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Myocardial damages after radiation therapy

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Case presentation

- A 60 year-old woman, with known case of hypothyroidism presented to our center with complaints of dyspnea on exertion and orthopnea, nor chest pain. She was a nonsmoker, had a body mass index of 21 kg/m^2, her blood pressure was 105/64 mmHg, heart rate was 110 bpm, and respiratory rate was 28/min. She had no family history of cardiomyopathy.
- She had been on daily oral levothyroxine .Six months before her referral, left breast cancer was diagnosed for the patient (invasive ductal cell carcinoma, positive estrogen receptor), and she underwent a left-sided mastectomy and conventional RT, which included 25 courses of 50-Gy external beam RT, delivered within 5 weeks.
- On physical examination, she had tachycardia and tachypnea; on auscultation, third and fourth heart sound (S3 and S4) and lung crackle were detected.

- TTE evaluation (performed before RT) showed an LV EF of 55% and a global longitudinal strain (GLS) of −19.2% .After RT, drop of LV EF to 30% (from 55%) and GLS to −11.2% (from 18.2%).
- The results of serum tests showed a high sensitivity troponin I level six times above the normal limit (up to 14 ng/L), as well as elevated N-terminal pro-B-type brain natriuretic peptide (NT pro-BNP) (six times above the normal limit). The results of CMR showed diffuse myocardial inflammation in T1 mapping and extracellular volume (ECV) map of LV, mid-wall late gadolinium enhancement (LGE) in basal segments of the interventricular septum (IVS), without an ischemic pattern of myocardial injury . Also, CT angiography follow-up showed patent coronary arteries.

Our challenges

- Matching the patient's clinical signs and symptoms with the European guideline for clinically suspected myocarditis, the diagnosis was considered as active myocarditis.

- signs & symptoms
- Diagnostic procedure
- therapeutic procedure

cardio toxic effects of RT is a known quantity, the frequency and severity of myocardial damage are not parallel in all patients and depend on several factors, including :

- the site of action
- radiation dose
- the method of administration
- and patients' characteristics
- underlying CVDs
- current or previous use of other antineoplastic therapies

Because of the proximity of the breast to the heart, RIHD can damage the heart and increase the risk of

- valvular heart disease
- coronary artery disease
- cardiomyopathy
- congestive heart failure
- acute myocardial infarction
- pericarditis (higher in those with left-sided breast cancer)

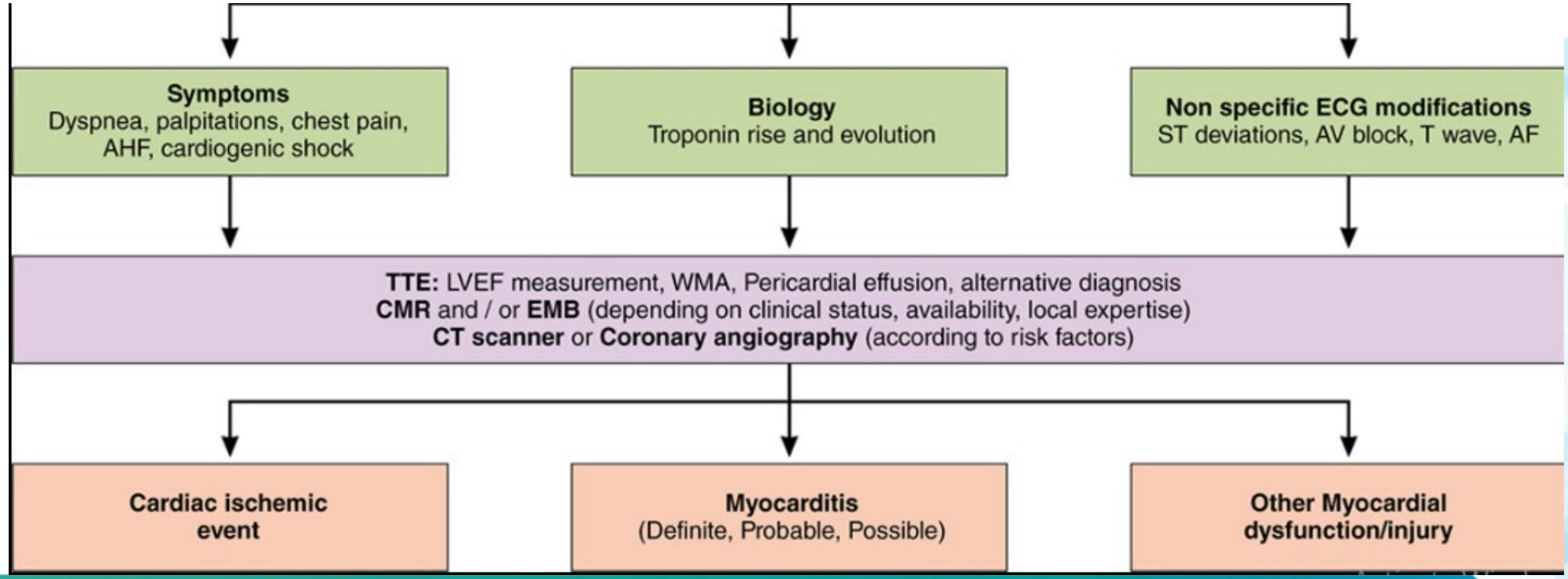
Myocarditis in Cancer Patients (Emerging Problem in Cardio-Oncology)

etiological factors for developing myocarditis:

- Classical or conventional chemotherapy
- radiation therapy
- immunotherapy
- Immunosuppression condition (bacterial and viral infections)

Definition of Myocarditis

- acute cardiac conditions without an alternative primary diagnosis (eg, acute coronary syndrome, trauma, etc).
- evidence of myocardial dysfunction and myocardial injury should be ascertained and accounted for even if not meeting a formal definition for myocarditis because these outcomes may represent subacute forms of myocarditis.



Clinical Presentation

Palpitations	chest pain	acute heart failure	chronic heart failure	pericarditis	pericardial effusion	mild degrees of ventricular dysfunction.

biomarker Elevations

- cardiac troponin
- CK-MB (creatine kinase–muscle/brain)
- total CK (creatine kinase)
- Natriuretic peptides

Biomarkers that may be useful for the diagnosis of myocarditis include markers of myonecrosis including

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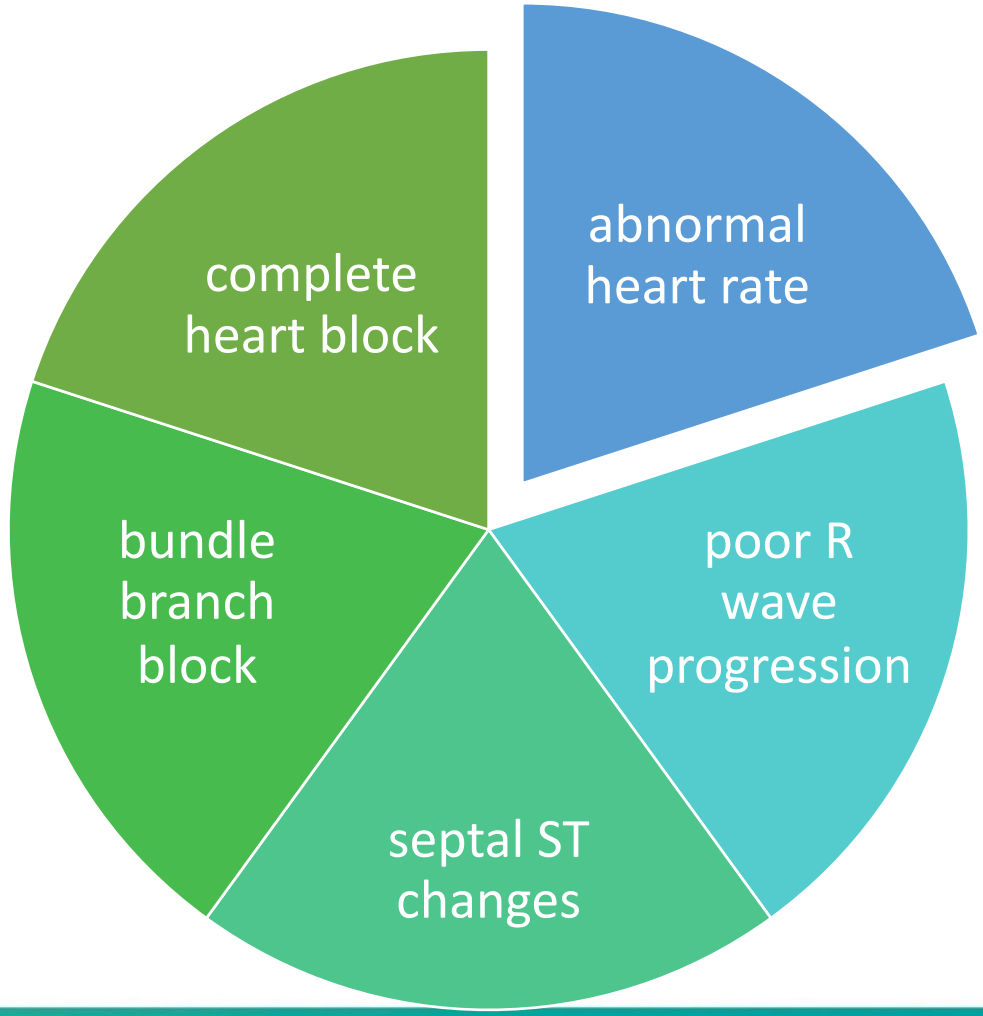
Natriuretic peptides are not specific for myocarditis but may be elevated in patients with significant left ventricular dysfunction and heart failure

ECG changes in acute phase



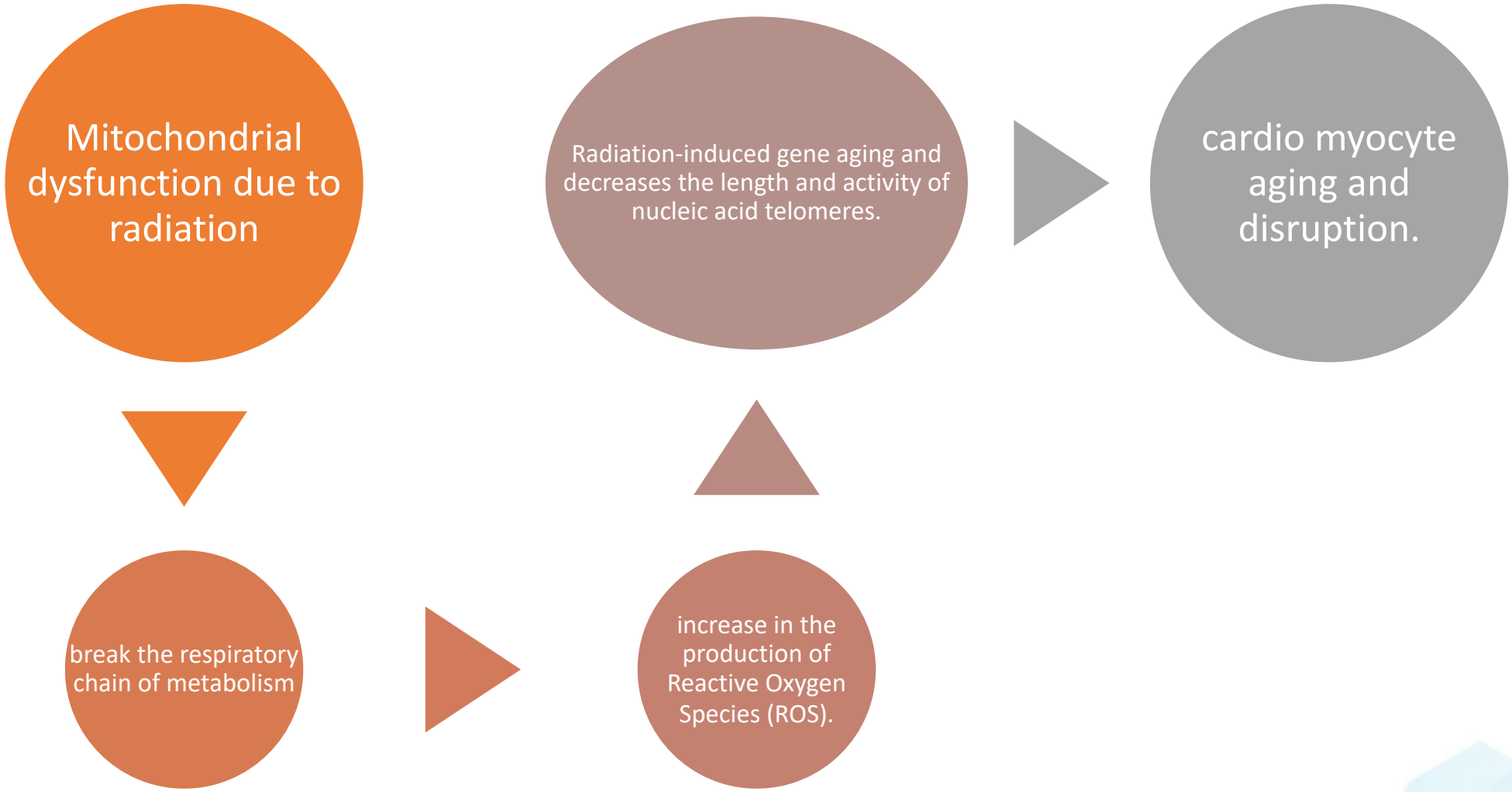
Imaging

echocardiography	• first line imaging study (diffuse , segmental wall motion abnormalities, and change in sphericity of the ventricle.) • Echocardiography is not specific for myocarditis and lacks sensitivity in cases in which systolic function is relatively preserved.
Cardiac magnetic resonance	• preferred imaging modality for the diagnosis • tissue characterization techniques
Positron emission tomography	• where CMR results are equivocal or patients not suitable for CMR

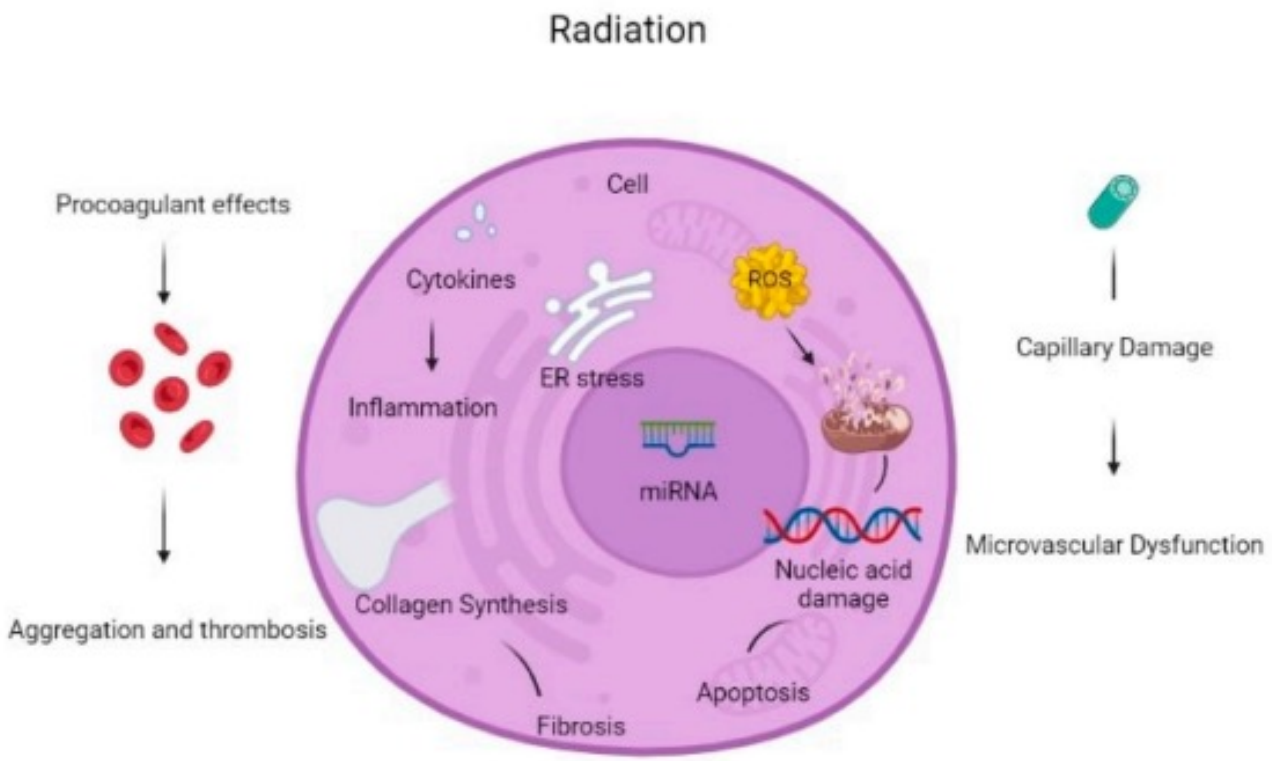
Endomyocardial Biopsy

endomyocardial biopsy should be considered when there is suspicion of the condition, and facilities and expertise should be made available for both the biopsy procedure and pathological processing and interpretation of the biopsy samples.

Mechanisms of Cardiotoxicity after Radiation Treatment



Summary of mechanisms of radiation-induced cardiac toxicities



Radiation significantly increases the risk of non-ischemic cardiomyopathies

The proinflammatory state

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differentiation of muscle cells into myofibroblasts

↓

collagen accumulation and fibrosis

↓

heart tissue remodeling

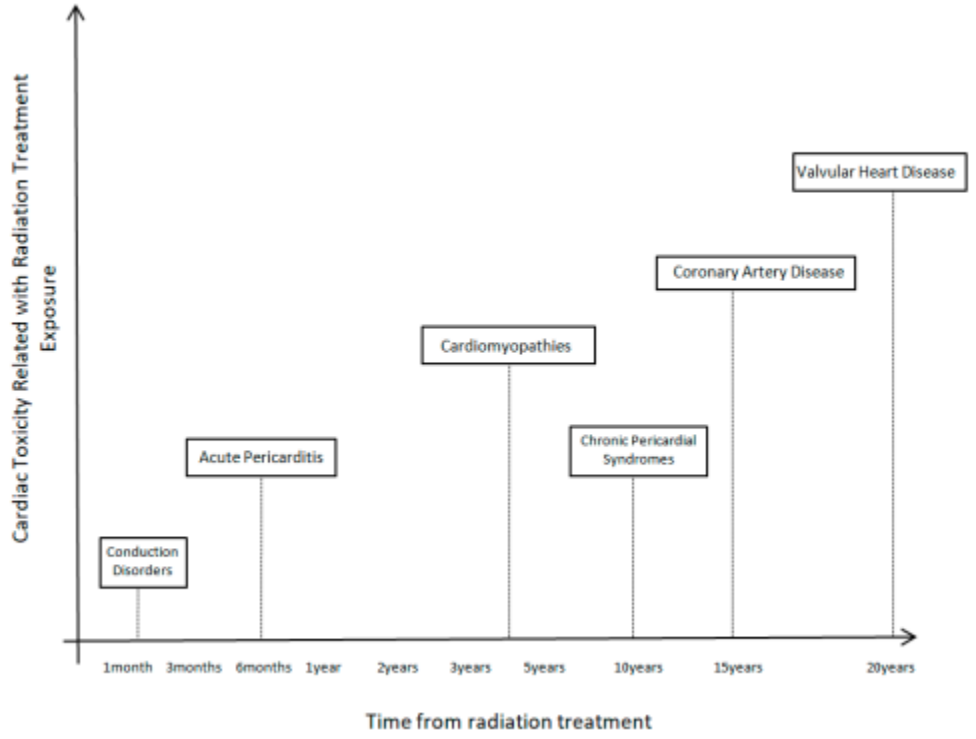
↓

diastolic dysfunction

Cardiac toxicities after radiation therapy exposure and chemotherapeutic agents

Cardiovascular System Adverse Effects of Cancer Treatments	Cardiac Toxicities of Radiation Therapy	Cardiac Toxicities of Chemotherapeutic Agents
Coronary Arteries	CAD	CAD (Fluoropyrimidines, VEGF inhibitors), Vasospasm, ACS (Fluoropyrimidines)
Valves	VHD	N/A
Heart Failure, Cardiomyopathies	HF	HF (Anthracyclines, Alkylating Agents, Proteasome Inhibitors, HER-2 antagonists, TKIs, VEGF, Taxanes)
Arrythmias	Conduction abnormalities	AF (Anthracyclines, Alkylating Agents, Fluoropyrimidines, TKIs, VEGF), Bradycardia (Taxanes)
Risk Factors	N/A	Hypertension (Proteasome Inhibitors)
Pericardial Syndromes	Acute and chronic	Acute pericarditis (Anthracyclines, Alkylating Agents), Chronic (ICI)
Thromboembolism	VTE, PE, Arterial	VTE, PE, Arterial (VEGF, Taxanes)
Myocardium	N/A	Myocarditis (ICI)
Pulmonary Vasculature	N/A	PH (TKIs)

Time course of cardiac toxicities after radiation treatment



- Treatment of myocarditis
- methylprednisolone 500–1000 mg i.v. bolus once daily for the first 3–5 days should be started as soon as possible, once the diagnosis is considered likely, to reduce MACE including mortality.
- If clinical improvement is observed (cTn reduced by .50% from peak level within 24–72 h and any LVD, AV block, and arrhythmias resolved), switching to oral prednisolone is recommended starting at 1 mg/kg up to 80 mg/day. reduction of oral prednisolone (most commonly by 10 mg per week) under clinical, ECG, and cTn surveillance should be considered . A reassessment of LV function and cTn should be considered when the prednisolone dose is reduced to 20 mg/day and then continue weaning the prednisolone by 5 mg per week to 5 mg/day, and a final reduction from 5 mg/day in 1-mg per week steps.

- If the troponin does not reduce significantly (.50% reduction from peak) and/or AV block, ventricular arrhythmias, or LVD persist despite 3 days of i.v. methylprednisolone plus cardiac treatments, then second-line immunosuppression should be considered.

Management (chronic phase)

- Heart failure symptoms from radiation are treated with standard medical therapy with beta blockers, angiotensin-converting enzyme inhibitors, and diuretics.
- In end-stage radiation-induced cardiomyopathy, cardiac transplant has shown to be an option although 5-year survival was lower in these patients compared with cardiomyopathy of other etiologies
- This was mostly attributed to early postoperative mortality from sternal wound dehiscence, wound infection, respiratory failure, and kidney injury. Death on the waiting list for transplant was not higher in patients having previously received radiation, suggesting that they were not sicker but had a more important operative risk. Although previous radiation therapy is not an absolute contraindication to cardiac transplantation, these patients should be carefully selected and monitored for postoperative complications.


Thank You