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SPECKLE TRACKING ECHOCARDIOGRAPHY IDENTIFIES CARDIAC DYSFUNCTION INDUCED BY THE ANTICANCER ERBB2 BLOCKER LAPATINIB

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Background: Anti-ErbB2 therapies have improved the prognosis of patients with breast cancer. Still, they are associated with an increased risk of left ventricular (LV) dysfunction. Trastuzumab (Herceptin) increases the frequency of asymptomatic decrease in LV ejection fraction (LVEF) by 3-18%, and the risk of heart failure (HF) by 2-4%. The newer agent Lapatinib (L) is associated with a lower risk of LV dysfunction. Traditional indexes of cardiac function *in vivo* (fractional shortening and ejection fraction) may underestimate subtle changes that occur with L. Here, we test whether early sensitive indices of LV dysfunction can reveal L-induced cardiotoxicity. **Methods:** In vivo cardiac function was measured with LV fractional shortening (FS) by M-mode echocardiography, and with radial myocardial strain (%) with Speckle tracking (ST) in sedated C57BL/6 mice (8-10wk. old) after 7 and 14 days of daily administration of 25 or 100 mg of L, and in control mice. After the echo studies, the hearts were excised, and interstitial fibrosis was evaluated with picrosirius red staining. **Results:** After 7 and 14 days of treatment, L 25mg did not affect FS nor strain. On the other hand, at 100mg of L, FS decrease was almost significant at 7 and 14 days (53±5% and 52±5% vs 60±1%; p=.08 and .07 vs sham, respectively), while there was a clear reduction in myocardial strain at both 7 and 14 days: 48±2% and 24±4%, respectively, vs 61±0.3%, both p<.02 vs sham. This early LV dysfunction detected with ST was paralleled by an increase in collagen content: 5±0.4% at 14 days vs 3±0.3% (sham; p=.005). **Conclusions:** Myocardial strain identifies LV systolic dysfunction earlier than conventional echocardiography, and parallels histological changes earlier than FS. Still, the clear mechanisms of anti ErbB2-induced cardiotoxicity are to be elucidated. We plan to study such mechanisms, and to apply ST technique in clinical practice, in order to evaluate the impact of early identification of L-related cardiotoxicity in the treatment of women affected by breast cancer.