

END OF CANCER THERAPY CV RISK ASSESSMENT

General Principles

End-of-cancer therapy CV risk assessment covers the first 12 months after the last cardiotoxic cancer treatment. Presented recommendations (Figures 1 and 2, Tables 1-4) are where cardiotoxic cancer therapy has been successfully completed with good long-term prognosis.¹ Recommendations for specific cardiac entities are presented in relevant Chapters.

1. Lyon AR, et al. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). *Eur Heart J*. 2022.

Table 1. ESC 2022 GL on cardio-oncology. Risk factors for future cardiovascular disease at the end-of-cancer therapy cardiovascular risk assessment

High-risk conditions
High- and very-high baseline CV toxicity risk based on HFA-ICOS assessment
Specific anticancer treatment proven to have a high risk of long-term CV complications ^a
Doxorubicin ^b ≥ 250 mg/m ²
RT > 15 Gy MHD ^c
Both doxorubicin ^b ≥ 100 mg/m ² and RT 5–15 Gy MHD ^d
High-risk HSCT patients ^e
Moderate or severe CTR-CVT during cancer treatment (especially CTRCD), ICI-related myocarditis, cardiac arrhythmias, or severe vascular toxicities (ACS, stroke, PVD)
New CV symptoms or new asymptomatic abnormalities in echocardiography and/or cardiac serum biomarkers at the end of therapy assessment

ACS, acute coronary syndromes; CTRCD, cancer therapy-related cardiac dysfunction; CTR-CVT, cancer therapy-related cardiovascular toxicity; CV, cardiovascular; CVD, cardiovascular disease; CVRF, cardiovascular risk factors; GVHD, graft vs. host disease; Gy, Gray; HFA, Heart Failure Association; HSCT, haematopoietic stem cell transplantation; ICI, immune checkpoint inhibitors; ICOS, International Cardio-Oncology Society; MHD, mean heart dose; PVD, peripheral vascular disease; RT, radiotherapy.

^aRT risk categorization based on MHD is recommended over categorization based on prescribed dose, which may not accurately reflect cardiac radiation exposure. Depending on dose distribution and exposure of specific cardiac substructures (as well as clinical risk factors), the treatment team may judge the patient to belong to a higher risk category. In addition, a patient may be judged to belong to a lower risk category if only a small part of the heart is exposed to a relatively high prescribed dose (i.e. RT to left breast or left chest wall only).

^bOr doxorubicin equivalent.

^cOr prescribed RT ≥ 35 Gy to a volume exposing the heart if MHD is not available.

^dOr prescribed RT 15–34 Gy to a volume exposing the heart if MHD is not available.

^eHigh-risk HSCT patients: allogeneic HSCT; pre-existing CVD or multiple uncontrolled CVRF; cancer treatment history (mediastinal or mantle field radiation, alkylating agents, >250 mg/m² doxorubicin or equivalent); conditioning schemes (total body irradiation, alkylating agents); development of GVHD.

Table 2. ESC 2022 GL on cardio-oncology. Recommendations for end-of-cancer therapy cardiovascular risk assessment

Educating and supporting patients with cancer to make appropriate healthy lifestyle choices ^a	I C
Education for patients with cancer regarding recognition for early signs and symptoms of CVD.	I C
CVRF assessment during the first year after cancer therapy ^a , And thereafter according to the 2021 ESC Guidelines on CVD prevention in clinical practice.	I B
In asymptomatic high-risk patients, ^b echocardiography and cardiac serum biomarkers at 3 and 12 months after completion of cancer therapy.	I B
In asymptomatic moderate-risk patients, ^c echocardiography and cardiac serum biomarkers within 12 months after completion of cancer therapy.	IIa B
In asymptomatic low-risk patients, ^c echocardiography and cardiac serum biomarkers within 12 months after completion of cancer therapy.	IIb C
Cardiology referral ^d in patients with cancer with new cardiac symptoms or new asymptomatic abnormalities in echocardiography and/or cardiac serum biomarkers at the end of therapy assessment.	I C

In selected patients with exercise intolerance persisting at 12 months after cancer treatment and with normal resting echocardiogram and cardiac biomarkers, exercise stress echocardiography and/or CPET I Ib C

Targeted cardiac rehabilitation in CS with high CV risk. IIa B

Long-term continuation of cardiac medication in patients who develop severe CTRCD during cancer therapy. I C

CV follow-up and treatment optimization in patients who developed TKI-mediated hypertension during cancer therapy. I C

CV follow-up and treatment optimization in patients who developed vascular toxicities during cancer therapy. I C

ECG follow-up in patients who developed QT lengthening or LQTS during cancer therapy. I C.

CPET, cardiopulmonary exercise testing; CS, cancer survivors; CTRCD, cancer therapy-related cardiac dysfunction; CV, cardiovascular; CVD, cardiovascular disease; CVRF, cardiovascular risk factors; DM, diabetes mellitus; ECG, electrocardiogram; ESC, European Society of Cardiology; LQTS, long QT syndrome; TKI, tyrosine kinase inhibitors.

a Including regulation of hypertension, DM, dyslipidaemia, smoking cessation, weight loss in case of obesity, and an adequate amount of exercise.

b High-risk patients

c Moderate- or low-risk patients: according to CV toxicity baseline risk stratification.

d Cardio-oncology referral is recommended when available; alternatively, the patient should be referred to a cardiologist with expertise in managing CVD in patients with cancer

Table 3. ESC 2022 GL on cardio-oncology. Risk categories for asymptomatic adult cancer survivors

Risk category ^a	Patient characteristics
Very high risk	• Very high baseline CV toxicity risk pre-treatment • Doxorubicin^b ≥ 400 mg/m² • RT > 25 Gy MHD^c • RT > 15–25 Gy MHD^c + doxorubicin^b ≥ 100 mg/m²
Early high risk (<5 years after therapy)	• High baseline CV toxicity risk • Symptomatic or asymptomatic moderate-to-severe CTRCD during treatment • Doxorubicin^b 250–399 mg/m² • High-risk HSCT^d
Late high risk	• RT > 15–25 Gy MHD^c • RT 5–15 Gy MHD^e + doxorubicin^b ≥ 100 mg/m² • Poorly controlled CVRF
Moderate risk	• Moderate baseline CV toxicity risk • Doxorubicin^b 100–249 mg/m² • RT 5–15 Gy MHD^e • RT < 5 Gy MHD^f + doxorubicin^b ≥ 100 mg/m²
Low risk	• Low baseline CV toxicity risk and normal end-of-therapy cardiac assessment • Mild CTRCD during therapy but recovered by the end of cancer therapy • RT < 5 Gy MHD^f • Doxorubicin^b < 100 mg/m²

CTRCD, cancer therapy-related cardiac dysfunction; CV, cardiovascular; CVD, cardiovascular disease; CVRF, cardiovascular risk factors; GVHD, graft vs. host disease; Gy, Gray; HSCT, haematopoietic stem cell transplantation; MHD, mean heart dose; RT, radiotherapy. References: ^{397,399,400,673,674}

^aRT risk categorization based on MHD is recommended over categorization based on prescribed dose, which may not accurately reflect cardiac radiation exposure. Depending on dose distribution and exposure of specific cardiac substructures (as well as clinical risk factors), the treatment team may judge the patient to belong to a higher risk category. In addition, a patient may be judged to belong to a lower risk category in case only a small part of the heart is exposed to a relatively high prescribed dose.

^bOr equivalent.

^cOr prescribed RT ≥ 35 Gy to a volume exposing the heart if MHD is not available. Note that in this case, the limited information about cardiac exposure does not allow one to distinguish between high- and very high-risk categories.

^dHigh-risk HSCT patients: allogeneic HSCT; pre-existing CVD or multiple uncontrolled CVRF; cancer treatment history (mediastinal or mantle field radiation, alkylating agents, >250 mg/m² doxorubicin or equivalent); conditioning schemes (total body irradiation, alkylating agents); development of GVHD.

^eOr prescribed RT 15–34 Gy to a volume exposing the heart if MHD is not available.

^fOr prescribed RT < 15 Gy to a volume exposing the heart if MHD is not available.

Table 4. ESC 2022 GL on cardio-oncology. Recommendations for cardiovascular surveillance in asymptomatic adult cancer survivors

Annual CV risk assessment, ^a including ECG and NP, and CVRF management in CS who were treated with a potentially cardiotoxic cancer drug or RT. ^b	I B
CV toxicity risk restratification ^c 5 years after therapy to organize long-term follow-up.	I C
Echocardiography at years 1, 3, and 5 after completion of cardiotoxic cancer therapy and every 5 years thereafter in asymptomatic very high- and early high-risk adult CS. ^d	IIa C
Echocardiography in asymptomatic late high-risk adult CS ^f starting at 5 years after radiation to a volume including the heart and then every 5 years.	IIa C
Echocardiography every 5 years in asymptomatic moderate-risk adult CS. ^d	IIb C
Non-invasive screening for CAD ^e every 5–10 years in asymptomatic patients who received >15 Gy MHD, ^b starting at 5 years after radiation.	IIa C
Carotid ultrasound imaging every 5 years in asymptomatic patients with a history of head/neck RT, starting at 5 years after radiation and every 5–10 years thereafter.	IIa C
Renal artery ultrasound in patients with a history of abdominal and pelvic radiation who present with worsening renal function and/or systemic hypertension.	IIa C

BP, blood pressure; CAD, coronary artery disease; CMR, cardiac magnetic resonance; CS, cancer survivors; CT, computed tomography; CTR-CVT, cancer therapy-related cardiovascular toxicity; CV, cardiovascular; CVD, cardiovascular disease; CVRF, cardiovascular risk factors; ECG, electrocardiogram; HbA1c, glycated haemoglobin; MHD, mean heart dose; NP, natriuretic peptides; RT, radiotherapy.

^a Clinical review, BP, lipid profile, HbA1c.

^b RT risk categorization based on MHD is recommended over categorization based on prescribed dose (≥ 35 Gy to a volume exposing the heart if MHD is not available).

^c Restratification includes evaluation of new or pre-existing CVRF and CVD (including CTR-CVT).

^d See Table 3

^e Stress echocardiography, cardiac CT, stress CMR, single-photon emission CT stress test, according to local protocol

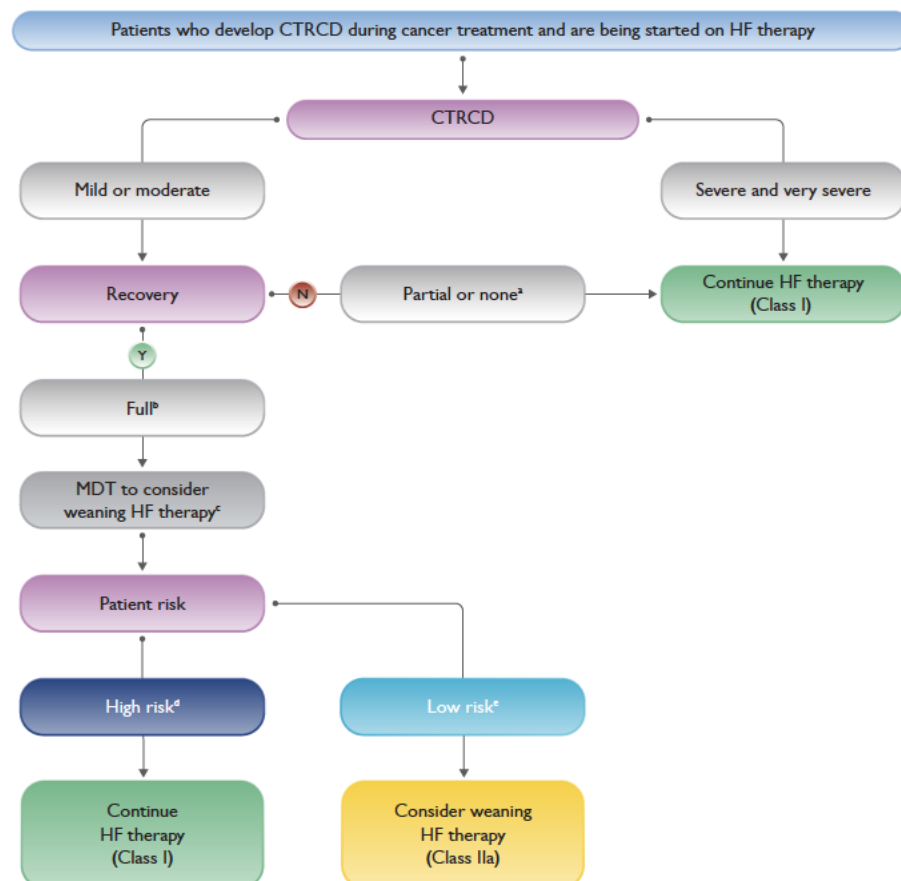


Figure 1. ESC 2022 GL on cardio-oncology. Management of cancer therapy-related cardiac dysfunction after cancer therapy.

CTRCD, cancer therapy-related cardiac dysfunction; CV, cardiovascular; GLS, global longitudinal strain; HF, heart failure; HFA, Heart Failure Association; ICOS, International Cardio-Oncology Society; LV, left ventricular; LVEF, left ventricular ejection fraction; MDT, multidisciplinary team; N, no; Y, yes.

a Partial or no recovery: patients who do not meet all of the criteria for full recovery.

b Full recovery: no signs or symptoms of HF + LVEF.50% + GLS within normal range or similar to baseline measurements + cardiac serum biomarkers within the normal range or similar to baseline measurements

c The CTRCD trajectory of each patient is unique and dynamic and withdrawal of HF therapy requires a MDT to consider several key points that help to stratify patients into low- or high-risk categories. Key points to consider during a MDT discussion are: HFA-ICOS baseline CV toxicity risk assessment, pre-existing indications for CV medication, class of cancer treatment causing CTRCD (generally reversible vs. generally irreversible), magnitude and duration of CTRCD before recovery, intensity of HF therapy needed to recover LV function, family history of cardiomyopathy or known cardiomyopathy gene carrier.

d See Table 1.

e Low-risk patient characteristics: low to moderate baseline CV toxicity risk (HFA-ICOS risk assessment), no pre-existing indications for CV medication, cancer treatment generally associated with reversible myocardial damage, asymptomatic mild CTRCD, early cardiac function recovery (3–6 months) under HF therapy, no family history of cardiomyopathy.

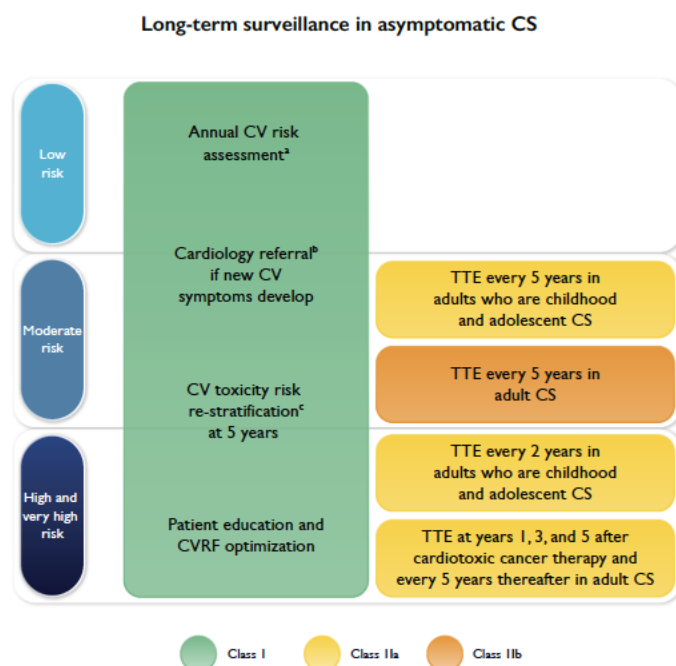


Figure 2. ESC 2022 GL on cardio-oncology. Long-term follow-up in cancer survivors.

BP, blood pressure; CAD, coronary artery disease; CS, cancer survivors; CTR-CVT, cancer therapy-related cardiovascular toxicity; CV, cardiovascular; CVD, cardiovascular disease; CVRF, cardiovascular risk factors; ECG, electrocardiogram; HbA1c, glycated haemoglobin; NP, natriuretic peptides; TTE, transthoracic echocardiography.

a Clinical review, BP, lipid profile, HbA1c, ECG, NP. In selected patients, non-invasive screening for CAD and carotid or renal diseases every 5–10 years, starting at 5 years after radiation may be considered.

b Cardio-oncology referral is recommended when available; alternatively, the patient should be referred to a specialized cardiologist with expertise in managing CVD in patients with cancer.

c Re-stratification includes evaluation of new or pre-existing CVRF and CVD (including CTR-CVT).