

# ACR Appropriateness Criteria® Assessment of Cardiac Function and Baseline Cardiac Risk Stratification in Oncology Patients

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Disclaimer: The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

## Abstract

Cardiac risk stratification is clinically useful prior to initiation of oncologic therapy in asymptomatic patients in order to guide treatment decisions and allow for initiation of cardioprotective therapy or modification of treatment regimens. Once oncology treatment is underway, patients may develop cardiac symptoms. In this setting, imaging can be used for assessment of ventricular and valvular function, myocardial characterization, pericardial effusion or constriction, as well as to evaluate for ischemia as a cause of symptoms. Results can help guide treatment choices and shared decision-making regarding modification or cessation of treatments with associated cardiotoxicity.

The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision process support the systematic analysis of the medical literature from peer reviewed journals. Established methodology principles such as Grading of Recommendations Assessment, Development, and Evaluation or GRADE are adapted to evaluate the evidence. The RAND/UCLA Appropriateness Method User Manual provides the methodology to determine the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where peer reviewed literature is lacking or equivocal, experts may be the primary evidentiary source available to formulate a recommendation.

**Key Words:** Appropriateness Criteria, appropriate use criteria, AUC, cardiac risk stratification, cardio-oncology, cardiotoxicity, oncologic therapy

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ACR Appropriateness Criteria® Assessment of Cardiac Function and Baseline Cardiac Risk Stratification in Oncology Patients. [Variants 1](#) and [2](#) and [Tables 1](#) and [2](#).

**Variant 1. Adult. Cardiac risk stratification prior to initiation of oncologic therapy. No cardiac symptoms. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
US echocardiography transthoracic resting	Usually Appropriate	O
MRI heart function and morphology without and with IV contrast	Usually Appropriate	O
MRI heart function and morphology without IV contrast	Usually Appropriate	O
Nuclear medicine ventriculography	Usually Appropriate	⊕⊕⊕
US echocardiography transesophageal	May Be Appropriate	O
US echocardiography transthoracic stress	May Be Appropriate	O
MRI heart function with stress without and with IV contrast	May Be Appropriate	O
MRI heart function with stress without IV contrast	May Be Appropriate	O
CT coronary calcium	May Be Appropriate	⊕⊕⊕
CTA coronary arteries with IV contrast	May Be Appropriate	⊕⊕⊕
N-13 ammonia PET/CT heart	May Be Appropriate	⊕⊕⊕
CT heart function and morphology with IV contrast	May Be Appropriate	⊕⊕⊕⊕
Rb-82 PET/CT heart	May Be Appropriate	⊕⊕⊕⊕
SPECT or SPECT/CT heart	May Be Appropriate	⊕⊕⊕⊕
US duplex Doppler lower extremity	Usually Not Appropriate	O
Radiography chest	Usually Not Appropriate	⊕
Arteriography coronary	Usually Not Appropriate	⊕⊕⊕
Arteriography coronary with ventriculography	Usually Not Appropriate	⊕⊕⊕
CT chest with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT chest without and with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT chest without IV contrast	Usually Not Appropriate	⊕⊕⊕
CTA chest with IV contrast	Usually Not Appropriate	⊕⊕⊕
CTA chest without and with IV contrast	Usually Not Appropriate	⊕⊕⊕
CTA pulmonary arteries with IV contrast	Usually Not Appropriate	⊕⊕⊕
PYP scan heart	Usually Not Appropriate	⊕⊕⊕
PYP scan with SPECT or SPECT/CT heart	Usually Not Appropriate	⊕⊕⊕

**Variant 2.** Adult. Assessment of cardiac function during oncologic therapy. Cardiac symptoms. Ischemia not excluded. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
US echocardiography transthoracic resting	Usually Appropriate	O
US echocardiography transthoracic stress	Usually Appropriate	O
MRI heart function and morphology without and with IV contrast	Usually Appropriate	O
MRI heart function and morphology without IV contrast	Usually Appropriate	O
MRI heart function with stress without and with IV contrast	Usually Appropriate	O
CTA coronary arteries with IV contrast	Usually Appropriate	⊕⊕⊕
Rb-82 PET/CT heart	Usually Appropriate	⊕⊕⊕⊕
SPECT or SPECT/CT heart	Usually Appropriate	⊕⊕⊕⊕
US echocardiography transesophageal	May Be Appropriate	O
Radiography chest	May Be Appropriate (Disagreement)	⊕
Arteriography coronary	May Be Appropriate	⊕⊕⊕
Arteriography coronary with ventriculography	May Be Appropriate	⊕⊕⊕
MRI heart function with stress without IV contrast	May Be Appropriate (Disagreement)	O
CTA pulmonary arteries with IV contrast	May Be Appropriate	⊕⊕⊕
N-13 ammonia PET/CT heart	May Be Appropriate (Disagreement)	⊕⊕⊕
Nuclear medicine ventriculography	May Be Appropriate	⊕⊕⊕
CT heart function and morphology with IV contrast	May Be Appropriate	⊕⊕⊕⊕
US duplex Doppler lower extremity	Usually Not Appropriate	O
CT chest with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT chest without and with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT chest without IV contrast	Usually Not Appropriate	⊕⊕⊕
CT coronary calcium	Usually Not Appropriate	⊕⊕⊕
CTA chest with IV contrast	Usually Not Appropriate	⊕⊕⊕
CTA chest without and with IV contrast	Usually Not Appropriate	⊕⊕⊕
PYP scan heart	Usually Not Appropriate	⊕⊕⊕
PYP scan with SPECT or SPECT/CT heart	Usually Not Appropriate	⊕⊕⊕

**Table 1.** Appropriateness category names and definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

**Table 2.** Relative radiation level designations

RRL	Adult Effective Dose Estimate Range (mSv)	Pediatric Effective Dose Estimate Range (mSv)
O	0	0
⊕	<0.1	<0.03
⊕⊕	0.1-1	0.03-0.3
⊕⊕⊕	1-10	0.3-3
⊕⊕⊕⊕	10-30	3-10
⊕⊕⊕⊕⊕	30-100	10-30

Note: Relative radiation level (RRL) assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "varies."

## SUMMARY OF LITERATURE REVIEW

### Introduction/Background

Patients with a diagnosis of cancer undergoing oncology treatment are at elevated risk for cardiovascular disease and adverse cardiovascular events [1-3]. Oncology patients who develop cardiovascular disease have a higher total mortality rate, and heart disease accounts for >75% of all cardiovascular disease mortality in cancer survivors [4]. Factors that contribute to poor outcomes if cardiac events do occur are still under investigation and may be related to medical frailty and the underlying malignancy itself or, alternatively, side effects from treatment. Systemic cancer therapies have varying degrees and types of cardiotoxicity. Major categories that are most associated with cardiotoxicity include anthracyclines, HER2-targeted therapies, vascular endothelial growth factor inhibitors, multitargeted kinase inhibitors, proteasome inhibitors and immunomodulatory drugs, immune checkpoint inhibitors, and androgen deprivation agents. Radiation therapy (RT) can cause short- and long-term cardiotoxicity including adverse effects on cardiac valves, the coronary arteries, and the pericardium. This document focuses on the use of imaging in cardiac risk stratification at baseline in asymptomatic patients who will undergo oncologic therapy, as well as the use of imaging to assess cardiac function if symptoms develop once oncologic therapy has commenced.

Cardiac risk stratification is clinically useful before the initiation of oncologic therapy in asymptomatic patients in order to guide treatment decisions and allow for initiation of cardioprotective therapy or modification of treatment regimens [1]. Specifically, expert consensus guidelines from the Heart Failure Association of the European Society of Cardiology (ESC) Cardio-Oncology Study Group in collaboration with the International Cardio-Oncology Society (ICOS) recommend evaluation of baseline ventricular ejection fraction (EF) and valvular function particularly before treatment that can potentially be cardiotoxic [2].

Once oncology treatment is underway, patients may develop cardiac symptoms. In this setting, imaging can be used for the assessment of ventricular and valvular function,

myocardial characterization, and pericardial effusion or constriction, as well as to evaluate for ischemia as a cause of symptoms. Results can help guide treatment choices and shared decision making regarding modification or cessation of treatments with associated cardiotoxicity. Appropriateness criteria have been developed for evaluation of suspected heart failure and of acute chest pain, which can be applied to the oncology patient population. See the ACR Appropriateness Criteria® topics on “Suspected New-Onset and Known Nonacute Heart Failure” [5], “Chest Pain-Possible Acute Coronary Syndrome” [6], and “Acute Nonspecific Chest Pain-Low Probability of Coronary Artery Disease” [7] for further guidance.

### Special Imaging Considerations

For the purposes of distinguishing between CT and CT angiography (CTA), ACR Appropriateness Criteria topics use the definition in the ACR–NASCI–SIR–SPR Practice Parameter for the Performance and Interpretation of Body Computed Tomography Angiography (CTA) [8]:

“CTA uses a thin-section CT acquisition that is timed to coincide with peak arterial and/or venous enhancement, depending on the vascular structures to be analyzed. The resultant volumetric data set is interpreted using primary transverse reconstructions as well as multiplanar reformations and 3-D renderings.”

All elements are essential: 1) timing, 2) reconstructions/reformats, and 3) 3-D renderings. Standard CTs with contrast also include timing issues and reconstructions/reformats. Only in CTA, however, is 3-D rendering a required element. This corresponds to the definitions that the CMS has applied to the Current Procedural Terminology codes.

### INITIAL IMAGING DEFINITION

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the

variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

- There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)  
OR
- There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient's care).

## DISCUSSION OF PROCEDURES BY VARIANT

### **Variant 1: Adult. Cardiac risk stratification prior to initiation of oncologic therapy. No cardiac symptoms. Initial imaging**

Cardiac risk stratification is thought useful and necessary before the initiation of oncologic therapy in asymptomatic patients, and evaluation of baseline ventricular EF and valvular function is the primary goal. Cardiac imaging that assesses ventricular function, however, can also provide potentially useful information on ischemia or plaque burden that may further assist in risk stratification. The role of imaging serves as a primary prevention strategy to recognize pre-existing yet unrecognized cardiovascular conditions and optimize the risk of cardiovascular complications during or after treatment. Oncology patients may have pre-existing cardiovascular disease even in the absence of symptoms, and detection may help guide decision making.

Cardiac risk stratification is clinically useful before the initiation of oncologic therapy in patients who do not have cardiac symptoms in order to guide treatment decisions. Chemotherapeutic agents have varying degrees and types of cardiotoxicity. Major categories of chemotherapeutic agents, which are most associated with cardiotoxicity, include anthracyclines, HER2-targeted therapies, vascular endothelial growth factor inhibitors, multitargeted kinase inhibitors, proteasome inhibitors and immunomodulatory drugs, immune checkpoint inhibitors, stem cell transplantation, cellular therapeutic agents, and androgen deprivation agents. RT can cause short- and long-term cardiotoxicity including adverse effects on cardiac valves, the coronary arteries, and the pericardium. Cardiac risk stratification may therefore help guide shared decision making regarding type or duration of oncologic therapy.

**Arteriography Coronary.** Coronary arteriography via left heart catheterization evaluates for obstructive coronary artery disease and does not characterize ventricular EF or valvular function. There is no relevant literature regarding the use of coronary arteriography in the evaluation of cardiac

risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

### **Arteriography Coronary With Ventriculography.**

Coronary arteriography with ventriculography evaluates for obstructive coronary artery disease and can be used to characterize ventricular function and aortic/mitral valvular function. There is no relevant literature regarding the use of coronary arteriography with ventriculography in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

### **CT Chest With IV Contrast.**

CT chest with intravenous (IV) contrast is performed in the oncology patient population for staging and treatment planning and provides limited incidental information on baseline cardiac abnormalities such as valvular or coronary artery calcification or chamber enlargement. However, assessment for presence of calcified plaque (qualitatively) has been shown to correlate with dedicated calcium score examination and confer information on the likelihood for significant obstructive coronary artery disease [9]. There is no relevant literature regarding the use of CT chest with IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms [9].

### **CT Chest Without and With IV Contrast.**

CT chest without and with IV contrast is performed in the oncology patient population for staging and treatment planning and provides limited incidental information on baseline cardiac abnormalities such as valvular or coronary artery calcification or chamber enlargement. However, assessment for presence of calcified plaque (qualitatively) has been shown to correlate with dedicated calcium score examination and confer information on the likelihood for significant obstructive coronary artery disease [9]. There is no relevant literature regarding the use of CT chest without and with IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

### **CT Chest Without IV Contrast.**

CT chest without IV contrast is performed in the oncology patient population for staging and treatment planning and provides limited incidental information on baseline cardiac abnormalities such as valvular or coronary artery calcification or chamber enlargement. However, assessment for the presence of calcified plaque (qualitatively) has been shown to correlate with dedicated calcium score examination and confer information on the likelihood for significant obstructive coronary artery disease [9]. There is no relevant literature regarding the use of CT chest without IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**CT Coronary Calcium.** Noncontrast CT coronary calcium for identification of coronary artery calcium plays an important role in cardiac risk stratification by detecting subclinical cardiovascular disease. In the current American College of Cardiology/American Heart Association (AHA) prevention guidelines for adults at intermediate risk for atherosclerotic cardiovascular disease, coronary artery calcium is a class IIA recommendation to stratify risk and target prevention strategies [10-12]. In addition, a calcium score of 0 allows downgrading of atherosclerotic cardiovascular disease risk in the absence of other risk factors [13]. A study of 333 patients with breast cancer demonstrated that median coronary artery calcium burden was not significantly different between patients who did and did not undergo RT ( $P = .982$ ), and this was also not significantly different between patients who underwent left- versus right-sided RT ( $P = .453$ ), suggesting that radiation-induced accelerated coronary artery disease is not an explanation for higher rates of heart disease [14]. There is no relevant literature regarding the use of CT coronary calcium in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**CT Heart Function and Morphology With IV Contrast.** CT of the heart function and morphology with IV contrast can evaluate ventricular EF at baseline prior to initiation of therapy. Valvular stenosis and insufficiency can be identified based on anatomic valve area; however, pressure gradients cannot be calculated. There is no relevant literature regarding the use of CT heart function and morphology with IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**CTA Chest With IV Contrast.** CTA chest with IV contrast can demonstrate baseline vascular pathology such as aortic aneurysm or stenosis of the origins of the arch vessels; however, it does not assess ventricular EF or valvular function. There is no relevant literature regarding the use of CTA chest with IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**CTA Chest Without and With IV Contrast.** CTA chest without and with IV contrast can demonstrate baseline vascular pathology such as aortic aneurysm or stenosis of the origins of the arch vessels; however, it does not assess ventricular EF or valvular function. There is no relevant literature regarding the use of CTA chest without and with IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**CTA Coronary Arteries With IV Contrast.** CTA of the coronary arteries with IV contrast can evaluate for the presence of coronary artery disease and degree of coronary artery stenosis; however, it does not assess ventricular EF or valvular function. There is no relevant literature regarding the use of CTA of the coronary arteries with IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**CTA Pulmonary Arteries With IV Contrast.** CTA pulmonary arteries with IV contrast is not typically used in asymptomatic patients or for risk stratification. There is no relevant literature regarding the use of CTA pulmonary arteries with IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**MRI Heart Function and Morphology Without and With IV Contrast.** MRI heart function and morphology with and without IV contrast can provide quantification of ventricular function to establish a baseline, as well as evaluate valvular disease, pericardial disease, and myocardial tissue characterization including edema, native parametric mapping values, or the presence of late gadolinium enhancement. Expert consensus guidelines by the American College of Cardiology Foundation and cosponsored by the ACR, AHA, North American Society for Cardiovascular Imaging, and the Society for Cardiovascular Magnetic Resonance Imaging describe that cine cardiac MRI for the evaluation of cardiac volumes and systolic function is considered a standard of reference by which other modalities are validated [15]. There is sparse literature [16] regarding the use of MRI heart function and morphology with and without IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in select settings.

**MRI Heart Function and Morphology Without IV Contrast.** MRI heart function and morphology without IV contrast can provide quantification of ventricular function to establish a baseline, as well as evaluate valvular disease, pericardial disease, and myocardial tissue characterization including edema and native parametric mapping values. There is sparse literature [16] regarding the use of MRI heart function and morphology without IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**MRI Heart Function With Stress Without and With IV Contrast.** MRI heart function with stress with and without IV contrast can demonstrate baseline ischemia via

stress-induced perfusion defects or wall motion abnormalities. As with other cardiac MRIs, this examination can also evaluate valvular disease, pericardial disease, and myocardial tissue characterization including edema, native parametric mapping values, and infiltrative process or infarction. There is sparse literature [16] regarding the use of MRI heart function with stress with and without IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

### MRI Heart Function With Stress Without IV Contrast.

MRI heart function with stress without IV contrast can demonstrate baseline ischemia via stress-induced wall motion abnormalities. As with other cardiac MRIs, this examination can also evaluate valvular disease, pericardial disease, and myocardial tissue characterization including edema and native parametric mapping values. There is no relevant literature regarding the use of MRI heart function with stress without IV contrast in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**N-13 Ammonia PET/CT Heart.** N-13 ammonia PET/CT of the heart can evaluate baseline parameters of perfusion such as myocardial flow reserve (MFR) and myocardial blood flow (MBF). A pilot study of 10 patients undergoing RT for locally advanced breast cancer demonstrated feasibility of N-13 ammonia PET imaging to evaluate MFR at baseline and at 1 year after RT. MFR decreased in 50% of the patients, which suggests it may be an indicator for early detection of cardiotoxicity in patients receiving chest wall RT [17]. A study of 20 patients with left-sided breast cancer who underwent RT did not show differences in rest or stress MBF between irradiated and nonirradiated myocardium several years after completing RT [18]. A study of 87 patients with breast cancer who underwent cardiac stress PET imaging with either N-13 ammonia or Rb-82 demonstrated that the lowest MFR tertile had a higher cumulative incidence of major adverse cardiovascular event (adjusted subdistribution hazard ratio 4.91; 95% confidence interval [CI], 1.68-14.38;  $P = .004$ ) compared with the highest MFR tertile, suggesting that MFR may have potential as a risk stratification biomarker [19].

**Nuclear Medicine Ventriculography.** Radionuclide ventriculography is commonly used for the assessment of left ventricular (LV) function [20]. A study of 177 patients with breast cancer evaluated potential early markers of LV dysfunction on baseline ventriculography including approximate entropy, synchrony, entropy, and SD from phase histogram. Eleven patients had a decline in LVEF of  $>10\%$  to an EF  $<50\%$  after treatment, and this group

had a significantly higher approximate entropy at baseline than those who did not experience a decrement in LVEF throughout treatment, suggesting that radionuclide ventriculography phase analysis using approximate entropy may help detect subclinical LV contraction abnormalities at baseline [21]. In another study of 593 patients with breast cancer, routine baseline ventriculography scans before adjuvant chemotherapy were abnormal and changed the treatment decision in only 2.5% and 2.0% of patients, respectively [22]. A recent study of 75 patients with cancer comparing radionuclide ventriculography EFs and cardiac MRI demonstrated that radionuclide ventriculography resulted in misclassification of 20% of patients as abnormal versus normal if an EF threshold of 55% was used and misclassification of 35% of patients if an EF threshold of 35% was used [23].

**PYP Scan Heart.** Pyrophosphate (PYP) scan heart is used for evaluation of cardiac amyloidosis, which is a risk factor for the development of chemotherapy-induced cardiotoxicity [2]. There is no relevant literature regarding the use of PYP scan heart in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**PYP Scan With SPECT or SPECT/CT Heart.** PYP scan with single-photon emission computed tomography (SPECT) or SPECT/CT heart is used for the evaluation of cardiac amyloidosis, which is a risk factor for development of chemotherapy-induced cardiotoxicity [2]. There is no relevant literature regarding the use of PYP scan with SPECT or SPECT/CT heart in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**Radiography Chest.** Chest radiography may be performed as part of staging for oncology patients and can demonstrate cardiomegaly, pulmonary edema, or advanced calcifications of the valves, aorta, and pericardium. There is no relevant literature regarding the use of chest radiography in the evaluation of cardiac risk stratification before the initiation of oncologic therapy in the absence of cardiac symptoms.

**Rb-82 PET/CT Heart.** Rb-82 PET/CT of the heart can evaluate baseline parameters of perfusion such as MFR and MBF. A study of 87 patients with breast cancer who underwent cardiac stress PET imaging with either N-13 ammonia or Rb-82 demonstrated that the lowest MFR tertile had a higher cumulative incidence of major adverse cardiovascular event (adjusted subdistribution hazard ratio 4.91; 95% CI, 1.68-14.38;  $P = .004$ ) compared with the highest MFR tertile, suggesting that

MFR may have potential as a risk stratification biomarker [19].

**SPECT or SPECT/CT Heart.** SPECT or SPECT/CT heart can evaluate for baseline ischemia or prior infarct as demonstrated by perfusion abnormalities at rest and stress. A study of SPECT-gated myocardial perfusion imaging in 18 patients with esophageal cancer undergoing RT showed significant decreases in wall motion (1/20 segments), wall thickening (2/20 segments), end-diastolic perfusion (5/20 segments), and end-systolic perfusion (8/20 segments) ( $P < .05$ ) as well as new myocardial perfusion defects in 8 of the patients. This suggests that early cardiotoxicity from RT can be demonstrated by SPECT performed at baseline and subsequently during RT [24].

**US Duplex Doppler Lower Extremity.** Ultrasound (US) duplex Doppler lower extremity evaluates patency of the lower extremity deep and superficial veins. There is no relevant literature regarding the use of US duplex Doppler lower extremity in the evaluation of cardiac risk stratification before the initiation of oncologic therapy.

**US Echocardiography Transesophageal.** Transesophageal echocardiography provides evaluation of ventricular function and of valvular disease. Expert guidelines by the ESC in collaboration with ICOS have incorporated echocardiography to establish ventricular EF and assess valvular function before therapy [1,2]. Although this test is typically not first-line, it may be used in select patients and does provide information on ventricular function.

**US Echocardiography Transthoracic Resting.** Transthoracic resting echocardiography provides evaluation of ventricular function and of valvular disease. Expert guidelines by the ESC in collaboration with ICOS have incorporated echocardiography to establish ventricular EF and assess valvular function before therapy [1,2]. The sensitivity and specificity of 2-D echocardiography in assessing LVEF  $<40\%$  in a study of 534 nononcology patients compared with ventriculography were 75% and 89%, respectively [25]. The addition of strain imaging has further been shown as an effective technique to identify patients who are at high risk for clinical events [26].

**US Echocardiography Transthoracic Stress.** Transthoracic stress echocardiography provides evaluation of the presence of stress-induced regional wall motion abnormalities that can indicate ischemia, and it can also assess ventricular function and of valvular disease. Expert guidelines by the ESC in collaboration with ICOS have incorporated echocardiography to establish ventricular EF and assess valvular function before therapy [1,2]. Stress studies are primarily intended to assess ischemia, but they can also provide information on ventricular function.

## Variant 2: Adult. Assessment of cardiac function during oncologic therapy. Cardiac symptoms. Ischemia not excluded. Initial imaging

After oncologic therapy is initiated, patients may develop cardiac symptoms due to either ischemic or nonischemic causes including depressed ventricular function, valvular disease, or pericardial disease. Assessment of cardiac function in this setting can include quantifying ventricular systolic function but also causes of cardiac symptoms including coronary artery disease and ischemia. Imaging plays a pertinent role in symptomatic patients for diagnoses of various cardiovascular complications that may arise during treatment.

**Arteriography Coronary.** A study of 480 patients with and without cancer who underwent coronary arteriography used a machine-learning neural-network-guided propensity-score-adjusted multivariable regression to assess coronary artery disease burden. Patients with cancer had fewer clinically significant lesions in the left anterior descending artery (25% versus 39.17%, respectively;  $P < .01$ ) and left circumflex artery (15.83% versus 30%, respectively;  $P < .001$ ), whereas left main and right coronary artery disease prevalence were similar. Patients with cancer were less likely to have multivessel coronary artery disease (odds ratio, 0.53; 95% CI, 0.29-0.98;  $P = .04$ ) and significant left circumflex artery lesions (odds ratio, 0.47; 95% CI, 0.26-0.85;  $P = .01$ ), independent of known coronary artery disease confounders [27]. A study of 94 patients with previous lung cancer who underwent coronary arteriography demonstrated that more severe anatomical coronary artery disease as evaluated by the SYNTAX score risk was increased by chemotherapy by 5.323 times (95% CI, 2.002-14.152) and by platinum-based regimens by 5.85 times (95% CI, 2.027-16.879) [28].

**Arteriography Coronary With Ventriculography.** Coronary arteriography with ventriculography evaluates for obstructive coronary artery disease and can be used to characterize ventricular function and aortic/mitral valvular function. There is no relevant literature regarding the use of coronary arteriography with ventriculography in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**CT Chest With IV Contrast.** CT chest with IV contrast can demonstrate causes of cardiac symptoms, including pericardial effusion, or secondary signs of depressed systolic function such as pulmonary edema or pleural effusions. There is no relevant literature regarding the use of CT chest with IV contrast in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**CT Chest Without and With IV Contrast.** CT chest without and with IV contrast can demonstrate causes of cardiac symptoms, including pericardial effusion, or secondary signs of depressed systolic function such as pulmonary edema or pleural effusions. There is no relevant literature regarding the use of CT chest without and with IV contrast in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**CT Chest Without IV Contrast.** CT chest without IV contrast can demonstrate causes of cardiac symptoms, including pericardial effusion, or secondary signs of depressed systolic function such as pulmonary edema or pleural effusions. There is no relevant literature regarding the use of CT chest without IV contrast in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**CT Coronary Calcium.** There is no relevant literature regarding the use of CT coronary calcium in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**CT Heart Function and Morphology With IV Contrast.** CT of the heart function and morphology with IV contrast can be used to evaluate ventricular and valvular function. Expert consensus guidelines by the Society of Cardiovascular Computed Tomography and recognized by the ICOS describe that EF can be calculated to assess systolic function, valves can be anatomically characterized, and the presence of pericardial thickening or effusion can be evaluated in the setting of cardiac symptoms after initiation of therapy [9,29]. There is no relevant literature regarding the use of CT of the heart function and morphology with IV contrast in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**CTA Chest With IV Contrast.** CTA chest with IV contrast can assess for vascular causes of chest pain including acute aortic syndromes. There is no relevant literature regarding the use of CTA chest with IV contrast in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**CTA Chest Without and With IV Contrast.** CTA chest without and with IV contrast can assess for vascular causes of chest pain including acute aortic syndromes. There is no relevant literature regarding the use of CTA chest without and with IV contrast in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**CTA Coronary Arteries With IV Contrast.** CTA of the coronary arteries with IV contrast can evaluate for coronary artery disease and stenosis as a cause of cardiac symptoms [9,29]. If CTA of the coronary arteries is performed with

retrospective electrocardiogram gating, ventricular EF can also be calculated.

**CTA Pulmonary Arteries With IV Contrast.** CTA pulmonary arteries with IV contrast can assess for pulmonary embolism as a cause of cardiac symptoms such as chest pain or dyspnea. There is no relevant literature regarding the use of CTA pulmonary arteries with IV contrast in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**MRI Heart Function and Morphology Without and With IV Contrast.** MRI heart function and morphology without and with IV contrast can provide assessment of ventricular function and help identify the cause for dysfunction. Additional information provided includes valvular disease, pericardial disease, and myocardial tissue characterization including edema, native parametric mapping values, or the presence of late gadolinium enhancement [30-36]. An observational study of patients receiving HER2-targeted therapy also demonstrated declines in right ventricular function, which is better assessed by cardiac MRI than by other modalities [37].

**MRI Heart Function and Morphology Without IV Contrast.** MRI heart function and morphology without IV contrast can provide assessment of ventricular function. Additional information provided includes valvular disease, pericardial disease, and myocardial tissue characterization including edema and native parametric mapping values [30-36]. An observational study of patients receiving HER2-targeted therapy also demonstrated declines in right ventricular function, which is better assessed by cardiac MRI than by other modalities [37].

**MRI Heart Function With Stress Without and With IV Contrast.** MRI heart function with stress without and with IV contrast can demonstrate ischemia via stress-induced perfusion defects or wall motion abnormalities as well as assessment of ventricular function. As with other cardiac MRIs, this examination can also evaluate valvular disease, pericardial disease, and myocardial tissue characterization including edema, native parametric mapping values, and the presence of late gadolinium enhancement [30-36].

**MRI Heart Function With Stress Without IV Contrast.** MRI heart function with stress without IV contrast can demonstrate ischemia via stress-induced wall motion abnormalities as well as assessment of ventricular function. As with other cardiac MRIs, this examination can also evaluate valvular disease, pericardial disease, and myocardial tissue characterization including edema and native parametric mapping values [30-36]. Late gadolinium enhancement and myocardial perfusion cannot be assessed without IV contrast.

**N-13 Ammonia PET/CT Heart.** N-13 ammonia PET/CT of the heart can evaluate parameters of perfusion such as MFR and MBF. There is no relevant literature regarding the use of N-13 ammonia PET/CT in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**Nuclear Medicine Ventriculography.** Radionuclide ventriculography, also known as multigated radionuclide angiography, has been commonly used for the assessment of LVEF with good accuracy and reproducibility [20]. However, a recent study of 75 patients with cancer comparing radionuclide ventriculography EFs and cardiac MRI demonstrated that radionuclide ventriculography resulted in misclassification of 20% of patients as abnormal versus normal if an EF threshold of 55% was used and misclassification of 35% of patients if an EF threshold of 35% was used [23]. Additional limitations include a lack of additional information about cardiac structure and morphology.

**PYP Scan Heart.** PYP scan heart can be used for the evaluation of cardiac amyloidosis in the setting of cardiac symptoms. There is no relevant literature regarding the use of PYP scan heart in the assessment of cardiac function after the initiation of oncologic therapy in the setting of cardiac symptoms.

**PYP Scan With SPECT or SPECT/CT Heart.** PYP scan with SPECT or SPECT/CT heart can be used for the evaluation of cardiac amyloidosis in the setting of cardiac symptoms. There is no relevant literature regarding the use of PYP scan heart in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**Radiography Chest.** Chest radiography can be used in the setting of cardiac symptoms to assess for signs of pulmonary edema or cardiomegaly. There is no relevant literature regarding the use of chest radiography in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**Rb-82 PET/CT Heart.** Rb-82 PET/CT of the heart can evaluate parameters of perfusion such as MFR and MBF. There is no relevant literature regarding the use of Rb-82 PET/CT in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**SPECT or SPECT/CT Heart.** SPECT or SPECT/CT heart can evaluate for ischemia as a cause of cardiac symptoms, as demonstrated by perfusion abnormalities at rest and stress. A study of SPECT-gated myocardial perfusion imaging in 18 patients with esophageal cancer undergoing RT showed significant decreases in wall motion (1/20 segments), wall thickening (2/20 segments), end-diastolic

perfusion (5/20 segments), and end-systolic perfusion (8/20 segments) ( $P < .05$ ) as well as new myocardial perfusion defects in 8 of the patients. This suggests that early cardiotoxicity from RT can be demonstrated by SPECT performed at baseline and subsequently during RT [24].

**US Duplex Doppler Lower Extremity.** Lower extremity venous US can be used in the setting of cardiac symptoms to assess for deep venous thrombosis that may lead to pulmonary embolism. There is no relevant literature regarding the use of lower extremity venous US in the assessment of cardiac function after initiation of oncologic therapy in the setting of cardiac symptoms.

**US Echocardiography Transesophageal.** Transesophageal echocardiography provides evaluation of ventricular function and of valvular disease. Expert guidelines by the European Association of Cardiovascular Imaging and American Society of Echocardiography have incorporated echocardiography to detect myocardial dysfunction induced by oncologic therapy [1,38-42]. An additional parameter that can be assessed is global longitudinal strain, which can be an early marker of impaired myocardial function [43-45].

**US Echocardiography Transthoracic Resting.** Transthoracic resting echocardiography provides evaluation of ventricular function and of valvular disease. Expert guidelines by the European Association of Cardiovascular Imaging and American Society of Echocardiography have incorporated echocardiography to detect myocardial dysfunction induced by oncologic therapy [1,38-42]. An additional parameter that can be assessed is global longitudinal strain, which can be an early marker of impaired myocardial function [43-45].

**US Echocardiography Transthoracic Stress.** Transthoracic stress echocardiography provides evaluation of ventricular function and of valvular disease, as well as the presence of stress-induced regional wall motion abnormalities that can indicate ischemia. Echocardiography is considered the modality of choice to detect myocardial dysfunction induced by oncologic therapy [1,38-42].

## SUMMARY OF HIGHLIGHTS

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

- **Variant 1:** For initial imaging for the purpose of cardiac risk stratification before the initiation of oncologic therapy when there are no cardiac symptoms present, transthoracic echocardiography, cardiac MRI, and nuclear medicine ventriculography are recommended

studies. Cardiac CT including coronary artery CTA, CT coronary calcium, and CT heart function and morphology may be appropriate to assess coronary arteries and/or coronary artery calcification, as well as complementary anatomic evaluation of the heart with ventricular function. Cardiac stress MRI, N-13 ammonia PET/CT, Rb-82 PET/CT heart, and SPECT may also be appropriate to assess ventricular function with complementary information regarding ischemia.

■ **Variant 2:** For the assessment of cardiac function during oncologic therapy when cardiac symptoms are present and ischemia has not been excluded, transthoracic echocardiography with or without stress, cardiac MRI with or without contrast, cardiac stress MRI with contrast, coronary artery CTA, Rb-82 PET/CT heart, and SPECT are recommended studies. Other studies that may be appropriate in specific clinical situations include transesophageal echocardiography, coronary arteriography with or without ventriculography, CTA pulmonary arteries, nuclear medicine ventriculography, and CT heart function and morphology. Chest radiography, cardiac stress MRI without contrast, and N-13 ammonia PET/CT were considered as possibilities but consensus on appropriateness was not reached.

## SUPPORTING DOCUMENTS

The evidence table, literature search, and appendix for this topic are available at <https://acsearch.acr.org/list>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to <https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria>.

## GENDER EQUALITY AND INCLUSIVITY CLAUSE

The ACR acknowledges the limitations in applying inclusive language when citing research studies that pre-dates the use of the current understanding of language inclusive of diversity in sex, intersex, gender and gender-diverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health [46].

## RELATIVE RADIATION LEVEL INFORMATION

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different

diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table 2). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [47].

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