Evaluation of analytical quality of cardiac biomarkers in the emergency laboratory by sigma metrics

Fatma Ceyla Eraldemir
Department of Biochemistry, Kocaeli University School of Medicine, Kocaeli, Turkey

Abstract

Aim: The analytic quality of cardiac biomarkers were investigated consecutive six months by sigma metric method in our emergency laboratory. Total allowable error ratio (TEa%)'s of AAB, BV, RCPA, Ricos, and Rilibak were used for calculation. Sigma levels are compared and used to decide which TEa% is appropriate for our laboratory for more accurate results. Material and Method: Sigma levels were calculated for cardiac biomarkers which include Troponin I (cTnI), Troponin T (cTnT), CKMB mass, Myoglobin (Mb) and NT-proBNP in our emergency laboratory department between December 2017 and May 2018. The internal quality control (IQC) and external quality control (EQC) assessment results and TEa%'s of AAB, BV, RCPA, Ricos, and Rilibak were used to calculate sigma metrics. The sigma metrics for tests were calculated by "Sigma = (TEa% – Bias%) / CV%" formula. Results: Considering different TEa% 's, it is evaluated that CKMB mass sigma level is at the "world-class quality". On the contrary, cTnT sigma level is found to be at the level of "poor quality". For AAB, BV, RCPA, Ricos and Rilibak, different sigma levels are observed. Discussion: Due to using different TEa%'s for each test, different sigma levels were determined. On the other hand, because of the "poor quality" level of cTnT sigma value, decision is taken for the improvement of cTnT in our laboratory. In addition, it is observed that there is no specified TEa% for whole blood samples. Therefore, it is concluded that, for more accurate and consistent evaluations, specified matrix of TEa% values are required for whole blood samples.

Keywords

Six Sigma; Analytical Quality Management; Emergency Units; Laboratory Markers; Cardiac Biomarkers

DOI: 10.4328/JCAM.6003 Received: 13.08.2018 Accepted: 28.08.2018 Published Online: 04.09.2018 Printed: 01.01.2019 J Clin Anal Med 2019;10(1): 35-40
Corresponding Author: Fatma Ceyla Eraldemir, Department of Biochemistry, Kocaeli University Facultyof Medicine, Kocaeli, Turkey.
T.: +90 2623037256 E-Mail: ceyeraldemir@gmail.com
ORCID ID: 0000-0001-9410-8554

Introduction

Accurate, precise and rapid test results are requested from emergency laboratories. Particularly, it is vital for the management of cardiac diseases such as acute coronary syndromes (ACS) and heart failure (HF). Cardiac biomarkers are valuable for the risk assessment of cardiovascular disease, as well [1, 2]. Radiometer AQT90 Flex allows receiving very quick (within approximately 11-21 min) cardiac biomarker results. The methodology of analysis relies on detection of monoclonal antibodies in the analyzer. CKMB mass, Myoglobin (Mb), NT-pro BNP, Troponin I (cTnI) and Troponin T (cTnT) in the whole blood are detected rapidly with this analyser. By this way, early detection of cardiac damages becomes possible.

Quality of preanalytical, analytical and postanalytical process is significant for the correct test results in laboratories. For quality of analytical process, each test is confirmed daily, with internal quality reference materials before analysis of patient's samples. Additional to daily controls, external quality assessments are performed every month. This confirmation methodology allows laboratories to compare their results with the same reference material and get aligned for the results.

Sigma metrics are calculated using internal quality control (IQC) and external quality control (EQC) data. And this simple calculation method allows laboratory experts to interpret analytical quality level of the test results. Sigma methodology shows the degree of process accuracy and stability in terms of quality. Processes having 4 sigma level are accepted as representing "average quality performance" with 63 defects per million, 6 sigma level is accepted as "the best" or ''world-class quality'' of performance with 0,002 defects per million [3,4]. Increase in sigma levels expresses reliable and better quality of test results. While sigma levels are calculated, total allowable error ratio (TEa%)'s are used. TEa% is a simple comparative quality concept used to define acceptable analytical performance same as IQC and EQC outcomes. TEa% defines maximum error limitation for running test in the laboratory. For each test, we may compare different TEa%'s from different references. It is important to decide which TEa% is appropriate for our laboratory.

In this study, TEa%s of American Association of Bioanalysts (AAB), 2004 update of the Spanish Society of Clinical Chemistry and Molecular Pathology table of desirable quality specifications based on Biological variation (BV), 2012 update of the Royal College of Pathologists of Australasia and the Australasian Clinical Biochemist association Quality Assurance Program (RCPA), Ricos and Rilibak were used to calculate sigma metrics. In this manner, the analytic quality of Radiometer AQT90 Flex cardiac biomarkers are investigated consecutive six months in our emergency laboratory by sigma metric method. Especially, the study was conducted to determine which TEa% is appropriate for our laboratory and perform improvement studies for poor quality tests.

Material and Method

The IQC and EQC data of 5 cardiac biomarkers of the emergency laboratory department between December 2017 and May 2018 were used to calculate sigma levels. The AQT90 FLEX (Radiometer) analyzer was used to measure cardiac biomarkers which include cTn I, cTn T, CKMB mass, Mb, and NT-proBNP. Two levels of internal control materials were obtained from Technopath Multi-check cardiac normal level-IQC1 and pathologic level-IQC2 (reference number: 944-513, 944-514). They were assayed once a day, two levels in the morning at 08:00 a.m. IQC data were used to calculate mean, standard deviation (SD) and coefficient of variation (CV)% of the tests separately for each month. CV% of the test were calculated with "CV% = (SD × 100) / mean" formula.

The mean of bias% separately for each month period was used for calculation of sigma levels. Data from EQC, were obtained once a month by External Quality Assurance Services (EQAS). Cardiac markers program BC39 was used to provide bias values with the mentioned formula: "Bias% = (mean of peer group – mean of our lab / mean of peer group) × 100".

TEa%'s of AAB, BV, RCPA, Ricos and Rilibak were used to calculate sigma metrics. The sigma metrics for 5 tests was calculated by "Sigma = (TEa% – Bias%) / CV%" formula. Among three Radiometer AQT90 Flex analyzers, the sigma levels of the most used analyzer were calculated for each month.

Results

TEa%'s of the tests according to AAB, BV, RCPA, Ricos, and Rilibak were presented in Table 1. CV%'s for IQC1 and IQC2 samples for each consecutive six months were shown in Table 2. Bias%'s were given in Table 3 and sigma levels according to AAB, BV, RCPA, Ricos and Rilibak TEa%'s were given in Table 4. The tests were divided into four groups according to their sigma levels.

Table 1. TEa%'s of the tests according to AAB, BV, RCPA, Ricos and Rilibak.

Tests	AAB TEa%	BV TEa%	RCPA TEa%	Ricos TEa%	Rilibak TEa%
CK MB mass	a	31.2%	c	30.06% (S)	d
Myoglobin	a	b	c	19.60% (S)	d
NT-proBNP	a	b	20% (>125 ng/L)	13.00% (S)	d
Troponin I	0.9 ng/mL or 30%	b	±0.002 up to 0.010µg/L; 20% >0.010µg/L	76.36%(P)	33.00%
Troponin T	0.1 ng/mL or 30%	b	±0.01 up to 0.050µg/L; 20% >0.050µg/L	48.9% (S)	33.00%

TEa: Total allowable error; AAB: American Association of Bioanalysts, BV: 2004 update of the Spanish Society of Clinical Chemistry and Molecular Pathology (SEQC) table of Desirable Quality Specifications based on Biological Variation, RCPA: 2012 update of the Royal College of Pathologists of Australasia and the Australasian Clinical Biochemist association Quality Assurance Program, aTEa: value is not available according to AAB. bTEa: value is not available according to BV, cTEa: value is not available according to RCPA, dTEa: value is not available according to Rilibak, S: serum, P:plasma.

Tests having sigma levels below 3.0 are evaluated as ''poor'' and named as Group 1 tests. Group 2 tests are the ones having sigma levels between 3.0 and 3.99, evaluated as ''acceptable''. Group 3 tests have sigma levels between 4 and 5.99 and named as ''good'', whereas group 4 have sigma levels above 6 named as ''world class quality''. For consecutive six months tests of groups 1,2,3 and 4 were given in Table 5. The analytical performance of the tests in Group 1 was poor whereas the tests in Group 4 had world-class analytical quality.

Table 2. CV%'s for IQC1 and IQC2 samples for consecutive six months.

	CV%											
Months Instruments	Dec2017 AQT902		Jan2018 AQT902		Feb2018 AQT902		March2018 AQT902		April 2018 AQT901		May2018 AQT901	
Tests	IQC1	IQC2	IQC1	IQC2	IQC1	IQC2	IQC1	IQC2	IQC1	IQC2	IQC1	IQC2
CK MB mass (ug/L)	5.11	23.99	5.74	2.48	2.79	4.25	4.04	1.65	3.61	3.1	3.65	4.06
Myoglobin (ug/L)	20.99	6,8	5.09	3.7	4.3	2.75	3.62	3.05	2.78	2.74	2.44	3.63
NT-proBNP (ng/L)	12.76	7.75	7.01	4.26	3.95	3.02	4.53	6.74	5.77	6.76	7.49	5.39
Troponin I (ug/L)	9.66	38.88	8.71	4.7	5.83	4.72	8.83	3.8	5.02	6.65	7.95	5.31
Troponin T (ug/L)	9.54	9.95	9.7	5.24	8.48	6.69	10.39	6.87	13.96	8.23	11.23	9.44

Note: IQC:internal quality control, EQC: External quality control

Table 3. Bias%'s calculated from EQC data.

Tests	Bias%					
Months	Dec 2017	Jan 2018	Feb 2018	March 2018	April 2018	May 2018
Instruments	AQT902	AQT902	AQT902	AQT902	AQT901	AQT901
CKMB mass (ug/L)	0.70	2.32	0.87	4.76	1.71	5.92
Myoglobin (ug/L)	4.76	3.50	15.68	13.63	0.56	0.56
NT-proBNP (ng/L)	4.91	8.72	1.58	1.63	1.03	2.99
Troponin I (ug/L)	0	4.16	1.56	16.66	5.55	2.96
Troponin T (ug/L)	12.34	33.63	39.48	16.86	7.72	1.44

Note. EQC: External quality control

Discussion

In order to manage vital cardiac diseases, the emergency laboratory should give test results in a short turnaround time (TAT) [5].

Laboratory experts prefer Radiometer Flex 90 hence it allows short TAT. At the same time, good quality test outcomes are also more important in the management of cardiac diseases in emergency units. For this purpose, analytic quality of cardiac biomarkers was evaluated in our emergency laboratory by six sigma metric. The tests were observed by dividing the tests into groups according to the sigma levels. The tests needed to be improved were identified by TEa% of AAB, BV, RCPA, Rilibak, Ricos.

TEa%'s for the CKMB mass are established by only BV and Ricos. According to both Ricos and BV, CKMB mass seemed to have problems only at IQC2 in December. In other months, performance was at good levels, even at world-class quality standards.

Mb could be evaluated only according to Ricos because of Ricos gave TEa% only for Mb. In December, February, and March, sigma levels for both IQC levels performed poorly. In January, IQC1 was evaluated as acceptable, IQC2 as good quality. In May, IQC2 was shown in good, IQC1 in world-class quality. In April, sigma levels were detected as world-class quality for Mb. Mb levels increase early from 90 pg/mL to 250 ng/mL within 90 min after acute myocardial infarction (AMI), vital rapidly diagnosis of cardiac disease [6,7,8].

For diagnosis of AMI in the emergency units, myoglobin is a better marker rather than CKMB mass or cTnT within 3-6 hours after inception of symptoms, while CKMB mass is better at 7th hours. The test features are affected by the possibility of the existence of AMI in the patients and by the size of infarct [9]. As a result, having correct values for all cardiac biomarkers are significant while clinicians decide about the diagnosis of cardiac diseases.

NT-proBNP was evaluated only according to RCPA and Ricos. In December, both IQC level were evaluated as "poor" by RCPA and Ricos. In January, only IQC2 was shown as ''poor'' by RCPA, but Ricos said "poor" for both two IQC levels. Therefore generally poor outcomes were received for Ricos and it was being evaluated for serum. RCPA TEa%'s were found to be suitable for our laboratory because our samples are whole blood samples.

Sigma levels of NT-proBNP were evaluated as ''acceptable'', ''good'' or ''world-class quality'' for February, March, April but generally at one IQC level. Therefore, NT-proBNP was reported as "improvement studies are required".

NT-proBNP ensures significant prognostic value for HF patients. It is important for discharge and for hospitalization of HF that are robust. Additionally, it is also robust and independent factor of all-cause death and HF rehospitalization [2, 10].

NT-proBNP is a significant biomarker of adverse events post-AMI such as death, HF and less strongly for recurrent cardiac ischemia [1].

TEa%'s of cTn I were identified as AAB 30%, RCPA 20%, Ricos 76.36% (for plasma), Rilibak 33% excepting BV. TEa% of Ricos was very high compared to others and was reported as the designated value for plasma. We did not choose the TEa%'s for Ricos serum because our samples were whole blood samples. Sigma levels of cTnI for IQC2 were detected as ''poor'' quality by AAB, Ricos, and Rilibak in January. According to RCPA, both two IQC levels showed ''poor'' sigma metric quality in this month. In December, while IQC1 of cTnI was ''world-class'' quality, IQC2 was ''poor'' by Ricos. Consequently, only cTnI was world-class quality in December only according to Ricos. Sigma levels of IQC1 were poor in January by AAB and RCPA. However, when IQC1 was evaluated by Ricos, it was world class quality. Because of this serious difference for evaluation results, it was decided to use TEa% of Rilibak (33%) in our laboratory for cTnI. While IQC2 (in December) and IQC1 (in March) was poor, IQC1 (in December) was evaluated as acceptable, IQC2 as good quality (Group 3). Generally, sigma levels of cTnI were acceptable or more world class quality for consequent six months.

According to the study conducted by Young et al., National Centre of Clinical Laboratories (NCCL) of China, TEa% is taken as 30% and sigma levels for cTn I and cTnT were calculated as 5 and 3.8 respectively. However, NCCL study was conducted by using a serum. [11].

Table 4. Sigma levels of the tests according to AAB, BV, RCPA, Ricos and Rilibak.

Months-Instrument	Tests	Sigma AAB		Sigma BV		Sigma RCPA		Sigma Ricos		Sigma Rilibak	
		IQC1	IQC2	IQC1	IQC2	IQC1	IQC2	IQC1	IQC2	IQC1	IQC2
Dec 2017 AQT902	CKMBmass(ug/L)			5.96	1.27			5.74	1.22		
	Myoglobin (ug/L)							0.70	2.18		
	NT-proBNP (ng/L)					1.19	1.94	0.63	1.04		
	Troponin I (ug/L)	3.10	0.77			2.07	0.51	7.90	1.96	3.41	0.84
	Troponin T (ug/L)	1.85	1.77			0.80	0.76	3.83	3.67	2.16	2.07
Jan 2018 AQT902	CKMBmass(ug/L)			5.03	11.74			3.42	11.18		
	Myoglobin (ug/L)							3.16	4.35		
	NT-proBNP (ng/L)					1.60	2.64	0.61	1.00		
	Troponin I (ug/L)	2.96	5.49			1.81	3.37	8.28	15.36	3.31	6.13
	Troponin T (ug/L)	*	*			*	*	1.57	2.91	*	*
Feb 2018 AQT902	CKMBmass(ug/L)			10.87	7.13			10.46	6.86		
	Myoglobin (ug/L)							0.91	1.42		
	NT-proBNP (ng/L)					4.66	6.09	2.89	3.78		
	Troponin I (ug/L)	4.87	6.02			3.16	3.90	12.83	15.84	5.39	6.66
	Troponin T (ug/L)	*	*			*	*	1.11	1.40	*	*
March 2018 AQT902	CKMBmass(ug/L)			6.54	16.02			6.26	15.33		
	Myoglobin (ug/L)							1.64	1.95		
	NT-proBNP (ng/L)					4.05	2.72	2.50	1.68		
	Troponin I (ug/L)	1.51	3.50			0.37	0.87	6.76	15.66	1,85	4.28
	Troponin T (ug/L)	1.26	1.91			0.30	0.45	3.08	4.66	1,55	2.34
April 2018 AQT901	CKMBmass(ug/L)			8.16	9.5			7.85	9.14		
	Myoglobin (ug/L)							6.84	6.94		
	NT-proBNP (ng/L)					3.28	2.80	2.03	1.77		
	Troponin I (ug/L)	4.87	3.67			2.87	2.16	14.10	10.64	5.46	4.12
	Troponin T (ug/L)	1.59	2.70			0.87	1.49	2.94	5.00	1.81	3.07
May 2018 AQT901	CKMBmass(ug/L)			6.92	6.22			6.66	5.94		
	Myoglobin (ug/L)							7.80	5.24		
	NT-proBNP (ng/L)					2.27	3.15	1.33	1.85		
	Troponin I (ug/L)	3.40	5.09			2.14	3.20	9.23	13.82	3.77	5.65
	Troponin T (ug/L)	2.54	3.02			1.65	1.96	4.22	5.02	2.81	3.34

*: bias% is higher than total allowable error ratio (TEa%), sigma level of test could not be calculated.
AAB: American Association of Bioanalysts, BV: 2004 update of the Spanish Society of Clinical Chemistry and Molecular Pathology (SEQC) table of Desirable Quality Specifications based on Biological Variation, RCPA: 2012 update of the Royal College of Pathologists of Australasia and the Australasian Clinical Biochemist association Quality Assurance Program, IQC:internal quality control, EQC: External quality control

The main problem in terms of sigma level was seemed to be in cTnT. It was remarkable because generally it was of poor sigma quality. TEa% for cTnT was not given by BV, therefore, it could not be evaluated according to BV standards. The cTnT gave poor sigma quality for both two IQC levels in December, February, and March by all evaluations except for Ricos. In January, all evaluation results were poor quality. In April, evaluation results were poor quality according to AAB and RCPA, where as only IQC1 was poor quality for Ricos. In May, IQC1 was poor quality for AAB and Rilibak, while both two IQC levels were poor quality for RCPA.

The sigma levels of tests below 3 are considered as the unacceptable level of quality. TEa% is a simple comparative quality concept used to define acceptable analytical performance.

However, our samples are whole blood samples and we could not meet TEa% for whole blood samples. The more reliable outcomes for our laboratory may be obtained TEa% with whole blood samples. The testing process runs quicker with whole blood samples because centrifugation and waiting for coagulation are not necessary. Therefore, it is appropriate for the emergency laboratory.

Conclusion

As a conclusion, due to using different TEa%'s for each test, different sigma levels were determined. On the other hand, because of "poor quality" sigma levels for cTnT by all references, the decision was taken for the improvement of cTnT in our laboratory. In addition, it was observed that there is no specified TEa% for whole blood samples. Therefore, it was concluded that, for more accurate and consistent evaluations, the specified matrix of TEa values are required for whole blood samples. It may be valuable suggestion for further assessment of cardiac biomarkers.

Table 5. Group1,2,3 and 4 of tests according to sigma levels for consecutive six months by AAB, BV, RCPA, Ricos and Rilibak. ts according to sigma levels for consecutive six months.

Months-Instrument	Sigma AAB		Sigma BV		Sigma RCPA		Sigma Ricos		Sigma Rilibak	
	IQC1	IQC2	IQC1	IQC2	IQC1	IQC2	IQC1	IQC2	IQC1	IQC2
Group 1 (sigma<3)										
December 2017 AQT902	Troponin T	Troponin I Troponin T		CKMB and mass	NT-proBNP Troponin I Troponin T	NT-proBNP Troponin I Troponin T	Myoglobin NT-proBNP	CKMB mass Myoglobin NT-proBNP Troponin I	Troponin T	Troponin I Troponin T
January 2018 AQT902	Troponin I Troponin T	Troponin T			Troponin I Troponin T	NT-proBNP Troponin T	NT-proBNP Troponin T	NT-proBNP Troponin T	Troponin T	Troponin T
February 2018 AQT902	Troponin T	Troponin T			Troponin T	Troponin T	Myoglobin NT-proBNP Troponin T	Myoglobin Troponin T	Troponin T	Troponin T
March 2018 AQT902	Troponin I Troponin T	Troponin T			Troponin I Troponin T	NT-proBNP Troponin I Troponin T	Myoglobin NT-proBNP	Myoglobin	Troponin I Troponin T	Troponin T
April 2018 AQT901	Troponin T	Troponin T			Troponin I Troponin T	NT-proBNP Troponin I Troponin T	NT-proBNP Troponin T	NT-proBNP		
May 2018 AQT901	Troponin T				NT-proBNP Troponin I Troponin T	Troponin T	NT-proBNP	NT-proBNP	Troponin T	
Group 2 (sigma: 3.0–3.99)										
December 2017 AQT902	Troponin I							Troponin T	Troponin I	
January 2018 AQT902						Troponin I	CKMB mass Myoglobin		Troponin I	
February 2018 AQT902					Troponin I	Troponin I		NT-proBNP		
March 2018 AQT902		Troponin I					Troponin T			
April 2018 AQT901		Troponin I			NT-proBNP					
May 2018 AQT901	Troponin I	Troponin T				NT-proBNP Troponin I			Troponin I	Troponin T
Group 3 (sigma: 4.0–5.99)										
December 2017 AQT902			CKMB and mass				CKMBmass Troponin T			
January 2018 AQT902		Troponin I	CKMB mass					Myoglobin		
February 2018 AQT902	Troponin I				NT-proBNP				Troponin I	
March 2018 AQT902					NT-proBNP			Troponin T		Troponin I
April 2018 AQT901	Troponin I							Troponin T	Troponin I	Troponin I
May 2018 AQT901		Troponin I					Troponin T	CKMBmass Myoglobin Troponin T		Troponin I
Group 4 (sigma: ≥6.0)										
December 2017 AQT902							Troponin I			
January 2018 AQT902				CKMB and mass				CKMBmass Troponin I		Troponin I
February 2018 AQT902	Troponin I		CKMB and mass	CKMB and mass		NT-proBNP	CKMBmass Troponin I	CKMBmass Troponin I		Troponin I
March 2018 AQT902			CKMB and mass	CKMB and mass			CKMBmass Troponin I	CKMBmass Troponin I		
April 2018 AQT901			CKMB and mass	CKMB and mass			CKMBmass Myoglobin Troponin I	CKMBmass Myoglobin Troponin I		
May 2018 AQT901			CKMB and mass	CKMB and mass			CKMBmass Myoglobin Troponin I	Troponin I		

Scientific Responsibility Statement

The author declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the author for this article.

Funding: None

Conflict of interest

None of the author received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Aldous SJ. Cardiac biomarkers in acute myocardial infarction. Int J Cardiol. 2013;164(3): 282-94. DOI: 10.1016/j.ijcard.2012.01.081.
2. Hill SA, Booth RA, Santaguida PL, Don-Wauchope A, Brown JA, Oremus M, et al. Use of BNP and NT-proBNP for the diagnosis of heart failure in the emergency department: a systematic review of the evidence. Heart Fail Rev. 2014; 19(4): 421-38. DOI: 10.1007/s10741-014-9447-6.
3. Nevalainen D, Berte L, Kraft C, Leigh E, Picaso L, Morgan T. Evaluating laboratory performance on quality indicators with the six sigma scale. Arch Pathol Lab Med. 2000; 124(4): 516-9.
4. Bozkaya G, Murat Aksit M, Aksit MZ. Evaluation of clinical chemistry tests in emergency laboratory by sigma metrics. Turk J Biochem. 2018; 43(1): 9–14.
5. Lu Y, Leong W, Wei B, Yu P, Wang C, Ying Y, et al. An Evaluation of Laboratory Efficiency in Shanghai Emergency by Turn Around Times Level. J Clin Lab Anal. 2015; 29(4): 334-41. DOI: 10.1002/jcla.21775.
6. Sallach SM, Nowak R, Hudson MP, Tokarski G, Khoury N, Tomlanovich MC, et al. A Change in Serum Myoglobin to Detect Acute Myocardial Infarction in Patients with Normal Troponin I Levels. Am. J. Cardiol. 2004; 94: 864–7. DOI: 10.1016/j.amjcard.2004.06.019.
7. Wang Q, Liu F, Yang XH, Wang KM, Wang H, Deng X. Sensitive point-of-care monitoring of cardiac biomarker myoglobin using aptamer and ubiquitous personµal glucose meter. Biosens. Bioelectron. 2015; 64: 161–4. DOI: 10.1016/j.bios.2014.08.079.
8. Yang Z, Wang H, Guo P, Ding Y, Lei C, Luo Y. A Multi-Region Magnetoimpedance-Based Bio-Analytical System for Ultrasensitive Simultaneous Determination of Cardiac Biomarkers Myoglobin and C-Reactive Protein. Sensors (Basel). 2018; 18(6): 1765. DOI: 10.3390/s18061765
9. de Winter RJ, Koster RW, Sturk A, Sanders GT. Value of myoglobin, troponin T, and CK-MBmass in ruling out an acute myocardial infarction in the emergency room.Circulation. 1995; 92(12): 3401-7.
10. Linssen GCM, Jaarsma T, Hillege HL, Voors AA, van Veldhuisen DJ. A comparison of the prognostic value of BNP versus NT-proBNP after hospitalisation for heart failure. Neth Heart J. 2018. DOI: 10.1007/s12471-018-1145-x.
11. Xia Y, Xue H, Yan C, Li B, Zhang S, Li M, et al. Risk analysis and assessment based on Sigma metrics and intended use. Biochem Med (Zagreb). 2018; 28(2). DOI: 10.11613/BM.2018.020707.

How to cite this article:
Eraldemir FC. Evaluation of analytical quality of cardiac biomarkers in the emergency laboratory by sigma metrics. J Clin Anal Med 2019;10(1): 35-40.