Clinical Heart Failure Guidelines: are they different for cancer patients?

Guidelines for cardiac monitoring

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Do we need a guideline for cardiac monitoring in oncologic patients?
Onset of cancer in a patient with CVD
Onset of HF in a patient under active cancer treatment
Onset of HF in a long term survivor
HF is not the only possible cardiotoxicity!

Predisposing factors before treatment → Early signs of cardiotoxicity → Acute CVD during treatment → CVD after treatment → CVD in long-term survivors

CV prognosis → Oncologic prognosis
Do we need a guideline for cardiac monitoring in oncologic patients?

• A guideline to prevent.
• A guideline to determine which patients should be monitored and how.
• A guideline to early diagnose.
• A guideline to avoid unnecessary disruptions of oncologic treatment.
• A guideline to follow up.
Key recommendations:

• A monitoring schedule that assesses baseline and on-treatment cardiac function (every 4 months)
• Simplified recommendations for trastuzumab treatment interruption and restarting
• Clear advice on initiating an ACE inhibitor and when to consult a cardiologist.
cardiovascular toxicity induced by chemotherapy, targeted agents and radiotherapy: ESMO Clinical Practice Guidelines†

G. Curigliano¹, D. Cardinale², T. Suter³, G. Plataniotis⁴, E. de Azambuja⁵, M. T. Sandri⁶, C. Criscitiello⁷, A. Golchirsch⁸, C. Cipolla⁹ & F. Rilla⁹, on behalf of the ESMO Guidelines Working Group

Figure 1. Algorithm for the management of cardiotoxicity in patients receiving anthracyclines.

Figure 2. Algorithm for continuation and discontinuation of treatments based on LVEF assessments.
Increasing responsibility to identify patients with adverse health outcomes related to past cancer treatments.
Society Guidelines

Canadian Cardiovascular Society Guidelines for Evaluation and Management of Cardiovascular Complications of Cancer Therapy

Primary Panel: Sean A. Virani, MD, MSc, MPH, FRCPC, Co-Chair, 2, *
2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Developed with the special contribution of the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: Piotr Ponikowski* (Chairperson) (Poland), Adriaan A. Voors* (Co-Chairperson) (The Netherlands), Stefan D. Anker (Germany), Héctor Bueno (Spain), John G. F. Cleland (UK), Andrew J. S. Coats (UK), Volkmar Falk (Germany), José Ramón González-Juanatey (Spain), Veli-Pekka Harjola (Finland), Ewa A. Jankowska (Poland), Mariell Jessup (USA), Cecilia Linde (Sweden), Petros Nihoyannopoulos (UK), John T. Parissis (Greece), Burkert Pieske (Germany), Jillian P. Riley (UK), Giuseppe M. C. Rosano (UK/Italy), Luis M. Ruilope (Spain), Frank Ruschitzka (Switzerland), Frans H. Rutten (The Netherlands), Peter van der Meer (The Netherlands)
Table 3  Factors associated with risk of cardiotoxicity following anti-HER2 compounds and VEGF inhibitors

<table>
<thead>
<tr>
<th>Agent</th>
<th>Risk factors</th>
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<tbody>
<tr>
<td>Anti-HER2 compounds</td>
<td>Previous or concurrent anthracycline treatment (short time between anthracycline and anti-HER2 treatment)</td>
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<td>VEGF inhibitors</td>
<td>Previous history of hypertension</td>
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Table 4  Baseline risk factors for cardiotoxicity

<table>
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<tr>
<th>Current myocardial disease</th>
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<tr>
<td>Heart failure (with or without preserved or reduced ejection fraction)</td>
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<tr>
<td>Asymptomatic LV dysfunction (EF &gt;50% or high risk patients)</td>
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<tr>
<td>Evidence of CAD (previous myocardial infarction, angina, PCI or CABG, myocardial ischemia)</td>
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<tr>
<td>Moderate and severe LV with or without LV dysfunction</td>
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<tr>
<td>Hypertensive heart disease with LV hypertrophy</td>
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<tr>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
</tr>
<tr>
<td>Restrictive cardiomyopathy</td>
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<tr>
<td>Center involvement with myocardial ischemia</td>
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<tr>
<td>Significant cardiac arrhythmias (e.g., atrial fibrillation)</td>
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<tr>
<th>Demographic and other CV risk factors</th>
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<tr>
<td>Age (pediatric population) ≤10 years; ≥55 years for transmural; ≥65 years for anthracyclines</td>
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<tr>
<td>Family history of premature CV disease (≥50 years)</td>
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<tr>
<td>Arterial hypertension</td>
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<tr>
<td>Diabetes mellitus</td>
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<tr>
<td>Hypercholesterolemia</td>
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Previous cardiovascular cancer treatment                                                   Lifestyle risk factors

| Prior anthracycline use                                                                 |
| Prior refractory to chest or myocardium                                                  |

Smoking                                                                                     |
High cholesterol level                                                                     |
Obesity                                                                                    |
Sedentary habit                                                                             |

BMI = body mass index; CAD = coronary artery disease; HER2 = human epidermal growth factor receptor 2; LV = left ventricular; EF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; WHO = World Health Organization; EF = ejection fraction.
• Myocardial dysfunction and heart failure
• Coronary artery disease
• Valvular heart disease
• Arrhythmias and QT
• Arterial hypertension
• Thrombotic disease
• Peripheral vascular disease and stroke
• Pulmonary hypertension
• Pericardial complications
1. Which patients with cancer are at increased risk for developing cardiac dysfunction?
2. Which preventive strategies minimize risk before initiation of therapy?
3. Which preventive strategies are effective in minimizing risk during the administration of potentially cardiotoxic cancer therapy?
4. What are the preferred surveillance and monitoring approaches during treatment in patients at risk for cardiac dysfunction?
5. What are the preferred surveillance and monitoring approaches after treatment in patients at risk for cardiac dysfunction?
6. No recommendations can be made regarding continuation or discontinuation of cancer therapy in individuals with evidence of cardiac dysfunction.

Focused on HF and LVEF monitoring
• Evaluate left ventricular ejection fraction (LVEF) prior to and during treatment.
• The optimal frequency of LVEF assessment during adjuvant trastuzumab therapy is not known.
• The FDA label recommends LVEF measurements prior to initiation of trastuzumab and every 3m during therapy.
5 Warnings and Precautions

5.1 Cardiomyopathy

Herceptin can cause left ventricular cardiac dysfunction, arrhythmias, hypertension, disabling cardiac failure, cardiomyopathy, and cardiac death [see Boxed Warning: Cardiomyopathy]. Herceptin can also cause asymptomatic decline in left ventricular ejection fraction (LVEF).

There is a 4–6 fold increase in the incidence of symptomatic myocardial dysfunction among patients receiving Herceptin as a single agent or in combination therapy compared with those not receiving Herceptin. The highest absolute incidence occurs when Herceptin is administered with an anthracycline.

Withhold Herceptin for ≥ 16% absolute decrease in LVEF from pre-treatment values or an LVEF value below institutional limits of normal and ≥ 10% absolute decrease in LVEF from pretreatment values [see Dosage and Administration (2.3)]. The safety of continuation or resumption of Herceptin in patients with Herceptin-induced left ventricular cardiac dysfunction has not been studied.

Patients who receive anthracycline after stopping Herceptin may also be at increased risk of cardiac dysfunction [see Drug Interactions (7) and Clinical Pharmacology (12.3)].

Cardiac Monitoring

Conduct thorough cardiac assessment, including history, physical examination, and determination of LVEF by echocardiogram or MUGA scan. The following schedule is recommended:

- Baseline LVEF measurement immediately prior to initiation of Herceptin
- LVEF measurements every 3 months during and upon completion of Herceptin
- Repeat LVEF measurement at 4 week intervals if Herceptin is withheld for significant left ventricular cardiac dysfunction [see Dosage and Administration (2.3)]
- LVEF measurements every 6 months for at least 2 years following completion of Herceptin as a component of adjuvant therapy.
The meeting points between the guidelines

- Identifying the **high-risk** population
  - Patient related factors
  - Therapy related factors
- CV risk factors control and **life-style** intervention
- Detection and Prevention of Cardiotoxicity
  - Evaluation of LVEF **before initiation** of cancer treatments known to cause impairment in LV function.
  - Whenever needed, monitoring with the **same imaging** technique.
  - Subclinical LV dysfunction evaluation using novel echocardiographic techniques
  - Utility of **cardiac biomarkers** for the early detection of chemotherapy-mediated cardiotoxicity
- Baseline ECG and periodic monitoring of the QTc interval in patients receiving QT-prolonging drugs
- Recommendations for a **Multidisciplinary Approach** to Cardio-oncology
• Feasibility
• Cost effectiveness
• It is unclear if early detection strategies decrease the burden of CVD and ultimately improve the outcome of cancer survivors
• Lack of high-quality evidence for effective primary and secondary prevention strategies.
• When to stop a cancer therapy in individuals with evidence of cardiac dysfunction.
• Urgent need for collaborative studies to help guide patient management.
  ✓ Large prospective registries that enable the development of risk models.
  ✓ Multicentre randomized controlled trials for primary and secondary interventions.
  ✓ Genetic and epigenetic characterization to define susceptibility to cardiotoxicity
Modern-day cardio-oncology: a report from the ‘Heart Failure and World Congress on Acute Heart Failure 2018’

Markus S. Anker, Alessia Lena, Sara Hadzibegovic, Yury Belenkov, Jutta Bergler-Klein, Rudolf A. de Boer, Alain Cohen-Solal, Dimitrios Farmakis, Stephan von Haehling, Teresa López-Fernández, Radek Pudil, Thomas Suter, Carlo G. Tocchetti, Alexander R. Lyon for the Heart Failure Association Cardio-Oncology Study Group of the European Society of Cardiology

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**Figure 2** Role of cardiac imaging in cardio-oncology.

- **Before therapy**
  - Stratify Cardio-Toxicity risk
  - Optimize CV conditions
- **During therapy**
  - Reproducible EF: 3DE-MRI
  - Early diagnosis: GLS
  - Preventive strategies
  - ↓ Treatment interruptions
  - Minimize CV events
- **After therapy**
Unidad multidisciplinar de Cardio-Oncología. Visita inicial

Edad ………… Sexo ………… Peso ………… Talla ………… IMC ………… TA …………

Diagnóstico: ..........................................................................................................................

Esquema terapéutico:

Riesgos cardiovasculares potenciales del tratamiento:

- I. Cardiaca
- Cardiopatía isquémica
- Artritis
- Enfer. vascular periférica
- Trombosis
- HTA/DM/Dislipemia

Factores de riesgo cardiovascular:
- Fumador/exfumador
- Hipercolesterolemia (Objetivo LDL < 100)
- Hipertensión arterial (Objetivo < 130/80 mm Hg)
- Diabetes (Objetivo HbA1c < 7.5 - 8)
- Insuficiencia renal moderada-severa

Antecedentes de:
- Quimioterapia cardiotóxica
- Esquema
- Radioterapia torácica
- Fecha fin tratamiento
- Cardiotoxicidad
- Cardiopatía conocida
- Sospecha cardiopatía
- Disnea de esfuerzo
- Síncope o presíncope
- Edemas
- Dolor precordial

Pruebas complementarias basales:
- Todos
- Analítica basal *
- Troponina
- Perfil lipídico
- Hb A1c
- ECG basal
- Ecocardiograma si:
  - >65 años
  - > 2 FRCV

Optimizar tratamiento (solicitar interconsulta electrónica rápida en caso necesario)

Cualquier respuesta Sí
Enviar a consulta de Cardio-Oncología (3CAR07)
Seguir protocolos específicos según patología

- Si ECG o ECO anormal
- Si Troponina elevada
Seguimiento durante el tratamiento

Pruebas complementarias

- TnI antes de cada ciclo iv / trimestral en tratamientos orales si ANT, anti HER2, MEKi, TKi

Factores de riesgo cardiovascular

- Fumador/exfumador
- Hipercolesterolemia (Objetivo LDL < 100)
- Hipertensión arterial (Objetivo < 130/80 mm Hg)
- Diabetes (Objetivo HbA1C <7,5-8)
- Insuficiencia renal moderada-severa
- Síntomas nuevos con sospecha de cardiopatía (disnea de esfuerzo, arritmias, síncope, edemas, dolor precordial)
- Elevación de TnI

Optimizar tratamiento (solicitar interconsulta electrónica rápida en caso necesario)

Cualquier respuesta Sí

Enviar a consulta de Cardio-Oncología (3CAR07)

Otras pruebas complementarias durante el tratamiento

ECG

- En tratamientos que prolonguen el QT seguimiento individualizado
- Fin de tratamiento

Ecocardiograma:

- Cada 6 m en pacientes con >2FRCV y tratamiento prolongado con ANT, HER2, MEKi, TKi
- Previo a trasplante de progenitores hematopoyéticos (TPH) y a los 100 días
- Fin de tratamiento a todos (en los siguientes 6-8 meses)

Pacientes tratados sólo con radioterapia torácica

- Visita inicio: Check List de FRCV, cardiopatía y tratamientos previos
  - Analítica (Perfil lipídico y Hb A1c)
  - ECG
  - ECO (alteraciones ECG, cardiopatía o tratamientos antitumorales previos)
- Seguimiento clínico. Control de FRCV. Si sospecha de cardiopatía remitir al cardiólogo
- Fin de tratamiento: ECG y ECO al año

Largos supervivientes

- Control estricto de FRCV
- ECG 1, 2 y 5 años post tratamiento
- ECO a los 5 años si FRCV, antraciclinas, radioterapia torácica o tratamiento con <15 años.
- Interconsulta a la unidad de cardio-oncología
  1. Cáncer + síntomas nuevos o mal control de FRCV a pesar de ajuste de medicación
  2. Alteraciones nuevas en el ECG
  3. Tratamiento con cardiotóxicos sin monitorización específica durante el tratamiento
  4. Antes de una gestación
• We should continue to look for a more cost-effective way of detecting cardiotoxicity, with the primary objective to improve outcomes.
• Additional research is needed to better define monitoring guidelines.
• An effective cardio-oncology team work is crucial in order to improve CV health in cancer patients.
• 31 y.o pregnant woman (week 36)
• Admitted for acute pulmonary edema
• Hodgkin lymphoma 13 years before (QT and RT)
• Obese, BMI 36
• Sedentary
• Arterial HT
Teorema de Pitágoras

En un triángulo rectángulo, el cuadrado de la hipotenusa es igual a la suma de los cuadrados de los catetos.

\[ a^2 + b^2 = c^2 \]