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Original Article

Blood urea nitrogen/creatinine change ratio as a delta check method for dialysis specimens

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Abstract: The delta check is used in clinical laboratories to detect specimen mislabeling or misidentification. However, test results can differ markedly pre-versus post-dialysis, and the delta check in fact typically has little value, as well as being labor intensive. We propose the "blood urea nitrogen/creatinine change ratio" (BCCR) as a new delta check method for dialysis cases. A total of 1,116 specimens with same-day pre- and post-dialysis test results were analyzed. Also, the performance of the BCCR was evaluated by simulating specimen mix-up. Among the 1,116 specimens, the median BCCR was 0.80 and the 2.5th, 25th, 75th, and 97.5th percentiles were 0.62, 0.74. 0.84, and 0.93, respectively. In the simulated misidentification dataset, the median BCCR was 0.79 and the 2.5th, 25th, 75th, and 97.5th percentiles were 0.34, 0.61, 1.02, and 1.77, respectively. When the 2.5th and 97.5th percentile values of the BCCR were set as the upper and lower limits, the delta check detected 61.0% of the simulated misidentified specimens. In summary, the BCCR enables detection of changes in important measures and could reduce the rate of false-positives.

Keywords: Delta check, BUN/Cr, dialysis, blood urea nitrogen/creatinine change ratio, BCCR

Introduction

Recent advances in laboratory automation have enhanced the test capacity of clinical laboratories. However, the processing of specimens, such as phlebotomy and labeling, remains dependent on manual labor. During pre-analytical preparatory processing, samples can be misidentified or mislabeled [1]. Such errors are not easily detected using the test results currently obtained, and are typically only reported by clinicians when a result shows a discrepancy with the clinical state of the patient.

The delta check is performed in clinical laboratories to detect such errors and involves comparing current and previous test results. The delta check methods used most frequently in clinical laboratories are the delta difference (difference between the current value and a previous value), the delta percentage change (ratio of the delta difference to the current value), the rate difference (ratio of the delta difference to the delta interval, which is the period between the previous and current results), and the rate percentage change (ratio of the delta percentage change to the delta interval) [2, 3]. The delta check method is largely dependent on variation in the test item over time [4, 5].

Test results flagged by a laboratory information system as exceeding a preset delta check limit should be reviewed to determine the cause of the variation, which could be misidentification [3, 6]. However, in patients undergoing dialysis, pre- and post-dialysis test results differ significantly, and a delta check typically has little value and requires considerable labor, so it is often not performed.

We evaluated differences in common biochemical measures pre-versus-post-dialysis, and suggest the BCCR as a new delta check method for dialysis cases.

Materials and methods

The same-day pre- and post-dialysis test results for blood urea nitrogen (BUN), creatinine (Cr), sodium (Na), potassium (K), chloride (Cl), total

calcium (Ca), phosphorus (P), and total CO_2, of 1,116 specimens, were used in the analysis. The delta check limits were calculated as follows:

• Delta difference = current value - previous value

• Delta percent change = delta difference ÷ previous value

• Rate difference = delta difference ÷ delta time*

• Rate percent change = delta percentage change ÷ delta time*

*Delta time = current test date - previous test date

However, because the pre- and post-dialysis tests were performed on the same day, the rate difference and percentage change were not evaluated. The BCCR was calculated as follows:

(BUN/Cr ratio post-dialysis) ÷ (BUN/Cr ratio pre-dialysis).

To evaluate sample misidentification, post-dialysis test results were simulated. To this end, the post-dialysis specimen identification numbers were shuffled and randomly matched to those of pre-dialysis specimens. The results of one post-dialysis specimen were changed to those of another post-dialysis specimen. The pre- and post-dialysis results had distinct distributions, and only the post-dialysis specimen was considered to be misidentified.

The Wilcoxon test was used for the analysis; $P < 0.05$ was considered indicative of statistical significance. Statistical analyses and misidentification simulations were performed using code written in the R language and graphics were produced using the ggplot2 package.

Results

Table 1 shows the results of the 1,116 pre- and post-dialysis blood specimens, and **Figure 1** shows the distribution of the test results. The results of all test items differed significantly between the pre- and post-dialysis specimens ($P < 0.05$). The median delta differences and delta percentage changes in BUN, Ca, Cl, Cr, K, Na, P, and TCO_2 were -40.70 (-68.94%), 1.90 (21.79%), -1.0 (-1.0%), -6.30 (-61.11%), -1.50 (-29.17%), 1.0 (0.72%), -2.50 (-51.43%), and 5.00 (26.09%), respectively. Although BUN and Cr showed the most marked changes, and Na and Cl the least marked, the BUN/Cr ratios of pre- and post-dialysis samples were strongly correlated ($r^2 = 0.8975261$, $P < 0.05$) (**Figure 2**).

The median BCCR was 0.80 and the 2.5th, 25th, 75th, and 97.5th percentiles were 0.62, 0.74. 0.84, and 0.93, respectively. For the simulated misidentified post-dialysis specimens, the median BCCR was 0.79 and the 2.5th, 25th, 75th, and 97.5th percentiles were 0.34, 0.61, 1.02, and 1.77, respectively. **Figure 3** shows that the simulated BCCR distribution was wider than that of the actual specimens. When the 2.5th and 97.5th percentile values of the BCCR were set as the delta limits, 61.0% (681/1116) of the simulated misidentified specimens were out of limits.

Discussion

Clinical laboratory testing can be divided into preanalytic, analytic, and postanalytic phases, all of which are potential sources of error. However, the preanalytic phase is the most vulnerable to error. Although specimen mix-up is rare, it is the one of the most serious errors and a major concern for clinical laboratories in the preanalytic phase [6-8]. Delta check, which involves comparing current and previous results to determine whether the difference is within a predefined acceptable range, is used in clinical laboratories to detect specimen mix-up [2, 3].

Various methods and limits have been suggested to increase the accuracy of delta check. For instance, a multivariate delta check using multiple test items and machine learning of the characteristics of a given test item have been proposed [5, 8-10]. However, the most commonly used delta check methods are the absolute change and percentage change over time. Because most current laboratory information systems and middleware products do not support multi-analyte delta check, clinical laboratories focus on single analytes [11]. The most common cause of delta check alerts is a treatment effect, followed by a change in physiologic state as indicated by hemolysis, lipemia, or icteric specimens [2].

Table 1. Distribution of the pre- and post-dialysis test results, and delta check values

	Mean		SD		Median		P	Delta Difference (%)			Delta Percentage Change (%)		
	Pre	Post	Pre	Post	Pre	Post		2.5 Percentile	Median	97.5 Percentile	2.5 Percentile	Median	97.5 Percentile
BUN	61.00	19.00	17.80	7.77	58.80	17.90	< 0.05	-72.51	-40.70	-20.44	-82.43	-68.94	-53.77
Ca	8.92	10.80	0.83	0.94	8.90	10.90	< 0.05	-0.20	1.90	3.90	-1.83	21.79	50.00
Cl	99.50	98.50	3.30	2.63	99.00	99.00	< 0.05	-8.00	-1.00	6.00	-7.55	-1.00	6.13
Cr	10.30	4.03	3.09	1.53	10.20	3.80	< 0.05	-10.01	-6.30	-2.79	-72.97	-61.11	-45.65
K	5.17	3.64	0.75	0.40	5.15	3.60	< 0.05	-2.90	-1.50	-0.50	-45.35	-29.17	-12.73
Na	137.00	138.00	2.81	2.35	137.00	138.00	< 0.05	-4.00	1.00	7.00	-.82	0.72	5.22
P	5.19	2.50	1.55	0.68	5.00	2.40	< 0.05	-5.40	-2.50	-0.80	-68.97	-1.43	-23.01
TCO_2	21.00	26.20	3.42	2.51	21.00	26.00	< 0.05	-2.00	5.00	11.00	-7.14	26.09	68.75

BUN, blood urea nitrogen; Ca, total calcium; Cl, chloride; Cr, creatinine; K, potassium; Na, sodium; P, phosphorus; TCO_2, total CO_2.

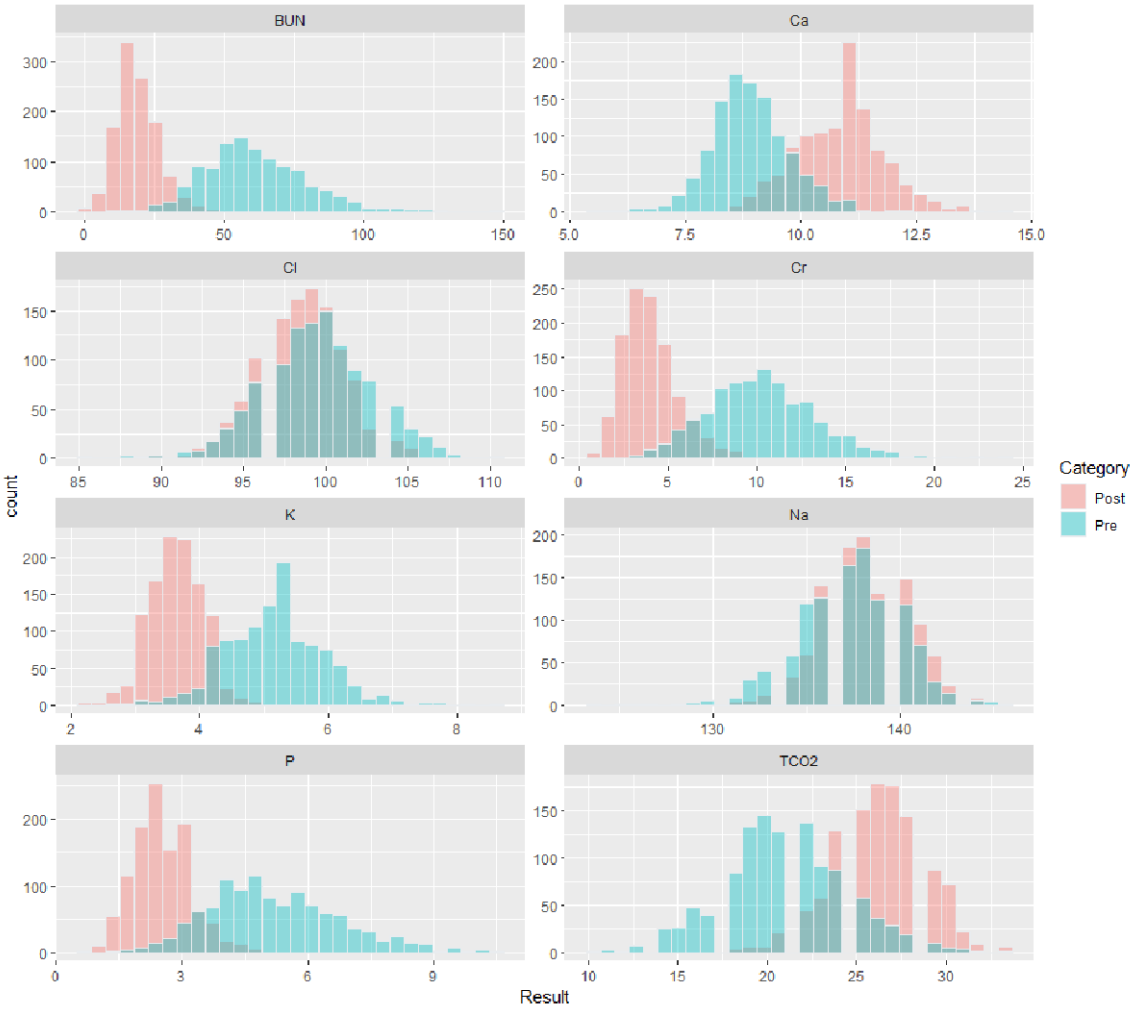

Figure 1. Distribution of the pre- and post-dialysis test results.

End-stage renal disease patients require renal replacement therapy. In such patients, a battery of tests is performed to evaluate renal function and the adequacy of dialysis, including BUN, Ca, Cl, Cr, K, Na, P, and TCO_2 tests. The BUN level indicates how effectively dialysis removes waste; the recommended minimum reduction in urea level is 65% [12].

In the CAP survey, the median change in the delta difference of BUN, Ca, Cl, Cr, K, Na, P, and TCO_2 was 20 mg/dL, 2 mg/dL, 10 mEq/L, 1 mg/dL, 1 mEq/L, 9 mEq/L, 2 mg/dL, and 8 mEq/L, respectively; the median percent change was 50%, 15%, 12%, 30%, 20%, 5%, 50%, and 20%, respectively [3].

In this study, the median delta percentage changes in BUN, Ca, Cl, Cr, K, Na, P, TCO_2, BUN, and Cr differed significantly between pre- and post-dialysis specimens. Using the median absolute change and percentage change of the CAP survey, the BUN and Cr results of 97.5% of our post-dialysis specimens were out of limits by both criteria. The high out of limits rate of dialysis specimens shows the inaccuracy of the delta check.

The BUN/Cr ratio is used to distinguish prerenal azotemia from acute tubular necrosis and is associated with all-cause mortality of dialysis patients [13, 14]. In this study, the BUN/Cr ratios of pre- and post-dialysis specimens were strongly correlated ($r^2 = 0.90$, $P < 0.05$).

For the above reasons, we developed the BCCR based on the pre- and post-dialysis BUN/Cr ratio. To evaluate the performance of this no-

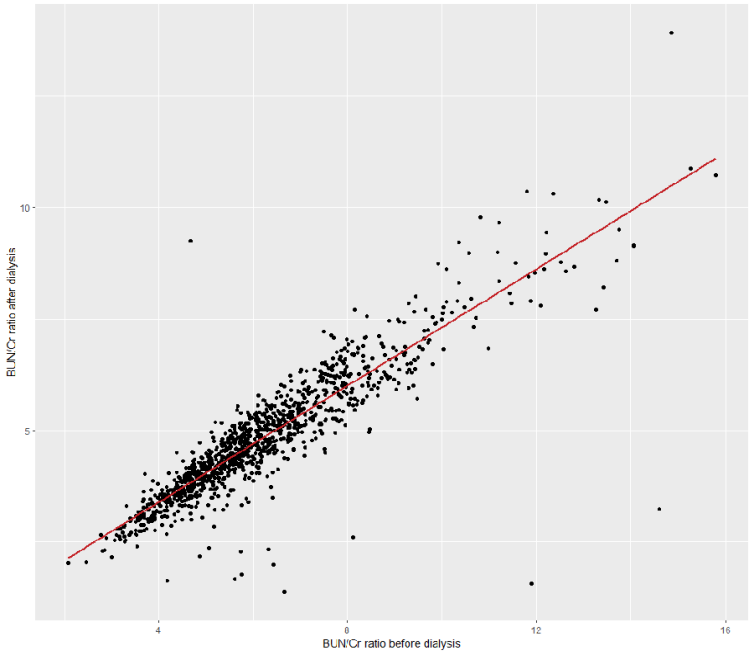

Figure 2. BUN/Cr ratio of pre- and post-dialysis specimens.

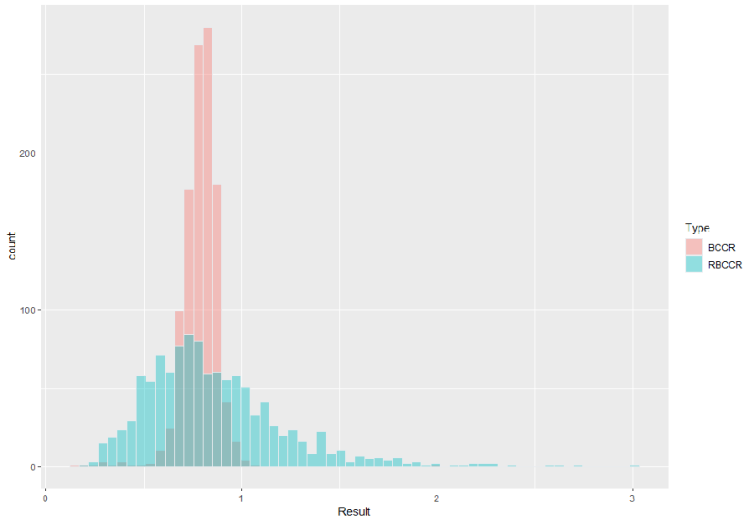

Figure 3. BCCRs of dialysis specimens and simulated misidentification specimens.

vel delta check method, a simulation-based approach is typically used. This is because it is not always possible to ascertain whether or not a specimen is correctly labeled, and the mislabeling rate is usually too low to provide sufficient power for prospective evaluation of delta check performance [9-11].

We shuffled the post-dialysis specimen identification numbers to simulate misidentification. In the original dataset, the median BCCR was 0.80 and the 2.5th, 25th, 75th, and 97.5th percentiles were 0.62, 0.74. 0.84, and 0.93, respectively. In the simulated misidentification dataset, the median BCCR was 0.79 and the 2.5th, 25th, 75th, and 97.5th percentiles were 0.34, 0.61, 1.02, and 1.77, respectively. Therefore, the interquartile range of the simulated specimens was larger than that of the actual 1,116 specimens. When the 2.5th and 97.5th percentile values of the BCCR were set as the upper and lower limits, the delta check detected 61.0% of the simulated misidentified specimens. The false positive rate of frequently used absolute and percentage change methods was over 95% of the 1,116 post-dialysis specimens; by contrast, the false positive rate of the algorithm was only 5%.

In conclusion, the BCCR enabled detection of changes in important clinical parameters and could reduce the rate of false-positives. However, its implementation requires the use of a laboratory information system.

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Disclosure of conflict of interest

None.

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