Florida CHAPTER

Cardiac Imaging for Early Detection of Cancer Therapeutics-Related Cardiac Dysfunction

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CANCER BACKGROUND

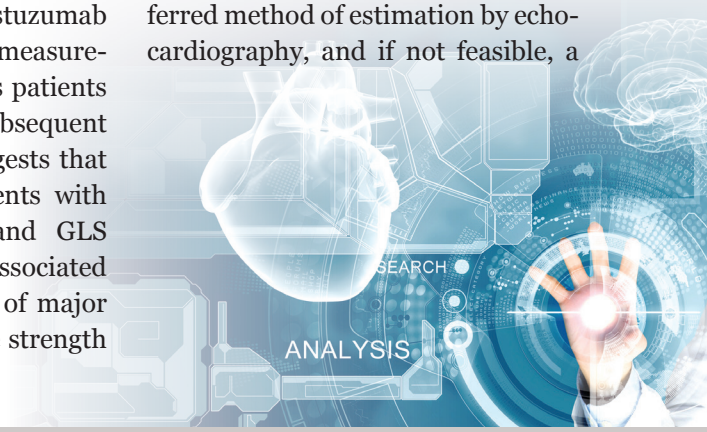
Cancer Therapeutics-Related Cardiac Dysfunction (CTRCD) is defined as a drop in Left Ventricular Ejection Fraction (LVEF) of > 5% in symptomatic patients or a drop in LVEF of >10% to < 53% in asymptomatic patients as a result of exposure to cancer therapies. Advanced multimodality imaging plays a role in the pretreatment risk assessment of CTRCD; the early detection of cardiac injury; the identification of cardiovascular complications of cancer therapies and may forecast recovery. The findings of imaging studies should not be the sole indicator to direct or alter cancer therapy. A multidisciplinary approach that weighs patient characteristics possible alternative therapies and the patient's preferences must be considered.

AVAILABLE IMAGING

Echocardiography has become the preferred imaging modality to assess CTRCD because of the ability to provide comprehensive assessment of cardiac function beyond left ventricular ejection fraction. The main role of echo is to assess cardiac function by measurement of LVEF, the standard to define CTRCD. A limitation of echo is that changes in EF usually occur at a later stage when significant toxicity has already occurred. Rendering the most accurate estimation of LVEF and detection of subclinical cardiac dysfunction are the ultimate goals to identify the patients at risk of CTRCD. Early initiation of cardio-protective medical therapy in patients with cardiac toxicity is associated with an increased likelihood of subsequent improvement in LVEF. The impact of poorly performed or inconsistency in technique is the potential impact to the patient of unnecessary withdrawal of lifesaving cancer therapy.

Myocardial Strain Imaging. There is solid evidence of the applicability of myocardial strain imaging for pretreatment risk assessment and detection of subclinical myocardial dysfunction. Global longitudinal strain (GLS) has been the most applied to cardio-oncology and is a surrogate for myocardial contractility. Specifically, in patients receiving anthracycline and /or trastuzumab therapy, pretreatment measurements of GLS differentiates patients more likely to develop subsequent CTRCD. Other studies suggests that anthracycline treated patients with LVEF between 50-59% and GLS greater than (-)16% were associated with a 4.7-fold higher risk of major adverse cardiac events. The strength of strain imaging is in its robust reproducibility (although vendor specific) and sequential analysis to define cardio-toxicity by the detection of changes in myocardial contractility prior to changes in LVEF. Whether cardiac interventions for isolated reduction in GLS improves long-term cardiovascular outcomes in patients receiving cancer therapy is unknown. This question, is the subject of the ongoing, multi-center, randomized controlled SUCCOUR trial.

Three-Dimensional Echo increases the accuracy of detecting subtle changes in LVEF, with higher reproducibility when compared to estimations of LVEF by 2D. The 3D LVEF is calculated by volumetric changes and does not assume a standard LV geometry. Therefore, it is comparable to LVEF by Cardiac Magnetic Resonance Imaging, long considered the gold standard for LV assessment. The 3D LVEF is the preferred method of estimation by echocardiography, and if not feasible, a



Cardiac Imaging *continued*

2D LVEF calculation with contrast may improve accuracy.

Multiple-gated acquisition (MUGA) was previously the main technique for estimation of LVEF due to high reproducibility. The use of MUGA has become more restricted as a result of the limited information it can provide regarding cardiovascular function (diastolic and systolic) and structure (valve and pericardial abnormalities). Due to the need for repetitive measurements and radiation exposure during the course of cancer therapy, as well as its higher cost compared to echo has led to limited use.

Cardiac Magnetic Resonance Imaging (CMR) is the gold standard for detection of ventricular volumes and function. It has greater intra and inter-observer reproducibility than echocardiography. CMR also affords the opportunity for non-invasive tissue characterization including myocardial edema, inflammation and fibrosis which may be associated with early and late stage CTRCD. Myocardial deformity imaging such as global longitudinal strain can also be calculated with great reliability. CMR is also helpful in the tissue characterization of intra-cardiac masses (thrombus versus tumor) identified in the cancer patient during routine imaging. The limitations are the lack of universal availability, higher cost and patient-related factors such as ferromagnetic devices and claustrophobia.

Positron Emission Tomography (PET) allows for the determination of viability and occasionally can help with cardiac metastatic disease via glucose metabolism.

REFERENCES

Expert Consensus for Multimodality Imaging Evaluation of Adult Patients during and after Cancer Therapy. A report from the American Society of Echo and the European Association of Cardiovascular Imaging. Journal of the American Society of Echocardiography 2014 27.911-939

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Detailed algorithms regarding imaging and treatment available above