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Troponin Delta: guideline on z-scores

Serial changes in cardiac troponin (cTn)

The definition of myocardial infarction includes a "typical" rise or fall in serial cTn levels. A z-score is a statistical parameter that can be used to determine the significance of the difference between serial results, thus assisting in classifying the difference as "typical" or not.

In order to decide whether a change between successive cTn values (ΔcTn) is real or a result of "noise", we need to isolate the components that contribute to uncertainty.[1]

Analytical variation ($SD_{Analytical}$) is the result of small mechanical and electrical errors in the measurement process. When the analytical process is well-controlled these errors are numerically small in real terms at low levels and increase predictably at higher levels.

Biological variation ($SD_{Biological}$) is the normal physiological fluctuation of cTn in an individual over time and results from the variable release into, and clearance from peripheral blood. We have experimentally determined the magnitude of this variance for the current cTn assay and it is numerically small in healthy individuals.

The smallest significant Δ or ***reference change value*** (RCV) can be calculated from this information:

$$RCV = z \times \sqrt{2(SD^2_{Analytical} + SD^2_{Biological})}$$

where $\sqrt{2(SD^2_{Analytical} + SD^2_{Biological})} = \sqrt{SD^2_{Difference}}$

In figure 1,[2] the significant Δ and Δ% values (RCVs) were calculated with z = 2. The RCVs are a function of the mean cTn concentration.

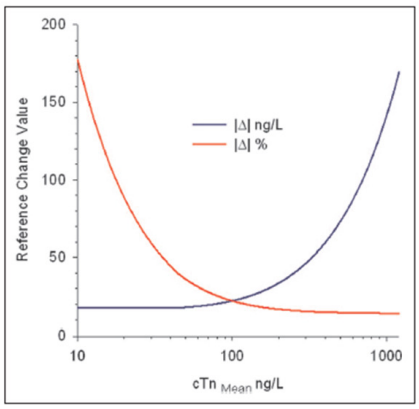

Figure 1. The relationship between the Beckman Coulter cTnI mean cardiac troponin level and the reference change values of relative and actual differences.

Calculation of z-scores

The *probability* of an observed ΔcTn being a chance finding can be isolated from the above:[1]

$$z = \Delta cTn \Big/ \sqrt{2(SD^2_{Analytical} + SD^2_{Biological})}$$

Z-scores are automatically calculated in Auslab between consecutive cTn results, if the two requests occur within an 8 hour window from each other.

How to interpret z-scores?

A z-score outside the ±2 interval tells us that a ΔcTn of this magnitude is expected to occur due to chance in less than 5% of instances ($p < 0.05$).

A z-score outside ±3 is expected to occur due to chance in less than 1% of cases ($p < 0.01$).

In Auslab, z-scores greater than ±3 will be highlighted in yellow.

Elevated z-scores can occur due to an error in the measurement of cTn and also when there is a pathological release into the circulation.

IMPORTANT:
Not all statistically significant ΔcTn results are equivalent to a clinical diagnosis of myocardial infarction.

Z-scores do not diminish the importance of clinical judgment in establishing a diagnosis of acute coronary syndrome.

Z-scores may assist in objectively assessing the significance of ΔcTn. This approach was preliminary validated in a population with clinically well-defined acute coronary syndrome.[2]

References

1. Serial cardiac troponin differences measured on four contemporary analyzers: Relative differences, actual differences and reference change values compared. CJ Pretorius, U Wilgen, JPJ Ungerer. Clin Chim Acta 2012;413:1786–91.
2. Towards a consistent definition of a significant delta troponin with z-scores: a way out of chaos? CJ Pretorius, L Cullen, WA Parsonage, JH Greenslade, JR Tate, U Wilgen, JPJ Ungerer. European Heart Journal: Acute Cardiovascular Care 2014;3:149-57.

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