Canadian Journal of Cardiology 35 (2019) 545.e1–545.e2 www.onlinecjc.ca

Letters to the Editor

Longitudinal High-Sensitivity Cardiac Troponin I Measurements in Patients With Breast Cancer Receiving Trastuzumab

To the Editor:

Studies assessing cardiac troponin for predicting a change in left ventricular ejection fraction (LVEF) in patients with breast cancer receiving trastuzumab have had mixed results, with 1 publication using the high-sensitivity cardiac troponin T (hs-cTnT) assay demonstrating no association with LVEF decrease or in the detection of cardiotoxic effects.[1] Of note, although not emphasized in the publication, was the high prevalence of myocardial injury in patients completing the anthracycline-containing chemotherapy and before trastuzumab treatment, with approximately 50% of the patients having hs-cTnT concentrations ≥ 99th percentile (14 ng/L).[1] Longitudinally in this study population, the hs-cTnT elevations persisted through 12 weeks and then proceeded to trend to normal levels.[1]

The profile of persistent elevated cardiac troponin is suggestive of chronic injury, yet it is unclear why hs-cTnT elevations persist over the first 3 months on trastuzumab therapy.[1] There are subtle differences between hs-cTnT and high-sensitivity cardiac troponin I (hs-cTnI), and even between hs-cTnI assays for interpreting persistently high concentrations.[2] Accordingly, our objective was to determine the longitudinal profile and prevalence of hs-cTnI concentrations above the 99th percentile in women being treated with trastuzumab using the regulatory-approved Beckman Coulter (Brea, CA) Access hsTnI assay.[3]

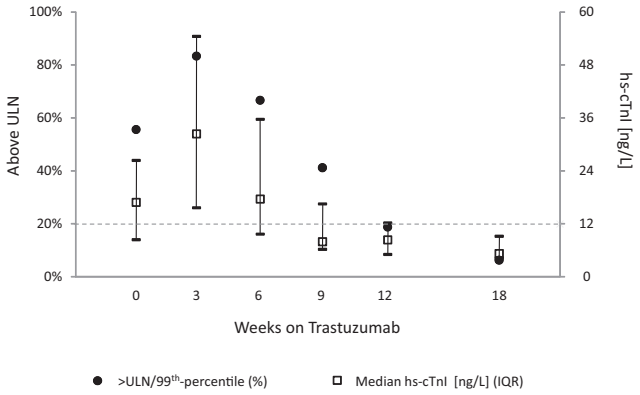

Figure 1. The longitudinal profile on the prevalence of concentration greater than upper limit of normal (ULN) (%) and high-sensitivity cardiac troponin I (hs-cTnI) (median, interquartile range [IQR]) concentrations in women with breast cancer who completed chemotherapy and started trastuzumab treatment (the **dashed line** is the ULN/99th percentile concentration cutoff of 12 ng/L).

After ethics board approval, 21 women with HER-2 positive early-stage breast cancer consented to have blood draws (ethylenediaminetetraacetic acid plasma/stored −70°C) before and after initiation of trastuzumab therapy (October 2010 to March 2016). For this analysis, only participants with a baseline LVEF obtained before initiation of trastuzumab (n = 18; median age, 51, years; interquartile range [IQR], 43-57) were selected with hs-cTnI testing performed on plasma samples collected before trastuzumab administration at baseline (n = 18), 3 weeks (n = 18), 6 weeks (n = 18), 9 weeks (n = 17), 12 weeks (n = 16), and 18 weeks (n = 16). The female 99th percentile cutoff/upper limit of normal (ULN) (> 12 ng/L) for the Access hs-cTnI assay was used to retrospectively identify those patients with elevations.[4]

After completion of an anthracycline-based chemotherapy regimen and before trastuzumab, the median LVEF was 60% (IQR, 56-63) and the median hs-cTnI concentration was 17 ng/L (IQR, 8-26) (10/18 patients with an hs-cTnI level greater than ULN). The hs-cTnI concentrations in the cohort were the highest at 3 weeks (hs-cTnI median = 32 ng/L; IQR, 15-54) and the lowest at 18 weeks (hs-cTnI median = 5 ng/L; IQR, 4-9) ($P < 0.01$) (Fig. 1). Before 12 weeks, 2 participants stopped treatment (3-week hs-cTnI concentrations: 76 ng/L and 10 ng/L), with no significant decrease in the LVEF in the remaining 16 patients at the 12-week scan (LVEF median = 58%; IQR, 54-62) and LVEF median difference from baseline = −5% (IQR, −6 to 0).

There are persistent elevations in hs-cTnI within the first 12 weeks after initiation of trastuzumab after an anthracycline regimen, similar to what was observed for hs-cTnT. Caution is warranted in interpreting high-sensitivity cardiac troponin solely on the basis of the ULN in this setting.

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https://doi.org/10.1016/j.cjca.2018.12.023

Funding Sources

Juravinski Cancer Center Foundation Grant (Dr Dhesy-Thind) and hs-cTnI reagent from Beckman Coulter (Dr Kavsak). The funding organizations had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the final approval of the manuscript.

Disclosures

Dr Kavsak has received speaker fees and grant support from Abbott Laboratories, Beckman Coulter, Roche Diagnostics, Randox Ltd., and Siemens Healthcare, and is listed as an inventor on patents filed by McMaster University related to laboratory testing in acute cardiac care. The other authors have no conflicts of interest to disclose.

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