CADTH OPTIMAL USE REPORT

Point-of-Care Troponin Testing in Patients With Symptoms Suggestive of Acute Coronary Syndrome: Recommendations

Recommendations Report

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Table of Contents

ABBREVIATIONS .................................................................................................................. II

1. SUMMARY OF RECOMMENDATIONS .............................................................................. 1
   1.1 Technology .................................................................................................................. 1

2. METHODS .......................................................................................................................... 2

3. DETAILED RECOMMENDATIONS .................................................................................. 2
   3.1 Rationale .................................................................................................................... 2
   3.2 Considerations ............................................................................................................ 2

4. BACKGROUND .................................................................................................................. 4
   4.1 Research Questions .................................................................................................... 4
   4.2 Summary of the Clinical Evidence ............................................................................. 4
   4.3 Summary of the Economic Evidence ......................................................................... 5

REFERENCES ....................................................................................................................... 7

APPENDIX 1: HEALTH TECHNOLOGY EXPERT REVIEW PANEL ..................................... 8
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS</td>
<td>acute coronary syndrome</td>
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<tr>
<td>AMI</td>
<td>acute myocardial infarction</td>
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<tr>
<td>cTn</td>
<td>cardiac troponin</td>
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<td>ECG</td>
<td>electrocardiogram</td>
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<tr>
<td>HTERP</td>
<td>Health Technology Expert Review Panel</td>
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<tr>
<td>NSTEMI</td>
<td>non–ST-segment elevation myocardial infarction</td>
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<td>POC</td>
<td>point of care</td>
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<tr>
<td>STEMI</td>
<td>ST-segment elevation myocardial infarction</td>
</tr>
</tbody>
</table>
1. Summary of Recommendations

The American Cardiovascular Society recommends measuring cardiac troponin (cTn) I or T levels in patients presenting with symptoms of acute coronary syndrome (ACS). cTn levels increase with damage to the heart from an insufficient blood supply, and measuring these levels is a sensitive test for the detection of heart muscle damage. However, cTn levels may also be elevated in other conditions, and therefore clinical assessment and electrocardiogram (ECG) findings are also required to diagnose myocardial infarction (MI). ACS includes ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina. Because NSTEMI does not exhibit changes typical of an MI on ECG, measurement of cTn is important for diagnosis.

Troponin is typically measured by central laboratory testing; however, central laboratories are not always available, particularly in rural or remote settings. Point-of-care (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 [ED]), and settings with no immediate access to a central laboratory (such as rural hospitals or health care centres, remote settings, or remote nursing stations) were considered.

1.1 Technology

Central laboratories are not always onsite, nor available for use 24 hours a day, seven days a week. 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 a short turnaround time for biomarker detection, typically providing results within 10 to 20 minutes. In a central laboratory, the recommended turnaround time for troponin is one hour. POC cTn testing is being used with the goal of expediting patient care in hospital EDs, with the hope of improving patient flow, reducing congestion, and speeding up therapeutic decisions regarding hospital admission and discharge for patients presenting with ACS. It is also being used in various settings where central laboratory testing is not available, such as by paramedics in land or air ambulances, and health personnel in rural hospitals or health care centres, or remote health care stations, with the hope of speeding up therapeutic decisions regarding patient transfers, and decreasing the number of unnecessary transfers of patients to larger hospitals for further assessment and management. Ultimately, these outcomes may potentially result in cost reductions due to fewer unnecessary hospital admissions and laboratory costs.

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

CADTH conducted an HTA on the clinical and cost-effectiveness of POC troponin testing in patients with symptoms suggestive of ACS. 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 (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 is found on the HTERP page of the CADTH website: www.cadth.ca/collaboration-and-outreach/advisory-bodies/health-technology-expert-review-panel

3. 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 ACS. Immediate access to a central laboratory is defined as the ability to obtain troponin results in less than one hour, and is typically defined as an on-site laboratory. Settings with no immediate access to a central lab include rural hospitals or health care centres, remote health care stations, ambulances, or other similar settings. Standard care in these settings is defined as clinician assessment of risk, without the use of troponin testing or ECG.

In settings with no immediate access to central laboratory testing, HTERP recommends POC troponin testing for patients presenting with symptoms of ACS.

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

3.1 Rationale

- In settings without immediate access to a central laboratory, POC troponin testing may prevent unnecessary patient transfers, improve access to care and equity in care, and enable patients who do not have acute myocardial infarction (AMI) to remain in their community, thereby limiting disruption, stress, and expenses for patients and their families. Those patients with elevated troponin and suspected AMI based on clinician assessment can be transferred to a larger centre for further assessment.
- 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.

3.2 Considerations

As HTERP worked the POC troponin testing issue through its deliberative framework, the following considerations were put forth as part of its discussion.

HTERP considered the potential cost savings and the potential improvement in access to care with POC troponin testing in settings without immediate access to a central laboratory. POC troponin testing could help to ensure appropriate transfers — transferring patients who are likely experiencing an MI to larger centres, and not transferring patients who are likely not having an MI, instead allowing them to be cared for in their community. Reducing unnecessary transfers
may minimize harms arising from familial disruption, stress, loss of productivity, and financial strain. HTERP did note that the findings — i.e., that POC troponin testing is less effective but also less costly than standard care in settings without central laboratory access — were sensitive to POC troponin test characteristics and the characteristics of standard care, discussed below.

One of the factors that HTERP considered during its deliberations was the diagnostic accuracy of the POC troponin tests. In fact, there was considerable uncertainty about the diagnostic accuracy of POC troponin testing, with variability in reported sensitivity and specificity in the included studies (to the degree that pooling of the results was not possible). The reported sensitivity of POC cTn tests ranged from 26% to 88%, depending on a number of factors. The studies used different devices, different patient selection criteria, and different positive cut-off thresholds (some using the 99th percentile of a healthy population and others using the 10% coefficient of variance of the assay which, in most cases, is higher than the 99th percentile). HTERP acknowledged that further research to determine the diagnostic accuracy of POC troponin testing is needed. In the meantime, selection of a POC device, the threshold used as the positive cut-off, appropriate patient selection for testing, and serial testing will all enhance the diagnostic accuracy and improve patient outcomes. In addition, the choice of a desktop versus hand-held POC troponin device will be dependent on the specific setting. HTERP also recognized that POC cTn testing would always be conducted alongside clinician assessment, which the committee agreed would increase the overall accuracy of the assessment process. This, together with serial POC troponin testing, may also improve diagnostic accuracy of POC troponin testing.

HTERP acknowledged that there was some uncertainty regarding the model used for the economic analysis that had to be taken into consideration when deliberating the role of POC troponin testing. For example, when considering care that included POC troponin testing in settings with no immediate access to a central laboratory, it was compared with standard care (clinical assessment without troponin testing or ECG). Given the 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. These real-world variations in clinical risk assessment introduce uncertainty to the economic model. Another example stems from the considerable uncertainty about the diagnostic accuracy of POC troponin testing already discussed. The reported sensitivity and specificity in the included studies varied, and varying the sensitivity and the specificity in the economic analysis affected the results, shifting from POC troponin testing being less costly and less effective to being more effective.

HTERP also recognized that the 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. Limited data were 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 turnaround 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.
4. Background

The increasing diffusion of POC troponin testing in the diagnostic workup of patients presenting with symptoms of ACS, together with the uncertainty regarding its usefulness in different settings, warranted a review of its diagnostic accuracy, clinical utility, and economic effects. The review was conducted to inform decisions about its use in emergency rooms (where a clinical laboratory is available) or in areas where a central laboratory is not available, such as rural hospitals or in remote nursing stations.

The clinical and economic evidence used for developing this guidance was derived from the CADTH HTA report titled Point-of-Care Troponin Testing for Patients with Symptoms Suggestive of Acute Coronary Syndrome.  

4.1 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
   b. As compared with central laboratory methods in settings where a central laboratory is available

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
   b. As compared with central laboratory methods in settings where a central laboratory is available

4.2 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 negative predictive value, and higher specificity and positive predictive value than central lab methods. This trend was maintained across different POC devices, and with blood samples taken at admission, three hours and six hours after admission, and between six and nine hours after admission. POC cTn tests seem to have higher positive and negative likelihood ratios than central lab methods.

There was wide variability in the reported data on the diagnostic performance for the POC troponin devices. Different methodological aspects of POC troponin assays performed from studies that used different generations of POC troponin 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 assay results, ranging from materials to procedures. 6,7 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, because 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 and in settings where central lab tests are not available. In general, in settings where central laboratories are available, POC cTn testing tends to shorten turnaround time (time from blood draw to the result), length of stay (in ED or hospital), and time to decision compared with central laboratory testing. 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 with 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 ED and shortening time to clinical decision is an important effect. Patient quality of life was similar in those who were tested using POC troponin devices and those who were tested using central lab testing.

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 ED 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 with centres that did not use POC cTn tests. This reduction of emergency referrals may come at the cost of an increased risk of missing patients with AMI. However, the use of POC cTn testing in these settings may also help to inform decisions regarding additional assessment or appropriate patient transfer, and appropriate triage of patients with use of POC cTn in ambulance settings was shown to be feasible. POC devices operated in a moving ambulance were shown to provide reliable results compared with measurements by the same device in the ED. Additional equipment and training of staff are required for the implementation of POC testing in a pre-hospital 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 challenging geographic settings to facilitate AMI diagnosis and that outcomes are improved in patients with chest pain. Time to discharge was shorter in patients who received pre-hospital POC cTn testing compared with clinician assessment and usual care. In remote health care centres where central laboratories were not available, the implementation of POC testing increased the volume of patients tested and increased staff satisfaction. Ninety-five per cent of staff believed POC testing was more convenient than transporting patients to settings with a central lab. The information on the use of POC testing in rural 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 be a feasible option.

4.3 Summary of the Economic Evidence

The economic evaluation investigated the cost-effectiveness of POC cTn compared with central laboratory cTn testing. The model included costs for the testing strategies and resource utilization costs. POC cTn testing strategies were less effective compared with central laboratory cTn testing for patients presenting to the ED with symptoms suggestive of ACS. When POC cTn testing was compared with no cTn testing (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 quality-of-life scores for patients with NSTEMI who were admitted and assumed to receive treatment. When this parameter was lowered below the identified minimum quality-of-life score, 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 hand-held 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: Health Technology Expert Review Panel

The Health Technology Expert Review Panel (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.

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