

# Timing of Orthopaedic Surgery in Multiple Trauma Patients: Development of a Protocol for Early Appropriate Care

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**Objectives:** The purpose was to define which clinical conditions warrant delay of definitive fixation for pelvis, femur, acetabulum, and spine fractures. A model was developed to predict the complications.

**Design:** Statistical modeling based on retrospective database.

**Setting:** Level 1 trauma center.

**Patients:** A total of 1443 adults with pelvis (n = 291), acetabulum (n = 399), spine (n = 102), and/or proximal or diaphyseal femur (n = 851) fractures.

**Intervention:** All fractures were treated surgically.

**Main Outcome Measurements:** Univariate and multivariate analysis of variance assessed associations of parameters with complications. Logistic predictive models were developed with the incorporation of multiple fixed and random effect covariates. Odds ratios, *F* tests, and receiver operating characteristic curves were calculated.

**Results:** Twelve percent had pulmonary complications, with 8.2% overall developing pneumonia. The pH and base excess values were lower ( $P < 0.0001$ ) and the rate of improvement was also slower (all  $P$ s  $< 0.007$ ), with pneumonia or any pulmonary complication. Similarly, lactate values were greater with pulmonary complications (all  $P$ s  $< 0.02$ ), and lactate was the most specific predictor of complications. Chest injury was the strongest independent predictor of pulmonary complication. Initial lactate was a stronger predictor of pneumonia ( $P = 0.0006$ ) than initial pH ( $P = 0.047$ ) or the rate of improvement of pH over the first 8 hours ( $P = 0.0007$ ). An uncomplicated course was associated with the absence of chest injury ( $P < 0.0001$ ) and definitive fixation within 24 ( $P = 0.007$ ) or 48 hours ( $P = 0.005$ ). Models were developed to predict probability of complications with various injury combinations using specific laboratory parameters measuring residual acidosis.

**Conclusions:** Acidosis on presentation is associated with complications. Correction of pH within 8 hours to  $>7.25$  was associated with fewer pulmonary complications. Presence and severity of chest injury, number of fractures, and timing of fixation are other significant variables to include in a predictive model and algorithm development for Early Appropriate Care. The goal is to minimize complications by definitive management of major skeletal injury once the patient has been adequately resuscitated.

**Key Words:** damage control, multiple injury, polytrauma, acidosis, fixation timing

**Level of Evidence:** Prognostic Level II. See Instructions for Authors for a complete description of levels of evidence.

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## INTRODUCTION

Unstable fractures of the femoral shaft, proximal femur, and acetabulum generate pain and relegate injured patients to a recumbent position. Mechanically unstable axial skeletal injuries including thoracolumbar fractures and pelvic ring injuries are similar in their initial implications for patient immobility until fractures are reduced and stabilized. Each of these injuries predisposes to pulmonary compromise, systemic inflammation, and immune dysfunction, whereas fracture fixation provides pain relief and promotes mobility.<sup>1</sup> It is accepted that early stabilization of femoral shaft fractures<sup>2–11</sup> and unstable fractures of the pelvis,<sup>12–15</sup> acetabulum,<sup>15,16</sup> or spine<sup>17–23</sup> reduces complication rates, especially those related to pulmonary compromise and sepsis.<sup>7,24–29</sup> This is attributed to the elimination of prolonged skeletal traction and recumbency.<sup>5,30</sup> The benefits of early stabilization seem more profound in multiply injured patients versus those with isolated orthopaedic injury.<sup>5,8,9</sup>

“Early total care,” the early definitive management of all fractures, has been problematic because the additional hemorrhage with surgery may be associated with a deleterious systemic inflammatory response and related complications in underresuscitated patients, generating a “second hit” beyond the systemic impact of the injury itself (first hit).<sup>31–37</sup> Damage control (DCO) is an attractive alternative in severely injured patients to provide provisional stability, generally through external fixation.<sup>35,36,38–44</sup> This tactic is associated with decreased initial operative times and less bleeding than definitive fracture surgery.<sup>41</sup> However, many unstable pelvis and

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acetabulum fractures and thoracolumbar spinal fractures cannot be provisionally stabilized with external fixation; and for those patients treated with DCO, the need for further surgery and the additional implant and other hospital costs associated with this strategy should be considered.<sup>3,4,32,40,45,46</sup> Furthermore, the specific circumstances when a patient would benefit from a DCO strategy have not been clarified.<sup>47</sup> The majority of previous studies lack the rigor of a randomized prospective design and have limitations of small group size and variable definitions of “early” fixation timing. Confounding factors such as associated injuries to the head, chest, or abdomen and the severity of injury have not been accounted for in most of the published literature to date. Thus, conclusions are limited and treatment recommendations are unclear.<sup>7,25,36,48</sup>

The purposes of this project were (1) to define which injuries or clinical parameters warrant delay of definitive fracture management, with particular respect to the adequacy of resuscitation and (2) to determine what time interval for fracture fixation promotes optimal patient outcome, provided the patient has been adequately resuscitated. A model will be developed to predict complications and to reduce complications and costs in the management of patients with mechanically unstable fractures of the thoracolumbar spine, pelvic ring, acetabulum, and proximal and diaphyseal femur.

**PATIENTS AND METHODS**

After IRB approval, a database of 1443 adult patients treated surgically at a level 1 trauma center between 1999 and 2006 for fractures of the pelvis (n = 291), acetabulum (n = 399), spine (n = 102), and/or proximal or diaphyseal femur (n = 851) was developed. Femoral fractures were treated with open reduction and internal fixation using plates and screws (n = 256), reamed intramedullary nails (n = 567), or both (n = 28). The database included 1053 men and 390 women with mean age of 37.8 years (range, 15–89) and mean Injury Severity Score (ISS) of 24.7 (range, 9–57). Low-energy fractures, such as from a fall from standing height, were excluded. Fractures secondary to neoplasm and skeletally immature fractures were also excluded. The mechanism of injury was motor vehicle collision in 805 (56%), motorcycle collision in 216 (15%), fall from a height in 204 (14%), pedestrian versus motor vehicle in 114 (7.9%), gunshot in 51 (3.5%), crush in 42 (2.9%), and other in 11 (0.8%) patients.

Timing of definitive surgical treatment of these fractures was within 24 hours in 869 patients (defined as early fixation) and after 24 hours of injury in 574 patients (range, 2–17 days). There were no differences in age, gender, or ISS for early versus delayed fixation. Incremental analysis of the timing of fixation was included based on the number of hours from injury until the time of the start of the definitive procedure. When patients were treated for more than 1 fracture of interest, the time of completion of the final definitive fixation was determined. Nine patients each had provisional external fixation of their femur or pelvis, and only the time of definitive treatment was used in the analysis. Other extremity fractures, for example, ankle or forearm fractures that could be splinted, were not included in the analysis of fracture timing, whether treated in the same surgical setting or on a more delayed basis.

Associated injuries of the chest (n = 463), abdomen (n = 333), and head (n = 158) were present (Table 1). Validated scoring systems, the ISS,<sup>49</sup> the Abbreviated Injury Scores (AIS), and the Glasgow Coma Scale,<sup>50</sup> were used to grade the severity of injuries. When AIS was ≤2 the chest and abdominal injuries were defined as minor, whereas when the AIS was >2, they were defined as severe. Types of treatment of associated injuries including urgent and emergent surgeries were not included in the analysis. Fracture characteristics, associated injuries, medical comorbidities, and the timing and techniques of provisional treatment and surgical procedures were documented. Vital signs and laboratory parameters including hematocrit, pH, base excess (BE), and lactate were documented throughout the first 72 hours after injury and surgery. Transfusion requirements, length of ventilator assistance, length of intensive care unit stay, and length of hospitalization were determined. Complications related to injury and treatment were reviewed, including wound infection, pulmonary complications [adult respiratory distress syndrome (ARDS), pneumonia, pulmonary embolism], renal failure, multiple organ failure, and deep venous thrombosis (DVT).

Deep wound infection was defined as purulent drainage requiring surgical debridement. Sepsis was defined as positive blood cultures in the presence of elevated white blood count. ARDS was defined as PaO<sub>2</sub>/FiO<sub>2</sub> ratio of <200 for >4 consecutive days with diffuse infiltrates on chest radiographs, in the absence of pneumonia.<sup>51</sup> Pneumonia was defined by plain chest radiograph with a new pulmonary infiltrate in the presence of purulent sputum, temperature >38°C, and a white blood cell count >10,000. Pulmonary embolus was diagnosed by positive ventilation/perfusion scan or pulmonary embolism protocol computerized tomography of the chest. Acute renal failure was defined as blood urea nitrogen >100 mg/dL, creatinine ≥3.5 mg/dL, and urine output <150 mL per day for ≥2 days. Multiple organ failure was defined as 2 or more organs in failure for a minimum of 3 consecutive days with a score of ≥4 points.<sup>26</sup> DVT was documented with venous duplex scanning proximal to the knee.

Statistical analysis was performed with SAS software (version 9.2; SAS Institute, Inc, Cary, NC). Univariate

**TABLE 1. Associated Injuries**

	Fixation Within 24 h (n = 869)	Fixation After 24 h (n = 574)	Total (n = 1443)	P
Abdominal injury	160 (18%)	173 (30%)	333 (23%)	<0.0001
Minor (AIS ≤ 2)	89 (10%)	97 (17%)	186 (13%)	NS
Severe (AIS > 2)	71 (8.2%)	76 (13%)	147 (10%)	
Chest injury	233 (27%)	230 (40%)	463 (32%)	<0.0001
Minor (AIS ≤ 2)	106 (12%)	89 (16%)	195 (14%)	NS
Severe (AIS > 2)	127 (15%)	141 (24%)	268 (18%)	
Head injury	227 (26%)	202 (36%)	429 (30%)	0.0002
GCS < 8	77 (8.9%)	81 (14%)	158 (11%)	NS
GCS = 9–15	150 (17%)	121 (21%)	271 (19%)	

The numbers of patients with associated abdominal, chest, and/or head injuries are listed. P values are listed for comparisons of the groups treated within versus after 24 hours of injury. Percentages indicate the percentage of patients with that associated injury who were treated early versus delayed.

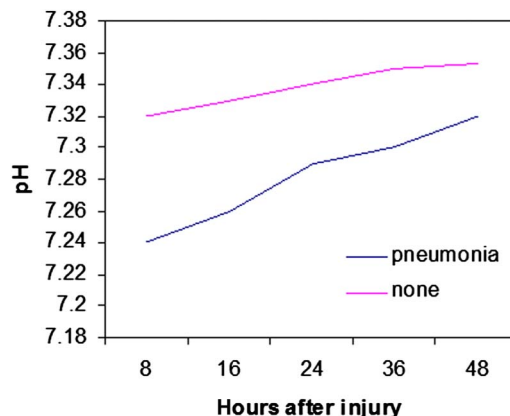
GCS, Glasgow Coma Scale; NS, not significant.

analysis of variance (ANOVA) and multivariate ANOVA (MANOVA) were used to assess associations of parameters over time with the occurrence of complications. Laboratory values were grouped in increments obtained within 8, 16, 24, 36, 48, and 72 hours of injury, and assessed for the development of various types of complications. Logistic predictive models were developed with the incorporation of multiple fixed and random effect covariates, including the effect of time.<sup>52-55</sup> Odds ratios, *F* tests, and receiver operating characteristic (ROC) curves were calculated based on the models. Statistical significance was defined as *P* < 0.05.

### RESULTS

Three hundred nineteen patients (22.1%) developed 354 complications during their initial episode of care (Table 2). The most frequent complications were pneumonia (8.2%) and DVT (6.4%). ANOVA and MANOVA showed that patients who developed pneumonia (Fig. 1), ARDS, any pulmonary complication, or any complication had significantly lower pH values at the time of presentation and within 8, 16, 24, 36, 48, and 72 hours of injury (all *P* < 0.0001). Similarly, BE and lactate values were also significantly worse at each of these time points in patients who developed pneumonia, ARDS, any pulmonary complication, or any complication. Table 3 presents some of the mean laboratory values for various groups of patients. The occurrence of complications was related to the initial objective laboratory measurements of acidosis and the rate of improvement of the values over time for each of these measurements of acidosis (*P* = 0.0009 for pH, *P* = 0.0008 for BE, and *P* = 0.014 for lactate related to complications). Hematocrit, platelets, INR, heart rate, blood pressure measurements, and transfusion requirements did not have an association with the development of complications.

Preliminary logistic predictive models were developed to predict pneumonia, ARDS, any pulmonary complication, and any complication, respectively. Presence and severity of chest injury, timing of definitive fracture fixation, and initial



**FIGURE 1.** Mean pH values improve over time. Patients who developed pneumonia had lower pH values and had significantly slower improvement of pH (both *P* < 0.001).

pH were associated with pneumonia with *P* = 0.0026, *P* = 0.0084, and *P* < 0.0001, respectively, and area under the ROC curve (AUROC) of 0.7647 (Fig. 2). The predicted probability of developing pneumonia based on initial pH and chest injury for patients definitively managed within 24 hours of injury (Fig. 3A) was lower than it was in those patients managed definitively after 72 hours (Fig. 3B). Presence and severity of chest injury and initial pH were also predictive of the development of ARDS with *P* < 0.0001 and *P* = 0.0022, respectively, with AUROC of 0.8198. Factors associated with an uncomplicated course included the absence of chest injury (*P* < 0.0001) and definitive fixation of fractures within the first 24 hours (*P* = 0.007) or 48 hours (*P* = 0.005). Multiple other preliminary models were generated including the presence and severity of abdominal injury, head injury, ISS, type of fracture, and the number of fractures treated. Of these, only ISS was weakly predictive of pneumonia. ROC curves for any pulmonary complication or for any complication had lower values for AUROC versus pneumonia.

Subsequent logistical predictive models incorporated the initial pH value and the magnitude and rate of change of the pH over time. When acidosis had not improved to normal within the first 24 hours, patients were more likely to develop pneumonia (*P* = 0.0007; AUROC = 0.7345) or any pulmonary complications (*P* = 0.024; AUROC = 0.7125). Incorporating time dependency of pH into the predictive model for pneumonia enhanced the AUROC to 0.7869 (Fig. 4) for the presence and severity of chest injury (*P* = 0.0049), timing of fixation (0.0015), and time-dependent pH (*P* < 0.0001). Subsequent models assessed the addition of BE and/or lactate and compared either or both of these parameters with pH as a predictor for pneumonia or other complications. Lactate was the most specific predictor of pneumonia, with *P* = 0.0006, versus pH (*P* = 0.047) or BE (*P* = 0.001). Final models were developed containing only one of these measurements of acidosis (pH, BE, or lactate) to avoid multicollinearity.

The next step was to analyze the data for predicted probability of pulmonary complications with incremental measurements of acidosis from a normal level. The first 2 measurements obtained within 16 hours of injury were used,

**TABLE 2.** Unadjusted Complications Based on Timing of Definitive Fracture Fixation

	Fixation Within 24 h (n = 869)	Fixation After 24 h (n = 574)	Total	<i>P</i>
Pneumonia	51 (5.9%)	67 (11.7%)	118 (8.2%)	<0.0001
ARDS	10 (1.2%)	23 (4.0%)	33 (2.3%)	0.0004
Renal failure	14 (1.6%)	10 (1.7%)	24 (1.7%)	NS
MOF	3 (0.35%)	2 (0.35%)	5 (0.35%)	NS
DVT	46 (5.3%)	46 (8.0%)	92 (6.4%)	0.038
PE	12 (1.4%)	10 (1.7%)	22 (1.5%)	NS
Wound infection	7 (0.81%)	5 (0.87%)	12 (0.83%)	NS
Sepsis	10 (1.2%)	23 (4.0%)	33 (2.3%)	0.0004
Death	8 (0.92%)	7 (1.2%)	15 (1.0%)	NS
Any complication	149 (17.1%)	170 (29.6%)	319 (22.1%)	<0.0001

MOF, multiple organ failure; NS, not significant; PE, pulmonary embolism.

**TABLE 3.** Mean Laboratory Values of pH, BE, and Lactate Were Obtained Upon Presentation and at Intervals of 8, 16, 24, and 36 Hours After the Injury

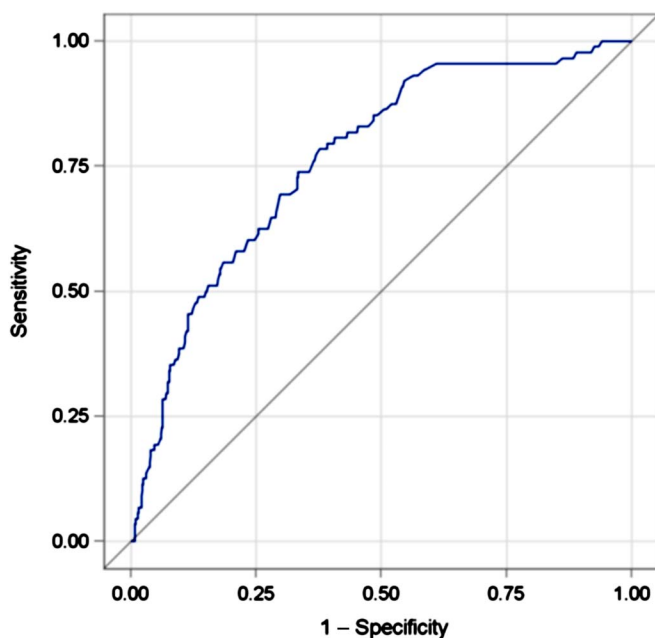
	All Patients	No Complications	Pneumonia	ARDS
Initial				
pH	7.31 ± 0.009 (6.86 to 7.56)	7.31 ± 0.005 (6.9 to 7.56)	7.24 ± 0.12 (6.86 to 7.47)	7.23 ± 0.20 (6.93 to 7.41)
BE, mmol/L	-6.24 ± 0.12 (0.3 to 24.2)	-6.13 ± 0.17 (0.3 to 9.1)	-8.66 ± 0.83 (-0.9 to 24.2)	-8.93 ± 0.81 (-8.1 to 20.8)
Lactate, mmol/L	3.03 ± 0.11 (0.7 to 8.8)	2.52 ± 0.18 (0.7 to 2.8)	4.01 ± 0.18 (1.2 to 8.8)	4.79 ± 0.46 (2.5 to 6.9)
After 8 h				
pH	7.31 ± 0.005 (7.01 to 7.43)	7.32 ± 0.003 (7.31 to 7.41)	7.27 ± 0.009 (7.01 to 7.43)	7.27 ± 0.022 (7.02 to 7.35)
BE, mmol/L	-5.62 ± 0.14 (-0.8 to 17.8)	-5.53 ± 0.12 (-0.8 to 4.9)	-7.43 ± 0.18 (-1.2 to 16.7)	-7.96 ± 0.71 (-7.2 to 17.8)
Lactate, mmol/L	3.16 ± 0.15 (0.9 to 7.0)	2.92 ± 0.18 (0.9 to 3.2)	3.90 ± 0.36 (3.3 to 7.0)	4.78 ± 0.50 (3.1 to 7.0)
After 16 h				
pH	7.33 ± 0.003 (7.07 to 7.44)	7.34 ± 0.003 (7.33 to 7.40)	7.29 ± 0.009 (7.07 to 7.41)	7.28 ± 0.017 (7.08 to 7.29)
BE, mmol/L	-5.00 ± 0.13 (-1.2 to 15.8)	-4.93 ± 0.12 (-1.2 to 5.1)	-6.17 ± 0.85 (-2.1 to 15.8)	-6.93 ± 0.92 (-5.9 to 15.1)
Lactate, mmol/L	3.11 ± 0.14 (1.0 to 6.9)	2.80 ± 0.17 (1.0 to 3.0)	3.77 ± 0.34 (3.0 to 6.7)	4.73 ± 0.48 (3.1 to 6.9)
After 24 h				
pH	7.34 ± 0.005 (7.09 to 7.41)	7.35 ± 0.003 (7.34 to 7.40)	7.30 ± 0.008 (7.12 to 7.41)	7.30 ± 0.17 (7.09 to 7.34)
BE, mmol/L	-4.41 ± 0.12 (-0.4 to 15.0)	-4.37 ± 0.12 (-0.4 to 3.7)	-6.03 ± 0.84 (-1.8 to 11.7)	-5.66 ± 0.97 (-5.8 to 15.0)
Lactate, mmol/L	3.06 ± 0.14 (1.0 to 6.7)	2.75 ± 0.16 (1.0 to 3.0)	3.79 ± 0.35 (2.9 to 6.7)	4.12 ± 0.43 (3.2 to 6.7)
After 36 h				
pH	7.35 ± 0.005 (7.09 to 7.41)	7.36 ± 0.003 (7.35 to 7.41)	7.32 ± 0.008 (7.15 to 7.40)	7.32 ± 0.016 (7.09 to 7.35)
BE, mmol/L	-3.91 ± 0.14 (-0.9 to 10.9)	-3.86 ± 0.12 (-0.9 to 3.2)	-5.25 ± 0.14 (-1.6 to 10.7)	-5.14 ± 0.75 (-1.5 to 10.9)
Lactate, mmol/L	3.02 ± 0.12 (1.0 to 5.6)	2.61 ± 0.17 (1.0 to 2.8)	3.66 ± 0.25 (2.8 to 5.5)	4.13 ± 0.86 (2.1 to 5.6)

Values are displayed for patients with an uncomplicated course of care, and those patients who developed pneumonia or ARDS. Each value is shown with the SD and range. At each time point, values for patients with pneumonia or ARDS were significantly different from those with no complications.

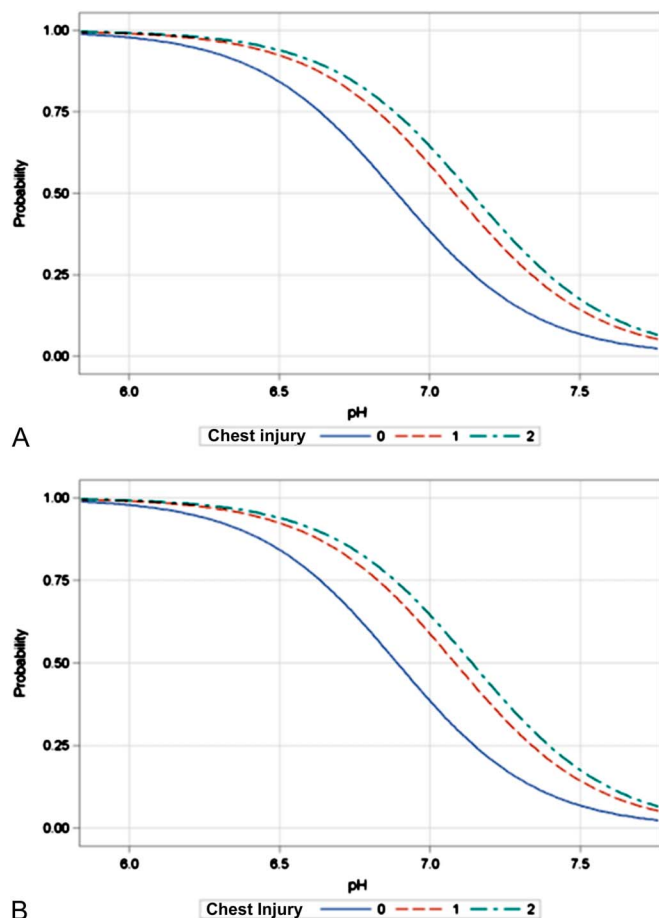
including the magnitude of the value and the rate and direction of change of the value. The pH, BE, and lactate values were each assessed in 0.05 increments to develop cutoff values beyond which the probability of a complication

would diminish to an acceptable level. To predict pulmonary complications (both pneumonia and ARDS) at a frequency below 20%, a minimum level of resuscitation and improvement in acidosis was recommended. For pH, the calculated recommended value was  $\geq 7.25$ . BE at or above  $-5.5$  mmol/L and lactate  $< 4.0$  mmol/L were also identified. Each of these cutoff values was then incorporated into probability models including the presence and severity of chest injury and timing of fracture fixation. In predicting pneumonia, AUROC for lactate  $< 4.0$  mmol/L was 0.7717, AUROC for pH  $\geq 7.25$  was 0.7478, and AUROC for BE at or above  $-5.5$  mmol/L was 0.7669. Notably, for each parameter, 3 incremental values in each direction were also modeled, and the AUROC in all cases was lower than the AUROC with the selected cutoff value.

Figure 5A depicts the AUROC for the model with lactate  $< 4.0$  mmol/L, chest injury, and timing of fixation. Figure 5B shows the predicted probability for pneumonia based on the presence and severity of chest injury, the interval within which definitive fracture fixation took place, and the lactate level within 8 hours of injury ( $< 4.0$  or  $\geq 4.0$  mmol/L). For example, the probability of a patient with severe chest injury, lactate  $< 4.0$  mmol/L, and fracture fixation within 24 hours has a 13% probability of developing pneumonia. The same patient without chest injury has a 3.6% probability of developing pneumonia. A patient with severe chest injury, fixation  $> 48$  hours after injury, and lactate  $\geq 4.0$  mmol/L within 8 hours of injury has a 52% probability of developing pneumonia, whereas the same patient having lactate  $< 4.0$  mmol/L has a 23% probability of developing pneumonia. These examples highlight the independent effects of the presence and severity



**FIGURE 2.** ROC curve for the logistic regression model predicting pneumonia and incorporating chest injury, timing of fixation, and initial pH. Area under the curve is 0.7647.



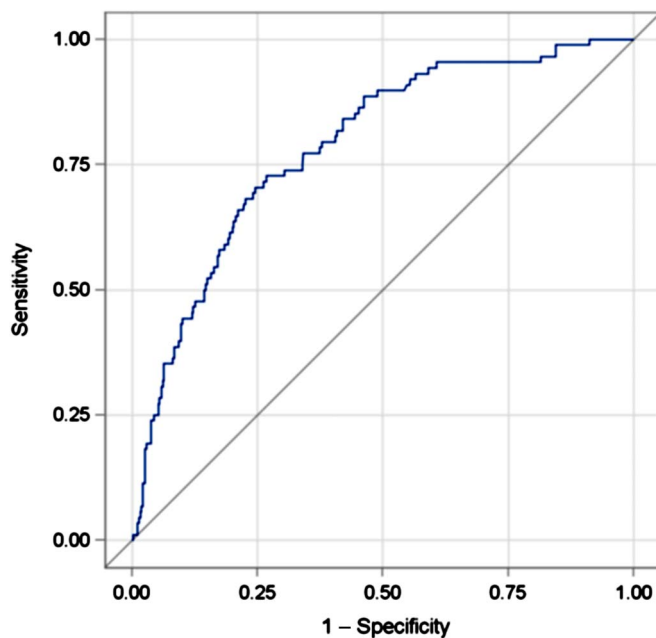
**FIGURE 3.** Predicted probability (1.00 = 100%) for developing pneumonia based on initial pH and the presence and severity of chest injury [0 = none, 1 = AIS ≤ 2 (minor), 2 = AIS ≥ 3 (severe)] for patients with definitive fracture fixation within 24 hours of injury (A) or >72 hours after injury (B).

of chest injury, magnitude and duration of acidosis, and timing of fixation on the development of pneumonia.

**DISCUSSION**

Complications are minimized when isolated fractures of the femur, pelvis, acetabulum, and spine are stabilized on an early basis. However, in patients with injuries to other body systems and/or severe hemorrhage, a DCO tactic may be advisable to prevent a heightened inflammatory response. The purposes of this project were to define which injuries or clinical parameters warrant delay of definitive fracture management, with particular respect to the course of resuscitation and to determine what time interval for fracture fixation promotes optimal patient outcome, provided the patient has been adequately resuscitated. Models were developed to predict and minimize complications in the management of patients with mechanically unstable fractures of the thoracolumbar spine, pelvic ring, acetabulum, and proximal and diaphyseal femur.

Previous studies on this topic have addressed changes in clinical practice over time. Rixen et al<sup>40</sup> performed a comprehensive literature review on the timing of treatment of

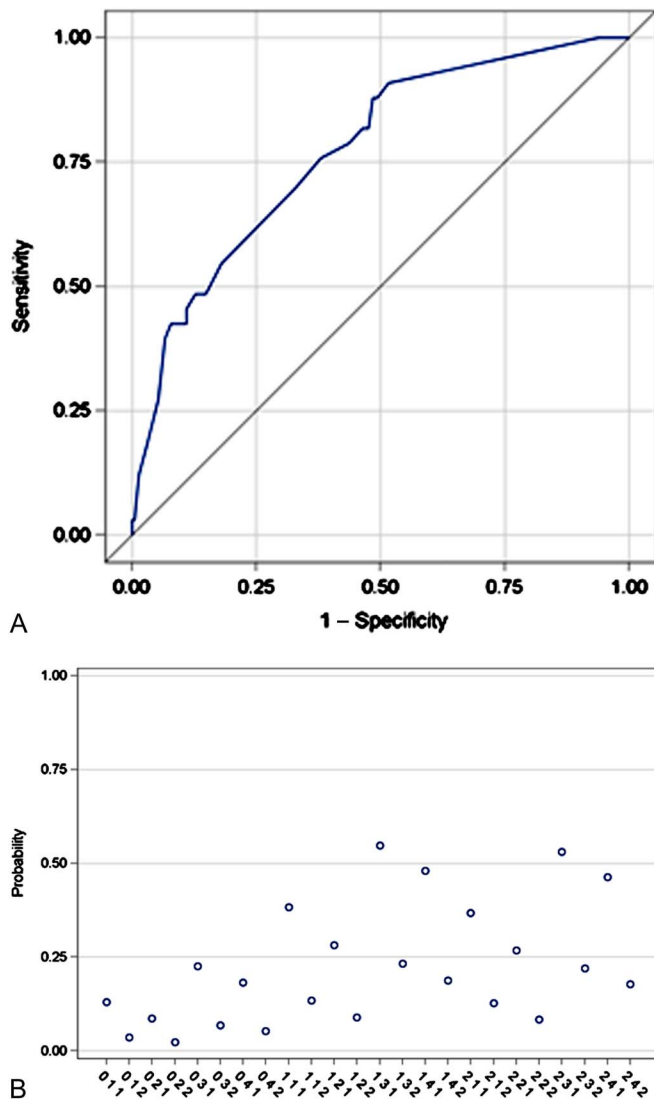


**FIGURE 4.** ROC curve for the logistic regression model predicting pneumonia and incorporating chest injury, timing of fixation, and time-dependent effect of pH within the first 16 hours after injury.

femoral shaft fractures. No definite advantage or disadvantage was identified for “early definitive” fracture stabilization. However, the level of evidence in most studies was quite poor. These authors also reviewed the German Trauma Society registry, which encompassed 1465 femoral shaft fractures treated over 8 years. The use of provisional or definitive external fixation in these patients increased over time and was more likely associated with an increased ISS, a lower Glasgow Coma Scale, thoracic trauma, a base deficit >6.0 mmol/L, or an elevated prothrombin time. However, no advantage to external fixation versus primary femoral stabilization with a nail or plate was seen, in any of these patient groups. They concluded that further study is warranted and suggested that “risk-adapted DCO orthopaedics” may be the best approach.<sup>40</sup>

The impact of definitive fixation of unstable spine, pelvis, and/or femoral fractures in patients with other major systemic injury has not been well studied. Clearly, severe chest injury is a risk factor for pulmonary complications, regardless of the type of musculoskeletal injury and methods of treatment.<sup>6,10,15,28,29,38,56</sup> We identified chest injury to be the strongest independent predictor of pulmonary complication. However, the reality is that many severely injured patients have some chest trauma, and their associated fractures must also be managed. Our data provide risk assessment for patients with chest injury and suggest that achieving a certain level of resuscitation before definitive stabilization of major fractures is helpful in reducing pulmonary complications.

The optimal type, timing, and sequence of treatment of combined abdominal and musculoskeletal injury are also unknown, although severe abdominal injuries frequently have massive associated hemorrhage, which can contribute to difficulty in initial resuscitation.<sup>6,7,10,29</sup> One of the weaknesses of this article



**FIGURE 5.** A, ROC curve for the logistic regression model predicting pneumonia, incorporating chest injury, timing of fixation, and lactate within 8 hours of injury. B, shows the probability of pneumonia (1.0 = 100%) where the first digit on the x axis corresponds to the presence and severity of chest injury: 0 = none, 1 = AIS  $\leq$  2 (minor), and 2 = AIS  $\geq$  3 (severe). The second digit on the x axis corresponds to definitive fracture fixation within 24 hours of injury (1), 24–48 hours after injury (2), 48–72 hours after injury (3), or >72 hours after injury (4). The third digit on the x axis refers to lactate  $\geq$  4.0 mmol/L within 8 hours of injury (1) or lactate < 4.0 (2).

is that details about various emergent and urgent procedures by other surgical services were not studied, for example, exploratory laparotomy may have been life saving and would have contributed to the control of hemorrhage and improvement of acidosis. Although we included all of the available laboratory information in developing our predictive models, we did not specifically record such nonorthopaedic procedures. Nevertheless, it seems that the patient's physiological status measured by acidosis seems to be predictive of complications whether sustaining other system injuries to the abdomen or head or not.

Many trauma patients exhibit acidosis secondary to rapid blood loss. Admission pH and BE values are proportional to the magnitude of the resuscitation needed, including blood and blood products.<sup>57</sup> These markers on presentation provide prognosis about morbidity and mortality. Inability to respond to resuscitation and normalize acidosis is associated with ARDS,<sup>58–60</sup> organ failure,<sup>59,61–63</sup> and death.<sup>64–69</sup> Our data support these findings, as patients who developed pneumonia, ARDS, or any complication had significantly lower pH, BE, and lactate levels on presentation to our hospital and incrementally over the first 72 hours. When acidosis had not improved to normal within 24 hours of injury, our patients were more likely to develop pneumonia or any pulmonary complication. Consistent with this theme, another recent study concluded that early reamed femoral nailing is safe in patients with ISS >17 provided they have been adequately resuscitated, as defined by significant improvement in serum lactate, with ARDS occurring in only 1.5%.<sup>38</sup> Previous work suggests that BE is superior to pH in evaluating acidosis associated with trauma,<sup>70,71</sup> but lactate may be the most specific measurement versus pH or BE.<sup>60,72</sup> Our data support this premise because lactate was the most specific predictor of pneumonia (vs. BE and pH). However, some measurement of acidosis, whether pH, BE, or lactate, is critical in assessing readiness for definitive fracture care.<sup>58</sup> During development of our model, only one of these types of values was needed to avoid multicollinearity. Serum lactate is easier to obtain than pH and BE, which are determined from an arterial sample.

Expedient resuscitation is critical in minimizing morbidity and preventing death in patients with severe acidosis from massive hemorrhage. Reduction and fixation of fractures can aid in control of hemorrhage; however, the additional bleeding associated with surgical procedures must be anticipated when planning the best course of care. Probst et al<sup>73</sup> performed a retrospective study of the German Trauma Registry and analyzed for independent effects of duration (<1, 1–3, and >3 hours) and timing (early = within 24 hours, intermediate = 24–72 hours, and late = >3 days) on outcomes of patients with pelvic ring injury. Delayed procedures or early short procedures had the lowest rates of organ failure and mortality in patients with ISS  $\geq$  16. Although we did not specify the duration of surgery in our modeling, we did include the number of fractures of interest. We also sought to determine a safe level of acidosis, in other words, a response to injury and resuscitation to permit definitive fracture management. Our tactic differs from these authors in that no measurement of their patients' physiological status was described, although longer procedures may be associated with more bleeding and coagulopathy, which could be problematic in underresuscitated patients.

Most literature on early fixation versus DCO has focused on femoral shaft fractures. Pape et al have suggested that patients with femoral shaft fractures may be classified into stable, borderline, unstable, and in extremis groups at the time of presentation.<sup>36,39</sup> Each of these groups was defined based on temperature, coagulation, and shock. Presence and severity of injury to the pelvis, abdomen, chest, and extremities were also included. DCO was recommended for those patients who are unstable or in extremis. However, the optimal type and timing of treatment for patients who are borderline remain controversial. Although it seems appropriate to

consider the magnitude of shock and the types and severity of injury to other systems when designing a plan for fracture management, to our knowledge, no models have been previously developed to determine the risk of pulmonary or other complications. A recommended level of resuscitation has not been prospectively tested in this population. To our knowledge, no parameters measuring acidosis have been prospectively assessed to determine their efficacy in minimizing complications in patients with major orthopaedic trauma with or without other system injury.

Those authors recommended DCO for those patients who are unstable or in extremis, as defined by hypotension (lactate  $> 2.5$  mmol/L, “severe acidosis”), coagulopathy (platelets  $< 70,000$  and abnormal D-dimer), and body temperature  $\leq 32^{\circ}\text{C}$ .<sup>36,39</sup> Borderline patients have less systemic injury and a lower level of hypotension and acidosis. Forty-four borderline patients with femoral shaft fractures were randomized prospectively into DCO and early treatment groups to determine the potential for complications with either strategy.<sup>36</sup> A borderline status was defined by at least 3 of the following: systolic blood pressure 80–100 mm Hg or lactate  $\geq 2.5$  mmol/L; platelets 90,000–110,000 per microliter, temperature 33–35°C; and chest AIS  $\geq 2$ , extremity AIS 2 or 3, or pelvic fracture. Time points of measurements were not specified. Early and DCO groups had no differences in the frequency of pneumonia, ARDS, multiple organ failure, or sepsis. However, acute lung injury, defined as bilateral diffuse infiltrates and  $\text{PaO}_2:\text{FiO}_2 < 300$ , was noted less often after DCO (16.7% vs. 52.4%,  $P = 0.048$ ). The clinical relevance of acute lung injury was not described.

We agree with these investigators in incorporating measurements of resuscitation and the type and severity of associated injury when considering the type and timing of orthopaedic care. In developing our model, we identified the presence and severity of chest trauma, initial magnitude of and response to acidosis, and timing of definitive fracture care as key determinants of pulmonary risk. We believe it is rational to apply these criteria to fractures other than the femoral shaft, as such injuries present the patient with a similar burden of recumbency and pain.

Our study is limited by its retrospective design in that there was no standardized protocol for timing and sequence of fracture fixation. Our general practice has been to limit definitive management of fractures that can be splinted until systemic status has normalized. However, without a standard protocol, the initial early treatment of some of these injuries could have contributed to prolonged surgical times, increased hemorrhage, and overall delay in achieving complete resuscitation. This may have had an unaccounted deleterious effect on those patients defined as having received “early care” for their pelvis, femur, or spine. As was stated previously, we did not incorporate the duration of surgical care into our models. Another limitation of our project was the absence of a defined protocol for laboratory measurements. Laboratory data were available at inconsistent time points, which limit the usefulness of strict conclusions about incremental improvement over time. Despite this, we analyzed all available parameters to groups within 8, 16, 24, 36, 48, and 72 hours of injury. We chose classic statistical methods, including multivariate logistic regression to adjust confounding effects. With a very large

sample, this methodology should be appropriate. A validation study would better serve to validate the cutoff values and the predictive ability of the proposed models. Our study is also limited by the definition of pneumonia, which may have resulted in a greater number of patients with pulmonary complications than if a more stringent definition were used.<sup>74</sup> This has been noted to be problematic in recent literature, and future work may benefit from quantitative cultures from the lower airways. Some of the strengths of this study include a large patient sample, within which confounding factors of fracture types and other injury types and severity could be accounted for. In addition, our hospital has standardized protocols for perioperative antibiotics, DVT prophylaxis and assessment, and nutrition.

We believe our findings can be applicable to other hospital systems. Based on our data, we have implemented a prospective protocol to standardize patient physiological assessment and to recommend timing of definitive fracture care according to the response to resuscitation. Such an approach requires team-based planning and communication incorporating input from specialists in general trauma, neurosurgery, and anesthesia, along with orthopaedic traumatology. It also requires operational support from the hospital to provide timely operating room access with experienced staff and appropriate equipment every day. Our protocol for Early Appropriate Care (EAC) recommends definitive management of mechanically unstable fractures of the pelvis, acetabulum, proximal femur, femoral shaft, and spine within 36 hours of injury as long as the patient has demonstrated response to resuscitation as based on improvement of acidosis with lactate  $< 4.0$  mmol/L, pH  $> 7.25$ , or BE less than  $-5.5$  mmol/L. During persistent acidosis, a DCO strategy is used, and the patient is continually reassessed to determine the timing of definitive care.

In conclusion, early recognition and control of hemorrhage and aggressive resuscitation to improve acidosis are critical in reducing morbidity and mortality. Acidosis on presentation as measured by pH, BE, or lactate is predictive of complications, and early definitive fixation in resuscitated patients is favorable. Within the first 8 hours, correction of lactate  $< 4.0$  mmol/L, pH  $> 7.25$ , or BE less than 5.5 mmol/L is associated with a reduced risk of pulmonary complications. Presence and severity of chest injury, number of fractures to be treated, and timing of fixation are other significant variables to include in a predictive model for pulmonary complications. The goal is to minimize complications by definitive management of major skeletal injury once the patient has been adequately resuscitated. This should translate into shorter length of hospital stay and lower costs of care.

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