Can We Skip LV Ejection Fraction Measurements in the Surveillance of Patients Undergoing Cancer Treatment with Cardiotoxic Drugs? Results from the CORE Registry

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Background

Serial measurements of LV ejection fraction (EF) have been established to assess cardiotoxic effects of cancer drugs. However, injection of ultrasound contrast is often necessary to ensure accuracy and good reproducibility of EF measurements.

Global longitudinal strain and strain rate have been shown to be more sensitive in detecting myocardial impairment from cardiotoxic drugs. Therefore monitoring of strain parameters seems to be a better alternative to sequential EF measurements. No study has demonstrated that abnormal EF is associated with abnormal GLS and GLSr values in cancer patients.

Objective

To perform global longitudinal strain and strain rate measurements in cancer patients with a reduced EF(<55%).

Method

The Cardiac Oncology Research (CORE) registry prospectively includes patients with cancer undergoing chemotherapy with cardiotoxic drugs**.** EF was measured using biplane contrast-enhanced (CE) Simpson method for optimizing the endocardial definition. In 101 out of 1141 exams the EF was reduced: 50 – 55%: n= 51, <50% n=50.

To evaluate longitudinal LV function, 2D non-contrast and native images of apical four-chamber, two-chamber and three-chamber views were obtained by Philips IE33 with the highest possible frame rates. The measurements of peak systolic global longitudinal strain (GLS), peak systolic and early diastolic strain rates (GLS SRs, GLS SRe) were performed with QLAB by two independent observers.

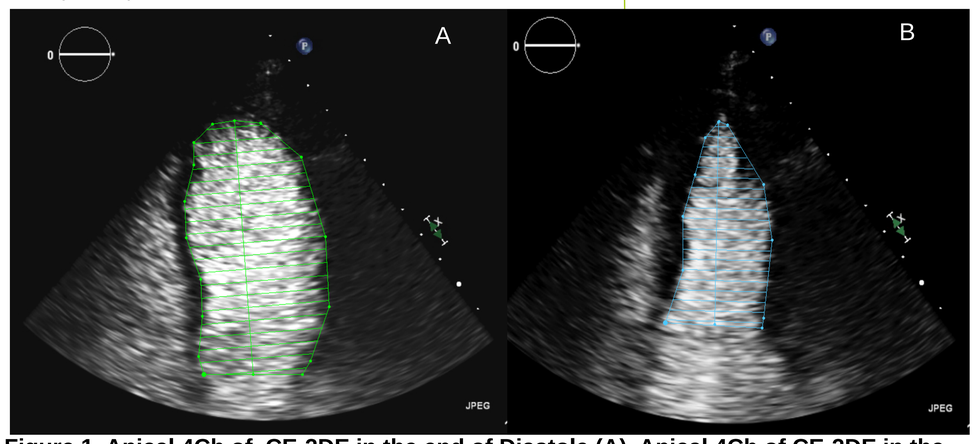

Figure 1. Apical 4Ch of CE-2DE in the end of Diastole (A). Apical 4Ch of CE-2DE in the end of Systole(B)

STRAIN AND STRAIN RATE \ EF		Number (percentage) of Patients with EF <50% (n=46)	Number (percentage) of Patients with EF 50-55% (n=45)
GLS	>-18 %	45(97.8%)	30 (66.7%)
	>-20 %	46 (100%)	41 (91.1%)
GLS SRs	<1.0 s^{-1}	40 (87.0%)	22 (48.9%)
	<1.2 s^{-1}	45 (97.8%)	43 (95.6%)
GLS SRe	<1.0 s^{-1}	41(91.1%)	24 (53.3%)
	<1.2 s^{-1}	43 (93.5%)	38 (84.4%)

Table.1 Myocardium deformation parameters within two groups of patients using different thresholds (black and blue),

Results

Strain and strain rate measurements could not be performed in 11/101 patients (10.9%), whereas contrast echocardiography was possible in all patients.

Table 1 shows the number of patients with GLS worse than – 18% and -20% and strain rate measurements < 1 s^{-1} and <1.2 s^{-1}. Using these thresholds in most patients with an ejection fraction < 50% , abnormal strain parameters are found.

However,, in patients with an EF of 50- 55% there were 33.3% with a GLS better than 18% and 46.7-51.1% with strain rates > 1 s^{-1}.

GLS inter-observer variability: bias 0.38% and 95% limits of agreement (-2.2 to 2.9%). EF inter-observer variability: bias 0.0 and 95% LOA (-2.8 to 3.5%)

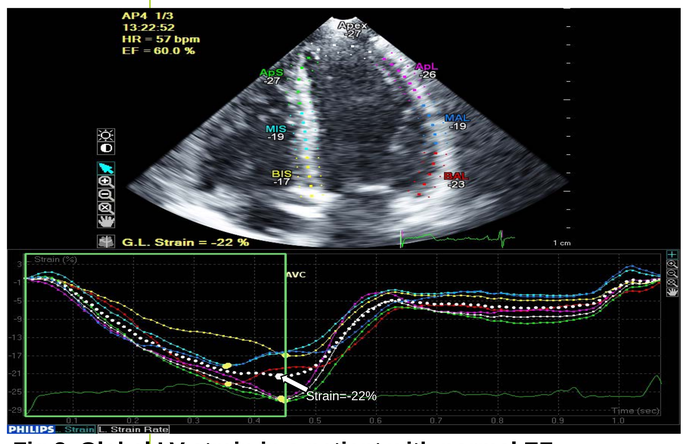

Fig 2 Global LV strain in a patient with normal EF

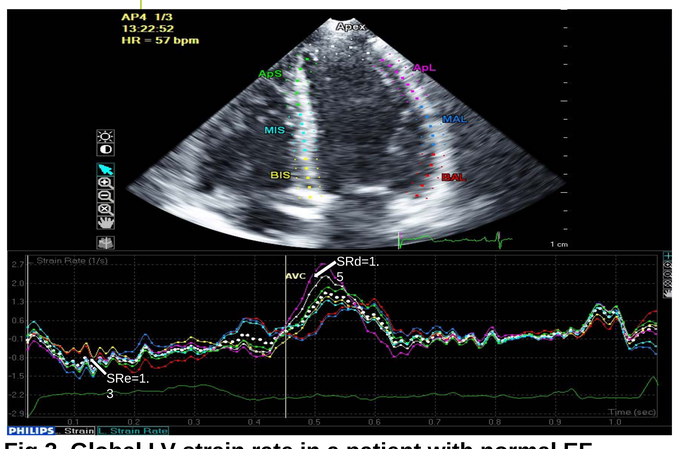

Fig 3 Global LV strain rate in a patient with normal EF

Discussion

A recent systemic review has confirmed the value of echocardiographic myocardial deformation parameters for the early detection of myocardial changes and prediction of cardiotoxicity in patients receiving cancer therapy. [1] Therefore we expected low GLS values in patients with mildly reduced LV ejection fraction.

However, in our study there are a considerable number of patients with normal global strain values despite mildly reduced ejection fraction (50-55%). It is not likely that the discrepancies between normal GLS values and abnormal EF measurements are due to inaccurate EF measurements. This study built on our previous work in showing that contrast echocardiography can be performed with excellent feasibility and reproducibility, which was confirmed again in this study.[2]

GLS measurements (which are performed on native recordings) are affected by image quality which may result in 'normal' strain despite reduced EF. Based on our results GLS should be used in conjunction with an accurate measurements for EF (such as contrast echocardiography) or only recordings with very good image quality should be used. Alternatively a higher threshold for GLS may be considered if one wants to perform F/U studies with GLS only.

Further studies on larger cohorts are needed to define these thresholds.

Conclusion

There are a considerable number of normal strain values in cancer patients with reduced ejection fraction – particularly in patients with EF between 50 and 55%. This limits the exclusive use of myocardial deformation imaging for monitoring cardiotoxic effects.

References

1. Thavendiranathan P, Poulin F, et al. Use of Myocardial Strain Imaging by Echocardiography for the Early Detection of Cardiotoxicity in Patients During and After Cancer Chemotherapy-A Systematic Review. The Am J Cardiol 2014 ; 113:395-401. JACC 2014:In Press

2. He W, Leung E, Becher H, ett al. Contrast echocardiography for monitoring cardiotoxic effects of chemotherapy: quality control in clinical practice with sonographer administered contrast.JASE 2013 26(6): B39-40.