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Single Versus Standard Multiview Assessment of Global Longitudinal Strain for the Diagnosis of Cardiotoxicity During Cancer Therapy

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ABSTRACT

OBJECTIVES The goal of this study was to compare echocardiographic measurements of global longitudinal strain (GLS) (using 3 apical views) with single-view longitudinal strain (LS, 4- or 2-chamber [4CV_LS and 2CV_LS, respectively]) for detection of cancer-therapy related cardiotoxicity.

BACKGROUND GLS is useful for the detection of cardiotoxicity, but the need for repeated measurements poses a significant burden on busy echocardiography laboratories. A single-view LS measurement, possibly at point of care, could improve efficiency.

METHODS Seventeen international centers prospectively recruited 108 patients (mean age 54 ± 13 years) at high risk for cardiotoxicity as part of the ongoing SUCCOUR (Strain Surveillance for Improving Cardiovascular Outcomes During Chemotherapy) randomized controlled trial. Echocardiography performed at baseline and follow-up were analyzed in a core laboratory setting blinded to clinical information. Peak systolic GLS and LS were measured from raw data. Cardiotoxicity was defined by reduction in left ventricular ejection fraction >0.10 to <0.55 or a relative drop in GLS by ≥12%.

RESULTS Cardiotoxicity developed in 46 patients by either criteria. Baseline and follow-up 2-dimensional left ventricular ejection fraction were 61 ± 4% and 58 ± 5%, respectively ($p < 0.001$). The baseline GLS (-20.9 ± 2.4%) was not different from 4CV_LS (-20.7 ± 2.5%; $p = 0.09$) or 2CV_LS (-21.1 ± 3.1%; $p = 0.25$). The follow-up GLS (-19.5 ± 2.4%) was also similar to 4CV_LS (-19.5 ± 2.6%; $p = 0.80$) and 2CV_LS (-19.7 ± 3.1%; $p = 0.19$). There was good correlation between GLS and 4CV_LS at baseline ($r = 0.86$; $p < 0.001$) and follow-up ($r = 0.89$; $p < 0.001$) and with 2CV_LS at baseline ($r = 0.87$; $p < 0.001$) and follow-up ($r = 0.88$; $p < 0.001$). However, there was 15% to 22% disagreement between GLS and 4CV_LS or 2CV_LS for the detection of cardiotoxicity. The interobserver and intraobserver reproducibility was higher for GLS (intraclass correlation: 0.93 to 0.95; coefficient of variance: 2.9% to 3.7%) compared with either single-chamber-based LS measurement (intraclass correlation: 0.85 to 0.91; coefficient of variance: 4.1% to 4.8%).

CONCLUSIONS Although there was good correlation between GLS and single-view LS measurements, single-view LS measurement led to disagreement in the diagnosis of cardiotoxicity in up to 22% of patients. GLS measurements were more reproducible than single-view LS. GLS based on 3 apical views should remain the preferred technique for detection of cardiotoxicity. (Strain Surveillance for Improving Cardiovascular Outcomes During Chemotherapy [SUCCOUR]; ACTRN12614000341628.) (J Am Coll Cardiol Img 2018;■:■-■) © 2018 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

2CV = 2-chamber view

4CV = 4-chamber view

AUC = area under the curve

CI = confidence interval

GLS = global longitudinal strain (using 3 apical views)

LVEF = left ventricular ejection fraction

LS = single-view longitudinal strain (4- or 2-chamber)

Peak systolic global longitudinal strain (GLS) measured using echocardiography has emerged as a sensitive marker of left ventricular systolic dysfunction. Its use has gained particular interest in the field of "cardio-oncology" to facilitate detection of early cardiotoxicity (1). A 10% to 15% relative drop in GLS early during cancer therapy identifies patients at risk of later reduction in left ventricular ejection fraction (LVEF) or development of congestive heart failure (2–4).

Standard GLS is calculated from 3 apical images. This method requires careful attention to optimizing 3 views, ensuring consistent heart rate and frame rate during acquisition, and post-processing of 3 datasets. In most cancers, patients receiving cancer therapy require repeated testing to identify cardiotoxicity. There is evidence that reversibility of left ventricular dysfunction is associated with early initiation of heart failure therapy after the onset of cardiotoxicity (5). A single long-axis view could improve efficiency and promote uptake of this technique in busy echocardiography laboratories, or even be applied to imaging approaches at point of care (6), allowing prompt detection of cardiotoxicity (7). Moreover, because cardiotoxicity is believed to be a diffuse process, longitudinal strain (LS) measurements from a single 4-chamber (4CV_LS) or 2-chamber (2CV_LS) view GLS could substitute for traditional GLS measurements. Using such an approach would enable LS measurements to be gathered easily as part of the routine evaluation after each round of chemotherapy, with a higher likelihood of rapid recognition of cardiotoxicity. We hypothesized that single-view LS measurements correlate with GLS, have acceptable measurement reproducibility, and could be used as an alternative to GLS in the detection of cardiotoxicity.

METHODS

PATIENTS. The study cohort consisted of patients recruited to the SUCCOUR (Strain Surveillance During Chemotherapy for Improving Cardiovascular Outcomes) trial. SUCCOUR is a multicenter, international, randomized controlled trial comparing the use of GLS versus LVEF by echocardiography for early detection and management of cardiotoxicity in patients receiving potentially cardiotoxic cancer treatment. Those who have an absolute reduction in LVEF (>0.10 reduction to <0.55) or a relative reduction in GLS (≥12% relative) in the strain arm are treated with a combination of angiotensin-converting enzyme inhibitors and beta-blockers. The primary outcome is a change in LVEF between baseline and the end of 3-year follow-up.

In this baseline substudy, we examined the first 108 patients (enrolled between January 2014 and September 2016), without reference to the outcome standard in the study, and with no knowledge about the patient's randomization status. The measurements in this study were obtained from the core laboratory, which are independent of the GLS or EF analysis being done to guide management in the clinical trial, which are local to the sites. Core laboratory measurements are not sent back to local sites and do not influence clinical management.

ECHOCARDIOGRAPHY. Transthoracic echocardiography was performed before initiation of cancer therapy and repeated every 3 months during treatment. For patients receiving anthracycline-based therapy, the baseline study was performed at the time of initiation of anthracycline; in those receiving anthracycline followed by trastuzumab, the baseline study was performed before trastuzumab initiation but after anthracycline completion. All studies were performed on standard, commercially available echocardiographic systems (Vivid 7 and E9, GE Medical, Milwaukee, Wisconsin).

Apical 2- and 4-chamber views were obtained for calculation of LVEF using the biplane Simpson method. Three long-axis images were recorded with the optimal frame rate (55 to 80 frames/s), stored in raw data format and transferred to the central core laboratory for analysis. Before the start of the study all involved centers participated in a calibration session to ensure uniform technique in image acquisition for strain and EF measurements (8). For this

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