

# Cancer Association of South Africa (CANSA)



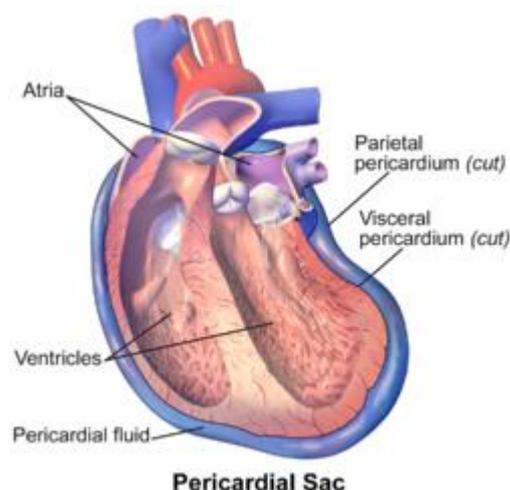
## Fact Sheet on Pericardial Effusion Caused by Cancer or Cancer Treatment

### Introduction

The pericardium is a double-walled sac containing the heart and the roots of the great blood vessels.

The pericardium has two layers: the fibrous pericardium is the outer layer. It is made from thick connective tissue and is attached to the diaphragm. It holds the heart in place in the chest cavity and protects it from infections; the serous pericardium is the inner layer. It is further divided into two more layers: the visceral (directly part of outer part of the heart) and parietal layers (an outer layer). The serous pericardium helps to lubricate the heart.

[Picture Credit: Pericardium]



The potential space between the two layers contains no more than 50mL of serous fluid under normal circumstances. The pericardium restrains acute dilation of the heart chambers, but it accommodates dilation and fluid accumulation to a certain extent. An abnormal collection of serous fluid in the pericardial space is referred to as pericardial effusion.

### Pericardial Effusion

Pericardial effusion, sometimes referred to as "fluid around the heart," is the abnormal build-up of excess fluid that develops between the pericardium, the covering sack around the heart, and the heart itself.

Pericardial effusion may be:

- Transudative effusion (congestive heart failure, myxoedema, nephrotic syndrome),
- Exudative effusion (tuberculosis, spread from empyema)
- Haemorrhagic effusion (trauma, rupture of aneurysms, malignant effusion).
- Malignant effusion (due to fluid accumulation caused by cancer or cancer treatment). Malignant Pericardial Effusion - a condition in which cancer causes extra fluid to collect inside the sac around the heart. The extra fluid causes pressure on the heart, which keeps it from pumping blood normally. Lymph vessels may be blocked, which can cause infection. Malignant pericardial effusions are most often caused by lung cancer, breast cancer, melanoma, lymphoma, and leukaemia.

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Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

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**Burazor, I., Imazio, M. Markel, G. & Adler, Y. 2013.**

“Malignant pericardial effusion is a common and serious manifestation in malignancies. The origins of the malignant process include solid tumors or hematological malignancies, while primary neoplasms of the pericardium are less common. In the oncological patient, pericardial effusion may develop by several different mechanisms, namely by direct or metastatic spread of the primary process or as a complication of antineoplastic therapies. In some cases, pericardial effusion may be the first manifestation of the disease, and that is why malignancy must be excluded in every case of an acute pericardial disease with cardiac tamponade at presentation, rapidly increasing pericardial effusion and an incessant or recurrent course. Thus, the definite differentiation of malignant pericardial effusion and rapid diagnosis are of particular therapeutic and prognostic importance. Management of these patients is multidisciplinary and requires team work, but at present there is a need for further research. An individual treatment plan should be established, taking into account cancer stage, the patient's prognosis, local availability and experience. In emergency cases with cardiac tamponade or significant effusion, initial relief can be obtained with pericardiocentesis. Despite the magnitude of this serious problem, little progress has been made in the treatment of pericardial effusion secondary to malignant disease.”

**Rousseau-Bussac, G., Crequit, P., Alifano, M. & Chouaid, C. 2014.**

“Acute pericarditis associated with lung cancer is a relatively frequent complication but is usually not symptomatic unless it causes tamponade. The clinical presentation is classically with dyspnea, thoracic pain, signs of right cardiac failure then left cardiac failure and syncope but it is often a difficult diagnosis in a patient with multi-symptomatic disease. The diagnosis is based on cardiac echography. Toxicity due to radiotherapy or more rarely an infectious etiology must be considered. Clinically significant effusions must be drained because of the high rate of recurrence after a simple aspiration. Drainage is formally indicated when, at echocardiography, the effusion exceeds 20mm in diastole, in cases of tamponade or in cases of compromised hemodynamic status. The formation of a pericardial window at thoracotomy prevents recurrences. Based on old, retrospective, very heterogeneous case series the prognosis, is generally considered to be poor with a median survival which does not exceed 100 days and a one year survival generally lower than 10%. Prognosis is better where diagnosis occurs at an earlier stage allowing regular follow-up and surgical intervention in a non-emergency setting.”

**Vakamudi, S., Ho, N. & Cremer, P.C. 2017.**

“The presentation of a patient with a pericardial effusion can range from an incidental finding to a life-threatening emergency. Accordingly, the causes of pericardial effusions are numerous and can generally be divided into inflammatory and non-inflammatory etiologies. For all patients with a suspected pericardial effusion, echocardiography is essential to define the location and size of an effusion. In pericardial tamponade, the hemodynamics relate to decreased pericardial compliance, ventricular interdependence, and an inspiratory decrease in the pressure gradient for left ventricular filling. Echocardiography provides insight into the pathophysiologic alterations, primarily through an assessment of chamber collapse, inferior vena cava plethora, and marked respiratory variation in mitral and tricuspid inflow. Once diagnosed, pericardiocentesis is performed in patients with tamponade, preferably with echocardiographic guidance. With a large effusion but no tamponade, pericardiocentesis is rarely needed for diagnostic purposes, though is performed if there is concern for a bacterial infection. In patients with malignancy, pericardial window is preferred given the risk for recurrence. Finally, large effusions can progress to tamponade, but can generally be followed closely until the extent of the effusion facilitates safe pericardiocentesis.”

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Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

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## Signs and Symptoms of Pericardial Effusion

Signs and symptoms of pericardial effusion may include:

- Chest pain
- Feeling of pressure in the chest
- Discomfort feeling in the chest
- Light-headedness
- Syncope
- Palpitations
- Cough
- Dyspnoea
- Hoarseness
- Anxiety and confusion
- Hiccoughs

## Causes and Risk Factors of Pericardial Effusion

Causes of pericardial effusion may include:

Inflammation of the pericardium following heart surgery or a heart attack. Autoimmune disorders, such as rheumatoid arthritis or lupus. Spread of cancer (metastasis), particularly lung cancer, breast cancer, melanoma, leukaemia, non-Hodgkin's lymphoma or Hodgkin's disease (which is serious and should be diagnosed and treated promptly)

The extra fluid causes pressure on the heart, which keeps it from pumping blood normally. Lymph vessels may be blocked, which can cause infection. Malignant pericardial effusions are most often caused by lung cancer, breast cancer, melanoma, lymphoma, and leukaemia.

In most cases, inflammation of the pericardial sac, a condition called pericarditis, leads to the effusion. As it becomes inflamed, more fluid is produced.

Viral infections are one of the main causes of the inflammation and the effusions it leads to. These infections include:

- Cytomegalovirus
- Coxsackieviruses
- Echoviruses
- Human Immunodeficiency Virus (HIV)

Other conditions that can cause pericardial effusions include:

- Cancer
- Injury to the sac or heart from a medical procedure
- Heart attack
- Severe kidney failure, also called uremia
- Autoimmune diseases (lupus, rheumatoid arthritis, and others)
- Bacterial infections, including tuberculosis

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Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

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In many cases, no cause can be found. One's doctor may call these 'idiopathic pericardial effusions'.

**Takata, N., Kataoka, M., Hamamoto, Y., Tsuruoka, S., Kanzaki, J., Uwatsu, K., Nagasaki, K. & Mochizuki, T. 2018.**

"Pericardial effusion is an important late toxicity after concurrent chemoradiotherapy (CCRT) for locally advanced esophageal cancer. We investigated the clinical and dosimetric factors that were related to pericardial effusion among patients with thoracic esophageal cancer who were treated with definitive CCRT using the two opposed fields technique (TFT) or the four-field technique (FFT), as well as the effectiveness of FFT. During 2007-2015, 169 patients with middle and/or lower thoracic esophageal cancer received definitive CCRT, and 94 patients were evaluable (51 FFT cases and 43 TFT cases). Pericardial effusion was observed in 74 patients (79%) and appeared at 1-18.5 months (median: 5.25 months) after CCRT. The 1-year incidences of pericardial effusions were 73.2% and 76.7% in the FFT and TFT groups, respectively ( $P = 0.6395$ ). The mean doses to the pericardium were 28.6 Gy and 31.8 Gy in the FFT and TFT groups, respectively ( $P = 0.0259$ ), and the V40 Gy proportions were 33.5% and 48.2% in the FFT and TFT groups, respectively ( $P < 0.0001$ ). Grade 3 pericardial effusion was not observed in patients with a pericardial V40 Gy of  $<40\%$ , or in patients who were treated using the FFT. Although the mean pericardial dose and V40 Gy in the FFT group were smaller than those in the TFT group, the incidences of pericardial effusion after CCRT were similar in both groups. As symptomatic pericardial effusion was not observed in patients with a pericardial V40 Gy of  $<40\%$  or in the FFT group, it appears that FFT with a V40 Gy of  $<40\%$  could help minimize symptomatic pericardial effusion."

### **Diagnosis of Pericardial Effusion**

If one's doctor suspects someone to suffering from a pericardial effusion, he or she will do a series of tests to look for it, identify possible causes in order to determine treatment.

**Medical examination** - The doctor will perform a medical examination, including listening to the heart with a stethoscope.

**Echocardiogram** - An echocardiogram uses sound waves to create real-time images of the heart. With this procedure, a cardiologist can see the extent of pericardial effusion based on the amount of space between the two layers of the pericardium. An echocardiogram can also show decreased heart function due to pressure on the heart (tamponade).

A cardiologist might be able to see whether one or more chambers of the heart have collapsed and how efficiently the heart is pumping blood. There are two types of echocardiograms:

- **Transthoracic echocardiogram** - this test uses a sound-emitting device (transducer) that is placed on the chest over the heart.
- **Transoesophageal echocardiogram** - a tiny transducer on a tube is put down the part of the digestive tract that runs from the throat to the stomach (oesophagus). Because the oesophagus lies close to the heart, having the transducer placed there often provides a more-detailed image of the heart.

**Electrocardiogram** - an electrocardiogram — also called an ECG or EKG — records electrical signals as they travel through the heart. A cardiologist can look for patterns that suggest tamponade.

**Chest X-ray** - this can show an enlarged heart silhouette if the amount of fluid in the pericardium is large.

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Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

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Other imaging technologies - computerized tomography (CT) scans and magnetic resonance imaging (MRI) are imaging technologies that can detect pericardial effusion, although they're not generally used to look for the disorder. However, pericardial effusion may be diagnosed when these tests are done for other reasons. Other tests - if there is evidence of pericardial effusion, the doctor may order blood tests or other diagnostic tests to identify the cause.

Examination findings in patients with pericardial effusion may include the following:

- Classic Beck triad of pericardial tamponade: Hypotension, muffled heart sounds, jugular venous distention
- Pulsus paradoxus
- Pericardial friction rub
- Tachycardia
- Hepatojugular reflux
- Tachypnoea
- Decreased breath sounds
- Ewart sign: Dullness to percussion beneath the angle of left scapula
- Hepatosplenomegaly
- Weakened peripheral pulses, oedema, and cyanosis

The following lab studies may be performed in patients with suspected pericardial effusion:

- Electrolytes - To assess for metabolic abnormalities (e.g., renal failure)
- Complete blood count (CBC) with differential - Leukocytosis for evidence of infection, as well as cytopenias, as signs of underlying chronic disease (e.g., cancer, HIV)
- Cardiac biomarkers
- Other markers of inflammation, such as erythrocyte sedimentation rate and C-Reactive protein - While these do not aid in identifying specifics, they can be used to potentially assess the need for anti-inflammatory agents (i.e., corticosteroids, colchicine, NSAIDs), especially in the setting of recurrent effusions
- Thyroid-stimulating hormone - Thyroid-stimulating hormone screen for hypothyroidism
- Blood cultures in the presence of systemic inflammatory response syndrome (SIRS) or fever; in general, specific viral studies are low yield and therefore not recommended
- Rheumatoid factor, immunoglobulin complexes, antinuclear antibody test (ANA), and complement levels (which would be diminished) - In suspected rheumatologic causes
- Specific infectious disease testing, based upon clinical suspicion, such as (1) tuberculin skin testing or QuantiFERON-TB assay; (2) rickettsial antibodies if there is a high index of suspicion for tick-borne disease; and HIV serology

**Kalogeraki, A., Lazopoulos, G., Papadakis, G.Z., Tamiolakis, D., Karvela-Kalogeraki, I., Karvelas-Kalogerakis, M., Segredakis, J. & Chalkiadakis, G.E. 2016.**

**BACKGROUND:** Malignant pericardial effusion occurs in one tenth of all cancers. It is a very serious disorder that is mainly a secondary process due to metastasis because primary neoplasms of the pericardium such as mesotheliomas, sarcomas being exceedingly rare [corrected]. Pericardial effusion specimens are uncommon and to the best of our knowledge the current study is the largest systematic evaluation of pericardial fluid cytology performed to date.

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Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

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**MATERIAL AND METHODS:** Pericardial effusion specimens from 145 patients collected over a 25 [corrected] year period were studied by cytology [corrected]. The minimum pericardial fluid volume used for adequate cytologic diagnosis in these patients was more than 60 mL.

**RESULTS:** Cytological diagnosis revealed malignant pericardial exudates in 100% of the studied patients [corrected].

**CONCLUSIONS:** Cytology provides an immediate and accurate means of diagnosis. Immunocytology is very important in the diagnostic evaluation.

### **Treatment of Pericardial Effusion**

Treatment of pericardial effusion is based on the underlying condition that is causing it and if the effusion is leading to severe symptoms, such as shortness of breath or difficulty breathing.

The goal of medical management for pericardial effusions is to treat the underlying cause. Medical therapies for pericardial effusions may include:

- Non-steroidal anti-inflammatory medications (NSAIDs) can be used to treat pericardial effusions caused by inflammation.
- Diuretics and other heart failure medications can be used to treat pericardial effusions caused by heart failure.
- Antibiotics are used to treat pericardial effusions caused by an infection.
- If a pericardial effusion is related to the presence of cancer, treatment may include chemotherapy, radiation therapy, or medication infused within the chest.

Large pericardial effusions may be drained through:

- Ultrasound-guided pericardiocentesis, a safe and effective procedure to remove excess fluid from the pericardium. This is most common followed by fluoroscopy.
- Video-assisted thoracoscopic surgery (VATS), also known as thoracoscopy is a minimally-invasive technique performed under general anaesthesia. VATS allows for visual evaluation of the pericardium and is used when the diagnosis of pericardial effusion has remained undiagnosed despite previous, less-invasive tests. It is also used to drain the excess fluid and prevent its re-accumulation.

**Palaskas, N., Morgan, J., Daigle, T., Banchs, J., Durand, J.B., Hong, D., Naing, A., Le, H., Hassan, S.A., Karimzad, K., Mouhayar, E., Kim, P., Lopez-Mattei, J., Thompson, K., Yusuf, S.W. & Iliescu, C. 2019.**

“Targeted cancer therapies with pericardial effusions requiring pericardiocentesis focusing on immune checkpoint inhibitors. *Am J Cardiol.* 2019 Apr 15;123(8):1351-1357. doi: 10.1016/j.amjcard.2019.01.013. Epub 2019 Jan 25. PMID: 30765065

“Case reports have reported immune checkpoint inhibitors (ICI), especially nivolumab, are associated with recurrent pericardial effusions. Our objective was to determine how often patients being treated with ICI develop hemodynamically significant pericardial effusion requiring pericardiocentesis compared with other cancer therapeutics and whether the survival of patients who underwent pericardiocentesis differs according to ICI use versus standard cancer therapeutics. Our institutional review board approved catheterization laboratory data collection for all pericardiocenteses performed and all patients receiving ICI from January 1, 2015 to December 31, 2017. Retrospective review of the electronic medical record was performed to identify cancer therapeutics given preceding pericardiocentesis. Log-rank analysis was performed to compare survival

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in patients requiring pericardiocentesis between those on ICI and those not on ICI. Overall, 3,966 patients received ICI of which only 15 pericardiocenteses were required, including 1 repeat pericardiocentesis in a patient on nivolumab. The prevalence of pericardiocentesis among patients on ICI was 0.38% (15/3,966). Eleven pericardiocenteses were performed after nivolumab infusion, 3 after pembrolizumab, and 1 after atezolizumab, with pericardiocentesis prevalences for each agent of 0.61% (11/1,798), 0.19% (3/1,560), and 0.32% (1/309), respectively. One hundred and twenty pericardiocenteses were performed on patients receiving other cancer therapeutics although no therapeutic agent was associated with more pericardiocenteses than nivolumab. In conclusion, the prevalence of hemodynamically significant pericardial effusions and ICI administration is uncommon, and survival durations after pericardiocentesis for patients receiving ICI and those not receiving ICI are similar, suggesting that frequent echocardiographic monitoring for pericardial effusions is not necessary.”

### Medical Disclaimer

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### Sources and References Consulted and/or Utilised

- Burazor, I., Imazio, M. Markel, G. & Adler, Y.** 2013. Malignant pericardial effusion. *Cardiology*. 2013;124(4):224-32. doi: 10.1159/000348559. Epub 2013 Apr 5.
- Hoit, B.C.** 2017. Pericardial effusion and cardiac tamponade in the new millennium. *Curr Cardiol Rep*. 2017 Jul;19(7):57. doi: 10.1007/s11886-017-0867-5.
- Istomin, V., Blondheim, D.S., Meisel, S.R., Frimerman, A., Lapidot, M. & Rachmilevitch, R.** 2016. Pericardial effusion due to primary malignant pericardial mesothelioma: a common finding but an uncommon cause. *Case Reports in Medicine*. Volume 2016, Article ID 4810901.
- Jama, G.M., Scarci, M., Bowden, J., Marciniak, S.J.** 2014. Palliative treatment for symptomatic malignant pericardial effusion. *Interact Cardiovas Thorac Surg*. 2014 Dec;19(6):1019-26. doi: 10.1093/icvts/ivu267. Epub 2014 Aug 20.
- Kalogeraki, A., Lazopoulos, G., Papadakis, G.Z., Tamiolakis, D., Karvela-Kalogeraki, I., Karvelas-Kalogerakis, M., Segredakis, J. & Chalkiadakis, G.E.** 2016. Cytology of pericardial effusion due to malignancy. *Rom J Intern Med*. 2016 Sep 1;54(3):179-183. doi: 10.1515/rjim-2016-0026.
- Niclauss, L., Montemurro, M. & Prêtre, R.** 2015. Survival after surgical drainage of malignant pericardial effusion. *World J Surg*. 2015 Jul;39(7):1767-72. doi: 10.1007/s00268-015-3025-5.

Palaskas, N., Morgan, J., Daigle, T., Banchs, J., Durand, J.B., Hong, D., Naing, A., Le, H., Hassan, S.A., Karimzad, K., Mouhayar, E., Kim, P., Lopez-Mattei, J., Thompson, K., Yusuf, S.W. & Iliescu, C. 2019. Targeted cancer therapies with pericardial effusions requiring pericardiocentesis focusing on immune checkpoint inhibitors. *Am J Cardiol.* 2019 Apr 15;123(8):1351-1357. doi: 10.1016/j.amjcard.2019.01.013. Epub 2019 Jan 25. PMID: 30765065

#### **Pericardial Effusion**

<https://www.cancer.gov/publications/dictionaries/cancer-terms/def/malignant-pericardial-effusion>

<https://www.webmd.com/heart-disease/guide/pericardial-effusion#1>

<https://www.mayoclinic.org/diseases-conditions/pericardial-effusion/diagnosis-treatment/drc-20353724>

<https://www.uptodate.com/contents/diagnosis-and-treatment-of-pericardial-effusion>

<https://emedicine.medscape.com/article/157325-overview>

<https://emedicine.medscape.com/article/157325-workup#c8>

<https://my.clevelandclinic.org/health/diseases/17351-pericardial-effusion/diagnosis-and-tests>

#### **Pericarditis**

<https://www.webmd.com/heart-disease/guide/pericardial-effusion#1>

#### **Pericardial Effusion Following Cancer Treatment**

<https://www.webmd.com/heart-disease/guide/pericardial-effusion#1>

#### **Pericardium**

<https://en.wikipedia.org/wiki/Pericardium>

Rousseau-Bussac, G., Crequit, P., Alifano, M. & Chouaid, C. 2014. Management of malignant pericardial effusion in lung cancer. *Rev Mal Respir.* 2014 Oct;31(8):746-53. doi: 10.1016/j.rmr.2014.02.011. Epub 2014 Apr 24.

Takata, N., Kataoka, M., Hamamoto, Y., Tsuruoka, S., Kanzaki, J., Uwatsu, K., Nagasaki, K. & Mochizuki, T. 2018. Risk factors for pericardial effusion after chemoradiotherapy for thoracic esophageal cancer-comparison of four-field technique and traditional two opposed fields technique. *J Radiat Res.* 2018 May 1;59(3):291-297. doi: 10.1093/jrr/rry029.

Tsang, T.S.M., Seward, J.B., Barnes, M.E., Bailey, K.R., Sinak, L.J., Urban, L.H. & Hayes, S.N. 2000. Outcomes of Primary and Secondary Treatment of Pericardial Effusion in Patients With Malignancy. <https://doi.org/10.4054/75.3.248>.

Vakamudi, S., Ho, N. & Cremer, P.C. 2017. Pericardial effusions: causes, diagnosis, and management. *Prog Cardiovasc Dis.* 2017 Jan - Feb;59(4):380-388. doi: 10.1016/j.pcad.2016.12.009. Epub 2017 Jan 4.