



Prediction of trastuzumab-induced cardiotoxicity in breast cancer patients receiving anthracycline-based chemotherapy: methodological issues

Mehdi Naderi¹ · Siamak Sabour^{2,3}

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Dear Editor

We were interested to read the paper by El-Sherbeny et al. published in Aug 2018 issue of the J Echocardiogr [1]. The purpose of the authors was to investigate whether myocardial strain imaging and level of N-terminal pro-brain natriuretic peptide (NT-pro BNP) could predict subsequent reduction in left ventricular ejection fraction (LVEF) in breast cancer patients who received adjuvant trastuzumab. Sixty-one cancer breast female patients with pathologically proven breast cancer HER-2 positive received AC (doxorubicin–cyclophosphamide) for four cycles, followed by paclitaxel with trastuzumab were enrolled. Clinical, conventional echocardiographic parameters, myocardial strain imaging [global longitudinal peak systolic strain (GLS), radial and circumferential systolic strain and level of NT-pro BNP were measured at baseline, after 3, 6, 9 and 12 months of trastuzumab therapy. Authors reported that 18 patients (29.5%) developed trastuzumab-induced cardiomyopathy (CM) at 6 and

9 months of therapy (LVEF declines $\geq 10\%$), GLS and radial strain significantly decreased in CM group at 3 months of trastuzumab treatment, the value of GLS at 3 months was the strongest predictor of cardiotoxicity and its area under the curve (AUC 0.98) with an optimal cutoff for GLS (-18%) having 92.5% sensitivity and 83% specificity. NT-pro BNP levels were not predictive of later trastuzumab-induced cardiac dysfunction [1].

The AUC is usually used to evaluate the accuracy of a diagnostic model. Moreover, AUC even though statistically significant, does not guarantee prediction. Moreover, for prediction studies, we need data from two different cohorts or at least from one cohort divided into two to first develop a prediction model and subsequently validate it. Misleading results are generally the main outcome of research that fails to validate its prediction models. Validation of a prediction model can be done by applying different approaches such as split file, bootstrapping, or other well-known validation methods. Moreover, for prediction of an outcome, we must assess the interactions between important variables [2–6].

Authors concluded that myocardial strain imaging has been able to predict pre-clinical changes in LV systolic function and GLS is an independent early predictor of subsequent reduction in EF in breast cancer patients treated with trastuzumab. Briefly, in prediction studies, the main purpose is to provide a model, index, or score applicable to an individual (patient). Finally, associations, even those that are statistically significant, do not guarantee prediction [2, 3].

In this letter, we discussed methodologic issues on prediction studies. Any prediction should be supported by the aforementioned methodologic issues.

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✉ Siamak Sabour
s.sabour@sbmu.ac.ir

¹ Department of Operating Room, School of Paramedical, Kermanshah University of Medical Sciences, Kermanshah, Iran

² Department of Clinical Epidemiology, School of Health, Safety Promotion and Injury Prevention Research Center, Shahid Beheshti University of Medical Sciences, Chamran Highway, Velenjak, Daneshjoo Blvd, Tehran 198353-5511, Iran

³ Safety Promotions and Injury Prevention Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Compliance with ethical standards

Conflict of interest Mehdi, Naderi and Siamak, Sabour declare that they have no conflict of interest.

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