J Bras Patol Med Lab. 2020; 56: 1-5.

10.5935/1676-2444.20200020

Performance analysis of commercial rapid tests for serum troponin detection

Análise do desempenho de testes rápidos comerciais para detecção de troponina I sérica

Raquel Ida Ferreira; Marcela R. Amaral; Maytê S. R. Brito; Matheus P. Pinto; Ana Carolina R. Maranhão; Lucas R. R. Costa; Rômulo C. Vaz de Melo

Faculdade de Medicina de Barbacena, Barbacena, Minas Gerais, Brazil.

ABSTRACT

Introduction: Rapid tests represent an important diagnostic tool, providing results in a short period of time and eliminating the use of large automated equipment. **Objective:** To evaluate the performance of five rapid test kits for troponin I detection in serum. **Materials and methods:** Samples from 100 patients with suspected acute myocardial infarction (AMI) were selected from a hospital in Barbacena, MG, Brazil. They were tested in the five troponin I commercial rapid test kits and the results were compared with the study reference method (quantitative chemiluminescent immunoassay). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and correlation coefficients of the rapid tests against the reference method were defined. **Results:** The kits from Abon®, Interteck®, Medtest® and Wama® presented the same performance, reaching equal levels of sensitivity (98.08%), specificity (100%), PPV (100%), NPV (97.96%), and correlation coefficient (0.99). The Eco Diagnostica® kit presented lower sensitivity (82.69%), low correlation coefficient (0.91) and NPV (84.21%), not reaching ideal levels even though lying within the confidence interval. **Discussion:** The results obtained with the Abon®, Interteck®, Medtest® and Wama® test kits corroborate pre-existing literature data on the diagnostic accuracy of rapid tests for troponin detection. These tests are allowed for immediate decision making by physicians and can be used to reduce unnecessary hospitalization time and costs associated with a suspected AMI. **Conclusion:** The kits from Abon®, Interteck®, Medtest® and Wama® showed excellent diagnostic performance, what makes them an important diagnostic tool in smaller laboratories without automated equipment.

Key words: myocardial infarction; troponin I; diagnostic techniques, cardiovascular.

RESUMO

Introdução: *Atualmente, os testes rápidos representam importante ferramenta diagnóstica, fornecendo resultados em curto espaço de tempo e dispensando a utilização de grandes automações.* ***Objetivo:*** *Avaliar o desempenho de cinco* kits *de testes rápidos para pesquisa sérica de troponina I.* ***Materiais e métodos:*** *Foram selecionadas 100 amostras de pacientes com suspeita de infarto agudo do miocárdio (IAM) de um hospital do município de Barbacena, Minas Gerais, Brasil. As amostras foram testadas nos cinco* kits *comerciais de teste rápido de troponina I e o resultado foi comparado com o método considerado referência no estudo (imunoensaio quimioluminescente quantitativo). Em seguida, foram definidos níveis de sensibilidade, especificidade, valor preditivo positivo (VPP), valor preditivo negativo (VPN) e coeficiente de correlação dos testes rápidos em relação ao método de referência.* ***Resultados:*** *Os* kits *Abon®, Interteck®, Medtest® e Wama® apresentaram o mesmo desempenho, atingindo níveis iguais de sensibilidade (98,08%), especificidade (100%), VPP (100%), VPN (97,96%) e coeficiente de correlação (0,99). O* kit *Eco Diagnóstica® apresentou 82,69% de sensibilidade, 0,91 de coeficiente de correlação e 84,21% de VPN, não atingindo os níveis ideais, mesmo dentro do intervalo de confiança.* ***Discussão:*** *Os resultados obtidos com os* kits *Abon®, Interteck®, Medtest® e Wama® confirmam dados preexistentes na literatura sobre a exatidão diagnóstica dos testes rápidos para detecção de troponina. Esses testes permitem a tomada de decisão imediata pelo médico e podem ser usados para reduzir tempo e custos de internações desnecessárias na suspeita de IAM.* ***Conclusão:*** *Os* kits *Abon®, Interteck®, Medtest® e Wama® apresentaram excelente desempenho diagnóstico e constituem importante ferramenta diagnóstica em laboratórios menores, sem equipamentos automatizados.*

Unitermos: *infarto do miocárdio; troponina I; técnicas de diagnóstico cardiovascular.*

First submission on 08/15/19; last submission on 08/19/19; accepted for publication on 08/26/19; published on 03/03/20

RESUMEN

Introducción: *Hoy en día, las pruebas rápidas representan importante herramienta diagnóstica, ofrecen resultados en corto espacio de tempo y dispensan el uso de equipos automatizados.* ***Objetivo:*** *Evaluar el desempeño de cinco* kits *de pruebas rápidas para detectar troponina I en suero.* ***Material y métodos:*** *Se eligieron 100 especímenes de pacientes sospechosos de infarto agudo de miocardio (IAM) de un hospital en el municipio de Barbacena, Minas Gerais, Brasil. Los especímenes fueron testados en los cinco* kits *comerciales de prueba rápida de troponina I y el resultado se comparó con el método considerado referencia en el estudio (inmunoensayo quimioluminiscente cuantitativo). Luego, se establecieron los niveles de sensibilidad, especificidad, valor predictivo positivo (VPP), valor predictivo negativo (VPN) y coeficiente de correlación de las pruebas rápidas con respecto al método de referencia.* ***Resultados:*** *Las marcas Abon®, Interteck®, Medtest® y Wama® tuvieron el mismo desempeño, alcanzando niveles iguales de sensibilidad (98,08%), especificidad (100%), VPP (100%), VPN (97,96%) y coeficiente de correlación (0,99), mientras la marca Eco Diagnóstica® presentó 82,69% de sensibilidad, 0,91 de coeficiente de correlación y 84,21% de VPN, no alcanzando los niveles ideales, aunque dentro del intervalo de confianza.* ***Discusión:*** *Los resultados obtenidos con las marcas Abon®, Interteck®, Medtest® e Wama® confirman datos preexistentes en la literatura sobre la precisión diagnóstica de las pruebas rápidas para detectar troponina. Esas pruebas permiten a los médicos adoptar decisiones de forma inmediata y pueden ser usados para reducir tiempo y costos de internaciones innecesarias cuando hay sospecha de IAM.* ***Conclusión:*** *Las marcas Abon®, Interteck®, Medtest® e Wama® presentaron excelente desempeño diagnóstico y representan importante herramienta diagnóstica en laboratorios menores, sin equipos automatizados.*

Palabras clave: *infarto del miocardio; troponina I; técnicas de diagnóstico cardiovascular.*

INTRODUCTION

Cardiovascular diseases (CVD) are the main cause of mortality globally. In 2015, 31% of deaths in the world were due to CVD. Coronary cardiac diseases are estimated to be responsible for 7.4 million of those losses[1].

The diagnosis of acute myocardial infarction (AMI) can be made with the rise or fall of cardiac biomarkers, and at least one of the following: presence of ischemic symptoms, electrocardiogram (ECG) changes indicative of ischemia (ST-segment elevation or depression, or new left bundle branch block), development of pathological Q waves on the ECG, or imaging evidence of loss of myocardial viability or abnormal segmental contractility[2-4]. However, many cases do not present typical symptoms, and ECG is nonspecific in 50% of the patients with AMI[5].

In this regard, cardiac biomarkers are fundamental for diagnosis of AMI and acute coronary syndrome (ACS). Cardiac troponin is considered the biomarker with the highest sensitivity and specificity to detect myocardial lesion; troponins I and T can be used in this diagnosis, presenting similar performance[2, 5, 6].

Since the beginning of the 1990's there are quantitative assays for serum troponin measurement, and current protocols for infarct diagnosis consider them as tests of choice. Nowadays, a measurement of troponin is recommended upon patient admission, and at least another one must be performed after 6-12 hours[5, 7]. It is important that the result is released as soon as possible, since early coronary reperfusion can improve patient prognosis. However, not all laboratories in the country have automated equipment to carry out this test[8, 9].

Rapid tests could solve problems of lack of automated equipment and time of assay development, as they do not require the use of instruments, are eye-readable and provide results in few minutes. But although rapid tests are widely available in the market and their manufacturers have to present validation procedures to the Brazilian Health Regulatory Agency (Anvisa), those procedures and their results are not disclosed, therefore, there is not the necessary knowledge on sensitivity and specificity of the tests for AMI diagnosis in the medical setting. Thus, it is essential to undertake researches to assess that performance, corroborating or not the use of those tests in places of low demand, without possibility of using automated methods.

OBJECTIVE

The objective of this study was to assess the performance of five commercial kits of rapid tests for the detection of troponin I in serum from patients with suspected AMI at an emergency unit.

MATERIALS AND METHODS

Study design

This is a diagnostic accuracy study of five commercial kits of rapid tests for investigation of serum troponin I, approved by the Research Ethics Committee of Faculdade de Medicina de Barbacena (record 2.893.449, CAAE: 97475518.7.0000.8307).

Specimen collection

As a reference for the method, the technical norms recommended by the Clinical and Laboratory Standards Institute (CLSI) 2008[10] were used.

A hundred blood specimens were selected and referred to Laboratório São José de Barbacena, Minas Gerais – a reference in analysis of cardiac markers in the region –, from patients at the emergency sector of Hospital Ibiapaba/Cebams, Barbacena, Minas Gerais, with suspected AMI. Selection was made for convenience, according to the demand for the laboratory service, including samples from patients who had undergone measurements of cardiac markers creatine phosphokinase or troponin. Insufficient, hemolyzed, lipemic, and icteric blood specimens were excluded from the research.

Specimens were analyzed for troponin I by the chemiluminescent quantitative method in the Access® (Beckman, Coulter®) instrument, considered, in this study, the reference method. Specimens were considered positive with values of troponin I ≥ 0.5 ng/ml, and negative with troponin I < 0.5 ng/ml. Later, they were tested in five commercial rapid test kits for troponin I serum detection, following recommendations by the manufacturers. Nine rapid tests kits were pre-selected for troponin I as they were the most used by diagnostic laboratories: Abon®, Bioclin®, Eco Diagnóstica®, Interteck®, Invitro®, Katal®, Laborimport®, Medtest®, OrangeLife® and Wama®. Among them, five were selected, with priority for those with longer shelf life: Abon®, Eco Diagnóstica®, Interteck®, Medtest® and Wama®.

Tests were conducted by the laboratory researchers, under supervision of duly qualified clinical pathology technicians and biochemists. During the experiment, the tests were identified with the name and record number of each patient. In order to avoid errors, just five specimens were assessed in each moment. Each manufacturer's recommendations were followed about specimen type (serum or whole blood), amount of necessary reagent, and time for reading the tests, which ranged from 10 to 15 minutes. The procedure for evaluation of five specimens, since identification until reading and result processing, lasted, on average, 30 minutes.

An agreement of 99% was aimed between results of rapid tests and the reference method. The authors declared absence of any conflicts of financial, personal or professional interests with the suppliers of kits for measurement of troponin I.

Statistical analysis

The achieved results were transcribed into the database and entered into an Excel spreadsheet. Data were analyzed by the statistical software Stata version 9.2. Comparison between the reference method for troponin I measurement and the rapid tests was done by means of the Pearson (chi-square) and Fischer exact test. Levels of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and coefficient of correlation were obtained between the rapid tests and the reference method. For this study, the reference method was considered the gold standard, with sensitivity and specificity of 100%. Results were calculated considering a 95% confidence interval (CI).

RESULTS

The study population comprised 100 patients, with 51 (51%) females and 49 (49%) males. The mean age was 65 years, with standard deviation of 12.35.

Troponin I measurement by the quantitative (reference) method showed 48 negative and 52 positive results. The rapid tests Abon®, Interteck®, Medtest® and Wama® presented disagreeing results in just one of the 100 analyzed specimens, with result of troponin I of 0.95 ng/ml, positive in the reference method and negative in the other tests; for rapid tests, such a value is considered a false-negative result. The evaluation of Eco Diagnóstica® rapid tests showed disagreement in nine specimens, with results of troponin I of: 0.62; 0.9; 0.95; 0.97; 1.08; 2.22; 2.52; 3.5 and 34.1 ng/dl, all of them positive in the reference method and negative in the rapid test in question, considered false-negative results. False-positive results were not found in any of the assessed tests.

The **Table** presents the values of sensitivity, specificity, PPV, NPV, accuracy, and coefficient of correlation (*r*) between the commercial rapid tests and the reference method. One can observe that the Abon®, Interteck®, Medtest® and Wama® tests presented identical performance, reaching excellent levels of diagnostic accuracy and coefficient of correlation in relation to the reference method; all measurements reached ideal levels (100%) within the CI.

The Eco Diagnóstica® test presented lower levels of sensitivity (82.69%) and NPV (84.21%), and, even within the CI, did not

TABLE – Specifications of diagnostic accuracy and CI of rapid tests to detect serum troponin I compared with those of the chemiluminescent method (Access® – Beckman-Coulter®) in blood specimens from patients with suspected AMI at Hospital Ibiapaba/Cebams, Barbacena, Minas Gerais, Brazil

	S	Sp	PPV	NPV	*r*	Accuracy
Abon®	98.1 (95.4-100)	100 (100-100)	100 (100-100)	97.9 (95.2-100)	0.99 (0.97-1)	99 (97-100)
Eco diagnóstica®	82.7 (75.3-90.1)	100 (100-100)	100 (100-100)	84.2 (77.1-91.4)	0.91 (0.85-0.96)	91 (85-96)
Interteck®	98.1 (95.4-100)	100 (100-100)	100 (100-100)	97.9 (95.2-100)	0.99 (0.97-1)	99 (97-100)
Medtest®	98.1 (95.4-100)	100 (100-100)	100 (100-100)	97.9 (95.2-100)	0.99 (0.97-1)	99 (97-100)
Wama®	98.1 (95.4-100)	100 (100-100)	100 (100-100)	97.9 (95.2-100)	0.99 (0.97-1)	99 (97-100)

All measurements presented p *value < 0.01.*

CI: confidence interval; AMI: acute myocardial infarction; S: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value; r*: coefficient of correlation.*

reach the ideal level (100%). Besides, the coefficient of correlation relative to the reference method was also lower than the others (0.91) – it did not reach the ideal level within the CI.

DISCUSSION

Early diagnosis and rapid beginning of therapeutical measures present direct impact on morbidity and mortality of patients with ACS[11]. Several studies like this state that rapid tests for detection of troponin I are adequate to evaluate subjects with ACS symptoms in emergency services, being an alternative to reduce time and costs of unnecessary hospitalizations, besides allowing for immediate decision taking by the attending physicians[8, 11, 12].

Clinical implications

This study did not evaluate the direct use of rapid tests for detection of troponin I in the diagnosis of AMI. However, the potential of those tests was analyzed in an indirect manner in this diagnosis by a comparison with the results of a recognized and widely used laboratory test. The implementation of rapid tests in emergency sectors can reduce diagnosis time, cost with hospitalization, and time of hospital stay, as already noted in the literature[13, 14].

Abon®, Interteck®, Medtest® and Wama® rapid tests for troponin I presented excellent diagnostic accuracy, with ideal levels of specificity and PPV. The levels of sensitivity and NPV were very high, besides the coefficient of correlation of 0.99, reaching perfection within the CI. Thus, the results from the study corroborate pre-existing data in the literature about diagnostic accuracy of rapid tests for troponin detection[7, 13, 15].

It is important to highlight that just a specimen presented disagreeing results between rapid tests and the reference method. There was no possibility of confirming the result of the quantitative immunoassay, as the specimen quantity was not sufficient for additional testing. Therefore, although the quantitative immunoassay has been considered the reference method for this study, we cannot rule-out the possibility of this result being a false positive in this test and a true negative in the rapid tests.

The researchers considered the performance of the Eco Diagnóstica® test insufficient for clinical use, because sensitivity and NPV and coefficient of correlation in relation to the reference method were low, not reaching satisfactory levels within the CI. It happened mainly because this test has presented false-negative results in samples with different troponin I concentration levels, what is against the preconized by the literature, which, for AMI management, recommends tests with high levels of sensitivity[15].

Limitations

A limitation of the study was the incapacity of conducting clinical validation of results, with the verification of medical records and confirmation of AMI. However, the number of specimens and the results demonstrated that this validation perhaps would not bring further information. Another limitation is related to the use of chemiluminescent quantitative immunoassay as the reference method for validation; such a choice was taken because the method was practical and of easy access. Assuming the results of this test are the standard for comparison, an error might have occurred in the analysis. Yet, by the almost perfect correlation among the main tests, we believe that if this error occurred, it was not relevant for final analysis.

CONCLUSION

The present study demonstrated that the Abon®, Interteck®, Medtest® and Wama® rapid tests for serum troponin I detection presented excellent diagnostic performance, being an important tool in small laboratories, with no automated instruments, which perform tests in patients with suspected AMI in emergency units.

REFERENCES

1. WHO. World Health Organization. Cardiovascular diseases (CVDs) [Internet]. 2016. Available at: http://www.who.int/mediacentre/factsheets/fs317/en/index.html.

2. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD. Fourth universal definition of myocardial infarction. Circulation. 2018; 138(20): e620-45.

3. Palamalai V, Murakami MM, Apple FS. Diagnostic performance of four point of care cardiac troponin I assays to rule in and rule out acute myocardial infarction. Clin Biochem. 2013; 46(16-17): 1631-5. PubMed PMID: 23850852.

4. Greiser A, Winter T, Mahfoud H, et al. The 99th percentile and imprecision of point-of-care cardiac troponin I in comparison to central laboratory tests in a large reference population. Clin Biochem. 2017; 50(18): 1198-1202. PubMed PMID: 28803961.

5. Heeschen C, Goldmann BU, Moeller RH, Hamm CW. Analytical performance and clinical application of a new rapid bedside assay for the detection of serum cardiac troponin I. Clin Chem. 1998; 44(9): 1925-30. PubMed PMID: 9732978.

6. Suzuki K, Komukai K, Nakata K, et al. The usefulness and limitations of point-of-care cardiac troponin measurement in the emergency department. Intern Med. 2018; 57(12): 1673-80. PubMed PMID: 29434124.

7. Christ M, Geier F, Blaschke S, et al. Clinical performance of a new point-of-care cardiac troponin I test. Clin Chem Lab Med. 2018; 56(8): 1336-44. PubMed PMID: 29630502.

8. Juliano M, Wason C. Comparison of point-of-care versus laboratory troponin testing in an emergency department setting. Mil Med. 2017; 182(7): e1938-e40. PubMed PMID: 29630502.

9. Hirschl MH, Herkner H, Laggner AN, et al. Analytical and clinical performance of an improved qualitative troponin T rapid test in laboratories and critical care units. Arch Pathol Lab Med. 2000; 124(4): 583-7. PubMed PMID: 10747317.

10. Garret PE, Lasky FD, Meier KL. User protocol for evolution of qualitative test performance; approved guideline. Clinical and Laboratory Standards Institute (CLSI). 2008; 28(2).

11. Singer AJ, Williams J, Taylor M, Le Blanc D, Thode HC Jr. Comprehensive bedside point of care testing in critical ED patients: a before and after study. Am J Emerg Med. 2015; 33(6): 776-80. PubMed PMID: 25836947.

12. Suh D, Keller DI, Hof D, et al. Rule-out of non-ST elevation myocardial infarction by five point of care cardiac troponin assays according to the 0 h/3 h algorithm of the European Society of Cardiology. Clin Chem Lab Med. 2018; 56(4): 649-57. PubMed PMID: 29257750.

13. Sardi AR, Lamoureux JA, Phillip-Samuel SG. Point-of-care testing of troponin levels compared with automated laboratory evaluation: a reliability study. Crit Care Nurs Q. 2016; 39(4): 345-51. PubMed PMID: 27575797.

14. Cramer GE, Kievit PC, Brouwer MA, Keijzer MH, Luijten HE, Verheugt FWA. 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(2): 164-66.

15. Ramparany L, Ramirez J, Nizou JY, Le Saux D, Richard V, Talarmin A. Evaluation of four rapid immunochromatographic tests for the detection of cardiac troponin I. Clin Vaccine Immunol. 2011; 18(3): 414-17.

CORRESPONDING AUTHOR

Raquel Ida Ferreira ID 0000-0003-1533-8971
e-mail: raquelidaferreira@yahoo.com