An innovative approach to predict the development of adult respiratory distress syndrome in patients with blunt trauma

Robert D. Becher, MD, Alexander L. Colonna, MD, Toby M. Enniss, MD, Ashley A. Weaver, MS, Daniel K. Crane, MD, R. Shayn Martin, MD, Nathan T. Mowery, MD, Preston R. Miller, MD, Joel D. Stitzel, PhD, and J. Jason Hoth, MD, PhD, *Winston-Salem, North Carolina*

| BACKGROUND: METHODS: | Pulmonary contusion (PC) is a common injury associated with blunt chest trauma. Complications such as pneumonia and adult respiratory distress syndrome (ARDS) occur in up to 50% of patients with PC. The ability to predict which PC patients are at increased risk of developing complications would be of tremendous clinical utility. In this study, we test the hypothesis that a novel method that objectively measures percent PC can be used to identify patients at risk to develop ARDS after injury. Patients with unilateral or bilateral PC with an admission chest computed tomographic angiogram were identified from the trauma registry. Demographic, infectious, and outcome data were collected. Percent PC was determined on admission chest computed tomography using our novel semiautomated, attenuation-defined computer-based algorithm, in which the lung was segmented with minimal manual editing. Factors contributing to the development of ARDS were identified by both univariate and multivariable logistic regression analyses. ARDS was defined as PaO ₂ /FiO ₂ ratio of less than 200 with diffuse bilateral infilterates on sheat rediograph with end and as PaO ₂ /FiO ₂ ratio of less than 200 with diffuse bilateral |
|-------------------------|---|
| RESULTS: | Quantifying percent PC from our objective computer-based approach proved successful. We found that a contusion size of 24% of total lung volume or greater was most significant at predicting ARDS, which occurred in 78% of these patients. Such patients also had a significantly higher incidence of pneumonia when compared with those with contusions less than 24%. The specificity of contusion size of 24% or greater was 94%, although sensitivity was 37%; positive predictive value was 72% |
| CONCLUSION: | We developed and describe a software-based methodology to accurately measure the size of lung contusion in patients of blunt trauma. In our analyses, contusions of 24% or greater most significantly predict the development of ARDS. Such an objective approach can identify patients with PC who are at increased risk for developing respiratory complications before they happen. Further research is needed to use this novel methodology as a means to prevent posttraumatic lung injury in patients with blunt trauma. (<i>J Trauma Acute Care Surg.</i> 2012;73: 1229–1235. Copyright © 2012 by Lippincott Williams & Wilkins) |
| LEVEL OF EVIDENCE: | Prognostic/epidemiologic study, level III; diagnostic study, level IV. |
| KEY WORDS: | Pulmonary contusion; ARDS; automated CT. |

P ulmonary contusion (PC) is a common injury seen after blunt trauma that is associated with significant morbidity and mortality.^{1–3} Complications stemming from a contused lung occur in up to 50% of patients with PC and include pneumonia, respiratory failure requiring prolonged mechanical ventilation, and adult respiratory distress syndrome (ARDS). PC is an independent risk factor of death in patients

DOI: 10.1097/TA.0b013e31825b2124

J Trauma Acute Care Surg Volume 73, Number 5 with trauma, with estimates of mortality as high as 25%; when PC is complicated by ARDS, mortality can reach 50%.³⁻⁶

Symptoms of PC evolve during the first 24 hours after admission and vary from simple dyspnea to severe respiratory failure.¹ Pathophysiologically, PC causes a parenchymal lung injury resulting in inefficient gas exchange and hypoxia caused by ventilation/perfusion mismatching from alveolar collapse and lung consolidation.¹ In addition, PC activates inflammatory mechanisms both locally and systemically, which have been shown to contribute to worsening hypoxia, ARDS, remote organ dysfunction, and death.⁷ This inflammatory response has delayed repercussions in that it also "primes" inflammatory cells for exaggerated responses to subsequent stimuli resulting in the second hit phenomenon, which is observed clinically.⁸

Given the delay in the onset of clinical symptoms and the immediate and delayed effects on inflammation, a potential therapeutic window exists for patients who have sustained PC during which preventive measures may be used. In fact, PC has previously been identified as an independent risk factor for acute lung injury (ALI), on which can be intervened.⁹ Thus, early identification of patients who are at high risk for the severe complications stemming from PC is warranted.

Submitted: October 7, 2010, Revised: April 17, 2012, Accepted: April 18, 2012. Published online: August 20, 2012.

From the Department of Surgery (R.D.B., A.L.C., R.S.M., N.T.M., P.R.M., J.J.H.) and Virginia Tech-Wake Forest University Center for Injury Biomechanics (A.A.W., J.D.S.), Wake Forest University School of Medicine, Winston-Salem, North Carolina; Department of Surgery (T.M.E.), University of Utah Health Science Center, Salt Lake City, Utah; and the Emergency Medicine (D.K.C.), University of Alabama at Birmingham, Birmingham, Alabama.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.jtrauma.com).

R.D.B. and A.L.C. contributed equally to the study.

Address for reprints: J. Jason Hoth, MD, PhD, Department of Surgery, Wake Forest University School of Medicine, Medical Center Blvd, Winston-Salem, NC 27157; email: jhoth@wakehealth.edu.

To predict complications from PC, previous studies have focused on quantifying the size of PC as a percentage of total lung volume (TLV) using computed tomographic (CT) angiogram of the chest obtained at the time of admission. Patients with contusions of greater than 20% TLV were shown to be more likely to require mechanical ventilation and develop ARDS.^{6,10} These studies quantified PC as a percentage of TLV in a semiquantitative manner, using CT imaging with expert opinion or computer-assisted measurement. Both of these methods are cumbersome to perform and have inherent interobserver error that can potentially reduce the accuracy of the predicted contusion size.^{4,11} These currently used methodologies of quantifying percent PC from CT images have been shown to be antiquated, overly subjective, and highly variable in nature.¹²

Taking advantage of modern, advanced CT imaging should be fundamental to an imaging-based prediction model. Such a methodology could rapidly and accurately quantify PC size to predict which patients are at increased risk of developing complications; this would be of tremendous clinical utility.

To specifically address this, we have developed an objective, computer-based analysis program that rapidly quantifies PC size in relation to TLV from three-dimensional CT images. Our hypothesis is that this modern technique of objectively assessing lung injury can expeditiously and accurately measure the size of PC and that PC size will enable the clinician to reliably predict which patients are at increased risk to develop ARDS and other complications after injury.

PATIENTS AND METHODS

Patient Characteristics and Selection

Approval was obtained from the Wake Forest University Baptist Medical Center Institutional Review Board (#BG03-081). Patients were retrospectively identified from the trauma registry of our Level I trauma center during a 12-month period. We included patients who were diagnosed with a unilateral or bilateral PC on admission chest CT scan. Patient medical records were reviewed for demographic information, admission physiologic parameters, and arterial blood gas measurements in the first 72 hours of admission. Outcome metrics were also collected, including the onset of ARDS within the first 72 hours of admission, pneumonia, hospital length of stay, and in-hospital mortality. ARDS was defined as PaO2/FiO2 ratio of less than 200 with diffuse bilateral infiltrates on chest roentgenogram with no evidence of congestive heart failure.13 Pneumonia was diagnosed by bronchoalveolar lavage and defined as 10⁵ colony-forming units per milliliter or greater. Our institution participates in the National Heart, Lung, and Blood Institute's ARDS Network.¹⁴ Mechanical ventilator settings, both in the emergency department and in the trauma intensive care unit, were determined according to ARDS Network protocols; ventilator settings were not influenced by initial CT scan findings. Patients younger than 16 years were excluded because they are not included in the trauma registry.

PC Measurement

A computerized, semiautonomous method for quantifying volumes of injured lung has been previously described and published by our institution.^{2,15} These methods were initially developed using positron emission tomography and CT scans to quantify pulmonary pathology in rats subjected to a direct lung impact. The pathologic contused lung volumes coupled with experimental impact data were used to validate an injury prediction model of rat lungs by means of imaging-based finite elements, also known as segmentation. In the current study, a methodology similar to but unique from the initial approach for segmenting the rat CT data was used. In this newer approach, we created a computer-based model to isolate and differentiate normal from pathologic lung tissue on chest CT scan (complete methods, including color version of Figure 1, are provided in the Supplemental Digital Content 1, http://links.lww.com/TA/A163). This is a semiautomated, attenuation-defined approach designed specifically to segment CT scans in patients sustaining blunt chest trauma.

Statistical Analysis

Statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC). χ^2 analysis or Fisher's exact test was used to compare differences in proportions of categorical variables; such data were presented as percentages. Student's t tests were used to compare normally distributed continuous variables; such data were presented as mean (SD). Wilcoxon rank sum tests were used to compare nonnormally distributed continuous variables; such data were presented as median values with interquartile ranges. Contributing factors to the development of ARDS were identified by both univariate and multivariable logistic regression analyses. Candidate covariates for multivariable regression were included based on their statistical significance using stepwise selection; a significance level of 0.15 was required to enter the model, and one of 0.05 was required to stay in the model. Significance was defined as p < 0.05 throughout.

RESULTS

Patient Characteristics

A total of 202 patients with PC on admission CT scan were identified during the 1-year period (Table 1). Most of the patients were involved in motor vehicle accidents and were severely injured with a median Injury Severity Score (ISS) of 22 and chest Abbreviated Injury Scale (AIS) score of 3. The mean PC volume was 12.9%; 26 patients (13%) developed pneumonia, and 75 patients (37%) developed ARDS. Mean length of stay was 13 days, and 18 patients (9%) died during their hospitalization.

Pulmonary Function, Severity of Contusion, and Outcome

Logistic regression analysis was used to determine if PC size was an independent predictor for the development of ARDS within the first 72 hours of admission (Table 2). In the univariate analysis, myriad candidate covariates significantly increased the risk of subsequent ARDS; these variables were admission lactate, systolic blood pressure (SBP), total Glasgow Coma Scale (GCS) score, motor GCS score, ISS, chest AIS score, extremity AIS score, need for blood transfusion, and size of PC. In the multivariable analysis, the following four variables were found to be independently predictive of the development of ARDS: size of PC, ISS, admission GCS score, and administration of blood products.

TABLE 1. Overall Patient Characteristics

| Patient Characteristic | Value (n = 202) | |
|---------------------------------------|-----------------|--|
| Demographics | | |
| Age, y | 36 (17) | |
| Female | 61 (30.2) | |
| Physiologic parameters | | |
| Lactate | 3.0 (2.2) | |
| SBP | 130 (23) | |
| Injury severity measures | | |
| GCS, total score | 15 (13–15) | |
| GCS, motor score | 6 (6–6) | |
| ISS | 22 (18-29) | |
| AIS score, chest | 3 (3–4) | |
| AIS score, extremity | 2 (2–3) | |
| Patients requiring blood transfusions | 43 (21.3) | |
| Pulmonary status and outcomes | | |
| Size PC, % | 12.9 (13.5) | |
| Patients developing pneumonia | 26 (12.9) | |
| Patients developing ARDS | 75 (37.1) | |
| Ventilator days | 4.7 (10.2) | |
| Patient outcomes | | |
| Length of total hospital stay, d | 13.1 (17.6) | |
| Mortality | 18 (9.0) | |

Categorical variables are presented as n (%); continuous data are presented as mean (SD); and nonnormally distributed continuous variables as median (interquartile range).

A PC of 24% was most significant at predicting development of ARDS and portended the poorest prognosis to develop ARDS. For patients with less than 24% PC, the incidence of ARDS was 28%; for patients with 24% PC or greater, the incidence of ARDS was 78% (Table 3). The patients with 24% PC or greater were more severely injured overall, with higher ISS and chest AIS scores, with lower admission GCS scores, and received significantly more blood transfusions in the first 24 hours after admission. These patients also had a higher incidence of pneumonia and longer hospital stays; however, there was no difference in mortality.

ARDS Versus No ARDS

Overall, 75 patients (37%) developed ARDS (Table 4). Patients who developed ARDS had significantly larger PCs (19.2% vs. 9.1%), significantly higher rates of pneumonia (32% vs. 1.6%), and a much higher rate of mortality (21.3% vs. 1.6%). Of injury severity measures, the patients who went on to develop ARDS had a higher median ISS, chest AIS score, GCS score, and motor GCS score; patients with ARDS also required significantly more blood transfusions in the first 24 hours of their hospitalization.

In the 127 patients who did not develop ARDS, 119 had contusions of less than 24% and 8 had contusions of 24% or greater; this translates into a specificity of 94% for PC of 24% or greater. Of the 75 patients with ARDS, 28 had PC 24% or greater, whereas 47 had contusions of less than 24%; this indicates that the sensitivity of a contusion of 24% or greater is 37%. As such, the positive predictive value of a patient with a PC of 24% or greater was 78% in our patient population; the negative predictive value of a contusion <24% was 72% (note that positive predictive value and negative predictive value are dependent on prevalence and are therefore totally determined by local rates of ARDS). The area under the receiver operating characteristic curve was 0.8916.

Pneumonia Versus No Pneumonia

Of the 202 patients, 26 (12.9%) developed pneumonia (Table 5); the pneumonia versus no pneumonia cohorts were compared to examine the relationship between contusion size and the development of pulmonary infection. Patients who developed pneumonia had higher admission ISS and lower

| | Univariate Logistic Regression Models | | Multivariable Logistic Regression Model* | |
|------------------------------------|---------------------------------------|------------|--|---------------|
| Variable | OR (95% CI) | p † | OR (95% CI) | p^{\dagger} |
| Demographics | | | | |
| Age, y | 1.01 (1.00-1.03) | 0.0993 | _ | _ |
| Female | 0.68 (0.36-1.30) | 0.2484 | _ | _ |
| Physiologic parameters | | | | |
| Lactate | 1.28 (1.09–1.51) | 0.0029 | _ | _ |
| SBP | 0.98 (0.97-0.99) | 0.0032 | _ | _ |
| Injury severity measures | | | | |
| GCS, total score | 0.82 (0.75-0.88) | < 0.0001 | _ | _ |
| GCS, motor score | 0.65 (0.55-0.77) | < 0.0001 | 0.70 (0.58-0.85) | 0.0003 |
| ISS | 1.10 (1.06–1.14) | < 0.0001 | 1.07 (1.02–1.11) | 0.0046 |
| Chest AIS score ≥ 4 | 2.20 (1.23-3.93) | 0.0080 | _ | _ |
| Extremety AIS score ≥ 3 | 2.36 (1.26-4.40) | 0.0071 | _ | _ |
| Patient received blood transfusion | 7.85 (3.64–16.94) | < 0.0001 | 5.09 (2.02–12.83) | 0.0005 |
| Pulmonary status and outcomes | | | | |
| Size PC | 1.06 (1.04–1.09) | < 0.0001 | 1.06 (1.03–1.09) | 0.0003 |

 $\dagger p < 0.05$ was considered statistically significant.

CI, confidence interval; OR, odds ratio.

| TABLE 3. Patient Characteristics by Size of PC | | | |
|--|-----------------------|---|---------------|
| Variable* | PC < 24% (n = 166) | $\begin{array}{l} PC \geq 24\% \\ (n=36) \end{array}$ | p^{\dagger} |
| Demographics | | | |
| Age, y | 37 (17) | 35 (14) | 0.0831 |
| Female | 49 (29.5) | 12 (33.3) | 0.6513 |
| Physiologic parameters | | | |
| Lactate | 2.8 (2.2) | 3.5 (2.2) | 0.0867 |
| SBP | 131.5 (21.4) | 122.2 (28.6) | 0.0292 |
| Injury severity measures | | | |
| GCS, total score | 15 (14–15) | 14 (6–15) | 0.0133 |
| GCS, motor score | 6 (6–6) | 6 (1-6) | 0.0092 |
| ISS | 22 (17–29) | 29 (20-34) | 0.0037 |
| AIS score, chest | 3 (3–4) | 4 (3-4) | < 0.0001 |
| AIS score, extremity | 2 (2–3) | 3 (2–3) | 0.1810 |
| Patients requiring blood transfusions | 28 (16.9) | 15 (41.7) | 0.0010 |
| Pulmonary status and outcomes: | | | |
| Size PC, % | 7.8 (6.6) | 36.3 (12.2) | < 0.0001 |
| Patients developing pneumonia | 15 (9.0) | 11 (30.6) | 0.0005 |
| Patients developing ARDS | 47 (28.3) | 28 (77.8) | < 0.0001 |
| Ventilator days | 3.1 (6.9) | 12.3 (17.3) | < 0.0001 |
| Patient outcomes | | | |
| Length of total hospital stay, d | 10.6 (14.6) | 24.9 (24.5) | < 0.0001 |
| Mortality | 13 (7.8) | 5 (13.9) | 0.2475 |

*Categorical variables are presented as n (%); continuous data are presented as mean (SD); and nonnormally distributed continuous variables as median (interquartile range). †*p* values for overall tests of difference are from χ^2 analysis for categorical variables and Student's *t* test for continuous variables; a *p* < 0.05 was considered statistically significant.

GCS score and required significantly more blood transfusions. The PC size was, on average, higher in the group that developed pneumonia (21.0% vs. 11.7%). Of the patients, 92.3% who developed pneumonia also antecedently developed ARDS; this is contrasted to the 29.0% of patients without pneumonia who developed ARDS.

DISCUSSION

PC is a common injury after blunt trauma, with a complex pathophysiology, resulting from direct tissue damage and activation of both local and systemic inflammatory mechanisms, causing significant morbidity and mortality.¹⁶⁻²¹ Given that the onset of symptoms from PC is frequently delayed and that the effects that PC has on inflammation are sustained with potentially dire consequences, early identification of patients with PC at high risk for complications is indicated because these patients may benefit from early intervention. Accordingly, the ability to use an admission CT scan early in a hospitalization to rapidly and accurately identify patients with a PC who are at high risk to experience infectious morbidity, ARDS, remote organ failure, or death would be of tremendous clinical utility. The current study presents such an innovative prediction tool. We have developed an objective, computer-based analysis program that rapidly, easily, and accurately quantifies percentage of PC from three-dimensional CT images. This modern technique of objectively assessing lung injury allows us to predict ARDS within 72 hours of blunt lung injury.

Previous studies based their findings on contusion sizes measured either by subjective expert opinion or by semiobjective computer-assisted measurement.^{6,10,11,22} Both of these methods have inherent interobserver error that potentially reduces the accuracy of contusion size reported in these studies. The strength of the current study is the semiautomated, computerbased method to derive an estimate of PC from admission CT scan that is nearly entirely quantitative; this innovative approach attempts to remove the inherent error introduced by previous methods by standardizing the objective measurement of highopacity lung, which serves as a proxy for PC. This unique methodology is highly accurate, eliminates interobserver error/ bias, and allows for significantly enhanced precision in the measurement of contusion size. Furthermore, this tool is rapid (results obtained within minutes), is reproducible, and can be used both in the study of human subjects and in animal models of PC.^{2,3,23}

In the current study, size of PC was a continuous variable in the analyses. Older methods described by Miller et al.¹⁰ analyzed contusion volumes as a categorical, noncontinuous variable; patients were stratified into groups based on contusion severity using increments of 10%. An increase in the incidence of ARDS was seen at the 20% threshold, although this cutoff lacks accuracy and precision given its derivation from noncontinuous data. In a separate study, Miller et al.²⁰ analyzed 4,397

| TABLE 4. Patient Characteristics by ARDS Status | | | |
|---|------------------|----------------------|----------|
| Variable* | ARDS (n = 75) | No ARDS (n = 127) | p† |
| Demographics | | | |
| Age, y | 39 (19) | 35 (15) | 0.0975 |
| Female | 19 (25.3) | 42 (33.1) | 0.2472 |
| Physiologic parameters | | | |
| Lactate | 3.6 (2.4) | 2.6 (2.0) | 0.0008 |
| SBP | 123.6 (28.4) | 133.7 (18.3) | 0.0024 |
| Injury severity measures | | | |
| GCS, total score | 14 (3–15) | 15 (14–15) | < 0.0001 |
| GCS, motor score | 6 (1–6) | 6 (6–6) | < 0.0001 |
| ISS | 29 (21–34) | 22 (14–26) | < 0.0001 |
| AIS score, chest | 4 (3–4) | 3 (3–4) | 0.0055 |
| AIS score, extremity | 3 (2–3) | 2 (2–3) | 0.0783 |
| Patients requiring blood transfusions | 32 (42.7) | 11 (8.7) | < 0.0001 |
| Pulmonary status and outcomes | | | |
| Size PC, % | 19.2 (16.7) | 9.1 (9.4) | < 0.0001 |
| Patients developing pneumonia | 24 (32.0) | 2 (1.6) | < 0.0001 |
| Ventilator days | 11.0 (14.1) | 1.0 (3.2) | < 0.0001 |
| Patient outcomes | | | |
| Length of total hospital stay, d | 21.7 (21.5) | 8.1 (12.4) | < 0.0001 |
| Mortality | 16 (21.3) | 2 (1.6) | < 0.0001 |

*Categorical variables are presented as n (%); continuous data are presented as mean (SD); and nonnormally distributed continuous variables as median (interquartile range).

 $\dagger p$ values for overall tests of difference are from χ^2 analysis for categorical variables and Student's *t* test for continuous variables; a p < 0.05 was considered statistically significant.

| Variable* | Pneumonia (n = 26) | No Pneumonia (n = 176) | p† |
|--|-----------------------|---------------------------|----------|
| Demographics: | | | |
| Age, y | 41.0 (19.2) | 35.7 (16.3) | 0.1321 |
| Female | 9 (34.6) | 52 (29.6) | 0.5992 |
| Physiologic parameters | | | |
| Lactate | 3.6 (2.1) | 2.9 (2.2) | 0.0940 |
| SBP | 116.7 (29.7) | 131.9 (21.3) | 0.0015 |
| Injury severity measures | | | |
| GCS, total score | 9.5 (3–15) | 15 (14–15) | 0.0005 |
| GCS, motor score | 2 (1-6) | 6 (6–6) | < 0.0001 |
| ISS | 29 (22–34) | 22 (17-29) | 0.0006 |
| AIS score, chest | 4 (3–4) | 3 (3–4) | 0.0801 |
| AIS score, extremity | 3 (2–3) | 2 (2–3) | 0.0231 |
| Patients requiring blood transfusions | 13 (50.0) | 30 (17.1) | 0.0001 |
| Pulmonary status and outcomes | | | |
| Size PC, % | 21.0 (19.9) | 11.7 (11.9) | 0.0010 |
| Patients developing ARDS | 24 (92.3) | 51 (29.0) | < 0.0001 |
| Ventilator days | 24.4 (15.2) | 1.8 (4.4) | < 0.0001 |
| Patient outcomes | | | |
| Length of total hospital stay, d | 41.1 (23.0) | 9.0 (12.1) | < 0.0001 |
| Mortality | 5 (19.2) | 13 (7.4) | 0.0478 |

| TABLE 5. | Patient Characteristics by Presence of Pneum | onia |
|----------|--|------|

*Categorical variables are presented as n (%); continuous data are presented as mean (SD); and nonnormally distributed continuous variables as median (interquartile range).

p values for overall tests of difference are from χ^2 analysis for categorical variables and Student's *t* test for continuous variables; a p < 0.05 was considered statistically significant.

patients that sustained blunt trauma and identified independent risk factors for ARDS. One of the risk factors providing the greatest contribution to ARDS development was PC. However, in that study, PC was defined as a binary yes/no variable, and therefore, the percent contusion volume was not analyzed. Another study by Hamrick et al.⁶ calculated percent PC for 152 patients and analyzed the risk of assisted ventilation; the risk of ARDS was not correlated with the size of PC. In this study, the TLV and PC volume were estimated using an ellipsoid mathematical formula, meaning they were not directly measured but rather were calculated via standard geometric equations by assuming each lung is one half of an ellipsoid.

The current study represents a substantial leap forward in the evolution of measuring the size of PC and predicting the development of ARDS. We calculated contusion volume as a percentage of TLV for 202 PC patients. This is a larger sample size than those of Miller et al.¹⁰ and Hamrick et al.⁶ In fact, the sample size in the current study is the largest reported in the literature for studies correlating percent PC volume with incidence of ARDS. Our methodology is an innovative, semiautomated method that does not rely on the approach used by Miller et al. or an ellipse-based approach used by Hamrick et al. to estimate the TLV. Furthermore, a receiver operating characteristic curve analysis was used in our study to determine the threshold for percent PC that best discriminated for ARDS development. This differed from statistical methods used by

© 2012 Lippincott Williams & Wilkins

Miller et al. who used noncontinuous bins of 10% to determine the percent contusion thresholds that discriminated for ARDS development.¹⁰

Previous studies have identified contusion sizes of 20% of TLV as being predictive of significant lung injury and ARDS.6,10 Our analysis, using a larger number of patients and more accurate methodology to measure contusion size, demonstrated a sharp increase in the incidence of ARDS when contusion size was greater than 24% of TLV. Specifically, when contusion sized was 24% of TLV or greater, the ARDS occurred 78% of the time. In addition, these patients had a significantly higher incidence of pneumonia when compared with those with contusions less than 24%, confirming the association between contusion and pneumonia demonstrated by others.²⁴ It remains unknown whether this association is caused by prolonged mechanical ventilation, the amount of injured lung tissue, or immune dysregulation that has been described to occur after injury. Not surprisingly, patients with contusion size greater than 24% of TLV, the presence of ARDS within 72 hours of admission, and the development of pneumonia had significantly greater ISSs as well as reduced SBP and GCS score at



Figure 1. CT imaging and segmentation results in patient with PC. Automatic three-dimensional rendering (A1-D1) of the lungs using software for image viewing, with left-sided unilateral PC. Three-dimensional rendering of the segmentation results (A2-D2) in the same patient that allowed for calculation of percent contusion. High-opacity tissue is depicted in *blue* with the following views labeled: anterior (A1, A2); top (B1, B2); left (C1, C2); isometric (D1, D2). Right (R), left (L), anterior (A), posterior (P). See supplemental digital content for color version of Figure 1, http://links.lww.com/TA/A163.

admission. These findings underscore the association between contusion and significant multisystem trauma.

Potentially confounding variables that could affect our ability to isolate the association of contusion size on the development of ARDS were included in the multivariable regression analysis to account for their effects. These included severe injury (via ISS), shock (via SBP as a continuous variable), brain injury (via both overall GCS score and motor GCS score), the requirement for red blood cell transfusions, and extremity fractures; all of these variables have been shown to be independently associated with posttraumatic ARDS.²⁰ However, after controlling for these, size of PC remained significantly associated with ARDS. Only the development of ARDS within 72 hours of admission was used in the current study; this was done in an attempt to exclude ARDS caused by nosocomial infections or factors not related to injury, which can occur after 72 hours.

Owing to the retrospective nature of the study, we are unable to control for all potential confounding variables. As such, there may be other variables not identified here, which predict the development of ARDS within 72 hours after major thoracic trauma. Another limitation is that the percentage of high opacity lung is used as proxy for size of PC, which is an objective construct and may potentially not represent actual contused lung. In addition to PC, the high opacity categorization also includes atelectasis and aspiration. Therefore, the percent of TLV that represents PC is only as good as our ability to discriminate.

In addition, many PCs are not clinically significant and will not substantially impact a patient's morbidity or mortality. To address this, we used size of PC as a continuous variable, and it remained a significant predictor of mortality even in a multivariable analysis. Although the analysis demonstrated a cutoff of 24% representing the most clinically significant, we cannot say with accuracy that all contusions less than 24% are insignificant and that all contusions 24% or greater are significant. Lastly, only 18 of 202 patients died during their hospitalization; therefore, lack of significant differences with mortality could represent a type II error (Table 3), and significant differences in mortality could represent a type I error (Tables 4 and 5).

A major strength of this study is the development and implementation of a semiautomated method of quantifying contusion size that is highly accurate, is simple to implement, and rapidly yields results. This methodology potentially could be used to screen and identify patients at high risk for ARDS as defined by contusion size at the time of admission. These patients could then be placed in areas of higher acuity such as the intensive care unit or could be the subject of interventional studies. Toward this end, there has been increasing interest in prospectively identifying patients at risk for ALI or ARDS so that preventive management strategies can be initiated; the lung injury prediction score study is one such prospective, multicenter study, which validated the use of lung injury prediction score to assist clinicians in identifying patients at high risk for ALI to facilitate implementation of ALI prevention strategies.⁹

CONCLUSION

PC is associated with significant morbidity and mortality. We describe an automated methodology that can be used to measure contusion size with a high degree of accuracy. Our findings indicated that contusion size is an independent risk factor for ARDS within 72 hours of injury, independent of shock, head injury, ISS, and need for blood transfusions. These patients should be monitored closely for the development of pulmonary complications. Further studies are needed to characterize the precise inflammatory response caused by PC in humans and to develop new interventions to decrease the odds of these adverse sequelae.

AUTHORSHIP

R.D.B., A.L.C., T.M.E., R.S.M., N.T.M., P.R.M., and J.J.H. designed the study. R.D.B., A.L.C., A.A.W., D.K.C., and J.D.S. collected the data. R.D.B., A.L.C., A.A.W., and J.D.S. analyzed the data. R.D.B., A.L.C., R.S.M., N.T.M., P.R.M., and J.J.H. interpreted the data. R.D.B., A.L.C., and J.J.H. conducted the literature search. R.D.B., A.L.C., A.A.W., J.D.S., and J.J.H. prepared the manuscript.

DISCLOSURE

This research was supported by NIH-GM083154 (J.J.H.) and AAST/ACS/ NIGMS-Clowes Award (J.J.H.).

REFERENCES

- Allen GS, Coates NE. Pulmonary contusion: a collective review. Am Surg. 1996;62:895–900.
- Weaver AA, Gayzik FS, Stitzel JD. Biomechanical analysis of pulmonary contusion in motor vehicle crash victims: a crash injury research and engineering network (ciren) study - biomed 2009. *Biomed Sci Instrum.* 2009;45:364–369.
- Stitzel JD, Gayzik FS, Hoth JJ, Mercier J, Gage HD, Morton KA, Duma SM, Payne RM. Development of a finite element-based injury metric for pulmonary contusion part I: model development and validation. *Stapp Car Crash J.* 2005;49:271–289.
- 4. Wu JS, Sheng L, Wang SH, Gu J, Ma YF, Zhang M, Gan JX, Xu SW, Zhou W, Xu SX. et al. The impact of clinical risk factors in the conversion from acute lung injury to acute respiratory distress syndrome in severe multiple trauma patients. *J Int Med Res.* 2008; 36:579–586.
- Wu J, Sheng L, Ma Y, Wang SH, Zhou W, Chen JM, Zhang M, Xu SW, Jiang GY. The analysis of risk factors of impacting mortality rate in severe multiple trauma patients with posttraumatic acute respiratory distress syndrome. *Am J Emerg Med.* 2008;26:419–424.
- Hamrick MC, Duhn RD, Ochsner MG. Critical evaluation of pulmonary contusion in the early post-traumatic period: risk of assisted ventilation. *Am Surg.* 2009;75:1054–1058.
- Hoth JJ, Burch PT, Bullock TK, Cheadle WG, Richardson JD. Pathogenesis of posttraumatic empyema: the impact of pneumonia on pleural space infections. *Surg Infect (Larchmt)*. 2003;4:29–35.
- Hoth JJ, Martin RS, Yoza BK, Wells JD, Meredith JW, McCall CE. Pulmonary contusion primes systemic innate immunity responses. J Trauma. 2009;67:14–21; discussion 21–22.
- Gajic O, Dabbagh O, Park PK, Adesanya A, Chang SY, Hou P, Anderson H, Hoth JJ, Mikkelsen ME, Gentile NT. et al. Early identification of patients at risk of acute lung injury: evaluation of lung injury prediction score in a multicenter cohort study. *Am J Respir Crit Care Med*. 2011;183:462–470.
- Miller PR, Croce MA, Bee TK, Qaisi WG, Smith CP, Collins GL, Fabian TC. ARDS after pulmonary contusion: accurate measurement of contusion volume identifies high-risk patients. *J Trauma*. 2001;51: 223–228; discussion 229–230.
- Tyburski JG, Collinge JD, Wilson RF, Eachempati SR. Pulmonary contusions: quantifying the lesions on chest X-ray films and the factors affecting prognosis. *J Trauma*. 1999;46:833–838.
- 12. Trupka A, Waydhas C, Hallfeldt KK, Nast-Kolb D, Pfeifer KJ, Schweiberer L. Value of thoracic computed tomography in the first

assessment of severely injured patients with blunt chest trauma: results of a prospective study. *J Trauma*. 1997;43:405–411; discussion 411–412.

- Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, Lamy M, LeGall JR, Morris A, Spragg R. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med*. 1994;149(3 Pt 1):818–824.
- Anon. National Heart, Lung, and Blood Institute (NHLBI) Acute Respiratory Distress Syndrome (ARDS) Network homepage. Available at: http://www.ardsnet.org/. Accessed November 4, 2011.
- Gayzik FS, Hoth JJ, Daly M, Meredith JW, Stitzel JD. A finite elementbased injury metric for pulmonary contusion: investigation of candidate metrics through correlation with computed tomography. *Stapp Car Crash J.* 2007;51:189–209.
- Rodrigues RS, Miller PR, Bozza FA, Marchiori E, Zimmerman GA, Hoffman JM, Morton KA. FDG-PET in patients at risk for acute respiratory distress syndrome: a preliminary report. *Intensive Care Med.* 2008;34:2273–2278.
- 17. Schroeder JE, Weiss YG, Mosheiff R. The current state in the evaluation and treatment of ARDS and SIRS. *Injury*. 2009;40(Suppl 4):S82–S89.
- Kishikawa M, Yoshioka T, Shimazu T, Sugimoto H, Yoshioka T, Sugimoto T. Pulmonary contusion causes long-term respiratory dysfunction with

decreased functional residual capacity. J Trauma. 1991;31:1203-1208; discussion 1208-1210.

- Hardaway RM. A brief overview of acute respiratory distress syndrome. World J Surg. 2006;30:1829–1834; discussion 1835.
- Miller PR, Croce MA, Kilgo PD, Scott J, Fabian TC. Acute respiratory distress syndrome in blunt trauma: identification of independent risk factors. *Am Surg.* 2002;68:845–850; discussion 850–851.
- Hoth JJ, Stitzel JD, Gayzik FS, Brownlee NA, Miller PR, Yoza BK, McCall CE, Meredith JW, Payne RM. The pathogenesis of pulmonary contusion: an open chest model in the rat. *J Trauma*. 2006;61:32–44; discussion 44–45.
- Deunk J, Poels TC, Brink M, Dekker HM, Kool DR, Blickman JG, van Vugt AB, Edwards MJ. The clinical outcome of occult pulmonary contusion on multidetector-row computed tomography in blunt trauma patients. *J Trauma*. 2010;68:387–394.
- Daly M, Miller PR, Carr JJ, Gayzik FS, Hoth JJ, Meredith JW, Stitzel JD. Traumatic pulmonary pathology measured with computed tomography and a semiautomated analytic method. *Clin Imaging*. 2008;32:346–354.
- Croce MA, Fabian TC, Davis KA, Gavin TJ. Early and late acute respiratory distress syndrome: two distinct clinical entities. *J Trauma*. 1999;46:361–366; discussion 366–368.