High sensitive methods for cardiac troponin assay: analytical characteristics and pathophysiological aspects

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In 2000, the European Society of Cardiology/American College of Cardiology (ESC/ACC) consensus conference along with the American Heart Association (AHA)/ACC guidelines for differentiating acute myocardial infarction (AMI) and unstable angina codified the role of cardiac troponin monitoring by advocating that (a) diagnosis of AMI and (b) risk stratification are based on the increase in cardiac troponin I (cTnI) or T (cTnT), in an appropriate clinical setting; in 2007, these recommendations were confirmed by the so-called "Universal Definition of Myocardial Infarction". Moreover, in 2001 the IFCC C-SMCD established recommended quality specifications for cardiac troponin assay. In particular, these guidelines recommend that an increased concentration of cardiac troponin should be defined as a measurement exceeding the 99th percentile of the distribution of cardiac troponin concentrations in the reference group. A total imprecision (CV) at this decision limit of 10% is recommended. Unfortunately, at present time, analytical imprecision is not uniform among different commercial immunoassays for cardiac troponins, mainly within the low concentration range, and therefore some troponin assays do not fit the goals recommended for functional sensitivity. As a result, a new generation of more sensitive and standardized cTnI immunoassays should show a ratio of 10% CV concentration to 99th percentile limit equal or even less than 1.

In our laboratory we evaluated the analytical and clinical performance of the TnI-Ultra immunoassay for cardiac Troponin I (cTnI) measurement, carried out on the fully automated ADVIA Centaur CP® platforms (Siemens Medical Solutions Diagnostics SrL). The distribution of cTnI values was calculated in a population including 692 healthy subjects (311 males and 381 females; age range from 11 to 89 years); log-transformed values of original cTnI concentration approximated to a symmetrical distribution with a calculated 99th percentile of 0.072 μg/L. As a result, the ratio between 10% CV concentration and 99th percentile values was less than 1 (i.e., 0.057/0.072= 0.79). A significant difference was found between the cTnI values in men and women (men: median 0.012 μg/L, range from undetectable values to 0.196 μg/L; women: median 0.008 μg/L, range from undetectable values to 0.130 μg/L; $p < 0.0001$ by Mann-Whitney U test). When a multiple regression analysis was performed, NT-proBNP, gender and age significantly contributed to the regression with cTnI ($R= 0.444$, $p < 0.0001$). Furthermore, a close linear regression was found between the cTnI values obtained with the TnI-Ultra method and the Access AccuTnI™, carried out on the UniCell® DxI 800 platform (Beckman Coulter, Inc., Fullerton) in 230 patients with cardiovascular diseases, including 70 samples with a cTnI value higher than the decision level for acute myocardial infarction (TnI-Ultra= -0.192 + 1.434 AccuTnI^{T}; $R= 0.976$; $n= 230$).

Our data indicate that cut-off values, based on 99th percentile of cTnI distribution in apparently healthy subjects, can significantly vary according to age and gender of the reference population. From a physiological point of view, cTnI circulating levels are independently related to gender, age, and NT-proBNP values. As a work hypothesis, we can assume that, if heart dysfunction is an inevitable, ultimate fate, the measurement of cardiac troponins and natriuretic peptides should be used to detect people, who are at risk of a more rapid progression toward symptomatic cardiac failure, thus needing a specific clinical care.

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