SUPPLEMENTAL FIGURES AND TABLES

The diagnostic accuracy of clinical examination for estimating cardiac index in critically ill patients: the Simple Intensive Care Studies-I

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Content

SUPPLEMENTAL FIGURES AND TABLES

Descriptives

e-Table 1. Description of collected variables and percentage of missingness

Variable	Method of measuring	Missing %
Age, years	Patient's electronic chart	0.0
Male gender	Patient's electronic chart	0.0
Mechanical ventilation		
PEEP, cmH$_2$O	mechanical ventilator	0.0
Set respiratory rate, per minute	mechanical ventilator	0.0
Vasoactive medication, µg·kg^{-1}·min^{-1}	Infusion pump inspection at bedside	0.0
Central circulation		
Respiratory rate, per minute	bedside (electrocardiographic) monitor	0.0
Heart rate, beats per minute	bedside (electrocardiographic) monitor	0.0
Heart rhythm	bedside (electrocardiographic) monitor	0.0
Systolic blood pressure, mmHg	arterial line and sphygmomanometer	0.2
Diastolic blood pressure, mmHg	arterial line and sphygmomanometer	0.2
Mean arterial pressure, mmHg	arterial line and sphygmomanometer	0.3
Central venous pressure, mmHg	central venous line in internal jugular, subclavian or femoral vein	76.5*
Cardiac murmurs	Auscultation at the 2nd intercostal space left and right, 4th or 5th intercostal space left and apex	9.6
Pulmonary crepitations or crackles	Auscultation of the chest at the superior, inferior and basal lung fields	1.3
Organ perfusion		
Mental state (alert/voice/pain/ unresponsive)	Observation	0.0
Sedative medication, µg·kg^{-1}·min^{-1}	Infusion pump inspection at bedside	4.9
Urine output, ml·kg^{-1}·h^{-1}	Patient's electronic chart	1.9
Central temperature, °C	Bladder thermistor catheter	1.5
Skin temperature dorsum foot, °C	skin temperature of dorsum foot using skin probe	15.3
Skin temperature big toe, °C	skin temperature of big toe using skin probe	9.9
Δ-Temperature or ΔTc-p	Bladder to dorsum foot or big toe difference	15.3
Cold extremities, cold or warm	Subjective assessment	0.6
Capillary refill time sternum, s	Palpation	13.7
Capillary refill time finger, s	Palpation	2.5
Capillary refill time knee, s	Palpation	9.9
Mottling severity, score from 0 to 5	Observation of mottling area on the legs, scoring system according to Ait-Oufella.	10.1
Critical care ultrasonography		
Cardiac output, L·min^{-1}	Critical care ultrasonography	22.8
Cardiac output adjusted for body surface area (cardiac index), L·min^{-1}·m^{-2}	Critical care ultrasonography	22.8

*Central venous pressure was missing in > 50% of the patients and was excluded from the multiple imputations and multivariable analyses.

Supplemental figures and tables

Primary analysis: univariable (unadjusted) analyses

e-Table 2. Univariable associations of clinical examination with cardiac index as a continuous variable

Variable	Coefficient	SE	98.5% CI	R^2	P-Value
Covariates					
Age, years	0.00	0.00	-0.01 to 0.00	0.002	0.24
Male gender	-0.32	0.07	-0.48 to -0.15	0.028	<0.001
Mechanical ventilation	-0.28	0.07	-0.44 to -0.12	0.023	<0.001
PEEP, cm H_2O	-0.03	0.01	-0.05 to -0.01	0.020	<0.001
Noradrenaline dose, $\mu g \cdot kg^{-1} \cdot min^{-1}$	0.31	0.19	-0.14 to 0.76	0.004	0.10
Central circulation					
Respiratory rate, per minute	0.01	0.01	0.00 to 0.02	0.004	0.08
Heart rate, beats per minute	0.02	0.00	0.01 to 0.02	0.142	<0.001
Atrial fibrillation	-0.18	0.13	-0.49 to 0.13	0.003	0.16
Systolic blood pressure, mmHg	0.01	0.00	0.00 to 0.01	0.020	<0.001
Diastolic blood pressure, mmHg	0.00	0.00	-0.01 to 0.00	0.003	0.14
Mean arterial pressure, mmHg	0.00	0.00	0.00 to 0.01	0.003	0.14
Central venous pressure, mmHg	-0.01	0.01	-0.04 to 0.02	0.007	0.30
Cardiac murmurs	0.32	0.11	0.04 to 0.59	0.013	0.005
Crepitations	0.12	0.09	-0.11 to 0.35	0.003	0.21
Organ perfusion					
Consciousness, n (%)					
alert		Reference		0.028	
reacting to voice	0.28	0.09	0.05 to 0.50		0.003
reacting to pain	0.00	0.17	-0.40 to 0.40		0.99
unresponsive	0.06	0.14	-0.28 to 0.40		0.65
Urine output last hour, $ml \cdot kg^{-1} \cdot h^{-1}$	0.06	0.03	-0.02 to 0.14	0.004	0.08
Urine output in 6 hours, $ml \cdot kg^{-1} \cdot h^{-1}$	0.09	0.04	-0.01 to 0.20	0.007	0.032
Central temperature, °C	0.19	0.04	0.11 to 0.28	0.038	<0.001
ΔTc-p, central to dorsum foot, °C	-0.06	0.01	-0.09 to -0.04	0.048	<0.001
ΔTc-p, central to big toe, °C	-0.05	0.01	-0.07 to -0.03	0.044	<0.001
Cold extremities, subjective	0.34	0.07	0.18 to 0.51	0.032	<0.001
Capillary refill time sternum, s	-0.13	0.03	-0.20 to -0.06	0.028	<0.001
Capillary refill time finger, s	-0.06	0.01	-0.09 to -0.02	0.019	<0.001
Capillary refill time knee, s	-0.06	0.01	-0.09 to -0.02	0.024	<0.001
Skin mottling severity, n (%)					
Mild (0-1)		Reference		0.004	
Moderate (2-3)	-0.11	0.08	-0.30 to 0.08		0.17
Severe (4-5)	-0.13	0.20	-0.60 to 0.35		0.53

Abbreviations: SE, standard error; PEEP, positive end expiratory pressure; ΔTc-p, central-to-peripheral temperature difference.

Supplemental figures and tables

Primary analysis: internal validation and diagnostics of the multivariable linear regression

e-Table 3. Multivariable linear regression, predictors for cardiac index as a continuous variable

Variable	B	SE	98.5% CI	P value	β	Significant # out of 100
Covariates						
Male gender	-0.24	0.06	-0.38 to -0.10	<0.001	-0.12	97
Mechanical ventilation	-0.14	0.06	-0.29 to 0.01	0.021	-0.08	91
Noradrenaline per $\mu g \cdot kg^{-1} \cdot min^{-1}$ increase	0.17	0.17	-0.26 to 0.59	0.339	0.03	53
Clinical signs reflecting the central circulation						
Respiratory rate per minute increase	-0.02	0.01	-0.03 to 0.00	0.003	-0.10	85
Heart rate in beats per minute	0.02	0.00	0.02 to 0.02	<0.001	0.47	100
Atrial fibrillation	-0.37	0.11	-0.64 to -0.10	0.001	-0.10	91
Systolic blood pressure per mmHg increase	0.01	0.00	0.01 to 0.01	<0.001	0.27	100
Diastolic blood pressure per mmHg increase	-0.02	0.00	-0.02 to -0.01	<0.001	-0.20	100
Cardiac murmurs	0.22	0.09	-0.01 to 0.45	0.018	0.07	72
Clinical signs reflecting organ perfusion						
CRT on the sternum per sec increase	-0.08	0.03	-0.15 to -0.01	0.005	-0.10	91
ΔTc-p, central to big toe per °C increase	-0.04	0.01	-0.06 to -0.02	<0.001	-0.16	100
R²	*0.32*		*0.28 to 0.37*			
Adjusted R²	*0.31*		*0.27 to 0.35*			

Abbreviations: R², R squared; B, coefficient in the linear regression model; SE, standard error; CI, confidence interval; ß, standardized ß-coefficient in the linear regression model; CRT, capillary refill time; ΔTc-p, central-to-peripheral temperature difference.

Supplemental figures and tables

e-Figure 1. Linear relationship between cardiac output and heart rate
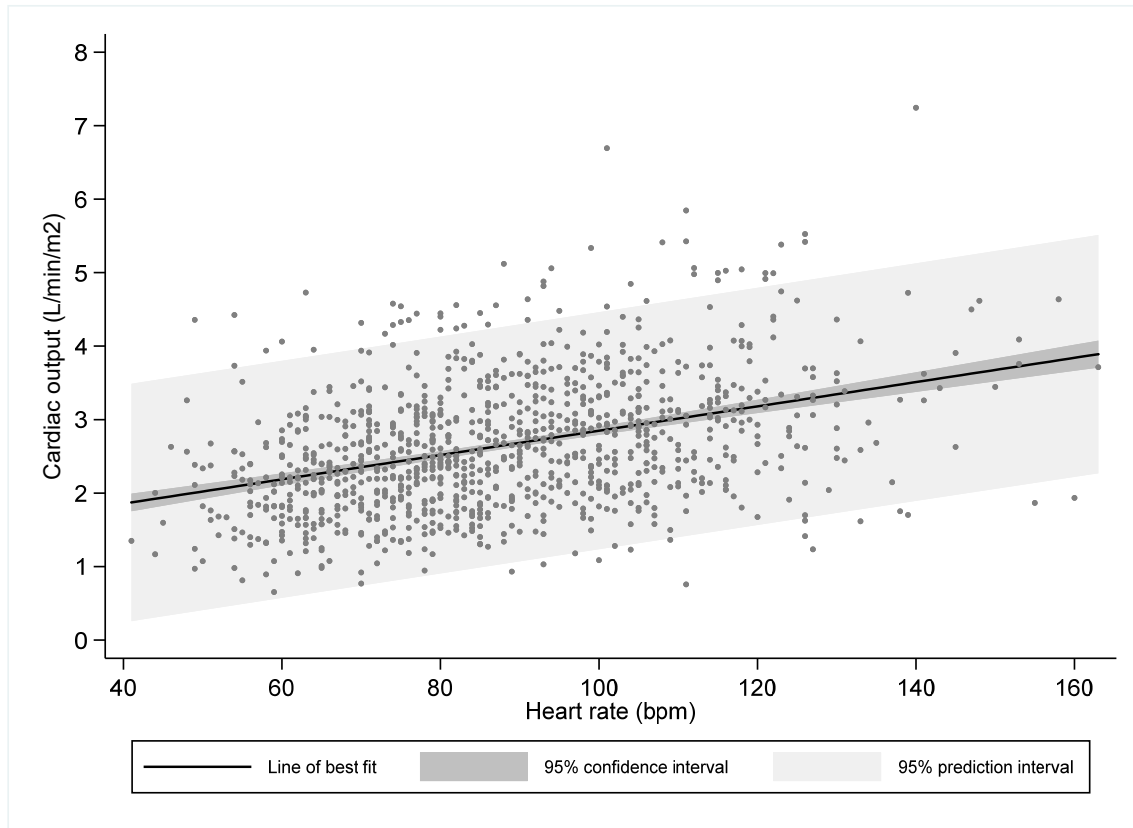
e-Figure 2. Kernel plot of standardized residuals

kernel = epanechnikov, bandwidth = 0.1518
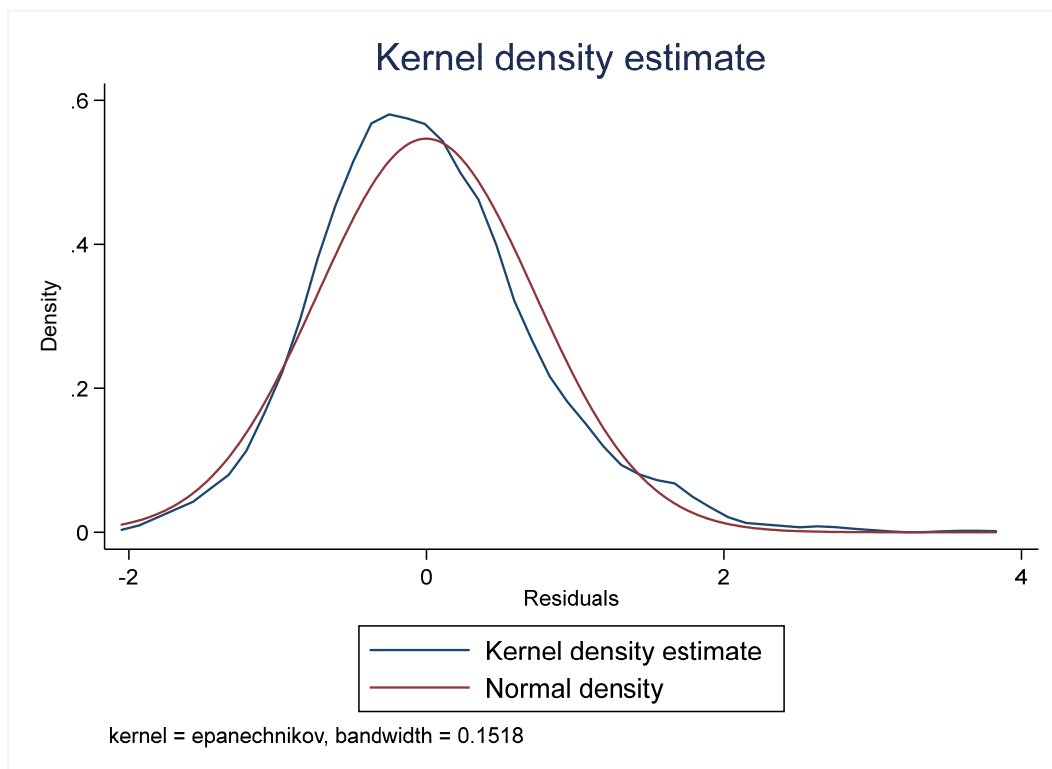
Comment: the Kernel density estimate of the multivariable regression model closely follows the distribution of a normal density plot

Supplemental figures and tables

e-Figure 3. Probability P-P Plot of the residuals
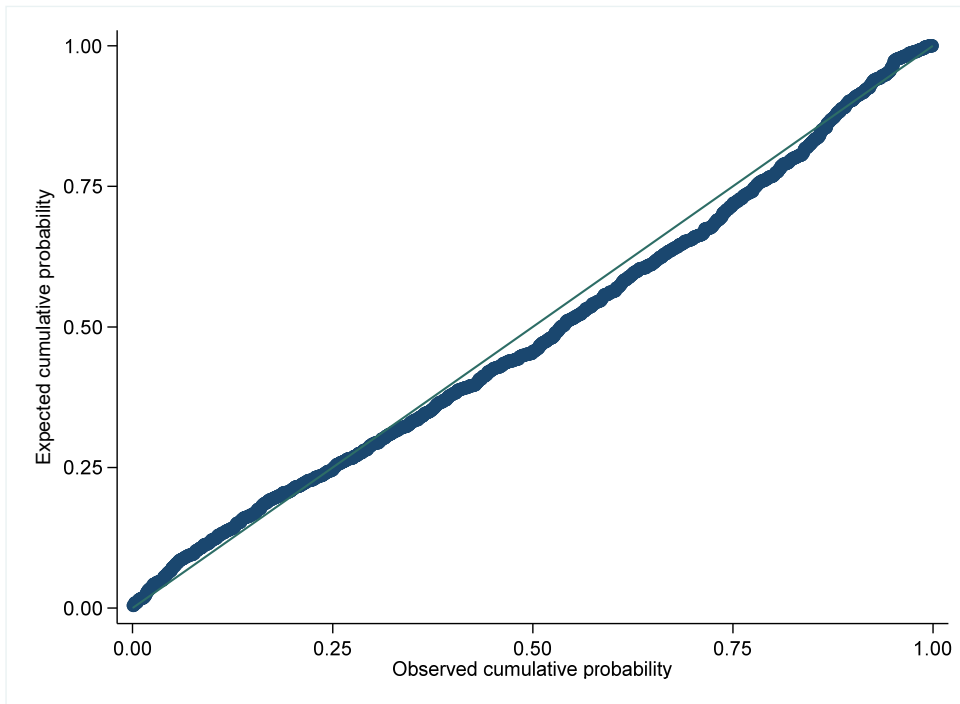
Comment: there is some deviation in the center of the plot, but we still assume normality as there are no drastic deviations from the diagonal (normality) line.

e-Figure 4. Scatterplot of the residuals
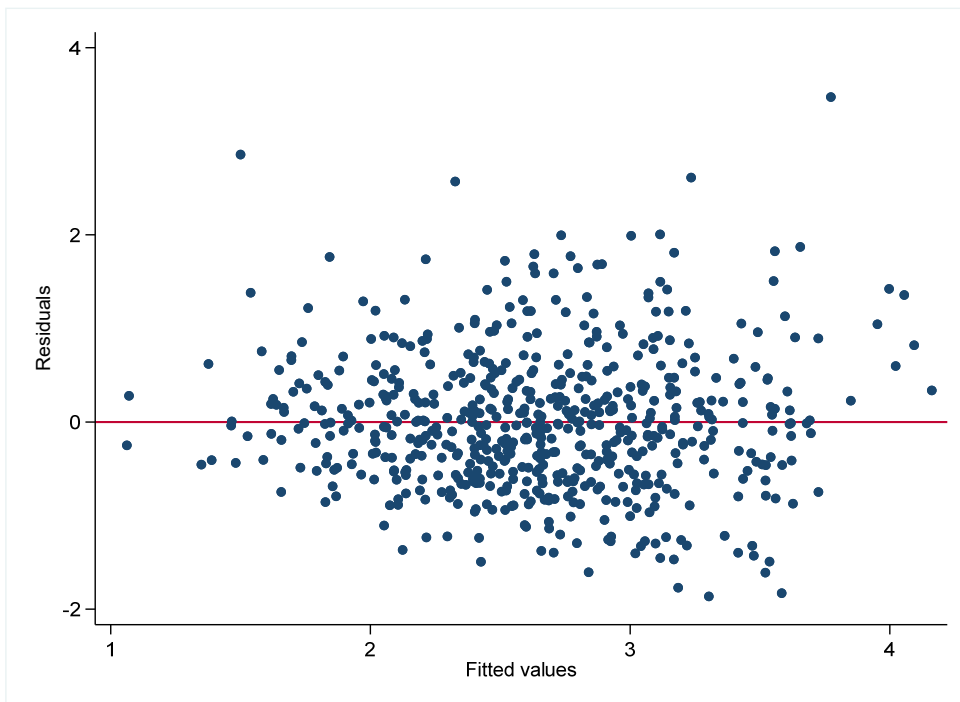
Comment: the scatterplot of the residuals shows no clear pattern to the residuals plotted against the fitted values. Therefore, we assume homoscedasticity of the residuals.

Supplemental figures and tables

e-Table 4. Variance inflation factors and tolerance

Variable	Variance inflation factor	Tolerance
Covariates		
Male gender	1.01	0.99
Mechanical ventilation	1.21	0.83
Norepinephrine dose per µg·kg^{-1}·min^{-1} increase	1.29	0.78
Clinical signs reflecting the central circulation		
Respiratory rate per minute increase	1.18	0.85
Heart rate in beats per minute	1.27	0.78
Atrial fibrillation	1.05	0.96
Systolic blood pressure per mmHg increase	1.61	0.62
Diastolic blood pressure per mmHg increase	1.49	0.67
Cardiac murmurs	1.02	0.98
Clinical signs reflecting organ perfusion		
CRT on the sternum per sec increase	1.14	0.88
ΔTc-p, central to big toe per °C increase	1.13	0.89

Comment: there are no signs for multicollinearity, as none of the variables has a variance inflation factor that exceeds 10 or a tolerance below 0.1.

e-Table 5. Independent predictors of cardiac output on complete cases (non-imputed data)

Variable	B	SE	95% CI	P value	β
Covariates					
Male gender	-0.24	0.06	-0.36 to -0.11	<0.001	-0.13
Mechanical ventilation	-0.17	0.07	-0.30 to -0.04	0.012	-0.09
Norepinephrine dose per µg·kg^{-1}·min^{-1} increase	0.16	0.20	-0.22 to 0.55	0.407	0.03
Clinical signs reflecting the central circulation					
Respiratory rate per minute increase	-0.02	0.01	-0.03 to -0.01	0.001	-0.12
Heart rate in beats per minute	0.02	0.00	0.02 to 0.02	<0.001	0.46
Atrial fibrillation	-0.52	0.14	-0.79 to -0.25	<0.001	-0.13
Systolic blood pressure per mmHg increase	0.01	0.00	0.01 to 0.01	<0.001	0.28
Diastolic blood pressure per mmHg increase	-0.02	0.00	-0.02 to -0.01	<0.001	-0.21
Cardiac murmurs	0.24	0.10	0.04 to 0.45	0.020	0.08
Clinical signs reflecting organ perfusion					
CRT on the sternum per sec increase	-0.09	0.03	-0.15 to -0.03	0.003	-0.11
ΔTc-p, central to big toe per °C increase	-0.04	0.01	-0.06 to -0.02	<0.001	-0.16
R^2	*0.34*				
Adjusted R^2	*0.32*				

All patients with complete data were included. The model included 595 patients. Abbreviations: R^2, R squared; CI, confidence interval; ß, standardised ß-coefficient in the linear regression model; CRT, capillary refill time.
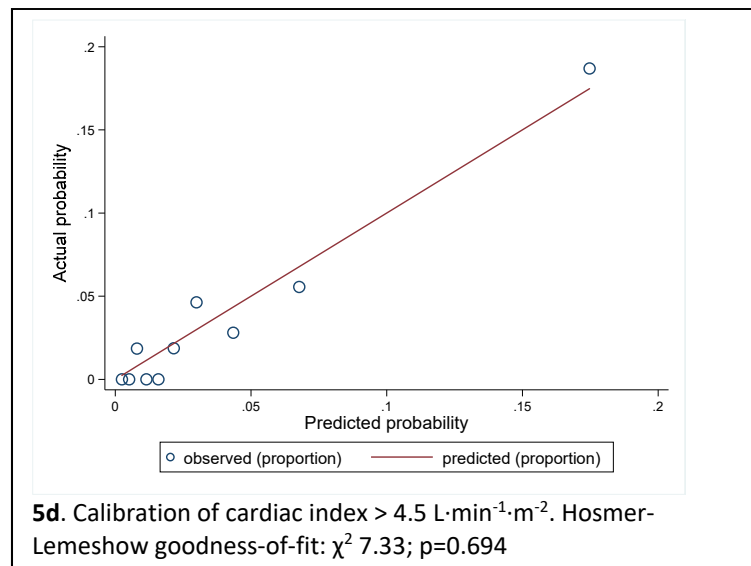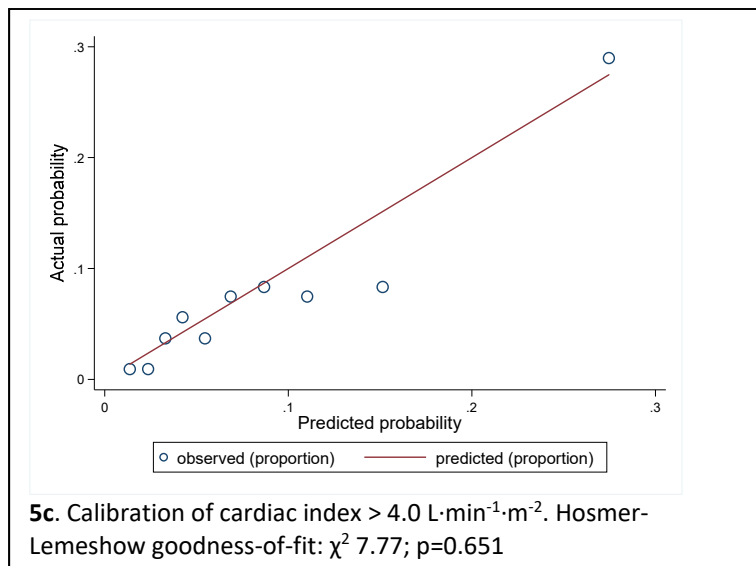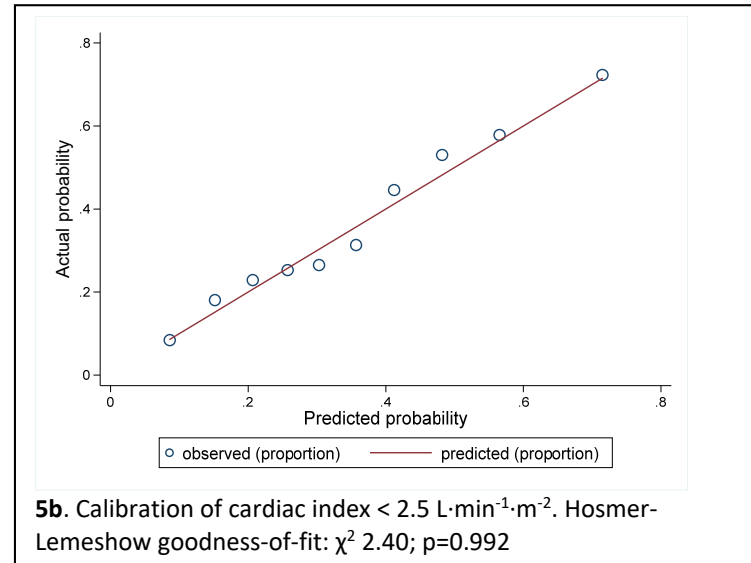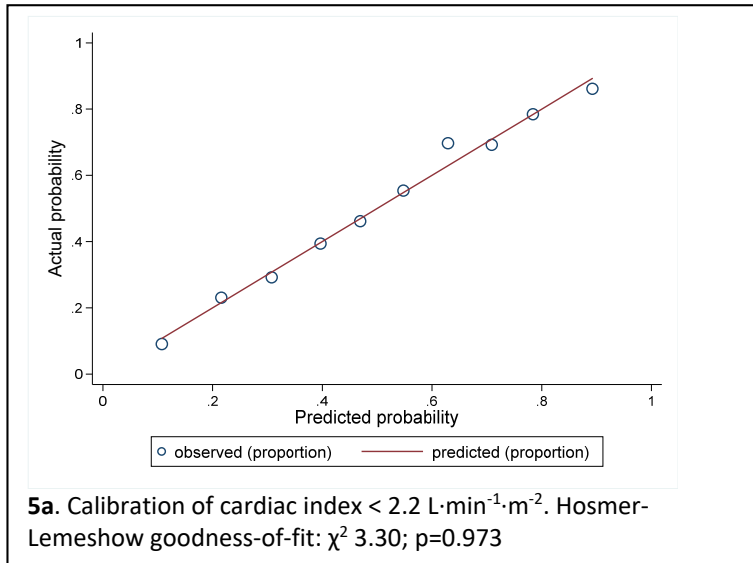
Secondary analysis: diagnostic performance

e-Table 6. Significant associations for different cardiac index cut-off values using multivariable logistic regression

Variable	Odds ratio	95% CI	P-value	Independent contribution %
Cardiac index < 2.2 L·min^{-1}·m^{-2}				AUC 0.74 (0.70 - 0.78)
Gender	1.62	1.16 - 2.27	0.005	4
Noradrenaline dose per μg·kg^{-1}·min^{-1}	1.69	0.63 - 4.53	0.296	1
Central circulation				
Respiratory rate per minute	1.04	1.01 - 1.07	0.021	2
Heart rate in beats per minute	0.96	0.95 - 0.97	<0.001	46
Atrial fibrillation	2.42	1.31 - 4.46	0.005	3
Systolic blood pressure per mmHg	0.98	0.97 - 0.99	<0.001	14
Diastolic blood pressure per mmHg	1.04	1.02 - 1.06	<0.001	8
Organ perfusion				
CRT on the sternum per sec	1.17	1.00 - 1.37	0.046	8
ΔTc-p, central to big toe per °C	1.10	1.05 - 1.15	<0.001	15
Cardiac index < 2.5 L·min^{-1}·m^{-2}				AUC 0.76 (0.72 - 0.79)
Gender	1.53	1.10 - 2.11	0.011	3
Noradrenaline dose per μg·kg^{-1}·min^{-1}	1.01	0.38 - 2.66	0.989	1
Central circulation				
Respiratory rate per minute	1.04	1.00 - 1.07	0.024	2
Heart rate in beats per minute	0.96	0.95 - 0.97	<0.001	50
Atrial fibrillation	2.34	1.25 - 4.36	0.008	2
Systolic blood pressure per mmHg	0.97	0.97 - 0.98	<0.001	15
Diastolic blood pressure per mmHg	1.04	1.02 - 1.06	<0.001	5
Organ perfusion				
CRT on the sternum per sec	1.23	1.05 - 1.46	0.012	8
ΔTc-p, central to big toe per °C	1.11	1.06 - 1.16	<0.001	14
Cardiac index > 4.0 L·min^{-1}·m^{-2}				AUC 0.75 (0.69 - 0.81)
Noradrenaline dose per μg·kg^{-1}·min^{-1}	2.89	0.88 - 9.44	0.080	5
Heart rate in beats per minute	1.04	1.03 - 1.05	<0.001	66
Systolic blood pressure per mmHg	1.01	1.00 - 1.02	0.044	9
ΔTc-p, central to foot per °C	0.86	0.78 - 0.94	0.001	20
Cardiac index > 4.5 L·min^{-1}·m^{-2}				AUC 0.86 (0.79 - 0.93)
Noradrenaline dose per μg·kg^{-1}·min^{-1}	2.47	0.49 - 12.4	0.272	4
Heart rate in beats per minute	1.06	1.04 - 1.09	<0.001	70
Systolic blood pressure per mmHg	1.02	1.00 - 1.03	0.026	6
ΔTc-p, central to foot per °C	0.83	0.72 - 0.96	0.011	21

The models included all 783 patients with validated cardiac index measurements. Abbreviations: CRT, capillary refill time; ΔTc-p, central-to-peripheral temperature difference; AUC, area under the receiver-operating-curve.

Supplemental figures and tables

5a. Calibration of cardiac index < 2.2 L·min^{-1}·m^{-2}. Hosmer-Lemeshow goodness-of-fit: χ^2 3.30; p=0.973

5b. Calibration of cardiac index < 2.5 L·min^{-1}·m^{-2}. Hosmer-Lemeshow goodness-of-fit: χ^2 2.40; p=0.992

5c. Calibration of cardiac index > 4.0 L·min^{-1}·m^{-2}. Hosmer-Lemeshow goodness-of-fit: χ^2 7.77; p=0.651

5d. Calibration of cardiac index > 4.5 L·min^{-1}·m^{-2}. Hosmer-Lemeshow goodness-of-fit: χ^2 7.33; p=0.694

e-Table 7a. Diagnosing a low cardiac index: tabular display derived from the 2x2 matrix for each clinical sign

Results for each clinical sign	N	Cardiac index < 2.2 L·min^{-1}·m^{-2}				Cardiac index < 2.5 L·min^{-1}·m^{-2}			
		A = True positive	B = False positive	C = False negative	D = True negative	A = True positive	B = False positive	C = False negative	D = True negative
Central circulation									
Respiratory rate > 22 pm	783	216	334	64	169	286	264	99	134
Heart rate < 100 bpm	783	229	342	51	161	314	257	71	141
Atrial fibrillation	783	26	30	254	473	33	23	352	375
SBP < 90 mmHg	783	18	38	262	465	28	28	357	370
DBP < 45 mmHg	783	13	27	267	476	21	19	364	379
MAP < 65 mmHg	783	32	65	248	438	49	48	336	350
Cardiac murmurs	783	18	57	262	446	30	45	355	353
Crepitations	783	36	79	244	424	49	66	336	332
Organ perfusion									
Consciousness									
reacting to voice	783	31	90	249	413	47	74	338	324
reacting to pain	783	14	19	266	484	18	15	367	383
unresponsive	783	19	31	261	472	26	24	359	374
Urine output <0.5 ml·kg^{-1}·h^{-1}									
Over 1 hour	783	132	213	148	290	183	162	202	236
Over 6 hours	783	111	177	169	326	153	135	232	263
Skin temperature cold*									
ΔTc-p, dorsum foot	783	182	220	98	283	237	165	148	233
ΔTc-p, big toe	783	217	304	63	199	290	231	95	167
Cold subjective	785	132	153	148	352	175	110	210	288
CRT prolonged**									
Sternum	783	29	33	251	470	39	23	346	375
Finger	783	71	76	209	427	88	59	297	339
Knee	783	92	107	188	396	118	81	267	317
Skin mottling severity***									
Over the knee (≥3)	783	45	47	235	456	53	39	332	359
Severe (≥4)	783	9	14	271	489	12	11	373	387

*ΔTc-p was considered cold if >7 °C. **CRT was considered prolonged if >4.5 seconds. ***Mottling was scored according to Ait-Oufella et al. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; ΔTc-p, central-to-peripheral temperature difference; CRT, capillary refill time.

Supplemental figures and tables

e-Table 7b. Diagnosing a low cardiac index: Outcome measures for each clinical sign

Performance of each clinical sign	Cardiac index < 2.2 L·min⁻¹·m⁻²							Cardiac index < 2.5 L·min⁻¹·m⁻²						
	Sens.	Spec.	PPV	NPV	Accuracy	LR +	LR -	Sens.	Spec.	PPV	NPV	Accuracy	LR +	LR -
Central circulation														
Respiratory rate > 22 pm	0.77	0.34	0.39	0.73	0.49	1.16	0.68	0.74	0.34	0.52	0.58	0.54	1.12	0.76
Heart rate < 100 bpm	0.82	0.32	0.40	0.76	0.50	1.20	0.57	0.82	0.35	0.55	0.67	0.58	1.26	0.52
Atrial fibrillation	0.09	0.94	0.46	0.65	0.64	1.56	0.96	0.09	0.94	0.59	0.53	0.52	1.48	0.97
SBP < 90 mmHg	0.06	0.92	0.32	0.64	0.62	0.85	1.01	0.07	0.93	0.50	0.49	0.51	1.03	1.00
DBP < 45 mmHg	0.05	0.95	0.33	0.64	0.62	0.86	1.01	0.05	0.95	0.53	0.52	0.51	1.14	0.99
MAP < 65 mmHg	0.11	0.87	0.33	0.64	0.60	0.88	1.02	0.13	0.88	0.51	0.49	0.51	1.06	0.99
Cardiac murmurs	0.06	0.89	0.24	0.63	0.59	0.57	1.06	0.08	0.89	0.40	0.50	0.49	0.69	1.04
Crepitations	0.13	0.84	0.31	0.63	0.59	0.82	1.03	0.13	0.83	0.43	0.00	0.49	0.77	1.05
Organ perfusion														
Consciousness														
reacting to voice	0.11	0.82	0.26	0.62	0.57	0.62	1.08	0.12	0.81	0.39	0.51	0.47	0.66	1.08
reacting to pain	0.05	0.96	0.42	0.65	0.64	1.32	0.99	0.05	0.96	0.55	0.51	0.51	1.24	0.99
unresponsive	0.07	0.94	0.38	0.64	0.63	1.10	0.99	0.07	0.94	0.52	0.54	0.51	1.12	0.99
Urine output <0.5 ml·kg⁻¹·h⁻¹														
Over 1 hour	0.47	0.58	0.38	0.66	0.54	1.11	0.92	0.48	0.59	0.53	0.53	0.54	1.17	0.88
Over 6 hours	0.40	0.65	0.39	0.66	0.56	1.13	0.93	0.40	0.66	0.53	0.61	0.53	1.17	0.91
Skin temperature cold*														
Δ-T, dorsum foot	0.78	0.40	0.42	0.76	0.53	1.28	0.57	0.62	0.59	0.59	0.64	0.60	1.48	0.66
Δ-T, big toe	0.65	0.56	0.45	0.74	0.59	1.49	0.62	0.75	0.42	0.56	0.58	0.58	1.30	0.59
Cold subjective	0.47	0.70	0.46	0.70	0.62	1.56	0.76	0.45	0.72	0.61	0.52	0.59	1.64	0.75
CRT prolonged**														
Sternum	0.10	0.93	0.47	0.65	0.64	1.58	0.96	0.10	0.94	0.63	0.53	0.53	1.75	0.95
Finger	0.25	0.85	0.48	0.67	0.64	1.68	0.88	0.23	0.85	0.60	0.54	0.55	1.54	0.91
Knee	0.33	0.79	0.46	0.68	0.62	1.54	0.85	0.31	0.80	0.59	0.52	0.56	1.51	0.87
Skin mottling severity***														
Over the knee (≥3)	0.16	0.91	0.49	0.66	0.64	1.72	0.93	0.14	0.90	0.58	0.51	0.53	1.40	0.96
Severe (≥4)	0.03	0.97	0.39	0.64	0.64	1.15	1.00	0.03	0.97	0.52	0.50	0.51	1.13	1.00

*ΔTc-p was considered cold if >7 °C. **CRT was considered prolonged if >4.5 seconds. ***Mottling was scored according to Ait-Oufella et al. Abbreviations: Sens, sensitivity; Spec, specificity PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; ΔTc-p, central-to-peripheral temperature difference; CRT, capillary refill time.

Supplemental figures and tables

e-Table 8a. Diagnosing a high cardiac index: tabular display derived from the 2x2 matrix for each clinical sign

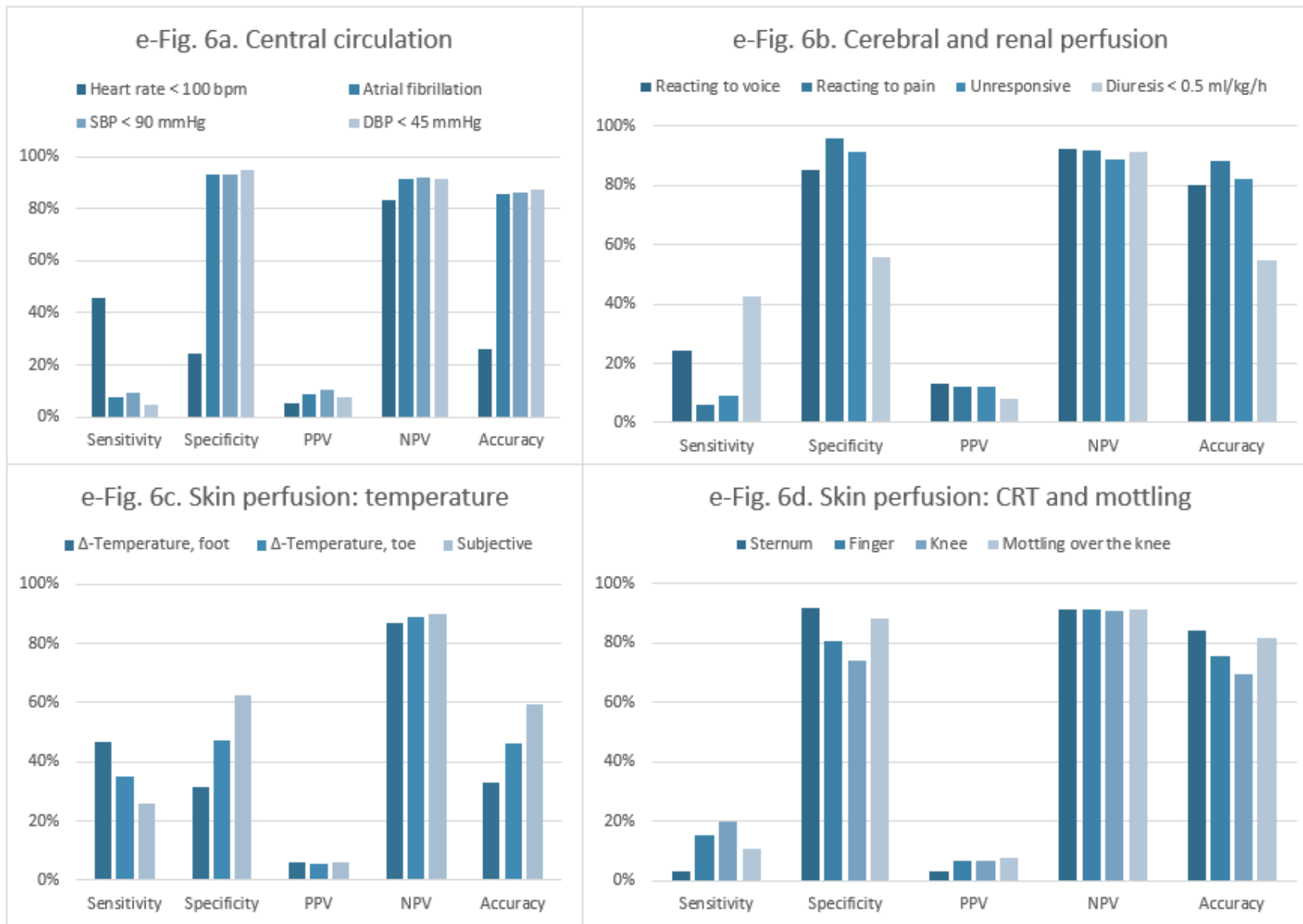| Results for each clinical sign		Cardiac index > 4.0 L·min^{-1}·m^{-2}				Cardiac index > 4.5 L·min^{-1}·m^{-2}			
	N	A = True positive	B = False positive	C = False negative	D = True negative	A = True positive	B = False positive	C = False negative	D = True negative
Central circulation									
Respiratory rate > 22 pm	783	43	507	23	210	20	530	10	223
Heart rate < 100 bpm	783	30	541	36	176	8	563	22	190
Atrial fibrillation	783	5	51	61	666	0	56	30	697
SBP < 90 mmHg	783	6	50	60	667	3	53	27	700
DBP < 45 mmHg	783	3	37	63	680	2	38	28	715
MAP < 65 mmHg	783	9	88	57	629	5	92	25	661
Cardiac murmurs	783	11	64	55	653	5	70	25	683
Crepitations	783	14	101	52	616	5	110	25	643
Organ perfusion									
Consciousness									
reacting to voice	783	16	105	50	612	7	114	23	639
reacting to pain	783	4	29	62	688	2	31	28	722
unresponsive	583	6	44	60	473	3	47	27	706
Urine output <0.5 ml·kg^{-1}·h^{-1}									
Over 1 hour	783	28	317	38	400	11	334	19	419
Over 6 hours	783	23	265	43	452	11	277	19	476
Skin temperature cold*									
ΔTc-p, dorsum foot	783	23	379	43	338	10	392	20	361
ΔTc-p, big toe	783	31	490	35	227	15	506	15	247
Cold subjective	783	17	268	49	449	7	278	23	475
CRT prolonged***									
Sternum	783	2	60	64	657	1	61	29	692
Finger	783	10	137	56	580	6	141	24	612
Knee	783	13	186	53	531	7	192	23	561
Skin mottling severity***									
Over the knee (≥3)	783	7	85	59	632	3	89	27	664
Severe (≥4)	783	1	22	65	695	0	23	30	730

*ΔTc-p was considered cold if >7 °C. **CRT was considered prolonged if >4.5 seconds. ***Mottling was scored according to Ait-Oufella et al. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; ΔTc-p, central-to-peripheral temperature difference; CRT, capillary refill time.

Supplemental figures and tables

e-Table 8b. Diagnosing a high cardiac index: Outcome measures for each clinical sign

Performance of each clinical sign	Cardiac index > 4.0 L·min⁻¹·m⁻²							Cardiac index > 4.5 L·min⁻¹·m⁻²						
	Sens.	Spec.	PPV	NPV	Accuracy	LR +	LR -	Sens.	Spec.	PPV	NPV	Accuracy	LR +	LR -
Central circulation														
Respiratory rate > 22 pm	0.65	0.29	0.08	0.90	0.32	0.92	1.19	0.67	0.30	0.04	0.96	0.31	0.95	1.13
Heart rate < 100 bpm	0.45	0.25	0.05	0.83	0.26	0.60	2.22	0.27	0.25	0.01	0.90	0.25	0.36	2.91
Atrial fibrillation	0.08	0.93	0.09	0.92	0.86	1.07	1.00	0.00	0.93	0.00	0.96	0.89	0.00	1.08
SBP < 90 mmHg	0.09	0.93	0.11	0.92	0.86	1.30	0.98	0.10	0.93	0.05	0.96	0.90	1.42	0.97
DBP < 45 mmHg	0.05	0.95	0.08	0.92	0.87	0.88	1.01	0.07	0.95	0.05	0.96	0.92	1.32	0.98
MAP < 65 mmHg	0.14	0.88	0.09	0.92	0.81	1.11	0.98	0.17	0.88	0.05	0.96	0.85	1.36	0.95
Cardiac murmurs	0.17	0.91	0.15	0.92	0.85	1.87	0.92	0.17	0.91	0.07	0.96	0.88	1.79	0.92
Crepitations	0.21	0.86	0.12	0.92	0.80	1.51	0.92	0.17	0.85	0.04	0.00	0.83	1.14	0.98
Organ perfusion														
Consciousness														
reacting to voice	0.24	0.85	0.13	0.92	0.80	1.66	0.89	0.23	0.85	0.06	0.96	0.83	1.54	0.90
reacting to pain	0.06	0.96	0.12	0.92	0.88	1.50	0.98	0.07	0.96	0.06	0.97	0.92	1.62	0.97
unresponsive	0.09	0.91	0.12	0.89	0.82	1.07	0.99	0.10	0.94	0.06	0.96	0.91	1.60	0.96
Urine output <0.5 ml·kg⁻¹·h⁻¹														
Over 1 hour	0.42	0.56	0.08	0.91	0.55	0.96	1.03	0.37	0.56	0.03	0.96	0.55	0.83	1.14
Over 6 hours	0.35	0.63	0.08	0.91	0.61	0.94	1.03	0.37	0.63	0.04	0.96	0.62	1.00	1.00
Skin temperature cold*														
Δ-T, dorsum foot	0.47	0.32	0.06	0.87	0.33	0.69	1.68	0.33	0.48	0.02	0.96	0.47	0.64	1.39
Δ-T, big toe	0.35	0.47	0.06	0.89	0.46	0.66	1.38	0.50	0.33	0.03	0.95	0.33	0.74	1.52
Cold subjective	0.26	0.63	0.06	0.90	0.60	0.69	1.19	0.23	0.63	0.02	0.94	0.62	0.63	1.22
CRT prolonged**														
Sternum	0.03	0.92	0.03	0.91	0.84	0.36	1.06	0.03	0.92	0.02	0.95	0.89	0.41	1.05
Finger	0.15	0.81	0.07	0.91	0.75	0.79	1.05	0.20	0.81	0.04	0.96	0.79	1.07	0.98
Knee	0.20	0.74	0.07	0.91	0.69	0.76	1.08	0.23	0.75	0.04	0.96	0.73	0.92	1.03
Skin mottling severity***														
Over the knee (≥3)	0.11	0.88	0.08	0.91	0.82	0.89	1.01	0.10	0.88	0.03	0.96	0.85	0.85	1.02
Severe (≥4)	0.02	0.97	0.04	0.91	0.89	0.49	1.02	0.00	0.97	0.00	0.96	0.93	0.00	1.03

*ΔTc-p was considered cold if >7 °C. **CRT was considered prolonged if >4.5 seconds. ***Mottling was scored according to Ait-Oufella et al. Abbreviations: Sens, sensitivity; Spec, specificity PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; ΔTc-p, central-to-peripheral temperature difference.

Supplemental figures and tables

e-Fig. 6: Diagnostic performance for clinical signs to diagnose a cardiac index above 4.0 L·min^{-1}·m^{-2}

Supplemental figures and tables

e-Fig. 7: Results for each clinical sign in subgroup analyses

| | Subgroup 1: split by norepinephrine | | | | | | | | | | Subgroup 2: clinically different groups | | | | | | | | | | | | | | | | | | | | | | | | |
	No norepinephrine *Prevalence 30%; n = 547*					Norepinephrine *Prevalence 39%; n = 528*					Heart failure *Prevalence 57%; n = 63*					Cardiac arrest *Prevalence 66%; n = 125*					Liver failure *Prevalence 15%; n = 54*					Septic shock *Prevalence 33%; n = 156*					CNS pathologies *Prevalence 33%; n = 144*				
	Sens.	Spec.	PPV	NPV	Acc.	Sens.	Spec.	PPV	NPV	Acc.	Sens.	Spec.	PPV	NPV	Acc.	Sens.	Spec.	PPV	NPV	Acc.	Sens.	Spec.	PPV	NPV	Acc.	Sens.	Spec.	PPV	NPV	Acc.	Sens.	Spec.	PPV	NPV	Acc.
Central circulation																																			
Respiratory rate > 22	68%	42%	33%	76%	50%	88%	20%	41%	73%	46%	81%	30%	60%	53%	59%	96%	2%	65%	25%	64%	75%	46%	19%	91%	50%	98%	3%	33%	75%	34%	74%	32%	35%	72%	46%
Heart rate																																			
< 100 bpm	83%	28%	33%	80%	45%	82%	42%	47%	79%	58%	64%	44%	61%	48%	56%	95%	12%	67%	56%	66%	88%	30%	18%	93%	39%	63%	60%	43%	77%	61%	96%	10%	34%	83%	38%
< 90 bpm	74%	42%	35%	79%	51%	73%	63%	56%	79%	67%	56%	56%	63%	48%	56%	89%	23%	69%	53%	66%	75%	54%	22%	93%	57%	57%	82%	60%	80%	74%	89%	19%	35%	78%	42%
< 80 bpm	55%	62%	38%	76%	60%	55%	76%	60%	73%	68%	36%	89%	81%	51%	59%	70%	44%	70%	43%	61%	50%	65%	20%	88%	63%	39%	90%	65%	75%	73%	74%	31%	34%	71%	45%
< 70 bpm	34%	83%	46%	75%	68%	32%	91%	69%	68%	68%	14%	100%	100%	47%	51%	59%	70%	79%	47%	62%	13%	87%	14%	85%	76%	25%	99%	93%	73%	75%	47%	60%	36%	70%	56%
Atrial fibrillation	8%	94%	37%	71%	69%	9%	92%	42%	61%	60%	17%	89%	67%	44%	48%	4%	95%	60%	34%	35%	0%	96%	0%	85%	81%	16%	92%	50%	69%	67%	4%	93%	22%	67%	64%
Systolic blood pressure																																			
< 100 mmHg	17%	90%	42%	72%	68%	42%	66%	44%	64%	56%	42%	63%	60%	45%	51%	32%	79%	74%	38%	48%	25%	76%	15%	85%	69%	45%	66%	39%	71%	59%	13%	97%	67%	70%	69%
< 90 mmHg	2%	97%	24%	70%	69%	15%	84%	37%	61%	57%	19%	93%	78%	46%	51%	9%	95%	78%	35%	38%	0%	87%	0%	83%	74%	12%	85%	27%	66%	64%	4%	100%	100%	68%	69%
Diastolic blood pressure																																			
< 50 mmHg	13%	86%	30%	71%	65%	17%	76%	30%	59%	53%	8%	70%	27%	37%	35%	13%	91%	73%	35%	40%	13%	76%	8%	83%	67%	12%	85%	27%	66%	61%	9%	94%	40%	68%	66%
< 45 mmHg	2%	96%	20%	70%	68%	6%	90%	28%	60%	58%	3%	85%	20%	40%	38%	6%	95%	71%	35%	37%	6%	89%	0%	84%	76%	6%	90%	23%	66%	63%	2%	99%	50%	68%	67%
Mean arterial pressure																																			
< 70 mmHg	20%	84%	35%	71%	65%	43%	55%	38%	60%	50%	44%	59%	59%	44%	51%	30%	67%	64%	34%	43%	38%	39%	10%	78%	39%	49%	56%	35%	69%	54%	9%	93%	36%	68%	65%
< 65 mmHg	8%	93%	33%	70%	68%	19%	78%	35%	60%	55%	14%	78%	45%	40%	41%	10%	86%	57%	33%	36%	38%	85%	30%	89%	78%	22%	81%	35%	68%	62%	6%	99%	75%	69%	69%
Cardiac murmurs	7%	88%	21%	69%	64%	5%	91%	27%	60%	58%	3%	85%	20%	40%	38%	4%	98%	75%	35%	36%	13%	80%	10%	84%	70%	4%	93%	22%	67%	64%	9%	92%	33%	67%	65%
Crepitations	17%	86%	33%	71%	65%	10%	85%	30%	60%	56%	31%	63%	52%	40%	44%	10%	91%	67%	35%	38%	0%	89%	0%	84%	76%	12%	78%	21%	65%	56%	4%	96%	33%	67%	66%
Organ perfusion																																			
Consciousness																																			
Voice	28%	66%	26%	68%	55%	22%	77%	38%	61%	56%	19%	89%	70%	45%	49%	13%	74%	50%	31%	34%	13%	67%	6%	82%	59%	25%	75%	33%	68%	59%	60%	41%	33%	68%	47%
Pain	6%	95%	34%	70%	69%	3%	98%	50%	61%	61%	3%	100%	100%	44%	44%	2%	98%	67%	34%	35%	0%	98%	0%	85%	83%	6%	97%	50%	68%	67%	13%	84%	27%	66%	60%
Unresponsive	7%	93%	30%	70%	67%	7%	92%	38%	61%	59%	11%	100%	100%	46%	49%	4%	84%	30%	31%	31%	0%	93%	0%	84%	80%	6%	93%	30%	67%	65%	15%	84%	30%	67%	61%
Diuresis < 0.5 ml·kg⁻¹·h⁻¹																																			
Over 1 hour	31%	71%	32%	71%	59%	49%	53%	40%	62%	51%	39%	63%	58%	44%	49%	40%	58%	65%	34%	46%	75%	43%	19%	91%	48%	59%	50%	36%	71%	53%	32%	81%	45%	71%	65%
Over 6 hours	39%	64%	31%	71%	56%	58%	46%	41%	63%	51%	44%	59%	59%	44%	51%	54%	44%	65%	33%	50%	88%	48%	23%	96%	54%	57%	47%	34%	69%	50%	38%	66%	35%	69%	57%
Skin temperature cold*																																			
Delta-T-foot	58%	60%	38%	77%	59%	70%	44%	44%	70%	54%	56%	52%	61%	47%	54%	84%	23%	68%	43%	63%	50%	70%	22%	89%	67%	67%	37%	34%	70%	47%	66%	59%	44%	78%	61%
Delta-T-toe	74%	47%	37%	81%	55%	84%	24%	41%	71%	48%	81%	44%	66%	63%	65%	91%	14%	67%	46%	65%	75%	41%	18%	90%	46%	76%	26%	33%	69%	42%	77%	42%	39%	78%	53%
Subjectively	36%	75%	38%	73%	63%	58%	60%	48%	69%	59%	47%	74%	71%	51%	59%	77%	40%	71%	47%	64%	38%	76%	21%	88%	70%	43%	55%	32%	67%	51%	43%	75%	45%	73%	65%
CRT prolonged**																																			
Sternum	17%	89%	40%	72%	68%	13%	91%	47%	62%	61%	6%	93%	50%	42%	43%	18%	79%	63%	34%	39%	0%	93%	0%	84%	80%	18%	89%	43%	69%	65%	4%	100%	100%	68%	69%
Finger	17%	89%	40%	72%	68%	33%	78%	48%	65%	60%	31%	96%	92%	51%	59%	48%	65%	72%	39%	54%	38%	89%	38%	89%	81%	25%	73%	32%	67%	58%	6%	93%	30%	67%	65%
Knee	22%	81%	33%	71%	63%	42%	70%	47%	66%	59%	39%	78%	70%	49%	56%	49%	56%	68%	36%	51%	50%	83%	33%	90%	78%	45%	61%	36%	70%	56%	15%	88%	37%	68%	64%
Skin mottling severity***																																			
>3 (knee)	12%	90%	34%	71%	67%	20%	88%	52%	64%	62%	14%	78%	45%	40%	41%	22%	79%	67%	35%	42%	25%	91%	33%	88%	81%	24%	85%	43%	70%	65%	13%	96%	60%	69%	69%
>4 (severe)	2%	98%	33%	70%	69%	4%	96%	43%	61%	61%	6%	100%	100%	44%	46%	2%	98%	67%	34%	35%	0%	93%	0%	84%	80%	10%	94%	45%	68%	67%	0%	100%		67%	67%

*ΔTc-p was considered cold if >7 °C. **CRT was considered prolonged if >4.5 seconds. ***Mottling was scored according to Ait-Oufella et al. Abbreviations: PPV, positive predictive value; NPV, negative predictive value; CRT, capillary refill time.

Supplemental figures and tables

Sensitivity analysis I: primary analysis with imputed cardiac index measurements

Univariable (unadjusted) analyses

e-Table 9. Univariable associations of clinical examination with cardiac index as a continuous variable

Variable	Coefficient	SE	95% CI	R^2	P-Value
Covariates					
Age, years	-0.01	0.00	-0.01 to 0.00	0.008	0.008
Male gender	-0.26	0.06	-0.38 to -0.13	0.019	<0.001
Mechanical ventilation	-0.32	0.06	-0.44 to -0.19	0.031	<0.001
PEEP, cm H_2O	-0.03	0.01	-0.05 to -0.02	0.024	<0.001
Noradrenaline dose, $\mu g \cdot kg^{-1} \cdot min^{-1}$	0.29	0.16	-0.03 to 0.62	0.004	0.077
Central circulation					
Respiratory rate, per minute	0.01	0.01	0.00 to 0.02	0.007	0.014
Heart rate, beats per minute	0.02	0.00	0.01 to 0.02	0.151	<0.001
Atrial fibrillation	-0.15	0.12	-0.39 to 0.08	0.002	0.195
Systolic blood pressure, mmHg	0.00	0.00	0.00 to 0.01	0.018	<0.001
Diastolic blood pressure, mmHg	0.00	0.00	-0.01 to 0.00	0.002	0.155
Mean arterial pressure, mmHg	0.00	0.00	0.00 to 0.01	0.003	0.136
Central venous pressure, mmHg	-0.01	0.01	-0.04 to 0.01	0.008	0.241
Cardiac murmurs	0.36	0.11	0.15 to 0.57	0.002	<0.001
Crepitations	0.10	0.09	-0.08 to 0.27	0.002	0.280
Organ perfusion					
Consciousness, n (%)					
alert	Reference			0.030	
reacting to voice	-0.10	0.09	-0.27 to 0.06		0.223
reacting to pain	-0.37	0.12	-0.60 to -0.15		0.001
unresponsive	-0.35	0.07	-0.49 to -0.20		<0.001
Urine output last hour, $ml \cdot kg^{-1} \cdot h^{-1}$	0.06	0.03	0.00 to 0.12	0.004	0.061
Urine output in 6 hours, $ml \cdot kg^{-1} \cdot h^{-1}$	0.07	0.04	0.00 to 0.15	0.005	0.044
Central temperature, °C	0.22	0.03	0.15 to 0.28	0.050	<0.001
ΔTc-p, central to dorsum foot, °C	-0.06	0.01	-0.07 to -0.03	0.048	<0.001
ΔTc-p, central to big toe, °C	-0.05	0.01	-0.08 to -0.04	0.044	<0.001
Cold extremities, subjective	0.34	0.06	0.22 to 0.46	0.033	<0.001
Capillary refill time sternum, s	-0.12	0.03	-0.18 to -0.06	0.025	<0.001
Capillary refill time finger, s	-0.05	0.01	-0.08 to -0.03	0.017	<0.001
Capillary refill time knee, s	-0.05	0.01	-0.08 to -0.03	0.022	<0.001
Skin mottling severity, n (%)					
Mild (0-1)	Reference			0.001	
Moderate (2-3)	-0.03	0.07	-0.17 to 0.11		0.644
Severe (4-5)	-0.10	0.17	-0.44 to 0.24		0.563

Abbreviations: SE, standard error; PEEP, positive end expiratory pressure; ΔTc-p, central-to-peripheral temperature difference.

Supplemental figures and tables

Multivariable linear regression, internal validation and diagnostics

e-Table 10. Multivariable linear regression, predictors for cardiac index as a continuous variable

Variable	B	SE	95% CI	P value	β	Significant # out of 100
Covariates						
Male gender	-0.20	0.06	-0.31 to -0.09	<0.001	-0.10	98
Mechanical ventilation	-0.19	0.06	-0.30 to -0.07	0.001	-0.10	93
Noradrenaline per µg·kg^{-1}·min^{-1} increase	0.32	0.16	0.01 to 0.63	0.046	0.06	53
Clinical signs reflecting the central circulation						
Respiratory rate per minute increase	-0.01	0.00	-0.02 to 0.00	0.004	-0.09	81
Heart rate in beats per minute	0.02	0.00	0.02 to 0.02	<0.001	0.43	100
Atrial fibrillation	-0.32	0.11	-0.52 to -0.11	0.003	-0.09	89
Systolic blood pressure per mmHg increase	0.01	0.00	0.01 to 0.01	<0.001	0.24	100
Diastolic blood pressure per mmHg increase	-0.01	0.00	-0.02 to -0.01	<0.001	-0.17	100
Cardiac murmurs	0.24	0.09	0.07 to 0.42	0.007	0.08	70
Central temperature per °C increase	0.09	0.03	0.03 to 0.15	0.002	0.09	87
Clinical signs reflecting organ perfusion						
CRT on the sternum per sec increase	-0.08	0.03	-0.13 to -0.02	0.005	-0.09	91
ΔTc-p, central to big toe per °C increase	-0.05	0.01	-0.06 to -0.03	<0.001	-0.18	100
R^2	*0.30*		*0.26 to 0.37*			
Adjusted R^2	*0.29*		*0.25 to 0.36*			

Abbreviations: R^2, R squared; B, coefficient in the linear regression model; SE, standard error; CI, confidence interval; ß, standardized ß-coefficient in the linear regression model; CRT, capillary refill time; ΔTc-p, central-to-peripheral temperature difference.

Sensitivity analysis II: diagnostic performance with imputed cardiac index measurements

e-Table 11a. Diagnosing a low cardiac index: tabular display derived from the 2x2 matrix for each clinical sign

Results for each clinical sign		Cardiac index < 2.2 L·min⁻¹·m⁻²				Cardiac index < 2.5 L·min⁻¹·m⁻²			
	N	A = True positive	B = False positive	C = False negative	D = True negative	A = True positive	B = False positive	C = False negative	D = True negative
Central circulation									
Respiratory rate > 22 pm	1075	292	481	76	226	405	368	121	181
Heart rate < 100 bpm	1075	304	462	64	245	429	337	97	212
Atrial fibrillation	1075	31	47	337	660	43	35	483	514
SBP < 90 mmHg	1075	34	65	334	642	50	49	476	500
DBP < 45 mmHg	1075	16	47	352	660	29	34	497	515
MAP < 65 mmHg	1075	52	98	316	609	76	74	450	475
Cardiac murmurs	1075	23	75	345	632	37	61	489	488
Crepitations	1075	47	102	321	605	66	83	460	466
Organ perfusion									
Consciousness									
reacting to voice	1075	91	204	277	503	136	159	390	390
reacting to pain	1075	17	26	351	681	22	21	504	528
unresponsive	1075	26	51	342	656	38	39	488	510
Urine output <0.5 ml·kg⁻¹·h⁻¹									
Over 1 hour	1075	182	313	186	394	261	234	265	315
Over 6 hours	1075	152	263	216	444	212	203	314	346
Skin temperature cold*									
ΔTc-p, dorsum foot	1075	74	260	294	446	118	216	408	332
ΔTc-p, big toe	1075	130	373	238	333	200	303	326	245
Cold subjective	1075	177	225	191	482	239	163	287	386
CRT prolonged**									
Sternum	1075	38	41	330	666	47	32	479	517
Finger	1075	94	113	274	594	162	130	364	419
Knee	1075	122	170	246	537	74	63	452	486
Skin mottling severity***									
Over the knee (≥3)	1075	61	76	307	631	74	63	452	486
Severe (≥4)	1075	13	20	355	687	17	16	509	533

*ΔTc-p was considered cold if >7 °C. **CRT was considered prolonged if >4.5 seconds. ***Mottling was scored according to Ait-Oufella et al. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; ΔTc-p, central-to-peripheral temperature difference; CRT, capillary refill time.

Supplemental figures and tables

e-Table 11b. Diagnosing a low cardiac index: Outcome measures for each clinical sign

Performance of each clinical sign	Cardiac index < 2.2 L·min⁻¹·m⁻²							Cardiac index < 2.5 L·min⁻¹·m⁻²						
	Sens.	Spec.	PPV	NPV	Accuracy	LR +	LR -	Sens.	Spec.	PPV	NPV	Accuracy	LR +	LR -
Central circulation														
Respiratory rate > 22 pm	0.79	0.32	0.38	0.75	0.54	1.17	0.65	0.77	0.33	0.52	0.60	0.57	1.15	0.70
Heart rate < 100 bpm	0.83	0.35	0.40	0.79	0.59	1.26	0.50	0.82	0.39	0.56	0.69	0.64	1.33	0.48
Atrial fibrillation	0.08	0.93	0.40	0.66	0.63	1.27	0.98	0.08	0.94	0.55	0.52	0.55	1.28	0.98
SBP < 90 mmHg	0.09	0.91	0.34	0.66	0.59	1.00	1.00	0.10	0.91	0.51	0.52	0.49	1.07	0.99
DBP < 45 mmHg	0.04	0.93	0.25	0.65	0.58	0.65	1.02	0.06	0.94	0.46	0.51	0.53	0.89	1.01
MAP < 65 mmHg	0.14	0.86	0.35	0.66	0.55	1.02	1.00	0.14	0.87	0.51	0.51	0.49	1.07	0.99
Cardiac murmurs	0.06	0.89	0.23	0.65	0.61	0.59	1.05	0.07	0.89	0.38	0.50	0.49	0.63	1.05
Crepitations	0.13	0.86	0.32	0.65	0.61	0.89	1.02	0.13	0.85	0.44	0.50	0.49	0.83	1.03
Organ perfusion														
Consciousness														
reacting to voice	0.25	0.71	0.31	0.64	0.65	0.86	1.06	0.26	0.71	0.46	0.50	0.51	0.89	1.04
reacting to pain	0.05	0.96	0.40	0.66	0.63	1.26	0.99	0.04	0.96	0.51	0.51	0.51	1.09	1.00
unresponsive	0.07	0.93	0.34	0.66	0.54	0.98	1.00	0.07	0.93	0.49	0.51	0.54	1.02	1.00
Urine output <0.5 ml·kg⁻¹·h⁻¹														
Over 1 hour	0.49	0.56	0.37	0.68	0.55	1.12	0.91	0.50	0.57	0.53	0.54	0.52	1.16	0.88
Over 6 hours	0.41	0.63	0.37	0.67	0.48	1.11	0.93	0.40	0.63	0.51	0.52	0.42	1.09	0.95
Skin temperature cold*														
Δ-T, dorsum foot	0.20	0.63	0.22	0.60	0.43	0.55	1.26	0.22	0.61	0.35	0.45	0.41	0.57	1.28
Δ-T, big toe	0.35	0.47	0.26	0.58	0.61	0.67	1.37	0.38	0.45	0.40	0.43	0.58	0.69	1.39
Cold subjective	0.48	0.68	0.44	0.72	0.65	1.51	0.76	0.45	0.70	0.59	0.57	0.52	1.53	0.78
CRT prolonged**														
Sternum	0.10	0.94	0.48	0.67	0.64	1.78	0.95	0.09	0.94	0.59	0.52	0.54	1.53	0.97
Finger	0.26	0.84	0.45	0.68	0.61	1.60	0.89	0.31	0.76	0.55	0.54	0.52	1.30	0.91
Knee	0.33	0.76	0.42	0.69	0.64	1.38	0.88	0.14	0.89	0.54	0.52	0.52	1.23	0.97
Skin mottling severity***														
Over the knee (≥3)	0.17	0.89	0.45	0.67	0.65	1.54	0.93	0.14	0.89	0.54	0.52	0.51	1.23	0.97
Severe (≥4)	0.04	0.97	0.39	0.66	0.61	1.25	0.99	0.03	0.97	0.52	0.51	0.49	1.11	1.00

*ΔTc-p was considered cold if >7 °C. **CRT was considered prolonged if >4.5 seconds. ***Mottling was scored according to Ait-Oufella et al. Abbreviations: Sens, sensitivity; Spec, specificity PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; ΔTc-p, central-to-peripheral temperature difference; CRT, capillary refill time.

Supplemental figures and tables

e-Table 12a. Diagnosing a high cardiac index: tabular display derived from the 2x2 matrix for each clinical sign

Results for each clinical sign	N	Cardiac index > 4.0 L·min^{-1}·m^{-2}				Cardiac index > 4.5 L·min^{-1}·m^{-2}			
		A = True positive	B = False positive	C = False negative	D = True negative	A = True positive	B = False positive	C = False negative	D = True negative
Central circulation									
Respiratory rate > 22 pm	1075	52	721	29	273	23	750	15	287
Heart rate < 100 bpm	1075	37	729	44	265	11	755	27	282
Atrial fibrillation	1075	6	72	75	922	0	78	38	959
SBP < 90 mmHg	1075	10	89	71	905	5	94	33	943
DBP < 45 mmHg	1075	7	56	74	938	4	59	34	978
MAP < 65 mmHg	1075	13	137	68	857	7	143	31	894
Cardiac murmurs	1075	16	82	65	912	8	90	30	947
Crepitations	1075	18	131	63	863	7	142	31	895
Organ perfusion									
Consciousness									
reacting to voice	1075	32	263	49	731	15	280	23	757
reacting to pain	1075	4	39	77	955	2	41	36	996
unresponsive	1075	9	68	72	926	4	73	34	964
Urine output <0.5 ml·kg^{-1}·h^{-1}									
Over 1 hour	1075	35	460	46	534	15	480	23	557
Over 6 hours	1075	29	385	52	609	15	399	23	638
Skin temperature cold*									
ΔTc-p, dorsum foot	1075	27	544	54	450	11	560	27	477
ΔTc-p, big toe	1075	39	701	42	293	18	722	20	315
Cold subjective	1075	21	381	60	613	7	395	31	642
CRT prolonged***									
Sternum	1075	3	76	78	918	1	78	37	959
Finger	1075	13	194	68	800	7	200	31	837
Knee	1075	18	274	63	720	8	284	30	753
Skin mottling severity***									
Over the knee (≥3)	1075	12	125	69	869	4	133	34	904
Severe (≥4)	1075	1	32	80	962	0	33	38	1004

*ΔTc-p was considered cold if >7 °C. **CRT was considered prolonged if >4.5 seconds. ***Mottling was scored according to Ait-Oufella et al. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; ΔTc-p, central-to-peripheral temperature difference; CRT, capillary refill time.

Supplemental figures and tables

e-Table 12b. Diagnosing a high cardiac index: Outcome measures for each clinical sign

Performance of each clinical sign	Cardiac index > 4.0 L·min⁻¹·m⁻²							Cardiac index > 4.5 L·min⁻¹·m⁻²						
	Sens.	Spec.	PPV	NPV	Accuracy	LR +	LR -	Sens.	Spec.	PPV	NPV	Accuracy	LR +	LR -
Central circulation														
Respiratory rate > 22 pm	0.64	0.27	0.07	0.90	0.30	0.89	1.30	0.61	0.28	0.03	0.95	0.29	0.84	1.43
Heart rate < 100 bpm	0.46	0.27	0.05	0.86	0.28	0.62	2.04	0.29	0.27	0.01	0.93	0.27	0.40	2.61
Atrial fibrillation	0.07	0.93	0.08	0.92	0.86	1.02	1.00	0.00	0.92	0.00	0.96	0.89	0.00	1.08
SBP < 90 mmHg	0.12	0.91	0.10	0.93	0.85	1.38	0.96	0.13	0.91	0.05	0.97	0.88	1.45	0.95
DBP < 45 mmHg	0.09	0.94	0.11	0.93	0.88	1.53	0.97	0.11	0.94	0.06	0.96	0.91	1.85	0.95
MAP < 65 mmHg	0.16	0.86	0.09	0.93	0.81	1.16	0.97	0.18	0.86	0.05	0.97	0.84	1.34	0.95
Cardiac murmurs	0.20	0.92	0.16	0.93	0.86	2.39	0.87	0.21	0.91	0.08	0.97	0.89	2.43	0.86
Crepitations	0.22	0.87	0.12	0.93	0.82	1.69	0.90	0.18	0.86	0.05	0.97	0.84	1.35	0.95
Organ perfusion														
Consciousness														
reacting to voice	0.40	0.74	0.11	0.94	0.71	1.49	0.82	0.39	0.73	0.05	0.97	0.72	1.46	0.83
reacting to pain	0.05	0.96	0.09	0.93	0.89	1.26	0.99	0.05	0.96	0.05	0.97	0.93	1.33	0.99
unresponsive	0.11	0.93	0.12	0.93	0.87	1.62	0.95	0.11	0.93	0.05	0.96	0.90	1.50	0.96
Urine output <0.5 ml·kg⁻¹·h⁻¹														
Over 1 hour	0.43	0.54	0.07	0.92	0.53	0.93	1.06	0.39	0.54	0.03	0.97	0.53	0.85	1.13
Over 6 hours	0.36	0.61	0.07	0.92	0.59	0.92	1.05	0.39	0.62	0.04	0.95	0.61	1.03	0.98
Skin temperature cold*														
Δ-T, dorsum foot	0.48	0.29	0.05	0.87	0.31	0.68	1.76	0.29	0.46	0.02	0.94	0.45	0.54	1.54
Δ-T, big toe	0.33	0.45	0.05	0.89	0.44	0.61	1.47	0.47	0.30	0.02	0.95	0.31	0.68	1.73
Cold subjective	0.26	0.62	0.05	0.91	0.59	0.68	1.20	0.18	0.62	0.02	0.96	0.60	0.48	1.32
CRT prolonged**														
Sternum	0.04	0.92	0.04	0.92	0.86	0.48	1.04	0.03	0.92	0.01	0.96	0.89	0.35	1.05
Finger	0.16	0.80	0.06	0.92	0.76	0.82	1.04	0.18	0.81	0.03	0.96	0.79	0.96	1.01
Knee	0.22	0.72	0.06	0.92	0.69	0.81	1.07	0.21	0.73	0.03	0.96	0.71	0.77	1.09
Skin mottling severity***														
Over the knee (≥3)	0.15	0.87	0.09	0.93	0.82	1.18	0.97	0.11	0.87	0.03	0.96	0.84	0.82	1.03
Severe (≥4)	0.01	0.97	0.03	0.92	0.90	0.38	1.02	0.00	0.97	0.00	0.97	0.93	0.00	1.03

*ΔTc-p was considered cold if >7 °C. **CRT was considered prolonged if >4.5 seconds. ***Mottling was scored according to Ait-Oufella et al. Abbreviations: Sens, sensitivity; Spec, specificity PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; ΔTc-p, central-to-peripheral temperature difference.

Supplemental figures and tables