Evaluation of Total Serum Calcium Critical Values

Joan H. Howanitz, MD; Peter J. Howanitz, MD

**Context.**—As a patient safety measure, laboratories are required by regulatory agencies to have a critical values policy. Total serum calcium commonly is included in critical results lists; however, a wide range of values are used and there is scant outcome data justifying inclusion of this analyte in these lists.

**Objective.**—To evaluate the appropriateness of the critical values for total serum calcium used in our institution.

**Design.**—We studied all critical total serum calcium results found during a 3-month period. The patients' medical records were evaluated for the presence of documented critical results call for calcium, clinician response, and patient outcome. The patients' outcomes were measured by time of clinical response, length of stay in the hospital, and mortality.

**Results.**—There were 722 (1.4%) critical results found in a total of 50,402 total serum calcium results. Using our criteria of 7 mg/dL or less as the low and 12 mg/dL or more as the high critical value, we found 171 patients with 608 critically low results and 47 patients with 114 critically high results. Eighty percent of patients with critically low results and 75% of patients with critically high results had length of stays greater than our average (5.58 days). Clinicians responded to 49% of the critical results calls within 4 hours. There was an overall mortality rate of greater than 25%, with more than half the mortality occurring in patients who had results within 0.5 mg/dL of the cutoff values used.

**Conclusion.**—Although broadening critical values limits would reduce required calls, this does not appear warranted. The disease severity of the patients as measured by length of stay and mortality, as well as the rapidity with which patients were treated, indicate that the current limits are appropriate and should not be widened.

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The reporting of critical laboratory results, sometimes called panic values, is a widespread practice now required by accrediting bodies. Critical results are considered those that indicate the patient is in imminent danger unless appropriate treatment is started promptly. However, data are not readily available to determine the effectiveness of inclusion of a given analyte on a critical values list or at what concentration a result should be considered critical. Changes in the critical limits used can lead to an increase in the number of required phone calls to clinicians regarding results without concomitant improvement in patient care or, in contrast, can cause failure in notifying clinicians of potential harmful situations.

Most clinical laboratories include total serum calcium in their critical values lists, albeit at different concentrations. Kost reported the range for low critical value limits for total serum calcium as 5.0 to 8.6 mg/dL, and the range for high critical results as 10.5 to 14.0 mg/dL. More recently, critical values used for total serum calcium also were found to vary significantly among hospitals in the United States. Ninety percent of laboratories reporting critical total serum calcium results used values below a lower limit of 7.0 mg/dL and above a higher limit of 12.0 mg/dL. We studied clinician responses and patient outcomes for critical total serum calcium results using 7.0 mg/dL or less for the lower limit and 12.0 mg/dL or greater for the upper limit.

**MATERIALS AND METHODS**

Total serum calcium results were evaluated for a 3-month period as part of a quality assurance project on reporting critical values. Total serum calcium assays were performed on an automated chemistry analyzer (Roche MODULAR, Indianapolis, Ind) using the o-cresolphthalein complexone method. The reference range for total serum calcium was 8.5 to 10.5 mg/dL and, as approved by our Medical Board, the total serum critical calcium results were 7 mg/dL or less and 12 mg/dL or more for the low and high values, respectively. The electronic records of patients with results falling in the critical values ranges were evaluated for the following clinical parameters: patient age, amount of time of clinician response to critical result, diagnosis, length of stay (LOS), and whether the patient died during that hospital stay. As per policy, critical results were called to clerks, nursing personnel, or physicians. The times of the critical calls and the names of the individuals receiving the calls were documented in the laboratory computer system. Response to a critical result was defined as reordering either total serum calcium, ordering ionized calcium, or treating the underlying calcium disorder as documented in the electronic medical record.

**RESULTS**

Of the 50,402 total serum calcium results reported during the study period, 722 (1.4%) were critical (Table 1). There was documentation in the electronic records that calls were made for all 722 critical results. There were 608 critically low results (7.0 mg/dL or less) from 171 patients, including 14 outpatients or referral patients (specimens sent from other medical centers) and 157 inpatients. For
the inpatients with critically low total serum calcium results, the LOS ranged from 1 to 71 days, and for 126 (80%) of these patients, the LOS was 6 days or more (Table 2). The average LOS for the year in which the study occurred was 5.58 for general care, that is, for all patients except those under psychiatric and rehabilitation medicine care.

The 3 most common diagnoses in patients with hypocalcemia were renal failure (32), trauma (27), and gastrointestinal disorders (23). Table 3 shows the time frames in which critical values were acted on by reordering total serum calcium, ordering ionized calcium, or treating the hypercalcemia. Forty-five percent (67 patients) of the hypocalcemic patients were treated within 4 hours of the critical results call.

Of the 47 patients with critically high total serum calcium results, 24 were inpatients and 23 were outpatients or referral patients. For the hypercalcemic inpatients, the LOS ranged from 3 to 72 days, and for 18 (75%) of these 24 patients, the LOS was 6 days or more (Table 2). The 3 most common diagnoses in the hypercalcemic patients were hyperparathyroidism (13), renal failure (12), and malignancy (10). The hypercalcemia was caused by hyperparathyroidism in 3 patients. Fifty percent of the hypercalcemic inpatients were treated within 4 hours of the critical results call. Table 4 shows when the critical values were acted on by reordering total serum calcium, ordering ionized calcium, or treating the hypercalcemia.

Twenty-seven percent (46 patients) of the patients with critically low total serum calcium results died; 6 patients died during their hospitalization before further action was undertaken. Nineteen percent (9 patients) with critically high total serum calcium results died during the study period. Table 5 summarizes the critical value results for those patients who died during the study period.

**COMMENT**

As a patient safety measure, calling critical values is required for accreditation by various groups, including the College of American Pathologists and Joint Commission for Accreditation of Healthcare Organizations. Few data are available, however, on how critical values lists effect patient outcomes. Even when critical results are reported immediately by the laboratory personnel, they are not always acted on promptly for a variety of reasons. Not all analytes appearing on critical values lists fit the definition described originally by Lundberg1 as life-threatening unless something is done promptly. Because abnormal calcium levels are associated with serious health consequences, most institutions have critical value limits for both low and high total serum calcium results, but considerable variation occurs in the values used.2–4

The values chosen for any clinical result not only influence patient care, but they impact the institution’s workload. Calling critical values is problematic because notifying clinicians of critical results is labor-intensive for both laboratory personnel and clinicians. The mean time for laboratory personnel to complete a critical value call is approximately 6.1 minutes for hospital inpatients and 13.7 minutes for outpatients.3 If this average held true for our institution, we spent about 80 hours in calling critical total serum calcium results during the 3-month study period. Lowering of the high critical value limits for total serum calcium dramatically increases mandated calls.2 In contrast, failure to notify clinicians may lead to treatment delays with attendant untoward effects. In our study, treatment or repeat measurements were undertaken within 4 hours in more than half the patients.

Ordinarily, approximately 40% of serum calcium is protein-bound, of which 90% is bound to albumin, approximately 50% is free or ionized calcium, and the remaining 10% is complexed to carbonate, phosphate, citrate, lactate, and sulfate.6 Lacher et al7 reported data from more than 16,000 individuals that showed a mean total serum calci-
um of 9.28 mg/dL, with a between-individual variation of 4.7%. Even though total serum calcium results normally vary within these small ranges, a wide variety of values are used as critical total serum calcium limits. Ninety percent of the laboratory use between 6 and 7 mg/dL for the critical low results and between 12 and 14 mg/dL for the critical high values. We choose to use calcium results of 7 mg/dL or less and 12 mg/dL or more as our critical limits because of the potential serious consequences of these levels.

Hypocalcemia is associated with a poor outcome as measured either by survival or LOS in intensive care units. Some early symptoms of hypocalcemia such as muscle cramps and irritability are nonspecific and, as hypocalcemia becomes more severe, tetany, hypotension, and heart failure occur. Hypocalcemia is associated with a large number of underlying disorders including alkalosis, hypomagnesemia, and renal insufficiency. Hypocalcemia occurs frequently in critically ill patients, especially those with sepsis. In a study of medical patients in intensive care, 70% had decreased levels of total serum calcium and the mortality of hypocalcemic patients was significantly greater than that of normocalcemic patients. Critically ill surgical patients commonly have low total and ionized serum calcium levels. It is unclear whether hypocalcemia directly contributes to mortality or is simply a manifestation of severity of illness.

In our study, critically low total serum calcium results were more than 5 times as common as critically high results. The most common causes of these low results were renal failure, trauma, and gastrointestinal disease. Approximately 45% of the calls regarding patients with the low results were responded to with an order within 4 hours of the time of the critical result call. Most results were responded to within 24 hours, with more rapid responses tending to occur for patients with lower total serum calcium results. Reasons for delayed response may include that the appropriate clinician did not receive the results, there was clinical decision not to treat, or there was a delay in order documentation. Eighty percent of patients with critically low total serum calcium level results had a longer LOS than our average stay, and 27% of these patients died. For the hypocalcemic group of patients, the LOS varied widely (1–71 days), and for those who died, the LOS was greater than our average stay in almost 80% of patients. More than half the patients who died did not have severely depressed total serum calcium results; they had results ranging from 6.5 to 7.0 mg/dL.

Because hypercalcemia affects many organ systems, it can lead to a variety of clinical signs and symptoms including those related to gastrointestinal and neurologic systems. Hypercalcemia also affects the electrical conduction system of the heart. Most hypercalcemic patients do not have obvious symptoms until total serum calcium results exceed 12 mg/dL, whereas almost all patients become symptomatic when results are more than 14 mg/dL. Generally, immediate treatment is warranted for patients with total serum calcium results of 14 mg/dL or more.

Causes of hypercalcemia include hyperparathyroidism, malignancy, and granulomatous disease. In our patients, hyperparathyroidism, renal failure with secondary hyperparathyroidism, and malignancy were the most common causes of increased total serum calcium. Although critically ill surgical patients commonly have hypocalcemia, about 15% of these patients have hypercalcemia. In our study, most results were responded to within 24 hours, with response occurring within 4 hours 50% of the time. Our patients with critically high total calcium levels also had a variable LOS (from 3 to 72 days), with 75% having a longer LOS than our average stay. Almost 20% of patients died, but more than half the patients who died did not have marked increase in total calcium, they had results in the 12.0 to 12.5 mg/dL range.

For all diagnostic-related groups, severity of disease and mortality indices are the strongest predictors for LOS. In our patients, both low and high critical total serum calcium results were associated with prolonged LOS and high mortality. Broadening criteria for notifying physicians of critical total serum calcium results would markedly decrease the required number of critical result calls. Of the more than 5000 total serum calcium orders placed during the study period, only 1.4% were critical. Although calling these results represents considerable work, it does not appear warranted to broaden the critical total serum calcium limits when considering the seriousness of disease in our patients.

### References