Cancer and the Heart
An update on cardio-oncology

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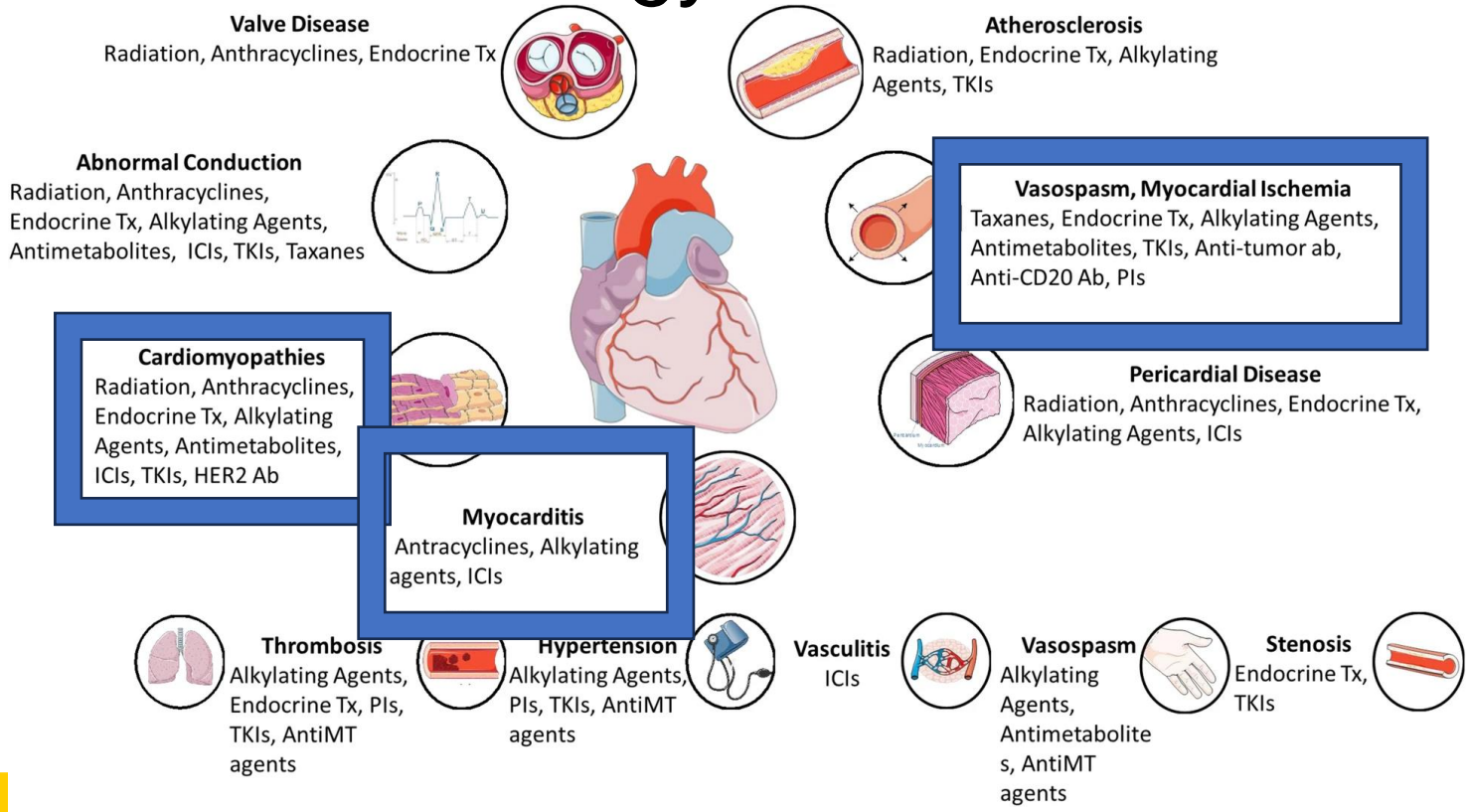
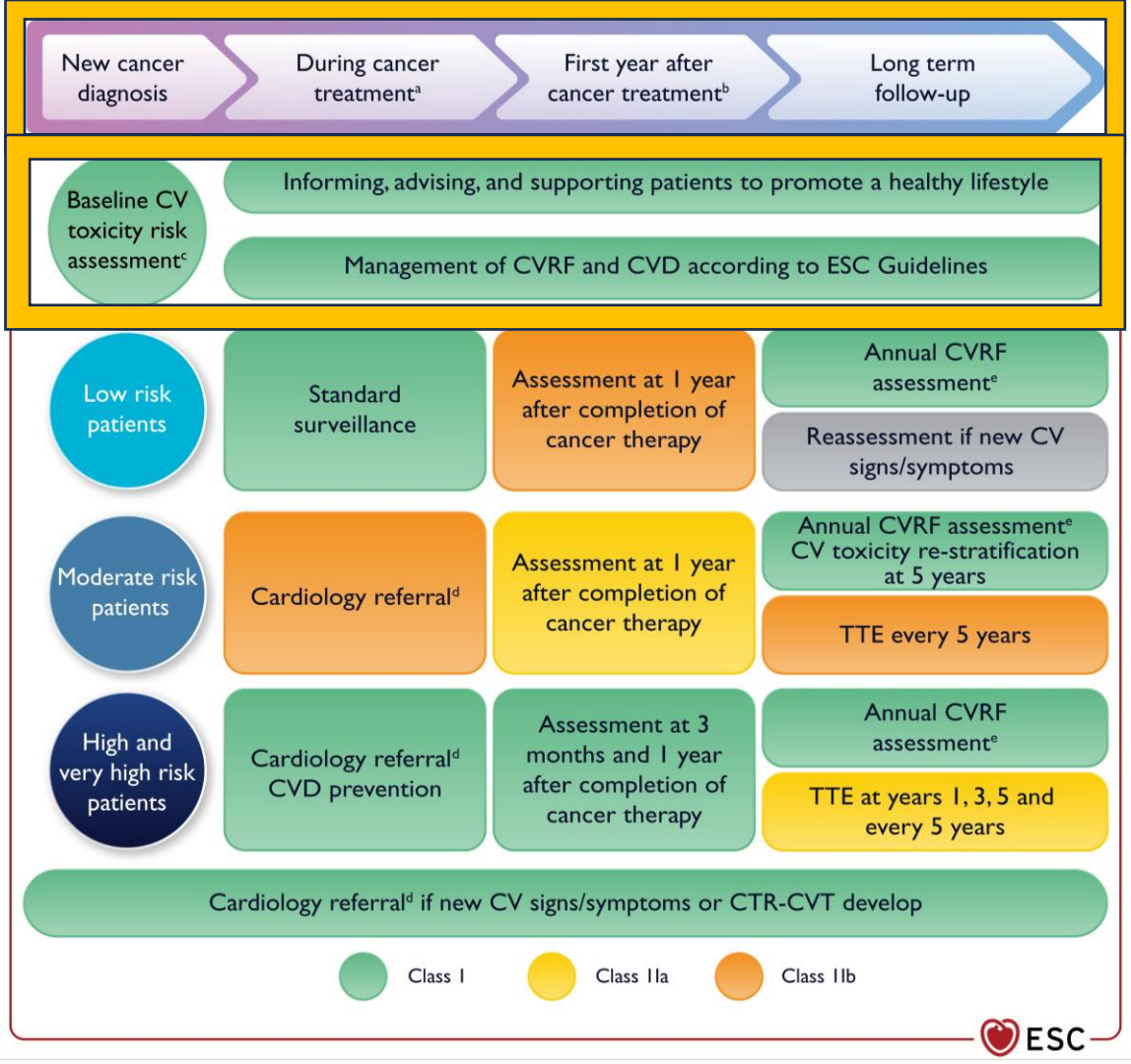
No disclosures.

What is cardio-oncology?





Cardio-oncology care

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Which patients are at increased risk for cardiotoxicity?

Treatment-specific risk factors
- High dose anthracycline (≥ 250mg/m^2 doxorubicin)
- High-dose radiotherapy (≥ 30Gy) with heart in the treatment field
- Low dose anthracycline + low dose RT
- Low dose anthracycline + anti-HER2 therapy
- Proteasome inhibitors
- Tyrosine kinase inhibitors (risk depends on profile of inhibition)
- VEGF inhibitors
- Immune checkpoint inhibitors - ICIs

Patient-specific risk factors
- ≥ 2 cardiovascular risk factors (e.g. smoking, hypertension, diabetes, hyperlipidemia, obesity)
- Age ≥ 60 years
- Compromised cardiac function (e.g. borderline low LVEF 50-55%, h/o myocardial infarction, > moderate valve disease)

Armenian et al. J Clin Oncol. 2017; 35: 893-911.

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Incidence of LV dysfunction with various Chemotherapeutics

Chemotherapy Agents	Frequency of Use	Incidence (%)	Prevention/Treatment
Anthracyclines			
Doxorubicin	++++	3-26	Monitor EF, GLS, troponin dexrazoxane, continuous infusion, liposomal preparation, BB/ACEI
Epirubicin	+	0.9-3.3	
Idarubicin	++	5-18	
Alkylating agents			
Cyclophosphamide	++++	7-28	
Ifosfamide	+++	17	
Antimetabolites			
Decitabine	++	5	
Clofarabine	+	27	
Antimicrotubule agents			
Docetaxel	++	2.3-8.0	
Monoclonal antibody-based tyrosine kinase inhibitors			
Trastuzumab	+++	2-28	Avoid concomitant use with anthracyclines
Bevacizumab	++	1.0-10.9	
Adotrastuzumab emtansine	+	1.8	
Pertuzumab	+	0.9-16.0	
Small molecule tyrosine kinase inhibitors			
Pazopanib	++++	0.6-11.0	Treat hypertension aggressively
Ponatinib	+	3-15	Ischemia workup and treatment
Sorafenib	++++	1.9-11.0	
Dabrafenib	++++	8-9	
Sunitinib	++++	1-27	
Dasatinib	++++	8-9	
Lapatinib	++++	0.9-4.9	
Trametanib	++++	7-11	
Proteasome inhibitor			
Carfilzomib	++	7	
Bortezomib	++	2-5	
Miscellaneous			
Tretinoin	++++	6	

Chang et al. J Am Coll Cardiol. 2017; 20:2536-51.

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Screening prior to treatment – ASCO and ESC

- Assessment and modification of risk factors
- TTE prior to initiation of potentially cardiotoxic therapies

- NT pro-BNP and troponin
  - Chemotherapy with anthracyclines, HER2 inhibitors and other Protease inhibitors in patients with significant CV risk factors or decreased LVEF at baseline
  - Immune checkpoint inhibitors

  - CAR-T cell therapy

Armenian et al. J Clin Oncol. 2017; 35: 893-911.

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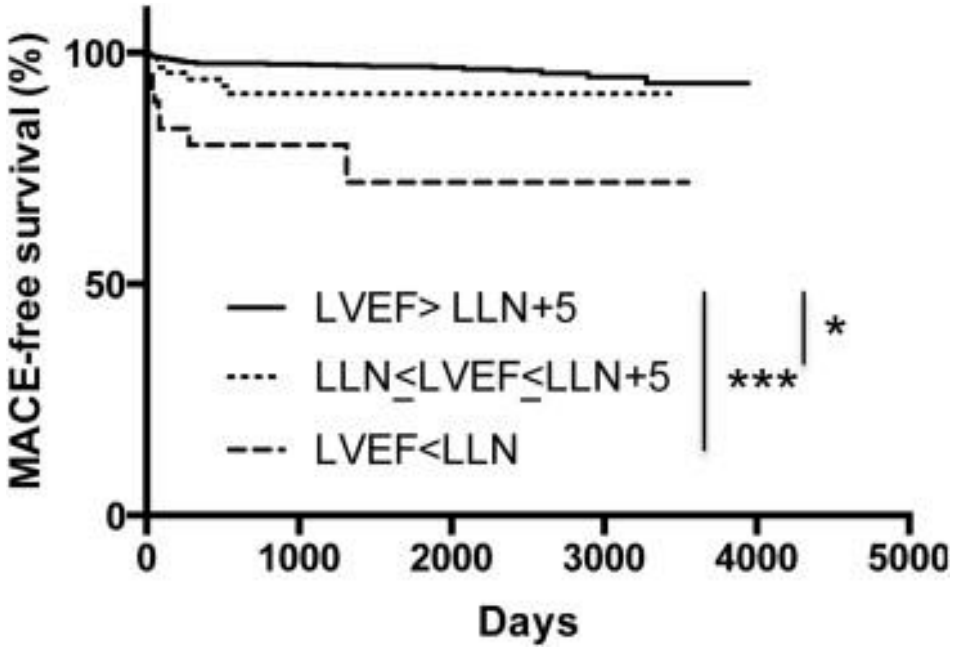
Why should I order a TTE before chemotherapy with cardiotoxic chemotherapy?
What should I order?

Baseline assessment: Does LVEF before therapy with anthracyclines predict the risk of MACE?



Wang et al, Am J Card, 2015

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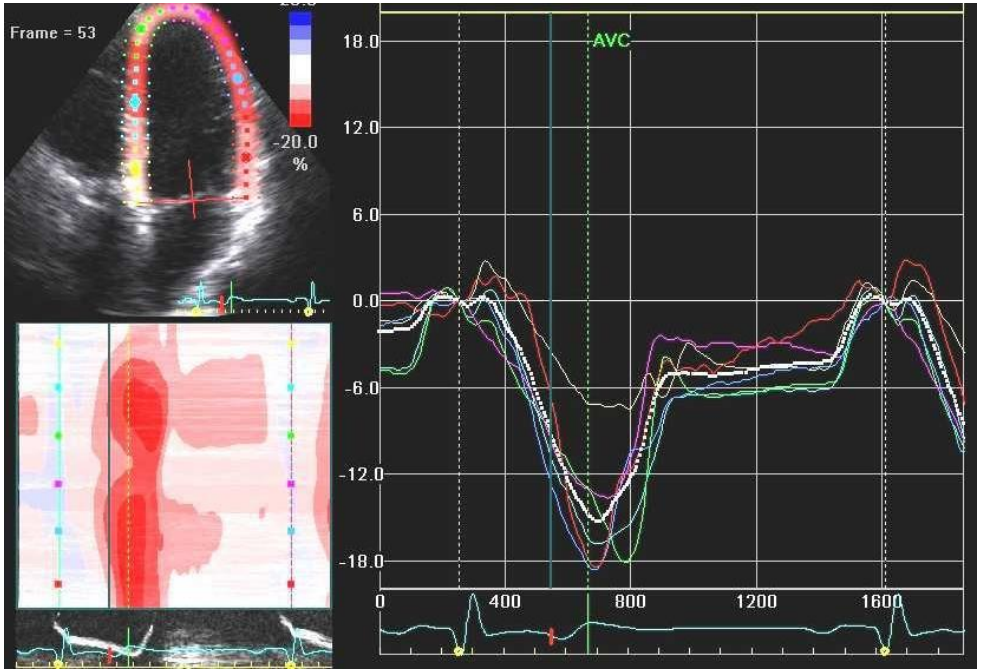
Recommended imaging

- TTE or cMRI
- TTE should include 3D EF and global longitudinal strain (GLS)



I have a referral for LV dysfunction under chemotherapy.
What should I do?

Cancer therapy-related cardiac dysfunction - Definition

CTRCD		
Symptomatic CTRCD (HF)[a,b]	Very severe	HF requiring inotropic support, mechanical circulatory support, or consideration of transplantation
	Severe	HF hospitalization
	Moderate	Need for outpatient intensification of diuretic and HF therapy
	Mild	Mild HF symptoms, no intensification of therapy required
Asymptomatic CTRCD	Severe	New LVEF reduction to <40%
	Moderate	New LVEF reduction by ≥10 percentage points to an LVEF of 40–49% *OR* New LVEF reduction by <10 percentage points to an LVEF of 40–49% AND either new relative decline in GLS by >15% from baseline OR new rise in cardiac biomarkers[c]
	Mild	LVEF ≥ ***50%*** AND new relative decline in GLS by >15% from baseline AND/OR new rise in cardiac biomarkers[c]

Eur Heart J, Volume 43, Issue 41, 1 November 2022,
Pages 4229–4361,
https://doi.org/10.1093/eurheartj/ehac244

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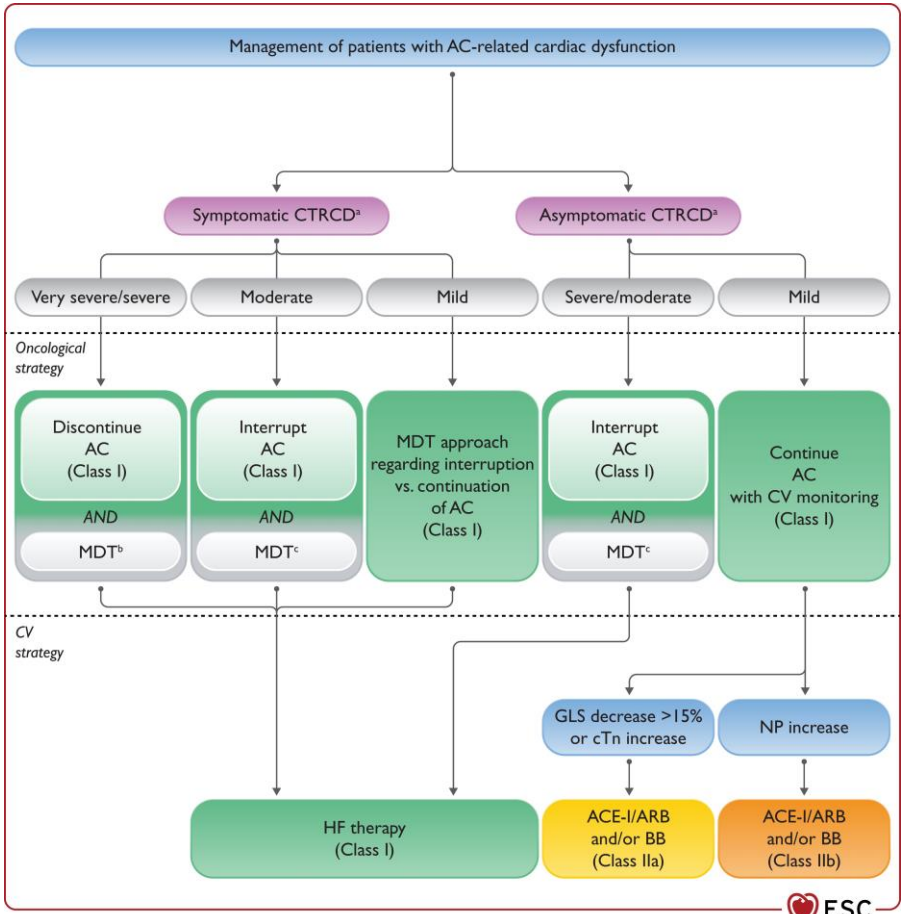
Management of anthracycline chemotherapy-related cardiac dysfunction.



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Management of human epidermal receptor 2-targeted therapy-related cardiac dysfunction.

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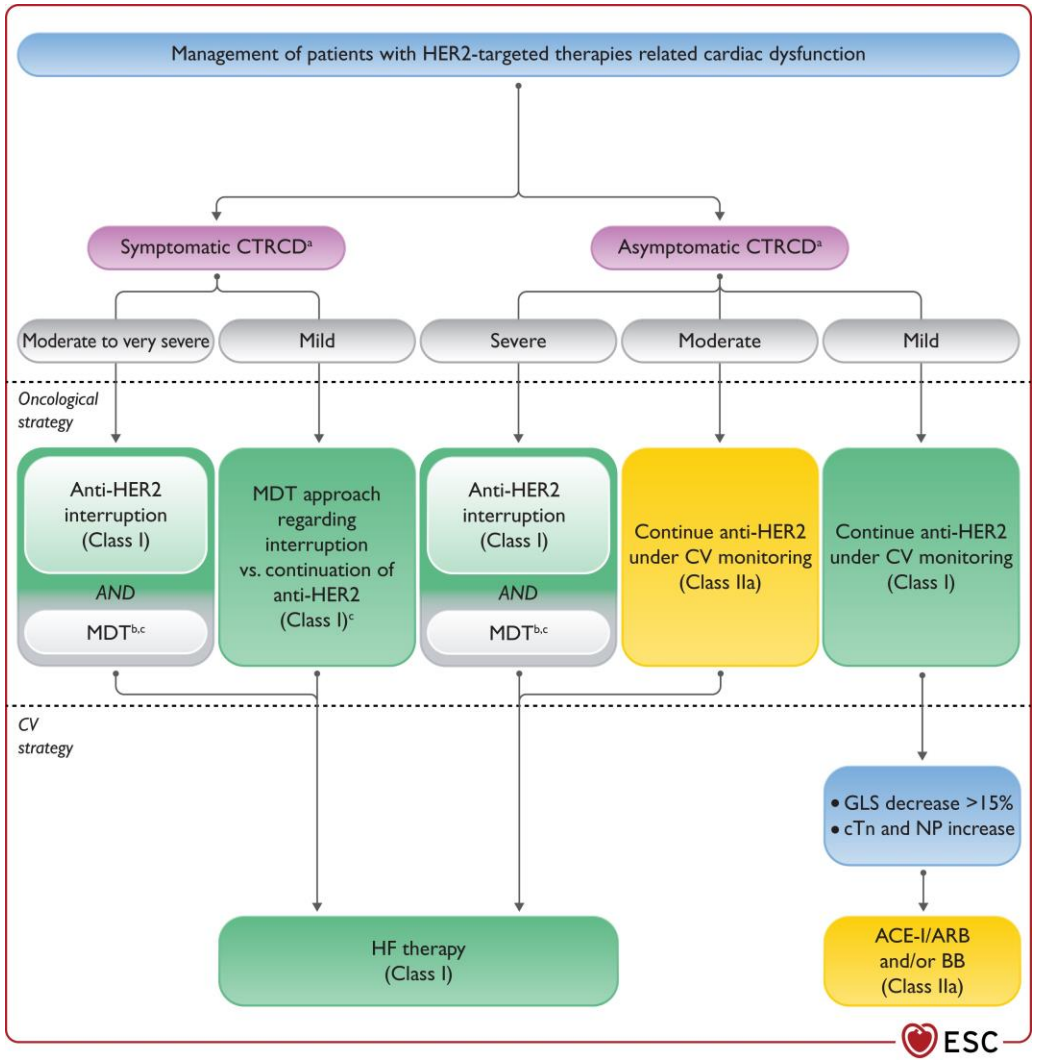
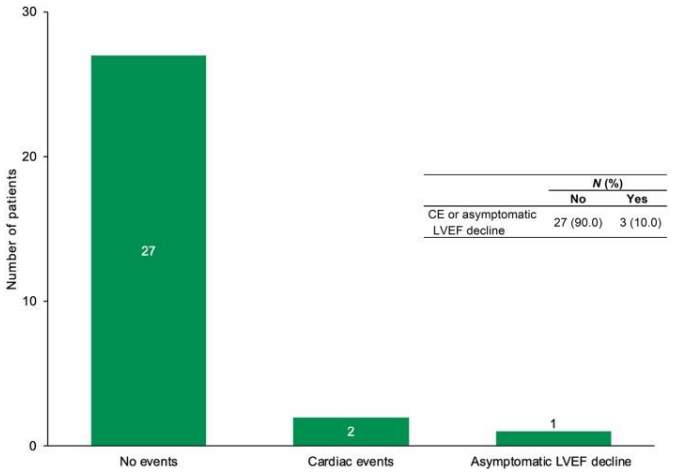
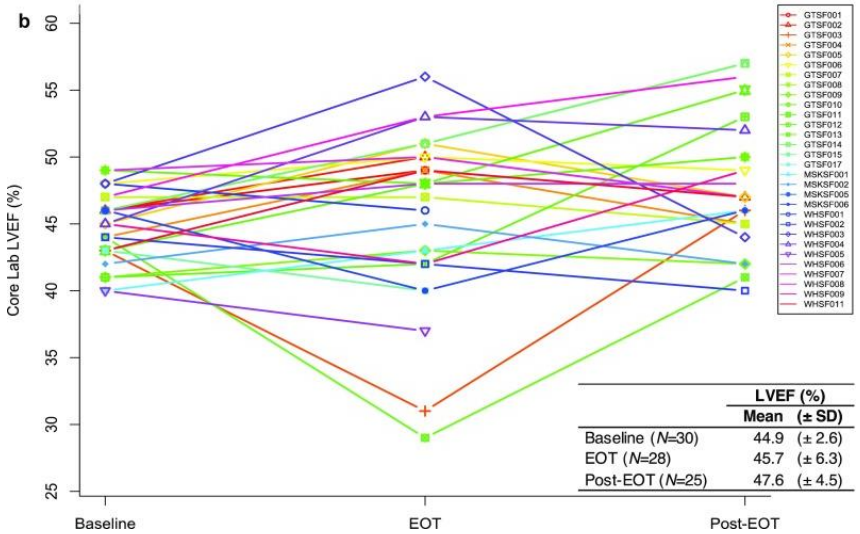


SAFE-HEART trial: can Her2 therapies be safely administered without interruptions in patients with cardiac dysfunction?





Lynce, Breast Cancer Res and Treatment, 2019

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How often do I order an imaging study during chemotherapy and for how long after?

Repeat imaging during chemotherapy

Anthracyclines:

- Repeat studies are recommended for symptomatic patients.
- Surveillance imaging may be offered during treatment in asymptomatic patients at increased risk.
- Frequency should be determined based on clinical judgment and circumstances.

HER2R inhibitors:

- Imaging every three months.

Imaging after end of chemotherapy

Anthracyclines:

- Low risk patients: In the first 6-12 months after end of chemotherapy, then every 5 years,
- High risk patients: In the first 3 years annually, and then once every ~ 3 years.

HER2 blockers:

- In the first 6-12 months after end of chemotherapy.

I have a referral for chest pain under 5-FU chemotherapy.
What should I consider?

5-FU-induced cardiotoxicity

- Oncologic mainstay (colon, breast, pancreatic, head/neck, esophageal and gastric cancers)
- Given as bolus or continuous infusion
- Capecitabine is a prodrug and given p.o.

- Cardiotoxicity (chest pain and ECG changes) known since the 1970's
- Causes vasospasm (other mechanisms implicated, including endothelial damage and cardiac metabolic derangement)
- Symptoms: chest pain, MI, stress-induced cardiomyopathy (Takotsubo), ventricular arrhythmias

5-FU-induced cardiotoxicity

- Change from Capecitabine or continuous infusion to bolus

- Work-up and treatment of CAD
- Consider stress test on 5FU
- Admission for next cycle 5FU
- Pretreatment with Nitrates and/or Nifedipine

I have heard that patients with immune checkpoint inhibitor myocarditis have a terrible prognosis.
What do I need to know?

Checkpoint inhibitor-induced myocarditis

- Clinical presentation:
  - Develops in the first weeks after start of treatment (~ day 40)
  - Is often accompanied by other symptoms, such as myositis
  - Heart failure symptoms are less common (50% have EF >50%)
  - Conduction disease, complete heart block, ventricular arrhythmias
- Incidence
  - ??? 0.1-5%, depending on criteria, higher with combination therapy
  - Less common than other CI side effects (diarrhea, colitis, rash)
- Outcome:
  - Major adverse cardiac endpoints (cardiovascular death, cardiac arrest, hemodynamically significant arrhythmias/heart block/cardiogenic shock) up to 50%;
  - Mortality 25-50%.

Mahmoud et al. J Am Coll Cardiol. 2018;71:1755-64. Escudier et al. Circulation. 2017. 136: 2085-87.

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Cardiovascular surveillance in patients treated with immune checkpoint inhibitors.

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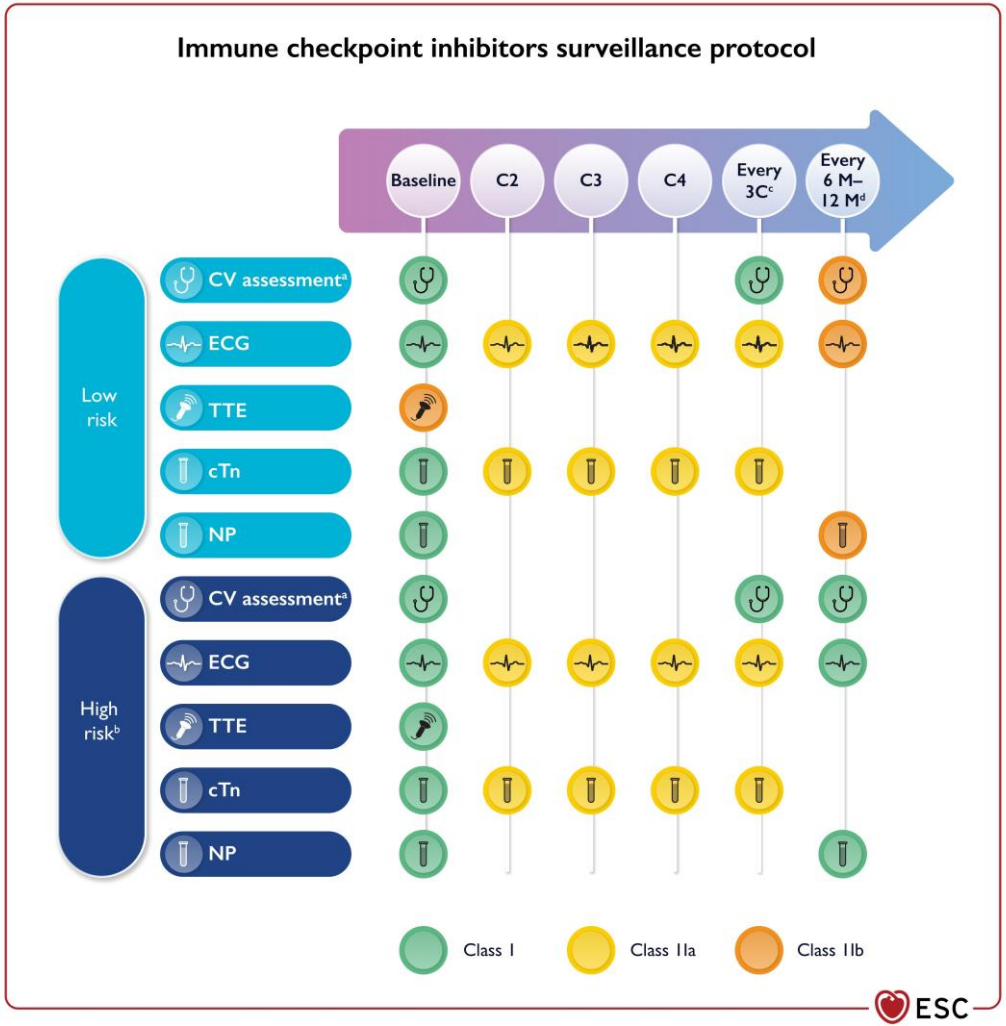

Diagnosis and management of immune checkpoint inhibitor-related myocarditis.

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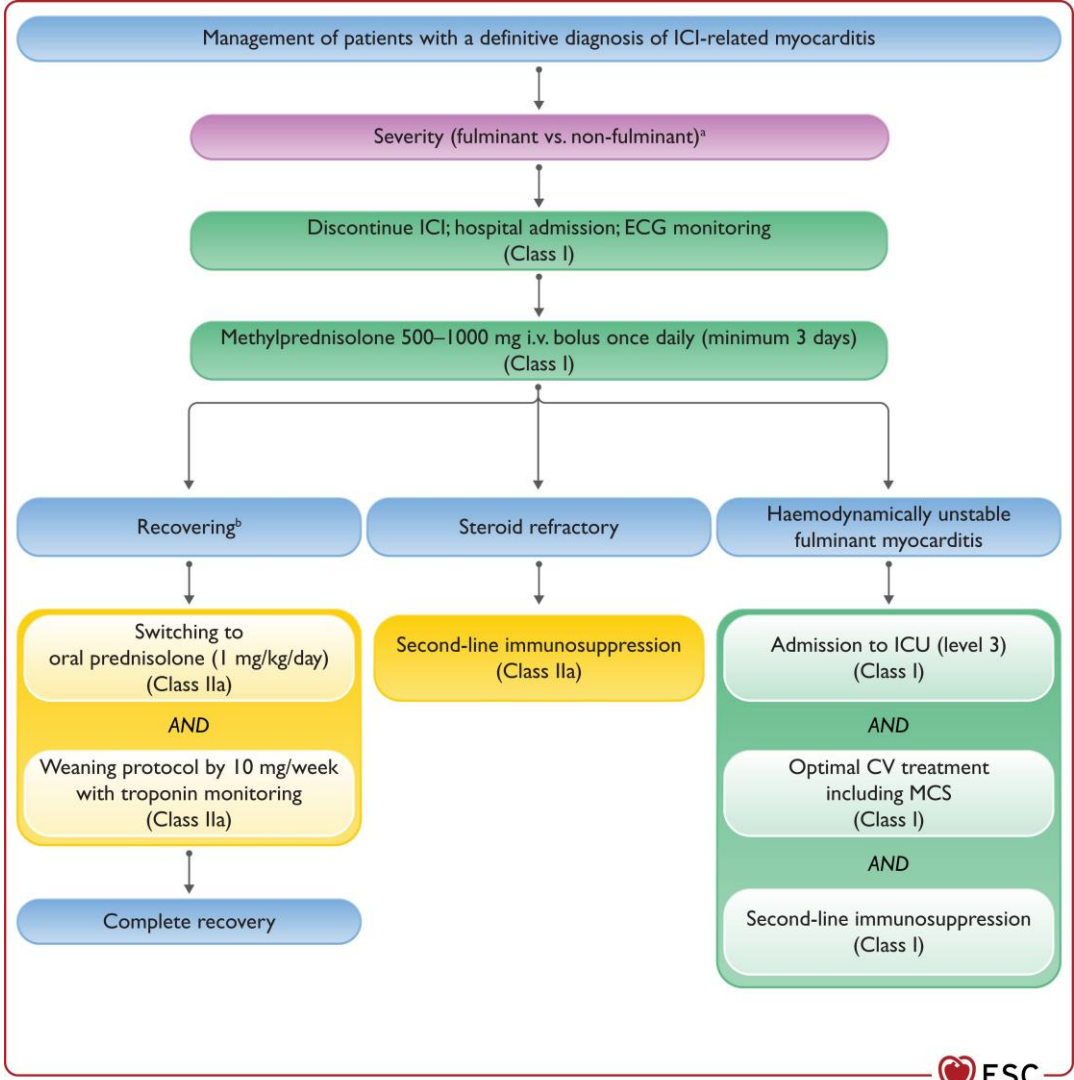

Cancer and the Heart

- Risk factor modification and guideline-directed CV therapy in patients at high risk of cardiotoxicity
- Baseline TTE, sometimes ECG and biomarkers for patient receiving cardiotoxic chemotherapy

- Surveillance of symptoms and imaging as needed until one year after end of chemotherapy for Dox and HER2R blockers
- Guideline-directed therapy for LV dysfunction, discuss discontinuation if LV < 40%
- 5FU –related symptoms: bolus 5FU, nitrates and nifedipine
- ICI myocarditis: rare but can be fulminant, high dose steroids as first line treatment

Questions?

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Thank you

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First TTE after 12 years: