Post Radiation Cardiopathy
From Diagnosis to Management

- Japanese Life Span Study
- Mayak Worker Cohort
- Scandinavian Breast Cancer


Ioannis A. Paraskevaidis
Radiation-Induced CV Disease

Cumulative Incidences of Radiation Induced HD in Childhood

J.R.Cuomo et al. World J Cardiol 2016 September 26; 8(9): 504-519

The spectrum of Radiation Induced HD

RIHD

- Pericarditis constriction
- Valvular heart disease
- Cardiomyopathy
- Arrhythmia
- Coronary artery disease

Heart failure

- Pericardiectomy
- Valve surgery
- Volume management
- Pacemaker ICD/CRT-D
- PCI vs. CABG

Mechanical circulatory support/heart (lung) transplantation
Radiation-Induced IHD

Radiation-Induced Valvular HD

Long-Term Survival of pts With Radiation HD Undergoing Cardiac Surgery

Radiation-Induced Pericardial Disease

- Early acute pericarditis
- Delayed chronic pericardial effusion
- Constrictive pericarditis

Radiation-Induced Cardiomyopathy

- Diastolic dysfunction - restrictive cardiomyopathy

- Systolic dysfunction (only in conjunction with cardiotoxic chemotherapeutic agents)

✓ Vascular disease
Potential Targets for New Pharmacotherapies

N. Donis et al. EXPERT OPINION ON PHARMACOTHERAPY, 2018 doi: 10.1080/14656566.2018.1446080
Proposed Algorithm for Cardio-Oncologic Screening Following Radiotherapy

Focused history with physical examination
Assess for comorbidities like DM, HT, CRD, hypercholesterolemia, metabolic syndrome, and preexisting history of CAD.
Evaluate if patient receives only radiation / or in addition receives cardiotoxic chemotherapy like anthracyclines or trastuzumab
At the end of therapy, assess with biomarkers like BNP, Troponin I and Troponin T (experimental basis) as well as cardiac dose volume histogram parameters

Low risk in the absence of co-morbidities, adherence to cardiac dose constraints
Echocardiography at 10 years/Noninvasive stress test if any symptoms arise

High risk in the presence of co-morbidities, cardiac dose constraints not met
Early surveillance with echocardiography from 5 years onwards, yearly cardiac evaluation with noninvasive stress test at 10 years

During RT and immediate post treatment elevation of biomarkers-evaluate and treat initially as indicated and follow up with close scrutiny for long term events
If cardio toxic chemotherapy has been used with RT, follow up 6 monthly with echocardiography


Algorithm for the Management of pts Undergoing Chest Radiotherapy

Risk factors for RIHD
- Age <15 and >60
- Anterior or left chest radiation therapy
- Presence and extent of tumor in or next to the heart
- Lack of shielding
- High dose RT fractions (>2 Gy/day) and/or high cumulative RT dose (>30 Gy) - a "safe" dose cutoff is not defined
- Concomitant chemotherapy
- Any CV risk factor
- Pre-existing CV disease, especially known CAD and prior MI

Define cardiac risk

Mediastinal/thoracic radiation therapy

Yearly HPI and physical

Signs or symptoms of cardiovascular disease?

Assess and optimize modifiable CV risk factors

Screening TTE
- Every 5 y, starting 5 y after RT in pt with one RIHD risk factor and 10 y after RT in pt with no RIHD risk factor

Screening stress test
(exercise echo ±O₂ consumption study preferred, may consider CCTA)
- Every 5 y after RT
- Additional early evaluation at 2 y after RT if >60 y, ≥1 CV risk factor, known CAD, or vasotoxic cancer drugs

Pericardial effusion or constriction
- TTE ± CT, MRI, or hemodynamic cath

Valvular heart disease
- TTE ± hemodynamic cath

Cardiomyopathy
- TTE ± hemodynamic cath

Arrhythmia
- ECG, Holter, event monitor

Coronary artery disease
- Coronary angiography

Gated chest CT for assessment of mediastinal fibrosis, porcelain aorta, internal mammary arteries, etc.
For interventional planning (catheter-based and/or surgical Heart Team approach)

Iliescu CA et al, Catheter Cardiovasc Interv 2016;87(5):E206
### Radiation-Induced Heart Disease: Diagnosis and Management

#### Pericardial Disease

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>6%–30%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Pericarditis (acute or chronic), pericardial effusion, pericardial constriction. Most common manifestation of radiation-induced heart disease, and a diagnosis of exclusion. Due to inflammation and impaired drainages to the pericardial surface, fibrotic changes to the parietal pericardium. Acute pericarditis is often self-limiting. Chronic pericarditis is often effusive-constrictive.</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Diagnosis of exclusion after other causes of pericardial disease have been ruled out</td>
</tr>
<tr>
<td>Management</td>
<td>Anti-inflammatory drugs for pericarditis, pericardiocentesis for large effusions or tamponade, pericardial window for recurrent pericardial effusions, pericardial stripping for constrictive pericarditis</td>
</tr>
</tbody>
</table>

#### Coronary Artery Disease

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Up to 85%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Due to epicardial coronary arteries and microcirculatory damage, and sustained inflammation. Usually occurs 10 yrs after radiation therapy. Involves the LM, ostial LAD, and RCA. Lesions are longer, concentric, and tubular.</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Stress echocardiography (could also screen for other causes of RIHD, other than CAD); or stress perfusion imaging; cardiac CTA; possible role for coronary calcium screening</td>
</tr>
<tr>
<td>Management</td>
<td>Percutaneous coronary angioplasty or coronary artery bypass graft (challenging surgery due to fibrosis of pericardium and mediastinum). Aggressive cardiovascular risk factor modification</td>
</tr>
</tbody>
</table>

#### Valvular Heart Disease

| Prevalence   | 10 yrs: 26% AI, 39% MR, 16% TR, and 7% PR  
20 yrs: 60% AI, 16% AS, 52% MR, 26% TR, and 12% PR |
<table>
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<tr>
<td>Description</td>
<td>Mean time interval of 12 yrs after radiation. Diffuse fibrosis of the valvular cusps or leaflets, with or without calcification; no post-inflammatory changes noted. Left-sided valves &gt; right-sided valves. Initial regurgitation related to valve retraction, later stenosis related to thickening/calcification</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Echocardiogram, cardiac magnetic resonance imaging</td>
</tr>
</tbody>
</table>
| Management   | Serial monitoring with timing of surgery as in ACC/AHA guidelines  
Valve replacement is preferred over valve repair  
Consider TAVR, if mediastinum and cardiac anatomy is not amenable to open heart surgery |
### TABLE 4  Radiation-Induced Heart Disease: Diagnosis and Management

#### Conduction System Abnormalities

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Up to 5%</th>
</tr>
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<tbody>
<tr>
<td>Description</td>
<td>A-V nodal block (including high-degree block), bundle branch block (right &gt; left), fascicular block. Tachycardia can be persistent, usually a result of autonomic dysfunction, similar to denervated hearts. Persistent tachycardia could increase risk of tachycardia-induced cardiomyopathy.</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>ECG, telemetry/ambulatory Holter monitor</td>
</tr>
<tr>
<td>Management</td>
<td>Permanent pacemaker for high-degree A-V block. ICD for life-threatening arrhythmia, sudden death, or secondary prevention. Consider subpectoral approach for device implantation, if subcutaneous involvement of thoracic radiation</td>
</tr>
</tbody>
</table>

#### Cardiomyopathy

<table>
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<tr>
<th>Prevalence</th>
<th>Up to 10%</th>
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<tr>
<td>Description</td>
<td>Diastolic dysfunction &gt; systolic dysfunction; right ventricle &gt; left ventricle. Due to increased fibrosis in all 3 layers of the ventricular walls (epicardium, myocardium, and endocardium). May lead to restrictive cardiomyopathy, and rarely to systolic dysfunction.</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Echocardiogram, cardiac magnetic resonance imaging</td>
</tr>
<tr>
<td>Management</td>
<td>Slow upward titration of ACEI, beta-blockade, and aldosterone inhibitors in patients with reduced left ventricular systolic function; optimize risk factors for diastolic dysfunction, exercise training; Inotropic support, VAD, heart transplantation</td>
</tr>
</tbody>
</table>
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Time trends of clinical and experimental studies reporting on radiation induced heart disease in PubMed


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