

Relationship between Delta Checks for Selected Chemistry Tests

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The correlation between delta differences for 20 serum chemistry tests was calculated for 2400 samples from 288 patients. There were 12 pairs of chemistry tests for which correlation coefficients of the delta checks exceeded 0.25; aspartate aminotransferase and alanine aminotransferase had the highest Pearson correlation coefficient, 0.915. The highest negative, indirect, correlation was between the delta checks of bicarbonate and chloride (-0.219). The relationship between delta differences may be used as a quality-control technique to detect analytical errors.

Additional Keyphrases: *statistics · quality control*

Laboratory errors can be detected by monitoring patients' results. Quality-control systems that make use of commercially available control sera are sensitive to intra-laboratory errors. Monitoring patients' laboratory data can detect pre-analytical, intralaboratory, and post-analytical errors, and may reflect biological variation and pathophysiological alterations in the patient (1).

Several statistical methods involving laboratory results for patients have been used as quality-control systems. Hoffman and Waid (2) described the "average of normals" method to detect systemic drift. Most laboratories have "panic" values that, when exceeded, may indicate important clinical changes or a laboratory error. Another popular method involving patients' results is the delta check. Laboratory computer systems use delta check methods based on differences or percent change of current results for a patient from previous values for that patient.

Delta checks are usually performed on a single analytical test. Delta check methods based on multiple tests can increase the efficiency of error detection. Delta differences of anion gap or the urea nitrogen/creatinine ratio are examples of multiple-test delta checks (3). Iizuka et al. (4) proposed a multivariate delta check based on the Mahalanobis general distance to detect specimen mix-up. Slotnick and Etzell (5) used the multivariate Hotelling T^2 statistic on within-person test results to minimize false-positive and false-negative laboratory results.

Results for many laboratory tests are highly correlated in patients. In this study, I investigated the correlation between delta checks based on differences for 20 common chemistry tests. I then compared the correlation between the original test values and the delta check values.

Materials and Methods

Data Base

Data for 20 chemistry tests were collected at the Medical College Hospitals via a MV-15000 computer (Data General, Westboro, MA) with Meditech (Westwood, MA) laboratory software. Patients' laboratory data were obtained for

2400 samples on 288 patients from July–November, 1988. Serum sodium, potassium, chloride, bicarbonate, glucose, urea nitrogen, creatinine, calcium, phosphorus, uric acid, total protein, albumin, total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), creatine kinase, cholesterol, and triglycerides were analyzed in an Astra instrument (Beckman Instruments, Inc., Brea, CA).¹ No attempt was made to eliminate outlier data. Laboratory results were obtained mostly for inpatients, differing in age, gender, and clinical state. Multiple delta checks were obtained for most patients.

The adult reference ranges for these tests were sodium, 136–144 mmol/L; potassium, 3.3–4.8 mmol/L; chloride, 96–106 mmol/L; bicarbonate, 24–30 mmol/L; glucose, 70–1200 mg/L (3.9–6.7 mmol/L); urea nitrogen, 70–200 mg/L (2.5–7.1 mmol/L); creatinine, 7–15 mg/L (62–133 μ mol/L); calcium, 85–105 mg/L (2.12–2.62 μ mol/L); phosphorus, 26–48 mg/L (0.83–1.55 mmol/L); uric acid, 22–82 mg/L (131–488 μ mol/L); total protein, 60–80 g/L; albumin, 37–50 g/L; total bilirubin, 1–12 mg/L (2–20 μ mol/L); AST, 12–48 U/L; ALT, 9–45 U/L; LDH, 90–165 U/L; ALP, 30–90 U/L; creatine kinase, 30–270 U/L; cholesterol, <2000 mg/L (<5.17 mmol/L); triglycerides, 350–1600 mg/L (395–1806 mmol/L).

Statistical Analysis

The delta check was calculated as the current value minus the previous result. Descriptive statistics—including the average, standard deviation, and the 1, 5, 10, 50, 90, 95, and 99 percentiles—were calculated for the delta checks of chemistry tests. A correlation matrix was calculated for the original data and the delta checks for the 20 chemistry tests. Statistical analysis was carried out with the SAS statistical software package (SAS Institute, Inc., Cary, NC) (6).

Results

The descriptive statistics of delta differences for 20 chemistry tests are shown in Table 1. The median (50th percentile) delta difference for most tests was zero (indicating no change), but there was considerable variation. Positive delta differences indicate an increase in test values when comparing current and previous laboratory values. The distribution of delta differences for the chemical tests was symmetrical for most tests except enzymes.

The 12 greatest positive correlations between delta differences of test pairs and the greatest negative correlation are listed in Table 2. Qualitatively, for positively correlated delta differences, an increase in one chemistry test would generally be associated with an increase in another highly correlated test. For negative correlations, an increase in one chemistry test would be associated with a decrease in

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¹ Nonstandard abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; and ALP, alkaline phosphatase.

Table 1. Descriptive Statistics of Delta Differences

Tests and units	n	Delta difference ^a									
		Mean	SD	Percentiles							
				1	5	10	50	90	95	99	
Sodium, mmol/L	1912	0.097	3.21	-9	-5	-4	0	4	5	8	
Chloride, mmol/L	1912	0.069	3.59	-9	-6	-4	0	4	6	9	
Bicarbonate, mmol/L	1916	0.087	2.66	-7	-4	-3	0	3	4	7	
Calcium, mmol/L	1441	0.008	0.127	-0.40	-0.17	-0.12	0	0.15	0.20	0.32	
Urea nitrogen, mmol/L	1714	0.113	2.64	-8.53	-3.21	-1.78	0	2.14	3.57	8.57	
Creatinine, μmol/L	1714	-0.362	43.8	-124	-26.5	-17.7	0	17.7	35.4	141	
Uric acid, μmol/L	990	-2.688	54.2	-172	-95.2	-65.4	0	53.5	27.3	155	
Total protein, g/L	932	0.236	4.47	-13	-7	-5	0	5	7	11	
Albumin, g/L	1003	0.057	2.72	-7	-4	-3	0	3	4	8	
AST, U/L	926	-2.429	126	-258	-49	-21	-1	16	36	135	
ALT, U/L	920	-0.777	67.4	-143	-28	-14	0	10	22	94	
LDH, U/L	987	1.795	289	-421	-130	-76	-5	56	103	590	
ALP, U/L	1012	1.341	57.0	-172	-53	-23	0	34	58	221	
Cholesterol, mmol/L	916	0.0287	0.059	-2.12	-0.73	-0.49	0	0.55	0.78	1.32	
Glucose, mmol/L	1477	-0.0797	2.898	-8.83	-4.11	-2.50	-0.055	2.44	4.11	8.77	
Potassium, mmol/L	1970	0.0243	0.518	-1.4	-0.8	-0.5	0	0.6	0.9	1.4	
Phosphorus, mmol/L	1024	0.027	0.338	-0.90	-0.48	-0.32	0.032	0.39	0.55	1.00	
Total bilirubin, μmol/L	939	0.26	20.8	-63	-24	-12	0	8.6	27	91	
Creatine kinase, U/L	1041	-73.18	886	-2450	-494	-192	-4	69	215	1449	
Triglycerides, mg/L ^b	920	10.587	645	-1944	-719	-470	20	490	698	1568	

^a Delta difference = (current - previous value) expressed as units of measurement. ^b Conversion factors: mg/L → mmol/L: 1.129 × 10³.

Table 2. Correlation between Delta Differences and Original Test Values for Selected Chemistries

Test pair	Delta checks		Original test values	
	No. of comparisons	Pearson <i>r</i>	No. of comparisons	Pearson <i>r</i>
AST, ALT	918	0.915	1475	0.873
Total protein, albumin	925	0.761	1477	0.578
Urea nitrogen, creatinine	1708	0.618	1576	0.660
Sodium, chloride	1912	0.508	2364	0.644
Calcium, total protein	923	0.447	1475	0.383
Calcium, albumin	1000	0.444	1570	0.520
Cholesterol, total protein	915	0.435	1467	0.411
Urea nitrogen, uric acid	989	0.400	1563	0.469
ALP, cholesterol	915	0.326	1467	0.113
Cholesterol, albumin	915	0.318	1467	0.345
Uric acid, creatinine	989	0.315	1563	0.351
AST, LDH	925	0.259	1479	0.323
Bicarbonate, chloride	1912	-0.219	2364	-0.428

another test.

The correlation for the original laboratory data and the delta differences for highly correlated chemistry tests are also shown in Table 2. The correlations between delta differences were generally the same as the corresponding correlations between the original test values, but with some differences. The correlation for the delta difference between total protein and albumin (0.761) was higher than the corresponding correlation between the original test values (0.578). This may reflect increased covariation seen in disease (with therapeutic intervention) as opposed to a more random relationship seen in health. The sodium-chloride test pair had a higher test correlation (0.644) than their corresponding correlation for delta check (0.508). This may result from frequent monitoring of patients with small

changes in laboratory values, which can lead to a lower correlation. Also, multiple factors (medications, intravenous fluids, diet, etc.) may affect these tests differently and thereby reduce their covariance.

Discussion

Monitoring patients for important clinical changes is a frequent reason for ordering laboratory tests. Alterations in laboratory data reflect biological variations, pathophysiological changes, analytical errors of accuracy and precision, and pre- and post-analytical sources of variance. Delta checks or multivariate monitoring statistics can detect these sources of variance.

The distribution of delta differences (Table 1) compared

well with that in a previous study (7). Values exceeding the 5 and 95 percentiles may alert the technician or physician to potential analytical or clinical problems. Delta checks should be compared against method precision to determine significant differences (8). Also, the time between consecutive measurements should be considered. In addition, biological within- and between-person variability and clinical significance of test changes are important considerations for delta checks (9). Each laboratory should determine its own distribution and correlation of delta checks because of the differences in test methods and mix of patients.

Many delta checks are false positives, particularly in critically ill patients (10). False-negative delta checks may result from specimen mislabeling (3). False-positive delta checks may lead to increased physician ordering of tests or changes in patient care, whereas false-negative delta checks may lead to late detection of important clinical changes. It may be easier to detect laboratory errors if the correlation between delta checks is used.

The highly correlated delta checks generally reflect high correlations of the underlying tests (Table 2). The high correlations among tests reflect the underlying physiological relationships between tests, which can be greater during illness (e.g., the increase in serum urea nitrogen and serum creatinine during acute renal failure) or through therapeutic intervention (e.g., the increase in sodium and chloride as a response to intravenous salt therapy).

The correlation between delta check differences may be used to detect possible analytical error. The direction of relationship between two highly correlated delta checks

could be evaluated. A positive delta check correlation indicates a direct relationship between two tests of consecutive specimens from a patient. Thus, an indirect (negative) relationship between checks (e.g., the increase in AST associated with a decrease in ALT delta difference) could indicate laboratory error. More quantitatively, one may be able to form confidence intervals for predictivity between highly correlated delta differences.

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