n = 28$) was $4.66 \pm 0.8$ months, compared to $12.8 \pm 0.9$ months in patients with no malignant disease of the pericardium ($n = 22$) ($p = 0.026$). Fig. 4 demonstrates the difference in survival based on metastatic involvement of the pericardium.

We compared mean survival of patients with lung and esophageal cancer (LE; $n = 37$) with all other types of cancer (Oth; $n = 25$). The median survival of patients for LE group was 4.8 months and for Oth group was 13.4 months, $p = 0.064$ (statistically not significant). The one-year survival in the LE group was 28%, while it was 57% in the Oth group. The 2-year survival was 17.8% in the LE group, and 32% in

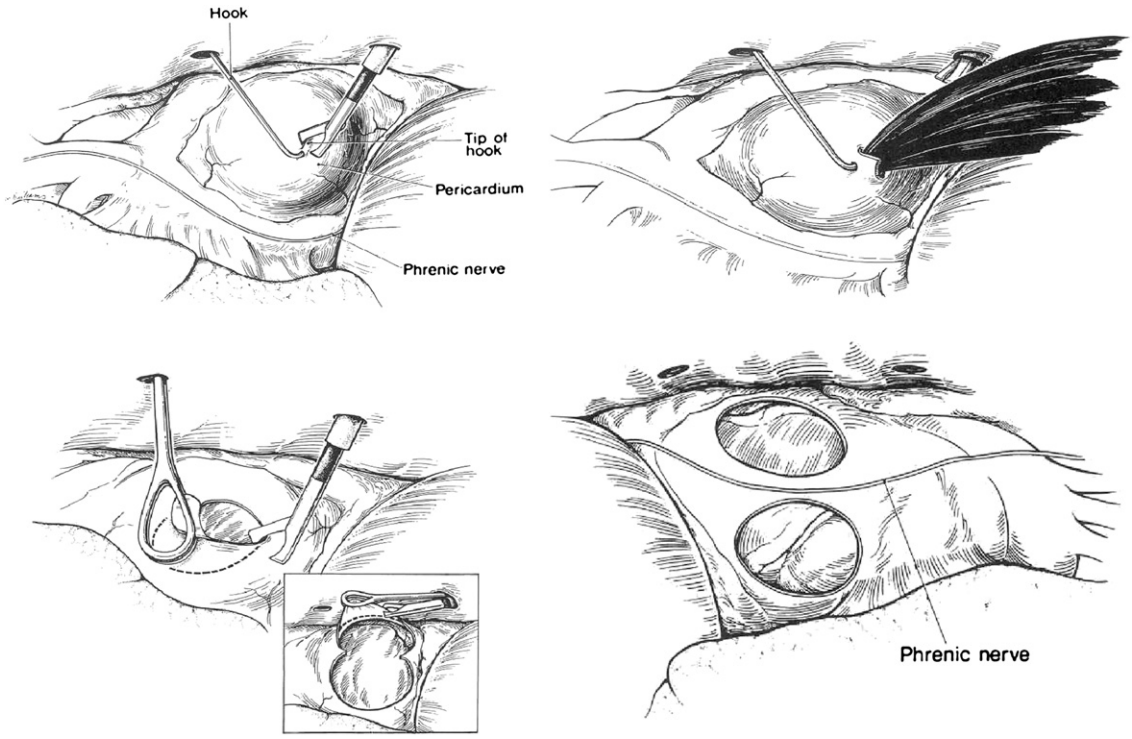


**Fig. 1 – Schematic illustration of operative approach. A. A nerve hook can be used to facilitate the initial incision into the distended pericardium. B. Release of fluid from the pericardium. C. A large window anterior (to phrenic nerve). D. Anterior and posterior pericardial windows and their relation to phrenic nerve.[22]**

the Oth group, ( $p = 0.06$). The 5-year survival in the Oth group was 16.2%, while none of the patients in the LE group was alive after 46 months (Fig. 5).

The majority of patients had only anterior pericardiectomy ($n = 48$; 77.4%), 3 patients had posterior pericardiectomy only, and 11 patients had combined anterior and posterior pericardiectomy. Seven patients (11%) needed a repeat pericardial window at a later time. Recurrent symptomatic effusion developed in 4 cases (6.45%) after an anterior pericardial window only, in 2 cases after posterior pericardial window only, and in 1 case after a combined anterior and posterior PW. The last case had a window placed from a left-sided approach, and subsequently developed a loculated symptomatic effusion on the right, which was drained with a right approach VATS and creation of a new pericardial window. There was no statistically significant correlation between the site of pericardicetomy and the recurrence rate. Concomitant pleurodesis was performed in 15 (24.2%) patients. The mean hospital stay was $8.7 \pm 5.5$ days. There was no correlation between length of hospital stay and long-term survival, nor between age and survival.

**Table 1 – The underlying pathology**

| Pathology of malignant pericardial effusion | *n* |
|---|---|
| NSCLC & SCLC | 32 |
| Breast cancer | 8 |
| Esophageal neoplasm | 5 |
| Non-Hodgkin-lymphoma | 5 |
| Leukemia | 3 |
| Other tumors and metastatic disease* | 10 |

* Thymoma 1, malignant melanoma 1, osteosarcoma 1, rhabdomyosarcoma 1, nerve sheath tumor 1, colon ca 2, ovarian ca 1, testicular ca 1, squamous cell cancer of unknown origin 1.

## 4. Discussion

Video-assisted thoracic surgery (VATS) pericardial window was safely and effectively applied to our cancer patient population with no perioperative deaths from the procedure. Furthermore, 43% of all patients survived over a year, despite the poor prognosis predicted from the previous literature. More importantly, we found that pericardial cytology

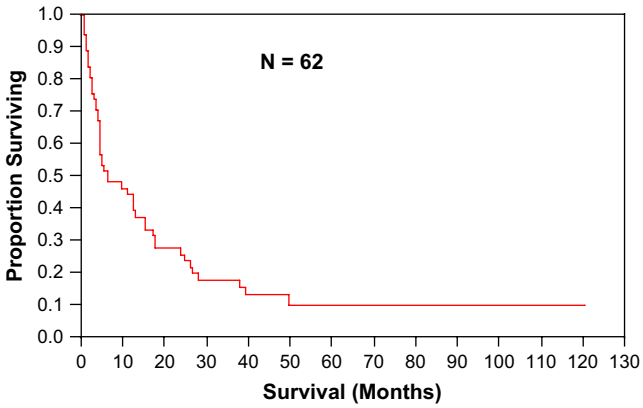


**Fig. 2 – Overall mean survival of patients.**

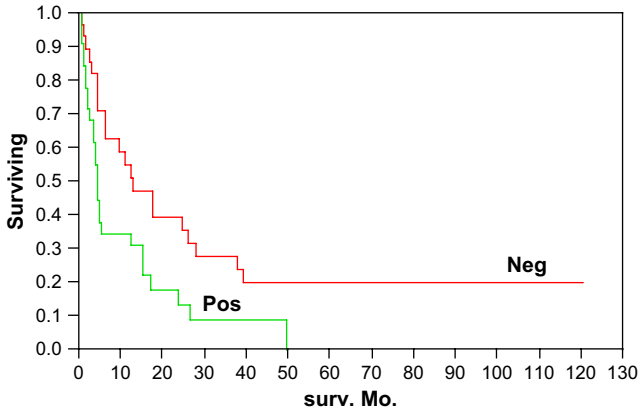


**Fig. 3 – Comparing the mean survival in patients with positive and negative cytology.**

predicted long-term survival, with 38% of patients with negative cytology living two years and 19% living 5 years, whereas no patients with positive cytology lived beyond 36 months. Metastatic involvement of the pericardium is another strong predictor of survival in this patient population, with 17% of patients with negative pericardial involvement living 5 years or longer, while none of the patients with metastatic disease of the pericardium were alive beyond 36 months. Cytologic analysis and evaluation of metastatic disease were performed in 48 (77.4%) and 50 (80.6%) patients, respectively.

Age had no influence on survival, nor did the site of the primary malignancy. This is likely due to the impact of the advanced malignancy on survival in all these patients, blunting the effect of these lesser influences.

The observation that a VATS pericardial window is safe and effective is supported by previous authors.[11,12] Mack et al.[11,12] previously reported that VATS for extensive pericardial resection was equivalent to open thoracotomy, but with morbidity less than or equal to a subxiphoid pericardial window.[12] Reitknecht et al.[8] published a series of 66 patients with malignant pericardial effusion treated by VATS pericardial window with no deaths or major complications attributed to the procedure. O'Brien et al.[9] compared the efficacy of 15 VATS pericardial windows with 71 subxiphoid approaches.

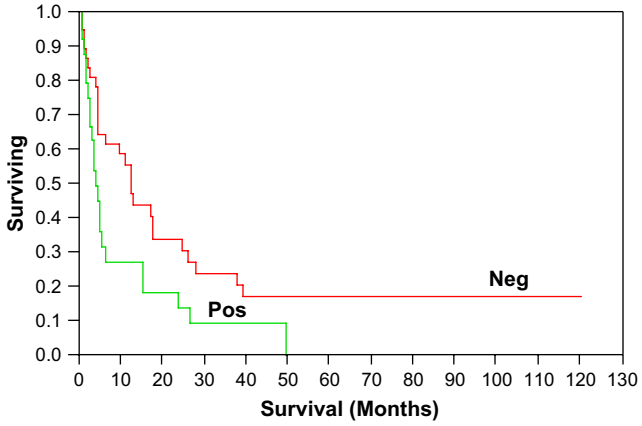


**Fig. 4 – Comparing the mean survival in patients with positive and negative metastatic disease of pericardium cytology.**

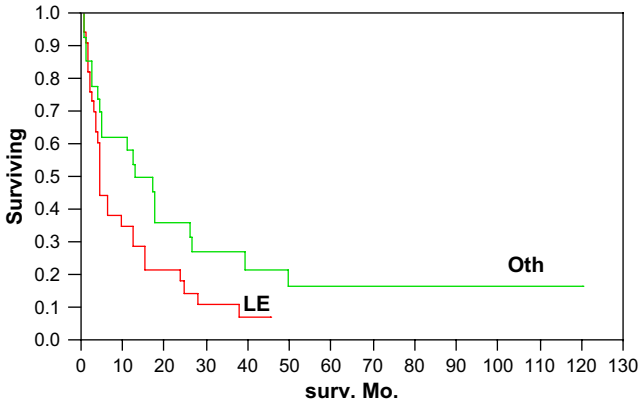


**Fig. 5 – Comparing the mean survival in patients with lung and esophagus vs patients with all other malignancies combined.**

They found no in-hospital mortality after the VATS procedure, compared to a 13% mortality following the subxiphoid procedure (perhaps due to moribund patients being offered subxiphoid technique with local anesthesia). Recurrence was observed in 1 patient after VATS (8%) and in 5 patients after subxiphoid approach (10%), similar to our recurrence rate.

Other authors have disagreed with our findings. In a series by Piehler et al., fifteen patients (10.3%) had late constriction or recurrent effusion. Six of these required re-operation.[16] O'Brien found a longer anesthesia time with the VATS procedure compared to the subxiphoid approach, and a slightly higher procedural morbidity (2.7% vs. 2%).[9] De la Gandara et al.[17] published a series of 13 patients with malignant pericardial effusion and tamponade. The mean survival in their small series was only 4 months. Anderson et al.[18] reported a median survival of 6 months after VATS pericardial window in a series of 59 cancer patients with malignant pericardial effusion. Cullinane et al.[19] reported in a series of 63 patients that survival correlates with type of malignancy (worse for NSCLC), concomitant presence of a pleural effusion, and positive pathologic or cytologic findings. Our data are in accordance with Cullinane's finding. Reitknecht et al. also reported that one-year survival following VATS pericardiotomy was only 26% with 50% of patients dead within 3 months of operation. They suggested that poor prognosis of the disease led to poor survival rates, but should not preclude palliating symptoms in this population.[8] We believe the primary driver of long-term survival is the tumor burden and biologic behavior within the patient population, and this likely explains the differences in survival rates between the author groups.

Although we are encouraged by our long-term results, we acknowledge that our analysis is retrospective and non-randomized. Also, the procedures were performed by a large group of thoracic surgeons, with different biases and slightly different techniques, thus limiting the uniformity of the procedure. Finally, in order to obtain enough data to analyze, we grouped together patients with the same operative intervention but with a heterogeneous group of malignancies with different biologic behaviors. These factors influence the power of our conclusions in terms of long-term results.

This cohort highlights a simple observation that a symptomatic pericardial effusion in a patient with a history of

malignancy may not, itself, be malignant, and thus may act like a benign effusion. Few of the previous authors evaluated the effect of positive cytology on survival. In our series, patients with positive cytology had a survival similar to the experience of the previous authors with a mean survival of 4.7 months. Patients with a negative cytology had a much better survival with 43% surviving over a year, and 19% living 5 years or more. In Piehler et al's series[17] the one year survival was 23% overall, but 85.6% for patients with idiopathic effusions after VATS pericardiotomy. Olsen et al.[20] performed a pericardial window using a small left anterior thoracotomy in 28 patients. In only 47% of patients, the etiology was malignant disease. The 5-year survival rate in patients with non-malignant effusions was 60%, while the 2-year survival in patients with malignant effusions was only 20%.[20] Benign causes of pericardial effusions in patients with malignancy include impaired immune system, impaired renal function, hypoalbuminemia, and impaired cardiac function.

Farsak et al.[21] conducted a prospective study in 150 patients with pericardial effusion. Half of the patients were treated with a pericardiectomy posterior to the phrenic nerve on the left side. The control group received conventional treatment only. A posterior pericardiotomy reduced the prevalence of early pericardial effusion, atrial fibrillation, and late pericardial effusion with tamponade.[21] In our series, a good number of patients ($n = 11$, 17%) had combined anterior and posterior pericardial window, which might explain the low recurrence rate in our series.

## 5. Conclusion

Video-assisted thoracoscopic pericardial window is an effective technique for pericardial drainage and can provide long term relief of bothersome symptoms. While our results compare favorably with the historic data in current literature, they also indicate that the short survival of patients is not a contra-indication for VATS pericardial window, and selected patients may achieve significant improvement in palliation and long-term survival with prompt recognition and appropriate intervention. The positive cytology of pericardial fluid and metastatic involvement of the pericardium are strong predictors of survival in this patient population.

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None declared.

*Funding*
None.

*Ethical approval*
None.

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