

## Large-magnitude Pelvic and Retroperitoneal Tissue Damage Predicts Organ Failure

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### Abstract

**Background** Pelvic and retroperitoneal trauma is a major cause of morbidity and mortality in multiply injured patients. The Injury Severity Score (ISS) has been criticized for underrepresenting and inaccurately defining mechanical injury. The influence of pelvic injury volume on organ dysfunction and multiple organ failure (MOF) has not been described. Through the use of CT, this investigation sought to precisely define volumes of mechanical tissue damage by anatomic region and examine its impact on organ failure.

**Questions/purposes** (1) Do patients with MOF have a greater volume of pelvic and retroperitoneal tissue damage when compared with those without MOF? (2) In patients

who sustained pelvic trauma, does the magnitude of pelvic injury differ in patients with MOF? (3) Does the magnitude of organ dysfunction correlate with pelvic tissue damage volume?

**Methods** Seventy-four multiply injured patients aged 18 to 65 years with an ISS  $\geq$  18 admitted to the intensive care unit for a minimum of 6 days with complete admission CT scans were analyzed. Each identifiable injury in the head/neck, chest, abdomen, and pelvis underwent volumetric determination using CT to generate regional tissue damage volume scores. Primary outcomes were the development of MOF as measured by the Denver MOF score and the degree of organ dysfunction by utilization of the Sequential Organ Failure Assessment (SOFA) score. Mean pelvic and retroperitoneal tissue damage volumes were compared in patients who developed MOF and those who did not develop MOF using Student's t-test. Among patients who sustained pelvic injuries, we compared mean volume of tissue damaged in patients who developed MOF and those who did not. We assessed whether there was a correlation between organ dysfunction, as measured by the SOFA score as a continuous variable, and the volume of pelvic and retroperitoneal tissue damage using the Pearson product-moment correlation coefficient.

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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**Results** The average volume of tissue damage was greater in patients with MOF when compared with those without (MOF:  $685.667 \pm 1081.344$ ; non-MOF:  $195.511 \pm 381.436$ ; mean difference  $490.156$  cc [95% confidence interval {CI},  $50.076$ – $930.237$  cc],  $p = 0.030$ ). Among patients who sustained pelvic injuries, those with MOF had higher average tissue damage volumes than those without MOF (MOF:  $1322.000 \pm 1197.050$ ; non-MOF:  $382.750 \pm 465.005$ ; mean difference  $939.250$  [95% CI,  $229.267$ – $1649.233$ ],  $p = 0.013$ ). Organ dysfunction (SOFA score) correlated with higher volumes of pelvic tissue damage ( $r = 0.570$ ,  $p < 0.001$ ).

**Conclusions** This investigation demonstrated that greater degrees of pelvic and retroperitoneal tissue damage calculated from injury CT scans in multiply injured patients is associated with more severe organ dysfunction and an increased risk of developing MOF. Early identification of polytrauma patients at risk of MOF allows clinicians to implement appropriate resuscitative strategies early in the disease course. Improved stratification of injury severity and a patient's anticipated clinical course may aid in the planning and execution of staged orthopaedic interventions. Future avenues of study should incorporate the ischemic/hypoperfusion component of pelvic injury in conjunction with the mechanical component presented here for improved stratification of multiply injured patients at higher risk of MOF.

**Level of Evidence** Level III, prognostic study.

## Introduction

Despite advances in resuscitative care of multiply injured patients (MIPs), predicting the clinical trajectory of these patients remains challenging. It is widely known that trauma is the leading cause of death for people younger than 45 years old [3]. For those who survive the initial traumatic insult, the most common cause of death is multiple organ failure (MOF) [6, 13]. Although the incidence of MOF has slightly decreased over the last 15 years, MOF-related complications, intensive care unit (ICU) length of stay (LOS), and mortality have remained relatively constant [6, 22]. Mechanical tissue damage, ischemic tissue injury (shock), preexisting host factors (age, comorbidities), and the host response all contribute to the development of MOF [24]. MOF prediction models have been described based on age and global physiologic response to injury and resuscitation [24, 29]. The Injury Severity Score (ISS) is the most commonly used instrument to summate regional and whole-body trauma, but this index does not quantify tissue damage volumes.

However, there are limited data to help us understand how the physical components of injury, specifically magnitude

and distribution of tissue injury, correspond to the development of organ failure. ISS has been heavily scrutinized for its underrepresentation of multiple severe injuries in one bodily region, underestimation of multiple extremity injury, and its retrospective nature has limited predictive capacity [5, 26]. Reports have implicated head injury, chest injury, and abdominal injury in the etiology of organ dysfunction [17, 24]. Although surgeons have hypothesized that injury magnitude and distribution affect outcomes after injury, mechanical tissue damage has never been precisely quantified in trauma patients. Accurate quantification of mechanical tissue injury, a patient-specific signature of tissue damage, may provide insight toward clinical trajectory and further pathophysiologic understanding of organ dysfunction in trauma patients. Prompt stratification of MIPs at greatest risk to develop MOF and complicated clinical courses may allow early intervention [7]. Pelvic and retroperitoneal trauma has been recognized as a major cause of morbidity and mortality in trauma patients [8]. However, the extent to which pelvic injury corresponds to MOF has, to our knowledge, not been described.

We therefore asked: (1) Do patients with MOF have a greater volume of pelvic and retroperitoneal tissue damage when compared with those without MOF? (2) In patients who sustained pelvic trauma, does the magnitude of pelvic injury differ in patients with MOF? (3) Does the magnitude of organ dysfunction correlate with pelvic tissue damage volume?

## Patients and Methods

### Study Design and Setting

This is an institutional review board-approved retrospective study from a prospectively collected database and medical records of MIPs at a Level I trauma center. All MIPs initially admitted to the ICU or taken to the operating room were identified through querying a trauma database from 2011 to 2012.

### Participants

Polytrauma patients aged 18 to 65 years with an ISS  $\geq 18$  ( $n = 467$ ) admitted to the ICU ( $n = 353$ ) for a minimum of 6 days ( $n = 81$ ) were included in this investigation. All eligible participants were required to have CT of the head/neck, chest, abdomen, and pelvis within 24 hours of presentation (three excluded). Patients with a known history of preexisting organ failure, hematologic disease, immune disorder, and/or currently taking immunomodulating drugs were excluded ( $n = 4$ ). The remaining 74 patients formed the population of interest.

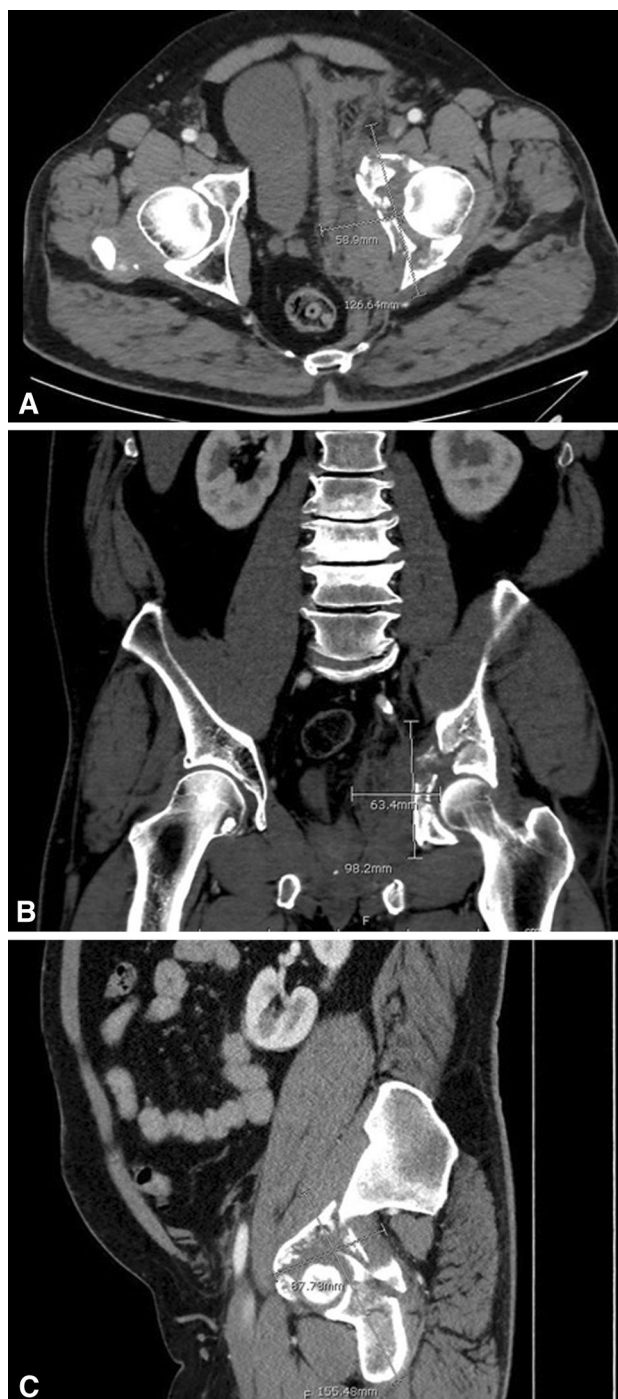
## Description of the Experiment

Tissue damage was quantified using admission CT scans and imaging software. Each identifiable injury in the head/neck, chest, abdomen, and pelvis underwent volumetric determination using CT. Each injury and surrounding tissue damage had three orthogonal characteristic diameters measured on two orthogonal CT images. Characteristic diameters spanned the region of parenchymal damage and surrounding hematoma. The mean of the three measurements served as the representative diameter of injury. Each injury was assumed to be spherical in nature and the characteristic radius was used to calculate the volume ( $V = 4/3\pi r^3$ ) (Fig. 1). In less than 2% of injuries, imaging precluded precise measurement in all three dimensions and thus only recordings deemed accurate were used.

Volumes of all injuries were reported as cubic centimeters and summed to generate a total body tissue damage volume score. Tissue damage was categorized by four body regions: (1) head/neck (all injuries superior to the C7/T1 articulation); (2) chest (heart, lungs, chest wall, diaphragm, ribs, thoracic spine, clavicle, and scapula); (3) abdomen (stomach, liver, spleen, gastrointestinal tract to the sigmoid colon, pancreas, abdominal wall); and (4) pelvis/retroperitoneum (pelvis, acetabulum, sacrum, lumbosacral spine, kidneys, urinary bladder, sigmoid colon, rectum, uterus, and testicles). This investigation focused on the impact of pelvic and retroperitoneal tissue damage volumes and the influence of chest, abdomen, and head injury was not explored in this analysis. CT scanning of extremity injuries was inconsistent; therefore, we did not include extremity tissue damage volumes in calculations. Although it can be assumed that 5 cc of intracranial injury will have a larger impact on overall physiology than 5 cc of pelvic hematoma, organ-specific injury analysis was not conducted in this investigation.

## Variables, Outcome Measures, Data Sources, and Bias

The primary outcome measures were MOF as defined by the Denver MOF Score and organ dysfunction as measured by the Sequential Organ Functional Assessment (SOFA) score. Both outcome instruments have been validated in a trauma population [1, 9, 23]. MOF was described as a score of  $\geq 4$  with involvement of at least two organ systems for the Denver score [23, 24]. The SOFA score evaluates the following six organ systems with an increasing score of dysfunction from 0 to 4: cardiovascular, respiratory, hepatic, renal, hematologic, and neurologic; the Denver MOF score evaluates the following four organ systems with an increasing score of dysfunction from 0 to 3: cardiac, pulmonary, hepatic, and renal (Table 1).



**Fig. 1A–C** This is an example of CT-based measurements of an acetabular fracture and the surrounding soft tissue injury with characteristic diameters on axial (A), coronal (B), and sagittal (C) cuts.

The SOFA score provides an ongoing measure of organ dysfunction. Higher scores within each organ system correspond with greater degrees of organ dysfunction and SOFA scores were thus measured as a continuous variable. The mean total maximum SOFA score, admission SOFA

**Table 1.** Denver MOF score and SOFA score [1, 12, 13, 23]

Organ system	Measure of dysfunction	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
<b>Denver MOF score</b>						
Cardiac	Inotrope support*	None	Minimal	Moderate	High	
Pulmonary	PaO <sub>2</sub> /FIO <sub>2</sub> ratio (mmHg)	> 250	200–250	100–199	< 100	
Hepatic	Bilirubin (mg/dL)	< 1.0	1.0–4.0	4.1–8.0	> 8.0	
Renal	Creatinine (mg/dL)	< 1.8	1.8–2.5	2.6–5.0	> 5.0	
<b>SOFA score</b>						
Cardiovascular	MAP or vasopressors	None	MAP < 70 mmHg	Dopamine ≤ 5 or dobutamine (any dose)	Dopamine > 5 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1	Dopamine > 15 or epinephrine > 0.1 or norepinephrine > 0.1
Respiratory	PaO <sub>2</sub> /FIO <sub>2</sub> ratio (mmHg)	> 400	301–400	201–300	101–200 (with respiratory support)	≤ 100 (with respiratory support)
Hepatic	Bilirubin (mg/dL)	< 1.2	1.2–1.9	2.0–5.9	6.0–11.9	≥ 12.0
Renal	Creatinine (mg/dL)	< 1.2	1.2–1.9	2.0–3.4	3.5–4.9	≥ 5.0
Hematologic	Platelets x 10 <sup>7</sup> /μL	> 150	101–150	51–100	21–50	≤ 20
Neurologic	Glasgow Coma Scale	15	13–14	10–12	6–9	≤ 5

Greater scores are indicative of increasing organ dysfunction; MOF was defined as a score of ≥ 4 with involvement of two or more organ systems; \* inotrope support definitions: minimal = one agent at a small dose; moderate = any agent at a moderate dose or more than one at a small dose; high = any agent at large dose or more than two at moderate doses; MOF = multiple organ failure; SOFA = Sequential Organ Functional Assessment; MAP = mean arterial pressure.

**Table 2.** Descriptive patient demographics and outcome statistics

Demographic	Mean	SD
Age (years)	38.92	14.01
Sex	56 M; 18 F	
ISS	31.65	9.90
BMI	30.34	7.32
ICU days	15.81	7.72
Death	6/74 (8.11%)	

M = male; F = female; ISS = Injury Severity Score; BMI = body mass index; ICU = intensive care unit.

score, and delta SOFA (mean total maximum SOFA minus admission SOFA) have all been shown to correlate well with complications and mortality [1, 14]. Comparisons between both widely used outcome instruments for the diagnosis of MOF have demonstrated higher sensitivity with the SOFA score and higher specificity with the Denver MOF score [9].

Neurologic data through Glasgow Coma Scale scores may be inaccurate in therapeutically sedated and obtunded patients and tend to inflate the degree of central nervous system organ failure [9]. For this reason, a modified SOFA score was used in this analysis by excluding the neurologic component.

#### Statistical Analysis

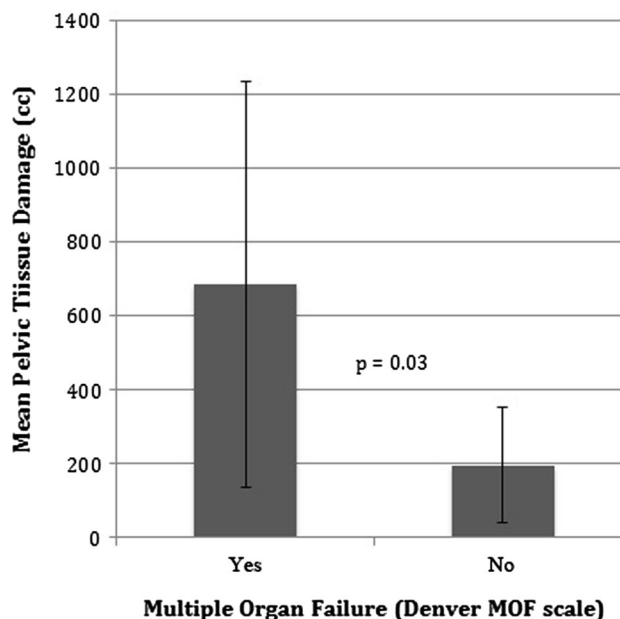
Pelvic tissue damage volumes were analyzed as a continuous variable. Descriptive statistics were calculated for all patients. Continuous variables were assessed using one-way analysis of variance or Student's t-test and categorical variables were assessed using chi-square tests. The relationship between mean SOFA scores and volume of pelvic tissue injured was evaluated using Pearson product-moment correlation coefficients. All tests were two-sided and alpha was set at 0.05.

#### Demographics

The cohort was comprised of severely injured polytrauma patients admitted to the ICU for a minimum of 1 week. Demographic data collected included: age, gender, ISS, body mass index, ICU LOS, and mortality (Table 2).

#### Results

The volume of pelvic and retroperitoneal tissue damage was greater in patients with MOF when compared with those without (MOF:  $685.667 \pm 1081.344$ ; non-MOF:



**Fig. 2** Patients who developed MOF had higher mean pelvic and retroperitoneal tissue damage volume scores than those who did not succumb to MOF.

$195.511 \pm 381.436$ ; mean difference 490.156 cc [95% confidence interval {CI}, 50.076–930.237 cc],  $p = 0.030$ ) (Fig. 2).

Among patients who sustained pelvic injuries, those with MOF had higher average tissue damage volumes than those without MOF (MOF:  $1322.000 \pm 1197.050$ ; non-MOF:  $382.750 \pm 465.005$ ; mean difference 939.250 [95% CI, 229.267–1649.233],  $p = 0.013$ ).

Larger magnitudes of pelvic tissue damage (cc) were correlated with higher levels of organ dysfunction as measured by the mean modified SOFA score ( $r = 0.570$ ,  $p < 0.001$ ).

#### Discussion

MOF is the leading cause of death in MIPs who survive major trauma [5, 12]. Although clinicians have rightfully focused on correspondence among head, chest, and abdominal injury with MOF, few studies have evaluated the impact and severity of pelvic trauma on the development of MOF [16, 23]. ISS has long been used as a surrogate of mechanical injury; however, it has been shown to consistently underestimate mechanical injury [4, 25]. Additionally, ISS is a retrospective index and thus inherently limited in its use in prospectively stratifying patient trajectory. We therefore asked the question: Can CT-based imaging provide a more accurate prospective representation of the amount of tissue injured in trauma patients and



does the volume of injury correlate to patient outcomes? Precise metrics of injury quantification available to the clinician within hours of presentation will allow an enhanced predictive capacity of a patient's clinical course and aid in decision-making such as resuscitative care and resource allocation. This investigation demonstrated that pelvic tissue damage volumes identified patients at risk of MOF and corresponded to severity of organ dysfunction.

This study had a number of limitations. There was potential for selection bias in this study given this cohort represents a severely injured group of patients who were admitted to the ICU for a minimum of 1 week. Regional tissue damage profiles in less severe trauma patients may exhibit different patterns of organ dysfunction and therefore the results presented in this study cannot be extrapolated to a general trauma population. Second, although CT-based injury measurements were derived from multiple axial thin-slice (2 mm) and reconstructed images, injuries were assumed to be spherical for calculation of individual injury. This methodology likely overestimates individual injury damage volumes because actual tissue damage is not uniformly spherical and a sphere has the greatest volume/surface ratio of any geometric figure. Therefore, the mean values of pelvic tissue damage predictive of MOF and organ dysfunction are likely lower than our calculations. However, all patients had consistent measurement techniques to facilitate between-group comparisons. Additionally, less than 2% of measurements had injury volumes derived from two reconstructed images instead of three. This was the result of the injury measurement on a third plane being less than 3 mm. Extremity injury analysis was not conducted because most patients with extremity injury did not have a CT scan of the affected limb. Radiographic estimation of injury is considerably inaccurate compared with CT. Although this study focused solely on pelvic and retroperitoneal injury, future investigations of whole-body tissue damage should include methodology to estimate extremity injury.

Our techniques quantified all injury within each region including parenchymal injury and surrounding hematoma. Although hematomas contain inflammatory mediators, the incorporation of hematoma may overestimate the amount of injured tissue. Therefore, larger magnitude pelvic injuries are partly explained by large hematomas.

Patients with MOF have much greater volume of pelvic and retroperitoneal tissue damage, and such damage may predict development of MOF. Previous investigations have focused on the regional impact of head, chest, and/or abdominal trauma on organ dysfunction [7, 10, 17, 22, 24, 27]. These findings parallel previous observations that severity of regional injury may have greater systemic consequences than the mere presence of a regional insult.

Multiple studies have shown that MIPs with axial orthopaedic injuries are at risk of developing systemic complications [2, 15, 18, 19, 28]. Timing and choices of interventions in these patients remain controversial and are largely anecdotal [10–12, 16, 20, 21, 27]. Surgeons readily agree that invasive operations must be carefully staged in MIPs at risk for organ dysfunction. However, judging which patients are at elevated risk of organ dysfunction is typically elusive. The findings of this study indicate that patients sustaining greater degrees of pelvic and retroperitoneal tissue damage are more likely to develop MOF and higher levels of organ dysfunction. This risk can be numerically stratified from routine admission CT. Understanding these risks can guide surgical decisions for staged orthopaedic interventions in MIPs.

Greater levels of pelvic and retroperitoneal tissue damage are positively correlated with higher levels of organ dysfunction. Previous studies have largely focused on the association of pelvic injury with mortality [4, 25]. For example, in 30,000 trauma patients of whom over 1000 had a pelvic injury, Schulman et al. [25] found the presence of a pelvic ring injury to be an independent risk factor for mortality after controlling for other systemic injury. In contrast, the effect of pelvic and retroperitoneal injury on the development of organ failure has not been explored. Our results revealed increasing volumes of pelvic tissue damage were correlated with higher levels of organ dysfunction in this population of critically injured patients.

Patients with pelvic injuries are known to have an increased risk of mortality [4, 25]. Data from this investigation showed larger magnitude pelvic injuries correlate with higher levels of organ dysfunction and predicted MOF. Early identification of polytrauma patients at risk of MOF permits patient-specific injury stratification and institution of early treatment strategies. The timing and magnitude of subsequent orthopaedic interventions may be more effectively implemented with an enhanced understanding of a patient's risk of developing organ failure and a complicated clinical course. Future research should focus on refinement of the volumetric quantification methods used here to more precisely define the injury burden in a prospective fashion.

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