1 **Table 1:** A multivariable predictive model for 30-day mortality using logistic regression in 4867 patients.

Variable	No. of patients (%)	30-day mortality (%)	OR (95% CI)*	% missing
Barthel index at admission	-		-	28.4%
≥75	1556 (44.6%)	60 (3.9%)	1	
50-74	912(26.2%)	76 (8.3%)	1.52 (1.07-2.16)	
25-49	614 (17.6%)	98 (16.0%)	2.34 (1.61-3.38)	
<25	404 (11.6%)	125 (30.9%)	3.99 (2.69-5.92)	
Systolic blood pressure (mm Hg)				2.0%
≥155	1443 (30.3%)	89 (6.2%)	1	
140-154	991 (20.8%)	81 (8.2%)	1.52 (1.08-2.15)	
125-139	986 (20.7%)	105 (10.7%)	2.06 (1.48-2.86)	
110-124	845 (17.7%)	114 (13.5%)	2.56 (1.85-3.56)	
95-109	357 (7.5%)	56 (15.7%)	2.52 (1.67-3.78)	
<95	146 (3.1%)	41 (28.1%)	3.03 (1.82-5.06)	
Age (years)				0.3%
<75	1227 (25.3%)	61 (5.0%)	1	
75-79	911 (18.8%)	71 (7.8%)	1.59 (1.08-2.33)	
80-84	1116 (23.0%)	112 (10.0%)	1.74 (1.22-2.49)	
85-89	1054 (21.7%)	139 (13.2%)	1.72 (1.21-2.45)	
>=90	546 (11.3%)	117 (21.4%)	2.62 (1.79-3.83)	
NT-proBNP (pg/mL)				59.8%
<8000	1412 (72.2%)	84 (6.0%)	1	
8000-15999	285 (14.6%)	38 (13.3%)	1.64 (1.08-2.49)	
16000-23999	110 (5.6%)	26 (23.6%)	2.04 (1.25-3.34)	
>24000	148 (7.6%)	42 (28.4.1%)	2.59 (1.68-3.99)	
Potassium (mEq/L)				4.9%
<3.5	249 (5.4%)	32 (12.9%)	1.48 (0.95-2.30)	
3.5-4.9	3536 (76.5%)	284 (8.0%)	1	
5-5.5	508 (11.0%)	73 (14.4%)	1.35 (0.98-1.87)	
>5.5	332 (7.2%)	78 (23.5%)	2.09 (1.48-2.94)	
Positive troponin level	1286 (45.1%)	198 (15.4%)	1.75 (1.32-2.30)	41.4%
NYHA class IV at admission	2148 (46.1%)	340 (15.8%)	1.63 (1.28-2.09)	4.2%
Respiratory rate (breaths/min)				29.5%
<25	2305 (67.2%)	189 (8.2%)	1	
25-29	540 (15.7%)	76 (14.1%)	1.35 (0.96-1.88)	
>=30	585 (17.1%)	109 (18.6%)	1.69 (1.23-2.32)	
Low output symptoms*	792 (17.5%)	161 (20.3%)	1.48 (1.15-1.90)	6.9%
Oxygen saturation (%)				4.0%
95-100	1830 (39.2%)	127 (6.9%)	1	
90-94	1675 (35.8%)	159 (9.5%)	1.19 (0.90-1.56)	
84-89	689 (14.7%)	98 (14.2%)	1.34 (0.97-1.86)	
<85%	479 (10.3%)	98 (20.5%)	1.67 (1.18-2.36)	
Episode associated with ACS**	134 (2.8%)	36 (26.9%)	2.02 (1.25-3.27)	2.9%
Hypertrophy at ECG***	290 (6.2%)	38 (13.1%)	1.59 (1.05-2.40)	3.4%
Creatinine (mg/dL)				1.8%
<1.5	3401 (71.1%)	263 (7.7%)	1	
1.5-2.4	1054 (22.1%)	156 (14.8%)	1.27 (0.99-1.64)	
>=2.5	326 (6.8%)	67 (20.6%)	1.46 (1.00-2.13)	

2 ACS is acute coronary syndrome; ECG, electrocardiogram; NYHA, New York Heart Association; OR, odds ratio.

\* Defined by confusion, weakness, cold periphery and any sign: poor peripheral perfusion, anuria or oliguria.

\*\*Defined by the presence of at least two of the following three criteria: symptoms of chest pain, ECG abnormalities, and positive
tropoinin.

6 \*\*\*Defined by the Sokolow-Lyon index.

7 ‡ Multivariable predictive model for 30-day mortality using logistic regression. Each quantitative predictor variable has been

8 grouped into appropriate categories. The odds ratio for each category is the change in the odds of dying within 30 days relative to

9 the reference category (e.g. age<75 years). The coefficient for each variable can be obtained as the log (odds ratio). Multiple 10 imputation using chained was used for missing data.

<sup>11</sup> <sup>+</sup> The intercept was -5.40, which is the log (odds) of dying within 30 days for a patient who is in the reference category of every

12 variable. Such a patient has the most favourable characteristics possible and has a very low probability (0.5%) of dying within 30

13 days.

- 14 **Table 2** Analysis of 30-day mortality stratified by type of hospital (university vs community) and ED volume of
- 15 attendances (low-medium vs high volume)

Risk Quintile	30-day mortality in university hospitals	30-day mortality in community hospitals	P-value*	30-day mortality in high-volume ED	30-day mortality in low/medium- volume ED	P-value**
Bottom quintile	6 (0.7%)	1 (0.7%)	0.65	2 (0.3%)	5 (1.3%)	0.74
2 <sup>nd</sup> quintile	15 (1.8%)	3 (2.4%)		11 (1.8%)	7 (2.0%)	
3 <sup>rd</sup> quintile	50 (5.9%)	8 (6.7%)		36 (6.0%)	22 (6.0%)	
4 <sup>th</sup> quintile	83 (9.9%)	19 (15.5%)		64 (10.4%)	38 (10.8%)	
Next decile	86 (20.5%)	12 (19.1%)		66 (20.9%)	32 (19.3%)	
Top decile	193 (45.8%)	24 (38.7%)		142 (44.5%)	75 (45.7%)	

17 ED: emergency department

\* P-value for Mantel Haenszel test. The c-statistic value for our model within university hospitals was 0.839
(95% CI 0.820-0.858), comparable to that obtained within community hospitals 0.812 (95% CI 0.761-0.862).

4193 patients were admitted to university hospitals (presenting 433 outcomes), whilst 626 patients were
admitted to community hospitals (presenting 67 outcomes)

22 \*\* P-value for Mantel Haenszel test. The c-statistic value for our model within high-volume hospital was 0.842

23 (95% CI 0.820-0.863), comparable to that obtained within medium/low-volume hospitals 0.824 (95% CI 0.791-

0.867). 3045 patients were admitted to high-volume hospitals (presenting 321 outcomes), whilst 1774 patients

25 were admitted to intermediate/low-volume hospitals (presenting 179 outcomes)

- 27 Figure 1: Risk score distribution (bars) and predicted 30-day mortality risk (line) from the model obtained in
- the derivation cohort.



For a patient in the reference category of every variable in Table 1 the estimated log(odds) of dying within 30 days is -5.40 (Intercept of the logistic model), meaning that the risk of dying within 30 days for a patient at the most extreme low risk (-5.40) is 0.5%. To calculate any individual patient's log(odds) of dying within 30 days one adds up their relevant coefficients in table 1 on top of this intercept value. Call this x. Then their probability of dying within 30 days is  $e^{x}/(1 + e^{x})$ . To facilitate this calculation for any patient we provide a website <u>http://bernalte.cat/calculadora/</u>

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**Figure 2:** Cumulative mortality for six risk groups. Risk groups 1–4 correspond to quintiles 1–4, with the top





Risk	Intervals	N	Probability of dying within 30 days
Low -	Bottom quintile	974	from 0.5% to 2.1%
	2 <sup>nd</sup> quintile	973	from 2.1% to 3.9%
Intermediate -	3 <sup>rd</sup> quintile	974	from 3.9% to 7.0%
	4 <sup>th</sup> quintile	973	from 7.0% to 14.5%
High	Next decile	487	from 14.5% to 25.7%
Very high	Top decile	486	from 25.8% to 89.8%

- 46 Figure 3: Assessment of risk discrimination and model goodness-of-fit in six risk groups (4 quintiles and the
- 47 top 2 deciles) from low to very high risk for the derivation cohort (top) and for the validation cohort (bottom).



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49 Q1 to Q4 denote quintiles 1 to 4; D9 and 10 denote deciles 9 and 10.

0.2

Predicted 30-day mortality

0.3

0.1

0.0

0.5

0.4

51 Appendix 1: Full list of participants in the ICA-SEMES Research Group (Research Group on Acute Heart Failure

52 of the Spanish Society of Emergency Medicine).

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#### 80 SUPPLEMENTAL MATERIAL

#### 81 **Table S1:** List of candidate predictor variables and units/definitions.

## Demographics

- Age (years)
- Gender (male/female)
- Body mass index (Kg/m<sup>2</sup>)

#### Vital signs

- Systolic blood pressure (mmHg)
- Diastolic blood pressure (mmHg)
- Heart rate (bpm)
- Respiratory rate (rpm)
- Arterial oxygen saturation (%)
- Temperature (ºC)

#### **Transfer & Triage**

- Triage level (severity)
- Type of transfer to Hospital
- Transfer to hospital with oxygen
- Transfer with diuretic, nitroglicerin or invasive ventilation

### **Medical history**

- Hypertension
- Diabetes Mellitus
- Dyslipidemia
- Ischemic Heart Disease
- Chronic Renal Failure (Creatinine >2mg/dL)
- Cerebrovascular Disease
- Atrial fibrillation
- Peripheral Arterial Disease
- Valvular heart disease
- Chronic obstructive pulmonary disease
- Dementia
- Neoplasia
- Cirrhosis

1 2

- Current smoker
- Prior congestive heart failure

- Prior echocardiography
- Type of ventricular
- dysfunction
- Left ventricular ejection fraction in the most recent echocardiogram (no older than 1 year before patients inclusion)

#### **Medical-social history**

- Incontinence
- Hearing impairment
- Social support
- Prior falls

## Status at admission

- Type of acute heart failure
- Symptoms of low output
- Cold skin
- Cutaneous pallor
- Delayed capillary refill
- Livedo reticularis
- Stupor or anxiety
- Dyspnea
- Ortopnea
- Paroxysmal nocturnal dyspnea
- Jugular venous pressure increased
- Hepatomegaly
- Edema
- Tachycardia
- Third sound auscultation
- Pulmonary rales
- Cardiomegaly (by chest Rx)
- Pleural effusion

#### Scores

- Barthel index at baseline
- Barthel index at admission
- NYHA at baseline
- NYHA at admission

## Precipitating factors

- Any precipitating factor
- Infection (precipitating factor)
- Fast Atrial Fibrillation (precipitating factor)
- Anemia (precipitating factor)
- Hypertensive crisis (precipitating factor)
- Non-compliance Treatment (precipitating factor)
- Others precipitating factors

#### **Blood tests**

- Hemoglobin (g/dL)
- Hematocrit (%)
- Red cell distribution width (%)
- White cells (number/mm3)
- Platelets (number/10e9/L)
- Platelets volume (fl)
- Glucose (mg/dL)
- Urea (mg/dL)
- Creatinine (mg/dL)
- Sodium (mEq/L)
- Potasium (mEq/L)
- Troponin
- BNP (pmol/L)
- NTproBNP (pmol/L)
- C-Reactive Protein (mg/dL)
- Procalcitonine
- pCO2 in arterial blood
- pH in arterial blood
- Lactic acid in blood (mmol/L)

#### ECG

- Sinus rhythm
- Atrial Fibrillation
- Left ventricular hypertrophy (according to Sokolow-Lyon index)
- Left bundle branch block

- Pacemaker rhythm

- **Table S2:** Collective descriptive missingness for key predictor variables in the whole both derivation
- 4 and validation cohorts.

Variable (% missingness)	30-day mortality if missing value (%)	30-day mortality if non-missing value (%)	p-value
Barthel index at admission (28.4%)	526 (9.8%)	273 (10.3%)	0.44
<b>Age</b> (0.3%)	0 (0%)	799 (10.0%)	0.40
Systolic BP (2.0%)	18 (10.7%)	781 (9.9%)	0.73
NYHA class IV at admission (4.2%)	40 (11.3%)	759 (9.9%)	0.39
Potassium (4.9%)	45 (11.0%)	754 (9.9%)	0.48
NT-proBNP (59.8%)	478 (10.2%)	321 (9.6%)	0.44
Positive troponin level (41.4%)	335 (9.9%)	464 (10.0%)	0.92
Low output symptoms (6.9%)	29 (8.5%)	770 (10.0%)	0.38
Respiratory rate (29.5%)	213 (8.6%)	586 (10.5%)	0.007
Episode associated with ACS (2.9%)	128 (9.7%)	771 (9.9%)	0.89
Oxygen saturation (4.0%)	30 (8.8%)	769 (10.0%)	0.48
Creatinine (1.8%)	19 (13.8%)	780 (9.9%)	0.129
Hypertrophy at ECG (3.4%)	30 (11.5%)	769 (9.9%)	0.39

**Table S3:** Description of the AUC ROC for each reduced-model and the full MEESSI-AHF model.

Model	c-statistic (95% CI)
Full model	0.836 (0.812-0.853)
Without NT-ProBNP	0.821 (0.803-0.840)
Without troponin	0.829 (0.811-0.848)
Without Barthel	0.817 (0.797-0.836)
Without NT-ProBNP and troponin	0.812 (0.792-0.831)
Without NT-ProBNP and Barthel	0.796 (0.776-0.816)
Without troponin and Barthel	0.809 (0.789-0.829)
Without NT-ProBNP, troponin and Barthel	0.784 (0.762-0.805)

**Table S4:** Comparison of key predictor variables between derivation and validation cohorts

Variable **Derivation cohort** Validation cohort Barthel index at admission, n (%) <25 404 (11.6%) 171 (8.8%) 25-49 614 (17.6%) 286 (14.7%) 50-74 912 (26.2%) 520 (26.7%) ≥75 971 (49.9%) 1556 (44.6%) Systolic BP (mm Hg), n (%) ≥155 1443 (30.3%) 873 (27.6%) 140-154 991 (20.8%) 747 (23.7%) 125-139 986 (20.7%) 681 (21.6%) 110-124 845 (17.7%) 570 (18.1%) 95-109 357 (7.5%) 210 (6.7%) <95 146 (3.1%) 77 (2.4%) Age (years), n (%) <75 1227 (25.3%) 783 (24.3%) 75-79 911 (18.8%) 580 (18.0%) 80-84 775 (24.0%) 1116 (23.0%) 85-89 657 (20.4%) 1054 (21.7%) >=90 546 (11.3%) 429 (13.3%) NT-proBNP (pg/mL), n (%) <8000 1412 (72.2%) 1060 (75.4%) 8000-15999 285 (14.6%) 195 (13.9%) 16000-23999 110 (5.6%) 61 (4.3%) >24000 148 (7.6%) 90 (6.4%) Potassium (mEq/L), n (%) <3.5 249 (5.4%) 150 (4.9%) 3.5-4.9 3536 (76.5%) 2397 (78.4%) 5-5.5 508 (11.0%) 311 (10.2%) >5.5 332 (7.2%) 200 (6.5%) Positive troponin level, n (%) 983 (53.5%) 1286 (45.1%) NYHA class IV at admission, n (%) 2148 (46.1%) 1329 (43.2%) Respiratory rate (bpm), n (%) <25 2305 (72.6%) 1575 (67.2%) 25-29 540 (11.6%) 252 (15.7%) >=30 585 (15.8%) 342 (17.1%) Low output symptoms, n (%) 792 (17.5%) 628 (19.5%) Oxygen saturation (%), n (%) 1292 (41.9%) 95-100 1830 (39.2%) 90-94 1098 (35.6%) 1675 (35.8%) 84-89 689 (14.7%) 398 (12.9%) <85% 479 (10.3%) 294 (9.5%) Episode associated with ACS, n (%) 134 (2.8%) 62 (2.0%) Hypertrophy at ECG, n (%) 290 (6.2%) 61 (2.0%) Creatinine (mg/dL), n (%) <1.5 3401 (71.1%) 2298 (72.3%) 1.5-2.4 1054 (22.1%) 676 (21.3%) >=2.5 326 (6.8%) 203 (6.4%)

12

ACS is acute coronary syndrome; ECG, electrocardiogram; NYHA, New York Heart Association; OR, odds ratio.

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## 15 Figure S1: Patient flow diagram







21 \*Each odds ratio is adjusted for all other variables in the model.





Receiver operating characteristic curve for risk 30-day mortality. Sensitivity and specificity of the risk threshold
for each category of the prediction model are plotted.





Of note, EHMRG score was conceived to predict 7-day and MEESSI predicts 30-day mortality. Between both validation and derivation cohorts, 2137 patients had available data to calculate the EHMRG score and therefore to perform the comparison between risk scores. The c-statistic for our model was 0.830 (95% CI: 0.804-0.857) and for EHMRG was 0.750 (95% CI: 0.719-0.783) (P-value for DeLong test P<0.001)

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