Necessity of Routine Repeat Testing of Critical Values in Various Working Shifts

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ABSTRACT

Background & Objective: Accurate and timely reporting of critical values is an important issue. There is some doubt whether repeat testing of critical values would offer any advantage over single testing or not. The aim of this study was evaluation of utility of routine repeat testing of critical values in our referral center and to compare probable variations in different working shifts.

Methods: Clinical results of serum Potassium, Calcium, Blood Hemoglobin and Prothrombin Time (INR: International Normalized Ratio) were evaluated for three months.

Results: Totally, 178, 96, 67 and 107 consecutive critical values for Potassium, Calcium, Hemoglobin and INR were reported, respectively. In potassium and Hemoglobin 5.05% and 1.17% of retest runs exceeded the acceptable tolerance limit. All of the calcium retest results were within the acceptable limit. For INR, 21/107 retest results did not meet the acceptable tolerance limit, nine still were critical. Afternoon working run performance was significantly better than the two others.

Conclusion: Our observation suggests that routine repeat of hematology and chemistry critical test result is not necessary and may adversely affect patient safety measure. However, attention should be paid to results greater than analytical measurement range and all such results should be repeated before reporting.

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Introduction

The concept of "Critical Value" was first introduced by Lundberg in 1972 and since then critical value reporting has been required by different regulations and accreditation programs (1-3).

The Joint Commission International, ISO 15189 and College of American Pathologists have published well defined requirements on the identification, handling and documentation of laboratory critical values (4-7). All laboratories should develop the list of their critical test values and a documented system for timely reporting of results to responsible health care provider (3).

There is no regulatory requirement to verify test result by repeating critical value testing (3). However, repeat critical values to ensure accuracy and avoiding false positive result is a common practice (3,8).

It appears that the repeat test practices date back to years ago when less sophisticated automatic systems have been used in laboratories (9). Given

ongoing improvements and technical advances in laboratory assays (1,10), over the past decades, repeat analysis of critical values have been questioned in recent years (3).

Analytical error rates in repeat testing is estimated about 2-3% but this step leads to delay rapid release of critical value (9) and hampers patient safety goals.

In a report by Dighe *et al.*, (1,11) about 70% of surveyed laboratories had policy on repeat critical values. A CAP Q-probe analysis of 86 clinical laboratories showed that routine repeat testing of chemistry critical values (60.8% of all laboratories) was more common in comparison with hematology critical values (52.6%) (8).

However, some reported this repeat testing was associated with about 10-14 minutes delay in reporting (8). Given the attention to patient safety measures and importance of timely reporting of critical results,

several issues arose concerning the eligibility of repeating critical values (12).

Several studies have been published regarding the utility of repeat critical testing (2,3,8,10,12).

In a Q-probe analysis by CAP they recommended that laboratories should assess the reproducibility of assays in their own laboratory and patient population and discuss the weight of probable discrepant results versus delayed reporting of critical values to determine either routine retesting is necessary or not (8).

We have not found any study that addresses the variations between reproducibility of critical values in different working shifts through 24 hour day.

The aim of this study was to evaluate the utility of routine repeat testing of critical values in Shariati hospital as a referral center affiliated with Tehran University of Medical Sciences and moreover to compare probable variations in different working shifts (morning, Afternoon and Night). Four tests from biochemistry, hematology and coagulation wards were selected as representative tests being performed by various automated analyzers as follow: Calcium (Biochemistry analyzer), Potassium (Electrolyte Analyzer), Hgb (Hematology analyzer) and PT (Coagulation Analyzer).

Materials and Methods

A Clinical results of serum potassium and Calcium, Blood Hemoglobin and Prothrombin Time (INR: International Normalized Ratio) were evaluated for three months (June 2018 to August 2018) in the central laboratory of a referral tertiary hospital. The clinical specimens were from patients suffering from various clinical conditions such as neoplasia, Infection, Chronic inflammatory Disease, Trauma, surgery and etc. The primary critical value and retest results for the mentioned analytical tests in various working shifts were obtained by automated analyzers. All of the clinical results were reported by making phone calls to the responsible nurse or medical staff immediately and then the test was repeated. All the primary and secondary results were recorded.

Serum specimens were analyzed for calcium by 902 Hitachi Automatic Analyzer (Roche Diagnostics GmbH Mannheim, Germany; Hitachi High-tech Science system corporation, Japan) and 917 Hitachi Automatic Analyzer (Boehringer Mannheim, Hitachi. Ltd. Tokyo, Japan) in the morning working run and two 717 Hitachi Automatic Analyzers (Boehringer Mannheim, Hitachi. Ltd. Tokyo, Japan) during the afternoon and night shifts.

Serum Potassium level were evaluated by ISE method using two IMS-972 (Shenzhen Xilaiheng Medical Electronics Co, Ltd.) Electrolyte Analyzers and four PL1000B Electrolyte Analyzers, (Perlong Medical Equipment Co. Ltd).

Blood Hemoglobin results were obtained by running EDTA blood specimen for Complete Blood Count (CBC) on the one of the hematology analyzers (XS800i and XS500i SYSMEX CORPORATION, KOBE, JAPAN in the morning and KX21 and XS500i SYSMEX CORPORATION in the other working runs).

Citrated blood specimens were analyzed by ACL Elite and ACL7000 during the morning working run and ACL7000 during the afternoon and night shifts.

All analyzers were calibrated and maintained daily for quality control according to the manufacturers' instructions. Moreover, although method Coefficient Variation (CV) for each analysis was not the same in all working runs, all were lower than Allowable CV of laboratory.

The repeat tests were performed either on the same analyzer or another one mentioned above. We developed a form and the staff were educated to document the repeat test results on that.

The cutoff range for critical values in our laboratory are summarized in Table 1.

All critical values, repeat test results and the absolute difference or percentage difference between two test results for the above mentioned tests were calculated and then compared with our laboratory acceptable Tolerance Limit for re-runs (Table 1). If the difference between two test runs were more than this limit we called it "Large difference" (2,3,13).

Table 1. Critical values and Acceptable Tolerance Limit range for various analyses in the laboratory

Test \ Value	Critical value	Acceptable Tolerance Limit
Potassium	≤2.7 MEq/L ≥6 MEq/L	0.5 MEq/L
Calcium	≤6.5 mg/dl ≥14mg/dl	1mg/dl
Hemoglobin	≤6g/dl or ≥ 24g/dl (0 t0 7 days) ≤6g/dl or ≥ 20g/dl (>7 days)	0.5 g/dl
PT(INR)	INR≥5	10%

Results

Totally, 178, 96, 67 and 107 consecutive critical values for Potassium, Calcium, Hemoglobin and INR were reported, respectively. The distribution of large differences and mean absolute differences in various working analytical shifts are summarized in Tables 2 and 3, respectively.

Totally, 6.65% of repeat test results were out of the tolerance limit of our laboratory.

Table 2. The distribution of large differences in various working analytical runs

Test Working shifts	Potassium	Calcium	Hemoglobin	INR
Morning	3/82	0/42	0/52	9/32
Afternoon	1/32	0/21	1/33	2/33
Night	5/64	0/33		10/42
Total	9/178(5.05%)	0/96(0.00%)	1/85(1.17%)	21/107(19.6%)

Potassium

During the morning analytical shifts, 82 repeat testing for potassium critical values were performed. Among them, 56 and 26 results were in low and high critical values, respectively. The mean absolute difference between two test results was 0.09 MEq/L. Three repeat test runs were more than acceptable limit (0.57, 0.51, and 0.8 MEq/L). Two of them were in high critical values and one in low level, the latter became non critical on retest (2.49 to 3 MEq/L). In summary, 3.65% of retests did not meet the acceptable tolerance limit.

In the afternoon working shifts, twenty and twelve low and high critical potassium values were reported, respectively. The mean absolute difference was the same as morning working shift (0.09MEq/L). Except for one retest run difference value which was 0.8 MEq/L, all other results were within acceptable limit. Totally in low and high values 3.1% of results were out of tolerance limit.

At night, totally, 64 critical value results were reported (high=41 and low=23). The mean absolute difference was 0.2 MEq/L. Although no repeat test result changed the critical status, five large differences were determined (7.81%). The greatest difference was 1.48 MEq/L (the level of serum potassium changed from 7.48 to 6MEq/L in re-testing) which was related to sample that the result was more than analytical measurement range (AMR) of the method.

Using repeated measurement analysis test, there was significant difference between various working runs, meaning that at night the mean absolute difference was much higher than the others ($P<0.001$), although it was still less than acceptable tolerance limit.

Calcium

Totally, 42, 21 and 33 critical results for calcium were reported during morning, afternoon and night working runs, respectively. Among them, eight showed high critical value. The maximum and mean absolute difference between two test results were 1,0.07; 0.6,0.15 and 0.7, 0.17 mg/dl during the morning,

afternoon and night working shifts, respectively. 54.8% and 42.9% of retest results were equal to initial result in the morning and afternoon, respectively.

None of the repeat test results were out of our tolerance limit.

Hemoglobin

Eighty five critical results were determined in various working shifts (morning=52, afternoon and night=33). During the morning, except for one, all other results were equal or less than 6gr/dl (low critical value). During the morning shift, 36/52 (69.2%) results were the same as initial result. The mean Absolute difference between two test runs was 0.05 g/dl. Except for two absolute differences of 0.4 and 0.3 all other retest result differences in the morning were equal or less than 0.2 mg/dl.

In the afternoon and night working shifts, however, one retest result exceeded the tolerance limit of the laboratory (5.4 to 6). The mean absolute difference was 0.14 gr/dl.

The absolute mean difference between retest results was significantly better in the morning in comparison with afternoon and night (0.05 versus 0.14) ($P<0.001$), still less than acceptable tolerance limit.

PT (INR)

A total of 107 INR values more than 5 were reported (32, 33 and 42 results in the morning, afternoon and night, respectively). Although 21 retest results did not meet the acceptable tolerance limit, twelve results became non-critical. Among retest results with large difference, one changed to 1.97, two between 2 and 3 and the others were still more than three; some still critical.

The mean percentage difference between two test results calculated as 28.12%, 6.06%, and 23.8% in the morning, afternoon and night shift, respectively.

Using repeated measurement analysis test, significant difference was observed between various working shifts performance ($P<0.001$). Based on the results, afternoon working run revealed the best performance.

Table 3. Mean Absolute difference (MAD) of retest results in various working shifts.

MAD in various working runs / Test	Potassium (MEq/L)	Calcium (mg/dl)	Hemoglobin (gr/dl)	INR (%)
Morning	0.09	0.07	0.05	28.12
Afternoon	0.09	0.15	0.14	6.06
Night	0.2	0.17		23.8

Discussion

Accurate and timely reporting of critical values has become an important issue and in 2004 the Joint Commission mandated that reporting of these values be included in its National Patient Safety Goals (12,13). Since then, the determination and communication of critical values has been recognized as patient safety measure (14).

There is no empirical evidence to indicate the necessity and benefit of repeat critical value (10); however, many laboratories do so to avoid false positive results (3,15).

Regarding the technical advances in automation and quality management issue in the clinical laboratories over the past decades, routine repeat testing of each critical value have been questioned (10,16).

Recent data have emphasized on errors in the pre and post analytical phases (17). While repeat testing may be an unnecessary step, it delays in reporting test results without adding any value to accuracy (8). On the other hand, such errors of delayed communication of critical values may be potentially a post analytical error (12,18).

In a Q-probe analysis by CAP, median delay due to repeat testing was 17-21 minutes for 10% of laboratories and about 20% of laboratories reported at least one incident that the delay adversely affected the patient (8).

In recent years, there has been some doubt whether repeat testing of critical values would offer any advantage over single testing or not.

Chima *et al.* (19) evaluated 580 repeat tests of different analyses including Sodium, Potassium, Platelet and PT. Their results revealed that about 95.3% of repeat results did not differ significantly and concluded repeating critical values did not yield better accuracy and is an unnecessary step for that purpose (2,3,19).

In a Q-probe analysis by CAP (8) (evaluation of 86 clinical laboratories for repeat testing of Potassium, Glucose, Platelet and White Blood Cell) they reported routine repeat analysis of critical values as a common practice. It was more common in Chemistry (60.8%) versus hematology (52.6%). Most laboratories did not have formal definition for significant difference between results. According to their findings more than 99% of repeat test results for Potassium, Glucose and WBC were still critical. For Platelet, 1.9% were no longer critical and 1.7% were considerably different. Finally,

they concluded that routine repeat analysis of automated chemistry and hematology critical values is unlikely to be useful and even may adversely affect patient care (8).

Munoz (20) believes that repeating critical hematology results is not warranted if analyzer does not flag the result (8,20).

There are some other studies discussing the utility of repeat testing of critical values (2,3,8,10,12,19-23).

However, to our knowledge, there are no data regarding the differences of performance in various analytical working shifts during a 24 hour period. Shortage of staff, tiredness, excess work load or other factors may adversely affect the quality of performance in both analytical and extra-analytical phases. So, in the present study we decided to evaluate the utility of repeat testing of critical values during a 24 hour cycle.

Regarding CAP Q-probe report, most laboratories did not have formal definition for significant difference between the results (8). This definition has been variable throughout the literature ranging from biologic variation, subjective expert opinion, clinical survey consensus, regulatory requirements or etc. (10,24). Some studies, have used CAP or CLIA total allowable error or proficiency testing criteria for comparison (2,10,12,25), while some others have had their own definition (3). We compared the results based on our laboratory acceptable tolerance limit, which we had defined based on our method imprecision, CAP or CLIA allowable error.

In our study, the total mean absolute difference for calcium in 24 hour evaluation was 0.13 mg/dl and all of the repeat critical values have been within acceptable tolerance limit. It was the same as reported by Motie *et al.* (2). However, 0.9% (10) and 4.9% (12) unacceptable results were reported in another study.

Totally 178 repeat testing of Potassium critical values were evaluated and 94.95% of retest results were within our acceptable tolerance limit.

Three sample results had become non-critical on repeat testing (one in the morning and two in the afternoon, among them one had become normal). The large differences (>0.5 MEq/L) were almost seen in high critical values, which on repeat testing the results were still critical. One of the most noticeable differences was related to the sample with values greater than the AMR

(Potassium=7.48 MEq/L) which on repeat test run decreased to 6MEq/L). In a study by Onyenekwu *et al.*, (12), 7.1% of Potassium critical values were out of acceptable limit (0.5MEq/L). The results with unacceptable difference were high critical values (8.5 to 7.4 and 7.8 to 6 MEq/L) (12). So, the pattern was in accordance with the present study.

We identified that the performance of the morning and afternoon working runs are much better than night regarding the differences in retest results. However, although more difference was observed, it was still less than tolerance limit and no change in critical status was reported. Thus, probably it is not clinically significant.

In hematology section, amongst 85 repeat test runs in various working runs, except for one, all were low critical results. Except for one, none of the repeat results were out of the acceptable tolerance limit and 36/52 and 14/33 repeat test results were the same as initial values in the morning and night shifts, respectively.

Moreover, except for two test results, the maximum absolute difference between two test runs in the morning was equal or less than 0.2 gr/dl, whereas at night 5 samples showed differences more than 0.2 gr/dl. These little variations especially in the morning shifts, could be due to low degree of imprecision inherent in automated hematology analyzers as mentioned by Toll *et al.* (3). However, at night we observed less reproducibility; although not adversely affected critical value reporting, it could be explained by some pre-analytical interferences such as inadequate inversion of sample when sampling or prior to analysis.

Motie *et al.*, (2) also did not find any unacceptable results in repeat testing of Hemoglobin critical values.

The most challenging test in our study was PT (INR). Among 107 repeat critical INR values, twenty one (19.6%) repeat results were out of our acceptable tolerance limits (9, 2 and 10 retest results in morning, afternoon and night, respectively). The frequency of large difference between two test runs was significantly different in various working runs and afternoon showed significantly better performance than the other two runs. Since the INR ≥ 5 is out of AMR of our analyzer, irrespective of critical status, it should be repeated as Niu *et al.*, (10) recommended for chemistry critical values.

In a study by Toll *et al.* (3), they subdivided high PT values in to three subgroups as high (37-49 sec), higher (50-62 sec) and highest (63-74 sec) (3). According to their observation, among the mean range of their critical PT values between 37.4 to 74.8 seconds, 99.4% of specimens on the repeat test runs showed a maximum difference of 4 seconds. INR status was not included in their report. In another study by Motie *et al.* (2), they observed that among 104 critical INR values, 25.96% of repeat samples had equal result as initial test run and the frequency of outliers were 4.8%. Their acceptable tolerance limit was +/-15% (2).

In our opinion, the discrepant result appears to be due to different policies for critical value definition and management. In our study, except for two, all other 19

significant different retest results showed PT values greater than 33 seconds which is again highly abnormal, though not critical in our laboratory.

On the other hand, INR ≥ 5 is out of our AMR, so, we recommend all INR values greater than 5 to be repeated before reporting the result in our laboratory in all working runs.

Conclusion

Finally, although some differences were observed between various working runs, they do not appear to be clinically significant. Thus, we suggest that in the absence of specific evidence (such as results greater than AMR), repeat critical values testing is not necessary and may adversely affect patient safety measure. We recommend that all laboratories should assess the reproducibility of their own implementation of critical value reporting policy.

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Conflict of Interest

The authors declared that there is no conflict of interest regarding the publication of this article.

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