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# Relevancy of Serum Calcium in Predicting Blood Product Transfusion in Trauma

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Uncontrolled hemorrhage is the leading cause of preventable mortality in trauma. Rapid identification of patients requiring blood transfusion during assessment and resuscitation is necessary for mortality reduction. Most pre-hospital or field medical criteria used to predict blood product needs in trauma patients rely on a combination of physiological, anatomic, and mechanism-of-injury components. Calcium (Ca) activates protein kinase C and is required for coagulation factors to bind properly in the clotting cascade. Ca has presented a novel laboratory test to predict early blood transfusion. The purpose of this study was to identify a relationship between serum Ca levels and the need for early transfusion. In this retrospective analysis, serum Ca <7.9 mg/dL was strongly associated with the need for blood product transfusion, as well as transfusion of more than four units within 4 hours, even after controlling for other clinical variables. This effect was age specific for the subject group aged 40 years and below. Patients with normal blood pressure could give medical teams a false sense of patient stability. Younger patients have a compensating capacity with blood loss and will not show signs of shock until they have exhausted this mechanism.

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Trauma resuscitation, blunt trauma, penetrating trauma, hypotension, anemia, calcium, transfusion, coagulopathy

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# TABLE OF CONTENTS

**Section** **Page**

# LIST OF TABLES

**Page**

## 1.0 SUMMARY

In this retrospective analysis, serum calcium <7.9 mg/dL was strongly associated with the need for blood product transfusion, as well as transfusion of more than four units within 4 hours, even after controlling for other clinical variables. This effect was age specific for the subject group aged 40 years and below. Younger patients have a compensating capacity with blood loss and will not show signs of shock until they have exhausted this mechanism.

## 2.0 INTRODUCTION

Uncontrolled hemorrhage is the leading cause of preventable mortality in trauma [1]. Rapid identification of patients requiring blood transfusion during assessment and resuscitation is necessary for mortality reduction [2]. Most pre-hospital or field medical criteria used to predict blood product needs in trauma patients rely on a combination of physiological, anatomic, and mechanism-of-injury components. Calcium (Ca) activates protein kinase C and is required for coagulation factors to bind properly in the clotting cascade. Ca has presented a novel laboratory test to predict early blood transfusion. The purpose of this study was to identify a relationship between serum calcium (sCa) levels and the need for early transfusion.

## 3.0 BACKGROUND

In the current conflicts, the most common causes of death in combat casualties have been head injury followed by truncal exsanguinations, and major hemorrhage remains the most frequent avoidable cause of early mortality in combat casualties [3]. Massively bleeding casualties die fast. Even in the civilian setting, those who survive at least 15 minutes into advanced trauma care go on to die of bleeding and half are dead within 2 hours. The most important advance in trauma transfusion medicine in the last decade has been the recognition of the acute coagulopathy of trauma and the need to supply coagulation factors (as plasma) and platelets in near-equivalence with red cells and do so quickly [4]. However, although large numbers of units of packed red blood cells (pRBCs) can be provided immediately upon arrival, equivalent proportions of platelets and plasma typically require a minimum of 20 minutes lead time to be thawed or otherwise processed and to arrive from the blood bank. In the military setting, where fresh whole blood may be available as a “walking blood bank,” appropriate donors need to be identified, prepped, and drawn. Advanced recognition of the need for blood transfusion from knowing the sCa levels can change outcomes and save lives.

Most pre-hospital, field medical criteria used to predict outcome and the need for interventions in trauma patients rely on a combination of physiological, anatomic, and mechanism-of-injury components that, in the experienced trauma clinician, are summed up as good clinical judgment. However, this approach still fails to identify a number of bleeding patients with severe injuries [3]. Civilian paramedic judgment has been assessed objectively and shown to provide little support in the diagnosis of major trauma, mainly due to differences across emergency medical and trauma care systems, individual experience levels, and incompatible methods of data collection. Patients with normal blood pressure could give medical teams a false sense of patient stability [5]. Despite the use of improving physiologic monitoring systems and better training to identify cardiorespiratory instability, in the civilian trauma system, rates of over-triage and under-triage remain high [3,4]. Likewise, once casualties reach advanced care, the number of individuals who receive one to four units of uncrossmatched group O pRBCs in the trauma center is surprisingly high, apparently based on the trauma team's assessment of the need for immediate transfusion. However, these casualties neither receive nor apparently require any other blood products in the first 24 hours and have good outcomes, raising the issue of whether they needed the blood—or the risk of transfusion—in the first place.

## 4.0 METHODS

An Institutional Review Board-approved retrospective review of adult subjects 18-65 years of age and presenting as level 1 trauma activations to an urban level 1 trauma center over a 48-month period was conducted. Deaths in the emergency department were excluded, as were subjects with labs drawn more than 60 minutes following arrival. Patient demographics, laboratory tests performed within 1 hour of arrival (including hemoglobin (HGB), international normalized ratio (INR), base excess (BE), and sCa), transfusion (including administration time), and outcome data were analyzed, using Student's t-test and chi-square analysis. Early transfusion was defined as blood product transfusion within 4 hours of arrival. Significant early transfusion was defined as at least four units of pRBCs transfused within 4 hours. Factors with $p<0.1$ on univariate analysis were entered into logistic regression analysis, with $p<0.05$ considered significant.

## 5.0 RESULTS

After exclusions, 488 subjects met criteria for analysis. Median age was 28.5 years (range: 18-65). Approximately half of the subjects presented with a penetrating mechanism of injury (n=253, 51.8%), and 207 (42.4%) subjects required red blood cell transfusions. There were no significant differences in age, but subjects receiving early transfusion presented with lower Revised Trauma Score (RTS), increased INR, decreased BE, and lower Ca (Table 1). On multiple logistic regression, early (<4 hours) transfusion was associated with systolic blood pressure (SBP) <110 mmHg (odds ratio (OR) 4.0, confidence interval (CI) 1.5-11.3, $p<0.01$) and hypocalcemia (Ca <7.9: OR 3.4, CI 1.2-9.6, p=0.02) (Table 2). Furthermore, transfusion of >4 units within 4 hours remained associated with hypocalcemia (OR 3.0, CI 1.4-6.0, p=0.001) (Table 3).

In subjects 40 years old or less who had sCa <8.0 and INR >1.1 (N=84), 77 (92%) received blood products. Fifty out of these 77 subjects (65%) had SBP >109 mmHg at time of arrival (TOA). Nineteen out of the total 84 subjects (23%) received massive blood product transfusion from TOA to 1 hour, and of these, 9 had SBP >109 mmHg (47%) at TOA.

**Table 1. Early Blood Transfusion Following Trauma**

| | pRBCs within 4 h (n=99) | No Early Transfusion (n=369) | *p*-value |
|---|---|---|---|
| Mean Age (yr) | 34 (23,48) | 31 (24, 44) | 0.13 |
| Mean RTS | 6.4 (3, 7.8) | 7.8 (6, 8) | 0.007 |
| Mean GCS | 13 (3, 15) | 15 (9.5, 15) | <0.001 |
| Mean SBP (mmHg) | 108 (82, 133) | 134 (116, 146) | <0.001 |
| Mean HGB (g/dL) | 11.6 (9.9, 13) | 13 (12, 14) | <0.001 |
| Mean INR | 1.1 (1, 1.8) | 1 (1, 1) | <0.001 |
| Mean BE (mmol/L) | -9 (-13.3, -4.3) | -5 (-8.8, -3) | 0.005 |
| Mean Ca (mg/dL) | 7.2 (6.7, 8) | 8 (7.9, 8,8) | <0.001 |

Note: >1 unit pRBCs in first 4 h.
GCS = Glasgow Coma Scale.

**Table 2. Predictors of Early Blood Transfusion Following Trauma**

| Factor | Univariate OR (95% CI) | *p*-value | Adjusted OR (95% CI) | *p*-value |
|---|---|---|---|---|
| Hypotension[a] | 6.35 (4.0, 10.2) | <0.001 | 4.07 (1.46, 11.35) | 0.007 |
| Anemia[b] | 4.2 (2.7, 6.6) | <0.001 | 1.97 (1.46, 11.35) | 0.218 |
| INR > 1.0 | 4.8 (3.0, 7.6) | <0.001 | 1.05 (0.35, 3.12) | 0.938 |
| BE < -6 | 4.4 (1.9, 10.3) | 0.001 | 2.49 (0.90, 6.88) | 0.079 |
| Hypocalcemia[c] | 6.8 (4.2, 10.9) | <0.001 | 3.38 (1.18, 9.63) | 0.022 |

[a]Hypotension defined as SBP <110 mmHg.
[b]Anemia: HGB <12 g/dL.
[c]Hypocalcemia: sCa <7.9.

**Table 3. Early Large Volume Transfusion Following Trauma**

| | ≥4 Units pRBCs within 4 h (n=66) | <4 units pRBCs within 4 h (n=402) | *p*-value |
|---|---|---|---|
| Mean Age (yr) | 34 (22, 47) | 31 (24, 44) | 0.12 |
| Mean RTS | 5 (2.9, 7.8) | 7.8 (6, 8) | 0.007 |
| Mean GCS | 10.5 (3, 15) | 15 (8, 15) | <0.001 |
| Mean SBP (mmHg) | 98 (85, 121) | 134 (116, 146) | <0.001 |
| Mean HGB (g/dL) | 11 (8.5, 12.4) | 13 (11.9, 14) | <0.001 |
| Mean INR | 1.3 (1, 2) | 1 (1, 1) | <0.001 |
| Mean BE (mmol/L) | -12.9 (-17.6, -6.1) | -5 (-9, -3) | 0.007 |
| Mean Ca (mg/dL) | 7.2 (6.7, 8) | 8 (7.9, 8.7) | <0.001 |

Note: >4 units pRBCs in first 4 h.

## 6.0 DISCUSSION

The results of this study will increase the knowledge of early indicators of blood product needs and conservation of resources through decreased mortality and will enhance accurate blood product delivery.

## 7.0 CONCLUSIONS

In this retrospective analysis, sCa <7.9 was strongly associated with the need for red blood cell transfusion, as well as transfusion of more than four units within 4 hours, even after controlling for other clinical variables. These results could be a significant tool to aid in the prioritization for evacuation to a higher level of care before deterioration. Further prospective analysis, for validation as well as the role of Ca replacement in hemostasis, is warranted.

## 8.0 REFERENCES


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# LIST OF ABBREVIATIONS AND ACRONYMS

| | |
|---|---|
| **BE** | base excess |
| **Ca** | calcium |
| **CI** | confidence interval |
| **GCS** | Glasgow Coma Scale |
| **HGB** | hemoglobin |
| **INR** | international normalized ratio |
| **OR** | odds ratio |
| **pRBC** | packed red blood cells |
| **RTS** | Revised Trauma Score |
| **SBP** | systolic blood pressure |
| **sCa** | serum calcium |
| **TOA** | time of arrival |