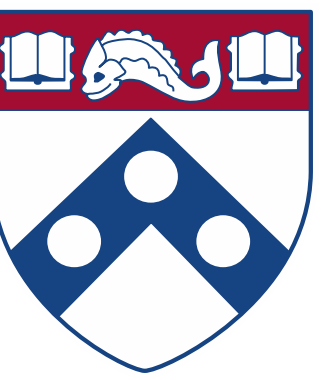# Cirrhosis is Associated with Higher Mortality and Organ Failure in Sepsis

Anushka Dasgupta[1], Ariel Weisman MRA[2], Caroline A.G. Ittner PhD[2], Todd Miano PharmD PhD[2], Oluwatosin Oniyide[2], Brian J. Anderson MD MSCE[2], Tiffanie K. Jones, MD MPH[2], Michael G.S. Shashaty MD MSCE[2,3], Nuala J. Meyer MD MS[2,3], and John P. Reilly MD MSCE[2,3]

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BACKGROUND

- Sepsis, a dysregulated host response to infection, is a leading cause of death in hospitalized patients in the US
- Patients with cirrhosis (liver fibrosis) are at a high risk of developing infection and sepsis

OBJECTIVE

- To evaluate if cirrhosis is associated with different septic characteristics
- To determine the association of preexisting cirrhosis with organ failure and mortality

METHODS

Design: Single center prospective cohort study

Study Population: Molecular epidemiology of Severe Sepsis in the ICU (MESSI) Cohort, 2008-2020: ICU subjects with sepsis or septic shock

- Sepsis-3 criteria as reason for ICU admission
  - Suspected or documented infection
  - Change in SOFA ≥ 2 points
- Exclusion criteria
  - Lack of informed consent
  - Palliative measures only on admission
  - Admitted from a long-term acute care hospital or previously enrolled

Exposure: Cirrhosis determined by H&P

Outcomes:
- 30-day Mortality
- Acute Respiratory Distress Syndrome (ARDS) by Berlin Criteria
- Acute Kidney Injury (AKI) by KDIGO Criteria

Statistical Analysis:
- **Unadjusted Analysis:** Wilcoxon rank-sum or Pearson χ^2 test as appropriate
- **Adjusted Analysis:** Multivariable Logistic regression adjusting for the pre-specified confounders: Age, race, and history of cancer, end stage renal disease, hypertension, and coronary artery disease

RESULTS

TABLE 1: Patient Characteristics by Cirrhosis Diagnosis

	No Cirrhosis (n = 2550)	Cirrhosis (n = 291)	p-value
Male Sex	1552 (61%)	179 (62%)	.15
Race			.036
White	1479 (58%)	194 (67%)	
Black	890 (35%)	83 (29%)	
Asian	94 (4%)	8 (3%)	
Other	87 (3%)	6 (2%)	
Hispanic Ethnicity	72 (3%)	12 (4%)	.29
Age	60 ± 16	57 ± 11	<.001
APACHE III	84 (60.2, 113)	101 (75, 127)	<.001
Cancer	584 (n = 2111, 28%)	37 (n = 212, 17%)	.001
End Stage Renal Disease	155 (6%)	29 (10%)	.002
Hypertension	1649 (n=2992, 55%)	164 (n = 339, 48%)	.018
Coronary Artery Disease	273 (n = 1961, 14%)	17 (n = 205, 8%)	.024

Continuous variables are expressed as median (IQR) and categorical variables are number (%). P values obtained using the Wilcoxon rank-sum or the Pearson χ^2 test.

TABLE 2: Physiologic and Lab Values by Cirrhosis Diagnosis

	No Cirrhosis (n = 2550)	Cirrhosis (n = 290)	p-value
Peak Heart Rate	119 (104, 136)	109 (97, 125)	<.001
Lowest Mean Arterial Pressure (MAP)	63 (55, 72)	59 (52, 66)	<.001
Peak Respiratory Rate	32 (26, 37)	30 (24, 36)	.0061
Highest White Blood Cell Count (WBC)	11.5 (5.3, 19.1)	12.3 (7.4, 18.0)	.049
Lowest Albumin	2.5 (2, 3)	2.5 (2, 3)	.68
Peak Bilirubin	1 (0.6, 1.9)	4.7 (1.8, 10.2)	<.001
Peak Sodium	139 (136, 142)	137 (134, 142)	<.001
Peak Creatinine	1.23 (0.8, 2.3)	2 (1.3, 3.1)	<.001

Continuous variables are expressed as median (IQR) and categorical variables are number (%). P values obtained using the Wilcoxon rank-sum or the Pearson χ^2 test.

TABLE 3: Cirrhosis and Mortality, ARDS Risk, and AKI Risk

	OR (95%CI)	p-value
ARDS	1.42 (1.08, 1.88)	.015
AKI	2.33 (1.76, 3.07)	<.001
30-Day Mortality	1.82 (1.45, 2.29)	<.001

Odds Ratios are for the association of Cirrhosis and each outcome adjusting for pre-specified confounders using multivariable logistic regression.

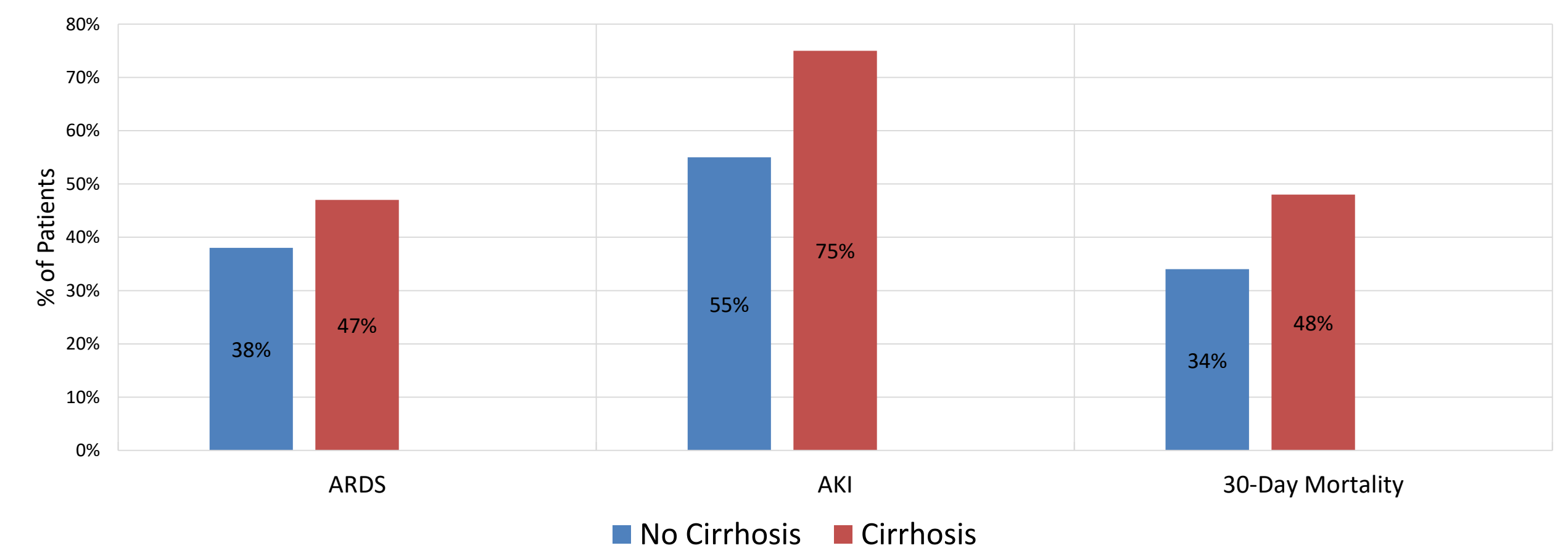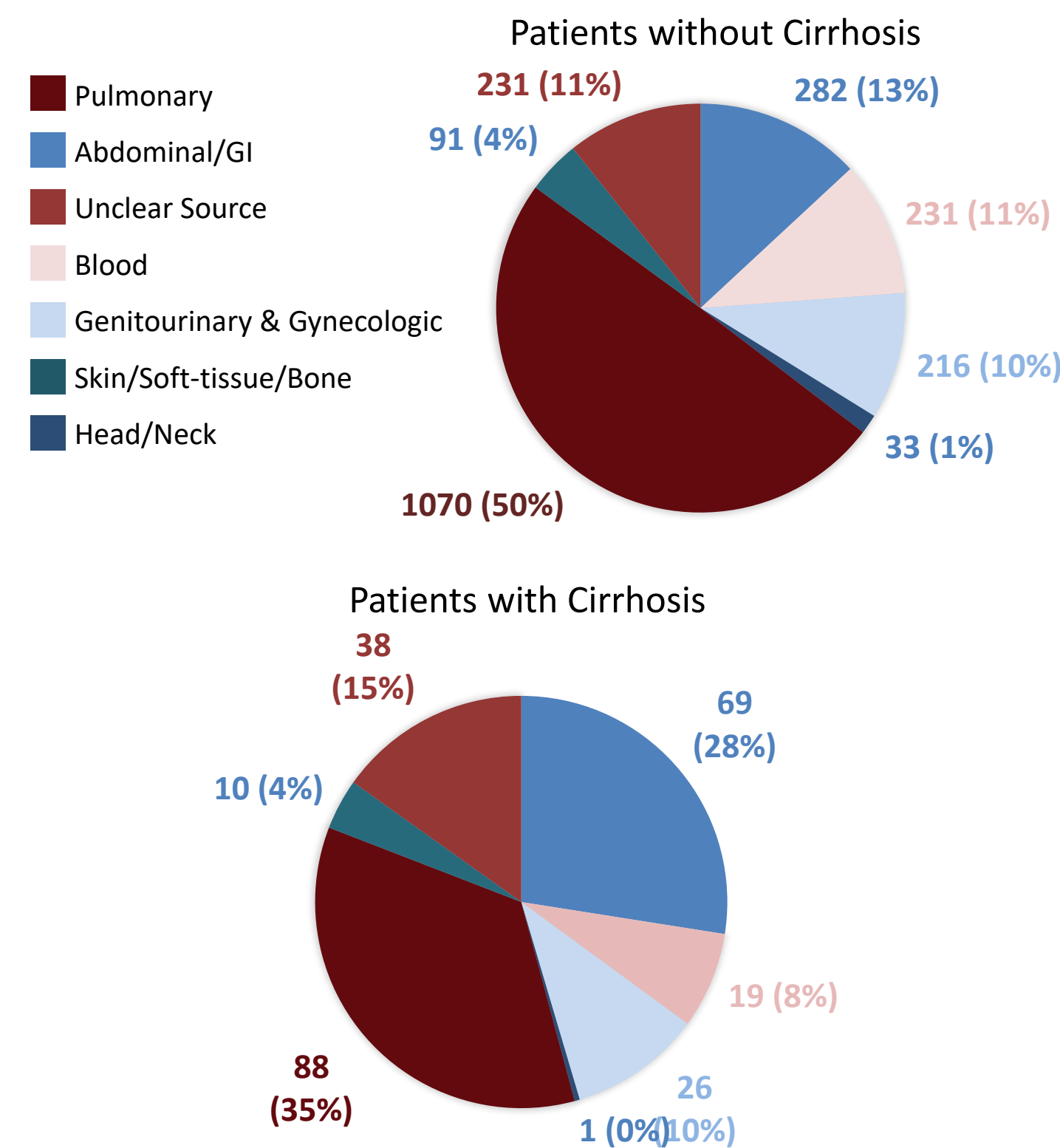### FIGURE 1: Cirrhosis is Associated with Higher Mortality and Higher Risk of ARDS and AKI

	No Cirrhosis	Cirrhosis
ARDS	38%	47%
AKI	55%	75%
30-Day Mortality	34%	48%

FIGURE 2: Source of Sepsis by Cirrhosis Diagnosis

Legend:
- Pulmonary
- Abdominal/GI
- Unclear Source
- Blood
- Genitourinary & Gynecologic
- Skin/Soft-tissue/Bone
- Head/Neck

Patients without Cirrhosis:
231 (11%), 282 (13%), 91 (4%), 231 (11%), 216 (10%), 33 (1%), 1070 (50%)

Patients with Cirrhosis:
38 (15%), 69 (28%), 10 (4%), 19 (8%), 26 (10%), 1 (0%), 88 (35%)

CONCLUSIONS

- Cirrhosis patients who develop sepsis have distinct characteristics;
  - higher APACHE III scores and more end stage renal disease
  - greater fraction of abdominal/GI infections, and less pneumonia
  - More physiologic and lab abnormalities including lower MAP, higher WBCs, higher bilirubin, and higher creatinine
- Cirrhosis is also independently associated with greater mortality, AKI, and ARDS in sepsis.
- Cirrhosis patients are high risk for poor sepsis outcomes and may benefit from targeted therapies to prevent or treat organ failure.

- Limitations: Single center study of a heterogeneous population.

CONTACT & FUNDING