# Evaluation of analytical quality of cardiac biomarkers in the Karapınar State Hospital emergency laboratory by sigma metrics

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# Summary

I will give an information about Six-Sigma Methodology and application of six sigma methodology to cardiac markers.

- This research was performed in Karapınar State Hospital and I will share our results in my presentation.

# CONTENT

**Six Sigma Metodology**

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# Introduction

- In clinical laboratories, clinical laboratory processes can be divided into five basic stages;
  pre-pre-analytical,
  pre-analytical,
  analytical
  post-analytical
  post-post-analytical.
- Errors that will appear in each phase may negatively affect the test results
- Total error should be calculated for each phase (1, 2).
- When the laboratory errors are evaluated according to these stages;
- Errors mostly occur at the pre-analytical phase(68%), secondly at post-analytical phase (19%) and finally the lowest rate is found at the analytical phase(13%) (3).

1. Coskun A. Six Sigma and laboratory consultation. Clin Chem Lab Med 2007; 45(1): 121–3.
2. Co kun A, Inal T, Unsal I, Serteser M. Six Sigma as a Quality Management Tool: Evaluation of Performance in Laboratory Medicine. Quality Management and Six Sigma 2010; 247–61.
3. Paolo C, Plebani M. Errors in a Stat Laboratory: Types and Frequencies 10 Years Later. Clin Chem 2007; 53(7):1338–42.

# Introduction

- There are two types of measurement errors: random and systematic errors.
- Inaccuracy and imprecision are basic parameters for systematic and random errors (4).
- These parameters are expressed as bias and coefficient of variation (CV), and can be used to calculate the total error (TE) (5).
- The total error of a test is calculated by: TE = Bias + 1.65CV.

4. Huysal K, Budak YU. Application of sigma metrics for the assessment of quality assurance using theMQ-2000 PT HbA1c analyzer. Biochem Med (Zagreb). 2015; 25(3): 416–20.
5. Westgard JO, Klee GG. Quality management. In: Burtis CA, Ashwood ER, Bruns DE, eds. Tietz textbook of clinical chemistry and molecular diagnostics St. Louis, MO: Elsevier Saunders, 2006: 485–529.


- The Six-Sigma Methodology evaluate the quality of the analytical phase by combining bias, imprecision and allowable total error (TEa) (2).

- TEa is a useful parameter for determinig required laboratory test quality which combines the effects of systematic and random errrors.

(3).

- The clinical application of Six-Sigma quality management involves the combined use of quality requirements and laboratory performance to evaluate whether a laboratory meets clinical testing standards.

**2. Coskun A, Inal T, Unsal I, Serteser M. Six Sigma as a Quality Management Tool: Evaluation of Performance in Laboratory Medicine. Quality Management and Six Sigma 2010; 247–61.**

**3. Paolo C, Plebani M. Errors in a Stat Laboratory: Types and Frequencies 10 Years Later. Clin Chem 2007; 53(7):1338–42.**

# Six Sigma Methodology

- Six Sigma metrics can serve as a self-assessment method in guiding clinical laboratory to make QC strategy and plan QC frequency.
- It's very helpful to implement this metrics into clinical laboratory daily analytical processes in order to produce accurate test results.

  High sigma values means low analytical errors and acceptable test results (9).

  Low sigma metric value is accepted as an error or a defect.
- The defect value is measured in defects per million (DPM) (10).

  The Six-Sigma is focused to control a process in 6 standard deviations (SD) and it is equal to 3,4 DPM.

  The success with Six Sigma Quality is accepted as the perfection goal.
- A performance at the 3-sigma level is considered as the minimum quality for manufacturing process (11,14).

Table: 1 Sigma conversion table

| *MFYO | Sigma (σ) |
|---|---|
| 690000 | 1,0 |
| 308000 | 2,0 |
| 66800 | 3,0 |
| 6210 | 4,0 |
| 320 | 5,0 |
| 3,4 | 6,0 |

# Aim

- In the present study , we aimed to evaluate the analytical performance of our emergency laboratory by using the internal quality control data of cardiac biomarkers(Troponin I (cTnI), CKMB mass, Myoglobin (Mb) and by calculating process sigma values.

# Material and Methods

- The present study was conducted in the clinical chemistry laboratory of the Karapınar State Hospital.
- Internal quality control (IQC) data of 3 analytes were analyzed retrospectively over a period of 4 months from January 2019 to April 2019 using Siemens Advia Centaur Classic (Siemens Healthcare Diagnostics, Tarrytown, NY, USA).
- 3 serum cardiac tests were included: Troponin I (cTnI), CKMB mass, Myoglobin (Mb). All reagents were obtained from Siemens and used according to the manufacturer's package inserts.
- Both normal (IQC1) and pathological (IQC2) levels of QC materials were assayed before analysing of patient samples every day.
- Serocheck NormControl and Serocheck PathControl QC materials were belong to Serocon Diagnostics company (Konya, Turkey).
- The instruments was calibrated regularly.
- IQC data were obtained from Laboratory Data Management System.
- Following the determination of mean and SD values, CV, bias and sigma values were calculated according to the following formulations.

# Material and Methods

## Coefficient of variation calculation

- Imprecision, expressed as coefficient of variation ( CV%) was determined from the calculated mean and Standard deviation evaluated from internal quality control (IQC) data.

- CV is the ratio of the SD which is obtained from a data set to the mean( $\bar{x}$) and it is expressed as a percentage of variance to the mean; CV(%)=(SD/ Mean of IQC data) × 100.

## Determination of Bias

Bias was calculated as the percentage difference of the average of observed results for each analyte from the target values provided in the serocheck control package inserts.

Percent bias values of each test were calculated separately between January and April 2019.

Bias%= [(our laboratory mean of IQC data–target mean of IQC data)/target mean of IQC data]×100

# Material and Methods

## Total Allowable error (TEa)

- The sigma metrics were calculated using TEa goals from one source in order to understand the effect of TEa on estimates of Sigma metrics: the Desirable Biological Variation Database (15).

  These source is regularly updated and can be freely accessed through http://www.westgard.com.

  The TEa values of each test are presented in Table II.

## Sigma metric calculation

- Sigma (s) value was used in order to determine the analytical performance characteristics of sigma value tests by using CV (obtained from IQC data), Bias% and TEa values.

  Sigma value calculated using the standard equation:

- Sigma metric (s)= (TEa%-Bias%) / CV%

**15. Aslan D, Demir S. Six-Sigma Quality Management in Laboratory Medicine. Turk J Biochem 2005; 30 (4); 272–8.**

# Material and Methods

- Sigma values were used to determine the analytical performance characteristics of the test.
- A sigma level <3 is an indication of a poor performance procedure.
- A good performance is indicated by a sigma level >3.
- Above six sigma level is a world class performance (16).


- **16. Lakshman M, Reddy BR, Bhulaxmi P, Malathi K, Salma M et al. Evaluation of sigma metrics in a Medical Biochemistry lab. International Journal of Biomedical Research 2015; 6(03): 164–71**

# Results

- Table I shows the target mean, laboratory mean and the calculated standard deviation values of the two levels namely normal (IQC1) and pathological (IQC2) quality controls run in our laboratory for the different parameters.

| Assay Name | IQC 1 | | | | | | | | | IQC 2 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Target Mean | January | | February | | March | | April | | | January | | February | | March | | April | |
| | | Lab mean | SD | Lab mean | SD | Lab mean | SD | Lab mean | SD | | Lab mean | SD | Lab mean | SD | Lab mean | SD | Lab mean | SD |
| Troponin | 0,06 | 0,07 | 0,02 | 0,05 | 0,01 | 0,054 | 0,02 | 0,06 | 0,02 | 2,81 | 2,46 | 0,53 | 2,17 | 0,51 | 2,39 | 0,43 | 2,56 | 0,59 |
| CK-MB | 1,23 | 1,65 | 0,32 | 2,06 | 0,39 | 1,87 | 0,32 | 1,99 | 0,13 | 10,41 | 9,86 | 2,17 | 9,71 | 1,52 | 10,7 | 2,11 | 11,02 | 1,62 |
| Miyoglobin | 30,25 | 30,04 | 6,8 | 25,53 | 2,88 | 32,05 | 2,17 | 30,02 | 2,2 | 57,03 | 58,5 | 9,7 | 48,63 | 11,62 | 56,09 | 2,42 | 51,65 | 11,7 |

# Results

- Table II shows TEa, bias and coefficient of variation (CV) sigma values of the two levels of quality control for the different parameters.
- The CV% values of pathological and normal level of IQC were found as > 5% for the tests including Troponin, CK-MB and Miyoglobin for 4 subsequent months.

Table 2. TEa, bias and CV values of the two levels of quality control for the assays.

| Assay Name | IQC 1 | | | | | | | | | IQC 2 | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Tea(%) | January | | February | | March | | April | | January | | February | | March | | April | |
| | | %CV | % Bias | %CV | % Bias | %CV | % Bias | %CV | % Bias | %CV | % Bias | %CV | % Bias | %CV | % Bias | %CV | % Bias |
| Troponin | 27,91 | 28,57 | 16,66 | 20 | 16,66 | 40 | 16,66 | 33,33 | 1,6 | 21,54 | 12,45 | 23,5 | 22,77 | 12,6 | 2,84 | 23,05 | 8,9 |
| CK-MB | 30,06 | 19,39 | 34,14 | 18,93 | 67,48 | 17,11 | 29,27 | 6,53 | 61,78 | 22,01 | 5,28 | 15,65 | 6,72 | 19,7 | 2,78 | 14,7 | 5,86 |
| Miyoglobin | 19,6 | 22,63 | 0,69 | 11,28 | 14,88 | 6,77 | 5,95 | 7,28 | 0,76 | 16,58 | 2,58 | 28,89 | 14,73 | 23,9 | 1,65 | 22,65 | 9,43 |

# Results

- Table III and Table IV show that complete sigma metrics for 3 assays.
- The sigma values of Troponin, CK-MB and Miyoglobin were found as <3.

Table 3. The sigma metrics for 4 months and overall sigma metrics for the assays

| Assay Name | January | | February | | March | | April | | overall 4 months sigma metrics | |
|---|---|---|---|---|---|---|---|---|---|---|
| | IQC 1 sigma metrics | IQC 2 sigma metrics | IQC 1 sigma metrics | IQC 2 sigma metrics | IQC 1 sigma metrics | IQC 2 sigma metrics | IQC 1 sigma metrics | IQC 2 sigma metrics | IQC 1 sigma metrics | IQC 2 sigma metrics |
| Troponin | 0,39 | 0,71 | 0,56 | 0,22 | 0,28 | 1,99 | 0,79 | 0,82 | 0,51 | 0,94 |
| CK-MB | 0,21 | 1,13 | 1,98 | 1,49 | 0,05 | 1,38 | 4,85 | 1,65 | 1,78 | 1,41 |
| Miyoglobin | 0,84 | 1,03 | 0,42 | 0,17 | 2,02 | 0,75 | 2,6 | 0,45 | 1,47 | 0,6 |

Table 4. The distribution of groups and tests according to sigma values.

| Sigma metrics | IQC 1 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | January | | February | | March | | April | |
| | | IQC 1 | IQC 2 | IQC 1 | IQC 2 | IQC 1 | IQC 2 | IQC 1 | IQC 2 |
| Grup 1 (<3) | | Troponin, CK-MB, Miyoglobin | Troponin, CK-MB, Miyoglobin | Troponin, CK-MB, Miyoglobin | Troponin, CK-MB, Miyoglobin | Troponin, CK-MB, Miyoglobin | Troponin, CK-MB, Miyoglobin | Troponin, CK-MB, Miyoglobin | Troponin, CK-MB, Miyoglobin |
| Grup 2 (3–6) | | | | | | | | | |
| Grup 3 (>6) | | | | | | | | | |

Table 4 also shows that complete sigma metrics for 3 assays.

# Discussion

In this study, we analysed 3 parameters over a period of 4 months.

According to our results, For all parameters troponin, CK-MB and miyoglobin sigma values were below 3.

We should strictly follow internal QC and Westgard multi rules and pay special attention to these cardiac parameters.

**17. Nanda SK, Ray L. Quantitative application of sigma metrics in medical biochemistry. J Clin Diagn Res 2013; 7(12): 2689–91.**

**18. Litten J, Lynne N, Johnson K, Shih J. Evaluation of technopath controls on the architect family of instruments. Clin Chem Lab Med 2015; 53, Special Suppl, pp S1–S1450.**

# Discussion

- In terms of clinical laboratory, the identification of test with low sigma values (< 3σ) indicate that actions should be taken to improve analytic quality or the laboratory should use alternate methods and reagents

- Variations between our statistical data and others were due to the difference in QC samples as well as instrument and method differences.
- Sigma metrics was calculated by using TEa, bias and CV. This method is not the ideal way, but the practical way.
- The ideal ways include using reference materials or comparison with reference methods.

# Conclusion

- The results from clinical laboratory have a large impact on patients' lives.
- However, there is no particular guideline of rules implementation based on the performance of each test and method, which can cause increase of false rejection and waste of control samples for testing laboratory.

- So, choosing a specific QC procedure will decrease the false rejection and maximize the error detection (22).

22. Theodorson E. Quality assurance in clinical chemistry: a touch of statistics and a lot of common sense. J Med Biochem 2016; 35: 103–12.

# Conclusion

- Clinical laboratory focus on producing exact test results, so it make sense to implement six sigma metrics into their daily analytical processes.
- Six Sigma metrics could serve as a self assessment method in guiding clinical laboratory to make QC strategy and plan QC regularity.
- It's very helpful to realize this metrics into our laboratory daily analytical processes in order to produce precise test results.

# THANK YOU.....