Medical Policy

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Title: Myocardial Strain Imaging

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Populations	Interventions	Comparators	Outcomes
Individuals: • With exposure to medications or radiation that could result in cardiotoxicity	Interventions of interest are: • myocardial strain imaging	Comparators of interest are: • left ventricular ejection fraction	Relevant outcomes include: • Symptoms • Morbid events • Quality of life • Treatment-related mortality • Treatment-related morbidity

DESCRIPTION

Myocardial strain refers to the deformation (shortening, lengthening, or thickening) of the myocardium through the cardiac cycle. Myocardial strain can be measured by tissue Doppler imaging or, more recently, speckle-tracking echocardiography. Speckle-tracking echocardiography uses imaging software to assess the movement of specific markers in the myocardium that are detected in standard echocardiograms. It is proposed that a reduction in myocardial strain may indicate sub-clinical impairment of the heart and can be used to inform treatment before the development of symptoms and irreversible myocardial dysfunction.

OBJECTIVE

The objective of this evidence review is to evaluate whether myocardial strain imaging improves the net health outcome in individuals exposed to medications or radiation that could result in cardiotoxicity.

BACKGROUND

The term 'strain' indicates dimensional or deformational change under force. When used in echocardiography, the term 'strain' is used to describe the magnitude of shortening, thickening, and lengthening of the myocardium through the cardiac cycle. The most frequent measure of myocardial strain is the deformation of the left ventricle in the long axis, termed global longitudinal strain. During systole, ventricular myocardial fibers shorten with movement from the base to the apex. Global longitudinal strain is used as a measure of global left ventricle function and provides a quantitative myocardial deformation analysis of each left ventricle segment. Myocardial strain imaging is intended to detect subclinical changes in left ventricle function in patients with a preserved left ventricle ejection fraction, allowing for early detection of systolic dysfunction. Since strain imaging can identify left ventricle dysfunction earlier than standard methods, this raises the possibility of heart failure prophylaxis and primary prevention before the patient develops symptoms and irreversible myocardial dysfunction. Potential applications of speckle-tracking echocardiography are coronary artery disease, ischemic cardiomyopathy, valvular heart disease, dilated cardiomyopathy, hypertrophic cardiomyopathies, stress cardiomyopathy, and chemotherapy-related cardiotoxicity.

Myocardial Strain Imaging

Myocardial strain can be measured by cardiac magnetic resonance imaging (MRI), tissue Doppler imaging, or by speckle-tracking echocardiography. Tissue Doppler strain imaging has been in use since the 1990s but has limitations that include angle dependency and significant noise. In 2016, Smiseth et al reported that the most widely used method of measuring myocardial strain is speckle-tracking echocardiography.[1,] In speckle-tracking echocardiography, natural acoustic markers generated by the interaction between the ultrasound beam and myocardial fibers form interference patterns (speckles). These markers are stable, and speckle-tracking echocardiography analyzes the spatial dislocation (tracking) of each point (speckle) on routine 2-dimensional sonograms. Echocardiograms are processed using specific acoustic-tracking software on dedicated workstations, with offline semiautomated analysis of myocardial strain. The 2-dimensional displacement is identified by a search with image processing algorithms for similar patterns across 2 frames. When tracked frame-to-frame, the spatiotemporal displacement of the speckles provides information about myocardial deformation across the cardiac cycle. Global longitudinal strain provides a quantitative analysis of each left ventricle segment, which is

expressed as a percentage. In addition to global longitudinal strain, speckle-tracking echocardiography allows evaluation of left ventricle rotational and torsional dynamics.

REGULATORY STATUS

A number of image analysis systems have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Examples of these are shown in Table 1. For example, the EcholnsightⓇ software system (Epsilon Imaging) "enables the production and visualization of 2-dimensional tissue motion measurements (including tissue velocities, strains, strain rates) and cardiac structural measurement information derived from tracking speckle in tissue regions visualized in any B mode (including harmonic) imagery loops as captured by most commercial ultrasound systems" (K110447). The FDA determined that this device was substantially equivalent to existing devices (eg, syngoⓇ US Workplace, Siemens, K091286) for analysis of ultrasound imaging of the human heart.

Table 1. Examples of Software That Have Received FDA Clearance

Brand Name	Manufacturer	510(k) Number	FDA Product Code	Clearance Date
Myostrain	Myocardial Solutions	K182756	LNH	02/14/2019
Vivid	GE	K181685	IYN	10/25/2018
Aplio	Toshiba	K173090	IYN	01/11/2018
2D CARDIAC PERFORMANCE ANALYSIS	Tomtec	K120135	LLZ	04/13/2012
Echolnsight	Epsilon Imaging	K110447	LLZ	05/27/2011
Q-lab	Phillips	K023877	LLZ	12/23/2002

FDA: Food and Drug Administration.

POLICY

A. Myocardial strain imaging in individuals who have exposure to medications or radiation that could result in cardiotoxicity is **experimental / investigational**.

B. Myocardial strain imaging is **experimental / investigational** in all other situations.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

This evidence review was created using searches of the PubMed database. The most recent literature update was performed through March 15, 2025.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

MYOCARDIAL STRAIN IMAGING TO DETECT CARDIOTOXICITY

Clinical Context and Test Purpose

The purpose of myocardial strain imaging in individuals who have an indication for a transthoracic echocardiogram is to inform a decision whether to modify monitoring and/or treatment before the patient develops symptoms and irreversible myocardial dysfunction.

In 2019, the American College of Cardiology, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and the Society of Thoracic Surgeons published appropriate use criteria for multimodality imaging in the assessment of cardiac structure and function in nonvalvular heart disease.[2,] In 2019, the American College of Cardiology et al considered strain imaging by speckle or tissue Doppler appropriate for the following indications:

- Initial evaluation prior to exposure to medications/radiation that could result in cardiotoxicity/heart failure,
- Re-evaluation (1 year) in an individual previously or currently undergoing therapy with potentially cardiotoxic agents,

- Periodic re-evaluation in an individual undergoing therapy with cardiotoxic agents with worsening symptoms, and
- Evaluation of suspected hypertrophic cardiomyopathy.

The American College of Cardiology et al recommended that myocardial strain imaging "may be appropriate" for indications that are described in Table 2, in the Supplemental Information section.

Cardiovascular complications of cancer treatment can be either acute or chronic (early or delayed) and include heart failure, myocardial ischemia or infarction, hypertension, thromboembolism, and arrhythmias. Presymptomatic detection of cardiotoxicity may allow modification of cancer therapy combinations or use of cardioprotective agents. Therefore, this evidence review will focus on clinical outcomes from use of strain imaging by speckle-tracking echocardiography or tissue Doppler imaging for the initial assessment and follow-up for cardiotoxicity.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals who have been exposed to cardiotoxic medications or radiation.

For individuals who are undergoing chemotherapy, current recommendations are to measure ejection fraction prior to chemotherapy, at completion of therapy, and 6 months later. It has been proposed that the measurement of myocardial strain in addition to ejection fraction will be helpful in cases when ejection fraction is in the lower normal range, and in these cases, the finding of subnormal strain should result in closer monitoring of cardiac function, modification of cancer therapy, and/or use of cardioprotective agents.

Interventions
The test being considered is myocardial strain imaging. Strain is a dimensionless measure of tissue deformation (L – L0)/L0, where L is final length and L0 the original length; positive values indicate lengthening, and negative values indicate shortening.[3,]

The most frequent measure of myocardial strain is global longitudinal strain, which averages values over the length of the myocardial wall. Greater deformation is indicated by lower strain values. Cardiac strain in a healthy individual is generally around 20%, indicated in echocardiography by a negative number (-20). In a meta-analysis of 24 studies (2597 healthy volunteers), Yingchoncharoen et al (2013), reported that global longitudinal strain varied from -15.9% to -22.1% (mean -19.7%; 95% confidence interval [CI], -18.9 to -20.4).[4,] Shortening of more than 20% is generally considered normal.

Comparators
Tagged magnetic resonance imaging (MRI) is considered the reference standard for myocardial strain imaging. However, its routine use is limited by high cost, limited availability, complexity of acquisition, and time-consuming image analysis. This evidence review will evaluate whether clinical outcomes are improved by myocardial strain imaging in comparison with ejection fraction.

Outcomes
The general outcomes of interest are symptoms and signs of cardiotoxicity. Cardiotoxicity is typically defined as a decline in ejection fraction, but there is little consensus regarding what level of decline in left ventricle ejection fraction constitutes cardiotoxicity.

The beneficial outcome of a true-positive test result would be an increase in monitoring or modification of treatment that would reduce cardiotoxicity.

The beneficial outcome of a true-negative test result would be avoiding unnecessary treatment.

A harmful outcome of a false-positive test result would be unnecessary therapy.

A harmful outcome of a false-negative test result would be failure to diagnose cardiotoxicity or progression of toxicity.

Cardiotoxicity may be measured by clinical symptoms and ejection fraction at 6 months and after 1, 2, and 3 years.

Study Selection Criteria
For the evaluation of clinical validity of myocardial strain imaging, studies that meet the following eligibility criteria were considered:
- Reported on clinical outcomes.
- Included a suitable reference standard (ejection fraction).
- Patient/sample clinical characteristics were described.
- Patient/sample selection criteria were described.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

REVIEW OF EVIDENCE

Systematic Review
Thavendiranathan et al (2014) conducted a systematic review of myocardial strain imaging for the early detection of cardiotoxicity in patients during and after cancer chemotherapy.[5,] Searches were conducted through November 2013. The reviewers included prospective or retrospective studies of at least 10 patients that used echocardiographic-based myocardial deformation parameters as the primary method to detect cardiotoxicity. Studies had to provide data on changes in deformation parameters and left ventricle ejection fraction during therapy. The authors focused the review on 3 clinical scenarios: 1) detection of early myocardial changes, 2) prediction of subsequent cardiotoxicity, and 3) detection of late consequences of therapy (>1 year posttreatment).

Detection of early myocardial changes: 13 single-center cohort studies (N=384) provided information on myocardial strain imaging parameters to detect early myocardial changes in patients treated with anthracycline-containing regimens. The earlier studies (n=7) used tissue Doppler imaging while more recent studies (n=6) used speckle-tracking echocardiography. There was heterogeneity regarding patient age, types of cancer, strain techniques, and timing of follow-

up, but all of the studies found that changes in myocardial deformation occurred earlier than changes in left ventricle ejection fraction. In addition, reductions in myocardial deformation occurred at doses lower than those historically considered cardiotoxic.

Prognosis for early cardiotoxicity: 8 observational studies (N=452) included in the systematic review evaluated the prognostic value of myocardial strain imaging for subsequent cardiotoxicity (left ventricle ejection fraction reduction or the development of heart failure). The studies differed in duration of follow-up (6 months vs. 12 to 15 months), treatment regimens, and other factors but used a similar definition of cardiotoxicity. The researchers found that an early fall in global longitudinal strain of 10% to 15% using speckle-tracking echocardiography predicted subsequent cardiotoxicity.

Prognosis for late cardiotoxicity: 9 case-control studies (N=436) were identified that compared findings in patients to controls. All of the studies used various myocardial deformation parameters to detect late subclinical cardiac injury, but none provided data on subsequent cardiac events.

The authors identified the following areas for future research:

- Determination of whether strain-based approaches could be reliably implemented in multiple centers, including nonacademic settings.
- Evaluate in larger multicenter studies and in cancers other than breast cancer.
- Need to determine the optimum sampling (single or multiple).
- Comparison with a traditional left ventricle ejection fraction based approach.
- Understanding the long-term effect of strain changes that occur during therapy.
- The use of vendor-neutral methods to measure strain.
- The prognostic significance of strain abnormalities in survivors of cancer and those receiving radiation therapy.
- Whether intervention would change the natural course of the cardiac disease.

Observational Studies

The BreAst Cancer and CArdiotoxicity Induced by RAdioTherapy (BACCARAT) study was a 2-year prospective cohort study aimed at predicting and preventing potential cardiotoxicity after radiotherapy in individuals with breast cancer through measurement of myocardial dysfunction based on global longitudinal strain via 2-dimensional (2D) speckle tracking echocardiography.[6,] Walker et al (2019) reported on 6 month interim results.[7,] The analysis consisted of 79 patients with chemotherapy- naive breast cancer treated with 3-D conformal radiotherapy. Global longitudinal strain was measured at baseline, 6 months, and 24 months post-radiotherapy. The association between subclinical left ventricular dysfunction and radiation dose was predefined as longitudinal strain reduction greater than 10%. Non-radiation factors, including age, body mass index, and various comorbidities, were considered for multivariate analyses. At 6 months, a mean decrease in global longitudinal strain of 6% was observed (-16.1% ± 2.7% pre-radiotherapy vs. -15.1% ± 3.2%; p=.01). Patients with left-sided breast cancer received mean heart and left ventricular radiation doses of 3.1 ± 1.3 Gray (Gy) and 6.7 ± 3.4 Gy, respectively, while those with right-sided cancer received lower doses of 0.7 ± 0.5 Gy and 0.1 Gy, respectively. In univariate analysis, associations between global longitudinal strain reduction greater than 10% (n=37) and mean doses to the heart and left ventricle were observed (odds ratio [OR] for mean dose to the heart, 1.37; 95% CI, 1.01 to 1.86; p=.04; OR for mean dose to the left ventricle, 1.14; 95% CI, 1.01 to 1.28; p=.03). When non-radiation factors

were accounted for, these associations did not remain significant. Additional analyses identified a subpopulation of participants with left ventricle volume 20 Gy exposed greater than 15% that had significant association with left ventricular dysfunction independent of other factors (OR, 3.97; 95% CI, 1.01 to 15.70; p=.048). Twenty-four month follow-up was available for 72 patients.[8,] No patient developed symptomatic cancer therapy-related cardiac dysfunction by 24 months. Global longitudinal strain reduction of more than 15% from baseline along with left ventricular ejection fraction was used in the detection of moderate and mild dysfunction. Asymptomatic dysfunction occurred in 44% of patients which was categorized as mild in 28%, moderate in 9%, and severe in 7%. The relative volumes exposed to at least 2 Gy (V2) of the left ventricle ≥36% and mean circumflex artery dose ≥1.40 Gy thresholds were determined to be optimal for predicting cancer therapy-related cardiac dysfunction, but there was no analysis specific to changes in global longitudinal strain.

The MEDIRAD EARLY HEART study was a 2-year prospective cohort study investigating associations between radiotherapy doses and myocardial dysfunction in patients with breast cancer undergoing radiotherapy without chemotherapy.[9,] Locquet et al (2022) reported a 6-month interim analysis.[10,] In this study, global longitudinal strain was measured at baseline and 6 months post-radiotherapy, and the association between subclinical left ventricular dysfunction and radiation doses was predefined as longitudinal strain reduction greater than 15%. Global longitudinal strain-based subclinical left ventricular dysfunction was observed in 22/186 patients (11.8%). A significantly higher mean radiation dose was observed in these patients compared to those without observed cardiotoxicity (mean whole heart dose, 2.66 ± 1.75 Gy vs. 1.64 ± 0.96 Gy, respectively; p=.01).

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, or avoid unnecessary therapy or testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

Randomized Controlled Trial
In the multicenter, prospective, randomized, controlled, Strain Surveillance of Chemotherapy for Improving Cardiovascular Outcomes (SUCCOUR) trial, anthracycline-treated patients with another heart failure risk factor (N=331) were randomly assigned to initiation of cardioprotective therapy guided by either a 12% or greater relative reduction in global longitudinal strain (n=166) or greater than 10% absolute reduction in left ventricular ejection fraction (n=165).[11,] Patients were enrolled at 28 centers from Australia, Asia, Europe, Canada, and the United States between January 2014 and December 2019. Cardioprotective therapy included initiation of an angiotensin converting enzyme (ACE) inhibitor (or an angiotensin receptor blocker [ARB], if the ACE inhibitor was not tolerated) followed by a beta-blocker, with doses titrated every 2 weeks until achievement of the maximal dose or development of intolerable side effects. The primary outcome was a difference in baseline to 1-year follow-up of left ventricular ejection fraction, preferentially based on 3D left ventricular ejection fraction, between the 2 groups. Twenty-four of the 331 randomized patients did not have a 1-year follow-up (2 died; 22 either withdrew consent

or did not return for imaging); 307 patients were included in the final analysis (154 in the global longitudinal strain surveillance arm and 153 in the left ventricular ejection fraction surveillance arm). The majority of patients were female (94%) and had breast cancer (91%). Most patients were of European descent (>60% in each group), followed by East Asian (between 20% to 28% per group), South Asian (3.3% to 7.2%), and African (0.7% in each group).

The primary endpoint was not met as the difference of left ventricular ejection fraction between groups at 1-year follow-up was not statistically significant (global longitudinal strain: 57% ± 6% vs. left ventricular ejection fraction: 55% ± 7%; p=.05).[11,] Of patients in the left ventricular ejection fraction surveillance group, 13.7% met criteria for cancer-therapy-related cardiac dysfunction versus 5.8% in the global longitudinal strain group (p=.02). A subgroup analysis revealed that patients receiving cardioprotective medications in the left ventricular ejection fraction surveillance group had larger reductions in left ventricular ejection fraction at follow-up than in the global longitudinal strain surveillance group (9.1% ± 10.9% vs. 2.9% ± 7.4%; p=.03). More patients in the global longitudinal strain surveillance group received cardioprotective treatment, which may account for this difference in ejection fraction. Limitations of the SUCCOUR trial include the potential for bias in local ejection fraction measurements since the sites were not blinded to study arm, the use of 2D left ventricular ejection fraction (instead of the preferential 3D) in some patients due to image quality, and a general shift toward use of non-anthracycline-based therapies in women with HER2+ breast cancer. With this shift, the focus on anthracycline-treated patients in the SUCCOUR trial may not be generalizable to those who are treated with non-anthracycline-based regimens. Of note, the adoption of global longitudinal strain-guided surveillance in routine practice also requires the commitment of echocardiography laboratories and training of analyzing/reporting clinicians.

Negishi et al reported results from a follow-up substudy of SUCCOUR.[12,] The primary endpoint was the change in 3D left ventricular ejection fraction from baseline to 3 years. Among the 331 patients enrolled in SUCCOUR, 255 patients (123 in the left ventricular ejection fraction group and 132 in the global longitudinal strain group) completed 3-year follow-up. Most patients (93%) had breast cancer, and anthracycline followed by trastuzumab was the most common chemotherapy regimen (84%). Cardioprotective therapy was administered to 18 patients (14.6%) in the ejection fraction group and 41 patients (31%) in the global longitudinal strain group (p=.03). The 3-year change in ejection fraction was -0.03% ± 7.9% and -0.02% ± 6.5% in the ejection fraction group and the global longitudinal strain group, respectively (p=.99), despite a significantly higher number of patients meeting criteria for cardioprotective therapy in the global longitudinal strain group (n=41 vs. n=18 in the ejection fraction group). At 3 years, 11 patients in the ejection fraction group had cancer therapeutics-related cardiac dysfunction compared to 6 patients in the global longitudinal strain group (p=.16); 1 patient in each group was admitted for heart failure.

Additional studies are indicated to better define the threshold for cardioprotective therapy and to assess whether a global longitudinal strain-guided approach to cardioprotective therapy reduces the long-term risk of heart failure and improves clinical outcomes.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Section Summary: Myocardial Strain Imaging to Detect Cardiotoxicity
A systematic review of 13 studies with 384 patients treated for cancer suggests that myocardial strain imaging with tissue Doppler imaging or speckle-tracking echocardiography may be able to identify changes in myocardial deformation that precede changes in left ventricle ejection fraction. Two recently published observational studies reported conflicting evidence at 6 months post-radiotherapy on whether longitudinal strain reduction was associated with radiotherapy dose. Although myocardial strain imaging may detect sub-clinical myocardial changes, the value of these changes in guiding therapy is uncertain. No studies were identified that evaluated the diagnostic accuracy of myocardial strain imaging compared to left ventricle ejection fraction. In the SUCCOUR trial, left ventricle surveillance with global longitudinal strain was associated with an increased use of cardioprotective therapy and a lower incidence of cancer-therapy-related cardiac dysfunction as compared to left ventricular ejection fraction surveillance. However, no difference in the primary endpoint of final left ventricular ejection fraction at 1-year follow-up was observed between the groups and interpretation of findings was limited by important design and relevance limitations. At 3-year follow-up, despite the increase in the use of cardioprotective therapies in the global longitudinal strain-guided group, there were minimal differences in the change in left ventricular ejection fraction between groups.

SUPPLEMENTAL INFORMATION
The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Cardiology et al
In 2019, the American College of Cardiology, American Association for Thoracic Surgery, American Heart Association (AHA), American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and the Society of Thoracic Surgeons published appropriate use criteria for multimodality imaging in the assessment of cardiac structure and function in nonvalvular heart disease (Table 2).[2,]

Using a modified Delphi approach, the panel rated indications as "appropriate", "may be appropriate", and "not appropriate".[13,] The specific studies that formed the basis of the American College of Cardiology guidelines are not cited; however, they note that they used American College of Cardiology/American Heart Association clinical practice guidelines whenever possible.

Of 81 indications considered for strain rate imaging, the panel rated only 4 as "appropriate" (Table 2). Three of the 4 concerned evaluation (initial or follow-up) in patients prior to and following exposure to potentially cardiotoxic agents. The other indication was follow-up testing to clarify initial diagnostic testing for patients with suspected hypertrophic cardiomyopathy. The

guidelines did not separate out imaging with speckle tracking and tissue Doppler and did not make recommendations related to the comparative effectiveness of these imaging modalities.

The panel rated 14 other indications "may be appropriate" (Table 2). According to the panel, interventions in this category should be performed depending on individual clinical patient circumstances and patient and provider preferences, including shared decision making.[13,]

Table 2. Summary of American College of Cardiology Appropriate Use Criteria for Myocardial Strain Imaging

Clinical Scenario and Indication	Rating
Initial evaluation in an asymptomatic patient:	
- Initial evaluation prior to exposure to medications/radiation that could result in cardiotoxicity/heart failure	Appropriate
- Initial cardiac evaluation of a known systemic, congenital, or acquired disease that could be associated with structural heart disease	May be appropriate
- Screening evaluation for structure and function in first-degree relatives of a patient with an inherited cardiomyopathy	May be appropriate
- Preparticipation assessment of an asymptomatic athlete with 1 or more of the following: abnormal examination, abnormal ECG, or definite (or high suspicion for) family history of inheritable heart disease)	May be appropriate
Initial evaluation of a patient with clinical signs and/or symptoms of heart disease:	
- Initial evaluation when symptoms or signs suggest heart disease	May be appropriate
- Arrhythmias or conduction disorders: Newly diagnosed LBBB; Nonsustained VT	May be appropriate
- Palpitations/presyncope/syncope: Clinical symptoms or signs consistent with a cardiac diagnosis known to cause presyncope/syncope (including but not limited to hypertrophic cardiomyopathy and heart failure)	May be appropriate
- Respiratory failure/exertional shortness of breath: Exertional shortness of breath/dyspnea or hypoxemia of uncertain etiology	May be appropriate
- HF/cardiomyopathy: Initial evaluation of known or suspected HF (systolic or diastolic) based on symptoms, signs, or abnormal test results to assess systolic or diastolic function and to assess for possible etiology (CAD, valvular disease); Suspected inherited or acquired cardiomyopathy (eg, restrictive, infiltrative, dilated, hypertrophic)	May be appropriate
- Device therapy: Known implanted pacing/ICD/CRT device with symptoms possibly due to suboptimal device settings	May be appropriate
- Cardiac transplantation: Monitoring for rejection or coronary arteriopathy in a cardiac transplant recipient	May be appropriate
- Other: Suspected pericardial diseases	May be appropriate
Sequential or follow-up testing to clarify initial diagnostic testing:	
- Evaluation of suspected hypertrophic cardiomyopathy	Appropriate

Clinical Scenario and Indication	Rating
- Re-evaluation (1 y) in a patient previously or currently undergoing therapy with potentially cardiotoxic agents	Appropriate
- Periodic reevaluation in a patient undergoing therapy with cardiotoxic agents and worsening symptoms	Appropriate
- Pulmonary hypertension in the absence of severe valvular disease	May be appropriate
- Comprehensive further evaluation of undefined cardiomyopathy	May be appropriate
- Evaluation of suspected cardiac amyloidosis	May be appropriate
Sequential or follow-up testing: new or worsening symptoms or to guide therapy	
Re-evaluation of known structural heart disease with change in clinical status or cardiac examination or to guide therapy	May be appropriate
Re-evaluation of known cardiomyopathy with a change in clinical status or cardiac examination or to guide therapy	May be appropriate
Re-evaluation of known HF (systolic or diastolic) with a change in clinical status or cardiac examination without a clear precipitating change in medication or diet	May be appropriate
Re-evaluation for CRT device optimization in a patient with worsening HF	May be appropriate

CAD: coronary artery disease; CRT: cardiac resynchronization therapy: ECG: electrocardiogram; HF: heart failure; ICD: implantable cardioverter-defibrillator; LBBB: left bundle branch block; VT: ventricular tachycardia.
Source: Adapted from Doherty et al (2019).[2,]

American Heat Association

A 2023 scientific statement from the AHA regarding cancer treatment-associated cardiovascular toxicity included some discussion of global longitudinal strain.[14,] The authors acknowledged that some definitions of cancer therapy-related cardiac dysfunction (CTRCD) rely on the use of changes in strain; however, there are no specific recommendations regarding appropriate use of global longitudinal strain in the statement.

American Society of Clinical Oncology

In 2017, the American Society of Clinical Oncology noted that measurement of strain has been demonstrated to have some diagnostic and prognostic use in patients with cancer receiving cardiotoxic therapies but that there have been no studies demonstrating that early intervention based on changes in strain alone can result in changes in risk and improved outcomes.[15,] The American Society of Clinical Oncology also notes that screening for asymptomatic cardiac dysfunction using advanced imaging could lead to added distress in cancer survivors.

International Cardio-Oncology Society

A 2021 consensus statement from the International Cardio-Oncology Society included global longitudinal strain in the definitions of mild and moderate asymptomatic CTRCD.[16,] Mild CTRCD was defined as an LVEF of at least 50% AND a new relative decline in global longitudinal strain by more than 15% from baseline AND/OR new rise in cardiac biomarker. Moderate CTRCD was defined as new LVEF reduction by at least 10% to an LVEF of 40% to 49% OR new LVEF

reduction by less than 10% to an LVEF of 40% to 49% AND new relative decline in global longitudinal strain by more than 15% from baseline AND/OR new rise in cardiac biomarker.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 3.

Table 3. Summary of Key Trials

Study	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04547465	The Role of 2D Speckle-tracking Echocardiography in Diagnosis Chemotherapy-induced Cardiomyopathy in Breast Cancer Patients with High Cardiovascular Risk Factors	300	Dec 2023 (unknown status)
NCT04429633	Strain-based vs. Left Ventricular Ejection Fraction-based Cardiotoxicity Prevention Strategy in Patients With Breast Cancer Who Treated With Adjuvant Trastuzumab	136	Jul 2023 (unknown status)

NCT: national clinical trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
93356	Myocardial strain imaging using speckle tracking-derived assessment of myocardial mechanics (List separately in addition to codes for echocardiography imaging)
C9762	Cardiac magnetic resonance imaging for morphology and function, quantification of segmental dysfunction; with strain imaging
C9763	Cardiac magnetic resonance imaging for morphology and function, quantification of segmental dysfunction; with stress imaging

REVISIONS	
05-18-2020	Policy published 05-18-2020. Policy effective 05-18-2020.
07-02-2021	Updated Description section
	Updated Rationale section
	Updated References section
08-11-2022	Updated Description Section
	Updated Rationale Section
	Updated Coding Section ▪ Added HCPCS codes: C9762 and C9763
	Updated References Section
06-27-2023	Updated Description Section
	Updated Rationale Section
	Updated Coding Section ▪ Removed ICD-10 Diagnosis Box
	Updated References Section
06-27-2024	Updated Description Section
	Updated Rationale Section
	Updated References Section
07-08-2025	Updated Description Section
	Updated Rationale Section
	Updated References Section

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