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Cardiac Troponins

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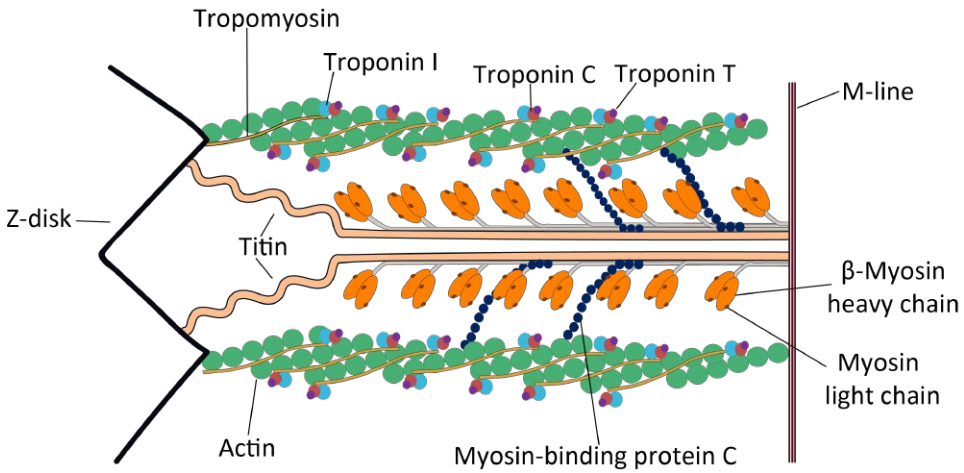
Introduction

Cardiac troponins have by and large replaced older cardiac assays like total creatine kinase (CK), creatine kinase-myocardial band (CK-MB), lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) to assess for cardiac tissue injury. The heterotrimeric troponins, consisting of Troponin T (TnT), Troponin I (TnI) and Troponin C (TnC) complexes with the tropomyosin molecule, which through conformational change following calcium binding, brings about muscle contraction (figure 1). Each of the troponin T and I subtypes, are encoded for on 3 distinct genes in the form of slow skeletal, fast skeletal and cardiac muscle. It is the presence of a distinct cardiac subtype that allows for specific cardiac immunoassays, used in the evaluation of myocardial injury.

In addition to the distinctive subtypes, cardiac tissue is considered as postmitotic and therefore not able to re-differentiate. Therefore, detection of extruded protein in blood, is interpreted as a sign of necrosis or injury. The progression from qualitative and low-sensitivity assays to high sensitivity assays (hs-cTn) further cemented its use in the evaluation of patients with chest pain and general risk stratification.

Figure 1. Coupling of the heterotrimeric troponins to the tropomyosin molecule By Mohamed Elshennawy, M.D. - Own work[12]



The presence of c-TnT in foetal skeletal muscle[1] has historically raised the question of whether it can be expressed in adult skeletal muscle[2]. This was demonstrated in patients with inherited and acquired skeletal myopathies[3], [4], [5], in addition to exercise studies[6], where hc-cTnT were demonstrated to be elevated but not hs-cTnI.

Comparing cTnI and cTnT

Comparison between the two markers is complicated by various issues. Firstly, from a pre-analytic viewpoint, both false positive and false negative results have been attributed to native antibody interference in both markers. Secondly, from an analytic stance, the hs-cTnT assay is only available from one manufacturer, Roche Diagnostics, due to patenting, whereas the hs-cTnI is offered by various manufacturers (Siemens, Abbott, Beckman Coulter amongst others).

This complicates comparison with varying reference ranges and assay harmonization. Lastly, with reference to the post-analytical, subsequent use of these markers in combination with other risk factors, various population groups and for clinical indications also affect its predictive value.

i. Diagnosis of AMI

Both assays perform similarly in their ability to serve as predictive markers for acute coronary events based on the results obtained from the APACE study[7], [8]. The use of both assays in combination has been proposed to overcome some of the pre-, post- and analytical issues discussed with some success, however, this effect is only marginal and not always practically justifiable.

ii. General population

The use of hs-cTn assays have been of interest as a marker for cardiovascular risk stratification in the general population. Despite its promise, studies are lack running both assays head-to-head, making comparison difficult owing to cohort differences. Comparison of data from studies run separately, demonstrate a slightly higher hazard ratio for future CVD events[9] as well as non-CVD death[10] using hs-cTnT over hs-cTnI. Of note, hs-cTnI show a greater predictive correlation in combination with age, male sex, body mass index and systolic pressure, whereas hs-cTnT shows greater predictive correlation in combination with diabetes[11].

Conclusion

No clear data currently justify the specific use of either hs-cTnT versus hs-cTnI in either the diagnosis of an AMI or as part of risk stratification. It is likely that genetic variation with regards to expression of these subsets as found within specific populations may guide future guidelines as to preferred use, however this is still lacking at this point.

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