Survival after cancer has greatly increased in the past few decades through advances in chemotherapy, as well as surgery, radiotherapy, and diagnostic imaging. Anthracyclines are effective and life-saving drugs that serve as the cornerstone of cancer chemotherapy. The current expected 5- to 10-year survival rate of patients with certain cancers, such as hematologic, breast, and childhood cancer, approaches 80%.1 However, cancer chemotherapy often causes acute and chronic cardiovascular complications. Cardiotoxicity from cancer chemotherapy has become a leading cause of morbidity and mortality in cancer survivors.2,3 Compared with siblings, cancer survivors are 10-fold more likely to develop coronary artery disease and 15-fold more likely to develop heart failure (HF).4 The high cardiac morbidity in cancer survivors is frequently from the cumulative, dose-dependent, irreversible myocyte necrosis caused by anthracyclines (type 1 cardiotoxicity). Furthermore, additional targeted receptor therapy with the monoclonal antibody trastuzumab may alter myocardial repair gene expression, which is reversible once the drug is withdrawn (type 2 cardiotoxicity).

Historically, several definitions of cardiotoxicity have been proposed.5 The most commonly used definition is ≥5% reduction in left ventricular ejection fraction (LVEF) after cancer chemotherapy. 

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Figure. Echocardiographic parameters and biomarkers for risk stratification and management of cardiotoxicity caused by anthracyclines. BNP, B-type natriuretic peptide; CV, cardiovascular; EF, ejection fraction; GLS, global longitudinal strain; LV, left ventricular; TTE, transthoracic echocardiography.
reduction in asymptomatic patients). LV peak systolic global longitudinal strain (GLS) derived from transthoracic echocardiography has emerged as a sensitive marker of subclinical LV dysfunction, and its use has gained particular interest in the field of “oncocardiology” to facilitate detection of early cardiotoxicity. A 10–15% relative drop in LV GLS early during cancer therapy identifies patients at higher risk of a later reduction in LVEF or the development of HF. During and even after cancer therapy, close cardiovascular monitoring should be applied for the early detection of cardiotoxicity and treatment of any cardiac dysfunction (Figure).

In this issue of the Journal, Hatazawa et al. examine the role of baseline echocardiographic parameters, including GLS, for the prediction of cardiotoxicity in 73 patients with malignant lymphoma who underwent anthracycline chemotherapy. Patients were followed for the occurrence of hospitalization for HF. After the completion of anthracycline chemotherapy, all patients underwent follow-up echocardiography. Importantly, only baseline GLS predicted the development of cancer therapy-related cardiac dysfunction (CTRCD). The optimal cutoff value of baseline GLS for the prediction of CTRCD was −19%, and patients with GLS >−19% had a higher rate of HF occurrence during follow-up, although the authors used the absolute value. Furthermore, baseline GLS provided incremental value for the prediction of CTRCD over clinical variables and LVEF. These new findings suggest that close follow-up might be needed for patients with impaired GLS at baseline. Conflicting results have been observed in previous studies of an association between baseline GLS and CTRCD. Mousavi et al. showed that baseline GLS, as well as LV end-diastolic volume index, predicted future cardiac death and HF development in 158 patients with LVEF of 50–59% treated with anthracycline chemotherapy. In contrast, Fallah-Rad et al. showed no significant difference in baseline GLS between patients with and without CTRCD among 42 patients who underwent trastuzumab therapy. Similar results were observed in 81 patients who underwent concurrent anthracycline and trastuzumab therapy. Furthermore, recent studies showed the usefulness of cardiac biomarkers for the prediction of CTRCD. Sawaya et al. demonstrated that serum troponin I levels measured at the termination of anthracycline therapy were useful for the prediction of subsequent cardiotoxicity. Serum B-type natriuretic peptide was also associated with the development of HF in 333 patients with cancer receiving anthracyclines. Future studies are warranted to determine whether baseline GLS predicts unfavorable cardiovascular events in a larger number of patients and whether its association is independent of these biomarkers.

Although we can detect subclinical LV dysfunction via deformation imaging, the benefit of early detection per se is still unknown. A limited number of studies have investigated the benefit of early intervention in asymptomatic patients with subclinical LV dysfunction, with conflicting results. Because of the lack of standardized methodology among vendors, it is essential that each echocardiography laboratory defines a normal range of strain values and ensures a high degree of reproducibility. In addition, when doing serial evaluations, the same equipment and algorithms for calculating strain should be used. Large, prospective trials are needed to evaluate whether early cardioprotective therapeutic interventions based on GLS have beneficial effects on cardiac function and lead to improvement in long-term clinical outcomes in patients treated with anthracyclines. Furthermore, impaired GLS at baseline should not preclude patients from receiving life-saving anthracycline chemotherapy, but close follow-up is needed in those patients.

Disclosures
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