Invited Editorial

Comments on new 2022 European Society of Cardiology guidelines on cardioncology

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Abbreviations

ACE-I - angiotensin-Converting Enzyme Inhibitor
ACS –acute coronary syndrome
ARB - angiotensin Receptor Blocker
CS- cancer survivors
cTn – cardiac troponin
CTRCD – cancer therapy-related cardiac dysfunction
CTR-CVT – cancer therapy-related cardiovascular toxicity
CVD – cardiovascular disease
ECG - electrocardiogram
ECHO - echocardiography
GLS – global longitudinal strain
HF – heart failure
HFA-ICOS – heart Failure Association International Cardio-Oncology Society
ICIs - immune checkpoint inhibitors
LVEF – left ventricular ejection fraction
MDT – multidisciplinary team
QTcF- corrected QT interval using Fridericia correction
RF - risk factor
RT - Radiotherapy

Emerging cardiovascular diseases (CVD) in cancer patients due to cancer therapy-related cardiovascular toxicity (CTR-CVT) take a significant proportion among causes of death in cancer survivors (CS) (1-3). CTR-CVT risk is a dynamic process, and the risk changes throughout the treatment course. CTR-CVT risk can be influenced by implementing primary prevention treatments, improving of pre-existing cardiovascular diseases treatment, dose, frequency, and duration of cancer treatment, and etc. Besides, the overall cumulative dose received, the time period since the cancer treatment was completed, and comorbidities may also impact on the risk (4).

A recently published the first ESC cardio-oncology Guideline includes current definitions and principles of diagnosis and treatment, thus summarizing all the available evidence on cardio-oncology to assist health professionals in selecting the best management strategies for oncologic patients, considering the impact on the outcome, as well as the risk-benefit ratio of particular diagnostic or therapeutic means.

Cancer therapy-related cardiac dysfunction (CTRCD)

CTRCD occurs in symptomatic and asymptomatic variants. Symptomatic CTRCD can be manifested in very severe form (need for inotropic support, mechanical circulatory support, or transplantation); severe (need for hospitalization due to developed heart failure (HF)); moderate (need for outpatient intensification of diuretic and HF therapy); and in mild form (mild HF symptoms, no need in intensification of HF therapy).

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Received: 14.01.2023 **Accepted:** 16.01.2023

doi: 10.24969/hvt.2022.370

Accordingly, asymptomatic CTRCD can also be severe (left ventricular ejection fraction (LVEF) reduction to <40%); moderate (LVEF reduction by 10 percentage points to a LVEF 40-49%, or LVEF reduction by <10 percentage points to an LVEF 40-49%, and either decline in GLS by >15% from baseline, or further rise in cardiac biomarkers); and mild (LVEF =50% and further relative reduction in GLS by >15% from baseline, and/or further rise in cardiac biomarkers).

Discontinuation of chemotherapy (mostly in cases of anthracyclines administration) is recommended for cancer patients who developed severe symptomatic CTRCD. Temporary interruption of chemotherapy is recommended for patients who developed moderate symptomatic and severe or moderate asymptomatic CTRCD. After recovery of LV function

under guideline-based HF therapy, a multidisciplinary team (MDT) discusses restarting anthracycline chemotherapy in these patients. ACE-I, ARB, and/or beta-blockers are considered in mild asymptomatic CTRCD, while anthracycline chemotherapy continues uninterrupted. If there is a compelling reason to continue anthracycline chemotherapy, three other strategies exist in addition to continuing ACE-I/ARB and beta-blockers in targeted doses for HF. First, minimizing the dose of anthracycline chemotherapy administered. Second, switching to liposomal anthracycline medications. Third, pre-treatment with dexrazoxane before each further cycle of anthracycline chemotherapy. Thorough cardiac monitoring every 1–2 cycles is recommended for patients who restart anthracycline chemotherapy following an episode of

CTRCD and in patients with mild asymptomatic CTRCD while they continue anthracycline chemotherapy.

Arrhythmias / QT interval prolongation

QTcF <480 ms – continuation of current treatment is indicated; QTcF 480-500 ms – proceeding with caution, correcting reversible causes, minimizing other QT-prolonging medications, repleting electrolytes; QTcF >500ms – stopping treatment and evaluation is needed. It may require dose reduction or alternative therapy.

Immune checkpoint inhibitors-related (ICI) myocarditis

The diagnosis of myocarditis is initially based on cTn elevation with one primary or two minor criteria after the exclusion of acute coronary syndrome (ACS) and acute infectious myocarditis. Major criterion: cardiac magnetic resonance diagnostics for acute myocarditis (modified Lake-Louise criteria). Minor criteria: clinical syndrome of myocarditis, including cardiogenic shock; ventricular arrhythmia and/or new conduction system disease; decline in LV systolic function, with or without regional wall motion abnormalities in a non-Takotsubo pattern; other immune-related adverse events.

All cases of ICI-associated myocarditis are classified according to severity: fulminant, non- fulminant, and steroid refractory. If myocarditis is suspected or confirmed, ICI therapy should be interrupted until stabilization, early high-dose methylprednisolone i.v. is recommended for 3-5 days, then switching to oral prednisolone until resolution of symptoms, LV systolic dysfunction and conduction abnormalities, and significant cTn reduction.

Vascular toxicity

Vascular toxicity can be symptomatic and asymptomatic. Symptomatic (stroke, transient ischemic attack, myocardial infarction, ACS, chronic coronary syndromes, peripheral artery disease, vasospastic angina, microvascular angina, Raynaud`s phenomenon); Asymptomatic (atherosclerosis, thrombosis, abnormal vasoactivity).

Hypertension

Treatment threshold =130 mm Hg systolic and/or =80 mm Hg diastolic pressure in patients with high CV risk (SCORE2, SCORE2-OP or equivalent); otherwise - =140 mm Hg systolic and/or =90 mm Hg diastolic. Cancer therapy holding threshold is =180 mm Hg systolic and/or =110 mm Hg diastolic.

Baseline cardiovascular toxicity risks stratification

A baseline CV risk assessment leading to a reduction in treatment interruptions is highly recommended for all cancer patients before starting anticancer therapy. Stratifying the risk of CTRCD requires a personalized/systematic approach using the HFA-ICOS form. It is performed by a treating oncologist/hematologist, with a cardiologist's consulting. These forms incorporate sets of risk factors (RFs) to determine specific cardiotoxicity risks: prior CVD, lifestyle factors, previous cancer history and therapy, ECG, physical and metabolic assessment, data on cardiac biomarkers and transthoracic echocardiography, and current cancer treatment. Cancer patients are stratified into low, medium, high, and very high groups at risk before starting treatments.

Low risk means no risk factors or one medium RF; moderate risk – from two to four medium RFs; high-risk – medium RFs =5 points, or one any high RF; very high risk – any very high RF. It is essential to identify patients with high and very high baseline risk for CV toxicity and refer them to cardiology settings to develop risk-mitigating strategies and manage CVD according to ESC Guidelines. CV toxicity risk and management strategies must be documented and conveyed
to patients. Moderate-risk patients may also benefit from a cardio-oncologist referral. Low-risk patients can be observed within the oncology program with referral to a cardio-oncologist if a CTR-CVT condition emerges or new or uncontrolled CV RFs appear. Regular clinical assessments and specific CV examinations (ECG, ECHO including 3D-LVEF and GLS, and
cardiac biomarkers) according created monitoring protocol are recommended during cancer treatment to detect early signs and symptoms of CTRCD.

End-of-cancer therapy CV risk assessment

End-of-cancer therapy CV risk assessment starts when cancer therapy is completed with a favorable long-term prognosis, and the focus of the cardio-oncology team shifts to the coordination of long-term surveillance planning. A new risk assessment is recommended to identify those at high risk based on the following criteria: high or very-high baseline CV risk based on HFA-ICOS risk assessment tools; cardiotoxic cancer therapy with an increased risk of long-term CV complications (doxorubicin = 250 mg/m2, RT >15 Gy; both doxorubicin =100 mg/m2 and RT >5–15 Gy; high-risk hematopoietic stem cell transplantation patients).

In asymptomatic high-risk patients, ECHO and cardiac biomarkers are recommended at 3 and 12 months after cancer therapy completion. In asymptomatic moderate-risk and low-risk patients, ECHO and cardiac biomarkers should be considered within 12 months after cancer therapy completion. CV risk assessment at the end of therapy identifies those CSs who require long-term cardiology follow-up beyond the first 12 months after completing their cancer treatment. Long-term follow-up surveillance includes annual CV risk assessment, including ECG, natriuretic peptides and RF management, patient education, promoting a healthy lifestyle, recognizing and reporting signs and symptoms of CVD to administer effective treatment. This can be done in collaboration with primary healthcare settings.

Peer-review: Internal
Conflict of interest: None to declare.
Authorship: ZT and SB equally contributed to the preparation of manuscript)
Acknowledgement and funding: None to declare
Authors disclosures: Authors are principal investigator and coordinator of the project "Development of a PRogram for Early DIagnosis and treatment of CArdiotoxic complications caused by chemoTherapy for BrEast cancer (PREDICATE)" funded by the Science Committee of the Ministry of Education and Science of the Republic of Kazakhstan (grant IRN AP09259524, state reg. No. 0121PK00565

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“T1N0M0”. Cancer is difficult to detect in time, because for a long time it can be asymptomatic, hidden.
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