HIGHLIGHTS FROM

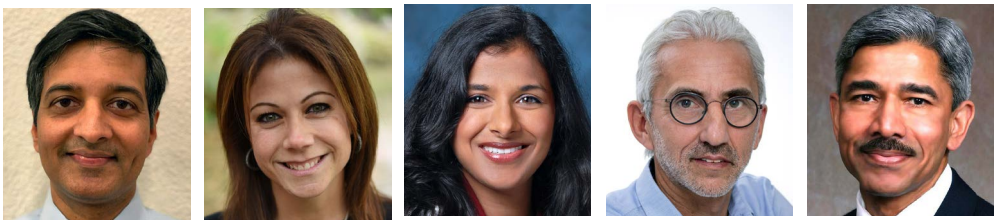
ASE'S MULTIMODALITY IMAGING FOR CARDIAC SURVEILLANCE OF CANCER TREATMENT IN CHILDREN GUIDELINE

Due to remarkable progress in pediatric cancer therapy over the past decades, more than 80% of children diagnosed with cancer today can expect to survive well into adulthood. At the same time, survivors face a high burden of morbidity and mortality, in particular cardiovascular disease (CVD), the leading non-cancer cause of late mortality in this population.

Current practice employs longitudinal monitoring of echocardiographic measures of the left ventricle (LV) systolic function for screening and detection strategies for CVD in children with cancer. However, there is significant variability in practice and lack of standardization in cardiovascular imaging methods used to perform cardiovascular screening in this population. The ASE guidelines developed by a multidisciplinary expert consensus panel of pediatric and adult cardiologists, pediatric oncologists, and experienced pediatric sonographers provide recommendations for the standardization of echocardiographic and multi-modality cardiovascular imaging assessment of cardiac function in pediatric cancer patients.

Cardiovascular complications after cancer treatment include LV dysfunction, cardiomyopathy, heart failure (HF), coronary artery disease, stroke, pericardial disease, and valvular and vascular dysfunction. The effects of anthracyclines and chest radiation have been well described. But there are several other established and newer cancer treatments with potential cardiovascular sequelae, and their cardiovascular toxicities are an area of active investigation (Figure 1). The primary goal of cardiac monitoring is to identify early signs of potentially reversible heart disease and seek to prevent progression of CVD to more advanced stages of heart failure. Prior to starting cardiotoxic treatment, a full baseline structural and functional echocardiogram should be performed. During the cancer treatment, echocardiographic screening for early detection of cardiac dysfunction is recommended. The frequency of screening will depend on the protocol and doses of cancer treat-

Contributed by **Hari Narayan, MD, FASE, MSCE, Melissa Wasserman, RDCS, RCCS, FASE, Ruchira Garg, MD, FASE, Luc Mertens, MD, PhD, FASE,** and **Gautam Singh, MD, FASE**



ment used and other coexisting risk factors. Withholding cancer treatment requires multidisciplinary decision-making and must be made cautiously. After completion of treatment, cardiac surveillance is recommended at least every two years for high-risk and every five years for moderate-risk patients.

Echocardiography

Echocardiography remains the primary cardiac imaging technique for children before, during, and after cancer therapy, with focus on both cardiac structure and function. This tailored echocardiogram should include assessment of LV dimensions, volumes and mass, as well as assessment of left and right ventricular systolic and diastolic function, valve function, and the pericardium. However, with so many echocardiographic techniques and measurements available, our aim is to provide guidance on which ones to use routinely in this specific patient population.

FIGURE 1: Overview of the cardiovascular effects of cancer treatments and use of imaging modalities. HTN, Hypertension; LVD, LV dysfunction; TK, tyrosine kinase.

Cardiac effect	LVD/HF	Myocarditis	Arterial Thrombosis	Athero-sclerosis, Coronary Spasm	Pericardial disease	Valve Disease	HTN	Pulmonary HTN or fibrosis
Conventional Therapies								
Anthracyclines	■				■			
Platinum-based Cisplatin			■	■			■	■
Alkylating Agents Cyclophosphamide, Ifosfamide	■		■		■			■
Vinca Alkaloids Vinblastine, Vincristine	■							
Antimetabolites 5-fluorouricil (5-FU), Capecitabine, Cytarabine			■	■	■			
Microtubule Inhibitors (primarily used in adults) Paclitaxel, Docetaxel	■		■					
Targeted Molecular Therapies (primarily used in adults)								
VEGF Antibodies Bevacizumab	■		■				■	
VEGF TK Inhibitors Sunitinib, Pazopanib	■		■				■	
BCR-ABL TK Inhibtors Imatinib	■	■	■	■	■	■		■
Proteasome Inhibitors Bortezomib, Carfilzomib	■		■				■	■
Radiation	■		■	■	■	■	■	■
Steroids				■			■	
Imaging								
Echo* (preferred screening modality)	■	■			■	■	■	■
CMR*	■	■	■		■	■	■	
CT*			■	■	■			■

For serial assessment of LV chamber size and wall thickness, linear dimensions of the LV cavity, interventricular septum, and posterior wall should be measured based on 2D or M-mode. For measuring LV volume and mass, the method of disks or area-length methods are recommended. The measurements should be corrected for body size, and Z scores should be included in the report. We recommend using the Pediatric Heart Network normative Z scores.

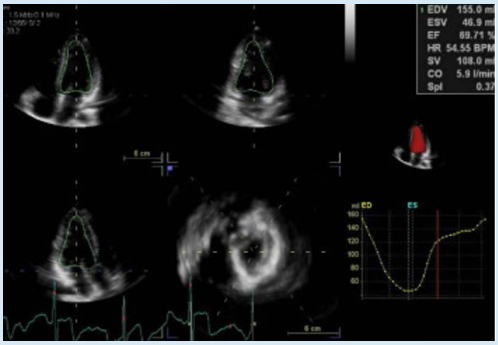
A standardized protocol for measuring functional parameters must be developed. Each laboratory should consistently utilize standardized methods for serial assessment of LV function. The method used should be identified in the report. We recommend the use of LV ejection fraction (EF) for monitoring LV function in children with cancer. We recommend using the biplane method of disks for calculating EF. In cases where the apical images are suboptimal, the 5/6 area-length method can be a recommended alternative. Global longitudinal strain (GLS) measurement by speckle-tracking echocardiography is a reproducible measurement of LV function that should be included in the assessment of LV function. Although, the predictive value of an early decrease in GLS during treatment and in long-term survivors is uncertain in the presence of preserved EF at the present, utilizing different measures of LV function for serial assessment, such as a 2D and 3D EF combined with GLS may allow reliable detection of early changes in cardiac function. We recommend adding GLS as an additional measurement to follow children after cancer treatment.

Evaluation of diastolic functional parameters, such as mitral inflow velocities, tissue Doppler velocities at the septal and mitral valve annulus and left atrial volume, are recommended, although their interpretation can be challenging. Left atrial volume is considered the most reliable parameter of diastolic function in children and should be included as part of a serial echocardiographic assessment. For right ventricular

TABLE 1

LVEF **Apical 4 chamber**
3D echo **3D volume**

- 3D volume should include entire LV avoid foreshortening or stitch artifacts.
- Temporal resolution of >20-25 volumes per second.
- Fully automated border detection available.

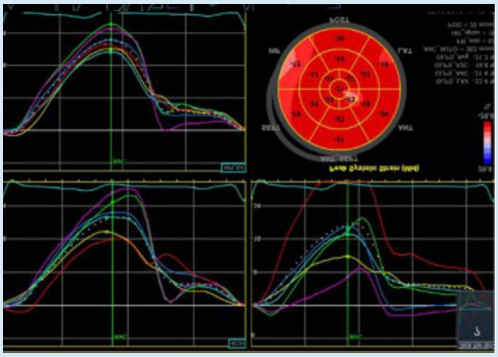


- No geometrical assumptions.
- Automated analysis available.
- Reproducible.
- Normative pediatric data available.

- Image quality- dependent.
- Lower temporal resolution.
- Requires cooperation.
- Specific transducers and software analysis package needed.

LV GLS **STE**
Apical 4 chamber,
Apical 2 chamber,
Apical 3 chamber

- Image optimized for myocardial definition; avoid foreshortening or dropout.
- 3 views selected should have similar heart and frame rates with clear electrocardiogram tracing
- Visual inspection to ensure accurate tracking of LV walls; analysis excluded if more than 2 segments per view show poor tracking.



- Highly reproducible.
- Automated analysis.

- Image quality dependent
- Heart and frame rates need to be comparable in all 3 views.
- Specific software analysis package needed.
- Vendor dependent.

(This figure is from Multimodality Imaging for Cardiac Surveillance of Cancer Treatment in Children: Recommendations From the American Society of Echocardiography, published in the December 2023 *Journal of the American Society of Echocardiography.* Reprinted with permission from Elsevier Inc.)

assessment, an RV size measurement, such as RV basal diameter, together with a right ventricular functional parameter such as RV FAC, is recommended.

We summarize the advantages and pitfalls, as well as how to perform all recommended echocardiographic measurements in a Table in the Guidelines, a part of which is reproduced for 3D LV EF and LV GLS in Table 1.

Guidance for monitoring of cardiac function in children with cancer during treatment with cardiotoxic agents is highlighted in Figure 2 and after treatment in Figure 3.

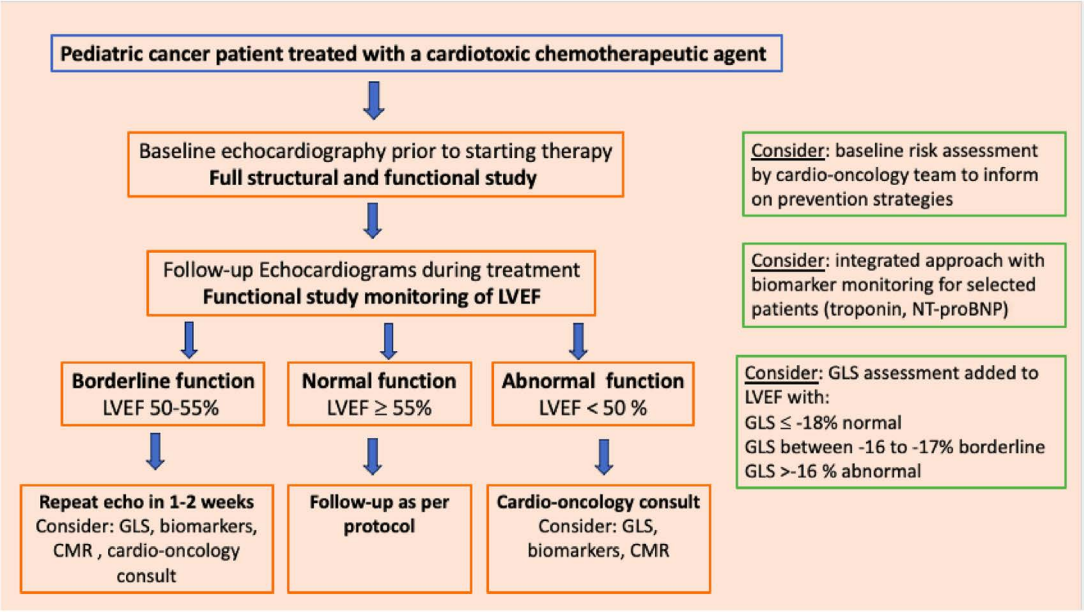


FIGURE 2: Monitoring of cardiac function in children with cancer during treatment with cardiotoxic agents

(This figure is from Multimodality Imaging for Cardiac Surveillance of Cancer Treatment in Children: Recommendations From the American Society of Echocardiography, published in the December 2023 *Journal of the American Society of Echocardiography.* Reprinted with permission from Elsevier Inc.)

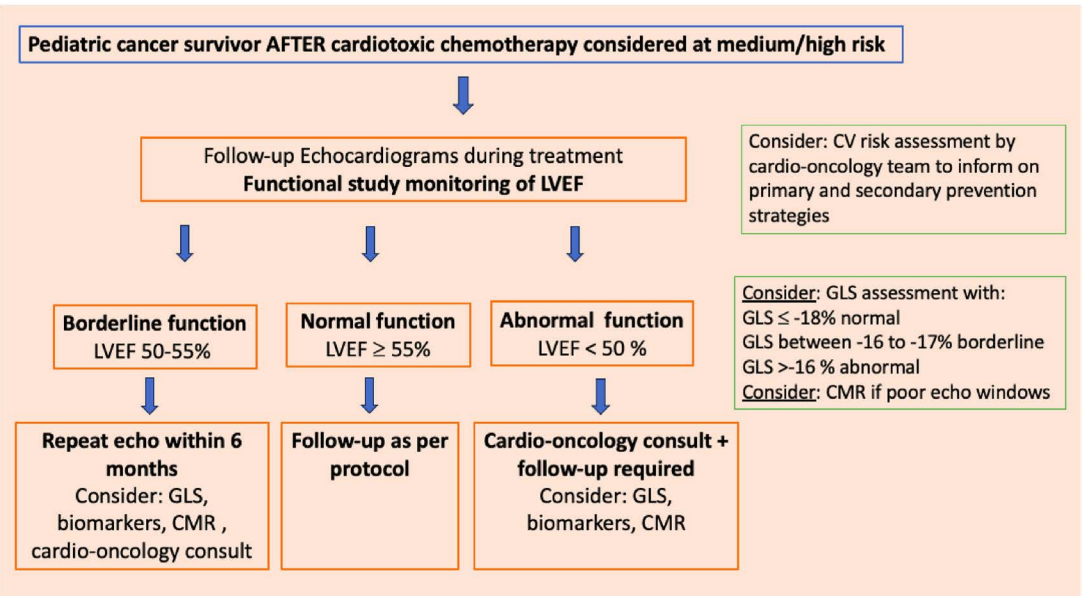


FIGURE 3: Monitoring of cardiac function in children with cancer after treatment with cardiotoxic agents.

(This figure is from Multimodality Imaging for Cardiac Surveillance of Cancer Treatment in Children: Recommendations From the American Society of Echocardiography, published in the December 2023 *Journal of the American Society of Echocardiography.* Reprinted with permission from Elsevier Inc.)

Use of CMR in Evaluating Children with Cancer

Echocardiography is the primary imaging modality for cardiac evaluation of this population; however, there are certain, specific indications for which CMR could be considered in pediatric cancer patients:

1. **If echocardiographic images are poor and it is difficult to reliably assess ventricular function**
2. **When borderline (EF 50-55%) or abnormal (EF <50%) LV function is detected by echocardiography and an alternative modality is desired.**
3. **For tissue characterization in suspected myocarditis.**
4. **For suspected constrictive pericarditis.**
5. **For cancer involving the heart.**

The protocol must include biventricular volumes, mass, and ejection fraction. All the other CMR techniques are considered optional and can be considered. These include assessment of LV diastolic function using phase-contrast or tissue-phase mapping, and measurement of atrial volumes. Also, myocardial deformation imaging by various techniques such as tagging, strain and feature tracking can be considered for advanced assessment of global and regional myocardial dysfunction. These advanced assessments of cardiac function by CMR have considerable technical variability and lack standard values in pediatric cancer patients to endorse routine use. Tissue characterization to assess myocardial fibrosis, edema and iron load can be included when clinically indicated.

Cardiac CT

When both echo and CMR are not adequate or feasible, cardiac CT can determine biventricular volumes and EF. Surveillance of adults for atherosclerotic coronary artery (CA) disease with CA calcium scans can be considered at 5–10-year intervals after radiation therapy (RT). Coronary CT angiography is appropriate in survivors >18 years to assess for RT-related atherosclerotic disease.

Knowledge Gaps

The guidelines highlight the gap in standardized approach in the current practice of cardiac monitoring and identify important knowledge gaps on the predictive value of echocardiographic measurements during and after cancer treatment.