31 GIORNATE CARDIOLOGICHE TORINESI

TURIN
October
24th-26th
2019

Cardioncology: is there a common clinical practice?

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Cardioncology Unit
European Institute of Oncology - Milan - Italy

Torino, 24th October 2019

4 KEY POINTS

RISK STRATIFICATION

PREVENTION

EARLY DETECTION

TREATMENT

ASCO SPECIAL ARTICLE

Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline

Clinical Question 1: Which patients with cancer are at increased risk for developing cardiac dysfunction?

Recommendation 1.1. It is recommended that patients with cancer who meet any of the following criteria should be considered at increased risk for developing cardiac dysfunction.

- Treatment that includes any of the following:
  - High-dose anthracycline (eg, doxorubicin ≥ 250 mg/m^2, epirubicin ≥ 600 mg/m^2)
  - High-dose RT (≥ 30 Gy) where the heart is in the treatment field
  - Lower-dose anthracycline (eg, doxorubicin < 250 mg/m^2, epirubicin < 600 mg/m^2) in combination with lower-dose RT (< 30 Gy) where the heart is in the treatment field
- Treatment with lower-dose anthracycline (eg, doxorubicin < 250 mg/m^2, epirubicin < 600 mg/m^2) or trastuzumab alone, and presence of any of the following risk factors:
  - Multiple cardiovascular risk factors (≥ two risk factors), including smoking, hypertension, diabetes, dyslipidemia, and obesity, during or after completion of therapy
  - Older age (≥ 60 years) at cancer treatment
  - Compromised cardiac function (eg, borderline low LVEF [50% to 55%], history of myocardial infarction, ≥ moderate valvular heart disease) at any time before or during treatment
- Treatment with lower-dose anthracycline (eg, doxorubicin < 250 mg/m^2, epirubicin < 600 mg/m^2) followed by trastuzumab (sequential therapy)

JCO 2016

European Heart Journal
doi:10.1093/eurheartj/ehw211

ESC CPG POSITION PAPER

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines

Table 4 Baseline risk factors for cardiotoxicity

Current myocardial disease	*Demographic and other CV risk factors*
• Heart failure (with either preserved or reduced ejection fraction) • Asymptomatic LV dysfunction (LVEF <50% or high natriuretic peptide[a]) • Evidence of CAD (previous myocardial infarction, angina, PCI or CABG, myocardial ischaemia) • Moderate and severe VHD with LVH or LV impairment • Hypertensive heart disease with LV hypertrophy • Hypertrophic cardiomyopathy • Dilated cardiomyopathy • Restrictive cardiomyopathy • Cardiac sarcoidosis with myocardial involvement • Significant cardiac arrhythmias (e.g. AF, ventricular tachyarrhythmias)	• Age (paediatric population <18 years; >50 years for trastuzumab; >65 years for anthracyclines) • Family history of premature CV disease (<50 years) • Arterial hypertension • Diabetes mellitus • Hypercholesterolaemia
Previous cardiotoxic cancer treatment	***Lifestyle risk factors***
• Prior anthracycline use • Prior radiotherapy to chest or mediastinum	• Smoking • High alcohol intake • Obesity • Sedentary habit

Dose??

Rationale for setting up a cardio-oncology unit: our experience at Mayo Clinic

MAYO CLINIC PROCEEDINGS

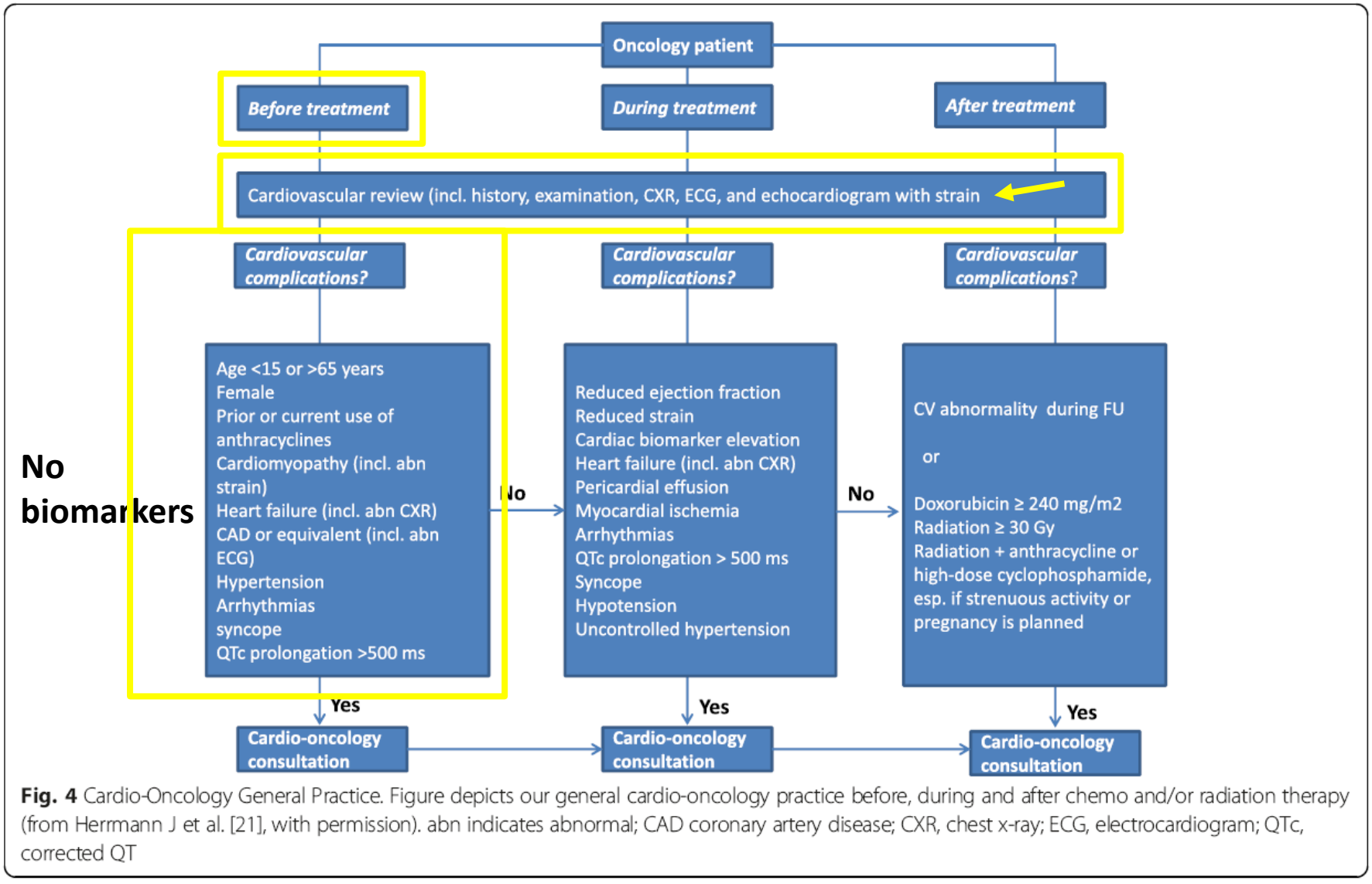

Fig. 4 Cardio-Oncology General Practice. Figure depicts our general cardio-oncology practice before, during and after chemo and/or radiation therapy (from Herrmann J et al. [21], with permission). abn indicates abnormal; CAD coronary artery disease; CXR, chest x-ray; ECG, electrocardiogram; QTc, corrected QT

Rev Esp Cardiol. 2017;70(6):474–486

Artículo especial

Cardio-Onco-Hematología en la práctica clínica. Documento de consenso y recomendaciones

Teresa López-Fernández[a,b,*], Ana Martín García[b,c], Ana Santaballa Beltrán[b,d], Ángel Montero Luis[b,e],

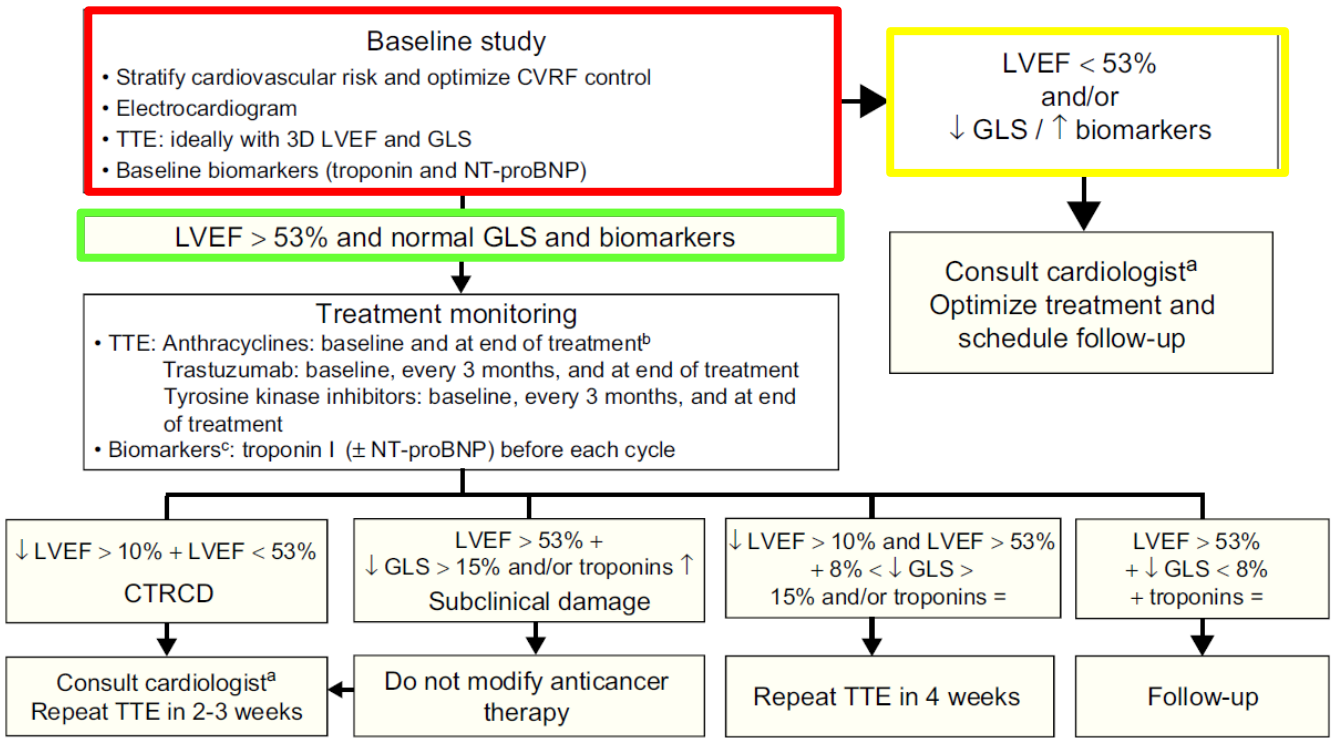

Figure 2. Monitoring algorithm for anticancer drug therapy.[14] 3D, 3-dimensional; CTRCD, cancer therapeutics-related cardiac dysfunction; CVRFs, cardiovascular risk factors; GLS, global longitudinal strain; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B type natriuretic peptide; TTE, transthoracic echocardiography. [a]Ideally, a specialist cardio-onco-hematology clinic. [b]Reevaluation of LVEF is recommended before treatment completion if the cumulative dose exceeds 240 mg/m^2. In these patients, the LVEF should be regularly monitored until the end of treatment. [c]In patients with low cardiovascular risk and without history of cardiotoxic treatment, determination of troponin levels before each cycle reduces the number of echocardiograms required and limits their use to symptomatic patients or those with troponin elevation.

Supplement submission

OPEN

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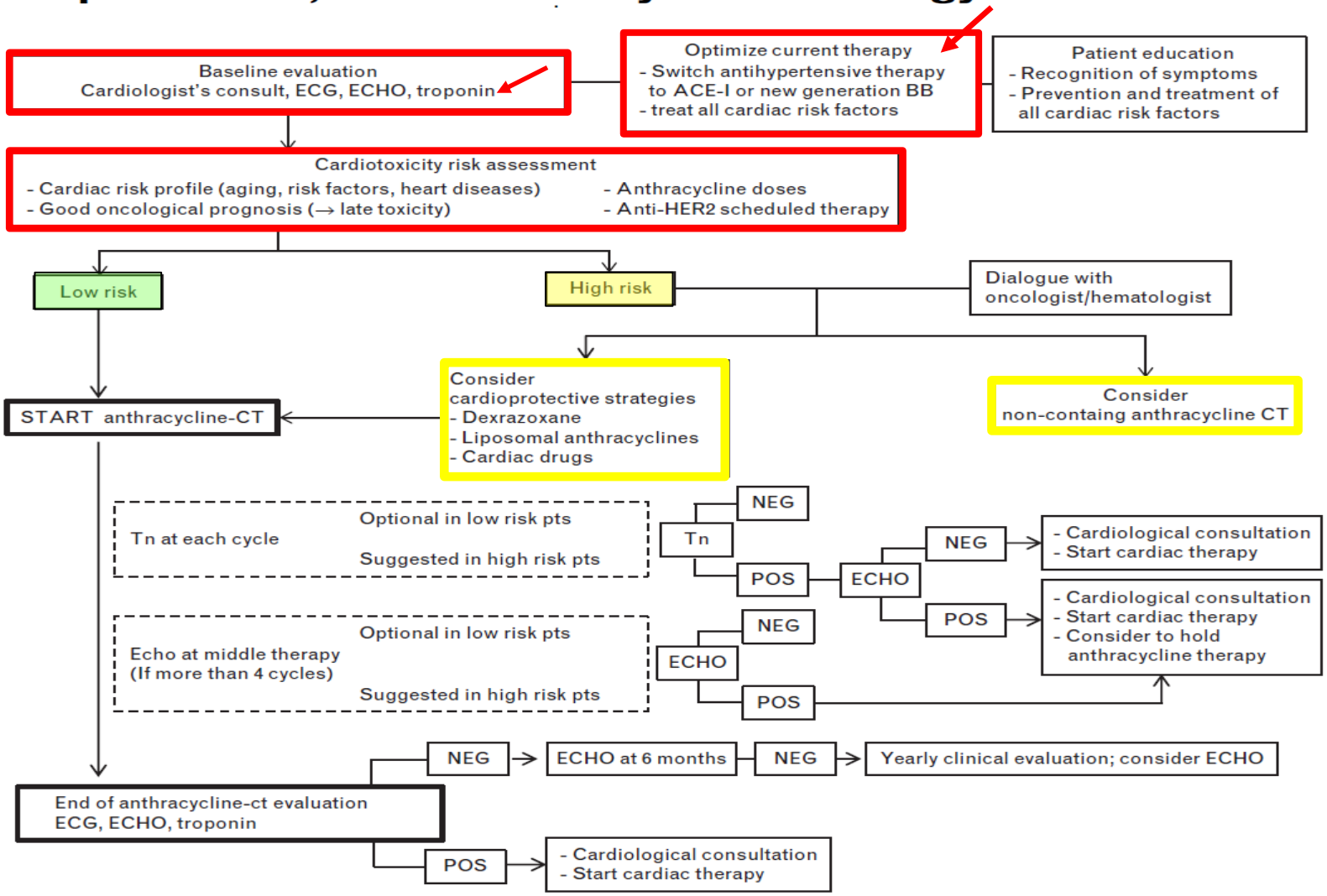
Italian Federation of Cardiology

A recommended practical approach to the management of anthracycline-based chemotherapy cardiotoxicity: an opinion paper of the working group on drug cardiotoxicity and cardioprotection, Italian Society of Cardiology



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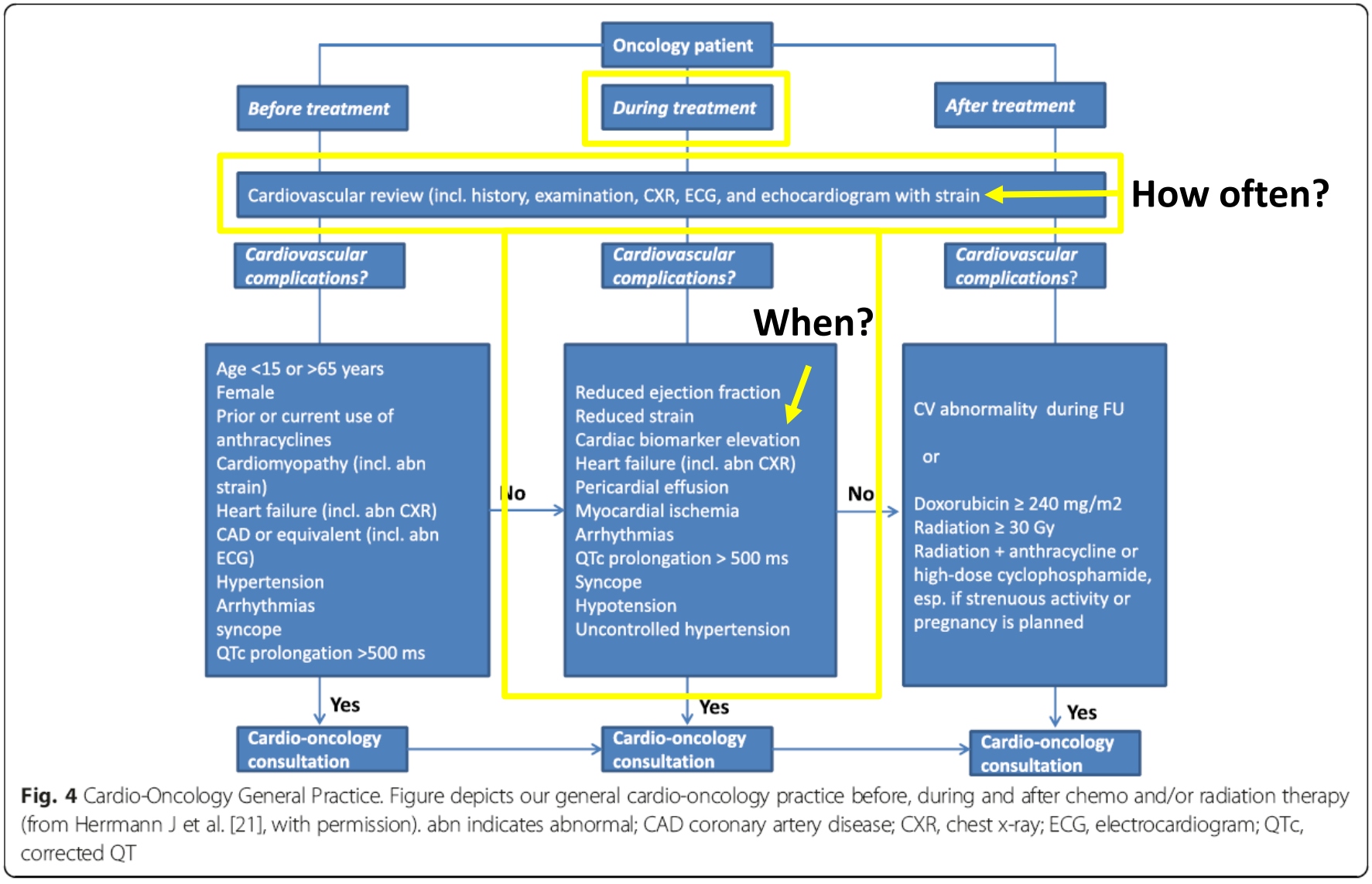

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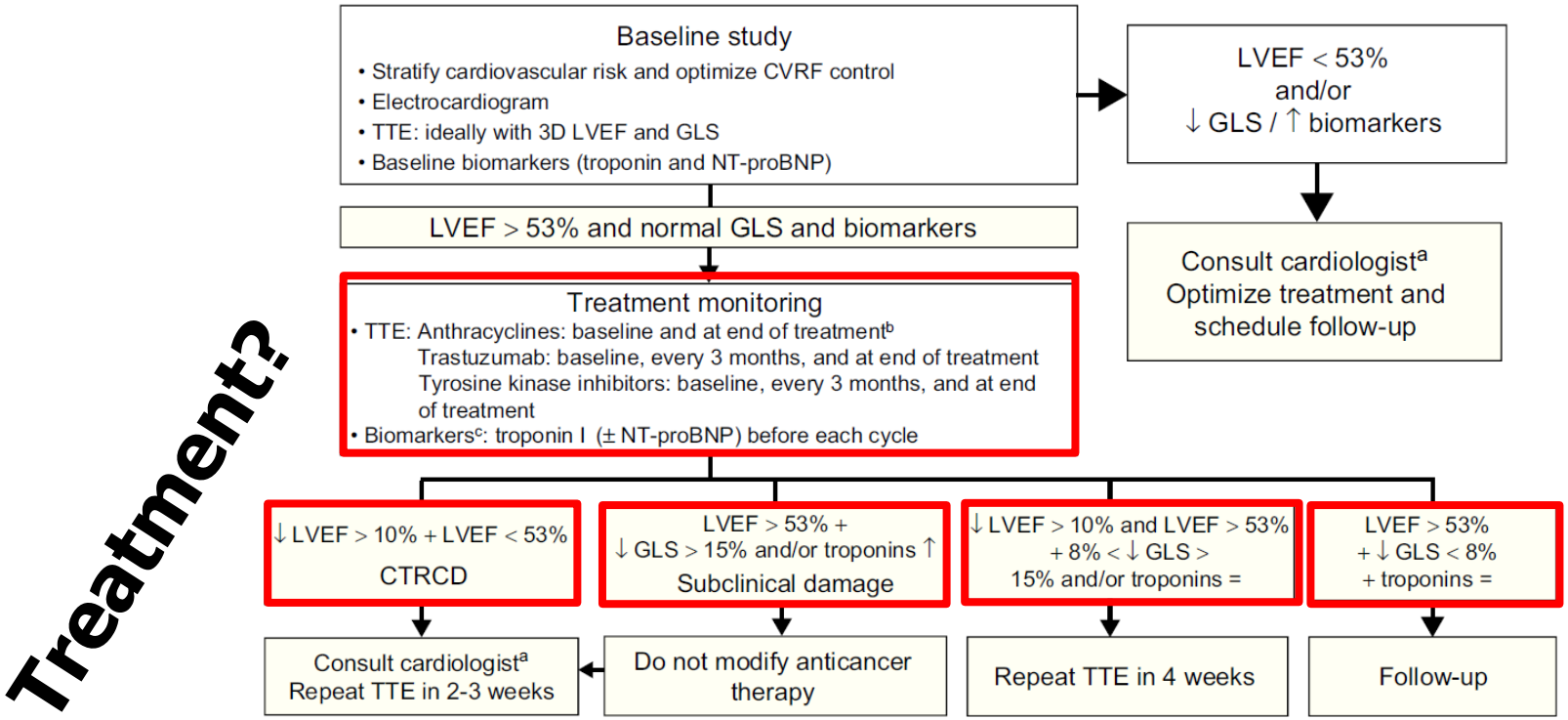

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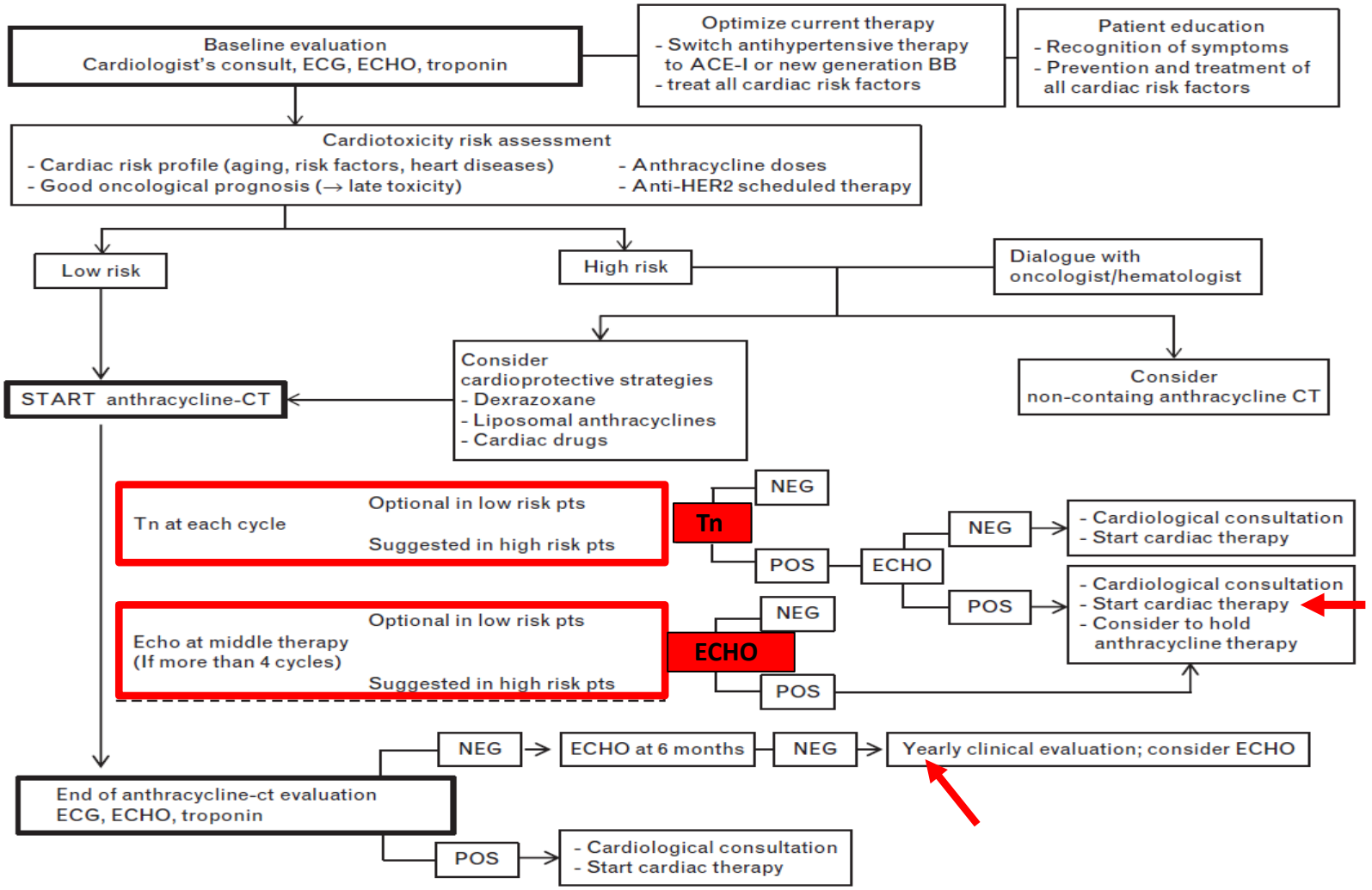

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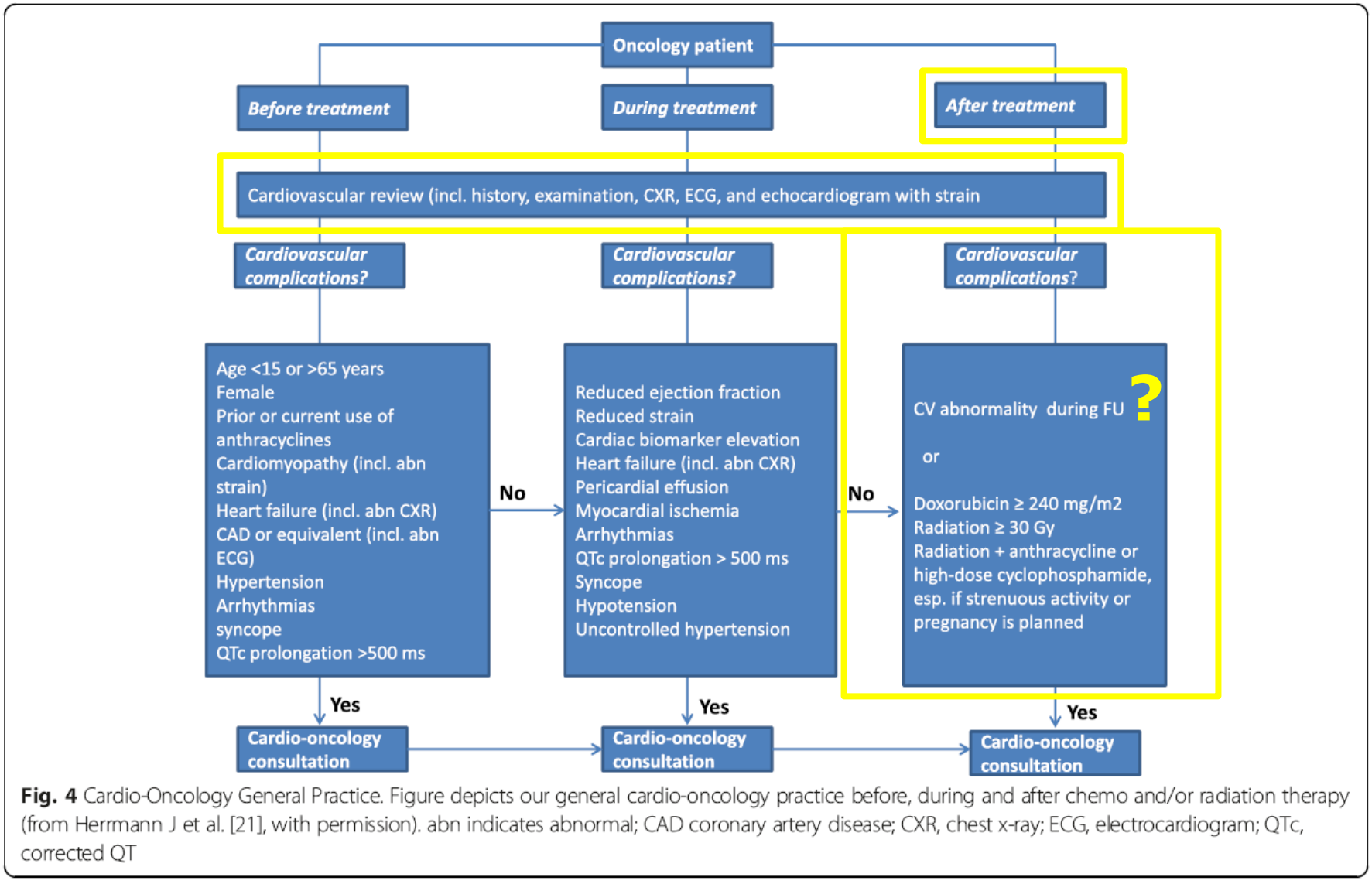

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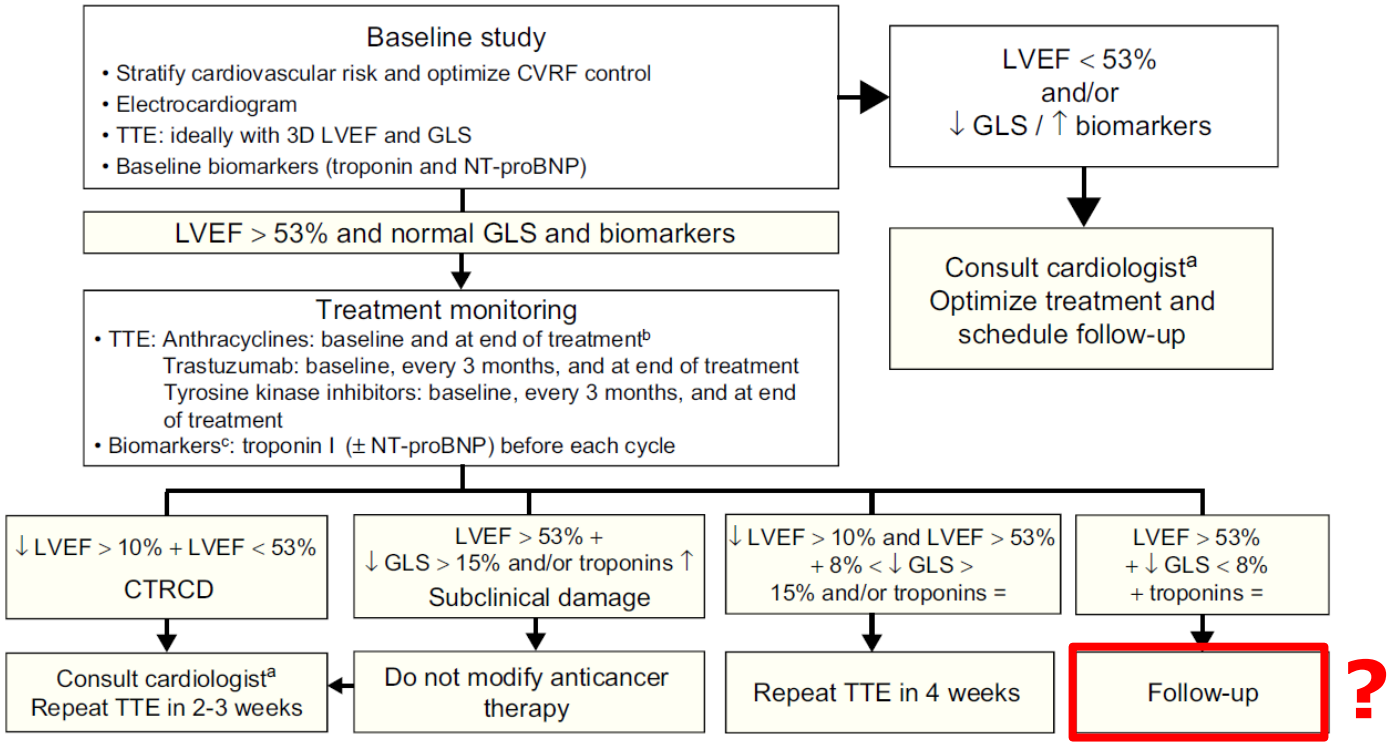

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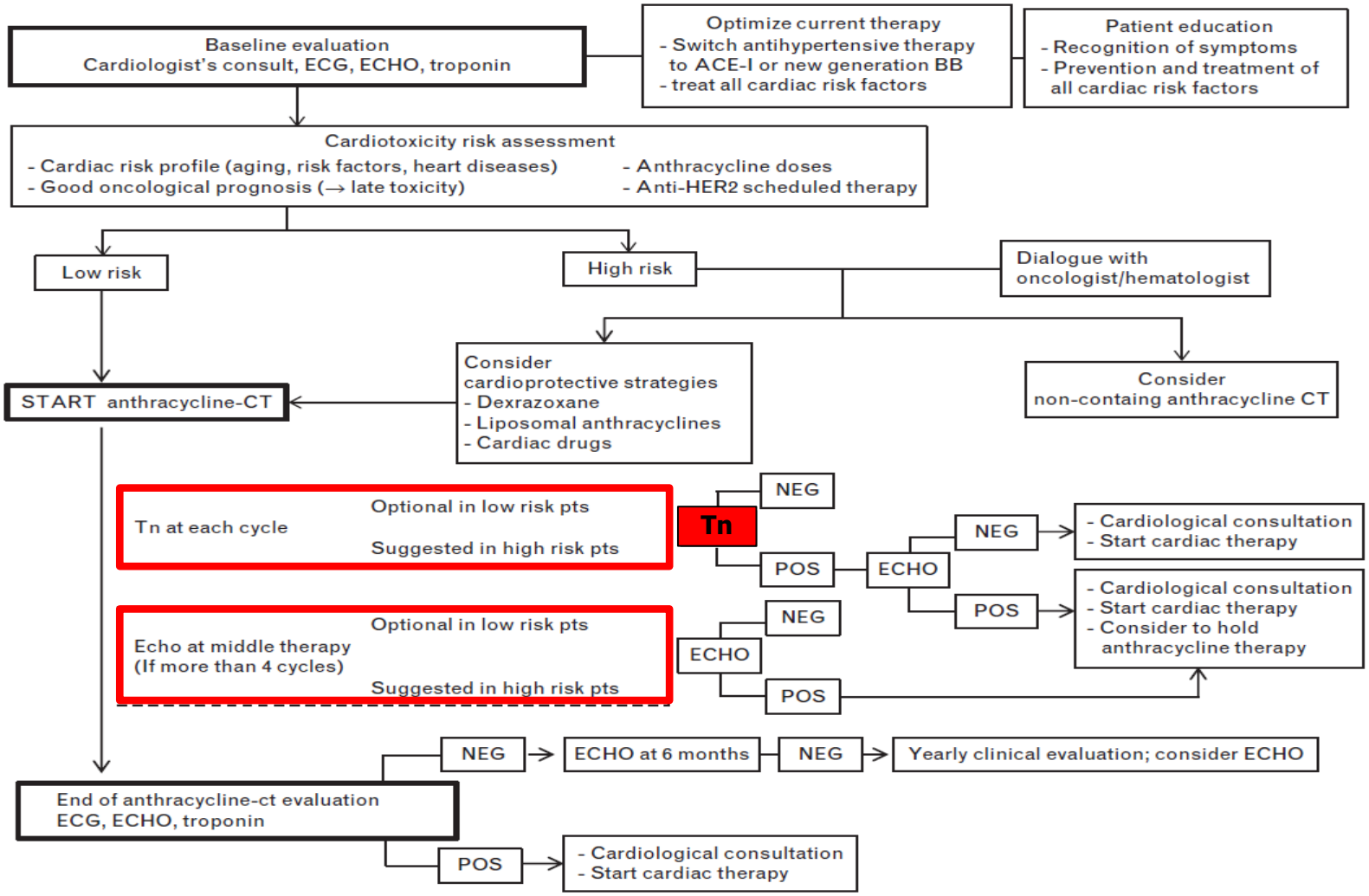

Cardiotoxic effects of anthracycline-based therapy: what is the evidence and what are the potential harms?

Bennett E Levis, Phillip F Binkley, Charles L Shapiro

Suggested approaches for prevention

For women without pre-existing cardiac risk factors receiving limited doses of anthracyclines, no cardiac imaging, biomarkers, or drug interventions are required.

Lancet Oncol 2017; 18: e445–56

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One unintended consequence of intensive cardiac surveillance and cardioprotective drugs is medicalisation.[72]

In addition to potentially unnecessary interventions, telling an individual that they have a heart problem can cause distress and anxiety, and reduce their health-related quality of life.

Another unintended consequence is the potential for increased health-care costs when the value of provision of that care is unknown. Value, in this case, would be defined as the prevention of heart failure or cardiac deaths relative to the total costs of the preventive care required.[74]

Lancet Oncol 2017; 18: e445–56

L.F., 40-year-old woman

- left sided breast cancer
- staging: pT2 pN3a (24/30) - grading MG2
- receptors: ER 80%, PR 90%, HER2 negative.

- no history of CV disease
- no CV risk factors
- baseline ECHO: normal - LVEF 66%

Cancer therapy

- 18/5/2018:
  left mastectomy + axillary dissection

- 6/7/2018 – 22/9/2018:
  Epirubicin 90 mg/m2 --> 140 mg tot
  Cyclophosphamide 600 mg/m2 --> 960 mg tot

  } X 4 cycles

- From 16/6/2018 to present:
  Decapeptyl 3.75 mg i.m. every 28 days

- From 5/10/2018 to present:
  Tamoxifen 20 mg/day

- 25/10/2018 – 15/11/2018:
  left side chest and supraclavicular lymph nodes radiotherapy (RT) with image-guided technique; total dose 40 Gy

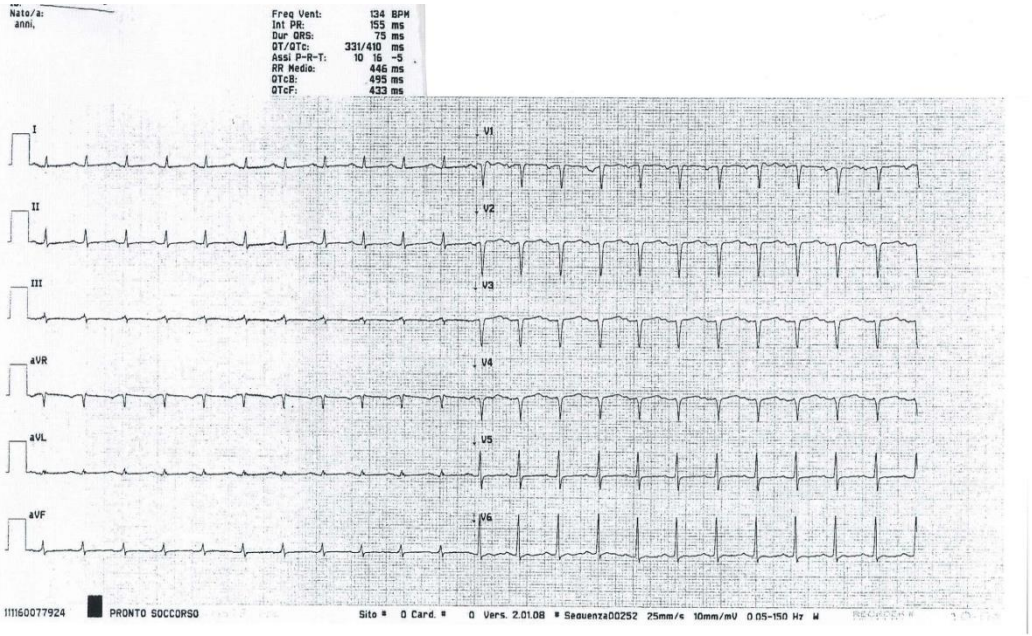
Follow-up 1

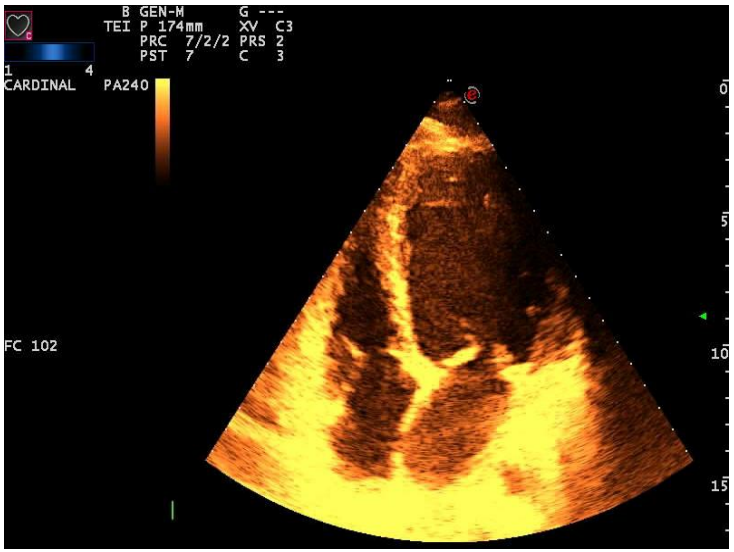
- She was considered at low risk for cardiotoxicity. She was not scheduled by oncologists for any cardiologic ± ECHO check during and after chemotherapy (CT) and RT.

Follow-up 1

- She was considered at low risk for cardiotoxicity. She was not scheduled by oncologists for any cardiologic ± ECHO check during and after chemotherapy (CT) and RT.

- 31 March 2019 (6 months after the end of CT): hospitalization for congestive heart failure. Evidence of hypokinetic cardiomyopathy with severe left ventricular dysfunction (LVEF = 16%) and bilateral pleural effusion. NT-proBNP = 12.862 ng/L.





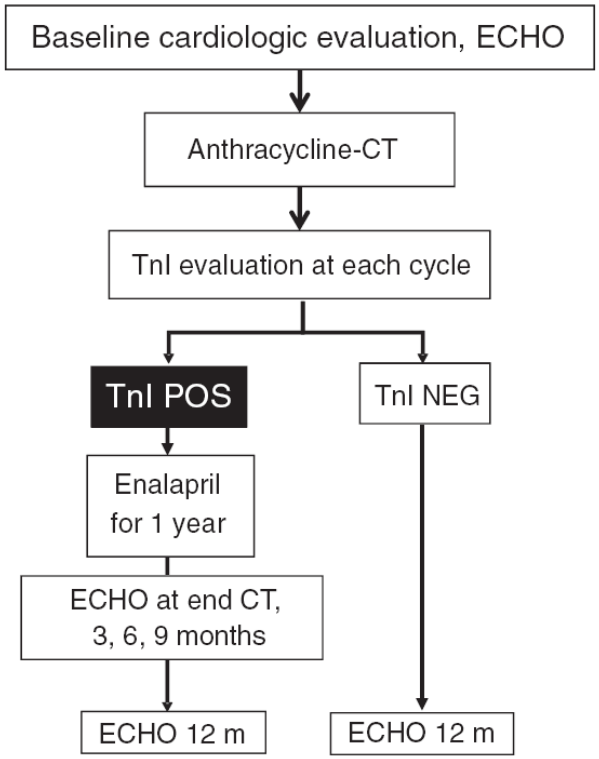


Fig. 1. Algorithm for the management of cardiotoxicity in patients receiving anthracyclines. CT = chemotherapy; ECHO = echocardiogram; TnI = Troponin I.

WE DON'T STOP CHEMOTHERAPY

IEO Istituto Europeo di Oncologia Unità di Cardiologia	CARDIOLOGICAL MONITORING IN PATIENTS UNDERGOING CANCER THERAPY	(CODE)
	(PROCEDURA)	Pagina 1 di 12

CARDIOLOGICAL MONITORING IN PATIENTS UNDERGOING CANCER THERAPY

Epirubicin + Cyclophosphamide x 4

	TnI before	TnI after		LVEF%	
EC 1°	0.002	0.001	n.v.<0.040	62	
EC 2°	0.002	0.003			
EC 3°	0.007	0.080		66	**Enalapril**
EC 4°	0.006	0.005		64	**Enalapril**
					Enalapril
after 2 months				62	
					Enalapril for 1 year
after 1 year				63	

D. Cardinale, M.T. Sandri / Progress in Pediatric Cardiology 39 (2015) 77–84

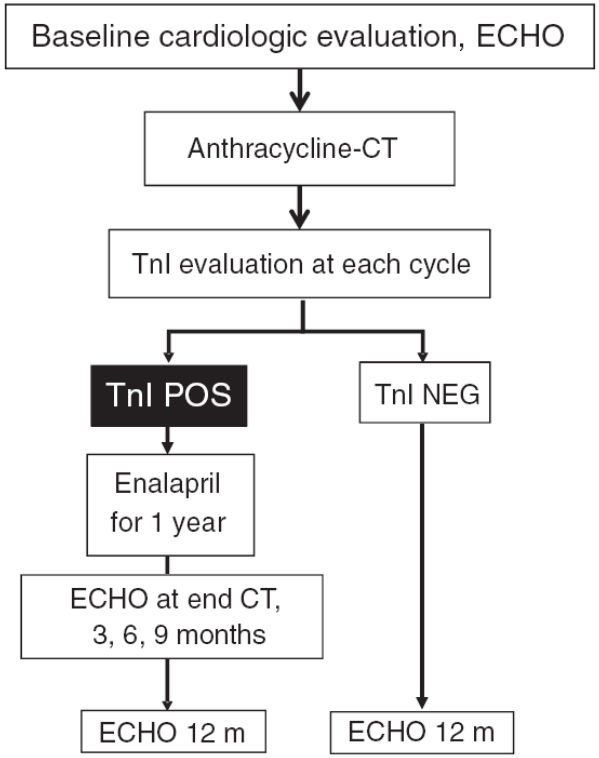


Fig. 1. Algorithm for the management of cardiotoxicity in patients receiving anthracyclines. CT = chemotherapy; ECHO = echocardiogram; TnI = Troponin I.

- 4284 post-study pts
- Negative cardiovascular history
- Different kinds of tumor
- Cardiotoxic oncologic treatments

- TnI before and after every CT cycle
- TnI + = n. 728 (17%)
- Enalapril in TNI+ pts
- Serial LVEF measurements

- 12 - year FU
- NO significant LVEF reduction from baseline

MV, 75-year-old man

- NSCLC IIIA pN2
- CV risk factors:
  - ✓ smoking
  - ✓ hypertension
  - ✓ diabetes
- Hypokinetic CMP (post-MI)
- Pre-CT baseline ECHO: LVEF 23%

Guideline-recommended oncologic treatment = neoadjuvant CT with Carboplatin + Gemcitabine followed by lung surgery

Multimarker approach in pts with cardiac disease

Patients are admitted to hospital to receive CT

Troponin + BNP approach

cycle n.	day	phase	TnI	BNP	EKG + visit	ECHO
1°	1°	baseline preCT	X	X	X	X
	2°	soon after CT	X	X	X	
	3°	before discharge	X	X	X	
2°	1°	baseline preCT	X	X	X	
	2°	soon after CT	X	X	X	
	3°	before discharge	X	X	X	
3°	1°	baseline preCT	X	X	X	X
	2°	soon after CT	X	X	X	
	3°	before discharge	X	X	X	
4°	1°	baseline preCT	X	X	X	
	2°	soon after CT	X	X	X	
	3°	before discharge	X	X	X	
After end CT		FU	X	X	X	X

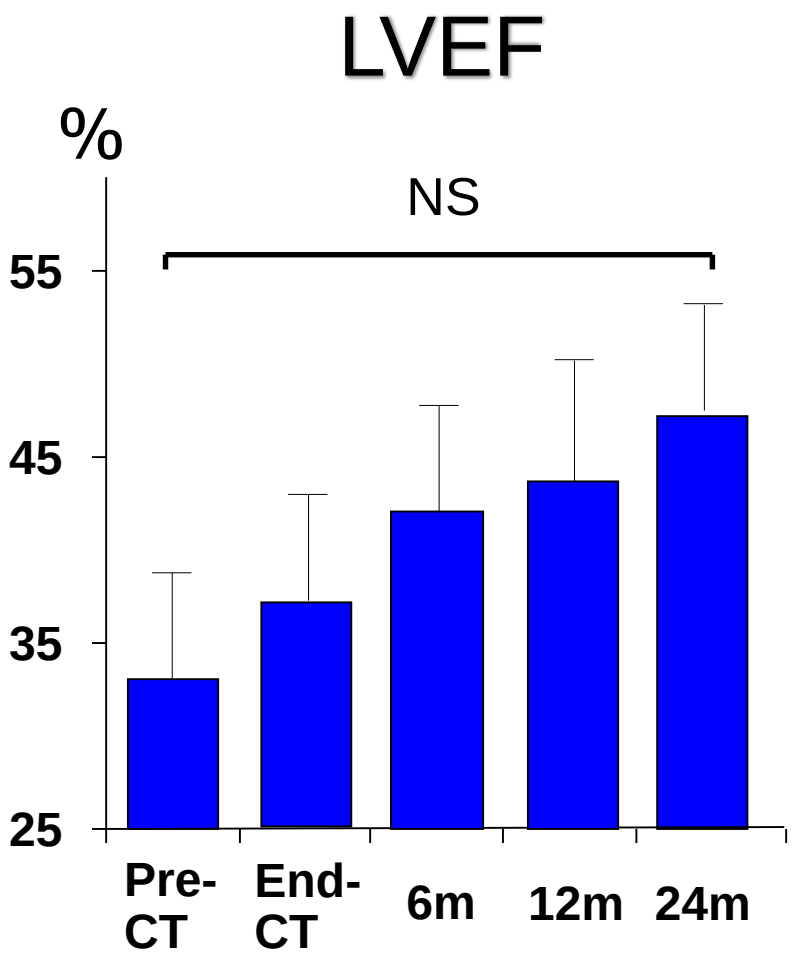
Multimarker approach in pts with cardiac disease

Troponin + BNP approach

- 435 pts
- Cardiac disease:
  - reduced LVEF
  - pre-existent or developed after CT
- Different kinds of tumor
- Liposomal AC, 5FU and platinum derivatives, targeted therapy

- TnI and BNP before and after every CT cycle
- Cardiologic therapy guided by biomarkers
- Serial LVEF measurements

- NO significant further LVEF reduction (in some cases LVEF improvement)
- NO cardiac events



Cardioncology: is there a common clinical practice?

The answer is NO.

Several guidelines/position papers with relevant differences in terms of:

- management of pts at standard/low risk
- diagnostic tools used in early identification
- primary prevention
- duration and intensity of follow-up no specified
- treatment no specified

Increased awareness and attention to the problem compared to the past.

CARDIONCOLOGY…..

…keeping the cancer patient treated today from becoming the heart patient of tomorrow.

Thank you!

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