COLLEGE of AMERICAN PATHOLOGISTS

Educational Discussion: Cardiac Markers

2015-A Cardiac Markers Survey (CAR)

In this first mailing of the year, two samples deserve special attention:
Sample CR-03 is a sample which we believe has no troponin in it, a topic we wrote about in the CAR-C 2014 Survey. We have included that discussion again at the end. The take-home message is that it is very important for laboratories to know, and make their providers aware of, their assay's lowest reporting limit (determined either by the laboratory or the manufacturer). There are three different ways of defining this lower limit – LOB, LOD, LOQ. In our opinion, the most appropriate limit for cardiac troponin is the LOD. Results should never be reported as zero, "0", but rather as less than some value (e.g., <0.02). Of interest, we did notice that laboratories, even using the same manufacturer's assay, reported values that had different numbers after the < sign (e.g., <0.01, <0.05, <1.0). Once again, we urge every laboratory to check their lower reporting limit.

Sample CR-05 provides additional information. It was designed to have a very low concentration of troponin. Because of the fact that these samples are non-commutable (i.e., they do not behave exactly like real patient samples), we do not expect all the different assays to get the same values. We might not even expect different assays to detect differences between Sample CR-03 and Sample CR-05. Both of these statements proved to be true, as shown in the table below.

Instrument	Most frequent result CR-03 (absent Troponin I)	Most frequent result CR-05 (low level Troponin I)
Abbott Architect i	<0.01	0.04
Beckman Access/2	0	0.03
Beckman Unicel DxI	<0.03	0.03
Roche e411/Elecsys STAT	<0.30	<0.30
Roche e600 ser/E170	<0.30	<0.30
Siemens Advia Centaur CP	<0.01	0.045
Siemens Advia Centaur/XP	<0.01	0.04
Siemens Dimension EXL	0.03	0.13
Siemens Dimension HM	<0.04	<0.04
Siemens Dimension Vista	0.045	0.13
Siemens Stratus CS	<0.03	<0.03
Vitros 3600, 5600, ECI/ECIQ	<0.01	0.02

To the extent that clinicians are focusing on lower detection limits and small differences between serial samples, knowing how our survey samples perform in the field is critically important.

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Discussion from CAR-C 2014 Survey

The majority of troponin values that clinical laboratories report can be grouped into “negative” or ”less than” categories. Up to now, the CAP has not included a challenge in this range because of the difficulties associated with their preparation and grading. These include, but are not limited to, issues associated with non-commutability (so-called “matrix effects”) and varying degrees of non-linearity at the lowest measurable concentrations.

In this mailing, we have included our first troponin challenge, CR-12 in this range because it makes clinical sense as it reflects a common test result range. After reviewing the results as well as the manufacturers’ performance specifications, we decided to use a threshold of 0.3 ng/mL or less as the criterion for acceptable performance.

We believe laboratories should take this opportunity to review how they report such values. Modern terminology for lowest reportable concentrations includes such terms as “limit of blank” (LoB), “limit of detection” (LoD), and “limit of quantitation” (LoQ).

Limit of Blank (LoB) LoB is the highest apparent analyte concentration expected to be found when replicates of a blank sample containing no analyte are tested.

Limit of Detection (LoD) The lowest analyte concentration likely to be reliably distinguished from the LoB and at which detection is feasible. LoD is determined by utilizing both the measured LoB and test replicates of a sample known to contain a low concentration of analyte.

Limit of Quantitation (LoQ) The lowest concentration at which the analyte can not only be reliably detected but at which some predefined goals for bias and imprecision are met. The LoQ may be equivalent to the LoD or it could be at a much higher concentration.

As most assays are non-linear at the very low end, “0” is not a reasonable choice; eg, results such as <0.02 ng/mL would be more appropriate. We recognize that some labs will have determined their own LoD or LoQ, which may differ from their manufacturer’s, but in all likelihood, the values will not be very different.

Most importantly; communication to the clinicians about the terms used, their meaning and clinical significance is paramount in appropriately utilizing these results. Lastly, these Proficiency Testing (PT) samples follow all of the existing CLIA requirements regarding PT processes ie, treat these PT samples as you would genuine samples – both in terms of analysis and reporting. Especially, if you report values as <0.03 ng/mL for patients, that’s how you should report the PT samples; if you report values as “NEGATIVE”, that is how you should report the PT samples.

References

1. Armbruster DA, Pry T. Limit of blank, limit of detection and limit of quantitation. Clin Biochem Rev. 2008 Aug;29 Suppl 1:S49-52.

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