Quality Improvement

High-Sensitivity Cardiac Troponin I vs a Clinical Chemistry Score for Predicting All-Cause Mortality in an Emergency Department Population

Peter A. Kavsak, PhD, Joshua O. Cerasuolo, MSc, Dennis T. Ko, MD, MSc, Jinhui Ma, PhD, Jonathan Sherbino, MD, MEd, Shawn E. Mondoux, MD, MSc, Richard Perez, MSc, Hsien Seow, PhD, and Andrew Worster, MD, MSc

Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada
ICES McMaster, Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada
ICES, Toronto, Ontario, Canada
Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, Ontario, Canada
Division of Emergency Medicine, McMaster University, Hamilton, Ontario, Canada

ABSTRACT

Background: For patients investigated for suspected acute coronary syndrome, there is uncertainty if a single measurement of high-sensitivity cardiac troponin I (hs-cTnI) at emergency department (ED) presentation can identify patients at both low and high risk for mortality.

Methods: We included consecutive adult patients in the ED who had a Clinical Chemistry Score (CCS) taken at presentation (ie, combination of glucose, creatinine for estimated glomerular filtration rate determination, and hs-cTnI assay) in a Canadian city between 2012 and 2013. Outcomes were 3-month, 1-year, and 5-year all-cause mortality using the provincial death registry. Mortality rates and test performance (eg, sensitivity and specificity) with 95% confidence intervals (CIs) were obtained for the CCS or hs-cTnI assay alone using established cutoffs for these tests.

Results: Our cohort included 5974 patients with a 1-year mortality rate of 17.2% (95% CI, 16.2-18.3). A CCS ≥ 1 yielded a sensitivity of ≥ 5 ng/L at emergency department (ED) presentation may be suitable to rule out myocardial infarction (MI) and identify a low-risk group of patients who may avoid unnecessary hospital admissions. These findings were generated with an Abbott Laboratories (Abbott Park, IL) hs-cTnI assay, and recent publications demonstrating a 5 ng/L cutoff might be suitable for one of Siemens Healthcare Diagnostics (Munich, Germany) hs-cTnI assays, suggesting an overall low concentration cutoff of 5 ng/L may be applicable to more than 1 hs-cTnI assay. Accordingly, this leads to the concept of a single rule-out cutoff when using hs-cTnI assays, which has been published by the European Society of Cardiology guidelines and most recently discussed in the Fourth Universal
99.2% (95% Cl, 98.4-99.6) compared with the hs-cTnI ≥ 5 ng/L cutoff sensitivity of 88.4% (95% Cl, 86.3-90.3), with the mortality rate being significantly lower for patients with CCS < 1 (2.0%; 95% CI, 0.9-4.0) vs patients with hs-cTnI < 5 ng/L (5.0%; 95% CI, 4.2-6.0) at 1 year (P = 0.01). A CCS of 5 also yielded a higher specificity (88.6%; 95% CI, 87.5-89.3) compared with hs-cTnI > 26 ng/L (83.9%; 95% CI, 82.9-84.9), with no difference in mortality rates (37.4% vs 36.3%; P = 0.66). This trend was consistent at 3-month and 5-year mortality.

**Conclusion:** For patients in the ED with a potential cardiac issue, using the CCS cutoffs can better identify patients at low and high risk for mortality than using published cutoffs for hs-cTnI alone.

Definition of MI, which provided the following balanced statement: “Some studies indicate that the single sample approach provides optimal sensitivity and negative predictive accuracy in patients otherwise at low risk and those with a normal electrocardiogram. However, one concern about short rule-out periods is that the precision of the assays may not permit small differences to be distinguished.”

In this regard, we have provided evidence of analytical issues that affect interpretation around and below 5 ng/L. Laboratory recommendations on appropriate monitoring of the hs-cTnI assays will help mitigate some of these issues; however, what has not been evaluated thoroughly is the impact of a low hs-cTnI result for risk stratification in a general ED population in North America. To address this gap, our goal was to compare Abbott hs-cTnI published cutoffs (eg, 5 ng/L and the overall 99th percentile of 26 ng/L) alone vs a simple laboratory algorithm (ie, Clinical Chemistry Score [CCS]) at presentation in a general ED population to determine low- and high-risk patients for subsequent all-cause death.

**Methods**

**Study design and population**

After research ethics board approval was obtained, from November 28, 2012, to February 28, 2013, all ethylenediaminetetraacetic acid blood samples from the ED at 3 adult hospitals in Hamilton, Ontario, Canada, that had an order for cardiac troponin had both the standard cardiac troponin I (cTnI) and hs-cTnI tests performed on the Abbott ARCHITECT instruments, with only the cTnI results being clinically reported. Patients included in this study were adult patients who were investigated for possible ACS as demonstrated by emergency staff ordering the “ED cardiac presentation panel,” which included troponin I, glucose, creatinine, and other laboratory tests at the Hamilton General Hospital, St. Joseph’s Healthcare Hamilton, and Juravinski Hospital (note, troponin I used for clinical decision making during this timeframe was the Abbott Laboratories contemporary sensitive cTnI assay). The Abbott hs-cTnI concentrations (limit of detection for the assay being 1 ng/L) were obtained in real-time and on the same instruments in the hospitals with the hs-cTnI results not reported to the treating physician.

The flow diagram in Supplemental Figure 1 shows the cohort selection. Briefly, only the presentation hs-cTnI result on the first ED encounter on 6641 patients who presented to the ED was used with further selection dependent on also having a glucose and creatinine result (ie, the “ED cardiac presentation panel,” with creatinine for an estimated glomerular filtration rate [eGFR] as calculated by the CKD-Epidemiology Collaboration equation). Patients were also excluded if they were not Ontario residents, if age and sex were missing in the registered persons database (n = 625 individuals excluded), or if they were not Ontario Health Insurance Plan eligible at baseline (n = 42). The final cohort consisted of 5974 individuals with the treating emergency physicians blinded to the hs-cTnI in addition to eGFR results calculated by the CKD-Epidemiology Collaboration equation.

**High-sensitivity cardiac troponin I cutoffs and CCS**

The cutoffs used for the Abbott Laboratories hs-cTnI assay were < 5 ng/L, 5 to 26 ng/L, and > 26 ng/L, as previously used in patients with suspected ACS. The simple laboratory algorithm or CCS has been published in both a multicenter Canadian study and an international study. The scores are generated as follows: glucose < 5.6 mmol/L = 0 points or ≥ 5.6 mmol/L = 1 point; eGFR ≥ 90 mL/min/1.73 m² = 0 points or < 90 mL/min/1.73 m² = 1 point; hs-cTnI < 4 ng/L = 0 points or 4-14 ng/L = 1 point or 15-30 ng/L = 2 points or > 30 ng/L = 3 points. The CCS was calculated by the sum of the points from glucose,
| Characteristic                                      | 0     | 1     | 2     | 3     | 4     | 5     | P value | hs-cTnI concentration |
|---------------------------------------------------|-------|-------|-------|-------|-------|-------|---------|-----------------------|
|                                                   | N = 399 | N = 923 | N = 1405 | N = 1486 | N = 853 | N = 908 |         | N = 2374 | N = 2324 | N = 1276 | P value |
| Age (y) Median (IQR)                              | 46 (36-53) | 53 (44-63) | 66 (56-78) | 77 (67-84) | 79 (67-86) | 80 (69-87) | < 0.001 | 58 (47-70) | 76 (65-84) | 78 (66-86) | < 0.001 |
| Sex, female N (%)                                 | 210 (52.6%) | 434 (47.0%) | 802 (57.1%) | 792 (53.3%) | 373 (43.7%) | 414 (45.6%) | < 0.001 | 1324 (55.8%) | 1154 (49.7%) | 547 (42.9%) | < 0.001 |
| Risk factors                                       |       |       |       |       |       |       |         |         |         |         |         |
| Arrhythmia N (%)                                  | 12 (3.0%) | 49 (5.3%) | 164 (11.7%) | 295 (19.9%) | 236 (27.7%) | 231 (25.4%) | < 0.001 | 157 (6.6%) | 509 (21.9%) | 321 (25.2%) | < 0.001 |
| Congestive heart failure N (%)                    | 11 (2.8%) | 49 (5.3%) | 177 (12.6%) | 381 (25.6%) | 329 (38.6%) | 343 (37.8%) | < 0.001 | 172 (7.2%) | 634 (27.3%) | 484 (37.9%) | < 0.001 |
| Diabetes N (%)                                    | 26 (6.5%) | 158 (17.1%) | 390 (27.8%) | 612 (41.2%) | 342 (40.1%) | 433 (47.7%) | < 0.001 | 526 (22.2%) | 906 (39.0%) | 529 (41.5%) | < 0.001 |
| Hypertension N (%)                                | 110 (27.6%) | 380 (41.2%) | 931 (66.3%) | 1181 (79.5%) | 691 (81.0%) | 752 (82.8%) | < 0.001 | 1181 (49.7%) | 1840 (79.2%) | 1024 (80.3%) | < 0.001 |
| MI N (%)                                          | 15 (3.8%) | 44 (4.8%) | 105 (7.5%) | 169 (11.4%) | 157 (18.4%) | 184 (20.3%) | < 0.001 | 121 (5.1%) | 318 (13.7%) | 235 (18.4%) | < 0.001 |
| Renal disease N (%)                               | 0 (0.0%) | 6 (0.7%) | 26 (1.9%) | 61 (4.1%) | 88 (10.3%) | 104 (11.5%) | < 0.001 | 15 (0.6%) | 124 (5.3%) | 146 (11.4%) | < 0.001 |
| Stroke N (%)                                      | ≤ 5  | 15 (1.6%) | 23 (1.6%) | 51 (3.4%) | 56 (6.2%) | < 0.001 | 35 (1.5%) | 87 (3.7%) | 64 (5.0%) | < 0.001 |
| Angina N (%)                                      | 12 (3.0%) | 27 (2.9%) | 79 (5.6%) | 118 (7.9%) | 79 (8.7%) | < 0.001 | 97 (4.1%) | 172 (7.4%) | 105 (8.2%) | < 0.001 |
| Percutaneous coronary intervention N (%)          | 7 (1.8%) | 31 (3.4%) | 68 (4.8%) | 78 (5.2%) | 56 (6.6%) | 66 (7.3%) | < 0.001 | 72 (3.0%) | 148 (6.4%) | 86 (6.7%) | < 0.001 |
| Coronary artery bypass grafting N (%)             | ≤ 5  | 7 (0.8%) | 29 (2.1%) | 41 (2.8%) | 40 (4.7%) | 29 (3.2%) | < 0.001 | 25 (1.1%) | 78 (3.4%) | 44 (3.4%) | < 0.001 |
| Serum creatinine, mmol/L                          | 4.98 ± 0.42 | 6.19 ± 2.17 | 7.03 ± 3.35 | 8.42 ± 5.60 | 7.92 ± 4.48 | 9.45 ± 4.82 | < 0.001 | 6.84 ± 3.34 | 7.95 ± 5.03 | 8.41 ± 4.55 | < 0.001 |
| Glucose, mmol/L                                   | 2 (1-2) | 2 (1-3) | 4 (2-6) | 8 (6-12) | 24 (18-42) | 67 (39-179) | < 0.001 | 2 (1-4) | 10 (7-15) | 62 (38-170) | < 0.001 |
| hs-cTnI, ng/L                                      | 94 (56-110) | 77 (63-87) | 63 (46-78) | 54 (34-76) | 46 (27-66) | < 0.001 | 86 (73-98) | 63 (44-81) | 49 (29-74) | < 0.001 |
| eGFR, mL/min/1.73 m²                               | 102 (96-110) | 77 (63-87) | 63 (46-78) | 54 (34-76) | 46 (27-66) | < 0.001 | 86 (73-98) | 63 (44-81) | 49 (29-74) | < 0.001 |
| Outpatient cardiologist follow-up: 30 d after ED visit | 25 (6.3%) | 71 (7.7%) | 133 (9.5%) | 192 (12.9%) | 152 (15.3%) | 155 (17.1%) | < 0.001 | 188 (7.9%) | 287 (12.3%) | 233 (18.3%) | < 0.001 |
| Outpatient GP/FP follow-up: 30 d after ED visit   | 190 (47.0%) | 405 (43.9%) | 673 (47.9%) | 699 (47.0%) | 380 (44.5%) | 403 (44.4%) | 1120 (47.2%) | 1094 (47.1%) | 536 (42.0%) |         |
| No outpatient follow-up: 30 d after ED visit      | 184 (46.1%) | 447 (48.4%) | 599 (42.6%) | 595 (40.0%) | 341 (40.0%) | 350 (38.5%) | 1066 (44.9%) | 943 (40.6%) | 507 (39.7%) |         |
| All-cause mortality, 90 d N (%)                    | ≤ 5  | 31 (3.4%) | 68 (4.8%) | 137 (9.2%) | 145 (17.0%) | 217 (23.9%) | < 0.001 | 65 (2.7%) | 254 (10.9%) | 282 (22.1%) | < 0.001 |
| All-cause mortality, 1 y  N (%)                    | 8 (2.0%) | 47 (5.1%) | 134 (9.5%) | 253 (17.0%) | 248 (29.1%) | 340 (37.4%) | < 0.001 | 119 (5.0%) | 448 (19.3%) | 463 (36.3%) | < 0.001 |
| All-cause mortality, 5 y N (%)                     | 32 (8.0%) | 137 (14.8%) | 335 (23.8%) | 657 (44.2%) | 526 (41.7%) | 612 (67.4%) | < 0.001 | 350 (14.7%) | 1113 (47.9%) | 836 (65.5%) | < 0.001 |

Medical history calculated using 5-y look-back.

CCS, Clinical Chemistry Score; ED, emergency department; eGFR, estimated glomerular filtration rate; FP, family practice; GP, general practice; hs-cTnI, high-sensitivity cardiac troponin I; IQR, interquartile range; MI, myocardial infarction.

* Suppressed for privacy reasons.
eGFR, and hs-cTnI. For example, a CCS < 1 (or CCS = 0) would be obtained if glucose < 5.6 mmol/L, eGFR ≥ 90 mL/min/1.73 m², and hs-cTnI < 4 ng/L, whereas a CCS = 5 would be obtained if glucose ≥ 5.6 mmol/L, eGFR < 90 mL/min/1.73 m², and hs-cTnI > 30 ng/L from the ED presentation blood work.

Outcomes and statistical analysis

We evaluated all-cause death at 3 months, 1 year, and 5 years after the presentation blood work. We compared baseline characteristics (demographic and clinical) with a 5-year look-back across the following categorizations: (1) hs-cTnI (<5 ng/L vs 5-26 ng/L vs >26 ng/L) and (2) CCS (all individual values on 0-5 ordinal scale). To assess test performance, we calculated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) (with 95% confidence intervals [CIs]). These metrics were calculated to assess the prognostic performance of hs-cTnI alone vs in combination with other laboratory tests to rule out those at low risk of experiencing the outcome and rule in those at high risk. We compared hs-cTnI ≥ 5 ng/L vs CCS ≥ 1 and hs-cTnI ≥ 5 ng/L vs CCS ≥ 2 to assess if sensitivity ≥ 99% or NPV ≥ 99.5%, 2 metrics that have been selected as necessities for a test to rule out. In contrast, for high risk, we compared hs-cTnI > 26 ng/L (the overall 99th percentile) vs CCS = 5 and hs-cTnI > 26 ng/L vs CCS ≥ 4 to assess if specificity ≥ 90% or PPV ≥ 75% could be attained. We also compared the rate of death between the CCS of < 1 or < 2 with that of hs-cTnI < 5 ng/L as surveys of Canadian, American, and Australasian ED physicians suggest a miss rate not exceed 2%. Kaplan–Meier survival curves for all-cause mortality over 5 years were also constructed for both the CCS categories and hs-cTnI ranges with censoring at the end of the 5-year observation window (P value by log-rank). Analyses were performed using SAS 9.1.3 software (SAS Institute Inc., Cary, NC) and MedCalc Statistical Software version 19.1.6 (MedCalc Software Ltd., Ostend, Belgium).

Results

The median age (interquartile range) for the study population was 70 years (56-82), 50.6% were female, and approximately one-third of the population (32.8%) had diabetes. The prevalence of cardiovascular disease and risk factors increased with the higher hs-cTnI concentrations and the higher CCS (Table 1), with survival curves also displaying separation of low- and high-risk groups per hs-cTnI ranges or the CCS over 5 years (Fig. 1). Overall, 40.8% of the population was discharged home from the ED with 79.4% (95% CI, 70.9-88.7) of patients with a CCS < 1 discharged compared with 64.4% (95% CI, 61.2-67.7) of patients with an hs-cTnI < 5 ng/L (P < 0.01). The mortality rate was ≤ 2.0% in patients (n = 399 or 6.7%...
of the total population) with a CCS < 1 (ie, CCS = 0) at both 3 months and 1 year compared with 2.7% and 5.0% in patients (n = 2374 or 39.7% of the total population) with hs-cTnI < 5 ng/L at these timeframes, respectively (Table 1). At 1 year, the difference in mortality rates was significant (CCS < 1 mortality was 2.0%; 95% CI, 0.9-4.0 vs mortality in patients with hs-cTnI < 5 ng/L of 5.0%; 95% CI, 4.2-6.0; P = 0.01). By applying the CCS cutoff of ≥ 1, the sensitivity for mortality was 99.5% (95% CI, 98.5-99.9) at 3 months, 99.2% (95% CI, 98.4-99.6) at 1 year, and 98.6% (95% CI, 98.0-99.0) at 5 years (Table 2). Patients with a CCS < 2 had outcome rates similar to those with only hs-cTnI < 5 ng/L; however, the sensitivities for a CCS ≥ 2 were higher (3-month sensitivity = 94.3% to 5-year sensitivity = 92.6%) than hs-cTnI ≥ 5 ng/L (3-month sensitivity = 89.1% to 5-year sensitivity = 84.7%) (Table 2). The highest observed NPV (99.2%; 95% CI, 97.8-99.8) was at 3 months when using the CCS cutoff ≥ 1. At 5 years, only the CCS of 5 yielded a specificity ≥ 90% (91.9%; 95% CI, 91.0-92.8) for all-cause mortality, with no PPVs > 75% for the CCS or hs-cTnI above the 99th percentile cutoffs.

**Discussion**

In an ED population who were investigated for ACS, were clinically managed with a contemporary cTnI assay, and had hs-cTnI results that were blinded to the treating physicians, our findings indicate that an hs-cTnI cutoff of ≥ 5 ng/L at ED presentation would not be sufficiently safe to rule out mortality because the sensitivity estimates were below 90%. Only a CCS ≥ 1 would yield diagnostic test estimates that could be considered safe for identifying low-risk patients because the sensitivity was > 99% and the event rate was ≤ 2% (for those with a CCS < 1) for up to 1 year after patient presentation. For identifying high-risk patients, only the CCS of 5 yielded a specificity > 90% for mortality, but this was evident at only 5 years. These data extend previous findings on the CCS to a general ED population, who are more representative of patients who have cardiac troponin ordered in the emergency setting. Moreover, these findings further support data that patients with hs-cTnI concentrations below the 99th percentile (or “normal levels”) early after ED presentation may still be at a higher risk for an adverse outcome over both the short and long term. Additional laboratory and clinical variables may further aid in risk stratification as demonstrated by the simple CCS in this setting.

**Limitations**

Our study includes some important limitations. First, we were unable to capture the time of pain onset and thus cannot differentiate early pain onset from late pain onset because hs-cTnI testing for rule-out is not recommended in the population with early chest pain onset. Second, we only included all-cause death, a hard end point, whereas others have also included MI and other cardiovascular outcomes. Third, the study population was derived from 3 hospitals from the same city. Further research could validate the results from other geographic locations. Fourth, the laboratory ordering practice of including glucose and creatinine with cardiac troponin (ie, the “ED cardiac presentation panel”) may differ at different hospitals. To our understanding, there are no

| Parameter | Time | Sensitivity | Specificity | PPV | NPV |
|-----------|------|-------------|-------------|-----|-----|
|            |      | 3 mo        | 5 y         | 5 y | 5 y |
| Rule-out   |      |             |             |     |     |
| CCS ≥ 1   |     | 0.988 (0.978-0.999) | 0.952 (0.938-0.967) | 0.739 (0.727-0.751) | 0.885 (0.874-0.896) |
|            |      | 0.986 (0.976-0.997) | 0.950 (0.937-0.966) | 0.736 (0.724-0.750) | 0.883 (0.872-0.892) |
| Rule-in    |      |             |             |     |     |
| CCS ≥ 2   |     | 0.980 (0.969-0.991) | 0.943 (0.930-0.957) | 0.729 (0.717-0.742) | 0.878 (0.867-0.889) |
|            |      | 0.978 (0.967-0.988) | 0.941 (0.928-0.955) | 0.727 (0.714-0.740) | 0.876 (0.865-0.885) |

Table 2. Prognostic performance of CCS ≥ 2 for rule-out and CCS ≥ 4 for rule-in vs hs-cTnI alone (≥ 5 ng/L for rule-out or > 26 ng/L for rule-in) for all-cause mortality. Bold text represent estimates that are > 99% sensitivity or ≥ 90% specificity.
recommendations on what laboratory tests besides cardiac troponin should be ordered when considering myocardial injury. Fifth, no adjustments were made for subsequent MI post-ED assessment, other cardiovascular disease risk factors, or medication use during the 5-year period for long-term mortality because there may be other important variables that have contributed to long-term mortality. Sixth, the prevalence of patients with a CCS < 1 (~7%) was approximately 6-fold lower compared with patients with an hs-cTnI < 5 ng/L (~40%). Clinicians may want to use additional screening tools, besides laboratory tests, to identify patients at low risk for an adverse outcome.

Conclusions

In patients in the ED being investigated for suspected ACS, using a simple CCS at presentation improves the ability to identify both low-risk and high-risk patients for short- and long-term mortality.

Funding Sources

This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care. Contents are based on data provided by CIHI. Analyses, opinions, and statements expressed are those of the authors and not necessarily those of CIHI; no endorsement is intended or should be inferred. The authors thank IMS Brogan Inc., for use of their Drug Information Database. This study was supported by a Canadian Institutes of Health Research grant (PK, Funding Reference #155964) with past financial and reagent support by Abbott Laboratories. The funding organizations had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or final approval of the manuscript.

Disclosures

Dr Kavsak has received grants/reagents/consultant/advisor/honoraria from Abbott Laboratories, Abbott Point of Care, Beckman Coulter, Ortho Clinical Diagnostics, Randox Laboratories, Roche Diagnostics, and Siemens Healthcare Diagnostics. McMaster University has filed patents with Drs Kavsak and Worster listed as an inventor in the acute diagnostics. McMaster University has honoraria from Abbott Laboratories, Abbott Point of Care, Beckman Coulter, Ortho Clinical Diagnostics, Randox Laboratories, Roche Diagnostics, and Siemens Healthcare Diagnostics. McMaster University has filed patents with Drs Kavsak and Worster listed as an inventor in the acute cardiovascular biomarker field; in particular, a patent has been filed on aspects related to the data presented in this study.

References

1. Shah AS, Anand A, Sandoval Y, Lee KK, et al. High-sensitivity cardiac troponin I at presentation in patients with suspected acute coronary syndrome: a cohort study. Lancet 2015;386:2481-8.
2. Chapman AR, Lee KK, McAllister DA, et al. Association of high-sensitivity cardiac troponin I concentration with cardiac outcomes in patients with suspected acute coronary syndrome. JAMA 2017;318:1913-24.
3. Bulaga A, Lee KK, Stewart S, et al. High-sensitivity troponin and the application of risk stratification thresholds in patients with suspected acute coronary syndrome. Circulation 2019;140:1557-68.
4. Chapman AR, Fujisawa T, Lee KK, et al. Novel high-sensitivity cardiac troponin I assay in patients with suspected acute coronary syndrome. Heart 2019;105:616-22.
5. Sandoval Y, Nowak R, deFilippis CR, et al. Myocardial infarction risk stratification with a single measurement of high-sensitivity troponin I. J Am Coll Cardiol 2019;74:271-82.
6. Rofigi M, Patrone C, Collet JP, et al. 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 2016;37:267-315.
7. Thygesen K, Alpert JS, Jaffe AS, et al. ESC Scientific Document Group. Fourth universal definition of myocardial infarction (2018). Eur Heart J 2019;40:2567-60.
8. Kavsak PA, Clark L, Jaffe AS. Effect of repeat measurements of high-sensitivity cardiac troponin on the same sample using the European Society of Cardiology 0-hour/1-hour or 2-hour algorithms for early rule-out and rule-in for myocardial infarction. Clin Chem 2017;63:1163-5.
9. Kavsak PA, Worster A, Oliver R, et al. Variability between reagent lots for high-sensitivity cardiac troponin I may affect performance of early rule-out strategies. Can J Cardiol 2018;34:209.e5-6.
10. Kavsak PA. External quality assessment testing near the limit of detection for high-sensitivity cardiac troponin assays. Clin Chem 2018;64:1402-4.
11. Kavsak PA, Ainsworth C, Clark L, Devereaux PJ, Worster A. Four different high-sensitivity cardiac troponin assays with important analytical performance differences. Can J Cardiol 2019;35:796.e17-8.
12. Kavsak PA, Petravaya E, Clark L. Analytical variation and Abbott diagnostics high-sensitivity cardiac troponin I risk categories in asymptomatic individuals. Can J Cardiol 2019;35:1605.e7-8.
13. Wu AHB, Christenson RH, Greene DN, 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 2018;64:645-55.
14. Kavsak PA, Neumann JT, Cullen L, et al. Clinical chemistry score versus high-sensitivity cardiac troponin I and T tests alone to identify patients at low or high risk for myocardial infarction or death at presentation to the emergency department. CMAJ 2018;190:E974-84.
15. Collinson PO, Saengker AK, Apple FS, IFCC C-CB. High sensitivity, contemporary and point-of-care cardiac troponin assays: educational aids developed by the IFCC Committee on Clinical Application of Cardiac Bio-Markers. Clin Chem Lab Med 2019;57:623-32.
16. Kavsak PA, Shortt C, Pond G, Worster A. High-sensitivity cardiac troponin I for predicting death in a female emergency department population. Clin Chem 2014;60:271-3.
17. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12.
18. Kavsak PA, McRae A, Vatanpour S, Ismail OZ, Worster A. 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;4:170-9.
19. Kavsak PA, Wang X, Ko DT, MacRae AR, Jaffe AS. Short- and long-term risk stratification using a next-generation, high-sensitivity research
cardiac troponin I (hs-cTnI) assay in an emergency department chest pain population. Clin Chem 2009;55:1809-15.

20. Than MP, Aldous SJ, Troughton RW, et al. Detectable high-sensitivity cardiac troponin within the population reference interval conveys high 5-year cardiovascular risk: an observational study. Clin Chem 2018;64:1044-53.

21. Lau G, Koh M, Kavsak PA, et al. Clinical outcomes for chest pain patients discharged home from emergency departments using high-sensitivity versus conventional cardiac troponin assays. Am Heart J 2020;221:84-94.

22. Than MP, Pickering JW, Sandoval Y, et al. Machine learning to predict the likelihood of acute myocardial infarction. Circulation 2019 Aug 16 [Epub ahead of print].

23. McRae AD, Innes G, Graham M, et al. Comparative evaluation of 2-hour rapid diagnostic algorithms for acute myocardial infarction using high-sensitivity cardiac troponin T. Can J Cardiol 2017;33:1006-12.

24. Neumann JT, Twerenbold R, Ojeda F, et al. Application of high-sensitivity troponin in suspected myocardial infarction. N Engl J Med 2019;380:2529-40.

Supplementary Material

To access the supplementary material accompanying this article, visit CJC Open at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2020.03.004.