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EARLY IDENTIFICATION OF LEFT VENTRICULAR DYSFUNCTION WITH SPECKLE TRACKING ECHOCARDIOGRAPHY IN ANTINEOPLASTIC THERAPY-INDUCED CARDIOTOXICITY

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Background: New anti-ErbB2 therapies have improved the prognosis of patients with breast cancer, but are associated with an increased risk of left ventricular (LV) dysfunction. Trastuzumab (T) can increase by 3-18% the frequency of asymptomatic decrease in LV ejection fraction (LVEF), and by 2-4% the risk of heart failure (HF). Opposite to the well known anthracyclin-induced cardiotoxicity, these conditions are reversible, in absence of apparent ultrastructural changes. Indexes of cardiac function such as fractional shortening (FS) and EF are not very sensitive in detecting early myocardial damage. Aim of this study is to evaluate whether myocardial strain by speckle tracking (ST) is able to identify early LV dysfunction in mice treated with doxorubicin (D) and T, alone or in combination (D+T). **Methods:** We measured radial myocardial strain (%) with ST, and FS by M-mode echocardiography in sedated C57BL/6 mice (8-10wk. old) at day 0, and after 2 and 6 days of daily administration of D (2.17 µg/g/day), T (2.25 µg/g/day), D + T (2.17 µg/g/day+2.25 µg/g/day respectively), and in a control group. **Results:** FS was able to identify early (2 days) LV dysfunction only in group D and D+T: 52±0.2% and 49±2%, respectively, both p<.001 vs 60±0.4% (sham), while in group T it decreased only at 6 days (49±1.5% vs 60±0.5%, p=.002). In contrast, after 2 days, myocardial strain was already reduced not only in D and D+T, but also in T alone: 43±3%, 49±1%, and 44±7%, respectively, all p<0.05 vs sham (66±0.6%). **Conclusions:** In mice treated with D or T, myocardial strain identifies LV systolic dysfunction earlier than conventional echocardiography. We plan to apply this technique to clinical studies, to evaluate the impact of early identification of T-related cardiotoxicity in the treatment of women affected by breast cancer, and to better elucidate the mechanisms of T myocardial effects.