Troponins in prediction of cardiotoxic effects

We read the work by Kilickap et al. [1] with great interest. These authors affirm that troponin T (cTnT) could be useful for the early detection of anthracycline-related cardiotoxicity. However, the role of cardiac troponins as indicators of early cardiotoxicity and as predictors of myocardial dysfunction has already been extensively demonstrated in animal models, as well as in children and adult patient populations treated with chemotherapy. We previously demonstrated that troponin I (cTnI) is a sensitive and specific marker for myocardial injury after high-dose chemotherapy, able to predict, in a very early phase, the development and severity of ventricular dysfunction [2]. More recently, these observations were extended to a larger population of >700 patients undergoing high-dose chemotherapy. During a follow-up of >3 years, a broad spectrum of adverse cardiac events was considered [3]. These data show clearly that cTnI release pattern identifies patients at different risk of cardiac events. It is quite surprising that the authors completely ignored these recent advances on the clinical and prognostic relevance of troponin increase after chemotherapy, and their statement ‘there was limited information regarding the usefulness of increased serum cTnT in detecting anthracycline-induced cardiotoxicity in its early stage’ appears inappropriate, and not updated. Notably, the pathophysiological and clinical relevance of cTnT and cTnI are equivalent from a cardiological point of view. In addition, the interest of troponins in the oncologic setting has recently moved to a further stage of investigation. Troponins have been proposed to assess the safety of new antineoplastic treatments, and to evaluate the effectiveness of cardioprotective strategies aimed at preventing or blunting troponin rise after chemotherapy [4].

The authors describe a relationship between cTnT levels and E/A ratio. cTnT values exceeded the upper limit of the normal range in only two patients, leading the authors to suggest the use of a new lower threshold for cTnT positivity for future studies on anthracycline cardiotoxicity. However, it must be considered that previous studies which had demonstrated a close correlation between troponin level increase and cardiac event occurrence used the standard cut-off for myocardial damage. Therefore, in our opinion the reduction of the diagnostic cut-off in this setting would only lead to decrease the marker specificity without additional clinical advantages. Moreover, Auner et al. [5] demonstrated the importance of serial measurement of troponins, especially after standard dose anthracycline. In our studies, repeated curves of cTnI samples, associated with a late measurement (1 month after the end of chemotherapy) were used, and a predictive negative value of 99% and a positive predictive value of 84% were found. Thus, the timing of detection of chemotherapy-induced cardiac injury, as revealed by troponins, more than their actual thresholds, represents the point we have to focus on in future studies. Finally, we found the possible correlation between cTnT increase and the development of diastolic dysfunction very interesting. Unfortunately, because of the short follow-up and the small study population, no conclusive information on the possible clinical relevance of this relationship can be drawn.

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references

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