

RESEARCH ARTICLE

# Treatment of Pericardial Effusion in Cancer Patients

Luis Alberto Chinchilla-Trigos<sup>1,2\*</sup>, Edgardo Jiménez-Fuentes<sup>2,3</sup>,  
Abelardo Meneses-García<sup>2,4</sup>, Mariana Cobos-Ortiz<sup>2,4</sup>

<sup>1</sup>Departamento de Oncología Torácica, Instituto Nacional de Cancerología, Mexico City, Mexico

<sup>2</sup>Universidad Nacional Autónoma de México, UNAM, Mexico City, Mexico

<sup>3</sup>Departamento de Neumología y Cirugía de Tórax, Instituto Nacional de Cancerología, Mexico City, Mexico

<sup>4</sup>Instituto Nacional de Cancerología, Mexico City, Mexico

**Abstract:** Pericardial effusion is the most common cardiac complication in cancer patients. Lung and breast cancers are the most common solid tumors associated with pericardial effusion. Multimodal tumor therapy improves the overall survival rate and reduces tumor complications. However, these patients need individualized treatment. This paper describes the treatment experience of pericardial effusion, from its pathophysiology, the correct classification of pericardial effusion related to malignant tumor, malignant pericardial effusion or pericardial cancer, to the methods of diagnosis and treatment. The incidence of pericardial effusion in our hospital was 12%. In 11 years of pericardial fenestration, pericardiectomy and subcutaneous catheter (tunneling) installation of pericardium or temporary pleurisy, the postoperative mortality was 1.2%, while the recurrence rate of pericardial effusion was 2.1%, and the recurrence rate of pericardial effusion was 33%. Malignant pericardial effusion is an oncologic emergency. It requires cost-effective management without increasing the incidence of patients who have deteriorated. Thoracoscopic pericardial fenestration (vats) and anterolateral small incision are ideal surgical approaches for malignant pericardial effusion.

**Keywords:** Tumor pericardium, Pericardial effusion, Pericardial window technique, Survival

**Received:** September 11, 2020  
**Accepted:** October 29, 2020  
**Published Online:** November 7, 2020

**\*CORRESPONDING AUTHOR**

Luis Alberto Chinchilla-Trigos  
E-mail:  
chinchillasurgery@hotmail.com

**CITATION**

Chinchilla-Trigos LA, Jiménez-Fuentes E, Meneses-García A, *et al.*, 2020, Treatment of Pericardial Effusion in Cancer Patients. *Cancer+*, 2(4):7–14.  
DOI: [10.18063/cp.v2i4.353](https://doi.org/10.18063/cp.v2i4.353)

**Copyright:** © 2020. Chinchilla-Trigos *et al.* This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (<http://creativecommons.org/licenses/by-nc/4.0/>), permitting all noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## 1. Introduction

Pericardial effusion is the most common cardiac complication in cancer patients. About 6 to 10% of cancer patients developed pericardial effusion. In a series of autopsy of tumor patients, it has been shown that 8.1% had pericardial effusion while 2.7% of the patients had at least one sign of pericardial effusion<sup>[1]</sup>. Cancer can affect pericardium through four mechanisms: (i) Implantation of tumor cells into the pericardium by direct extension or dissemination from the blood or lymph of the primary tumor; (ii) Chemotherapy toxicity; (iii) Radiotherapy toxicity; or (iv) Opportunistic infection related to cytotoxic immunosuppression and rapid immune response<sup>[2]</sup>. Before the introduction of multimodal management (chemotherapy, radiotherapy and targeted therapy), the incidence of pericardial effusion was 21%, the overall survival time after drainage was less than 12 weeks, and the recurrence rate of pericardial effusion was as high as 40%. At present, malignant pericardial effusion is still the most common cardiac complication in the, reference center, although the incidence is less than 1% to 10%. With the full clearance of pericardial effusion, the overall survival time can be increased to 28

weeks. In the case of no recurrence of pericardial effusion, the overall survival time can be increased to 20 years according to the patient's prognostic factors<sup>[3,4]</sup>.

Pericardial sac begins with the accumulation of liquid in its space, which will compress and hinder the functionality of heart pump. In 1829, Dominique Jean Larrey described the pericardial window as a free and continuous communication between the pericardium and the pleural cavity, subcutaneous tissue, and external media. Pericardiocentesis, which refers as percutaneous pericardial drainage, was not reported until 1840. In about 200 years later, in view of the life expectancy of primary tumors and the possibility of continuing tumor treatment, the discussion on how to maximally reduce pericardial effusion in cancer patients continues<sup>[5]</sup>.

Lung cancer accounts for 12.9% of all malignant tumors. The incidence of lung cancer in men is the highest, while the incidence in women is second to the breast and colorectal cancers. It remains the main cause of cancer death in the world<sup>[1,6]</sup>. Lung cancer is the most common primary tumor invading the pericardium. Breast cancer is the most common malignant tumor among women in developed countries. Progression in multimodal treatment has generally improved the overall survival rate of these two cancers at each clinical stage and also reduces tumor complications requiring individualized treatment, considering the overall condition of patients, life expectancy and the possibility of appropriate treatment of primary tumors<sup>[7-9]</sup>.

## 2. Natural history of pericardial effusion in cancer patients

It is important to understand the anatomical structure of pericardium. The pericardium has two leaves. The outer layer (fibrous pericardium) which is thick, with collagen fibers and elastin provides elasticity to the heart. The inner (serous pericardium) is thin and transparent structure that can be divided into parietal serosa and visceral serosa, are in close contact with epicardium and adventitia of large vessels. The pericardial space between fibrous pericardium and serous pericardium contains less than 50 ml of pericardial fluid, which is an ultrafiltered plasma. Pericardial effusion in cancer patients should be considered as a oncologic emergency, which is different from pericardial effusion associated with trauma, heart failure or other debilitating diseases<sup>[10-12]</sup>.

The evaluation and management of pericardial effusion should be carefully classified according to the following definitions.

(i) Pericardial effusion associated with malignant tumor: pericardial sac effusion in patients with tumor, and cytological examination showed no malignant cells or empty fluid cell mass (clinical case 1).

(ii) Malignant pericardial effusion: pericardial effusion,

and cytological examination shows malignant tumor cells or cell blocks, and there are no tumor cells in the pericardium (clinical case 2).

(iii) Pericardial carcinoma: macroscopic or microscopic identification of malignant cell implantation in the pericardial lobe, with or without tumor cells in pericardial fluid (clinical case 3).

The causes of pericardial effusion associated with malignant tumors include the chemical toxicity of drugs such as cyclophosphamide, cytarabine, adriamycin or gemcitabine, which can cause heart failure, myocarditis and pericarditis. It is reported that up to 20% of patients utilize these drugs in chemotherapy regimen<sup>[13]</sup>. The other factor related to pericardial effusion includes extensive radiotherapy in the chest, such as lymphoma, whole breast cycle or coverage after mastectomy, which can damage cardiomyocytes and change valve mechanics, resulting in heart failure, coronary artery spasm and pericardial fibrosis.

Opportunistic cytomegalovirus infection in patients with non-small cell lung cancer can occur through cytotoxic systemic therapy or targeted therapy (such as tyrosine kinase inhibitor (TKI) and epidermal growth factor receptor (EGFR) inhibitors (such as afatinib or erlotinib), mycobacteria and fungi, such as *Aspergillus* and *Candida*, and the same goes to bevacizumab, a monoclonal antibody against vascular endothelial growth factor (VEGF) used in breast cancer, as well as immunomodulators such as nivolumab and pd1-pd1-1 pathway inhibitors<sup>[2,14]</sup> in lung cancer and malignant pleural mesothelioma.

On the other hand, pericardial fluid accumulates slowly but gradually due to changes in the pericardial surface. Normal lymphatic flow in mediastinal tumors, lymphomas and reproductive tumors is blocked by tumor activity. The dissemination of malignant cells in the pericardium starts from the epicardial surface, continues to spread in the visceral pericardium, and finally spreads in the parietal pericardium. The dissemination channels of primary tumors at this time are blood and lymphatic vessels, which can be seen in different kinds of lung adenocarcinoma and breast cancer<sup>[15]</sup>.

When the spreading adjacent to the pericardium through the transepithelial pathway, the deposition of tumor cells occurs in the pericardial wall and then in the internal organs, which is common in small cell lung cancer, pleural malignant mesothelioma, ovarian adenocarcinoma and signet ring cell tumor subtypes. In addition to disrupting the secretion and absorption of pericardial fluid, the change of pericardial leaf mesothelial surface also allows the development of scars and adhesion between pericardial fibers and internal organs, so as to produce a partition wall and prevent the free flow of pericardial fluid as well as to buffer the respiratory changes transmitted to the ventricle.

The latter is considered as one of the reasons for the recurrence of pericardial effusion after pericardiocentesis, because the diaphragm does not allow the removal of all accumulated pericardial fluid<sup>[16]</sup>. The installation of pericardial window, pericardiectomy and temporary pericardial drainage system provides an operation field for extensive removal of parietal pericardial lobes, identification of macro implants and histopathological examination<sup>[17,18]</sup>.

### 3. Clinical features and prognostic factors

The presence of pericardial effusion reduces the possibility of any palliative treatment rather than provides better medical support since less than 2% of patients are with this complication<sup>[19]</sup>. The clinical spectrums of patients with pericardial effusion tumors include: (i) pericardial effusion with no hemodynamic effect, (ii) pericardial effusion with signs of hemodynamic effects, and (iii) cardiac tamponade. All these are related to the speed of pericardial effusion, the hardness of pericardial leaves and the changes of mesothelial surface<sup>[17-19]</sup>.

In about 70% of cases, pleural effusion in cancer patients has been accidentally discovered during the diagnosis, evaluation, treatment or follow-up of primary tumors. Although at least 60% of patients showed signs of hemodynamic effects, they could not reflect the severity of pericardial effusion, because 50% of patients were accompanied by pleural effusion, pulmonary edema, malnutrition and cardiotoxicity caused by treatment of primary tumors. In 80% of cases, the most common hemodynamic response is tachycardia. Other signs that include dyspnea, shortness of breath and abnormal pulse were 60%, 45% and 40% respectively. Cough, dyspnea and hypotension, which are early symptoms of cardiac tamponade occur in less than 25% of patients. Lastly, the typical beck triad, tachycardia, hypotension and reduced cardiac noise, is less than 15% in malignant pleural effusion. A variety of treatment options for pericardial effusion in cancer patients have been described, based on the hemodynamic effects, prognostic factors, such as functional status, life expectancy, histopathology and tumor biological behavior (assessed by Karnofsky index and Eastern Cooperative Oncology Group (ECOG) scale) as well as predictors of tumor treatment response<sup>[20,21]</sup>.

### 4. Early treatment of pericardial effusion in tumor patients

Considering the low overall incidence, life expectancy and recurrence rate of pericardial effusion, the ideal management of pericardial effusion in cancer patients should be a cost-effective, high-resolution, rapid and lasting measure. Traditional surgical options, such as subxiphoid pericardial window, anterolateral and posterolateral thoracotomy or thoracoscopic surgery,

application of pericardial hardener, temporary installation of pericardial drainage tube and image-guided pericardiocentesis require strict oncology standards, surgical skills and cardiopulmonary physiology knowledge<sup>[22-24]</sup>. All these operations are well tolerated in patients outside the surgical and medical control of primary tumors. However, the recurrence rate of pericardial effusion decreased (15%) and the 7-month overall survival rate increased in patients undergoing left anterolateral thoracotomy, while the recurrence rate and 3-month survival rate were only 31% in the image-guided percutaneous drainage group.<sup>[25]</sup>

In 1841 cases of pericardiocentesis, it was found that the survival rate of patients was related to the histological type of primary tumor and the possibility of systemic treatment. The >3-month survival rates of breast cancer were 93% and 72% respectively<sup>[9]</sup>. In another study by Patel *et al.*, clear percutaneous treatment was compared with open surgery plus insertion of temporary, portable and portable drainage catheters in 1,399 patients, and it was found that the incidence was the same: pericardiocentesis group 6% and open technology group 8%. Temporary pericardial subcutaneous (tunnel) catheter infection ("tunnel") occurred in 14 patients, which was not serious and related to poor nursing; the catheter needs to be pulled out within 20 days after installation<sup>[26]</sup>.

In the Memorial Sloan Kettering Series, we evaluated 72 patients with pericardial effusion, 37 underwent image-guided pericardiocentesis plus intrapericardial sclerotherapy, and 35 underwent pericardial fenestration. The survival time of the two groups was 97 days, and the cost of the operation group was higher. Due to the injection of hardener<sup>[27]</sup>, the recurrence rate of effusion in percutaneous drainage and pericardial window is the same. The results of intracardiac injection of cytotoxic drugs, such as cisplatin, were less encouraging because the overall survival rate did not increase, but the hematological toxicity was<sup>[28,29]</sup>.

## 5. Case reports

### 5.1. Clinical case 1: Pericardial effusion with malignant tumor

A 38-year old woman with bilateral synchronous, triple negative and locally advanced breast cancer was admitted to the hospital. She received neoadjuvant chemotherapy, followed by modified madden type bilateral radical mastectomy and postoperative radiotherapy. Breast reconstruction is late and staged.

She had a two-year disease-free period. During monitoring and follow-up, she was reported to have moderate effect and one month of progressive dyspnea. Karnoky's sinus tachycardia index was 70%.

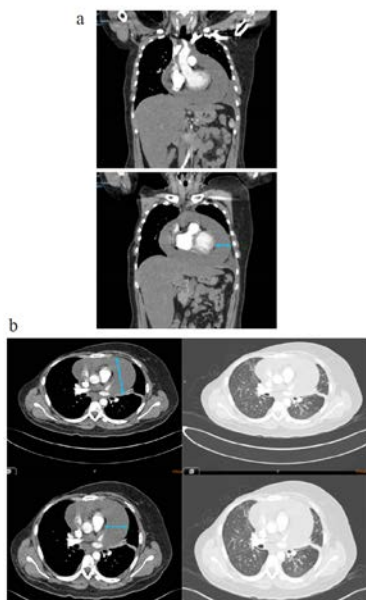
The electrocardiogram (ECG) showed signs of low voltage and disappearance of p wave. Chest x-ray showed

widening of mediastinal contour and disappearance of left costophrenic angle (**Figure 1**). Computed tomography (CT) of the chest showed pericardial effusion with an interval of 3.5 cm between the pericardial lobe and the left pleural effusion (**Figure 2**).

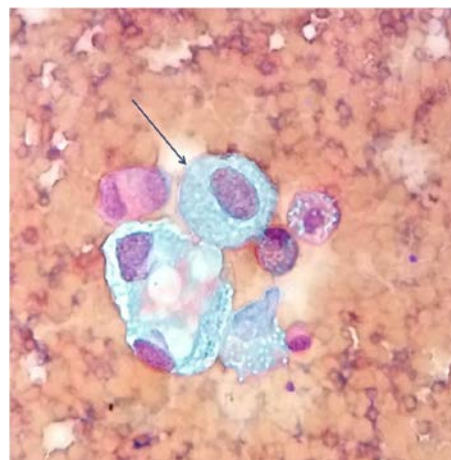
Pericardial window and pericardiotomy were performed, and the subpleural pericardial catheter (tunneling) was installed through the left thoracoscope. Pericardial fluid is areola color. No pleural or pericardial cancer was found. The cytological examination of pericardial fluid was negative for malignant tumor, and the histopathological examination of pericardial and parietal pleural biopsy was negative for reactive mesothelial malignant paraneoplastic tumor (**Figure 3**).



**Figure 1.** Chest film: pericardial effusion, enlarged myocardial mediastinal contour (dotted line) and left pleural effusion.



**Figure 2.** Chest CT. a. Coronal incision: uniform pericardial effusion without septum. b. Axial incision: the interval between pericardial lobes is 3.5 cm (double arrow). There was no pericardial thickening, and there was little pleural effusion on the left.



**Figure 3.** Pericardial fluid cytology background bleeding, changes in mesothelial cell reactivity, and no significant increase in nucleus and cytoplasm (arrow). Diagnosis: mesothelial reaction. Pasteurization, 40X.

Pericardial drainage for temporary pleurisy continued for 3 weeks until the volume was less than 50 ml. The chest x-ray showed the location of the pleural effusion catheter, the left lung was fully expanded and the myocardial mediastinal contour was reduced (**Figure 4**). The patient underwent cardiopulmonary rehabilitation (**Figure 5**).



**Figure 4.** Chest x-ray examination 3 weeks after pericardial window operation: left cardiothoracic catheter (arrow), appropriate expansion of left lung and reduction of thorax.



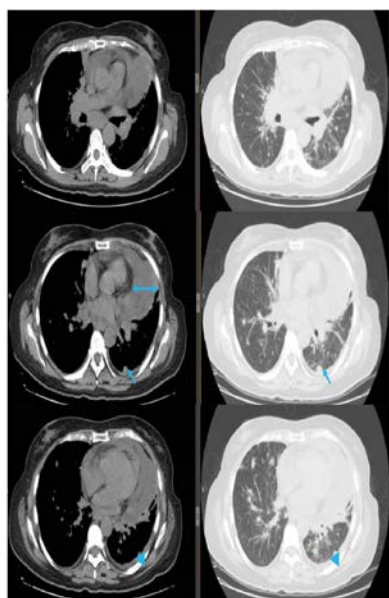


**Figure 5.** a: The pericardial catheter (arrow) was permeable and showed no signs of infection three weeks after installation. b and c: Postoperative cardiopulmonary rehabilitation.

In the evaluation of ventricular function by echocardiography, the ejection fraction was 55%, and there were signs of heart failure, which was related to cardiotoxicity.

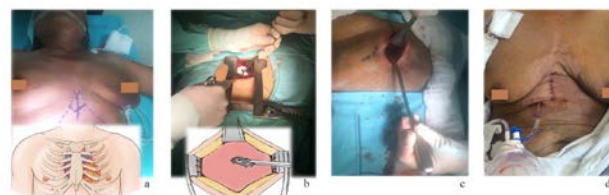
## 5.2. Clinical case 2: Malignant pericardial effusion

This is a 67-year old woman with T<sub>3</sub>N<sub>2</sub>M<sub>1a</sub> lung adenocarcinoma. Her clinical stage is stage IV and her ECOG score is grade 2. After chemotherapy, the pleural implants, pleural and pericardial thickening and pericardial effusion were observed by positron emission tomography (pet-CT). Progress has been made according to PET-CT (Positive Emission Tomography Response Criteria, PERIST). No signs of cardiac tamponade were observed (**Figure 6**).

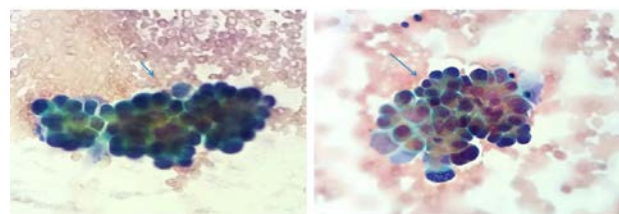


**Figure 6.** Mediastinum and lung window: pericardial effusion. The double arrow shows the pericardial interval of 2 cm, the arrow points to the pleural implant, and the arrow points to pleural thickening.

Installation of pericardial window and pericardial subcutaneous (tunnel) catheter under xiphoid process were performed (**Figure 7**). Cytological examination of pericardial fluid and cell mass showed serological characteristics; positive for malignant tumors: cancer (**Figure 8**). The histopathology removed from the pericardial window was negative. After 6 weeks, the patient underwent thoracoscopy to drain the left pleural effusion; pleural and lung biopsies were taken to evaluate the molecular characteristics of tissue samples.



**Figure 7.** Installation of subxiphoid pericardial window and subcutaneous pericardial catheter (tunneling): (a) mark xiphoid attachment and incision boundary; (b) pericardial sac exposure with finochietto separator, blunt anatomy and diaphragmatic and mediastinal fat separation; (c) treatment of pericardial effusion; (d) installation of subcardial (tunnel) catheter.



**Figure 8.** Cytological study of malignant pericardial effusion: a large number of tumor cells can be seen in the hemorrhagic background (short arrow) to form morula and rosette (long arrow). They have extensive cytoplasm and large pleomorphic nuclei. Cytological diagnosis of pericardial fluid: carcinoma pasteurization, 40x

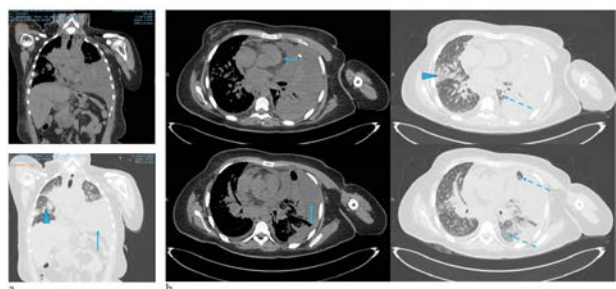
## 5.3. Clinical case 3: Pericardial carcinoma

This is a 39-year old woman with a left breast dependent ulcerative tumor. Histopathological incision biopsy shows that she had breast adenocarcinoma. She was reported to had dyspnea at admission, 30° jugular vein groin, abnormal pulse, tachycardia, epidural friction, anhydrous blister murmur in the left half of the chest.

Chest x-ray showed left pleural effusion and enlarged myocardial mediastinal contour (**Figure 9**). Chest CT showed pericardial effusion, septum, left pleural effusion, pleural and pericardial thickening (**Figure 10**).

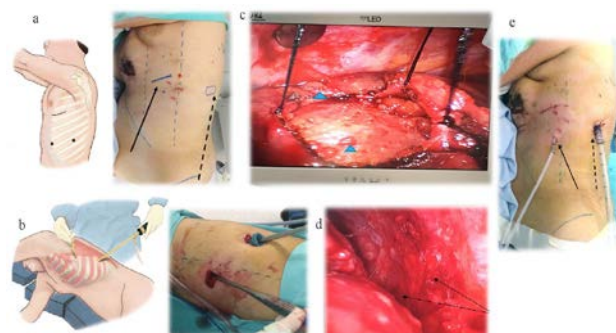


**Figure 9.** Chest x-ray: left pleural effusion. The arrow shows the opacity of the lower two-thirds of the left chest, and the dotted arrow is “lung encapsulation”. In the right half of the chest, opacity (ARROW) indicates cancerous lymphangitis in the context of the disease.



**Figure 10.** Chest axial CT examination: pleural effusion, pericardial effusion and pulmonary entrapment; (a) coronal incision and (b) axial incision. The arrows show images of carcinomatous lymphangitis, arrows, left pleural effusion and double arrow pericardial effusion, 1.2 cm from the pericardium. The dash arrow indicates the “depression” area of the lung.

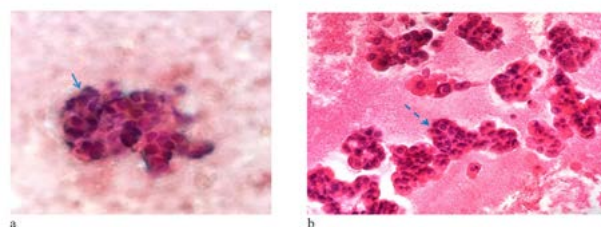
She underwent video assisted thoracotomy (VATS) of the left pericardial window and installed a temporary pericardial pleural subcutaneous catheter (tunneling) (**Figure 11**).



**Figure 11.** Thoracoscopic pericardial window. (a and b) schematics and photos show the layout of the patient in the right lying position. The dotted line indicates the incision of the thoracic cavity during thoracoscopy. The arrow points to the working cut of the cup; (c) thoracoscopic monitor image: arrows show tumor implants in the pericardium and viscera during

pericardial window surgery; (d) arrows point to implants in the visceral pleura and lungs; (e) the dash arrow shows the use of the camera port to place the thoracic tube. The arrow shows the exit of the pleural epicardial subcutaneous catheter (tunneling), 2 to 3 cm below the incision and above the axillary front line.

In cytology and pericardial fluid cell mass examination, malignant tumor was reported. Breast adenocarcinoma had been reported in pericardial histopathology. In immunohistochemistry, estrogen, progesterone receptor, GATA protein and lactoglobulin were positive, and proto-oncogene HER2/neu was negative (**Figure 12**).



**Figure 12.** (a) pericardial fluid cytology: a small number of epithelioid cells (arrow) can be seen in the hemorrhagic background, with mild atypia. Pasteurization, 40X; (b) pericardial fluid cell mass: it was observed that a group of epithelial cells formed glandular structure (dotted arrow), with oval nucleus, slightly atypical, chromatin mass and sparse cytoplasm; mesothelial cells are also rare. Hematoxylin and eosin, 100X.

## 6. Discussion

We believe that in addition to the known factors related to the occurrence of pericardial effusion, such as the relationship between pericardial to volume and accumulation time, the surface state of pericardial lobe will also increase in cancer patients. Therefore, the volume of patients with pericardial effusion associated with malignant tumor is between 500 and 1000 ml, and the hemodynamic changes are very small. Thrombosis and diaphragm formation contribute to recurrence after stroke.

Finally, in pericardial cancer, fibrous and restrictive pericardium can lead to small volume of fluid, leading to cardiac tamponade. Echocardiography is generally considered as a standard method to determine the presence, location, size and cardiac effects of pericardial effusion. Chest CT is not a good approach to evaluate pericardial effusion; however, CT and MRI may be superior to echocardiography in determining the presence and distribution of pericardial effusion and pericardial sac thickening<sup>[30,31]</sup>.

At the National Cancer Institute of Mexico, the incidence of pericardial effusion is about 12%. In 60% of cases, the diagnosis occurred accidentally during CT diagnosis or follow-up of primary tumor. The recurrence rate of pericardiocentesis was 33%<sup>[32]</sup>.

In the past 11 years, the time between the diagnosis of pericardial effusion with hemodynamic influence and the

completion of pericardial window was found to be 2.3 hours in 96 patients with cancer and pericardial effusion.

For patients without pericardial tamponade or other hemodynamic effects, the surgical procedure should be performed within 3 days after the diagnosis of pericardial effusion. After pericardial fenestration, 92% of the patients were transferred to the rehabilitation period, closely monitored during hospitalization, and carefully observed the changes of cardiac monitoring.

The syndrome after pericardiectomy is characterized by excessive dilation or dilation of the heart, decreased myocardial contractility or contractility, arrhythmia, mitral and tricuspid insufficiency. Only 4% of the cases shows symptoms and are successfully treated in the intensive care unit, including hemodynamic support, amines, beta blockers and amiodarone in the treatment of atrial fibrillation and drug cardioversion.

Pericardial window is a safe operation. The intraoperative mortality is 0% and the postoperative mortality is 1.2%. Surgery related morbidity was acceptable (2.3%), and in any case, the overall condition of patients before surgery did not deteriorate. The recurrence rate of pericardial effusion was 2.1%. The overall survival of 72% of patients increased to 8 months.

Thoracoscopic or anteroposterior thoracotomy on the subxiphoid pericardial window is recommended, because it can evaluate the pericardium under direct vision, conduct sufficient biopsy of pericardium and pleura, conduct extensive pericardiectomy in the case of pericardial cancer and restrictive pericarditis, and empty 45% of the concurrent pleural effusion. In addition, it allows the establishment of a cardiopleural drainage tube<sup>[33,34]</sup>.

## 7. Conclusion

Modern multidisciplinary cancer management, even in the advanced and metastatic stages, has transformed cancer disease into a chronic disease, prone to complications.

Malignant pericardial effusion is a kind of oncologic emergency, which can occur in solid tumors and hematological tumors. It requires cost-effective management, problem-solving, fast and lasting, without increasing the incidence of patients and deteriorating the overall situation. It requires individualized treatment to distinguish pericardial effusion, malignant pericardial effusion and pericardial cancer associated with malignant tumors.

In selected patients, VATS and anterolateral small incision are ideal approaches for malignant pericardial effusion, because in addition to allowing the discharge of pericardial effusion, in some cases, it also allows the evaluation of lung, pleura and pericardium under direct vision to solve pleural effusion and release stagnant lung. It allows biopsy of sufficient tissue for histopathological identification, immunohistochemistry and molecular

characteristics of primary malignant tumors.

## Conflict of interest

No conflict was declared.

## References

1. Klatt EC, Heitz DR, 1990, Cardiac Metastases. *Cancer*, 65:1456–9.
2. Pohjola-Sintonen S, Tötterman KJ, Salmo M, *et al.*, 1987, Late Cardiac Effects of Mediastinal Radiotherapy in Patients with Hodgkin's Disease. *Cancer*, 60:31–7.
3. Cullinane CA, Paz IB, Smith D, *et al.*, 2004, Prognostic Factors in the Surgical Management of Pericardial Effusion in the Patient with Concurrent Malignancy. *Chest*, 125:1328–34.
4. Gornik H, Gerhard-Herman M, Beckman JA, 2005, Abnormal Cytology Predicts Poor Prognosis in Cancer Patients with Pericardial Effusion. *J Clin Oncol*, 23:5211–6.
5. Tsang TS, Seward JB, Barnes ME, *et al.*, 2000, Outcomes of Primary and Secondary Treatment of Pericardial Effusion in Patients with Malignancy. *Mayo Clin Proc*, 75:248–53.
6. Ferlay J, Soerjomataram I, Dikshit R, *et al.*, 2014, Cancer Incidence and Mortality Worldwide: Sources, Methods and Major Patterns in GLOBOCAN 2012. *Int J Cancer*, 136:E359–86.
7. Abraham KP, Reddy V, Gattuso P, 1990, Neoplasms Metastatic to the Heart: Review of 3314 Consecutive Autopsies. *Am J Cardiovasc Pathol*, 3:195–8.
8. McDonald JM, Meyers BF, Guthrie TJ, *et al.*, 2003, Comparison of Open Subxiphoid Pericardial Drainage with Percutaneous Catheter Drainage for Symptomatic Pericardial Effusion. *Ann Thorac Surg*, 76:811–5.
9. Kim SH, Kwak MH, Park S, *et al.*, 2010, Clinical Characteristics of Malignant Pericardial Effusion Associated with Recurrence and Survival. *Cancer Res Treat*, 42:210–6.
10. Akhter SA, 2011, The Heart and Pericardium. *Thorac Surg Clin*, 21:205–17.
11. Kaiser L, Kron IL, Spray TL, 2013, *Mastery Cardiothoracic Surgery* (3<sup>rd</sup> edn.). Philadelphia: Wolters Kluwer, pp.289–95.
12. Echeverri D, Matta L, 2014, Pericarditis Tuberculosa. *Biomédica*, 34:528–34.
13. Gottdiener JS, Appelbaum FR, Ferrans VJ, *et al.*, 1981, Cardiotoxicity Associated with High-Dose cyclophosphamide Therapy. *Arch Intern Med*, 141:758–63.
14. Refaat MM, Katz WE, 2011, Neoplastic Pericardial Effusion. *Clin Cardiol*, 34:593–8.
15. Shields TW, 2009, *General Thoracic Surgery* (7<sup>th</sup> edn.).



- Philadelphia: Lippincott Williams & Wilkins, pp.885–90.
16. Tsang TS, Enriquez-Sarano M, Freeman WK, *et al.*, 2002, Consecutive 1127 Therapeutic Echocardiographically guided Pericardiocenteses: Clinical Profile, Practice Patterns, and Outcomes Spanning 21 Years. *Mayo Clin Proc*, 77:429–36.
  17. Burazor I, Imazio M, 2013, Malignant Pericardial Effusion. *Cardiology*, 124:224–32.
  18. Petrofsky M, 2014, Management of Malignant Pericardial Effusion. *J Adv Pract Oncol*, 5:281–9.
  19. Jama GM, 2014, Palliative Treatment for Symptomatic Malignant Pericardial Effusion. *Interact Cardiovasc Thorac Surg*, 19:1019–26.
  20. Karnofsky D, Burchenal J, 1949, The Clinical Evaluation of Chemotherapeutic Agents in Cancer. In: MacLeod C (ed.) *Evaluation of Chemotherapeutic Agents*. New York: Columbia University Press, pp.191–205.
  21. Oken MM, Creech RH, Tormey DC, *et al.*, 1982, Toxicity and Response Criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol*, 5:649–55.
  22. Campbell PT, 1992, Subxiphoid Pericardiotomy in the Diagnosis and Management of Large Pericardial Effusions Associated with Malignancy. *Chest*, 101:938–43.
  23. Hankins JR, Saterfield JR, 1980, Pericardial Window for Malignant Pericardial Effusion. *Ann Thorac Surg*, 30:465–71.
  24. Sugimoto JT, Little AG, Ferguson MK, *et al.*, 1990, Pericardial Window: Mechanisms of Efficacy. *Ann Thorac Surg*, 50:442–5.
  25. Celik S, Lestuzzi C, Cervesato E, *et al.*, 2014, Systemic Chemotherapy in Combination with Pericardial Window Has Better Outcomes in Malignant Pericardial Effusions. *J Thorac Cardiovasc Surg*, 148:2288–93.
  26. Patel N, Rafique AM, Eshaghian S, *et al.*, Retrospective Comparison of Outcomes, Diagnostic Value, and Complications of Percutaneous Prolonged Drainage Versus Surgical Pericardiotomy of Pericardial Effusion Associated with Malignancy. *Am J Cardiol*, 112:1235–9.
  27. Girardi LN, Ginsberg RJ, Burt ME, 1997, Pericardiocentesis and Intrapericardial Sclerosis: Effective Therapy for Malignant Pericardial Effusions. *Ann Thorac Surg*, 64:1422–8.
  28. Wilkes JD, Fidias P, Vaickus L, *et al.*, 1995, Malignancy-Related Pericardial Effusion. 127 Cases from the Roswell Park Cancer Institute. *Cancer*, 76:1377–87.
  29. Maisch B, Ristic AD, Pankuweit S, *et al.*, 2002, Neoplastic Pericardial Effusion. Efficacy and Safety of Intrapericardial Treatment with Cisplatin. *Eur Heart J*, 23:1625–31.
  30. Dequanter D, Lothaire P, Berghmans T, *et al.*, 2008, Severe Pericardial Effusion in Patients with Concurrent Malignancy: A Retrospective Analysis of Prognostic Factors Influencing Survival. *Ann Surg Oncol*, 15:3268–71.
  31. Lestuzzi C, 2010, Neoplastic Pericardial Disease: Old and Current Strategies for Diagnosis and Management. *World J Cardiol*, 2:270–9.
  32. Apodaca-Cruz A, Villarreal-Garza C, Torres-Ávila B, *et al.*, 2011, Effectiveness and Prognosis of Initial Pericardiocentesis in the Primary Management of Malignant Pericardial Effusion. *Interact Cardiovasc Thorac Surg*, 11:154–61.
  33. Gillen J, Lau C, 2013, Permanent Indwelling Catheters in the Management of Pleural Effusions. *Thoracic Surg Clin*, 23:63–71.
  34. Ahmad MM, 2011, The Pericardial Window: Is a Video Assisted Thoracoscopy Approach Better than Surgical Approach? *Interact Cardiovasc Thorac Surg*, 12:175–8.