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Early identification of trastuzumab-related cardiotoxicity with speckle-tracking echocardiography

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Background: New targeted therapies have improved the prognosis of patients with breast cancer but cause several off-target effects, such as left ventricular dysfunction and heart failure that has still a 5-years mortality of 50%. Adjuvant treatment of breast cancer consists of combination chemotherapy with anthracyclines (A) and, in women with ErbB2 over-expressing disease, trastuzumab (T). A can cause an irreversible left ventricular dysfunction, named type I cardiomyopathy. T causes can cause left ventricular systolic dysfunction between 3% and 18%, and heart failure between 2% and 4%, but these are reversible and there seems to be no apparent ultrastructural changes (II type cardiomyopathy). Methods for measuring cardiac function in Mmode
with shortening fraction (FA) and in B-mode with ejection fraction are not very sensitive in detecting early myocardial damage. The aim of this study was to evaluate if myocardial strain by speckle tracking technique (ST) was able to identify early left ventricular dysfunction in mice treated with doxorubicin (D) and T, alone or in combination (D+T).
Methods: We measured radial myocardial strain (%) with ST and FA by assessing M-mode short axis projection in C57BL/6 mice at time 0, 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: The second day we found a significant reduction of radial strain in the group D ($p = 0.003$), T ($p = 0.03$) and D+T ($p = 0.003$).
The FA was reduced significantly on day 2 only in group D ($p < 0.001$) and D+T ($p = 0.001$), whereas in group T was normal, and decreased only at day 6 ($p = 0.001$).
Conclusions: With myocardial strain obtained with ST technique it is possible to identify left ventricular systolic dysfunction early, before conventional echocardiography. The reason why this was found only in T group probably lies in the fact that T does not cause myocardial necrosis, in contrast to A, but reversible alterations (harder to detect early with the reduced FA). These studies will be extended to patients, to evaluate the clinical impact of early identification of T-related cardiotoxicity in the treatment of women affected by breast cancer.