Hypoalbuminemia is Independently Associated with Increased Risk of ARDS in Critically Ill Adults

Supplemental Information

VALID Inclusion and Exclusion Criteria

<u>VALID</u> Inclusion criteria: Patients in an intensive care unit (Medical ICU, Surgical ICU, Trauma ICU, Cardiovascular ICU patients) at VUMC who have reached ICU day 2 who are intubated and non-surgical and don't meet the following exclusion criteria:

a. ICU stay >2 days prior to enrollment
    i. Enroll patients who were admitted to ICU between 2200 two days before screening and 0200 day of screening
    ii. May be in OSH ICU up to 48 hours
b. Cardiac arrest prior to enrollment
c. Imminent death
d. Admission for uncomplicated drug overdose, uncomplicated GI bleed, DKA
e. History of pulmonary fibrosis, interstitial lung disease, use of continuous home oxygen, vent dependent (home vent for example), CF (if hx lung transplant, may enroll)
f. Anticipated transfer out of the ICU on day of screening
g. Currently pregnant
h. Medical students
i. In police custody (or if anticipated)
j. Mentally incapacitated at baseline
    i. Examples include dementia, Alzheimer's, hx TBI or stroke with cognitive deficits
k. <18 years of age
l. Jehovah's Witness
m. Non-English speaking
n. SICU patients whose primary service is TXL or TXB (Liver Transplant)
    i. Exclude patients who may be added to the liver transplant service as their primary team. For example, patients who have liver failure and may need transplant – use judgement
o. patients who are admitted to the ICU solely for frequency of nursing care (ex. Q 1 hour flap checks on a noncritically ill patient)
p. patient readmitted to the ICU after less than 24 hours off the unit

Albumin and Other Organ Failures

Sufficient data was available to score all six components of the Sequential Organ Failure Assessment scoring system for 801 of the 933 patients on study enrollment day in order to assess the relationship between hypoalbuminemia and organ dysfunction **(Supplemental Table 4)**. Patients with serum albumin levels at or below the median (2.7 g/dL) had higher overall SOFA scores (p<0.001) compared to those with levels above the median. The increase from a median SOFA score of 9 to 10 constitutes a predicted 23.3% increase in hospital mortality in these patients (1). Furthermore, there were significant increases in the hepatic (p<0.001), coagulation (p<0.001), and cardiac (p<0.001), and CNS (p=0.045) SOFA components in patients with serum albumin levels below the median.

Timing of albumin measurement

Because serum albumin measurements were not uniformly available prior to the onset of ARDS in this cohort, some albumin measurements were made after the onset of ARDS. In order to determine whether low serum albumin precedes the development of ARDS, we performed a sensitivity analysis excluding patients who only had serum albumin measured the day after enrollment. The logistic regression showed that albumin levels on the day before and of enrollment remained significantly associated with presence of ARDS, indicating low serum albumin may precede development of ARDS in this study (**Supplemental Table 5**).

Reporting on collinearity

Due to potential for multicollinearity between a priori confounders, we calculated the variance inflation factors for each variable in the logistic regression analyses in the manuscript and reported them below. Our findings indicate that some multicollinearity may exists, as indicated by the values being >5, however, no value in our analysis exceeded 10, a sign that collinearity is affecting the results. Due to these findings, we acknowledge that collinearity may be influencing effect estimates between ARDS and traditional risk factors in some way.

Analysis	Table 2	Supp. Table 2	Supp. Table 5	Supp Table 6
Age	7.2	7.5	6.2	7.1
Gender	6.0	6.1	5.3	5.9
Sepsis	9.1	7.6	7.0	8.5
APACHE II	8.2	7.8	7.3	8.1
eGFR	7.5	7.8	6.5	7.4
Fluid Balance	7.3	8.2	6.0	6.7
Chronic Liver Disease	6.9	5.8	5.9	N/A
Vasopressors	6.8	6.7	6.1	6.7
Serum Albumin	6.9	7.1	5.7	6.8

Variance Inflation Factors (VIF) for each variable in each respective logistic regression analysis

Other Risk Factors for ARDS in VALID

Other Risk Factors
Tumor Lysis
Sickle Crisis
Thymoglobulin
Bronchiolitis Obliterans Organizing Pneumonia

Reperfusion/Primary Graft Dysfunction
Alveolar Hemorrhage
Fat Emboli
Amiodarone Toxicity
Blast Crisis
Graft Vs Host Disease
Wegener's Granulomatosis
Acute Myelogenous Leukemia
IL-2 Toxicity
Spider Bite
Acute Eosinophilic Pneumonia
Eosinophilic Pneumonia
Pancytopenia
Alveolar Proteinosis
Drug Reaction
Trali
THC Vaping
Enterococcus Bacteremia

1.   Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. Crit Care Med. 1998;26(11):1793-800.