Clinica Chimica Acta 498 (2019) 27–29

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/cca

Letter to the editor

Long-term quality control testing on a high-sensitivity cardiac troponin I assay

To the Editor,

Monitoring high-sensitivity cardiac troponin assays at concentrations below and slightly above the 99th percentile is an important laboratory recommendation [1]. Guidelines and clinical studies have provided guidance on how absolute changes in cardiac troponin concentrations or percent changes can be used to aid in early decision-making for acute myocardial infarction and in the differentiation of acute versus chronic myocardial injury [2–4]. Our laboratory program has been utilizing patient-derived quality control (QC) material for nearly a decade [5,6], with both a normal concentration QC material (i.e. below the 99th percentile concentration) and a QC material around the 99th percentile concentration cutoff being produced when our sites transitioned to a high-sensitivity cardiac troponin assay [7,8]. These QC materials not only aided in the development of the total analytic error criterion for high-sensitivity cardiac troponin < 10 ng/l [9], but also demonstrated possible limitations for using small concentration changes in this range across multiple sites [8]. More recently, data using the normal concentration QC material has confirmed that once a day measurements are sufficient for monitoring purposes with within day imprecision being superior to between day imprecision [10].

However, there are limitations to the above analyses; in that typically the data were derived from 1 QC lot only. Because long-term assessment between different analyzers and lots of QC material have not been formally assessed, in the present analyses we assessed the variation and differences in concentrations between two analyzers that have been used for the validation, implementation and the clinical reporting of Abbott Diagnostics' high-sensitivity cardiac troponin I (hs-cTnI) assay across three lots of patient-derived QC material used during 2014 to 2019. Briefly, analyzer 1 (Architect ci8200) was from the Juravinski Hospital and analyzer 2 (Architect ci16200) was from the Hamilton General Hospital, Hamilton, Ontario, Canada [8,11]. The data from the different QC lots were obtained from the following timeframes on the respective analyzers: analyzer 1: lot A normal QC date range 10/15/2014 to 3/7/2016 and 99th percentile QC date range 10/16/2014 to 3/7/2016; lot B normal QC date range 2/17/2016 to 10/8/2017 and 99th percentile QC date range 2/17/2016 to 10/8/2017; lot C normal QC date range 9/17/2017 to 5/30/2019 and 99th percentile QC date range 9/17/2017 to 5/30/2019 and analyzer 2: lot A normal QC date range 10/15/2014 to 3/7/2016 and 99th percentile QC date range 9/20/2014 to 3/7/2016; lot B normal QC date range 2/17/2016 to 10/19/2017 and 99th percentile QC date range 2/17/2016 to 10/19/2017; lot C normal QC date range 10/11/2017 to 5/30/2019 and 99th percentile QC date range 10/11/2017 to 5/30/2019. The only QC data points that were eliminated from the analyses were those points where there was a mix-up/incorrect assignment in running the QC material (e.g., the normal QC material was ordered as the 99th percentile QC material etc.), with non-parametric analyses and percent frequency polygonal histograms used to assess and visualize differences between analyzers (Analyse-it and StatsDirect software).

For lot A there were 20 and 7 incorrect assigned QCs, for lot B there were 7 and 6 incorrect assigned QCs and for lot C there were 6 and 1 incorrect assigned QCs for analyzers 1 and 2, respectively, leaving a total of 4688 results for the normal QC material and 4720 results for the 99th percentile QC material. For the normal QC material, analyzer 1 (lot A n = 791 | median = 4.2 ng/l, lot B n = 907 | median = 4.0 ng/l, lot C n = 813 | median = 5.1 ng/l) yielded lower concentrations as compared to analyzer 2 (lot A n = 596 | median = 4.9 ng/l, lot B n = 750 | median = 4.5 ng/l, lot C n = 831 | median = 5.3 ng/l; $p < .0001$ for each comparison via Mann-Whitney test) (Fig. 1a). This minor difference of ≤1 ng/l between analyzers was also evident with the 99th percentile QC material with analyzer 1 yielding slightly lower results as compared to analyzer 2 (Fig. 1b). The maximum interquartile range (25th to 75th) and central 95th percentile range (2.5th to 97.5th) for the normal QC material was ≤1.0 ng/l and ≤2.6 ng/l, respectively, and for the 99th percentile QC material was ≤3.5 ng/l and ≤11.2 ng/l, respectively over these 3 lots.

Long-term testing using patient-derived QC material demonstrated that differences of approximately 1 ng/l between analyzers using the same reagent lots may be evident. This may be particular important for sites using an early rule-out protocol for myocardial infarction where concentrations < 10 ng/l and minor absolute changes between serial sampling have been proposed [2,4]. By measuring a low QC material, laboratories may help physicians in selecting the most appropriate

https://doi.org/10.1016/j.cca.2019.08.006
Received 16 July 2019; Received in revised form 11 August 2019; Accepted 12 August 2019
Available online 13 August 2019
0009-8981/

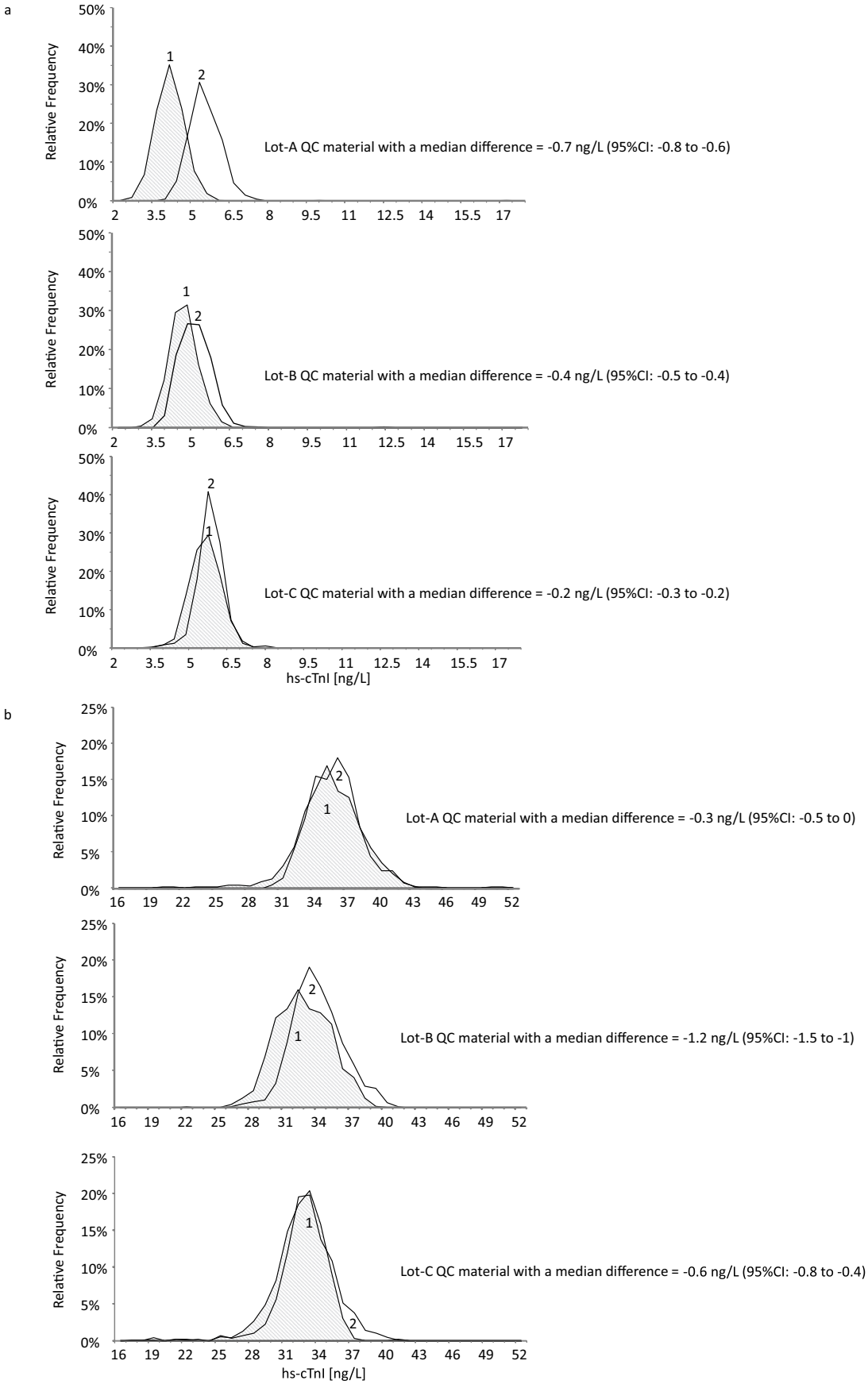

Fig. 1. Polygonal histogram plots: a) comparing three different lots (A,B,C) of QC material < 10 ng/l (i.e., normal QC material) between an ARCHITECT ci8200 (analyzer 1) and an ARCHITECT ci16200 (analyzer 2) and b) 3 different lots (A,B,C) of QC material > 30 ng/l (i.e., 99th percentile QC material) between an ARCHITECT ci8200 (analyzer 1) and an ARCHITECT ci16200 (analyzer 2).

change criteria for the application of high-sensitivity cardiac troponin testing in patients with possible acute coronary syndrome [4].

Declaration of Competing Interest

PK has received grants/ reagents/consultant/advisor/ honoraria from the laboratory diagnostic industry, specifically from Abbott Laboratories, Beckman Coulter, Ortho Clinical Diagnostics, Randox Laboratories, Roche Diagnostics and Siemens Healthcare Diagnostics. McMaster University has filed patents with PK listed as an inventor in the acute cardiovascular biomarker field.

References

[1] A.H.B. Wu, R.H. Christenson, D.N. Greene, A.S. Jaffe, P.A. Kavsak, J. Ordonez-Llanos, et al., Clinical laboratory practice recommendations for the use of cardiac troponin in acute coronary syndrome: expert opinion from the academy of the American Association for Clinical Chemistry and the task force on clinical applications of cardiac bio-markers of the International Federation of Clinical Chemistry and Laboratory Medicine, Clin. Chem. 64 (2018) 645–655.

[2] M. Roffi, C. Patrono, J.P. Collet, C. Mueller, M. Valgimigli, F. Andreotti, et al., ESC scientific document group. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC), Eur. Heart J. 37 (2016) 267–315.

[3] K. Thygesen, J.S. Alpert, A.S. Jaffe, B.R. Chaitman, J.J. Bax, D.A. Morrow, H.D. White, ESC Scientific Document Group, Fourth universal definition of myocardial infarction (2018), Eur. Heart J. 40 (2019) 237–269.

[4] J.T. Neumann, R. Twerenbold, F. Ojeda, N.A. Sörensen, A.R. Chapman, A.S.V. Shah, et al., Application of high-sensitivity troponin in suspected myocardial infarction, N. Engl. J. Med. 380 (2019) 2529–2540.

[5] P.A. Kavsak, Quality control material testing and the importance of "treating it like a patient's sample", Clin. Biochem. 47 (2014) 147–149.

[6] P.A. Kavsak, N. Caruso, J. Beattie, L. Clark, Centrifugation–an important pre-analytical factor for the Abbott Architect high-sensitivity cardiac troponin I assay, Clin. Chim. Acta 436 (2014) 273–275.

[7] P.A. Kavsak, J. Beattie, R. Pickersgill, L. Ford, N. Caruso, L. Clark, A practical approach for the validation and clinical implementation of a high-sensitivity cardiac troponin I assay across a North American city, Pract. Lab. Med. 1 (2015) 28–34.

[8] P.A. Kavsak, A.C. Don-Wauchope, S.A. Hill, A. Worster, Acceptable analytical variation may exceed high-sensitivity cardiac troponin I cutoffs in early rule-out and rule-in acute myocardial infarction algorithms, Clin. Chem. 62 (2016) 887–889.

[9] P.A. Kavsak, A.S. Jaffe, D.N. Greene, R.H. Christenson, F.S. Apple, A.H.B. Wu, Total analytic error for low cardiac troponin concentrations ($\leq$10 ng/l) by use of a high-sensitivity cardiac troponin assay, Clin. Chem. 63 (2017) 1043–1045.

[10] P.A. Kavsak, E. Millar, G. McLay, L. Clark, A.S. Jaffe, Between-day versus within-day imprecision using the Abbott high-sensitivity cardiac troponin I assay at concentrations around 5 ng/l, Clin. Chim. Acta 489 (2019) 58–60.

[11] P.A. Kavsak, A. McRae, S. Vatanpour, O.Z. Ismail, A. Worster, A multicenter assessment of the sensitivity and specificity for a single high-sensitivity cardiac troponin test at emergency department presentation for hospital admission, J. Appl. Lab. Med. (2019), https://doi.org/10.1373/jalm.2019.029512 Published July 2019.

Peter A. Kavsak[a,b,*], Kelsey MacEachern[a], Eleonora Petryayeva[a], Lorna Clark[b]

[a] *McMaster University, Hamilton, Ontario, Canada*

[b] *Hamilton Health Sciences, Hamilton, Ontario, Canada*

E-mail address: kavsakp@mcmaster.ca (P.A. Kavsak).

* Corresponding author at: Juravinski Hospital and Cancer Centre (Core Lab Section), 711 Concession Street, Hamilton, ON, Canada.