

Prognostic Value of Cardiac Biomarkers and National Early Warning Score 2 in Acute Dyspnea

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SUPPLEMENTARY TABLES AND FIGURES

Supplementary Table 1: Baseline characteristics HF subgroups (n=143)^a

	HF n=143	HF_{rEF} n=91	HF_{pEF} n=52	p
Age	78 (68-83)	74 (66-81)	81 (75-85)	0.003
Male sex	90 (63%)	69 (76%)	21 (40%)	<0.001
BMI	27 (22-29)	27 (22-29)	27 (23-30)	0.47
Smoking	30 (21%)	23 (25%)	7 (13%)	0.095
NYHA class IV	65 (45%)	42 (46%)	23 (44%)	0.82
History of:				
HF	87 (61%)	72 (79%)	15 (29%)	<0.001
AF	68 (48%)	45 (49%)	23 (44%)	0.55
COPD	61 (43%)	38 (42%)	23 (44%)	0.77
CAD	78 (55%)	62 (68%)	16 (31%)	<0.001
HT	69 (48%)	39 (43%)	30 (58%)	0.088
DM	43 (30%)	29 (32%)	14 (27%)	0.54
NEWS2 score	5 (3-7)	5 (3-7)	6 (3-8)	0.34
hs-cTnT	38 (22-75)	35 (23-74)	39 (19-96)	0.79
NT-proBNP	3600 (1601-8396)	4308 (2064-8738)	2293 (704-4536)	<0.001
CRP	13 (5-37)	13 (5-30)	17 (6-40)	0.26
eGFR	66 (47-81)	67 (45-81)	63 (47-82)	0.90

BMI, Body mass index; NYHA, New York Heart Association; HF, heart failure; AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; HT, hypertension; DM, diabetes mellitus; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate.

^a Data are presented as n (%) or median (Q1-Q3).

Supplementary Table 2: Heart failure medication at discharge

	HF <i>n=143</i>	HFrEF <i>n=91</i>	HFpEF <i>n=52</i>	<i>p</i>
Beta blocker	108 (76%)	75 (82%)	33 (63%)	0.011
ACEi/ARB	95 (66%)	66 (73%)	29 (56%)	0.041
MRA	25 (17%)	15 (16%)	10 (19%)	0.68
Loop diuretic	105 (73%)	71 (78%)	34 (65%)	0.10
Tiazid	13 (9%)	8 (9%)	5 (10%)	0.87
Digitalis	31 (22%)	22 (24%)	9 (17%)	0.34

ACEi, Angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist.

Supplementary Table 3: Variables associated with NEWS2 (n=314)

	<i>B</i>	<i>95% CI</i>
<i>Univariate linear regression</i>		
Age	0.036	0.013 - 0.060
Male sex	-0.366	-1.032 - 0.300
BMI	-0.041	-0.087 - 0.005
Smoking	-0.250	-0.999 - 0.498
NYHA class IV	1.934	1.298 - 2.570
<i>History of:</i>		
HF	0.058	-0.655 - 0.771
AF	0.237	-0.487 - 0.961
COPD	1.231	0.582 - 1.881
CAD	-0.286	-0.980 - 0.408
HT	0.806	0.129 - 1.483
DM	0.426	-0.378 - 1.230
lnhs-cTnT	0.685	0.413 - 0.956
lnNT-proBNP	0.327	0.153 - 0.501
lnCRP	0.602	0.383 - 0.820
lneGFR	-0.312	-1.073 - 0.449
<i>Multivariable linear regression (backward selection) (r²=0.20)</i>		
lnCRP	0.485	0.278 - 0.692
NYHA class IV	1.327	0.687 - 1.967
History of COPD	0.672	0.054 - 1.290
lnhs-cTnT	0.456	0.195 - 0.717

Abbreviations as described in Supplementary Table 1.

Supplementary Table 4: NEWS2 variables for AHF, HFrEF and HFpEF

<i>Variable</i>	<i>AHF</i> <i>n=143</i>	<i>HFrEF</i> <i>n=91</i>	<i>HFpEF</i> <i>n=52</i>	<i>p</i>
Respiratory rate (per minute)	24 (18-28)	23 (18-28)	24 (20-30)	0.45
O ₂ saturation (%)	94 (90-97)	95 (91-97)	92 (89-95)	0.005
Supplemental O ₂ (n, %)	64 (45%)	41 (45%)	23 (44%)	0.92
Systolic blood pressure (mmHg)	144 (123-166)	142 (119-171)	147 (129-165)	0.70
Heart rate (beats per minute)	88 (74-109)	88 (76-109)	89 (72-108)	0.74
Altered mental state (n, %)	0 (0%)	0 (0%)	0 (0%)	-
Temperature (°C)	36.8 (36.4-37.3)	36.8 (36.3-37.1)	37.0 (36.5-37.3)	0.029
NEWS2	5 (3-7)	5 (3-7)	6 (3-8)	0.34

Data are presented as n (%), or median (Q1-Q3) and compared using the Mann-Whitney U test.

Supplementary Table 5: Spearman's correlations between NEWS2 parameters and hs-cTnT/NT-proBNP

	<i>Hs-cTnT Corr.coeff.</i>	<i>p</i>	<i>NT-proBNP Corr.coeff.</i>	<i>p</i>
Respiratory rate	0.244	<0.001	0.167	<0.001
Saturation	-0.040	0.08	-0.046	0.045
Supplemental O2	0.166	<0.001	0.172	<0.001
Systolic blood pressure	0.069	0.003	0.063	0.007
Heart rate	0.029	0.214	0.007	0.76
Altered mental state	-	-	-	-
Temperature	0.008	0.74	-0.066	0.004
NEWS2	0.285	<0.001	0.197	<0.001

Supplementary Table 6: Hazard ratios for mortality in different prognostic models

<i>Model</i>	<i>Variables</i>	<i>HR (95% CI) Unadjusted</i>	<i>p^a</i>	<i>HR (95% CI) Adjusted</i>	<i>p^a</i>
1	Elevated NEWS2 clinical risk*	2.74 (1.66-4.51)	<0.001	2.11 (1.28-3.48) ^b	0.034
2	Elevated NEWS2 clinical risk, hs-cTnT and/or NT-proBNP above median**	5.64 (2.45-12.97)			
3	Respiratory rate, per minute	1.06 (1.04-1.09)		1.06 (1.04-1.09) ^c	
4	SpO2	0.96 (0.94-0.99)			
5	Supplemental O2	1.07 (1.00-1.15)			
6	Systolic Blood Pressure	0.99 (0.98-1.00)		0.99 (0.98-0.99) ^d	
7	Heart Rate	1.00 (0.99-1.01)			
8	Altered mental state	1.00 (-.)			
9	Temperature	0.89 (0.70-1.13)			

* Compared to low NEWS2 clinical risk

** Compared to low NEWS2 clinical risk and both cardiac biomarkers below median

^a *p* for trend

^b Adjusted for age, BMI, hs-cTnT, history of HF and history of COPD

^c Adjusted for systolic blood pressure

^d Adjusted for respiratory rate

Supplementary Table 7: Variables associated with all-cause mortality during follow-up for AHF patients (n=143)

	<i>HR</i>	<i>95% CI</i>
<i>Univariate</i>		
NEWS2 score	1.12	1.03 - 1.22
Age	1.04	1.02 - 1.07
Male sex	0.53	0.32 - 0.86
BMI	0.94	0.89 - 0.99
Smoking	0.88	0.48 - 1.62
NYHA class IV	2.01	1.23 - 3.29
<i>History of:</i>		
HF	1.43	0.86 - 2.38
AF	1.07	0.66 - 1.74
COPD	1.85	1.14 - 3.01
CAD	1.05	0.65 - 1.70
HT	0.83	0.51 - 1.36
DM	1.78	1.08 - 2.95
lnhs-cTnT	1.37	1.10 - 1.71
lnNT-proBNP	1.53	1.24 - 1.89
lnCRP	1.32	1.07 - 1.62
lneGFR	0.39	0.22 - 0.66
Multivariable (backward: LR)		
DM	2.26	1.31 - 3.87
lnNT-proBNP	1.46	1.17 - 1.83
Male sex	0.54	0.33 - 0.89
COPD	2.72	1.60 - 4.61
lneGFR	0.51	0.28 - 0.92

Abbreviations as described in Supplementary Table 1.

Supplementary Table 8: Comparison of AUCs for prognostic models

<i>Model</i>	<i>Cohort</i>	<i>Variables</i>	<i>AUC (95% CI)</i>	<i>p</i>
1	All patients	NEWS2	0.64 (0.58-0.71)	
2	All patients	hs-cTnT	0.69 (0.64-0.75)	0.22 ^a
3	All patients	NT-proBNP	0.67 (0.61-0.73)	0.64 ^a
4	All patients	hs-cTnT, NT-proBNP	0.70 (0.64-0.75)	
5	All patients	hs-cTnT, NT-proBNP, NEWS2	0.72 (0.66-0.78)	0.042 ^b
6	AHF	hs-cTnT, NT-proBNP	0.67 (0.58-0.76)	
7	AHF	hs-cTnT, NT-proBNP, NEWS2	0.70 (0.60-0.78)	0.014 ^c
8	AHF	NEWS2	0.65 (0.56-0.74)	
9	HFrEF	NEWS2	0.56 (0.43-0.68)	
10	HFpEF	NEWS2	0.80 (0.68-0.93)	0.005 ^d

Reference model compared with: ^a Model 1; ^b Model 4; ^c Model 6; ^d Model 9

Supplementary Figure: Survival curves for AHF patients stratified by NEWS2 clinical risk