Point of Care Troponin Testing in Patients with Symptoms Suggestive of Acute Coronary Syndrome: Recommendations Report

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## ABBREVIATIONS

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<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>HTERP</td>
<td>Health Technology Expert Review Panel</td>
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<td>POC</td>
<td>Point of care</td>
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<tr>
<td>cTn</td>
<td>Cardiac troponin</td>
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<td>ACS</td>
<td>Acute coronary syndrome</td>
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<td>AMI</td>
<td>Acute myocardial infarction</td>
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RECOMMENDATIONS IN BRIEF

Cardiac troponin I or T levels are recommended to be assessed patients presenting with symptoms of acute coronary syndrome (ACS).¹,² Cardiac troponins are sensitive for the detection of myocardial necrosis but may also be elevated in other conditions.{AHA} and therefore clinical assessment and electrocardiogram (ECG) findings are also required to diagnose myocardial infarction.¹ ACS includes ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina.² Since NSTEMI does not exhibit pathognomonic changes on ECG, measurement of cardiac troponin is important for diagnosis.

Troponin is typically measured by central laboratories; however, central laboratories are not always available, particularly in rural or remote settings. POC cTn testing therefore has the potential to improve patient care in these settings, reducing unnecessary and often expensive transfers to hospitals, and allowing patients to receive care in their community.

To assist decision makers considering the implementation of POC troponin testing, CADTH conducted a health technology assessment (HTA) on the clinical utility, diagnostic accuracy, and cost-effectiveness of POC troponin testing in different settings. Settings with access to a central laboratory, such as an emergency department, and settings with no access to a central laboratory, such as rural and remote hospitals and nursing stations, were considered.

Technology

Central laboratories are not always on-site, nor available for use 24 hours a day, seven days a week. Point-of-care (POC) testing is a care model that moves the analysis to the patient and therefore allows for testing without access to a central laboratory. POC cTn tests offer short turnaround time for biomarker detection, typically providing results within 10 to 20 minutes.³ In a central laboratory, the recommended turnaround time for troponin is one hour. POC cTn testing has been used with the goal to expedite patient care in hospital emergency departments, with the hope to improve patient flow, reduce congestion and speed up therapeutic decisions regarding hospital admission and discharge for patients presenting with ACS. It has also been used in various settings where central laboratory testing is not available, such as by paramedics
in land or air ambulance, and health personnel in rural or remote medical clinics, with the hope of speeding up therapeutic decisions around patient transfers, and decreasing the number of unnecessary patient transfers to larger hospitals for further assessment and management. Ultimately, these outcomes may result in cost reductions from fewer unnecessary hospital admissions and laboratory costs.4

There are several POC troponin devices available in Canada, produced by various manufacturers that test for one or both types of cardiac troponin: I and T. POC devices can be handheld devices, or desktop devices and some measure an array of biomarkers, including troponin.

**METHODS**

CADTH conducted an HTA on the clinical and cost-effectiveness of POC troponin testing in patients with symptoms suggestive of acute coronary syndrome.{add ref when published} HTERP developed recommendations on the use of POC troponin testing based on the evidence presented in the HTA report. HTERP members reviewed the evidence, discussed all elements of the HTERP deliberative framework, [https://www.cadth.ca/sites/default/files/pdf/hterp/HTERP_DFW_e.pdf](https://www.cadth.ca/sites/default/files/pdf/hterp/HTERP_DFW_e.pdf) and developed a consensus based recommendation through discussion and deliberation. Additional information on the HTERP process are found on the HTERP page of the CADTH website: [https://www.cadth.ca/collaboration-and-outreach/advisory-bodies/health-technology-expert-review-panel](https://www.cadth.ca/collaboration-and-outreach/advisory-bodies/health-technology-expert-review-panel)

**DETAILED RECOMMENDATIONS**

The objective of these recommendations is to provide advice for Canadian health care decision makers about the adoption of POC troponin testing. These recommendations are relevant for all adults with symptoms of acute coronary syndrome. Immediate access to a central laboratory is defined as the ability to obtain results in less than one hour, and it typically defined as an on-site laboratory. Standard care is defined as clinician assessment of risk, without the use of troponin testing or ECG.

In rural, remote, or other settings with no immediate access to central laboratory testing, HTERP recommends POC troponin testing for patients presenting with symptoms of acute coronary syndrome.

In settings with immediate access to central laboratory testing, HTERP does not recommend POC troponin testing for patients presenting with symptoms of acute coronary syndrome.
Rationale

- POC troponin testing may prevent unnecessary patient transfers, improve access and equity, and enable patients who do not have AMI to remain in their community, thereby limiting disruption, stress, and expenses for the patient and their family.
- POC troponin testing is less costly than standard care in settings with no immediate central laboratory access.
- The sensitivity and specificity of the troponin test is critical to the clinical and cost effectiveness of troponin testing.

Considerations

Although the economic review concluded that POC troponin is less effective than standard care in settings with no access to a central laboratory, it was also found to be less costly. This result was sensitive to the characteristics of the POC test and standard care. HTERP considered the cost savings and the potential improvement in access. Those in rural and remote settings who are not experiencing an MI are likely to wish to remain in their community for care. In this context, serial POC troponin testing may reduce unnecessary transfers to hospitals in large centres with central laboratory testing. Reducing unnecessary transfers may minimize harms due to familial disruption, stress, and other non-health benefits such as loss of productivity and financial strain. POC troponin would result in improved access and equity in these settings, as all patients could then benefit from the clinical assessment of risk and ECG evaluation in combination with troponin testing.

In settings with no immediate access to a central laboratory, POC troponin was compared with standard care. Given limited published data, the sensitivity for the clinical risk assessment used in the economic model was 93%, which may not be reflective of all clinical practice and which introduces uncertainty to the model. In addition, POC cTn testing would always be conducted alongside clinician assessment, which the committee agreed would increase the overall sensitivity of the assessment process and potentially further reduce the unnecessary transfers to hospitals in larger centres. The diagnostic accuracy of POC troponin testing would be improved with the addition of clinical assessment.

There was considerable uncertainty about the diagnostic accuracy of POC troponin testing, with variability in reported sensitivity and specificity in the included studies. This resulted in an inability to pool the data, which likewise introduced uncertainty to the economic model. The reported sensitivity of POC cTn tests ranged from 26% to 88%, depending on a number of factors. The studies used different devices, used different patient selection criteria, different positive cut-off thresholds (some using the 99th percentile of a healthy population and others using the 10% CV of the assay which in most cases is higher than the 99th percentile). Varying the sensitivity and specificity in the economic analysis affected the results and shifted from POC being less costly and less effective to more effective. Selection of a POC device, the threshold used as the positive cut-off, and appropriate patient selection for testing will all enhance the diagnostic accuracy and improve patient outcomes. In addition, the choice of a desktop versus handheld POC troponin device will be dependent on the specific setting. Further
research to determine the diagnostic accuracy of POC troponin testing is needed to improve the confidence in the estimate of effect.

Use of POC troponin in other settings without access to a central laboratory may also be feasible, such as in ambulance settings or in other settings by Emergency Medical Technicians. No data was identified on the effectiveness of POC troponin in such settings, although this would be an important area for future research.

Although HTERP does not recommend the use of POC troponin testing in settings with immediate access to a central laboratory, the hours of operation of the central laboratory and factors such as turn-around-time from test to results and time to discharge may be considered in this context. If the central laboratory is unable to provide results within the recommended time period of one hour, then POC troponin testing may be a consideration.

BACKGROUND

Given the introduction and increasing diffusion of POC troponin testing in the diagnostic work-up of patients presenting with symptoms of acute coronary syndrome (ACS), together with the uncertainty on its usefulness in different settings a review of its diagnostic accuracy, clinical utility and economic effects was conducted to inform decisions about its use in emergency rooms (where a clinical laboratory is available) or acquisition in remote and rural areas (where a clinical laboratory is not available).

The clinical and economic evidence used for developing this guidance was derived from the CADTH HTA: Point-of-Care Troponin Testing for Patients with Symptoms Suggestive of Acute Coronary Syndrome.(add ref when published)

Research questions

1. What is the diagnostic accuracy of POC cTn testing, using POC cTn devices approved by Health Canada, compared with central laboratory methods, in patients presenting with symptoms of ACS?

2. What is the clinical utility of POC cTn testing in altering the treatment and outcomes of patients presenting with symptoms of ACS?
   a. As compared with standard care in settings where a central laboratory is not available (pre-hospital setting; rural/remote settings)
   b. As compared with central laboratory methods in settings where a central laboratory is available (emergency departments, in hospital)

3. What is the cost-effectiveness of POC cTn testing in patients presenting with symptoms of ACS?
   a. As compared with standard care in settings where a central laboratory is not available (pre-hospital setting; rural/remote settings)
b. As compared with central laboratory methods in settings where a central laboratory is available (emergency departments, in hospital)

Summary of the Clinical Evidence

This systematic review on the diagnostic accuracy of POC cTn tests in patients with symptoms suggestive of ACS shows that currently available POC tests provide lower sensitivity and NPV, and higher specificity and PPV than central lab methods. This trend was maintained across different POC devices, and with blood samples taken at admission to three hours, six hours, and between six to nine hours after admission. POC cTn tests seem to have higher positive and negative likelihood ratios than central lab methods.

There was wide variability of the reported data on the diagnostic performance for the POC devices. Different methodological aspects of POC assays performed from studies that used different generations of POC assays, using fresh blood or frozen plasma, and by different clinical staff or technicians may have contributed to the large variability of the reported data. Patient selection, prior AMI, percentage of detected AMI, and device precision may also have affected the results, but given the limited amount of reported information on these variables, the effect on the overall findings is unclear. Diagnostic performance of commercial cTn assays was found to be variable in studies that identified lack of standardization among assays results, ranging from materials to procedures.5,6 The time of the patients’ presentation to the health care centre was variable across studies included in this review and this could have contributed to the observed variation in results, since the test sensitivity would increase with later presentation time. Some studies excluded patients with STEMI, and this patient selection may have affected the diagnostic test accuracy results.

The clinical utility of POC cTn testing in patients with symptoms suggestive of ACS can be categorized into two settings: in settings where central lab tests are available, in settings where central lab tests are not available (primary health care centres, remote or rural areas, and prehospital or ambulance settings). In general, in settings where central laboratories are available, POC cTn testing tends to shorten turn-around-time (time from blood draw to the result), length of stay (in emergency department or hospital), and time to decision compared with central lab. It is uncertain whether these changes are clinically significant, as the use of POC cTn did not statistically change mortality rates or severe adverse events compared to the central lab in up to one year of follow-up. In the majority of the studies, it was unclear if there was sufficient power to detect a clinically important effect, although it could be argued that saving time in the emergency department and shortening time to clinical decision is an important effect. Patient quality of life was similar in those who were tested using POC and those who were tested using central lab.

Although the evidence identified from primary studies on the clinical utility of POC cTn testing in settings with no central laboratory was limited, the data suggest that referrals to an emergency department can be reduced by use of POC cTn testing, and that use in ambulance settings may
be beneficial. Primary health care centres using POC cTn tests reduced the number of patients referred to an ED by 18% compared to centres without the use of POC cTn tests. This reduction of emergency referrals may come at the cost of an increased risk of missing patients with AMI.

Quantitative POC cTn testing proved to be feasible and reliable for patients transported by ambulance. POC devices operated in a moving ambulance were shown to provide reliable results compared to measurements by the same device in the ED. Additional equipment and training of staff are required for the implementation of POC testing in prehospital setting. The distance and time to a hospital may also be a consideration.

Other published information about the use of POC testing in rural areas suggests that POC troponin devices are being implemented in areas with challenging geographic settings to facilitate AMI diagnosis and that outcomes are improved in patients with chest pain. In remote health care centres where central labs were not available, the implementation of POC testing increased the volume of patients tested and increased staff satisfaction. Ninety-five percent of staff believed POC testing was more convenient than transporting patients to settings with central lab. The information on the use of POC testing in remote areas is most valuable from a Canadian perspective, but the evidence is limited to one Australian study. Use of POC troponin in rural Canadian settings may therefore be a feasible option.

Summary of the Economic Evidence

POC cTn testing strategies were less effective compared to central laboratory cTn testing for patients presenting to the ED with symptoms suggestive of ACS. Desktop POC cTn testing cost more than central laboratory, while handheld POC cTn testing strategies cost less per patient compared to central laboratory. When POC cTn testing was compared to no cTn testing (standard care/clinician assessment), POC cTn testing strategy was less effective and cost less per test.

In both contexts, the model was sensitive to the variability in the utility value for those with NSTEMI admitted and assumed to receive treatment. When this parameter was lowered below the identified threshold values, all of the POC cTn testing strategies became the dominant strategy. However, it is unknown if the threshold values evaluated were within the plausible range for the NSTEMI utility estimates. Sensitivity analyses varying the cost per assay and removing the POC device costs found that the model findings were not sensitive to variability in these costs.

The model results varied significantly with the estimates of diagnostic accuracy for both central laboratory and POC devices. Within plausible ranges of sensitivity and specificity, POC devices (both handheld and desktop) varied from less costly to more costly and less effective to more effective. There is significant uncertainty associated with the point estimates of cost-effectiveness due to the uncertainty in the diagnostic accuracy.
REFERENCES


APPENDIX 1: HTERP

HTERP consists of up to seven core members appointed to serve for all topics under consideration during their term of office, and up to five expert members appointed to provide their expertise for a specific topic. For this project, four expert members were appointed; their expertise included internal medicine, clinical chemistry, pathology, and family medicine. The core members include health care practitioners and other individuals with expertise and experience in evidence-based medicine, critical appraisal, health technology assessment, bioethics, and health economics. One public member is also appointed to the core panel to represent the broad public interest.

HTERP is an advisory body to CADTH and is convened to develop guidance or recommendations on non-drug health technologies to inform a range of stakeholders within the Canadian health care system. Further information regarding HTERP is available at www.cadth.ca/en/advisory-bodies/health-technology-expert-review-panel.

HTERP Core Members

Dr. Stirling Bryan (Chair)
Dr. Leslie Anne Campbell
Dr. Charlotte Moore
Dr. Lisa Schwartz
Dr. Jenny Basran
Dr. Hilary Jaegar
Dr. Jeremy Petch

Expert Members

Dr. Ronald A. Booth
Dr. Narmin Kassam
Dr. Michael O’Connor
Dr. Paul Salomon

Conflict of Interest

No members declared any conflicts of interest. Conflict of Interest Guidelines are posted on the CADTH website.