

SUPPLEMENTAL TABLES AND FIGURES

Unsupervised machine learning clustering to identify subphenotypes among cardiac intensive care unit patients with heart failure

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Supplemental Table 1

Supplemental Table 2

Supplemental Figure 1

Supplemental Figure 2

Supplemental Figure 3

Supplemental Figure 4

Supplemental Figure 5

Heart failure phenotypes in CICU

Supplemental Table 1: Univariable logistic regression models for prediction of in-hospital mortality with all available admission laboratory variables in the final study population.

Variable	OR	p value	Lower 95% CI	Upper 95% CI	N	N missing	AUC
<i>Complete blood count with differential</i>							
Hemoglobin	0.954	0.0258	0.915	0.994	4877	0	0.539
MCV	1.018	0.0139	1.004	1.032	4877	0	0.536
RDW	1.134	< 1e-04	1.096	1.172	4877	0	0.600
Platelets	1.000	0.5772	0.999	1.001	4877	0	0.522
WBC	1.069	< 1e-04	1.054	1.085	4877	0	0.616
Neutrophils	1.099	< 1e-04	1.081	1.118	4877	0	0.649
Lymphocytes	0.715	< 1e-04	0.615	0.826	4877	0	0.607
Monocytes	1.516	< 1e-04	1.273	1.807	4877	0	0.540
Eosinophils	0.045	< 1e-04	0.016	0.120	4877	0	0.616
NLR	1.032	< 1e-04	1.025	1.039	4877	0	0.677
PMN percent	17.104	< 1e-04	9.475	31.452	4877	0	0.650
Lymph percent	0.000	< 1e-04	0.000	0.001	4877	0	0.672
Mono percent	0.001	< 1e-04	0.000	0.020	4877	0	0.571
Eos percent	0.000	< 1e-04	0.000	0.000	4877	0	0.635
<i>Electrolytes and kidney function</i>							
Sodium	0.945	< 1e-04	0.929	0.961	4877	0	0.586
Potassium	1.324	< 1e-04	1.169	1.497	4877	0	0.552
Bicarbonate	0.967	0.0009	0.949	0.986	4877	0	0.555

Heart failure phenotypes in CICU

Variable	OR	p value	Lower 95% CI	Upper 95% CI	N	N missing	AUC
Chloride	0.950	< 1e-04	0.937	0.964	4877	0	0.589
Anion gap	1.119	< 1e-04	1.095	1.145	4877	0	0.612
BUN	1.017	< 1e-04	1.014	1.021	4877	0	0.642
Creatinine	1.174	< 1e-04	1.110	1.240	4877	0	0.614
Glucose	1.002	0.0017	1.001	1.003	3464	1413	0.562
Ionized Calcium	0.626	0.0031	0.459	0.852	1854	3023	0.577
Phosphorus	1.186	0.0002	1.081	1.297	2245	2632	0.516
Magnesium	1.724	< 1e-04	1.315	2.249	3339	1538	0.557
Other chemistries							
Albumin	0.441	< 1e-04	0.343	0.565	1560	3317	0.633
AST	1.000	< 1e-04	1.000	1.000	2682	2195	0.613
ALT	1.000	< 1e-04	1.000	1.001	2584	2293	0.582
Alk phos	1.002	0.0007	1.001	1.004	1931	2946	0.563
Bilirubin	1.104	0.0004	1.048	1.171	2111	2766	0.560
Lactate	1.257	< 1e-04	1.194	1.327	1691	3186	0.634
CRP	1.001	0.6569	0.997	1.004	438	4439	0.524
NT-proBNP	1.000	0.0003	1.000	1.000	1165	3712	0.630
Initial troponin T	1.022	0.2330	0.984	1.056	2901	1976	0.537
Arterial blood gas							
Arterial pH	0.045	< 1e-04	0.013	0.163	1781	3096	0.570
Arterial PCO2	0.996	0.4192	0.985	1.006	1784	3093	0.524

Heart failure phenotypes in CICU

Variable	OR	p value	Lower 95% CI	Upper 95% CI	N	N missing	AUC
Arterial PO2	1.001	0.1787	0.999	1.003	2336	2541	0.505
Arterial Base Excess	0.933	< 1e-04	0.912	0.954	1977	2900	0.608
PF Ratio	0.999	0.0447	0.998	1.000	1823	3054	0.549

Heart failure phenotypes in CICU

Supplemental Table 2: Baseline characteristics of the final study population and CICU patients with HF who were excluded due to one or missing laboratory variable of interest.

Variable	Excluded HF patients (N=1131)	Final study population (N=4877)	All CICU HF patients (N=6008)	p value
Demographics and outcomes				
Age	70.7 (14.7)	69.4 (14.9)	69.7 (14.8)	0.008
Female sex	451 (39.9%)	1872 (38.4%)	2323 (38.7%)	0.353
White race	1028 (90.9%)	4490 (92.1%)	5518 (91.8%)	0.195
ICU LOS	1.5 (3.4)	3.5 (6.1)	3.1 (5.7)	< 0.001
Hospital LOS	9.3 (13.5)	11.2 (17.9)	10.9 (17.2)	< 0.001
CICU_death	141 (12.5%)	276 (5.7%)	417 (6.9%)	< 0.001
Early death	96 (8.5%)	44 (0.9%)	140 (2.3%)	< 0.001
Hospital_death	212 (18.7%)	524 (10.7%)	736 (12.3%)	< 0.001
Severity of illness				
APACHE-3 score	66.7 (28.8)	67.6 (23.3)	67.4 (24.5)	0.306
Day 1 SOFA score	4.2 (3.8)	4.4 (3.2)	4.4 (3.3)	0.086
MCARS	2.7 (2.2)	3.0 (2.1)	2.9 (2.1)	< 0.001
Braden score	17.1 (3.5)	17.2 (3.4)	17.2 (3.4)	0.372
LVSD based on LVEF				0.445
- Normal	235 (30.2%)	1068 (29.0%)	1303 (29.2%)	
- Mild LVSD	114 (14.6%)	538 (14.6%)	652 (14.6%)	
- Moderate LVSD	178 (22.8%)	940 (25.6%)	1118 (25.1%)	
- Severe LVSD	252 (32.3%)	1132 (30.8%)	1384 (31.1%)	

Heart failure phenotypes in CICU

Variable	Excluded HF patients (N=1131)	Final study population (N=4877)	All CICU HF patients (N=6008)	p value
SCAI shock stage				< 0.001
- A	299 (34.1%)	1376 (37.3%)	1675 (36.7%)	
- B	310 (35.4%)	1252 (33.9%)	1562 (34.2%)	
- C	128 (14.6%)	630 (17.1%)	758 (16.6%)	
- D	114 (13.0%)	399 (10.8%)	513 (11.2%)	
- E	25 (2.9%)	31 (0.8%)	56 (1.2%)	
Comorbidities				
Prior MI	225 (19.9%)	1100 (22.6%)	1325 (22.1%)	0.052
Prior HF	433 (38.4%)	1792 (36.8%)	2225 (37.1%)	0.329
CCI	3.0 (2.8)	3.0 (2.8)	3.0 (2.8)	0.997
Prior DM	372 (33.0%)	1720 (35.3%)	2092 (34.9%)	0.133
Prior lung disease	264 (23.4%)	1151 (23.7%)	1415 (23.6%)	0.859
CKD	319 (28.3%)	1462 (30.0%)	1781 (29.7%)	0.242
Prior dialysis	58 (5.1%)	365 (7.5%)	423 (7.0%)	0.005
Ischemic etiology	512 (45.4%)	2415 (49.6%)	2927 (48.8%)	0.010
Admission diagnoses				
Cardiac arrest	169 (14.9%)	615 (12.6%)	784 (13.0%)	0.036
Shock	279 (24.7%)	1083 (22.2%)	1362 (22.7%)	0.075
CS	234 (20.7%)	900 (18.5%)	1134 (18.9%)	0.083
Sepsis	84 (7.4%)	454 (9.3%)	538 (9.0%)	0.046

Heart failure phenotypes in CICU

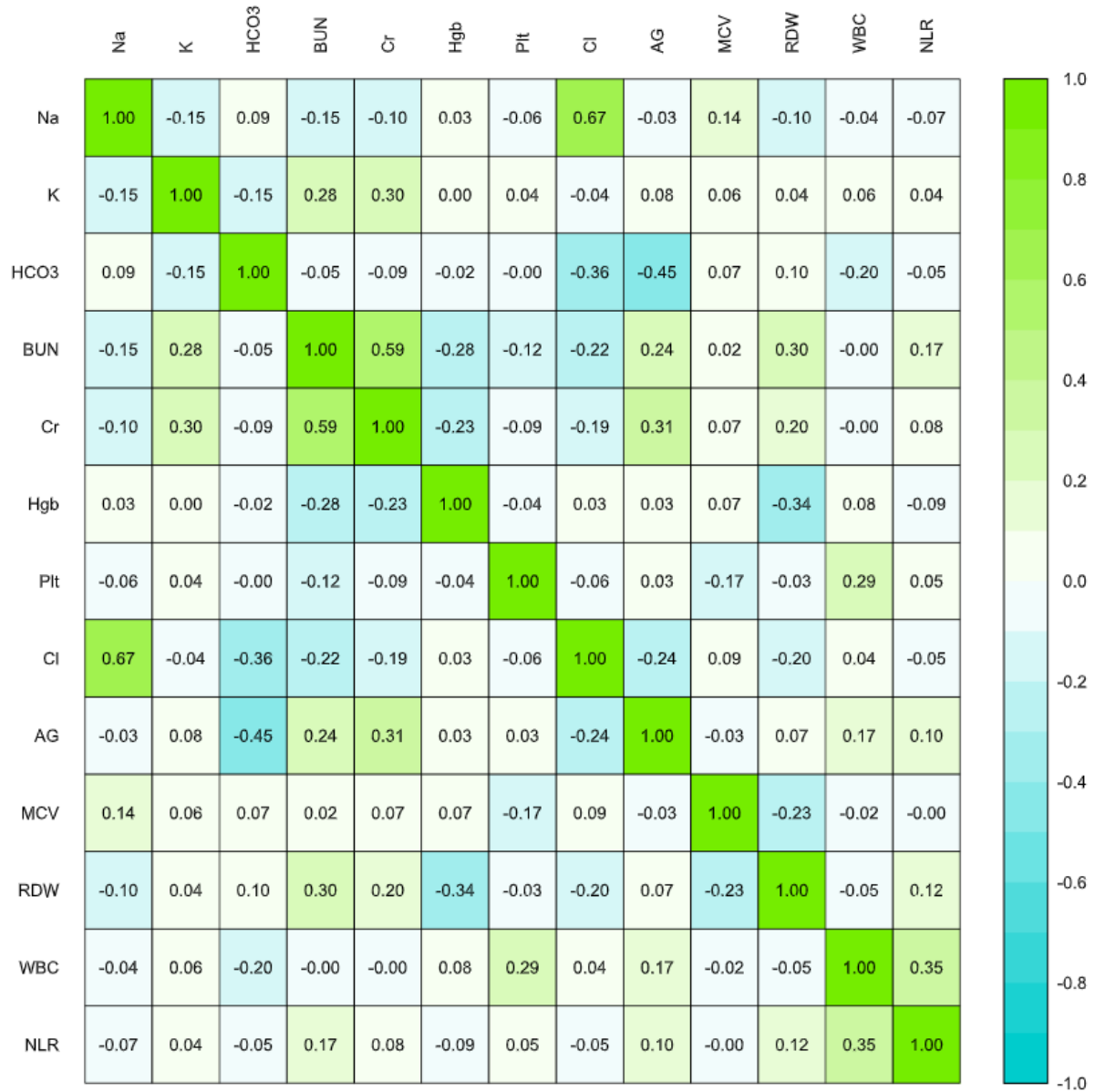
Variable	Excluded HF patients (N=1131)	Final study population (N=4877)	All CICU HF patients (N=6008)	p value
Respiratory failure	385 (34.0%)	1858 (38.1%)	2243 (37.3%)	0.011
ACS	384 (34.0%)	1779 (36.5%)	2163 (36.0%)	0.111
STEMI	188 (16.6%)	883 (18.1%)	1071 (17.8%)	0.240
Procedures and therapies				
IMV	217 (19.2%)	1093 (22.4%)	1310 (21.8%)	0.018
NIPPV	182 (16.1%)	1295 (26.6%)	1477 (24.6%)	< 0.001
CRRT	24 (2.1%)	181 (3.7%)	205 (3.4%)	0.008
Dialysis	91 (8.0%)	384 (7.9%)	475 (7.9%)	0.847
Vasopressors	381 (33.7%)	1372 (28.1%)	1753 (29.2%)	< 0.001
Inotropes	190 (16.8%)	805 (16.5%)	995 (16.6%)	0.811
Vasoactives	444 (39.3%)	1750 (35.9%)	2194 (36.5%)	0.034
IABP	123 (10.9%)	600 (12.3%)	723 (12.0%)	0.184
Impella/ECMO	14 (1.2%)	67 (1.4%)	81 (1.3%)	0.721
PAC	150 (13.3%)	865 (17.7%)	1015 (16.9%)	< 0.001
Cath	572 (50.6%)	2696 (55.3%)	3268 (54.4%)	0.004
PCI	288 (25.5%)	1244 (25.5%)	1532 (25.5%)	0.976
Transfusion	119 (10.5%)	694 (14.2%)	813 (13.5%)	0.001
IHCA	46 (4.1%)	120 (2.5%)	166 (2.8%)	0.003
Admission laboratory values				
Sodium	137.4 (5.2)	137.5 (4.8)	137.5 (4.9)	0.320

Heart failure phenotypes in CICU

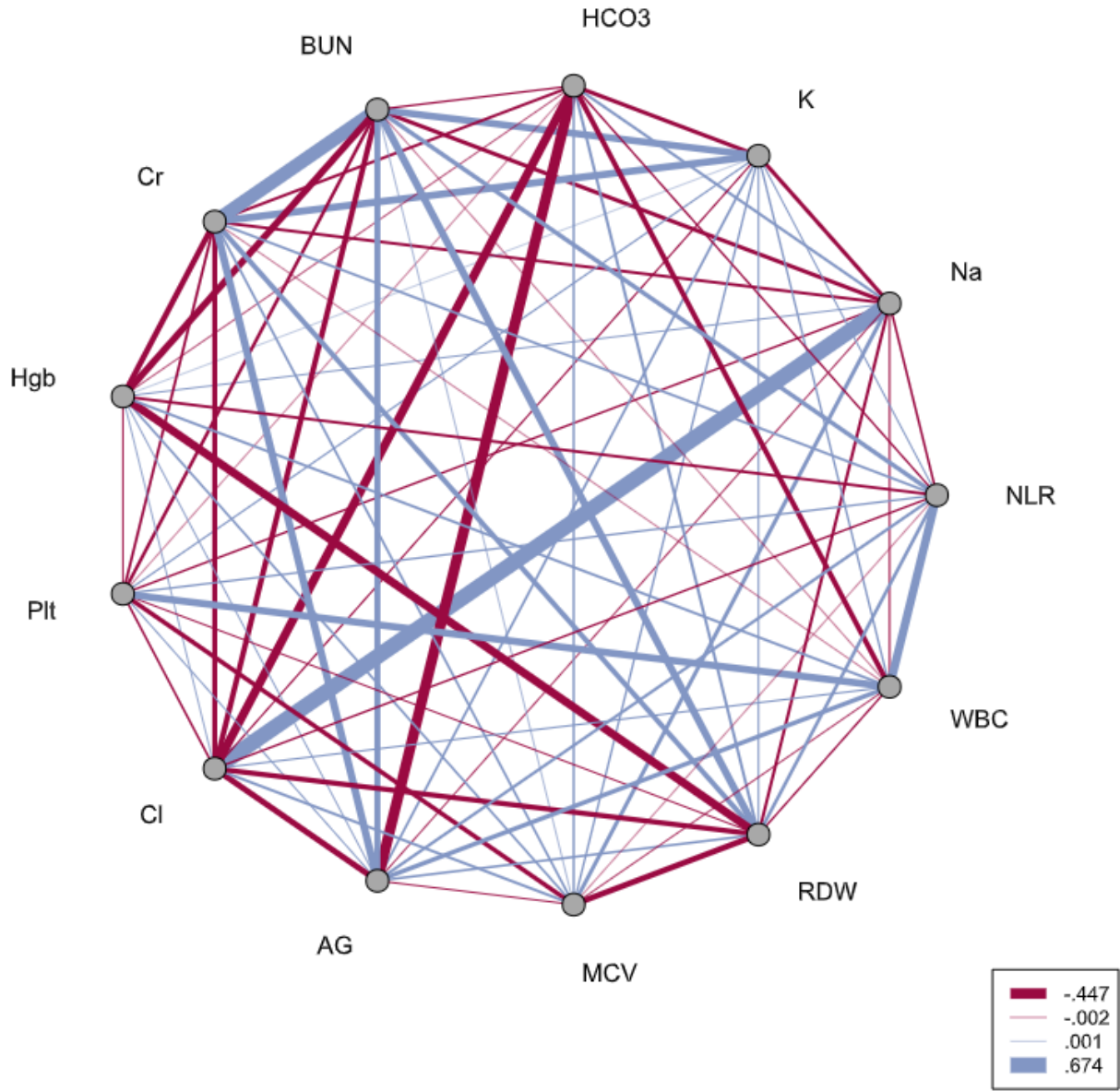
Variable	Excluded HF patients (N=1131)	Final study population (N=4877)	All CICU HF patients (N=6008)	p value
Potassium	4.3 (0.7)	4.3 (0.7)	4.3 (0.7)	0.324
Bicarbonate	24.0 (5.3)	24.1 (4.8)	24.1 (4.9)	0.651
BUN	33.0 (22.1)	32.9 (21.5)	32.9 (21.6)	0.856
Creatinine	1.6 (1.1)	1.6 (1.3)	1.6 (1.3)	0.274
Hemoglobin	11.5 (2.2)	11.8 (2.2)	11.7 (2.2)	0.005
Platelets	208.5 (106.1)	208.2 (87.6)	208.2 (90.8)	0.935
Chloride	101.2 (6.2)	100.8 (6.0)	100.9 (6.0)	0.066
Anion Gap	13.3 (4.4)	13.2 (3.7)	13.2 (3.8)	0.459
MCV	91.7 (7.6)	90.9 (6.6)	91.0 (6.7)	0.001
RDW	15.9 (2.8)	15.4 (2.3)	15.5 (2.4)	< 0.001
WBC	11.7 (13.3)	10.8 (6.0)	10.9 (7.6)	0.001
NLR	11.4 (12.1)	10.1 (11.1)	10.2 (11.1)	0.074

Heart failure phenotypes in CICU

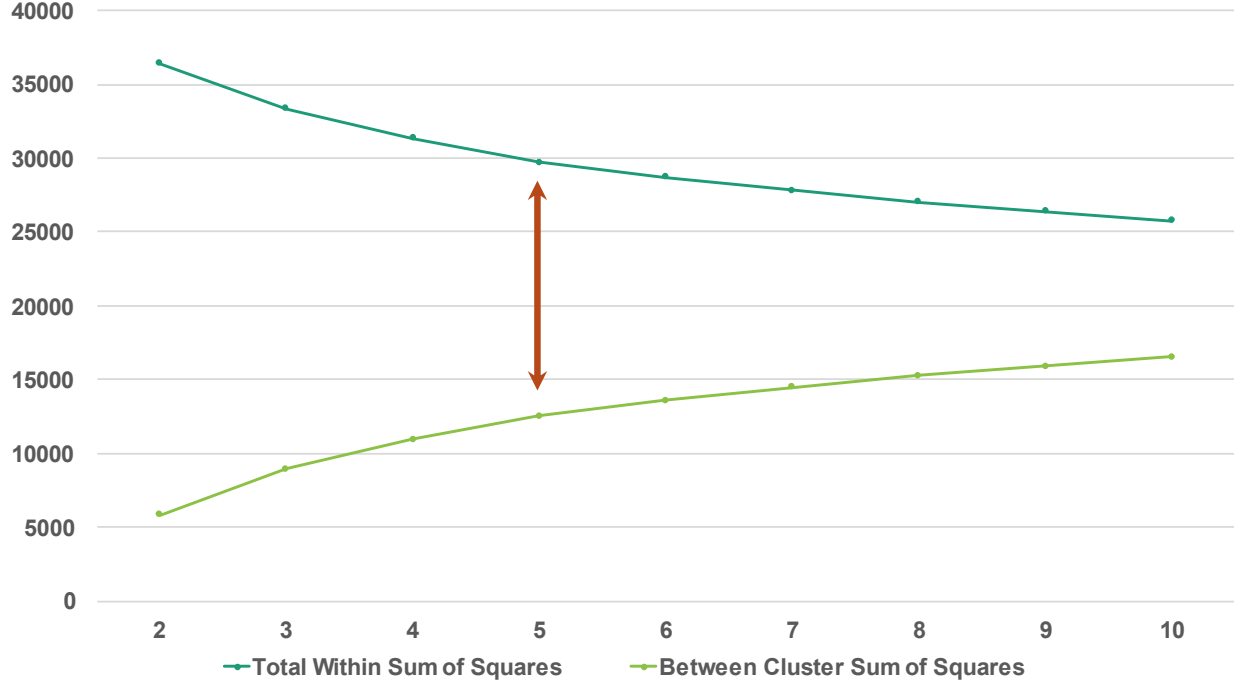
Supplemental Figure 1: Correlation matrix showing Pearson correlations among selected candidate laboratory feature variables in the final study cohort, with web plot demonstrating these same data.



Heart failure phenotypes in CICU



Supplemental Figure 2: Elbow plot demonstrating the between-clusters and within-clusters sum of squares, demonstrating a subtle inflection point at 5 clusters.

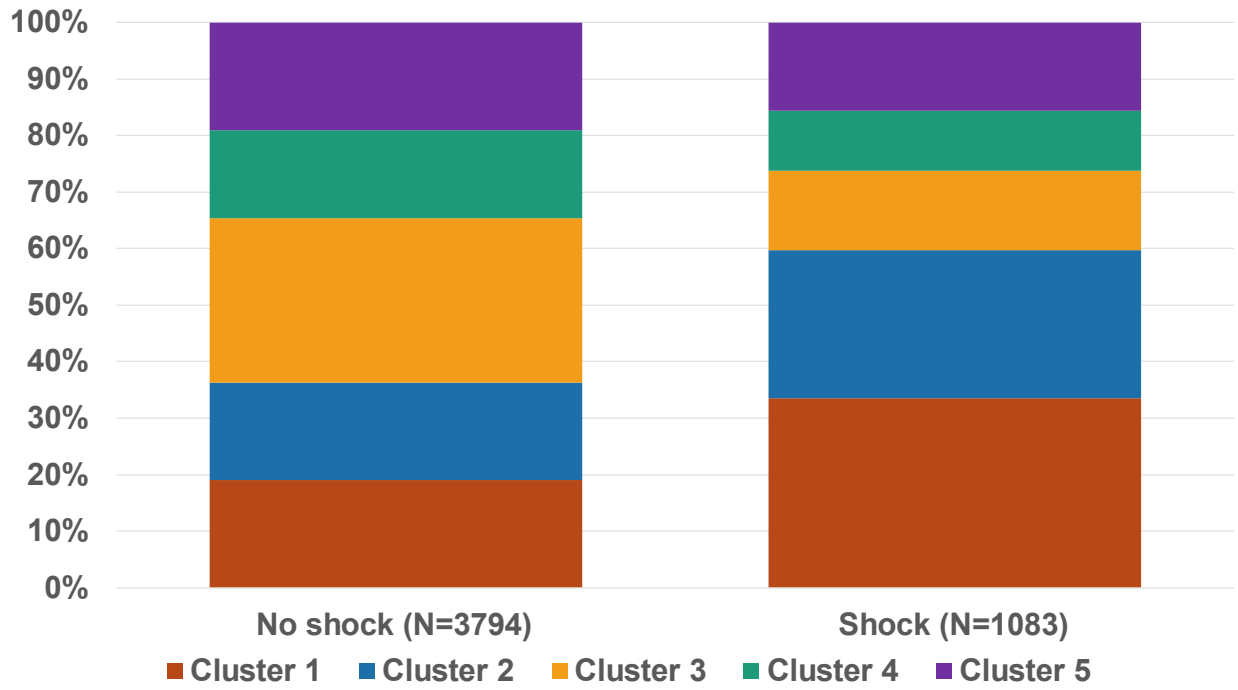
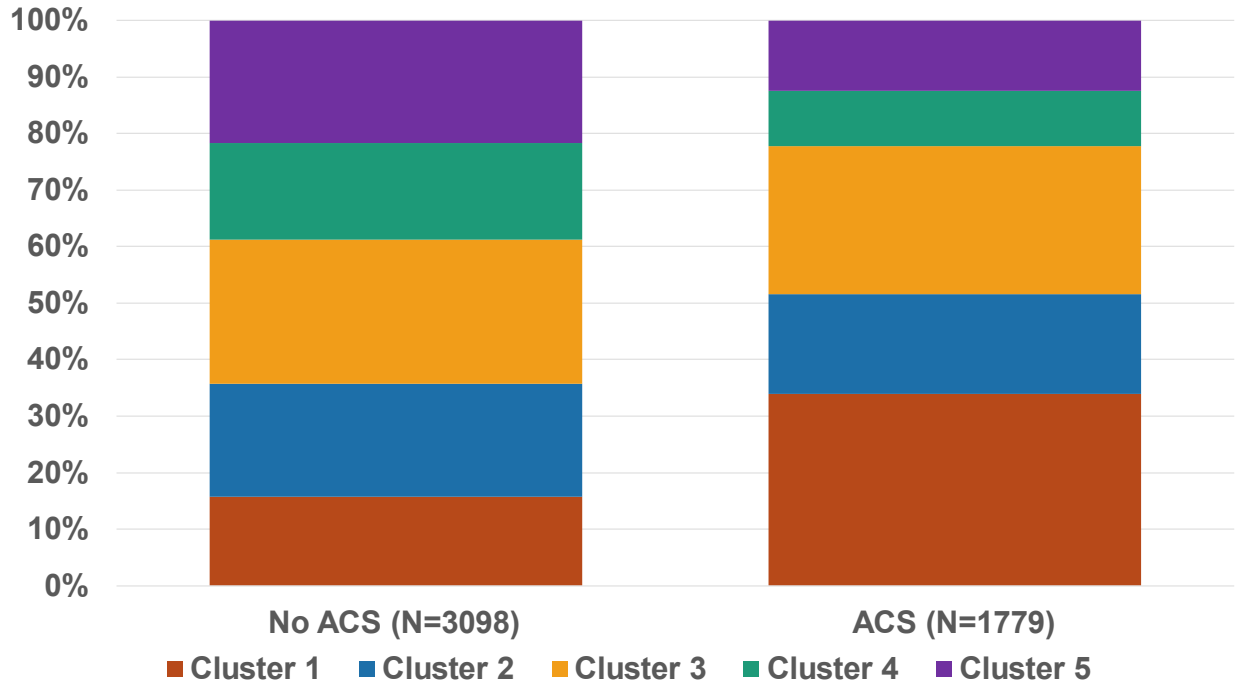


Heart failure phenotypes in CICU

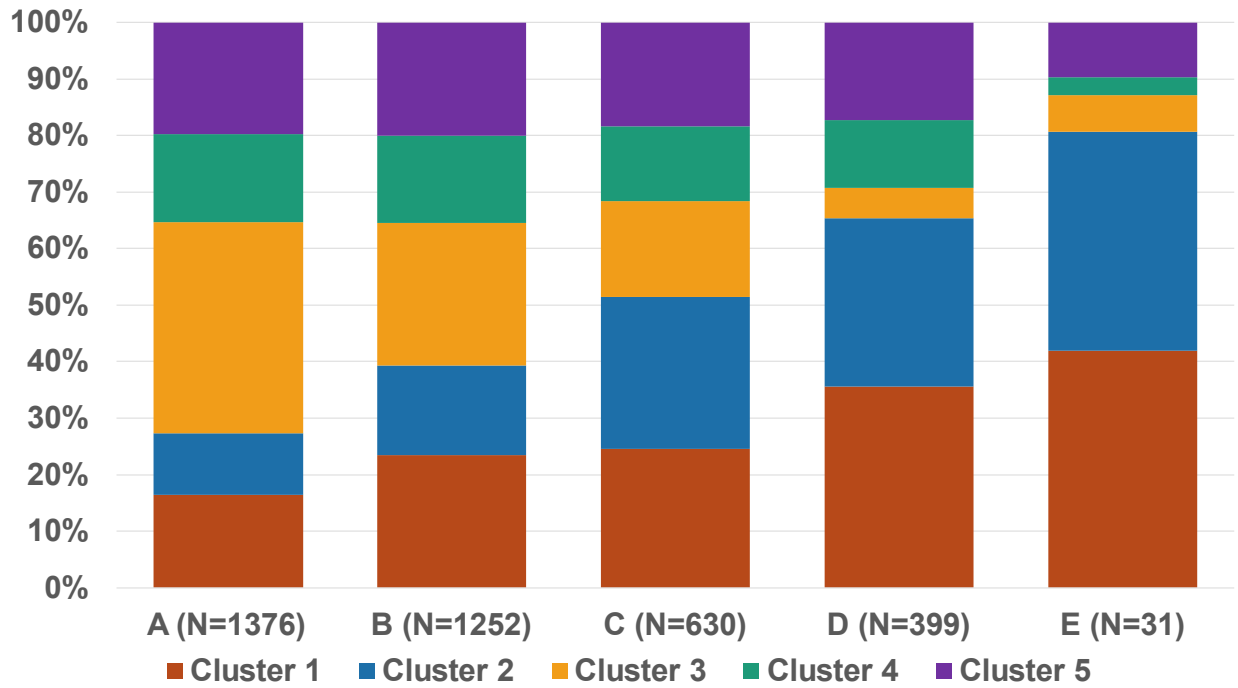
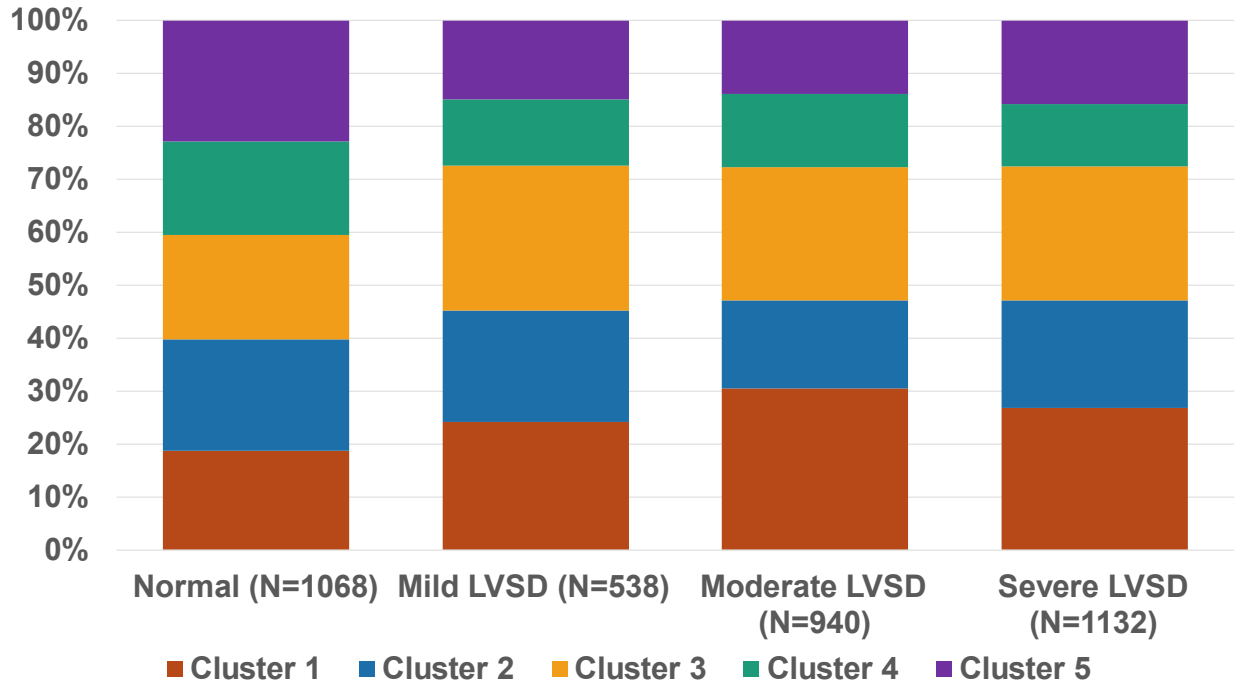
Supplemental Figure 3: Distribution of clusters according to patient characteristics. Cluster 1 = Inflamed; Cluster 2 = Hypoperfused; Cluster 3 = Uncomplicated; Cluster 4 = Iron-Deficient; Cluster 5 = Cardiorenal.



Heart failure phenotypes in CICU

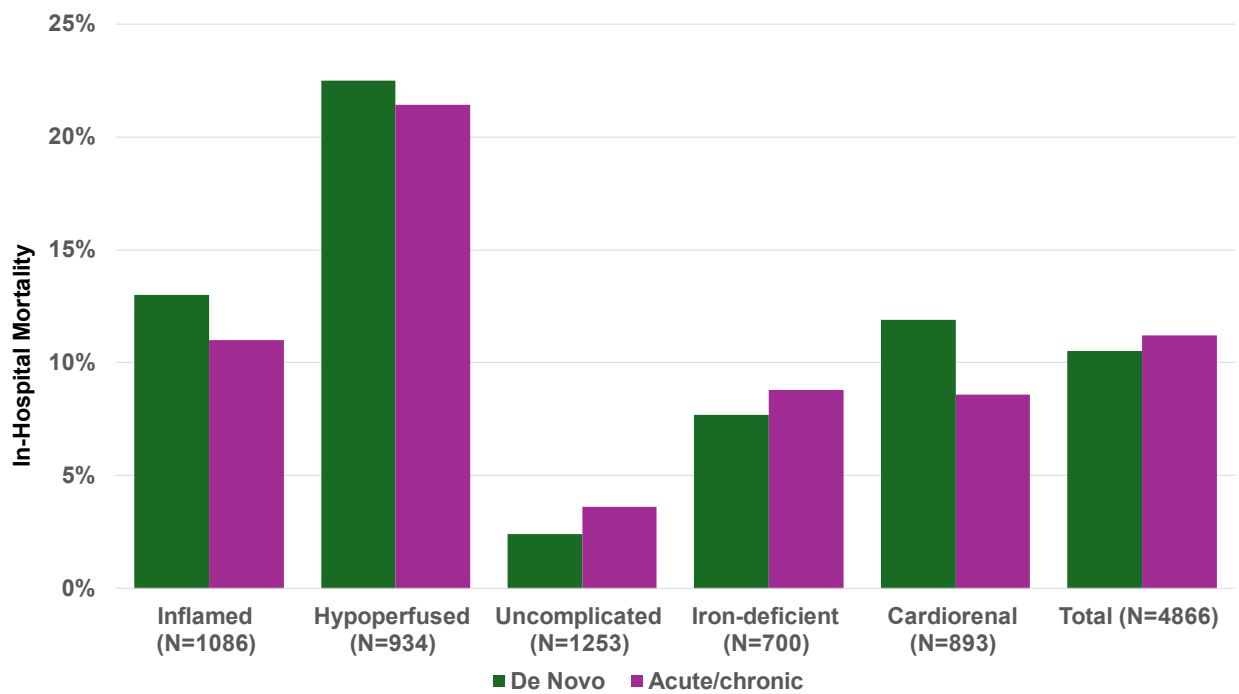
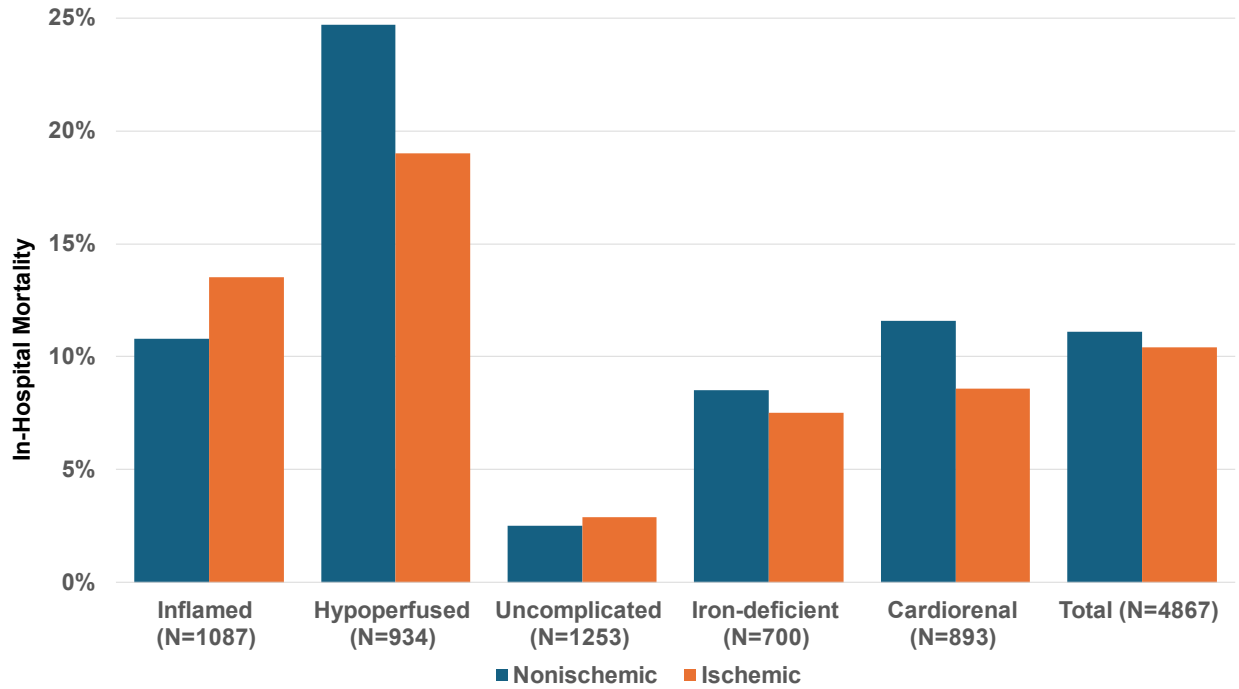


Heart failure phenotypes in CICU



Heart failure phenotypes in CICU

Supplemental Figure 4: In-hospital mortality according to subphenotype and etiology (ischemic versus nonischemic) or pattern (de novo versus acute on chronic) HF.



Heart failure phenotypes in CICU

Supplemental Figure 5: In-hospital mortality according to subphenotype and pattern of ventricular dysfunction based on moderate or greater RV and LV dysfunction by TTE.

