Primerjava hitrega, obposteljnega in laboratorijsko določenega troponina I

Comparison of point-of-care and laboratory troponin I assays

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Izvleček

Izhodišče: V zadnjih letih smo priča pojavu analizatorjev troponina, ki omogočajo hitro določitev troponina ob bolniku. Pojavila so se poročila o neskladnosti med laboratorijsko določeno vrednostjo troponina in rezultati hitrih obposteljnih testov. Z raziskavo smo primerjali rezultate laboratorijsko določenega in hitrega obposteljnega testa za troponin I (i-STAT cardiac troponin I test, Abbott Point of Care).

Metode: Opravljena je bila retrospektivna raziskava pri bolnikih s sumom na akutni koronarni sindrom, pri katerih smo hkrati odvzeli kri za določanje laboratorijskega in hitrega obposteljnega troponina I. Bolniki so bili obravnavani na Internistični nujni pomoči Univerzitetnega kliničnega centra Maribor med 23. novembrom in 21. decembrom 2010.

Rezultati: V analizo je bilo vključenih 112 bolnikov. Pri 105 (93,8 %) bolnikih so se rezultati obeh preiskav skladali. Ob predpostavki, da je laboratorijsko določena vrednost troponina »zlati standard« (diagnoza je bila postavljena na osnovi laboratorijskega testa), je bilo 6 izvidov (5,4 %) lažno negativnih in 1 (0,9 %) lažno pozitiven (občutljivost 81,2 %, specifičnost 98,7 %). Kljub temu nismo ugotovili statistično pomembne razlike med vrednostjo hitrega, obposteljnega troponina in laboratorijsko določeno vrednostjo troponina I ($p = 0{,}125$).

Zaključek: Glede na rezultate naše raziskave in podobnih raziskav smo se odločili za uporabo hitrega obposteljnega testa za troponin I pri bolnikih z visokim tveganjem za akutni koronarni sindrom brez dviga ST veznice. S hitrim testom dobimo dodaten podatek, ki lahko vpliva na izbiro načina zdravljenja. Za izključitev akutnega koronarnega sindroma brez dviga ST veznice pri bolnikih z nizkim tveganjem je smiselno laboratorijsko določanje troponina.

Abstract

Background: In recent years a number of point-of-care troponin assays have emerged. There have been reports of discrepancies between the results of point-of-care and laboratory assays. We sought to compare the results of point-of-care and laboratory troponin I assays in patients with suspected acute coronary syndromes.

Methods: A retrospective study was performed comparing the results of point-of-care (i-STAT cardiac troponin I test, Abbott Point of Care) and laboratory troponin I analysis in patients with suspected acute coronary syndrome treated in the Internal Medicine Emergency Department, University Medical Centre Maribor, between 23 November and 21 December 2010, who had blood samples drawn simultaneously for point-of-care and laboratory troponin I analysis.

Results: 112 patients were included in the analysis. There was an agreement between the results of point-of-care and laboratory troponin analysis in 105 (93.8 %) patients. If we consider the laboratory results as »gold standard« (diagnosis was based on laboratory troponin results), then 6 (5.4 %) false negative results and 1 (0.9 %) false positive result were found (sensitivity 81.2 %, specificity 98.7 %). However, there was no statistically significant difference between point-of-care and laboratory troponin I analysis ($p = 0.125$).

Conclusion: We detected lower sensitivity of point-of-care assay, but there was no statistically significant difference between point-of-care and laboratory troponin I analysis. We adopted a strategy of using point-of-care troponin assay primarily in patients at high-risk for acute coronary syndrome without ST elevation.

Introduction

Patients with chest pain make around 10 % of all emergency department visits.[1,2] In patients with chest pain and suspected acute coronary syndrome (ACS) cardiac troponins are important prognostic markers.[3] In the past, emergency departments depended on central hospital laboratories for troponin analysis. In central laboratories result turnaround-times (TAT) include time spent on delivery and preparation of blood samples, assay time and delivery of results. POC assays have reduced result TAT,[4-6] which could be potentially beneficial in diagnosing and early treatment of patients with suspected ACS.[3,5-8]

Performance of POC assays has been questioned.[8-10] Some reports have indicated that POC assays could represent an alternative to laboratory testing.[5,11,12] In our hospital, there have been individual reports of discordant troponin I (TnI) results between POC and laboratory analysis. We sought to compare the results of POC and laboratory TnI analysis in patients with suspected ACS treated in the Internal Medicine Emergency Department. Medical records of patients were reviewed for use of acetylsalicyclic acid (ASA), warfarin or exposure to diagnostic or therapeutic immunoglobins, which could interfere with the results.[13]

Methods

A retrospective study was conducted involving patients with suspected non-ST elevation ACS (NSTE-ACS),who had blood for POC and laboratory tests drawn simultaneously. The study population consisted of 112 patients. Patients were admitted to the Internal Medicine Emergency Department of the University Medical Centre Maribor, Slovenia, between 23 November and 21 December 2010. Laboratory TnI was measured using the high sensitivity Dimension Vista® 1500, Siemens assay at the Department of Biochemistry, University Medical Centre Maribor. The detection limit of the test is 0.02 µg/L and the 99th percentile cut-off point is at 0.045 µg/L.[14] It measures troponin I concentration using chemiluminescence method. The binding of human cardiac TnI to anti-TnI antibody triggers a reaction resulting in chemiluminescent signal proportional to TnI concentration in the sample.[14]

POC assay was performed using i-STAT cardiac troponin I test, Abbott Point of Care. i-STAT assay allows rapid, bedside TnI determination within 10 min using whole blood. The assay is quantitative. The detection limit is 0.02 µg/L and 99th percentile cutoff point is at 0.08 µg/L.[13] It uses enzyme-linked immunoabsorbant assay (ELISA) method. The cartridge contains antibodies specific for human cardiac TnI attached to working channel surface and a conjugate of alkaline phosphatase and an antibody specific for a separate part of TnI. TnI binds to both antibodies preventing alkaline phosphatase from being washed away later in the process. The fixed alkaline phosphatase reacts with a substrate, producing a detectable reactant, which is proportional to the concentration of TnI in the sample.[13]

i-STAT samples were collected and processed by trained personnel. 99th percentile cut-off assay values were used to separate positive from negative results. The between-assay level of concordance was determined. Concordance between POC and laboratory results was tested using the McNemar's test. P-value < 0.05 was regarded as statistically significant. Medical records were used to determine which patients were using ASA or warfarin or have been exposed to diagnostic or therapeutic immunoglobins, which could interfere with POC assay.[15] The relationship between ASA or warfarin use or exposure to immunoglobins and discordant results was tested using the Fisher's exact test. The relationship between lot numbers (with approximately 30 cartridges sharing the same lot number) was also tested using the Fisher's exact test. P-value < 0.05 was regarded as statistically significant.

Results

The analysis included 112 patients. The mean age of the study population was 64.8 ± 14.3 years; 60.7 % were males. ASA was used in 49.1 % and warfarin in 9.8 %. None was exposed to immunoglobulins. Po-

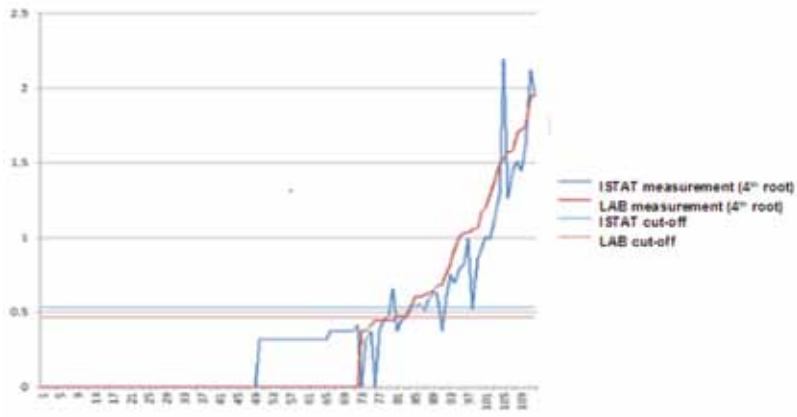

Figure 1: Comparison of the results of POC assay and laboratory analysis.

sitive POC TnI was measured in 27 (24.1 %) patients. Negative POC TnI was measured in 85 (75.9 %) patients. There was an agreement between the results of POC and laboratory Tn in 105 (93.8 %) patients. If we consider the laboratory results as »gold standard« then 6 (5.4 %) false negative results and 1 (0.9 %) false positive result were detected (Figure 1). However, there was no statistically significant difference between POC and laboratory TnI ($\chi^2(1) = 2.89$, $p = 0.125$).

Three patients with false negative POC assay results were diagnosed with non-ST elevation myocardial infarction (NSTEMI), 2 with pneumonia and sepsis and 1 with congestive heart failure. One patient with false positive POC assay was diagnosed with urosepsis. False negative results were not associated with use of ASA ($p = 0.095$), although the calculated odds of getting false negative results were 5.6 times higher if ASA was used, indicating that we might reach statistically significant difference between two groups if we increased the sample size. Use or warfarin was also not associated with false negative results ($p = 0.47$), with odds of getting false negative results being 1.96 times higher if warfarin was used. Lot number was not associated with false negative results ($p = 0.302$).

Discussion

POC assays have become commonplace in emergency departments, intensive care units and wherever a rapid laboratory analysis is required. The results that are issued need to be reliable and reproducible.

According to the producer, ASA and warfarin at therapeutic levels do not affect i-STAT method significantly. Significance is defined as < 10 % variation at TnI concentration of 2 ng/ml.[13] Due to the widespread use of ASA and warfarin in at-risk population (in our case 49.1 % and 9.8 %), we tested any association between false negatives and use of ASA or warfarin, and found none, with limitations of retrospective study and a relatively small sample considered. The method depends on antibodies binding to TnI. In patients who have been exposed to animals or have received immunoglobulins for therapeutic or diagnostic purposes, interfering antibodies may be present.[13,15] In our study, we found no evidence in medical data of any patient's exposure to immunoglobulins.

There have been reports of discrepancies in the results between POC and laboratory assays. Several studies have shown that a negative POC TnI did not exclude myocardial damage.[8-10] Use of POC TnI assays in TnI evaluation 6–12 h after the onset of pain did not rule out NSTE-ACS as well.[9,10] POC TnI I assays seem to be unable to identify patients with minor myocardial damage. Detecting minor elevations in TnI is important in patients with noncardiac conditions associated with troponin elevations as well. In our study, 3 patients with false negative POC assay results were in the later course of treatment diagnosed with NSTEMI (coronary angiography was performed in 2, 1 died), 2 with sepsis and pneumonia and 1 with congestive heart failure. One patient with false positive POC assay result was diagnosed with urosepsis. Repeated laboratory analysis of TnI was negative.

On the other hand, a positive POC TnI can predict elevated TnI levels[5,10] and points to patients at risk of adverse cardiac events.[10] POC TnI assays also allow for shorter result TAT,[16] with loss of significance for patient TAT when used for exclusion of NSTE--ACS.[17]

Our study was primarily aimed at the comparison of POC and laboratory TnI analysis. No statistically significant difference was detected between POC and laboratory TnI results. The results concerning sensitivity (81.2 %), specificity (98.7 %) (Figure

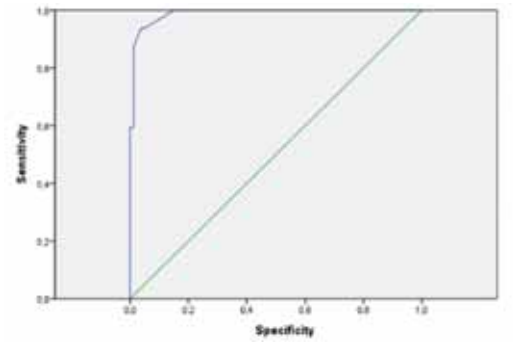

Figure 2: Receiver operating characteristic (ROC) curve of POC assay.

2) and false negatives (6 cases, 5.4 %) are comparable to other studies.[10] Low sensitivity cannot be explained by personnel experience (nurses have been trained in handling the assays, no invalid results have been reported), interactions due to the use of ASA or warfarin or linked to a single lot number (cartridges from 3 different lots have been tested, with no difference between lots).

Conclusion

POC TnI assays seem to have lower sensitivity when compared to laboratory TnI assay. We adopted a strategy of using POC TnI assay in patients at high risk for NSTE-ACS. Rapid confirmation of NSTE-ACS might be beneficial in risk-stratifying and earlier treatment of these patients. Laboratory TnI assays have higher sensitivity and are probably a safer option when excluding NSTE-ACS.

Literature

1. Fairbairn IP. Medical emergencies. J R Coll Physicians Edinb 2003; 33: 36–43.
2. Bhuiya FA, Pitts SR, McCaig LF. Emergency Department Visits for Chest Pain and Abdominal Pain: United States, 1999–2008. NCHS Data Brief 2010; 43: 1–8.
3. Task Force for Diagnosis and Treatment of Non--ST-Segment Elevation Acute Coronary Syndromes of European Society of Cardiology. Bassand JP, Hamm CW, Ardissino D, Boersma E, Budaj A, et al. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. Eur Heart J 2007; 28: 1598–660.
4. Singer AJ, Ardise J, Gulla J, Cangro J. Point-of--care testing reduces length of stay in emergency department chest pain patients. Ann Emerg Med 2005; 45: 587–91.
5. Možina H, Vukan V, Lenart K, Skitek M, Osredkar J. Quantitative Point-of-Care Troponin I in Emergency Department in Comparison With Troponin I in Central Laboratory. Point Care 2010; 9: 8–11.
6. Osredkar J. Use of POCT analyser PATHFAST in emergency service. In: Gričar M, Vajd R. 17th International Symposium on Emergency Medicine; 2010 Jun 9–12; Portorož, Slovenija. Ljubljana: Slovenian Society for Emergency Medicine; 2010.
7. Caragher TE, Fernandez BB, Jacobs FL, Barr LA. Evaluation of quantitative cardiac biomarker point-of-care testing in the emergency department. J Emerg Med 2002; 22: 1–7.
8. Cramer GE, Kievit PC, Brouwer MA, de Keijzer MH, Luijten HE, Verheugt FW. Lack of concordance between a rapid bedside and conventional laboratory method of cardiac troponin testing: impact on risk stratification of patients suspected of acute coronary syndrome. Clin Chim Acta 2007; 381: 164–6.
9. Venge P, Ohberg C, Flodin M, Lindahl B. Early and late outcome prediction of death in the emergency room setting by point-of-care and laboratory assays of cardiac troponin I. Am Heart J 2010; 160: 835–41.
10. James SK, Lindahl B, Armstrong P, Califf R, Simoons ML, Venge P, Wallentin L; GUSTO-IV ACS Investigators. A rapid troponin I assay is not optimal for determination of troponin status and prediction of subsequent cardiac events at suspicion of unstable coronary syndromes. Int J Cardiol 2004; 93: 113–20.
11. Heeschen C, Deu A, Langenbrink L, Goldmann BU, Hamm CW. Analytical and diagnostic performance of troponin assays in patients suspicious for acute coronary syndromes. Clin Biochem 2000; 33: 359–68.
12. Loten C, Attia J, Hullick C, Marley J, McElduff P. Validation of a point of care troponin assay in real life Emergency Department conditions.Emerg Med Australas 2009; 21: 286–92.
13. Cartridge and Test Information Sheets: Cardiac Troponin I/cTnI. Dosegljivo na: http://www.i-stat.com/products/ctisheets/715595-00L.pdf
14. LOCI Cardiac Troponin I. Dosegljivo na: http://www.medical.siemens.com
15. Kricka LJ. Commentary: interferences in laboratory tests. Clin Chem 2008; 54: 1245.
16. Lee-Lewandrowski E, Corboy D, Lewandrowski K, Sinclair J, McDermot S, Benzer TI. Implementation of a point-of-care satellite laboratory in the emergency department of an academic medical center. Impact on test turnaround time and patient emergency department length of stay. Arch Pathol Lab Med 2003; 127: 456–60.
17. Ryan RJ, Lindsell CJ, Hollander JE, O'Neil B, Jackson R, Schreiber D, et al. A multicenter randomized controlled trial comparing central laboratory and point-of-care cardiac marker testing strategies: the Disposition Impacted by Serial Point of Care Markers in Acute Coronary Syndromes (DISPO-ACS) trial. Ann Emerg Med 2009; 53: 321–8.