Modifications to the cardiomyopathy surveillance recommendations formulated in 2015 versus 2022

General recommendation	
Survivors treated with anthracyclines or chest radiation (RT) or both and their healthcare providers should be aware of the risk of cardiomyopathy	CAYA cancer survivors treated with anthracyclines, chest RT, or both (high-quality evidence), and their health care providers should be aware of the risk of cardiomyopathy (strong recommendation).
Who needs cardiomyopathy surveillance?	
Anthracyclines and/or mitoxantrone (as doxorubicin equivalent dose) alone	
Cardiomyopathy surveillance is recommended for survivors treated with high dose (≥250 mg/m^2) anthracyclines.	Cardiomyopathy surveillance is recommended for CAYA cancer survivors treated with high dose (≥250 mg/m^2) anthracyclines (high-quality evidence, strong recommendation)
Cardiomyopathy surveillance is reasonable for survivors treated with moderate dose (≥100 to <250 mg/m^2) anthracyclines.	Cardiomyopathy surveillance is reasonable for CAYA cancer survivors treated with moderate dose (≥100 to <250 mg/m^2) anthracyclines (high-quality evidence, moderate recommendation).
Cardiomyopathy surveillance may be reasonable for survivors treated with low dose (<100 mg/m^2) anthracyclines.	**Cardiomyopathy surveillance is not recommended for survivors treated with low dose (<100 mg/m^2) anthracyclines (high-quality evidence, strong recommendation).**
Chest-directed radiotherapy alone	
Cardiomyopathy surveillance is recommended for survivors treated with high dose (≥35 Gy) chest RT.	Cardiomyopathy surveillance is recommended for CAYA cancer survivors treated with high dose **(≥30 Gy)** chest RT (high-quality evidence, strong recommendation).
Cardiomyopathy surveillance may be reasonable for survivors treated with moderate dose (≥15 to <35 Gy) chest RT.	Cardiomyopathy surveillance is reasonable for CAYA cancer survivors treated with moderate dose **(≥15 to <30 Gy)** chest RT (high-quality evidence, moderate recommendation).
No recommendation can be formulated for cardiomyopathy surveillance for survivors treated with low dose (<15 Gy) chest RT with conventional fractionation.	**Cardiomyopathy surveillance is not recommended for CAYA cancer survivors treated with low dose (<15 Gy) chest RT with conventional fractionation (high-quality evidence, strong recommendation).**
Anthracyclines and chest-directed radiotherapy	
Cardiomyopathy surveillance is recommended for survivors treated with moderate to high dose anthracyclines (≥100 mg/m^2) and moderate to high dose chest RT (≥15 Gy).	Cardiomyopathy surveillance is recommended for CAYA cancer survivors treated with moderate to high dose anthracyclines (≥100 mg/m^2) and moderate to high dose chest RT (≥15 Gy) (high-quality evidence, strong recommendation).
Dexrazoxane	
-	No recommendation can be formulated to change cardiomyopathy surveillance in CAYA cancer survivors who received dexrazoxane cardioprotection with anthracycline administration (low-quality evidence).
Pregnancy	
Cardiomyopathy surveillance is reasonable before pregnancy or in the first trimester for all female survivors treated with anthracyclines or chest RT.	Cardiomyopathy surveillance is reasonable before pregnancy or in the first trimester for all female CAYA survivors treated with anthracyclines or chest RT (low-quality evidence, moderate recommendation).
No recommendations can be formulated for the frequency of ongoing surveillance in pregnant survivors who have normal left ventricular (LV) systolic function immediately before or during the first trimester of pregnancy.	Continuing cardiomyopathy surveillance is reasonable during pregnancy for female CAYA survivors treated with anthracyclines or chest RT who had a history of prior LV systolic dysfunction that has resolved even in the presence

	of a normal baseline ejection fraction in the first trimester (low-quality evidence, moderate recommendation).
Genetic variants	
-	No recommendation can be formulated for cardiomyopathy surveillance in CAYA cancer survivors carrying a genetic variant that increases or decreases the risk of developing cardiomyopathy (low-quality evidence).
What surveillance modality should be used?	
Echocardiography is recommended as the primary cardiomyopathy surveillance modality for assessment of LV systolic function in survivors treated with anthracyclines or chest RT.	LV ejection fraction measured with 2D or 3D echocardiography is recommended as the primary cardiomyopathy surveillance modality for assessment of LV systolic function in CAYA cancer survivors treated with anthracyclines or chest RT (moderate-quality evidence, strong recommendation).
Radionuclide angiography or CMR may be reasonable for cardiomyopathy surveillance in at-risk survivors for whom echocardiography is not technically feasible or optimal.	Cardiac magnetic resonance imaging may be reasonable for cardiomyopathy surveillance in at-risk CAYA cancer survivors for whom echocardiography is not technically feasible or optimal (expert opinion, moderate recommendation).
Assessment of cardiac blood biomarkers (e.g., natriuretic peptides) in conjunction with imaging studies may be reasonable in instances where symptomatic cardiomyopathy is strongly suspected or in individuals who have borderline cardiac function during primary surveillance.	Assessment of cardiac blood biomarkers (e.g., natriuretic peptides) in conjunction with imaging studies may be reasonable in instances where symptomatic cardiomyopathy is strongly suspected or in CAYA cancer survivors who have borderline cardiac function during primary surveillance (expert opinion, moderate recommendation).
Assessment of cardiac blood biomarkers (e.g., natriuretic peptides and troponins) is not recommended as the only strategy for cardiomyopathy surveillance in at-risk survivors.	Assessment of cardiac blood biomarkers (e.g., natriuretic peptides and troponins) is not recommended as the only strategy for cardiomyopathy surveillance in at-risk CAYA survivors (low- to moderate-quality evidence, strong recommendation).
At what frequency should cardiomyopathy surveillance be performed?	
High-risk CAYA cancer survivors	
Cardiomyopathy surveillance is recommended for high-risk survivors to begin no later than 2-years after completion of cardiotoxic therapy, repeated at 5-years after diagnosis and continued every 5 years thereafter.	Cardiomyopathy surveillance is recommended for high-risk CAYA cancer survivors to begin no later than 2 years after completion of cardiotoxic therapy and continued **every 2 years thereafter** (moderate-quality evidence, strong recommendation).
More frequent cardiomyopathy surveillance is reasonable for high-risk survivors.	-
Lifelong cardiomyopathy surveillance may be reasonable for high-risk survivors.	Lifelong cardiomyopathy surveillance is reasonable for high-risk CAYA cancer survivors (expert opinion, moderate recommendation).
Moderate-risk CAYA cancer survivors	
Cardiomyopathy surveillance is reasonable for moderate- and low-risk survivors to begin no later than 2 years after completion of cardiotoxic therapy, repeated at 5-years after diagnosis, and continue every 5 years thereafter.	Cardiomyopathy surveillance is reasonable for **moderate-risk** CAYA survivors to begin no later than 2 years after completion of cardiotoxic therapy, repeated at 5 years after diagnosis, and continue every 5 years thereafter (low-quality evidence, moderate recommendation).
More frequent cardiomyopathy surveillance may be reasonable for moderate- and low-risk survivors.	-

Lifelong cardiomyopathy surveillance may be reasonable for moderate- and low-risk survivors.	Lifelong cardiomyopathy surveillance is reasonable for moderate-risk CAYA cancer survivors (expert opinion, moderate recommendation).
Low-risk CAYA cancer survivors	
Cardiomyopathy surveillance is reasonable for moderate and low-risk survivors to begin no later than 2 years after completion of cardiotoxic therapy, repeated at 5 years after diagnosis and continue every 5 years thereafter.	Cardiomyopathy surveillance is not recommended in **low-risk** CAYA cancer survivors **(**moderate-quality evidence).
What should be done when abnormalities are identified?	
Cardiology consultation is recommended for survivors with asymptomatic cardiomyopathy following treatment with anthracyclines or chest RT.	Cardiology consultation is recommended for CAYA survivors with **asymptomatic LV systolic or diastolic dysfunction**** following treatment with anthracyclines or chest RT (expert opinion, strong recommendations).
-	Treatment with heart failure medications (ACE inhibitors, ARBs, beta-blockers) is recommended in CAYA cancer survivors with asymptomatic LV ejection fraction <40%, according to guidelines from the general population (low- to high-quality evidence in the general population, strong recommendation).
	No recommendations can be formulated about treatment with heart failure medications in CAYA cancer survivors with asymptomatic borderline (LV ejection fraction between 40% and the upper limit of normal) cardiac function (no studies in CAYA cancer survivors, no evidence in the general population).
Advice regarding physical activity and modifiable cardiovascular risk factors	
Cardiology consultation is recommended for survivors with asymptomatic cardiomyopathy to define limits and precautions for exercise.	Cardiology consultation is recommended for CAYA survivors with asymptomatic cardiomyopathy to define limits and precautions for exercise (expert opinion, strong recommendation).
Cardiology consultation may be reasonable for high-risk survivors who plan to participate in high intensity exercise to define limits and precautions for physical activity.	Cardiology consultation is reasonable for high-risk CAYA survivors who plan to participate in high intensity exercise to define limits and precautions for physical activity (expert opinion, moderate recommendation).
Screening for modifiable cardiovascular risk factors (hypertension, diabetes, dyslipidemia, and obesity) is recommended for all survivors treated with anthracyclines or chest RT so that necessary interventions can be initiated to help avert the risk of symptomatic cardiomyopathy.	Screening for and management of modifiable cardiovascular risk factors (hypertension, diabetes, dyslipidemia, obesity, smoking, alcohol intake) is recommended for all CAYA survivors treated with anthracyclines or chest RT to help avert the risk of symptomatic cardiomyopathy (evidence-based guidelines, strong recommendation).

*New cancer treatments: Tyrosine Kinase Inhibitors, demethylating agents, M-TOR inhibitors, Akt Inhibitors, PDK-1 inhibitors, RAF inhibitors, MEK inhibitors, FTS inhibitors, drugs targeting HER receptors, drugs targeting the c-MET receptor, drugs targeting IGF-IR receptor, SRC -targeting small molecule inhibitors, anti VEGF/VEGFR agents, vascular disrupting agents, heat shock protein inhibitors (HSP-90 inhibitors), inhibitors of ubiquitin proteosome system, PARP inhibitors, classes of histone deacetylases inhibitors, monoclonal antibodies, bevacizumab, Avastin

**LV systolic and diastolic dysfunction as defined by the America Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI) (Appendix D).

Color legend: Green=strong recommendation to do; Orange=moderate recommendation to do; Red=recommendation not to do

Abbreviations: 3D=three-dimensional; 2D=two-dimensional; ACE=angiotensin converting enzyme; ARB=angiotensin receptor blocker; ASE= America Society of Echocardiography; CAYA=childhood, adolescent and young adult; chest RT=chest-directed radiotherapy; c-MET= mesenchymal epithelial transition factor; CMR= cardiac magnetic resonance imaging; EACVI= European Association of Cardiovascular Imaging; FTS= feature tracking strain; Gy=Gray; HF=heart failure;

IGF-IR= Insulin-like growth factor 1 receptor; LV=left ventricular; <=less than; mg/m^2=milligrams per square meter; >=greater than or equal to; M-TOR=mammalian target of rapamycin; PDK= pyruvate dehydrogenase kinase; VEGF=vascular endothelial growth factor; VEGFR= vascular endothelial growth factor receptor; vs=versus