ACB Clinical Practice Section Troponin Working Group

Guidelines for use of Troponin Assays

A number of more sensitive troponin assays have been developed in recent years, all with different capabilities, and the term highly sensitive (hs) has been introduced to enable users to distinguish these from previous generations. However, developments in this field have continued with manufactures introducing various terminologies to describe their particular troponin assay. This has produced some confusion regarding assay capabilities and how each one could be applied to assist with the diagnosis or exclusion of AMI.

Laboratories have been faced with the not insignificant task of overseeing a transition to the new assays and ensuring that clinical users are as aware as possible of the implications and impact on patient investigation and care. A recent audit organised by the National Clinical Biochemistry Audit Group (NCBAG) has highlighted a number of inconsistencies in how laboratories have approached the implementation and oversight of more sensitive assays for troponin[1]. Due to the significant variations between manufacturers in assay performance and capabilities is it not possible to standardise specific parameters that will apply across the board, however, it is hoped that a more harmonised approach in how laboratories develop their troponin testing service can be achieved.

Laboratories should be aware of the recent guidelines on the use of highly sensitive troponin assays that have been published by NICE[2] and the IFCC[3] and of clinical guidelines produced by the European Society of Cardiology, the most recent update being published in August 2015[4-5]. This introduced a zero and one hour delta for the early rule-in and rule-out of AMI for three specific troponin assays (hs-cTnT-hs [Elecsys], hs-cTnI [Architect] & hs-cTnT [Dimension Vista]) which may particularly appeal to ED and cardiology colleagues. It is important that laboratories have clear guidelines on what troponin assay is available for use and highlight important information related to assay performance to users.

Furthermore, laboratories should participate in an EQA programme for Troponin that is designed and overseen by appropriately competent professionals including clinical oversight. Ideally, the distribution frequency should be at least monthly with commutable specimens that cover the whole clinical range and especially any clinical cut-offs for the assay employed. Each distribution cycle should include sufficient samples to provide evidence of reproducibility; selected distributions should include 'challenging' samples; and educational input. EQA samples should be 'blinded' to participants in relation to expected results with the samples treated as much as possible as if they were patient samples. The EQA programme should have mechanisms in place for the reporting of persistent poor performance to the appropriate regulatory/oversight body (in the UK this is the Chemical Pathology National Quality Assurance Advisory Panel) and the EQA programme should be accredited.

The following recommendations are made to improve the clinical utilisation of troponin assays and ensure that there is a more harmonised approach to the use of troponin across the UK.

1. Where possible, laboratories should provide a highly sensitive assay that is designated as Level 2 or above*.
2. Laboratories should be familiar with their troponin assay performance including Limit of detection (LOD), limit of quantitation (LOQ) and assay designation. This information should be available to all users.
3. Laboratories should report high sensitivity troponin results in ng/L.
4. Laboratories should have a protocol in place for the analysis of troponin in haemolysed samples.
5. Laboratories should verify assay imprecision at concentrations near the 99th percentile decision limit and below and provide such measurement uncertainty data to users.
6. Analytical variation across a network should be assessed and made available to users when there is more than one analyser used to measure troponin. Such data can be used to provide data on the significant of absolute incremental changes in troponin based on a reference change value.
7. Laboratories should be cautious about quoting high sensitivity troponin results as 'normal' or 'low risk' without appropriate clinical context.
8. The laboratory troponin service performance should be regularly assessed against current relevant professional key performance or key assurance indicators.
9. A 3 hour testing interval is recommended for the majority of high sensitivity troponin assays for the evaluation of a troponin change. New guidelines suggest a 1 hour interval for specified assays[5]. Information should be available to users regarding the ability to detect troponin changes from chest pain for their particular troponin assay and the minimal time required to sample for a significant change.
10. There should be continuous dialogue between laboratory professionals and clinical colleagues regarding the appropriate use of their troponin assay.
11. Laboratories should participate in an appropriate EQA programme (ideal characteristics noted above).

[*As defined by the Apple Scorecard[6]]

ACB Clinical Practice Section

[Lead author : Dr Gareth McKeeman]

22 February 2016

Table 1: Commonly used troponin assays ranked according to their sensitivity as defined by Apple Scorecard[6] and recent IFCC guidelines[3]. Manufacture quoted and evaluated 99th percentiles are shown along with assay LOD.

[Table adapted from McKeeman & Auld, 2015[1]].

Assay	Published Data / Sensitivity Designation				
	Published 99th percentile(s) M =Manufacturer E = Evaluated & LOD	Meets IFCC/NICE hs definition[12,13]		Apple Scorecard[A]	Designation
		≤ 10 % CV @ 99th percentile	Measure above LOD in > 50% healthy subjects		
Abbott hsTnI	**M:** 26 ng/L (M=34 ng/L; F=16 ng/L) **E:** 23, 27 ng/L **LOD**: 1.1-1.9 ng/L	Yes	Yes	Guideline Acceptable - Level 4	High Sensitivity
Roche TnThs	**M:** 14 ng/L **E:** 14, 15, 16 ng/L **LOD:** 5 ng/L	Yes	Yes	Guideline Acceptable - Level 2	High Sensitivity
Beckman AccuTnI+3	**M:** 40 ng/L **E:** 22, 32, 56 ng/L **LOD**: 2.5, 12 ng/L	Yes	N/A	Guideline Acceptable	High Sensitivity[B]
Siemens TnI Ultra	**M:** 40 ng/L **E:** 12 , 13, 21, 29, 40, 41, 60 ng/L **LOD:** 6 ng/L	Yes	No	Guideline Acceptable - Level 1	Sensitive
Ortho Vitros TnI ES	**M:** 34 ng/L **E:** 13, 19 ng/L **LOD**: 12 ng/L	Yes	No	Guideline Acceptable - Level 1	Sensitive
Siemens Stratus TnI	**M:** 70 ng/L **E:** 30, 40, 70 ng/L **LOD:** 30 ng/L	Yes	No	Guideline Acceptable - Level 1	Sensitive
Beckman AccuTnI	**M:** 40 ng/L **E:**, 43.8 ng/L **LOD**: 10 ng/L	No	Yes	Clinically Usable - Level 2	Non Sensitive
Abbott TnI	**M:** 28 ng/L **E:** 13 ng/L **LOD**: 9 ng/L	No	No	Clinically Usable - Level 1	Non Sensitive

[[A]Apple Scorecard Designations - **1. Acceptance Criteria:** Guideline acceptable (99th percentile CV ≤ 10%), Clinically usable (99th percentile CV > 10 to ≤ 20%), Not acceptable (99th percentile CV > 20%); **2. Designation:** Level 1 [contemporary] (< 50% measurable normal values below 99th percentile), Level 2 [first generation hs] (50 to < 75% measurable normal values below 99th percentile), Level 3 [second generation hs] (75 to < 95% measurable normal values below 99th percentile), Level 4 [third generation hs] (≥ 95% measurable normal values below 99th percentile[5]; [B] Beckmann AccuTnI+3 noted as a hs assay in the recent NICE diagnostics guidance[13]]

References

1. McKeeman GC & Auld PW. A national survey of troponin testing and recommendations for improved practice. *Ann Clin Biochem* 2015; 52: 527-42.

2. National Institute for Health and Care Excellence (NICE). Myocardial infarction (acute): early rule out using high-sensitivity troponin tests (Elecsys Troponin T high-sensitive, ARCHITECT STAT High Sensitive Troponin-I and AccuTnI+3 assays). NICE diagnostics guidance 15, www.nice.org.uk/dg15

3. International Federation of Clinical Chemistry and Laboratory Medicine – Scientific Division. Troponin assay analytical characteristics 2013. Scientific Division Documents, http://www.ifcc.org/media/245202/IFCC%20Troponin%20I%20and%20T%20%28ng_L%20units%29_%20update%20December%202013.pdf

4. Thygesen K, Alpert JS, Jaffe AS, et al. The writing group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. Third universal definition of myocardial infarction. *Eur Heart J* 2012; 33: 2551–2567.

5. Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J* doi:10.1093/eurheartj/ehv320 (Published online 11th September 2015: http://eurheartj.oxfordjournals.org/content/ehj/early/2015/09/09/eurheartj.ehv320.full.pdf

6. Apple FS. A new season for cardiac troponin assays: it's time to keep a scorecard. *Clin Chem* 2009; 55: 1303–1306.