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Alcohol Abuse Enhances Pulmonary Edema in Acute Respiratory Distress Syndrome

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Abstract

Background—Pulmonary edema is a cardinal feature of the life-threatening condition known as Acute Respiratory Distress Syndrome (ARDS). Patients with chronic alcohol abuse are known to be at increased risk of developing and dying from ARDS. Based upon preclinical data, we hypothesized that a history of chronic alcohol abuse in ARDS patients is associated with greater quantities and slower resolution of pulmonary edema compared to ARDS patients without a history of alcohol abuse.

Methods—A PiCCO™ transpulmonary thermodilution catheter was inserted into 35 patients within 72 hours of meeting American European Consensus Criteria definition of ARDS. Pulmonary edema was quantified as extravascular lung water (EVLW) and measured for up to 7 days in 13 patients with a history of chronic alcohol abuse and 22 patients without a history of chronic alcohol abuse.

Results—Mean EVLW was higher in patients with a history of chronic alcohol abuse (16.6mL/kg vs. 10.5mL/kg, $p<0.0001$). Patients with alcohol abuse had significantly greater EVLW over the duration of the study (RM-ANOVA $p=0.003$). There was a trend towards slower resolution of EVLW in patients with a history of alcohol abuse (a decrease of 0.5mL/kg vs. 2.4mL/kg, $p=0.17$) over the study period. A history of alcohol abuse conferred a greater than three-fold increased risk of elevated EVLW [OR 3.16, (1.26-7.93)] using multivariate logistic regression analysis.

Conclusions—In patients who develop ARDS, alcohol abuse is associated with greater levels EVLW and a trend towards slower resolution of EVLW. Combined with mechanistic and preclinical evidence linking chronic alcohol consumption and ARDS, targeted therapies should be developed for these patients.

Keywords

alcoholism; sepsis; respiratory distress syndrome (adult); pulmonary edema; extravascular lung water

Introduction

Acute respiratory distress syndrome (ARDS) is a heterogeneous clinical syndrome affecting between 100,000 and 200,000 Americans each year. (Rubenfeld et al., 2005; Ware and Matthay, 2000) The hallmark feature of ARDS is a pathologic accumulation of protein-rich alveolar fluid resulting from injury to the alveolar capillary barrier and a decrease in net alveolar fluid clearance. (Anderson and Thielen, 1992; Bachofen and Weibel, 1977; Pugin et al., 1999; Ware and Matthay, 2000) Acute medical (sepsis, aspiration, pancreatitis, hypertransfusion) and surgical (trauma, pulmonary contusion) diagnoses place a patient at risk for developing ARDS. Despite advances in ventilation strategy (Acute Respiratory Distress Syndrome Network Investigators, 2000) and fluid management (Wiedemann et al., 2006), ARDS mortality has remained unacceptably high at 30-60% for decades. (Rubenfeld et al., 2005; Ware and Matthay, 2000)

Alcohol is one of the most abused drugs worldwide and an estimated 17 million Americans currently suffer from alcohol abuse or dependence. (Grant et al., 2004) Nearly one-quarter of all Americans abuse alcohol at some point in their lives. (O'Connor and Schottenfeld, 1998) The healthcare implications of alcohol abuse is significant and accounts for up to 15% of health care costs in the United States. (O'Connor and Schottenfeld, 1998) The prevalence of alcohol abuse in hospitalized patients is often overlooked. Recent studies have shown that 20-40% of all hospitalized (Esper et al., 2006; O'Connor and Schottenfeld, 1998) patients and over 40% of both medical and surgical ICU patients (Moore, 2005) have a history of alcohol abuse.

A history of alcohol abuse is among the most potent chronic medical conditions to increase both the incidence and mortality of ARDS. (Moss et al., 1996) In patients at risk for developing ARDS, a history of alcohol abuse doubles their probability of developing ARDS and is independently associated with a twofold increase in mortality. (Moss et al., 1996) Depleted glutathione stores, an important anti-oxidant in the lung, are likely involved in the mechanism accounting for the increased susceptibility to ARDS. (Holguin et al., 1998) Impairment in glutathione homeostasis results in increased permeability of the alveolar capillary barrier, decreased fluid transport out of the alveolar space, and alterations in surfactant production and secretion. (Brown et al., 2001; Guidot and Roman, 2002; Holguin et al., 1998)

Measurement of extravascular lung water (EVLW) is a useful way to estimate the degree of pathologic fluid accumulation in the lung during ARDS. Sakka, et al, studied 373 critically ill patients and found that patients with ARDS has significantly higher EVLW than non-ARDS patients. (Sakka et al., 2002) In a recent study of patients with severe sepsis, we discovered that EVLW was higher in patients with chronic alcohol abuse irrespective of ARDS. (Martin et al., 2005) No study to date has examined the influence of chronic alcohol

abuse on EVLW in patients with ARDS. We hypothesized that chronic alcohol abuse in ARDS patients is associated with greater quantitative measures of EVLW and slower resolution of EVLW compared to ARDS patients without a history of alcohol abuse.

Methods

This study was reviewed and approved by the Institutional Review Board at Emory University School of Medicine and the Research Oversight Committee of Grady Memorial Hospital. Study participants were medical and surgical ICU patients at two large academic hospitals in Atlanta, Georgia (Grady Memorial Hospital and Emory Crawford Long Hospital). All ICU patients were screened for eligibility. Included patients were those who met the American-European Consensus Conference definition of ARDS as confirmed by both the study investigators and the primary team caring for the patient. (Bernard et al., 1994) Exclusion criteria included contraindication to femoral artery catheterization, risk factor for ARDS >10 days prior to eligibility, *Pneumocystis carinii* (*P. jiroveci*) pneumonia, partial or complete lung resection, age <18 years, pregnancy, inability to obtain consent from patient or surrogate, or the presence of ARDS for greater than 72 hours. All patient management decisions, including fluid management and ventilator therapy were at the discretion of the primary intensive care physicians caring for the patient. Data from eleven patients included in the present study has been reported previously. (Martin et al., 2005)

After informed consent was obtained, patient-specific data were collected, including medical history, risk factors for ARDS, Acute Physiology and Chronic Health Evaluation (APACHE) II and sequential organ failure assessment (SOFA) scores, lung injury score (LIS), (Murray et al., 1988) fluid management and daily weights. The Short Michigan Alcohol Screening Test (SMAST) and the Alcohol Use Disorder Identification Test (AUDIT) were administered to surrogates for each enrolled patient, as validated for reliable completion previously. (Donovan et al., 2004; Moss and Burnham, 2006) Once enrolled, a 5-F arterial catheter (Pulsiocath PV2015L20; Pulsion Medical Systems, Munich, Germany) was inserted into the descending aorta via the femoral artery using the Seldinger technique. A temperature sensor was connected to the distal port of a standard central venous catheter in either the internal jugular or subclavian location. The arterial and central venous catheters were connected to an integrated bedside monitor (PiCCO Plus™, Pulsion Medical Systems) for continuous hemodynamic monitoring. The catheter system was left in place for seven days, or removed earlier in the event of patient transfer from the ICU or death.

Measurements of Extravascular Lung Water

The PiCCO™ catheter system operates via a single thermal indicator technique to determine EVLW, cardiac output (CO), and volumetric parameters. Continuous CO calibration and EVLW measurements were obtained by triplicate central venous injections of 15-20cc of iced (<8°C) 0.9% saline and recorded as the mean of the three measurements. CO and EVLW measurements were performed immediately after catheter insertion and daily for the duration of the study. Thermodilution cardiac output was calculated by the Stewart-Hamilton method. (Goedje et al., 1999; Sakka et al., 1999) Volumetric parameters [Intrathoracic Thermal Volume (ITTV), Pulmonary Thermal Volume, Global End Diastolic

Volume (GEDV), and Intrathoracic Blood Volume (ITBV)], were derived as previously described (Martin et al., 2005; Neumann, 1999; Sakka et al., 2000) and EVLW calculated as the difference between ITTV and ITBV. (Neumann, 1999; Sakka et al., 2000; Sturm JA, 1990) The pulmonary vascular permeability index (PVPI) was calculated as the ratio of absolute (unindexed) EVLW to ITBV as a surrogate estimate of alveolar-capillary barrier dysfunction. (Groeneveld and Verheij, 2006; Holm et al., 2002; Honore et al., 2001; Martin et al., 2005; Monnet et al., 2007) All volumetric and hemodynamic parameters were indexed to body surface area (by Dubois Formula) except for EVLW and central venous pressure (CVP). EVLW is expressed as mL/kg and is indexed conventionally to actual body weight (determined by patient bedscale) and to predicted body weight (PBW), as indexing to PBW may more accurately characterize EVLW in patients with severe sepsis and ARDS. (Berkowitz et al., 2008; Phillips et al., 2008)

Outcome Variables

Patients were considered to have a history of chronic alcohol abuse if their score was ≥ 3 on the SMAST (Selzer et al., 1975) or ≥ 8 on the AUDIT. (Saunders et al., 1993) Patients were classified as having elevated EVLW if any measurement of EVLW was $>10\text{mL/kg}$ during the study period. This value is based on previous studies of EVLW in animal models without evidence of lung injury (Elings and Lewis, 1982; Fernandez-Mondejar et al., 2003; Katzenelson et al., 2004) and has been established as a threshold for acute lung injury in prior clinical studies. (Holm et al., 2002; Martin et al., 2005; Sakka et al., 2002) Patients were followed until time of hospital discharge to determine duration of mechanical ventilation, hospital length of stay (LOS), and in-hospital mortality.

Statistical Analysis

Data are presented as mean $\pm$ standard deviation or medians with interquartile range (IQR). Continuous variables were compared using t-tests for normally or Mann-Whitney U tests for non-normally distributed data. The χ^2 statistic was used to compare frequency proportions. Modeling by least squares linear regression for continuous outcome variables and maximum likelihood logistic regression for dichotomous outcome variables was used to assess individual effects while adjusting for individually significant covariables, defined by p-values <0.05 in bivariate analyses comparing the alcoholic and non-alcoholic groups and excluding the hemodynamic parameters. As multiple measurements of EVLW were taken from individual patients, repeated measure ANOVA (RM-ANOVA) testing was utilized to test for equality of means across longitudinal measurements and between groups. Statistical analysis was performed using NCSS 2001 software (NCSS, Inc., Kaysville, UT, USA) and Microsoft® Excel 2003 (Microsoft Corporation, Redmond, Washington, USA). All statistical tests were two-sided; p values <0.05 were considered significant and values >0.20 as not significant (NS).

Results

Demographics and Hemodynamics

The average age among the 35 enrolled patients was 46.6 years. Seventy-seven percent of study participants were male and 83% were African-American. Thirteen of 35 patients

(37%) met the criteria for alcohol abuse and had significantly higher SMAST and AUDIT scores (6.2 vs. 0.3 and 18.1 vs. 0.3, respectively). There was a tendency for patients with a history of alcohol abuse to be male (77% vs. 41%, $p=0.07$) and taller than patients who did not abuse alcohol (**Table 1**). There were no differences in baseline co-morbidities between those with alcohol abuse and those who did not abuse alcohol with the exception of a lower serum albumin level at enrollment (1.5 vs. 2.1 g/dL, $p=0.005$) and a trend towards a greater prevalence of chronic liver disease (23.1% vs. 4.5%, $p=0.13$) in those with alcohol abuse. Enrollment APACHE II, SOFA, and LIS were similar between the two groups. The most common risk factor for ARDS was sepsis and occurred at the same rate (77%) in patients with and without alcohol abuse. Just over half of all study patients had direct injury to the lung (defined as pneumonia, aspiration or lung trauma) prior to the onset of ARDS. See **Table 1** for details.

Central venous pressure measurements and all hemodynamics parameters measured by the PiCCO™ catheter system were similar between patients with and without alcohol abuse throughout the study, (**Table 2**) with the exception of stroke volume index, which was lower in patients with a history of alcohol abuse. Fluid management, which was not dictated by study protocol, was not statistically different in net balance between groups. On average, however, patients with a history of alcohol abuse received a total of 2L more intravenous fluids over the seven day study period. ICU LOS, hospital LOS, and days of mechanical ventilation were similar between groups.

Effect of Alcohol Abuse on EVLW

Initial measurements of unadjusted EVLW indexed to a patient's actual body weight were significantly higher in patients with a history of alcohol abuse (16.0 vs. 11.3 mL/kg, $p=0.03$). The overall mean unadjusted ELVW was also significantly higher in patients with a history of alcohol abuse (16.6 mL/kg for vs. 10.5 mL/kg, $p<0.0001$). Multivariable linear regression analysis was performed to adjust for baseline differences in groups, including albumin, age, sex, height and enrollment weight. After adjustment, initial EVLW (16.0 vs. 11.8mL/kg, $p=0.05$) and mean EVLW (16.0 vs. 10.6 mL/kg, $p<0.0001$) remained significantly greater in ARDS patients with a history of alcohol abuse than those without a history of alcohol abuse.

It has recently been reported that indexing EVLW to predicted body weight (PBW) rather than actual body weight (ActBW) may more accurately characterize EVLW in patients with ARDS and severe sepsis. (Berkowitz et al., 2008; Phillips et al., 2008) When EVLW was indexed to PBW instead of ActBW, patients with a history of alcohol abuse still had greater unadjusted mean EVLW (16.8 vs. 13.6 mL/kg, $p<0.001$) and adjusted mean EVLW (16.5 vs. 13.2 mL/kg, $p<0.001$).

Effect of Alcohol Abuse on ELVW Over Time

Using repeated measures ANOVA, patients with alcohol abuse had significantly greater EVLW over the duration of the study when compared to patients without a history of alcohol abuse (ANOVA $p=0.003$, see **Figure 1a**). The effects of alcohol abuse on EVLW over the duration of the study remained in a multivariable model when adjusting for baseline

differences between groups (ANOVA $p=0.008$). Repeated measure ANOVA indexing EVLW to PBW demonstrated a more modest difference between those with and without a history of alcohol abuse (ANOVA $p=0.08$).

Alcohol's Effect on Resolution of EVLW

Patients with a history of alcohol abuse also had a trend towards slower improvement in EVLW. EVLW decreased by an average of 2.4 mL/kg PBW in patients without a history of chronic alcohol abuse, while EVLW decreased by only 0.5 mL/kg PBW in patients with a history of alcohol abuse ($p=0.17$) over the study duration. This represented a non-significant 3% reduction in pulmonary edema from study entry in patients with chronic alcohol abuse compared to a 16% reduction in those without chronic alcohol abuse.

Predictors of Elevated EVLW

There was not an association between daily net fluid balance (daily net I/O) and daily EVLW indexed to actual body weight ($R^2=0.011$, $p=0.16$) and a weak association of daily net I/O and EVLW indexed to predicted body weight ($R^2=0.032$, $p=0.01$). Using multivariable logistic regression analysis to assess the independent effect of chronic alcohol use on accumulation of EVLW, a prior history of chronic alcohol use was associated with a greater than three-fold increased risk of having elevated EVLW [OR 3.16, (1.26-7.93)]. Albumin level did not influence whether a patient would have elevated EVLW. See **Table 4** for results of the multivariate regression analysis.

Discussion

The study results confirm our hypothesis that pulmonary edema, quantified as the accumulation of EVLW, is significantly greater in ARDS patients with a history of chronic alcohol abuse compared to ARDS patients without a history of alcohol abuse. This was seen both on initial measurement of EVLW (16.0 vs. 11.3 mL/kg, $p=0.03$), mean level of EVLW (16.6 vs. 10.5 mL/kg, $p<0.0001$) and trend for study duration (ANOVA $p=0.003$). These findings are consistent with animal models of alcohol abuse which demonstrate that chronic alcohol consumption leads to alveolar capillary barrier dysfunction and greater alveolar fluid accumulation. (Guidot et al., 2000; Guidot and Roman, 2002; Holguin et al., 1998)

Chronic alcohol use has been associated with decreased alveolar fluid clearance and increased protein leak. (Guidot et al., 2000) Over the duration of our study, patients with a history of chronic alcohol abuse had a trend towards slower resolution of elevated EVLW than those without a history of chronic alcohol use (0.52 vs. 2.37 mL/kg PBW). Although these results did not reach statistical significance, this trend indicates that patients with a history of alcohol abuse may require greater time to recover from ARDS. The reason for the persistent elevation in EVLW is multifactorial. The slower decline in EVLW over time may result from impaired fluid resorption, differential location of fluid accumulation (interstitium vs. alveoli), greater initial fluid extravasation, or a persistently injured alveolar-capillary membrane in patients with a history of alcohol abuse. The slower resolution of EVLW in ARDS patients with alcohol abuse may be one of the factors influencing prolonged

mechanical ventilation, greater illness severity and higher mortality in this patient population. (Moss et al., 1996; Moss et al., 2003; O'Brien, Jr. et al., 2007)

Our study may have implications for the management of chronic alcoholics with ARDS. Quantifying EVLW to assist in fluid management has been shown to decrease ICU LOS and days of mechanical ventilation, (Mitchell et al., 1992) and reducing pulmonary edema in ARDS through fluid restriction similarly improves outcomes. (Wiedemann et al., 2006) As we have demonstrated, ARDS patients with a history of chronic alcohol abuse have greater EVLW and a trend towards a slower decline in EVLW over time. Current standard of care directing fluid management may be suboptimal given that radiographs may underestimate the degree of pulmonary edema (Baudendistel et al., 1982; Eisenberg et al., 1987; Sivak et al., 1983) and pulmonary artery catheters alone may be inferior at guiding diuretic and fluid restriction therapies while introducing the risk of serious complications. (Wheeler et al., 2006) While our study did not observe a strong relationship between fluid balance and EVLW, we did not control diuretic administration and thus changes in fluid balance were modest compared to aggressive fluid reduction strategies. Thus, clinicians should recognize that ARDS patients with a history of chronic alcohol abuse will have persistently greater ELVW and should be managed at least as aggressively as in the seminal ARDSnet trial, (Wiedemann et al., 2006) and that they may require even greater diuresis and more stringent fluid restriction compared to ARDS patients without a history of alcohol abuse.

EVLW has historically been expressed as milliliters per kilogram of actual body weight (ActBW), although there is no scientific justification or clinical validation for this practice. We and others have recently demonstrated that indexing EVLW to predicted body weight (PBW) more accurately describes EVLW in patients with ARDS and severe sepsis. (Berkowitz et al., 2008; Phillips et al., 2008) As it is not known whether indexing EVLW to PBW is generalizable to all patients, we have chosen to express EVLW in the current study indexed to both ActBW and PBW. The current study results and conclusions related to alcohol abuse did not significantly change whether EVLW was indexed to ActBW or PBW.

This study has a several limitations. Although co-morbidities, severity of illness, and hemodynamic parameters were equally distributed between the two groups, the small sample size limits statistical comparisons and makes residual confounding impossible to exclude from our analyses. As such, it is impossible to completely differentiate effects of alcohol on the liver (e.g. cirrhosis) versus the lung or as a combination of organ systems. Patients with chronic alcohol abuse may have sought healthcare later than non-alcoholic patients, or received different sedative and analgesic medications or nutritional formulas and additives, which may influence severity of illness and the duration of mechanical ventilation, which were not statistically different in our study. Our rate of HIV infection (37%) is higher than other ARDS studies, (Moss et al., 2003; Wiedemann et al., 2006) however, patients were carefully evaluated and excluded if a diagnosis of *Pneumocystis carinii* (*P. jiroveci*) pneumonia was suspected or diagnosed. Although net fluid balance varied between groups, the difference was small over the entire seven days. Fluid administration was also less relevant because: EVLW differed between groups at baseline, there were no differences in hydrostatic pressures between groups, and there was no correlation between EVLW and fluid balance. Finally, although we have reported the PVPI

as it is commonly described and utilized in the research setting, it is as yet non-validated as a clinical measure of pulmonary permeability.

As anticipated, patients with a history of alcohol abuse had a greater incidence of chronic liver disease and lower levels of albumin. Hypoalbuminemia can affect EVLW by lowering intravascular oncotic pressure and decreasing the antioxidant capacity of the lungs. (Quinlan et al., 2004) The oncotic influence of serum albumin on EVLW may be small, as evidenced in our regression analysis. Because chronic liver disease lowers glutathione levels in the serum (Bianchi et al., 1997) and lung epithelial lining fluid, (Foreman et al., 2002) our findings may reflect impaired antioxidant capacity. Therefore, alcohol's affect on the development of ARDS may be via direct effects on glutathione and alveolar capillary barrier permeability (Burnham et al., 2003) and indirectly through the development of chronic liver disease with coincident reductions in antioxidants such as albumin and glutathione. (Quinlan et al., 2005)

In summary, ARDS patients with a history of chronic alcohol abuse have greater accumulation of pulmonary edema, as measured by EVLW, and a trend towards slower resolution of edema compared to ARDS patients without a history of alcohol abuse. Our study findings should alert the clinician to be more conscientious in identifying the need for and implementing strategies for minimizing edema accumulation (stringent fluid restriction and aggressive diuresis) in patients with chronic alcohol abuse who develop ARDS. Future investigations are needed to describe the pathophysiology behind the greater EVLW accumulation in patients with alcohol abuse. A better understanding of these mechanisms may lead to the development of preventive strategies and earlier interventions to decrease fluid extravasation and improve alveolar capillary barrier function and repair, and potentially to directed therapies for patients with chronic alcohol abuse.

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Dr. Martin serves on the Medical Advisory Board for Pulsion Medical Systems.

Abbreviations

ActBW	actual body weight
ALI	acute lung injury
APACHE	acute physiology and chronic health evaluation
ARDS	acute respiratory distress syndrome
AUDIT	alcohol use disorder identification test
CO	cardiac output
CVP	central venous pressure
EVLW	extravascular lung water

GEDV	global end-diastolic volume
ICU	intensive care unit
ITBV	intrathoracic blood volume
ITTV	intrathoracic thermal volume
LIS	lung injury score
PBW	predicted body weight
PiCCO	pulse contour cardiac output
PVPI	pulmonary vascular permeability index
RM-ANOVA	repeated measured analysis of variance
SMAST	short Michigan alcohol screening test
SOFA	sequential organ failure assessment

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Figure 1.

Mean EVLM (1a) and PVPI (1b) over the seven day study period: EVLM was significantly higher in patients with chronic abuse from time of enrollment and persisted throughout the study period. Pulmonary vascular permeability index (PVPI) was higher in patients with history of alcohol abuse. p-values calculated by repeated measure ANOVA.

Figure 2.

Absoluty change in unadjusted EVLM over the seven day study period. ARDS patients with a history of chronic alcohol abuse had less resolution of pulmonary edema (ELM) during the seven day study period.

Table 1

Baseline patient characteristics and co-morbidities: Data shown as mean $\pm$ standard deviation or percentage.

	Alcohol Abuse	No Alcohol Abuse	p-value
Total Number Patients	13	22	
Demographics and Co-morbidities			
% Male	77%	41%	0.07
Enrollment Actual Body Wt (kg)	77.8 $\pm$ 14.7	86.4 $\pm$ 22.0	0.22
Height (cm)	176.9 $\pm$ 9.0	171.5 $\pm$ 10.9	0.14
Predicted Body Weight (kg)	71.3 $\pm$ 9.9	64.7 $\pm$ 11.7	0.10
Enrollment BSA	1.9 $\pm$ 0.2	2.0 $\pm$ 0.2	NS
Age	50.6 $\pm$ 11.0	44.2 $\pm$ 15.3	0.19
Race (%African American)	77%	86%	NS
Chronic Heart Disease	0%	14%	NS
Hx Pulmonary Disease	8%	27%	NS
Hx Renal Disease	0%	0%	NS
Hx Hepatic Disease	23%	5%	0.13
Hx HIV	46%	32%	NS
Smoker	90%	69%	NS
AUDIT Score	18.1	0.3	<0.0001
SMAST Score	6.2	0.3	<0.0001
Characteristics at Enrollment			
APACHE II Score	25.5 $\pm$ 7.3	23.8 $\pm$ 1.2	NS
Lung Injury Score	2.8 $\pm$ 0.6	2.8 $\pm$ 0.6	NS
SOFA Score	10.7 $\pm$ 6.8	11.1 $\pm$ 2.3	NS
Creatinine	1.3 $\pm$ 1.0	1.6 $\pm$ 1.1	NS
Albumin	1.5 $\pm$ 0.3	2.1 $\pm$ 0.6	0.005
Primary ARDS Risk Factor			
Sepsis	77%	77%	NS
Aspiration	8%	23%	NS
Trauma	8%	0%	NS
Pancreatitis	8%	0%	NS
Direct Lung Injury	54%	55%	NS

BSA: Body Surface Area; AUDIT: Alcohol Use Disorder Identification Test; SMAST: Short Michigan Alcohol Screening Test; SOFA: Sequential Organ Failure Assessment; HIV: Human Immunodeficiency Virus

Table 2

Hemodynamics and outcomes: data shown as mean $\pm$ standard deviation or median (interquartile range).

	Alcohol Abuse	No Alcohol Abuse	p-value
Total Number Patients	13	22	
Net fluid balance (liters)	12.0 $\pm$ 7.0	9.7 $\pm$ 11.9	0.10
Mean values over study period			
CVP (mmHg)	13 $\pm$ 4	14 $\pm$ 5	NS
CI (L/min/m ²)	3.9 $\pm$ 1.3	4.0 $\pm$ 1.1	NS
SVRI (dyn*s*cm ⁻⁵ *m)	1607 $\pm$ 606	1590 $\pm$ 551	NS
GEDVI (mL/m ²)	688 $\pm$ 93	680 $\pm$ 257	NS
ITBVI (mL/m ²)	871 $\pm$ 138	840 $\pm$ 312	NS
SVV (%)	15 $\pm$ 6	14 $\pm$ 6	NS
SVI (mL/m ²)	43 $\pm$ 17	56 $\pm$ 25	0.0004
Outcomes			
ICU LOS	14 (7-27)	17 (14-24)	NS
Hospital LOS	25 (9-38)	28 (19-36)	NS
Days on Ventilator	10 (5-21)	14 (12-18)	NS
ICU Mortality	54%	36%	NS
Hospital Mortality	62%	41%	0.24

CVP: central venous pressure; CI: cardiac index; SVRI :Systemic Vascular Resistance Index; GEDVI :Global End Diastolic Volume Index ; ITBVI :Intrathoracic Blood Volume Index; SVV: Stroke Volume Variability; SVI: Stroke Volume Index

Table 3

Extravascular lung water (EVLW) measurements: EVLW (expressed as mL/kg) measurements were collected daily for seven days. Given greater EVLW, ARDS patients with alcohol abuse require greater diuresis and more stringent fluid restriction than does the general ARDS population.

n		Alcohol Abuse	No Alcohol Abuse	p-value
EVLW Indexed to Actual Body Weight				
35	Initial (Day 1) unadjusted EVLW (mL/kg)	16.0	11.3	0.03
34	Initial (Day 1) adjusted [*] EVLW	16.0	11.8	0.05
201	Unadjusted Mean EVLW	16.6	10.5	<0.0001
194	Adjusted [*] Mean EVLW	15.9	10.7	<0.0001
EVLW Indexed to Predicted Body Weight				
35	Initial (Day 1) unadjusted EVLW (mL/kg)	16.6	14.9	0.43
34	Initial (Day 1) adjusted [*] EVLW	16.7	14.4	0.28
201	Unadjusted Mean EVLW	16.7	13.6	0.0002
194	Adjusted [*] Mean EVLW	16.6	13.5	0.0002

* Adjusted for albumin, net fluid balance, age, sex, height and enrollment weight.

Table 4

OR for elevated EVLW (indexed to PBW). Alcohol was the only independent predictor of whether an ARDS patient would have elevated EVLW.

Variable	Odds Ratio	LCI	UCI
Age	1.00	0.97	1.03
Albumin	0.76	0.33	1.75
Alcohol	3.16	1.26	7.93
Enrollment weight	1.00	0.98	1.02
Height	0.91	0.98	0.97
Male Sex	0.54	0.16	1.75

Alcohol: positive history of alcohol abuse

Enroll wt: Actual Body weight at time of enrollment