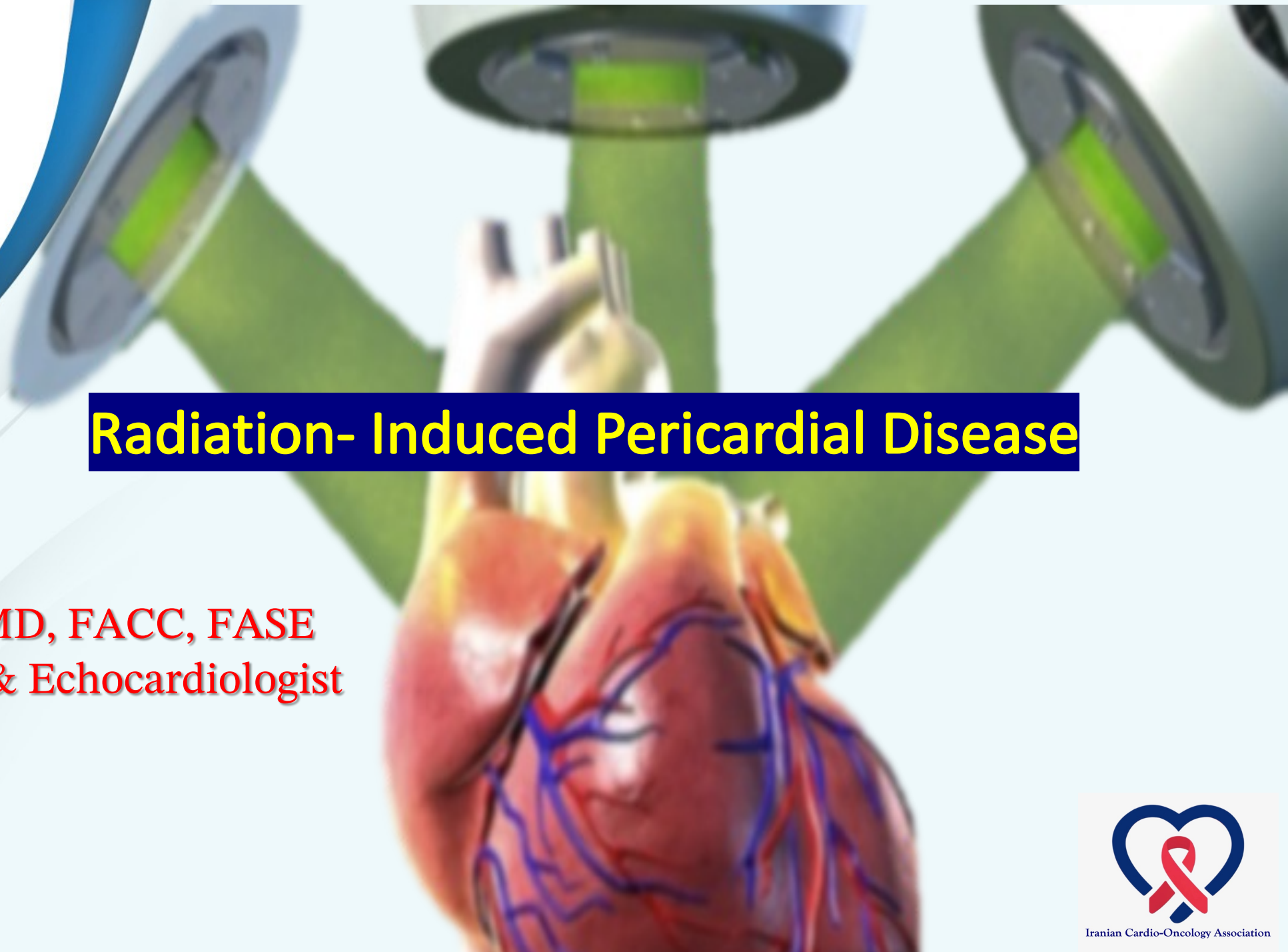
The 9th International
Clinical Oncology Congress

نوزدهمین کنگره سالیانه کلینیکال انکولوژی
فیزیک پزشکی، تکنولوژی پرتودرمانی،
رادیوبیولوژی و پرستاری انکولوژی

29-31 January 2025
Olympic hotel,Tehran ,IRAN



Radiation- Induced Pericardial Disease

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Cardio-Oncology Research Center

Iranian Cardio-Oncology Association

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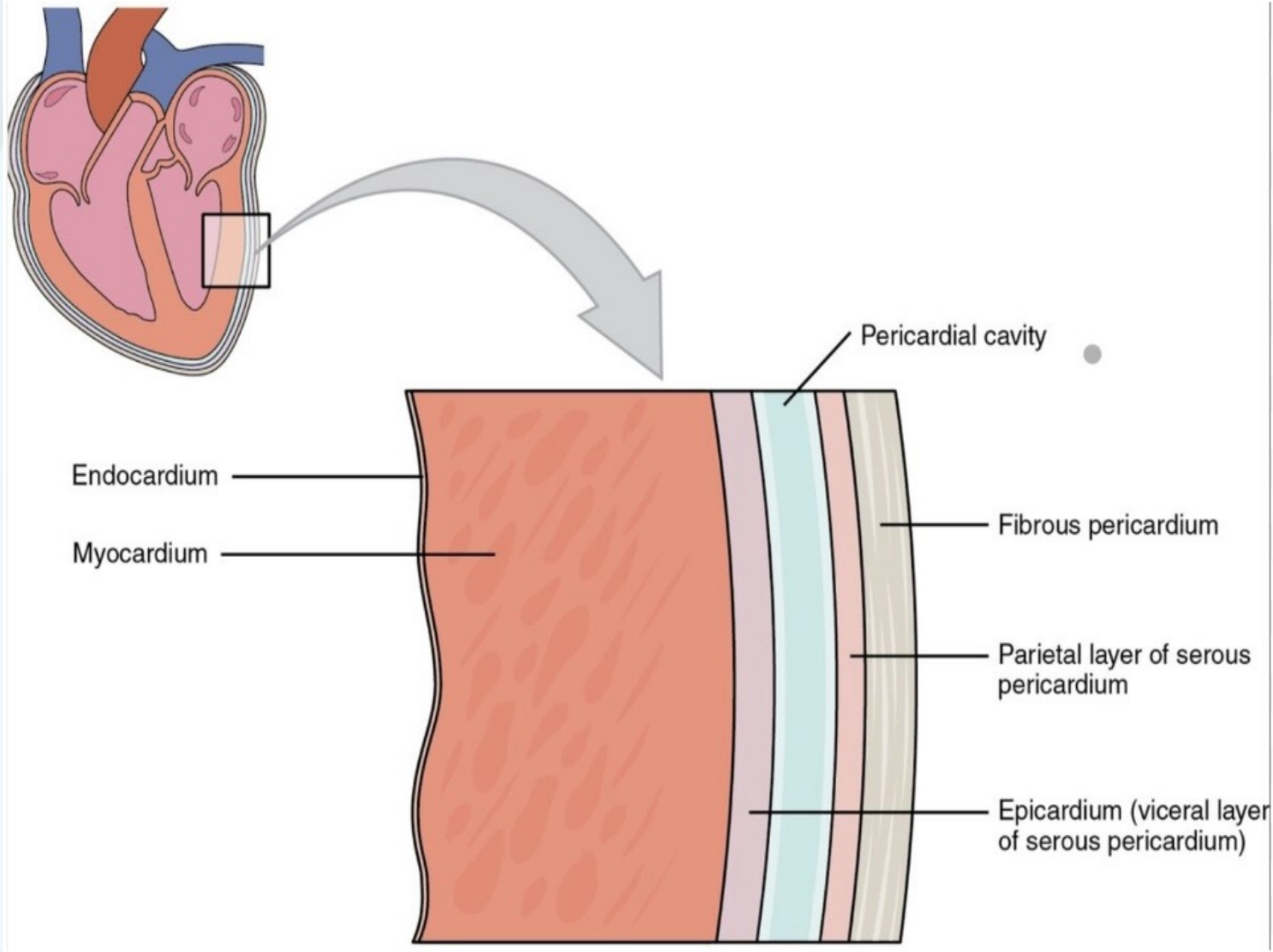


RT-related pericardial disease is relatively common.

***It is important to differentiate RT-related pericardial disease from disease progression of the primary neoplasm and from non-neoplastic causes of pericardial disease (e.g., infective pericarditis in immune compromised patients).

***The RT-related pericardial disease may manifest acutely early after treatment administration (acute toxicity), but it may also manifest very late, up to years and even decades after therapy completion (chronic toxicity).

von Kemp BA, Cosyns B. Radiation-Induced Pericardial Disease: Mechanisms, Diagnosis, and Treatment. Current Cardiology Reports. 2023;25(10):1113-21.

- ✓Direct radiation damage, leading to inflammation, fibrosis, and thickening of the pericardial layers.
- ✓Pericardial-Vascular injury may lead to intimal thickening and reduced vascular compliance, also contributing to pericardial inflammation.
- ✓Radiation may trigger an inflammatory response and the release of pro-inflammatory cytokines, such as TNF-α and IL-1, IL-6, that contribute to the development of pericardial inflammation.
- ✓In cases of prolonged inflammation due to radiation, excessive deposition of collagen and other extracellular matrix components within the pericardial layers can result in fibrotic changes.

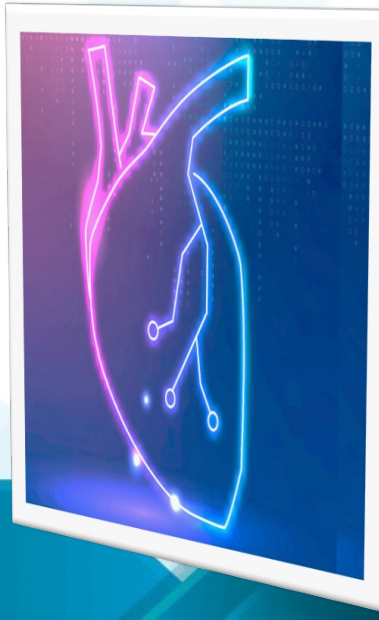
Szpakowski N, Desai MY. Radiation-associated pericardial disease. Current Cardiology Reports. 2019;21:1-10.

Radiation-induced generation of reactive oxygen species (ROS) can damage cellular components within the pericardium, including DNA, proteins, and lipids.

Radiation may further impair lymphatic drainage from the pericardial space, leading to the accumulation of fluid and proteins within the pericardial cavity .

Genetic factors and individual patient characteristics may influence the susceptibility to radiation-induced pericardial disease.

Variations in DNA repair mechanisms, antioxidant defense systems, and cellular responses to RT exposure contribute to differential risk among patients.



Gaya A, Ashford R. Cardiac complications of radiation therapy. Clinical oncology. 2005;17(3):153-9.

RF of RT-induced pericardial disease

Total cardiac dose > 30 gy

Daily dose fraction > 2 gy

Larger irradiated tissue volume

Lack of radiation shielding

Patient risk factors

Tumor location close to the heart

History of prior chest radiation

Pre-existing cardiovascular disease

Concomitant administration of chemotherapy

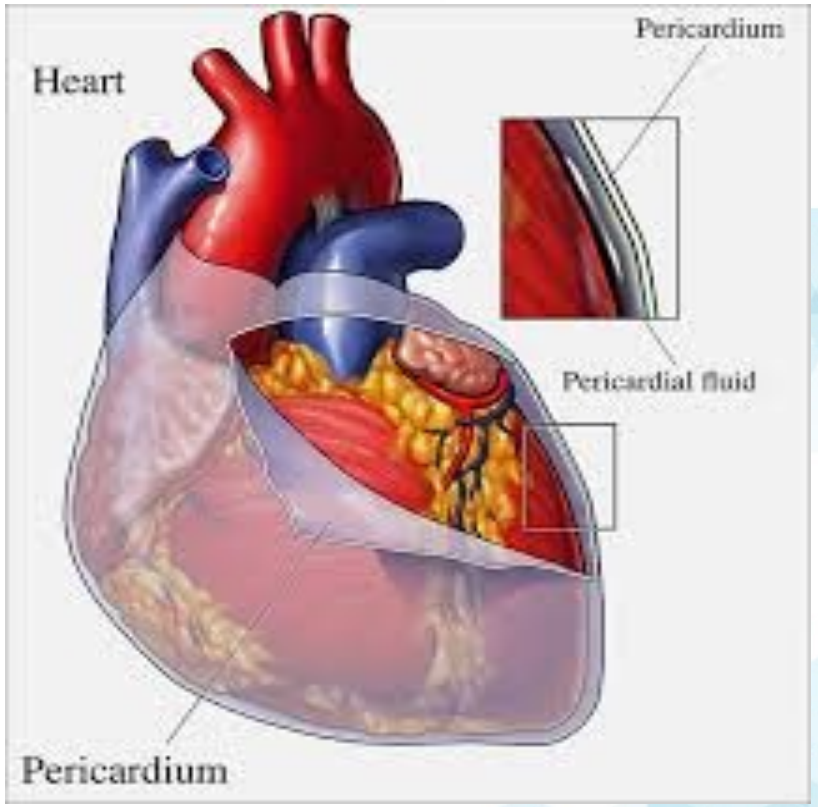
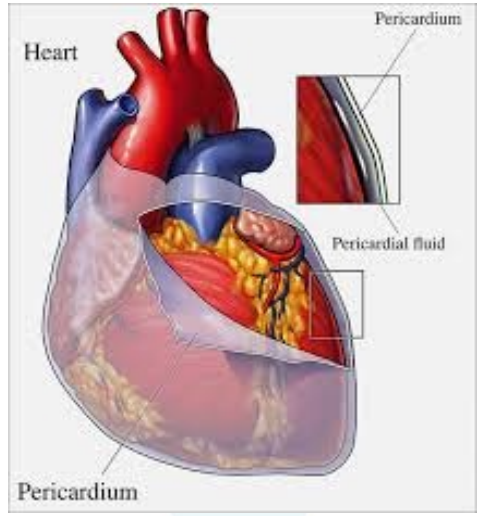


Table 1 Clinical manifestations of RT-induced pericardial disease

Clinical manifestation	Underlying disease mechanism
Acute pericarditis	RT-induced pericardial inflammation resulting in chest pain, fever, and pericardial friction rub
Pericardial effusion	RT-induced inflammation resulting in fluid accumulation (exudate), resulting in dyspnea, chest discomfort, and/or fluid retention
Cardiac tamponade	Rapid fluid accumulation within the pericardial sac, interfering with normal hemodynamics through cardiac compression and impaired filling
Chronic pericarditis	Persistent or recurrent pericardial inflammation, resulting in chest pain, fatigue, and exercise intolerance
Constrictive pericarditis	Fibrotic pericardial thickening, impairing myocardial relaxation and filling, resulting in fatigue, fluid retention, signs of right-sided heart failure
Pericardial calcifications	Pericardial calcium deposition as a late consequence of RT-induced inflammation
Pericardial fibrosis	Pericardial scarring and fibrotic thickening, resulting in loss of elasticity and compliance of the pericardial sac, contributing to constrictive physiology
Pericardial cysts	Fluid-filled pericardial collections, occurring either in isolation or secondary to RT exposure
Pericardial tumors	Very rare: development of secondary pericardial tumors after RT exposure (e.g., pericardial sarcoma)

Acute Radiotherapy-Induced Pericarditis

- Acute RT-related pericarditis has become rare in current RT treatment regimens.



- Acute pericarditis usually manifests early and may develop as soon as hours after RT administration, up to several weeks after the last RT dose.

- The volume of this PE may be limited to physiological quantities or more smaller effusions may cause increased friction of the inflamed pericardial tissue layers, resulting in a clinical presentation with **typical sharp pericardial/pleuritic chest pain syndrome.**

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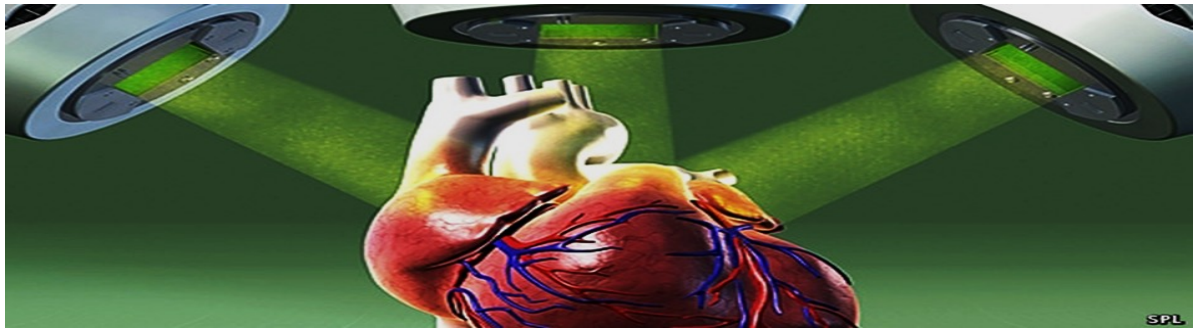
Acute RT-induced pericarditis	RT-induced pericardial effusion	Chronic / constrictive pericarditis
SYMPTOMS		
- Sharp chest pain, dyspnea - Fever - Pericardial friction rub	- May be asymptomatic - Dyspnea - Kussmaul sign, pulsus paradoxus	- Exertional dyspnea - Peripheral oedema, ascites
DIAGNOSIS		
- ECG - **TTE** - (CT/CMR/PET-CT)	- (ECG) - **TTE** - **CT/CMR/PET-CT** +/- pathology	- TTE - **CT/CMR** - **Right heart catheterization** +/- pathology
TREATMENT		
- Anti-inflammatory agents - Colchicine - Drainage if (pre-)tamponade	- Watchful waiting - Pericardiocentesis / fenestration if large effusion	- Loop diuretics if congestion - Anti-inflammatory agents - Surgical pericardiectomy (last resort)
Hours - Days - Weeks	Days – Weeks – Months	Years - Decades

Diagnosis

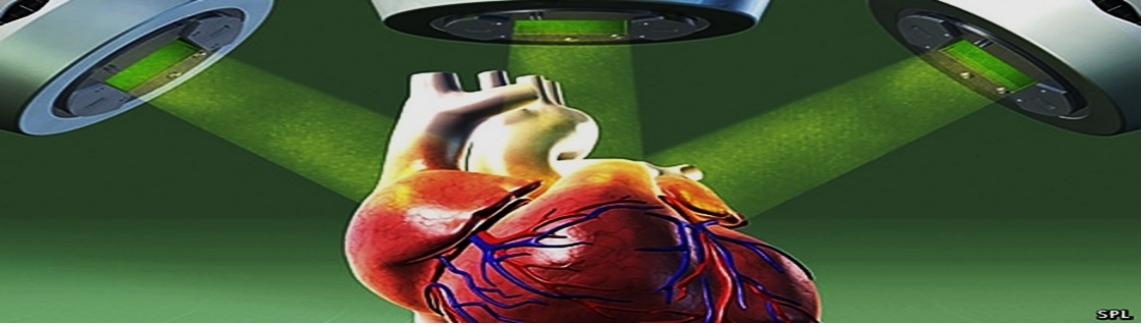


Pts presenting with chest pain and/or shortness of breath during or shortly after RT, acute RT-related pericarditis should be suspected.

However, since all CV structures are prone to undergo RT-related changes, the DD is very broad, and symptoms may be atypical.

This is further highlighted by the use of combined chemotherapy, and ICI may further predispose to the development of pericarditis and peri-myocarditis .

Zaghlol R, Pedersen L, Qamer S, Yoo SGK, Ladin DA, Parvathaneni A, et al. Cardiac Complications of Radiation Therapy. Cardiology clinics. 2025



- The decision whether or not to interrupt cancer treatment requires multidisciplinary discussion

- In most cases of acute RT-related pericarditis, radiotherapy may be completed if adequate symptom control can be obtained and if no hemodynamic compromise occurs.

- Regular reassessment is indicated (repeat echocardiography 7–14 days after diagnosis followed by 4–6 weekly intervals).

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Medical Treatment, Acute RT-Induced Pericarditis

- Pts presenting with acute RT-induced pericarditis are treated the same way as non-cancer pts

- Colchicine and anti-inflammatory agents as a first-line strategy. , a second-line treatment using systemic corticosteroids may be considered

- Cancer ps in particular present a high risk (20%) of progression towards CP, highlighting the importance of a complete and uninterrupted treatment .

Zaghlol R, Pedersen L, Qamer S, Yoo SGK, Ladin DA, Parvathaneni A, et al. Cardiac Complications of Radiation Therapy. Cardiology clinics. 2025

Cancer-Associated Pericardial effusion

- Pericardial effusions in cancer patients are **common.**
- Malignant pericardial effusion in **5–15%** of cancer patients.
- Non-malignant effusion in up to **7%** .
- Cancer-associated pericardial effusions confer a poor prognosis.
- **Pericardial effusions** after RT: may develop at **any** given moment.

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Cancer-Associated Pericardial effusion

- **Direct or metastatic invasion by a non-cardiac tumor (most commonly breast, lung cancer, but melanoma, gastro-intestinal cancers, and hematological malignancies may be implied as well)**

- **Primary pericardial malignancies are very rare but may include mesothelioma, sarcoma, and lymphoma, angiosarcoma, and fibrosarcoma.**

- **In order to differentiate an RT-related effusion from a malignant one, a cytological diagnosis of pericardial fluid is required.**

- **When a pericardial tumor is suspected, further diagnosis can be refined by tissue characterization using CMR.**

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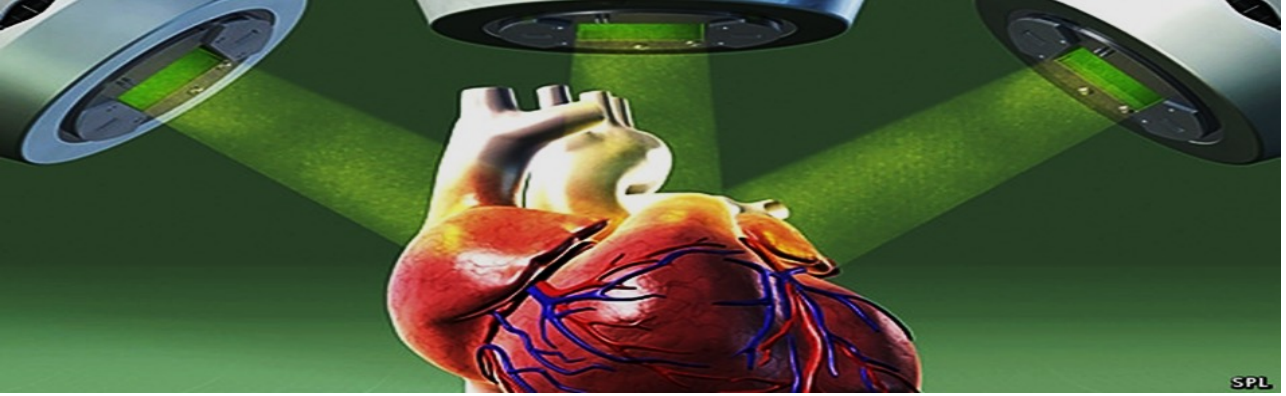


- Evolution towards tamponade with hemodynamic compromise is rare since these effusions generally develop very slowly over a prolonged period of time.

- Nevertheless, serial echocardiographic follow-up is recommended, and most effusions resolve spontaneously within 2 years or more.

Szpakowski N, Desai MY. Radiation-associated pericardial disease. Current Cardiology Reports. 2019;21:1-10.

It is important to note that pericardial effusion can occur with radiotherapy in general and is not limited to a specific type or technique.

RT-Induced Chronic Constrictive and Constrictive-Effusive Pericarditis

- CP and Effusive CP: will not manifest until very late (years or even decades) after radiotherapy.
- Echocardiography, CMR and invasive hemodynamic measurements can help differentiate it from restrictive cardiomyopathy.
- Pathology specimens should be obtained to exclude progressive malignancy.
- In classical cases, the only definitive treatment is surgical pericardiectomy.

- Echocardiography remains a cornerstone of the diagnosis, but multimodality imaging including CT and CMR may prove valuable allowing for better tissue characterization, especially in cases where malignant pericardial invasion is suspected.

- In ***CP***, right heart catheterization may be useful in differentiating from ***RCM***, and cardiac CT may aid in visualizing pericardial thickening and calcifications.

- In early disease stages, conservative medical treatment may be considered in order to mitigate residual pericardial inflammation using anti-inflammatory and corticosteroids drugs.

- In the case of symptoms of congestion (mainly ascites and/or peripheral edema), loop diuretics may help in diagnosis and treatment, progressive right sided congestion is to be expected.

- In pts presenting with CP and refractory congestive symptoms early surgical options may be considered.

Interventional Approach :

- In hemodynamically significant PE
- Tamponade
- Diuretic-refractory CP
- Elaborate the diagnostic framework by obtaining pathology specimens.

Zaghlol R, Pedersen L, Qamer S, Yoo SGK, Ladin DA, Parvathaneni A, et al. Cardiac Complications of Radiation Therapy. Cardiology clinics. 2025

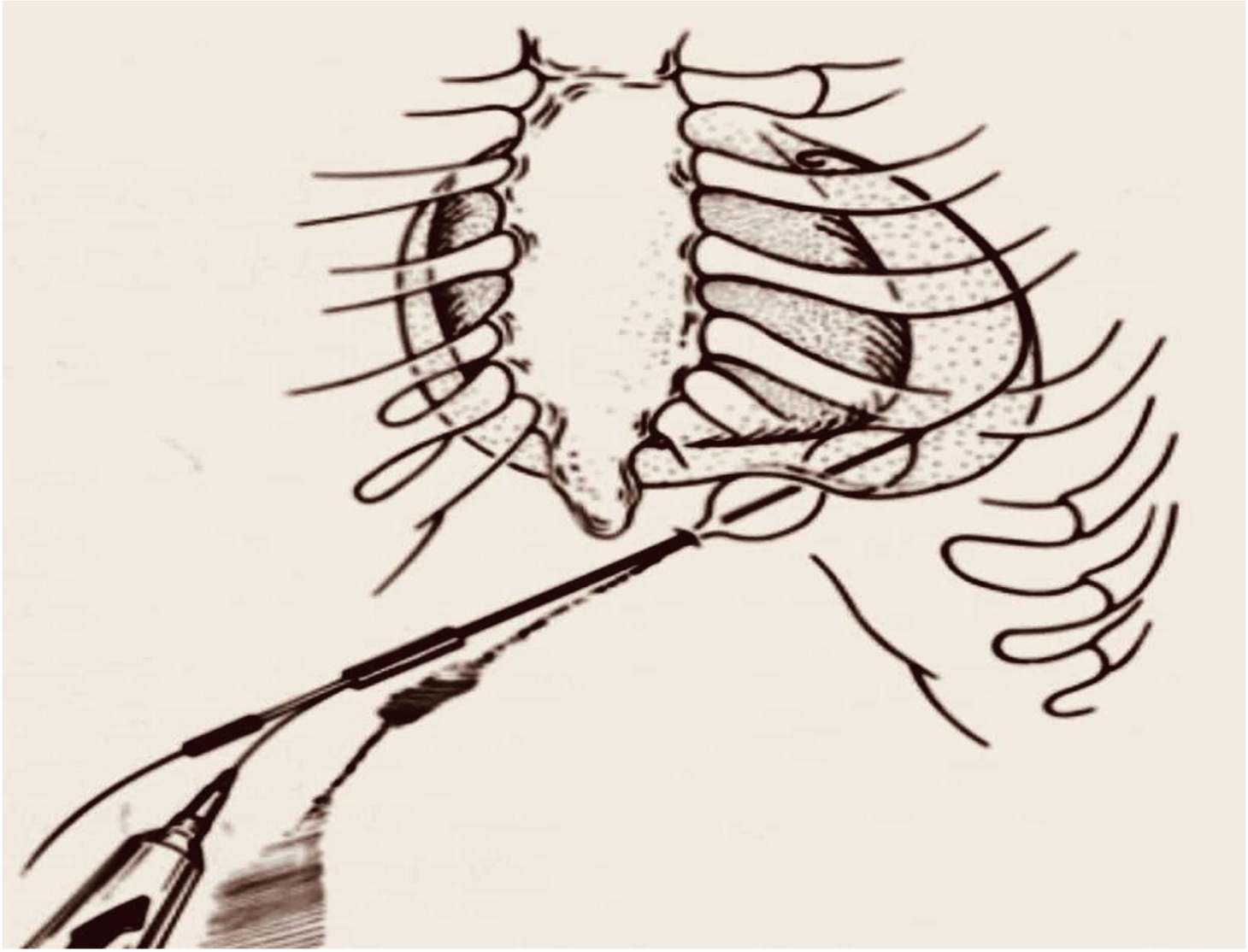
Pericardiocentesis

- For any cause of PE presenting by (pre-) or tamponade.
- Classical pericardiocentesis indications apply, besides intravenous fluid resuscitation in hypovolemic patients.
- Besides symptom relief and hemodynamic stabilization, pericardial fluid analysis may prove useful in differentiating the etiology.
- Prolonged drainage is generally preferred in order to avoid early recurrence
- In proven malignant effusions, intrapericardial treatment may be considered (using either cytotoxic or sclerosing agents)

Pericardial Fenestration

- In recurrent PE, repeat interventions can be avoided by creating a **pericardial window** (either by percutaneous balloon pericardiotomy or through a thoracoscopic or surgical approach).

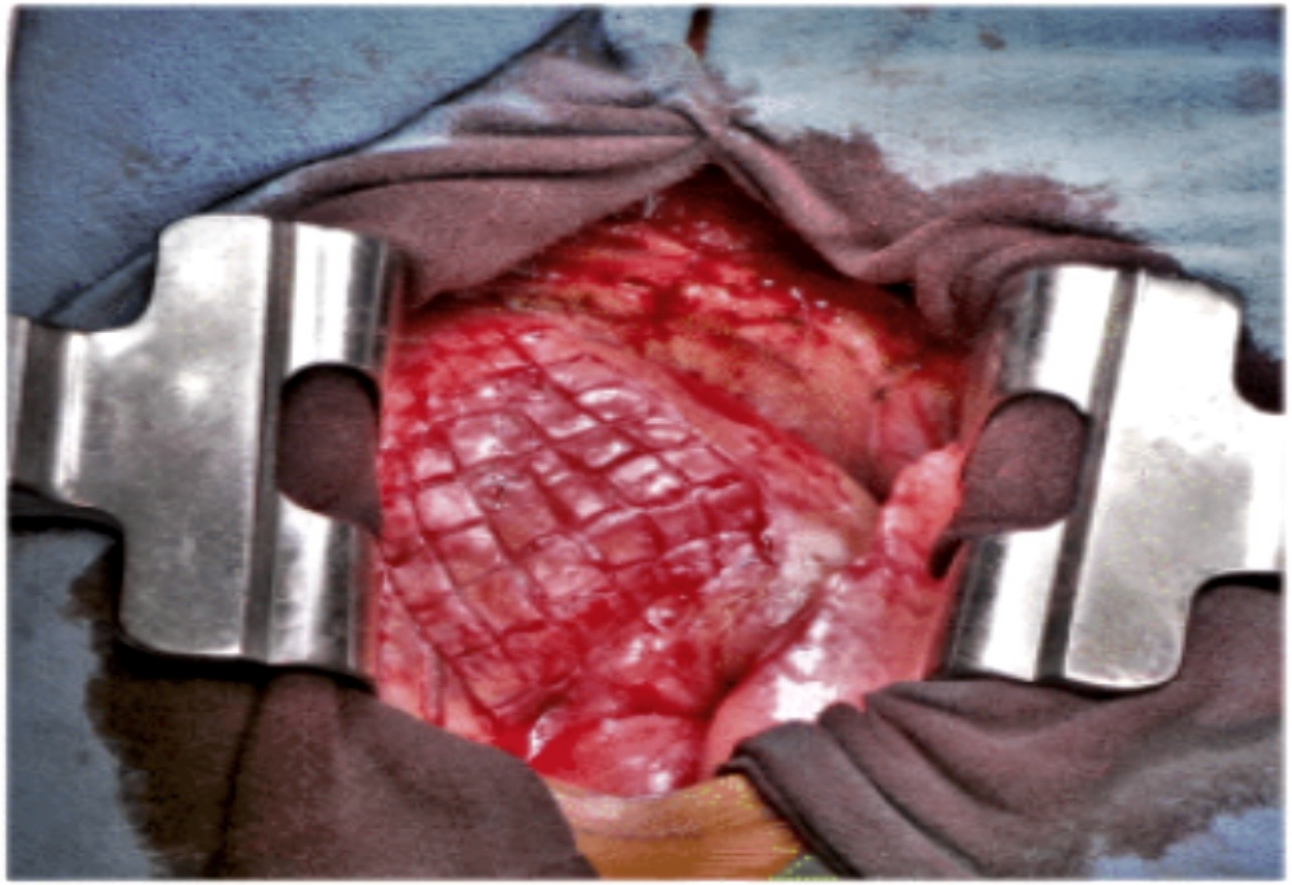
- This allows constant evacuation of pericardial fluid into an adjacent space, most often the **pleural cavity**.

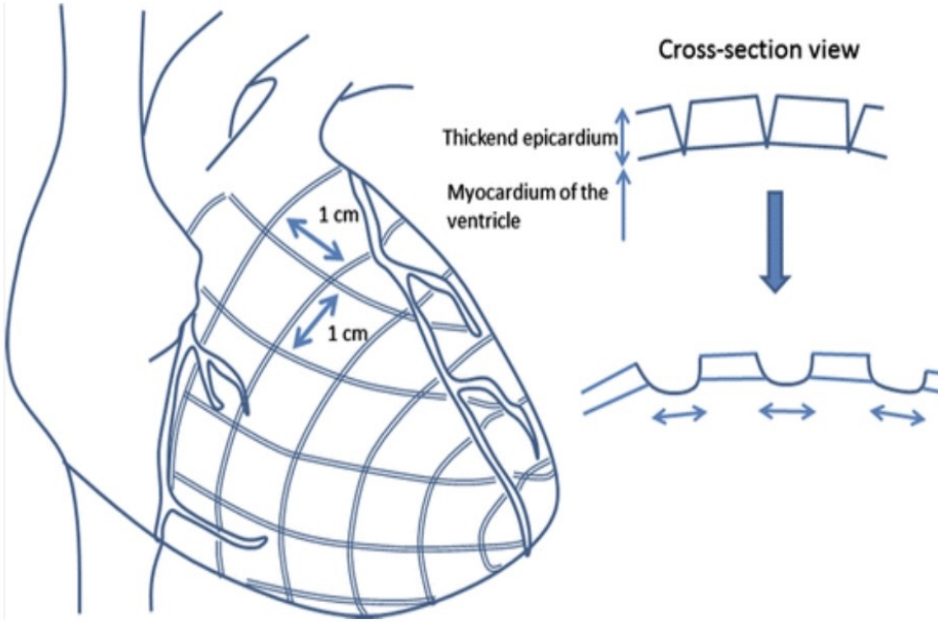


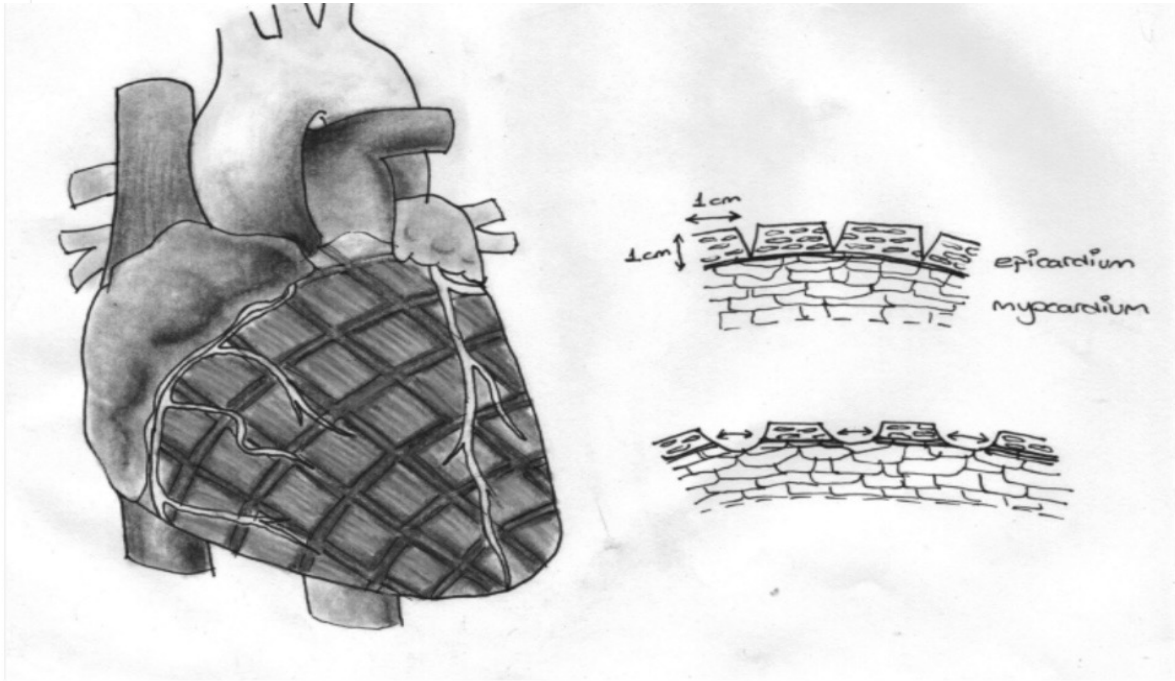
Surgical Pericardiectomy

- Symptomatic CP refractory to treatment with conservative measures (diuretics, anti-inflammatory agents and Corticosteroids).
- However, survival data for this intervention in RT-related CP are exceptionally poor (5-year survival rate post-pericardiectomy of 11%, compared to 80% in idiopathic CP).
- This is probably not only related to the complexity of pericardial and epicardial inflammation), but also to other RT-related abnormalities (notably RT-induced coronary and valvular heart disease which may require additional surgical intervention) as well as a coexisting RT-related RCM secondary to myocardial fibrosis.

Waffle procedure for the tight fibrotic epicardium




Cross-section view
Thickend epicardium
Myocardium of the ventricle
1 cm
1 cm

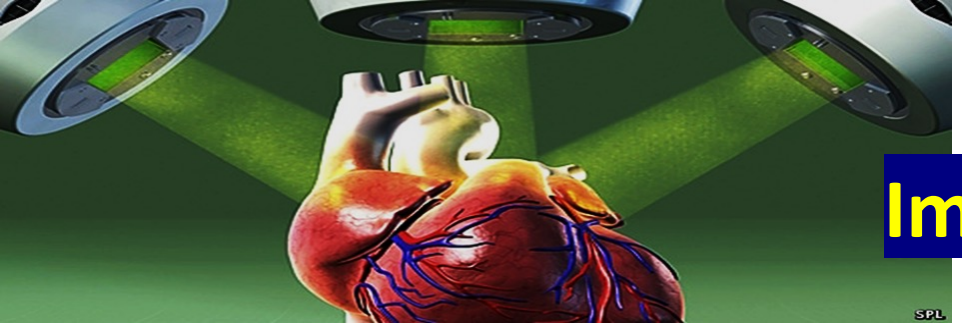

1cm
1cm
epicardium
myocardium

Cancer Therapy-Related Pericardial Diseases (Other reasons)

- In immunocompromised cancer pts, infectious causes of pericarditis (bacterial, viral, and fungal) should be excluded.

- ICI-induced pericarditis is a distinct entity, as it is a primarily immune-mediated, rather than tissue-toxic process, involving mainly T-lymphocytes as mediators of the inflammatory process. It may accompany ICI-mediated myocarditis, It develops typically soon after treatment initiation (within the first 3–4 treatment cycles and even sooner in dual ICI therapy) and requires a distinct treatment based on first-line therapy using corticosteroids rather than other anti-inflammatory drugs.

- Finally, after mediastinal surgery, classical postoperative pericarditis and/or pericardial effusion may occur.



Important POINTS:

- A Danish study demonstrated that in a large population of 13.759 patients presenting with new-onset pericarditis, 11% (1.550 pts) were diagnosed with cancer throughout the median follow-up period of 6.4 years.

- Workup of a new pericardial effusion with suspicion of underlying neoplastic of malignant disease requires multimodality imaging (TTE, CT, and CMR for optimal tissue characterization, eventually also PET as well as tissue diagnostics (pericardial fluid cytology analysis and/ or pericardial biopsies).

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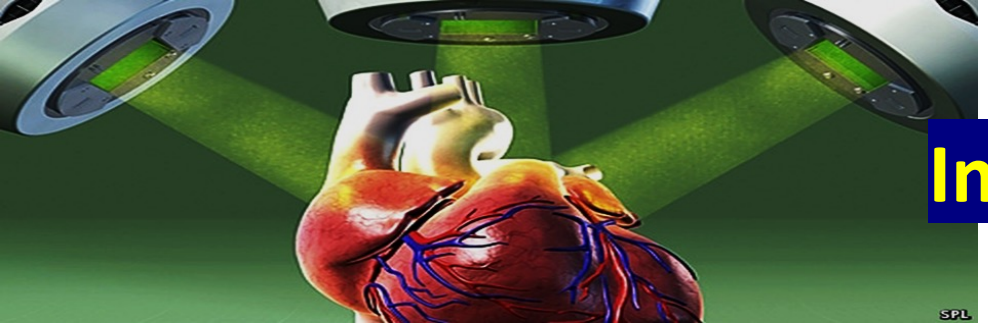

Important POINTS:

- New-onset pericardial disease in cancer pts can be caused by cancer therapy itself.
- It might also indicate progression of the primary neoplastic disease or Metastasis, treatment failure, or treatment resistance, which may require a change, rather than interruption of treatment.
- In most cases of acute pericarditis, RT can be completed if adequate symptom control can be achieved.
- Since CP is only a late disease manifestation occurring several years after RT exposure, and need precise consideration, diagnosis and treatment.

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Thank you
SO MUCH