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1 **Using Serial Hemoglobin Levels to Detect Occult Blood Loss in the**

2 **Early Evaluation of Blunt Trauma Patients**

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9

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18

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30

31Abstract

32**Objective:** Serial hemoglobin measurement (Δ Hgb) is intended to aid in the early identification
33of blunt trauma patients who have significant blood loss requiring intervention. However, the
34utility of Δ Hgb has yet to be rigorously studied. We sought to determine if Δ Hgb is a reliable
35diagnostic tool in assessing blood loss in blunt trauma patients.

36**Methods:** We enrolled consecutive blunt trauma patients 18 years of age and older, presenting to
37a level I trauma center. We measured two hemoglobin levels spaced five minutes apart and
38calculated the difference, Δ Hgb, for each patient. We also recorded whether each patient required
39any of the following interventions to treat their injuries; 1 - Operation or procedure to control
40hemorrhage, 2 - radiographic embolization, 3 - administration of blood and blood products, 4 -
41administration of three or more liters of IV fluids, 5 - exsanguination. Our primary outcome was
42the area under the receiver-operator curve (ROC).

43**Results:** We enrolled 251 patients, including 192 males and 59 females with a mean age of 40.
44Interventions occurred in 56 patients and were withheld in 195. The median Δ Hgb was -0.1
45gm/dl (Interquartile range: -0.5 gm/dl to 0.1 gm/dl) for patients requiring intervention, and 0.0
46gm/dl (Interquartile range: -0.6 gm/dl to 0.3 gm/dl) for patients not requiring intervention. We
47found the area under the ROC to be 0.53 (95% Confidence interval: 0.44 – 0.62).

48**Conclusions:** Our results indicated that Δ Hgb does not reliably distinguish between blunt trauma
49patients who require intervention, and those who do not.

51Introduction

52 Traumatic hemorrhage results in the loss of whole blood, including
53plasma and red blood cells. The resultant loss of intravascular volume
54triggers shifts of interstitial and intracellular fluid that act to restore overall
55intravascular volume, but do not restore erythrocyte and hemoglobin losses
56and result in a dilution of the intravascular concentration of red blood cells
57and hemoglobin. This conceptual framework provides the rationale for using
58measurements of hematocrit and hemoglobin concentration to assess blood
59loss in blunt trauma patients. However, baseline hematocrit and hemoglobin
60levels are affected by many factors not associated with bleeding such as
61age, gender, weight, volume of distribution, fluid status, and underlying
62conditions such as anemia.¹ As a result, single measurements have limited
63utility in the early assessment of blunt trauma patients.^{2,3}

64 Because the performance of single hemoglobin and hematocrit
65assessments is unreliable, serial measures have been suggested as a means
66of identifying patients who have decreasing values that might signify
67ongoing hemorrhage, and the use of serial hematocrit or serial hemoglobin
68measurements is now part of the routine evaluation of trauma patients at
69many institutions across the United States.⁴ However, recent studies on the
70utility of serial measurements have produced inconclusive results.^{1,4,5} These
71differing conclusions reflect differences in methodology, study populations,
72and the time frame of the serial evaluations.

73 The goal of our study was to prospectively examine the performance of
74serial hemoglobin (Δ Hgb) measurements in the early resuscitation of blunt

75trauma patients at five-minute intervals, and assess the ability of Δ Hgb to
76identify patients who require emergent intervention. The five-minute time
77interval was specifically chosen because of its relevance to typical trauma
78resuscitations and the ability of these measurements to identify patients and
79influence care in the early stages of trauma resuscitations where evaluations
80and decisions are made in relatively short time intervals. Furthermore, there
81is no current literature to illuminate the utility of serial hemoglobin
82measurements in this time frame.

83 We specifically wanted to examine the receiver-operator curve (ROC)
84to assess the discriminating capability of serial measurements.

85

86**Methods**

87**Study design and setting**

88 We conducted an observational study that enrolled consecutive blunt
89trauma patients 18 years of age and older, presenting to a level I trauma
90center. We excluded patients who were younger than 18 years of age,
91pregnant, were primarily burn victims, sustained penetrating trauma, were
92transferred from another hospital, or received interventions prior to the
93second hemoglobin measurement. The study involved recording the first two
94hemoglobin levels that were routinely assessed at five-minute intervals on all
95patients presenting to our institution for blunt trauma evaluations. Nursing
96personnel provided hemoglobin measurements to treating clinicians as part
97of normal practice, but study personnel did not inform the treating clinicians
98of any measurements or changes in hemoglobin levels, and the study did not

99interfere or otherwise alter the care of any patients. The study was reviewed
100by the UCLA Institutional Review Board and approval was granted under a
101waiver of informed consent.

102

103**Measurements and outcomes**

104 We calculated the difference, ΔHgb , for the two measured hemoglobin
105levels for each patient. We also recorded whether each patient required any
106of the following interventions to treat their injuries; 1 - Operation or
107procedure to control hemorrhage, 2 - radiographic embolization, 3 -
108administration of blood and blood products, 4 - administration of three or
109more liters of IV fluids, 5 - exsanguination. We counted only interventions
110that took place within the first 24-hours of the patient's arrival to the
111resuscitation suite. We documented interventions that occurred in the
112resuscitation area using direct observation. We had two trained and
113independent observers review case records to ascertain whether
114interventions were performed outside of the resuscitations area.
115Disagreements were resolved by third party assessments.

116

117**Analysis**

118 We calculated the sensitivity and specificity of each level of ΔHgb in
119predicting the need for any of the index interventions, and used these
120operator characteristics to construct a receiver-operator curve for ΔHgb . Our
121primary outcome was the area under this receiver-operator curve (ROC), and
122its corresponding confidence interval.⁶ We also calculated the maximum

123 Youden Index associated with the ROC. In determining our sample size, we
124 estimated that we would need 251 patients to estimate the optimal
125 sensitivity of serial hemoglobin measurements to within 5% (\pm 2.5%). In the
126 setting of acute hemorrhage, common practice is to withhold administration
127 of IV fluids and move straight to resuscitation with blood. Hence, we
128 calculated an additional area under the ROC where administration of 3 or
129 more liters of IV fluids was not considered an intervention.

130

131 **Results**

132 Our institution had 393 trauma activations between June 2016 and
133 October 2016. We excluded 142 patients because they either underwent an
134 index intervention prior to their second hemoglobin measurement, or met
135 one of the exclusion criteria. The remaining 251 patients, including 192
136 males and 59 females with a mean age of 40, form our cohort. We found that
137 no interventions were performed in 195 patients, while a total of 93
138 interventions were administered to the remaining 56 patients. Figure 1
139 provides the flow diagram for patient enrollment, and Table 1 documents the
140 distribution of interventions among our cohort. An operative procedure was
141 the only intervention provided to four patients (1.6% of all enrolled patients,
142 and 7.1% of the patients receiving some form of intervention). Of the 19
143 patients who received fluid support as their only intervention, ten exhibited
144 falling hemoglobin levels, five exhibited stable levels and four exhibited
145 rising levels.

146 The median Δ Hgb was -0.1 gm/dl (Interquartile range: -0.5 gm/dl to 0.1
147gm/dl) for patients requiring intervention, and 0.0 gm/dl (Interquartile range:
148-0.6 gm/dl to 0.3 gm/dl) for patients not requiring intervention. Figure 2
149depicts the frequency of Δ Hgb measurements as a function of Δ Hgb for cases
150with and without intervention.

151 Figure 3 presents the receiver operator curve for Δ Hgb, with an area
152under the ROC of 0.53 (95% Confidence interval: 0.44 – 0.62). The maximum
153Youden Index of 0.15 corresponded to a sensitivity of 71.4% and a specificity
154of 43.6%.

155 Our inter-rater assessment revealed that our raters agreed on 94.7% of
156their assessments, exhibiting a kappa value of 0.88.

157 Administration of 3 or more liters of IV fluids was the only intervention performed in 19
158of the 56 patients who received an intervention. Shifting these 19 patients into the non-
159intervention group left 37 patients who receive at least one of the remaining interventions, while
160214 patients received no intervention. We found the area under the Δ Hgb ROC for this revised
161classification to be unchanged at 0.53.

162

163**Limitations**

164 Because our study excluded patients who received interventions prior
165to a second hemoglobin measurement, it is possible that our study
166underestimates the benefit of Δ Hgb assessments that might be apparent had
167second measurements in these patients been obtained and included in our
168analysis. For example, many patients with obvious instability were rushed to
169the operating room prior to serial hemoglobin assessment. However, while it

170is likely that Δ Hgb measurements in these patients would have enhanced the
171apparent ability of Δ Hgb to detect the need for intervention, this additional
172information is mostly of academic interest as serial hemoglobin
173measurements were clearly of little value in determining the management of
174these patients. Thus, from a practical perspective, our study enrolled a
175suitable population for studying the effect of Δ Hgb on actual decision-
176making.

177 We specifically chose a short interval for our Δ Hgb assessments to
178focus on a time frame that is relevant to typical trauma resuscitations. It is
179possible that Δ Hgb assessments may have greater utility if measured on
180longer time intervals.

181 Our study also focused on the value of serial hemoglobin levels in
182assessing the need for intervention among blunt trauma patients. We
183specifically excluded patients with penetrating trauma because operative
184and interventional decisions frequently involve concerns such as visceral
185injury that may not be associated with extensive blood loss.

186 It is also worth noting that our study was conducted at a single tertiary
187center in an urban environment, and our findings may not generalize to
188other centers with differing spectra of patients and differing practice
189patterns.

190

191**Discussion**

192 The goal of early serial hemoglobin measurement is to aid in the
193detection of occult blood loss in the resuscitation suite, specifically in the

194 blunt trauma population of our study. However, our results indicate that
195 Δ Hgb is no better than a coin toss (AUC = 0.53) in identifying patients who
196 require intervention for ongoing hemorrhage. Many of our patients exhibited
197 rising Δ Hgb despite the fact that they had ongoing hemorrhage that
198 ultimately required an intervention. Conversely, other patients exhibited
199 falling Δ Hgb, despite the fact that they did not require any interventions.

200 Explanations for the poor performance of Δ Hgb are readily apparent in
201 view of the events and fluid shifts that typically occur during blunt trauma
202 resuscitations. Patients with risk of serious injuries typically receive
203 intravenous fluids in the pre-hospital setting and in the emergency
204 department prior to the first hemoglobin measurement. The administered
205 fluid acts to expand the intravascular volume resulting in decreased
206 hemoglobin concentrations that would be apparent on the initial hemoglobin
207 assessment. As the administered fluid redistributes to interstitial and
208 intracellular spaces, intravascular volume will decrease leading to a rise in
209 hemoglobin concentration that will be evident on subsequent hemoglobin
210 assessments. This process likely explains the rising Δ Hgb we found in many
211 of our patients who did not require intervention, but also likely explains the
212 increasing hemoglobin concentrations we found in patients who did require
213 intervention, where vigorous fluid resuscitation over-expanded the
214 intravascular volume despite modest ongoing blood loss.

215 In a similar fashion, patients who received vigorous fluid administration
216 after the initial hemoglobin measurement will be found to have decreasing
217 hemoglobin concentrations on subsequent measurements strictly as a

218consequence of the dilutional effect of the administered fluids, even in the
219absence of ongoing hemorrhage. This likely explains the falling hemoglobin
220levels we found in many of the patients who did not require intervention.

221 While studies testing the validity of Δ Hgb in blunt trauma patients is
222limited in literature, there is evidence suggesting that Δ Hgb provides little to
223no diagnostic value in the non-operative management of patients presenting
224with blunt splenic trauma.⁷ Our study extends this finding to the blunt
225trauma patient population as a whole. Early Δ Hgb assessments not only fail
226to aid in the detection of occult blood loss in blunt trauma patients, but likely
227act to confuse and misdirect physicians in the resuscitation suite.

228 It is important to note that our study focused on early serial
229hemoglobin measurements and their ability to inform interventions in the
230resuscitation suite, particularly within the first five minutes of arrival to the
231resuscitation suite. It is possible that the utility of serial measurements differ
232on other time scales, with most studies taking serial measurements two to
233six hours apart.⁸ Thorson and colleagues, in a study based on chart review,
234found that serial measurements were a good indicator of blood loss in
235trauma patients who had an initial assessment within the first 30 minutes of
236arrival and a second assessment within four hours,¹ but the study by Madsen
237suggests that serial measurements taken six hours apart rarely provide
238diagnostic information in trauma patients who are deemed stable for
239placement in observation units after the initial trauma screening.⁵ Given that
240our assessment of the utility of serial hemoglobin primarily focused on the

241first five minutes of arrival to the resuscitation suite, our results cannot be
242generalized to different interval scales for serial hemoglobin measurements.

243 In summary, the results of our study indicate that at a level I trauma
244center, where blunt trauma patients are first taken to the resuscitation suites
245prior to transport to the scanners, operating room, or observation units,
246serial hemoglobin provides little to no use in the detection of occult blood
247loss. Furthermore, serial hemoglobin potentially misdirects and confuses the
248physicians and the rest of the trauma team in the resuscitation suites,
249decreasing the efficiency of the code trauma.

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287

289**Table 1. The distribution of interventions among the blunt trauma**
290**cohort*.**

291

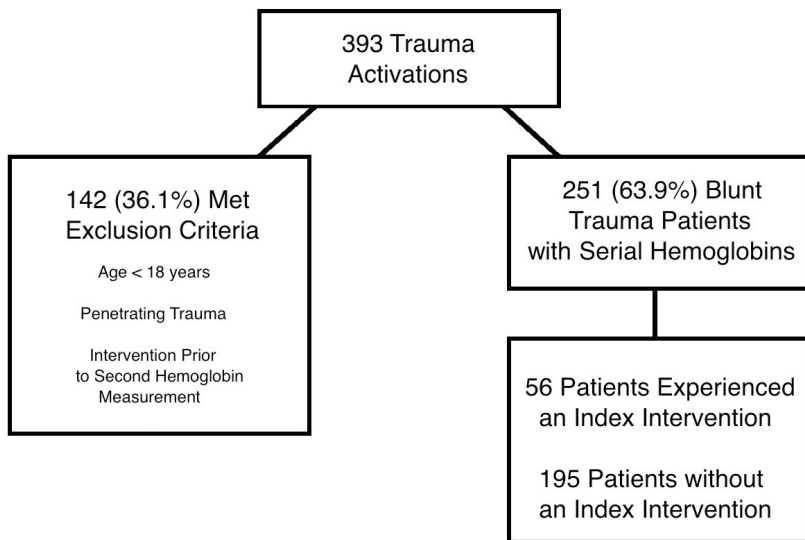
Intervention	Number of administrati ons	Proportion of all patients (N = 251)	Proportion of patients receiving any interventi on (N = 56)	Proportion of all interventio ns (N = 93)
Operation alone	4	1.6%	7.1%	4.3%
Embolizatio n	0	0%	0%	0%
Blood alone	4	1.6%	7.1%	4.3%
Fluids alone	19	7.6%	33.9%	20.4%
Exsanguinat ion	0	0%	0%	0%
Blood and fluids	20	8.0%	35.7%	21.5%
Fluids and operation	3	1.2%	5.4%	3.2%
Blood, fluids and operation	6	2.4%	10.7%	6.5%
Fluid, blood and embolizatio n	1	0.4%	1.8%	1.1%
Any fluid	48	19.1%	85.7%	51.6%
Any blood	31	12.4%	55.4%	33.3%
Any embolizatio n	1	0.4%	1.8%	1.1%
Any operation	13	5.2%	23.2%	14.0%

292

293*1 - Operation or procedure to control hemorrhage, 2 - radiographic
294embolization, 3 - administration of blood and blood products, 4 -
295administration of three or more liters of IV fluids, 5 - exsanguination.

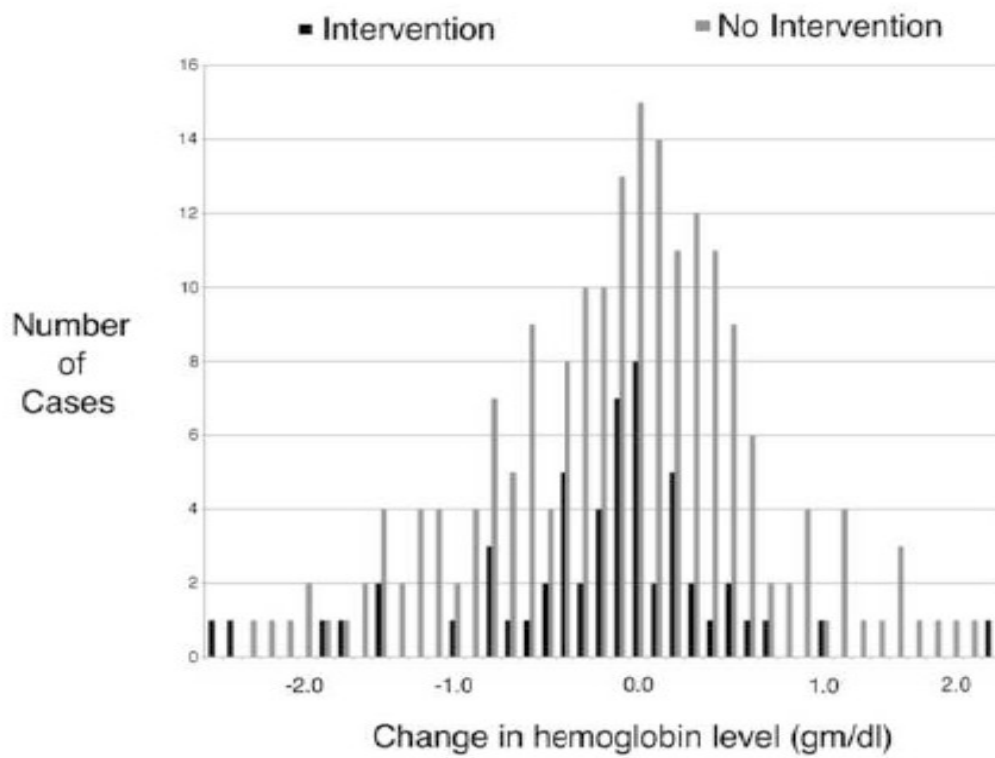
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297Figure 1 - Patient Flow Diagram



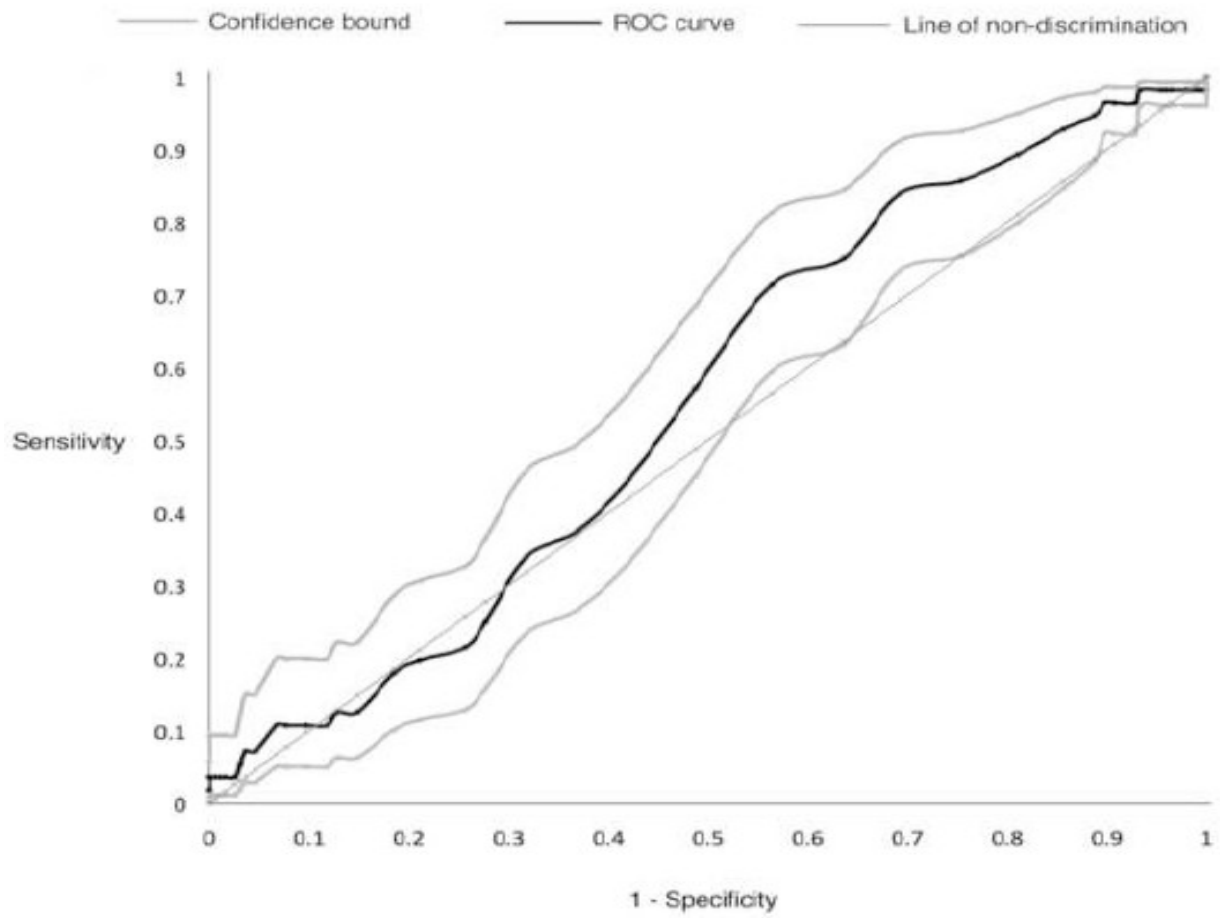
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300 Figure 2 - Number of Interventions at Different "Changes in Hemoglobin"
301 Levels
302
303



304
305

306 Figure 3 - Receiver Operator Curve for "Change in Hemoglobin"



307