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EDITORIAL
Special populations

Cardiotoxicity assessment in breast cancer patients: is it straining?

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This editorial refers to 'Serial changes of layer specific myocardial function according to chemotherapy regimen in patients with breast cancer', by M-N. Kim *et al.*, https://doi.org/10.1093/ehjopen/oeac008.

In the last 15 years, two-dimensional speckle tracking echocardiography has positioned itself as a method to detect cardiac toxicity before a drop in ejection fraction becomes eminent. Basic strain analysis by global longitudinal strain (GLS) can be performed with the majority of currently available ultrasound machines in <5 min during the echocardiographic examination, and importantly, with good inter- and intra-observer reproducibility.[1] Other domains of contractility (e.g. circumferential and radial strain) can be evaluated offline by stand-alone software packages once proper images are uploaded in DICOM format. These aspects are exemplified in the study by Kim *et al.*,[2] published in *EHJ Open*, which assessed several different strain parameters in 105 patients with breast cancer followed for 6 months.

The human heart, as described by Torrent-Guasp and coworkers,[3] has an outer and an inner arm that defines three layers of contractility: (i) endocardial level longitudinal fibres, (ii) mid-myocardial level fibres, and (iii) epicardial level fibres that contract circumferentially.[4] When histologically dissected, the orientation of these fibres spans from 90° at the endocardial level to 0° at the mid-myocardial level, and to 130° at the epicardial level.[4] This differential orientation may allow for a differential strain assessment of the different layers.[5] This very topic was addressed by Kim *et al.*, which is not an easy task, requiring methodological soundness and aspiring to provide meaningful impact. Based on the current analysis, one may conclude that assessing layer-specific strain values does not seem to add value to GLS, and GLS is to remain the gold standard for strain imaging for cardiotoxicity detection/prediction.[6]

A bigger question raised by the present study is the value of strain assessment in general. A significant decline in left ventricular ejection fraction (LVEF) at 3 months follow-up was noted already in those patients who developed a drop in LVEF by >10% at 6 months follow-up, which was the definition used for cardiotoxicity.[2] Who would need to add strain assessment, if we can tell by an early trend in LVEF dynamics? The relatively high incidence of cardiotoxicity (19%) within a 6-month observation period is also very striking and may have contributed to detection dynamics. Just over half of the patients (55%) received anthracyclines at <300 mg/m^2 and about half with the use of dexrazoxane; yet, even so, 19% incidence of cardiotoxicity. Trastuzumab was used in ~30% of the patients; only 10 patients had combined anthracycline–trastuzumab therapy, which showed the highest incidence of cardiotoxicity at 30%. This being said, even in patients on taxanes, 19% developed cardiotoxicity, and dynamics were rather similar across all subgroups.

Taken together, the article by Kim *et al.* pursued a novel layer-specific approach to strain imaging in breast cancer patients at risk of cardiotoxicity and provides an important impulse. The findings need to be reproduced and validated against the standard of GLS and its relative changes. Factors that can influence endocardial stress such as high afterload conditions need to be taken into account. Akin to the old differentiation of myocardial infarction, cardiotoxicity in breast cancer patients: is it endocardial, transmural, or of another kind? For this question to be answered, we need another find.

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