Cancer Therapeutics-Related Cardiac Dysfunction in a Large Clinical Cohort Undergoing Chemo-therapy with Trastuzumab

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Background

Two dimensional contrast echocardiography provides a reliable method to assess left ventricular ejection fraction (LV EF) for cancer patients exposed to potentially cardiotoxic chemotherapeutic agents. However, LV EF cannot detect early subclinical LV dysfunction and global longitudinal strain (GLS) has been recommended as an adjunct to LVEF. The incidence of cancer therapeutics-related cardiac dysfunction (CTRCD) has been reported in patients treated with trastuzumab only in small studies. We sought to elucidate the incidence and timing of CTRCD in a large cohort and to evaluate whether a drop in GLS consistently precedes a drop of more than 10% in LV EF as early marker to detect chemo-induced cardiotoxicity.

Objective

To perform serial GLS and EF measurements in patients with EF drop >10%.

Methods

The Cardiac Oncology Research (CORE) registry prospectively includes patients with cancer undergoing chemotherapy with cardiotoxic drugs**.** Sequential echocardiograms were performed in 177 consecutive female patients undergoing trastuzumab therapy for breast cancer before start and after 3, 6, 9, 12 months. LV EF was measured by biplane method of disks using bolus contrast echocardiography to optimize the endocardial definition (IE 33 or Epiq,Philips).

GLS was assessed by using cardiac performance analysis (Image Arena, TomTec) in three apical views.. The EF difference between baseline and follow up month (FUM) of lowest EF was investigated. In the CTRCD patients, the difference between GLS at baseline and the GLS in the FUM before the month of lowest EF was measured.

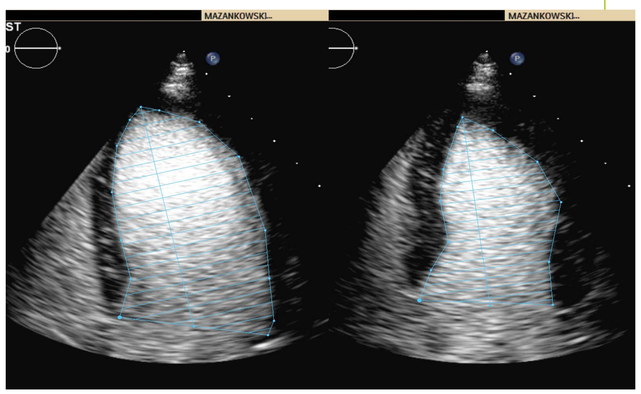

Figure 1. Apical 4Ch of CE-2DE in the end diastole and systole

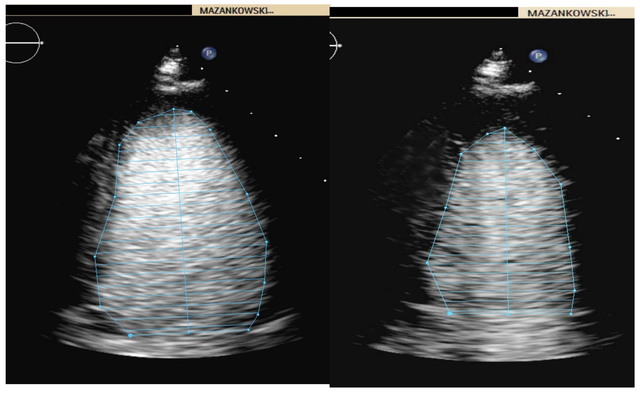

Figure 2. Apical 2Ch of CE-2DE in the end diastole and systole

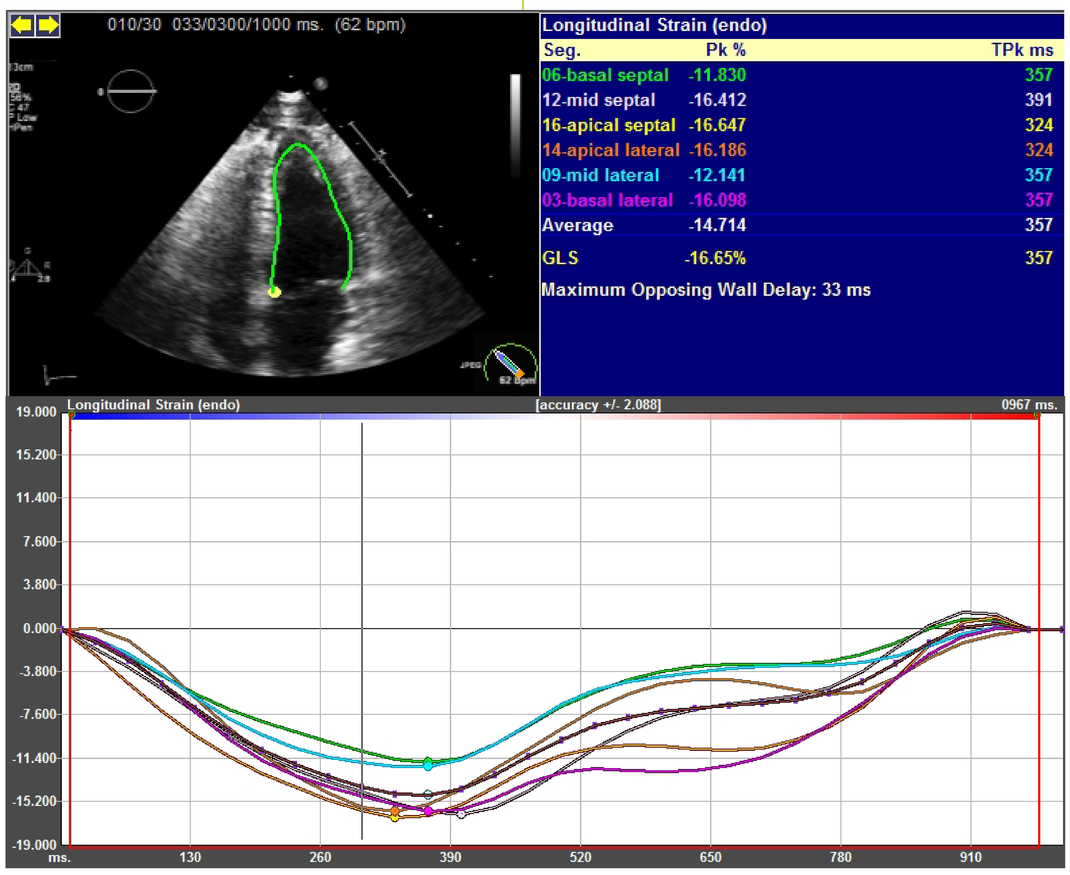

Fig 3. Four chamber view, longitudinal LV strain in a patient with EF = 48%

Results

• EF was >53% in all patients at baseline

•7.9% (n=14) out of 177 patients developed CTRCD with lowest EF<53% (48.9% ± 2.8%). In 14.1% (n=25) EF dropped >10% with lowest EF> 53% (59.5% ± 3.1%).

•The lowest EF was measured at 3 months in 6 patients, 6 months in 11 patients, 9 months in 11 patients and 12 months in 10 patients.

• In all but one patient the EF was back in the normal range at 12 months.

• In the 14 CTRCD patients, GLS dropped > 15% prior to drop in EF in 2 patients, while the maximum change in GLS was between 5.2% and -12.1% in 12 other patients.

Table 1. GLS drop timing compared to EF drop timing in patients with EF drop >10% and lowest EF <53%(n=14)

MONTH	0	3	6	9	12
pts. with drop of EF <53% and drop of EF>10%	n/a	4	3	3	4
Pts with drop of GLS >10%. preceding drop in EF	n/a	n/a	1	1	3
pts with drop of GLS >15% preceding drop in EF	n/a	n/a	0	0	2

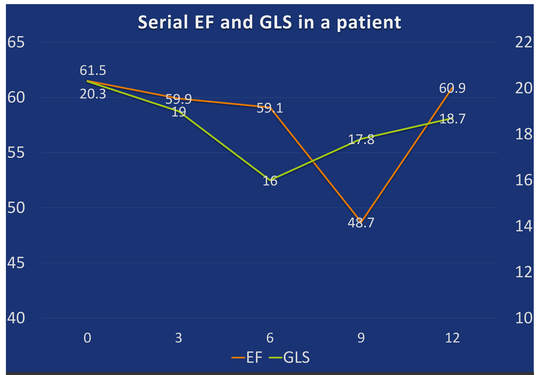

Fig 4. A patient in whom GLS drop preceded EF drop

Conclusion

•The incidence of CTRCD is low in a large cohort of patients mainly treated with trastuzumab and infrequent use of anthracycline. CTRCD could occur at any time during chemo-therapy. The strategy of every 3 months follow up cannot assure that a GLS drop >15% is detected before the LV EF drops.

References

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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.