**SUPPLEMENTARY FIGURES AND TABLES**

Clinical examination for the prediction of mortality in the critically ill: the Simple Intensive Care Studies-I

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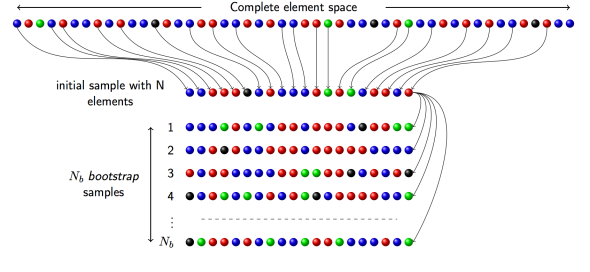
## Previous studies

#### eTable 1. Clinical examination findings associated with 90-day mortality identified in previous studies

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author, year | N | Population | Follow-up | Adjusted for | Clinical examination findings | | | | | | | | | |
|  |  |  |  |  | Age | Respiratory rate/expansion | Blood pressure | CVP | Heart rate/rhythm | Oliguria | Mottling | Capillary refill time | Skin temperature | Altered sensorium |
| Forrester, 1977 | 200 | AMI | Hospital discharge | - |  |  |  |  |  |  |  |  |  |  |
| Champion, 1980 | 360 | Critical injured patients | Hospital discharge | - |  |  |  |  |  |  |  |  |  |  |
| Parker, 1987 | 48 | Septic shock | ICU discharge | - |  |  |  |  |  |  |  |  |  |  |
| Tuchsmidt, 1989 | 145 | Septic shock | Hospital discharge | - |  |  |  |  |  |  |  |  |  |  |
| Bernardin, 1996 | 32 | Septic shock | Hospital discharge | - |  |  |  |  |  |  |  |  |  |  |
| Hasdai, 1999 | 2478 | Cardiogenic shock | 30 days | - |  |  |  |  |  |  |  |  |  |  |
| Varpula, 2005 | 111 | Sepsis | 30 days | - |  |  |  |  |  |  |  |  |  |  |
| Dünser, 2009 | 274 | Sepsis | 28 days | SAPS II |  |  |  |  |  |  |  |  |  |  |
| Macedo, 2011 | 317 | Critically ill | ICU discharge | Age, sepsis |  |  |  |  |  |  |  |  |  |  |
| Ait-Oufella, 2011 | 60 | Septic shock | 14 days | - |  |  |  |  |  |  |  |  |  |  |
| Van Genderen, 2012 | 25 | OHCA | 28 days | - |  |  |  |  |  |  |  |  |  |  |
| De Backer, 2013 | 252 | Severe sepsis | ICU discharge | APACHE II, SOFA |  |  |  |  |  |  |  |  |  |  |
| Coudroy, 2015 | 791 | Critically ill | ICU discharge | SAPS II |  |  |  |  |  |  |  |  |  |  |
| Ait-Oufella, 2014 | 59 | Septic shock | 14 days | - |  |  |  |  |  |  |  |  |  |  |
| De Moura, 2016 | 97 | Septic shock | 28 days | Age, SOFA |  |  |  |  |  |  |  |  |  |  |
| Vaara, 2016 | 1966 | Critically ill | 90 days | Age, APACHE II, SAPS II |  |  |  |  |  |  |  |  |  |  |
| Houwink, 2016 | 821 | Critically ill with infection | Hospital discharge | Age, APACHE IV (not shown) |  |  |  |  |  |  |  |  |  |  |
| Varis, 2016 | 496 | Septic shock | 90 days | SAPS II, SOFA |  |  |  |  |  |  |  |  |  |  |

Table legend.  = significant predictor in univariable analysis.  = significant predictor in multivariable analysis.  = very significant (p<0.015) predictor in multivariable analysis.  = nonsignificant (p>0.05) predictor in univariable analysis.  = nonsignificant predictor in multivariable analysis. Abbreviations: AMI, acute myocardial infarction; OHCA, out-of-hospital cardiac arrest; ICU, intensive care unit.

#### eFigure 1. Graphical representation of bootstrap sampling



Explanation: for each bootstrap sample, 1075 patients were drawn one by one from the imputed dataset with replacement. Drawing with replacement means that each selected case was placed back into the dataset so that it was available for the next draw. These 100 bootstrap samples are comparable, but not identical to the original data set. This process mimics the sampling from an underlying population.

## Descriptives and missing percentage

#### eTable 2. Description of collected variables and percentage of missingness

|  |  |  |
| --- | --- | --- |
| Variable | Method of measuring | Missing % |
| Age, years | Patient’s electronic chart | 0.0 |
| Sex, male | Patient’s electronic chart | 0.0 |
| Mechanical ventilation |  |  |
| Inspiratory O2, % | mechanical ventilator | 0.0 |
| PEEP, cm H2O | mechanical ventilator | 0.0 |
| Vasoactive medication, µg∙kg-1∙min-1 | Infusion pump inspection at bedside | 0.0 |
| Clinical examination |  |  |
| *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 | 76.6\* |
| 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 |
| *Tissue 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 | 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 score, 0 to 5 | Observation of mottling area on the legs, scoring system according to Ait-Oufella [19] | 10.1 |

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

#### eFigure 2. Graphical representation of missing values



## Primary analysis

#### eTable 3. Associations of clinical examination, biochemical and haemodynamic variables on 90-day mortality.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | OR | 95% CI | P-value | OR | 95% CI | P-value |
|  |  | *UNADJUSTED* |  | *AGE- AND SEX- ADJUSTED* | | |
| Age per year increase | 1.04 | 1.03 - 1.06 | <0.001 | - | - | - |
| Sex, male | 1.15 | 0.87 - 1.53 | 0.31 | - | - | - |
| Mechanical ventilation | 1.89 | 1.43 - 2.52 | <0.001 | 2.01 | 1.50 - 2.70 | <0.001 |
| PEEP per cm H2O increase | 1.12 | 1.05 - 1.20 | 0.001 | 1.14 | 1.06 - 1.23 | <0.001 |
| Norepinephrine dose, µg∙kg-1∙min-1 | 5.85 | 2.95 - 11.6 | <0.001 | 7.18 | 3.53 - 14.6 | <0.001 |
| Clinical examination |  |  |  |  |  |  |
| *Central circulation* |  |  |  |  |  |  |
| Respiratory rate per minute increase | 1.03 | 1.01 - 1.06 | 0.008 | 1.03 | 1.01 - 1.06 | 0.006 |
| Heart rate per minute increase | 1.01 | 1.00 - 1.01 | 0.06 | 1.01 | 1.00 - 1.01 | 0.012 |
| Atrial fibrillation | 2.40 | 1.51 - 3.84 | <0.001 | 1.48 | 0.91 - 2.42 | 0.11 |
| SBP per mmHg increase | 1.00 | 0.99 - 1.00 | 0.35 | 1.00 | 0.99 - 1.00 | 0.205 |
| DBP per mmHg decrease | 1.02 | 1.00 - 1.03 | 0.009 | 1.01 | 1.00 - 1.02 | 0.07 |
| MAP per mmHg decrease | 1.01 | 1.00 - 1.02 | 0.019 | 1.01 | 1.00 - 1.02 | 0.029 |
| Cardiac murmurs | 1.01 | 0.63 - 1.61 | 0.97 | 0.93 | 0.57 - 1.51 | 0.78 |
| Crackles or crepitations | 1.34 | 0.92 - 1.94 | 0.12 | 1.22 | 0.83 - 1.78 | 0.32 |
| *Organ perfusion* |  |  |  |  |  |  |
| Consciousness |  |  |  |  |  |  |
| alert | 1.00 | Reference | - | 1.00 | Reference |  |
| reacting to voice | 0.99 | 0.64 - 1.53 | 0.96 | 0.95 | 0.60 - 1.49 | 0.82 |
| reacting to pain | 2.25 | 1.35 - 3.74 | 0.002 | 2.34 | 1.38 - 3.99 | 0.002 |
| unresponsive | 2.18 | 1.56 - 3.03 | <0.001 | 2.33 | 1.65 - 3.28 | <0.001 |
| Urine output per ml∙kg-1∙h-1 decrease | 1.47 | 1.21 - 1.77 | <0.001 | 1.41 | 1.16 - 1.70 | <0.001 |
| Urine output per ml∙kg-1∙6h-1 decrease | 1.66 | 1.33 - 2.07 | <0.001 | 1.52 | 1.22 - 1.90 | <0.001 |
| Central temperature per °C decrease | 1.26 | 1.09 - 1.46 | 0.002 | 1.23 | 1.05 - 1.43 | 0.010 |
| ΔTc-p, dorsum foot per °C increase | 1.04 | 0.99 - 1.08 | 0.09 | 1.00 | 0.97 - 1.06 | 0.61 |
| ΔTc-p, toe per °C increase | 1.02 | 0.99 - 1.06 | 0.21 | 1.00 | 0.96 - 1.04 | 0.93 |
| Cold extremities, subjective | 1.41 | 0.54 - 0.93 | 0.015 | 1.22 | 0.62 - 1.09 | 0.17 |
| CRT sternum per second increase | 1.29 | 1.15 - 1.46 | <0.001 | 1.24 | 1.09 - 1.40 | 0.001 |
| CRT finger per second increase | 1.17 | 1.10 - 1.25 | <0.001 | 1.14 | 1.07 - 1.21 | <0.001 |
| CRT knee per second increase | 1.17 | 1.11 - 1.24 | <0.001 | 1.14 | 1.08 - 1.21 | <0.001 |
| Mottling rate |  |  |  |  |  |  |
| Mild (0-1) | 1.00 | Reference | - | 1.00 | Reference |  |
| Moderate (2-3) | 1.75 | 1.29 - 2.38 | <0.001 | 1.58 | 1.16 - 2.16 | 0.004 |
| Severe (4-5) | 3.63 | 1.66 - 6.75 | 0.001 | 3.42 | 1.65 - 7.07 | 0.001 |

Left: crude OR’s. Right: OR’s adjusted for age and sex. Abbreviations: OR, odds ratio; PEEP, positive end expiratory pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; CRT, capillary refill time; ΔTc-p, central-to-peripheral temperature difference.

eFigure 3. U-shaped association of systolic blood pressure with mortality using penalized spline regression



eFigure 4. Calibration plot of the clinical examination: observed versus predicted mortality across 10 equally sized groups



Comment: the actual probability deviates little from the predicted probability. Combined with a non-significant Hosmer Lemeshow test (χ2 7.01; p=0.72), we judged these deviations as acceptable.

eTable 4. Clinical examination model with systolic blood pressure in quartiles

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | OR | 95% CI | P-value |
| Age in years | 1.04 | 1.03 - 1.05 | <0.001 |
| Norepinephrine per µg∙kg-1∙min-1 | 3.15 | 1.45 - 6.85 | 0.004 |
| *Central circulation* |  |  |  |
| Respiratory rate per minute | 1.05 | 1.02 - 1.08 | <0.001 |
| Atrial fibrillation | 1.78 | 1.05 - 3.00 | 0.031 |
| Systolic blood pressure per quartile increase |  |  |  |
| 1st quartile (< 100 mmHg) | 1.00 | Reference |  |
| 2nd quartile (100 - 114 mmHg) | 1.17 | 0.77 - 1.78 | 0.45 |
| 3rd quartile (114 - 133 mmHg) | 1.04 | 0.68 - 1.61 | 0.85 |
| 4th quartile (> 133 mmHg) | 1.65 | 1.01 - 2.71 | 0.046 |
| Diastolic blood pressure per mmHg decrease | 1.01 | 1.00 - 1.03 | 0.07 |
| Central temperature per °C decrease | 1.22 | 1.04 - 1.44 | 0.012 |
| *Organ perfusion* |  |  |  |
| Consciousness |  |  |  |
| Alert | 0.93 | 0.58 - 1.50 | 0.78 |
| Reacting to voice | 2.75 | 1.57 - 4.81 | <0.001 |
| Reacting to pain | 2.30 | 1.55 - 3.39 | <0.001 |
| Unresponsive | 1.43 | 1.14 - 1.78 | 0.002 |
| Urine output per µg∙kg-1∙6h-1 decrease |  |  |  |
| Skin mottling severity | 1.00 | Reference |  |
| Mild (0-1) | 1.27 | 0.91 - 1.77 | 0.16 |
| Moderate (2-3) | 2.48 | 1.12 - 5.50 | 0.026 |
| Severe (4-5) | 1.04 | 1.03 - 1.05 | <0.001 |

The model included all 1075 patients of whom 298 died. Pseudo R2=0.13. Hosmer-Lemeshow goodness-of-fit test χ2 7.01; p=0.72. AUC = 0.74 (95% CI 0.71-0.78). Mottling was scored according to Ait-Oufella et al. [19]. Abbreviations: OR, odds ratio; CI, confidence interval.

eTable 5. Clinical examination model on complete cases (i.e. only patients without missing data)

|  |  |  |  |
| --- | --- | --- | --- |
| Clinical examination | OR | 95% CI | P-value |
| Age in years | 1.04 | 1.03 - 1.06 | <0.001 |
| Norepinephrine per µg∙kg-1∙min-1 | 4.51 | 1.88 - 10.8 | 0.001 |
| *Central circulation* |  |  |  |
| Respiratory rate per minute | 1.05 | 1.02 - 1.08 | <0.001 |
| Atrial fibrillation | 1.95 | 1.11 - 3.42 | 0.020 |
| Systolic blood pressure per mmHg increase | 1.01 | 1.00 - 1.02 | 0.009 |
| Diastolic blood pressure per mmHg decrease | 1.02 | 1.00 - 1.03 | 0.07 |
| Central temperature per °C decrease | 1.00 | 1.00 - 1.00 | <0.001 |
| *Organ perfusion* |  |  |  |
| Consciousness |  |  |  |
| Alert | 1.00 | Reference |  |
| Reacting to voice | 3.07 | 1.70 - 5.57 | <0.001 |
| Reacting to pain | 2.36 | 1.53 - 3.62 | <0.001 |
| Unresponsive | 1.33 | 1.06 - 1.68 | 0.016 |
| Urine output per µg∙kg-1∙h-1 decrease | 1.24 | 1.05 - 1.47 | 0.013 |
| Skin mottling severity |  |  |  |
| Mild (0-1) | 1.00 | Reference |  |
| Moderate (2-3) | 1.32 | 0.94 - 1.86 | 0.11 |
| Severe (4-5) | 2.90 | 1.27 - 6.62 | 0.012 |

The model included 916 patients of whom 257 died. Pseudo R2=0.14. Hosmer-Lemeshow goodness-of-fit test χ2 9.02; p=0.52. AUC = 0.75 (95% CI 0.71-0.78). Abbreviations: OR, odds ratio; CI, confidence interval.

## Sensitivity analysis

#### eTable 6. Associations of clinical examination on 7- and 30-day mortality.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | OR (95% CI)  *7-days* | P-value | OR (95% CI)  *30-days* | P-value |
| Age, year increase | 1.04 (1.03 - 1.06) | <0.001 | 1.04 (1.03 - 1.05) | <0.001 |
| Sex, male | 1.08 (0.75 - 1.55) | 0.67 | 1.05 (0.78 - 1.40) | 0.75 |
| Mechanical ventilation | 1.73 (1.19 - 2.50) | 0.004 | 1.87 (1.39 - 2.53) | <0.001 |
| PEEP, cm H2O increase | 1.13 (1.05 - 1.23) | 0.002 | 1.15 (1.07 - 1.23) | <0.001 |
| Norepinephrine dose, µg∙kg-1∙min-1 | 4.76 (2.31 - 9.82) | <0.001 | 4.84 (2.47 - 9.49) | <0.001 |
| *Central circulation* |  |  |  |  |
| Respiratory rate, minute increase | 1.04 (1.01 - 1.07) | 0.003 | 1.03 (1.01 - 1.06) | 0.009 |
| Heart rate, minute increase | 1.01 (1.00 - 1.01) | 0.11 | 1.00 (1.00 - 1.01) | 0.15 |
| Atrial fibrillation | 2.46 (1.44 - 4.19) | 0.001 | 2.28 (1.41 - 3.67) | 0.001 |
| SBP, mmHg increase | 0.99 (0.98 - 1.00) | 0.037 | 0.99 (0.99 - 1.00) | 0.08 |
| DBP, mmHg decrease | 1.02 (1.00 - 1.03) | 0.028 | 1.02 (1.00 - 1.03) | 0.009 |
| MAP, mmHg decrease | 1.02 (1.00 - 1.03) | 0.014 | 1.01 (1.00 - 1.02) | 0.018 |
| Cardiac murmurs | 1.03 (0.57 - 1.87) | 0.91 | 1.10 (0.68 - 1.79) | 0.69 |
| Crackles or crepitations | 0.76 (0.45 - 1.31) | 0.33 | 1.06 (0.71 - 1.59) | 0.77 |
| *Organ perfusion* |  |  |  |  |
| Consciousness |  |  |  |  |
| alert | 1.00 (Reference) |  | 1.00 (Reference) |  |
| reacting to voice | 0.98 (0.55 - 1.73) | 0.94 | 1.08 (0.68 - 1.72) | 0.73 |
| reacting to pain | 1.07 (0.51 - 2.25) | 0.87 | 1.85 (1.06 - 3.20) | 0.029 |
| unresponsive | 1.94 (1.27 - 2.96) | 0.002 | 2.23 (1.57 - 3.17) | <0.001 |
| Urine output, ml∙kg-1∙h-1 decrease | 1.62 (1.22 - 2.15) | 0.001 | 1.54 (1.25 - 1.91) | <0.001 |
| Urine output, ml∙kg-1∙6h-1 decrease | 1.81 (1.32 - 2.47) | 0.000 | 1.64 (1.29 - 2.07) | <0.001 |
| Central temperature, °C decrease | 1.28 (1.06 - 1.55) | 0.009 | 1.31 (1.12 - 1.54) | 0.001 |
| ΔTc-p, dorsum of foot, °C increase | 1.06 (1.00 - 1.12) | 0.033 | 1.04 (0.99 - 1.09) | 0.11 |
| ΔTc-p, toe, °C increase | 1.05 (1.00 - 1.10) | 0.044 | 1.02 (0.98 - 1.06) | 0.27 |
| Cold extremities, subjective | 1.58 (1.12 - 2.25) | 0.010 | 1.37 (1.03 - 1.83) | 0.030 |
| CRT sternum, second increase | 1.30 (1.13 - 1.50) | <0.001 | 1.22 (1.08 - 1.38) | 0.002 |
| CRT finger, second increase | 1.15 (1.07 - 1.23) | <0.001 | 1.12 (1.06 - 1.19) | <0.001 |
| CRT knee, second increase | 1.10 (1.04 - 1.17) | 0.001 | 1.11 (1.05 - 1.17) | <0.001 |
| Mottling rate |  |  |  |  |
| Mild (0-1) | 1.00 (Reference) |  | 1.00 (Reference) |  |
| Moderate (2-3) | 1.69 (1.14 - 2.54) | 0.009 | 1.74 (1.26 - 2.39) | 0.001 |
| Severe (4-5) | 4.41 (2.10 - 9.34) | <0.001 | 2.94 (1.44 - 5.98) | 0.003 |

Abbreviations: OR, odds ratio; PEEP, positive end expiratory pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; ΔTc-p, central-to-peripheral temperature difference; CRT, capillary refill time.

#### eTable 7. Clinical examination independently associated with 7-day (left) and 30-day (right) mortality

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | OR (95% CI) | P-value | OR (95% CI) | P-value |
| Age in years | 1.04 (1.02 - 1.05) | <0.001 | 1.03 (1.02 - 1.04) | <0.001 |
| Norepinephrine per µg∙kg-1∙min-1 | 2.76 (1.15 - 6.62) | 0.022 | 2.64 (1.21 - 5.74) | 0.014 |
| *Central circulation* |  |  |  |  |
| Respiratory rate per minute | 1.06 (1.02 - 1.09) | 0.001 | 1.05 (1.02 - 1.08) | <0.001 |
| Atrial fibrillation | 1.89 (1.05 - 3.41) | 0.035 | 1.85 (1.09 - 3.16) | 0.023 |
| SBP per mmHg increase | 1.00 (0.99 - 1.01) | 0.51 | 1.01 (1.00 - 1.01) | 0.09 |
| DBP per mmHg decrease | 0.99 (0.97 - 1.01) | 0.37 | 1.02 (1.00 - 1.03) | 0.07 |
| Central temperature per °C decrease | 0.82 (0.68 - 0.99) | 0.044 | 1.28 (1.09 - 1.51) | 0.003 |
| *Organ perfusion* |  |  |  |  |
| Consciousness | 1.00 (Reference) |  |  |  |
| Alert | 0.93 (0.51 - 1.70) | 0.81 | 1.00 (Reference) |  |
| Reacting to voice | 1.20 (0.54 - 2.62) | 0.66 | 1.08 (0.66 - 1.76) | 0.77 |
| Reacting to pain | 1.94 (1.19 - 3.17) | 0.008 | 2.19 (1.21 - 3.95) | 0.010 |
| Unresponsive | 1.45 (1.07 - 1.97) | 0.017 | 2.37 (1.58 - 3.56) | <0.001 |
| Urine output per µg∙kg-1∙6h-1 decrease |  |  | 1.40 (1.11 - 1.77) | 0.005 |
| Skin mottling score |  |  |  |  |
| Mild (0-1) | 1.00 (Reference) |  | 1.00 (Reference) |  |
| Moderate (2-3) | 1.25 (0.81 - 1.91) | 0.32 | 1.28 (0.91 - 1.81) | 0.15 |
| Severe (4-5) | 3.06 (1.34 - 6.98) | 0.008 | 2.04 (0.93 - 4.50) | 0.07 |

The7-day mortality model included 1075 patients of whom 151 died. Pseudo R2=0.11. Hosmer-Lemeshow goodness-of-fit test χ2 4.83; p=0.90. AUC = 0.74 (95% CI 0.70-0.78). The 30-day mortality model included 1075 patients of whom 255 died. Pseudo R2=0.11. Hosmer-Lemeshow goodness-of-fit test χ2 8.07; p=0.62. AUC = 0.73 (95% CI 0.70-0.76). eFigure 3 and 4 present information on model calibration and discrimination. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure.

eTable 8. Cox regression of clinical examination findings independently associated with 90-day mortality

|  |  |  |  |
| --- | --- | --- | --- |
| Clinical examination finding | Hazard ratio | 95% confidence interval | P-value |
| Age in years | 1.03 | 1.02 - 1.04 | <0.001 |
| Norepinephrine per µg∙kg-1∙min-1 | 2.21 | 1.31 - 3.74 | 0.003 |
| *Central circulation* |  |  |  |
| Respiratory rate per minute | 1.04 | 1.02 - 1.06 | <0.001 |
| Atrial fibrillation | 1.51 | 1.04 - 2.18 | 0.029 |
| Systolic blood pressure per mmHg increase | 1.01 | 1.00 - 1.01 | 0.037 |
| Diastolic blood pressure per mmHg decrease | 1.01 | 1.00 - 1.02 | 0.08 |
| Central temperature per °C decrease | 1.20 | 1.06 - 1.36 | 0.005 |
| *Organ perfusion* |  |  |  |
| Consciousness |  |  |  |
| Alert | 1.00 | Reference |  |
| Reacting to voice | 1.00 | 0.67 - 1.49 | 0.99 |
| Reacting to pain | 2.18 | 1.41 - 3.38 | <0.001 |
| Unresponsive | 2.01 | 1.46 - 2.76 | <0.001 |
| Urine output per µg∙kg-1∙h-1 decrease | 1.38 | 1.14 - 1.67 | 0.001 |
| Skin mottling severity |  |  |  |
| Mild (0-1) | 1.00 | Reference |  |
| Moderate (2-3) | 1.27 | 0.98 - 1.64 | 0.07 |
| Severe (4-5) | 1.92 | 1.14 - 3.25 | 0.015 |

The model included all 1075 patients of whom 298 died. Mottling was scored according to Ait-Oufella et al. [19].

## Subgroup analyses

**eFigure 5**. Clinical examination findings and 90-day mortality stratified by vasopressor use

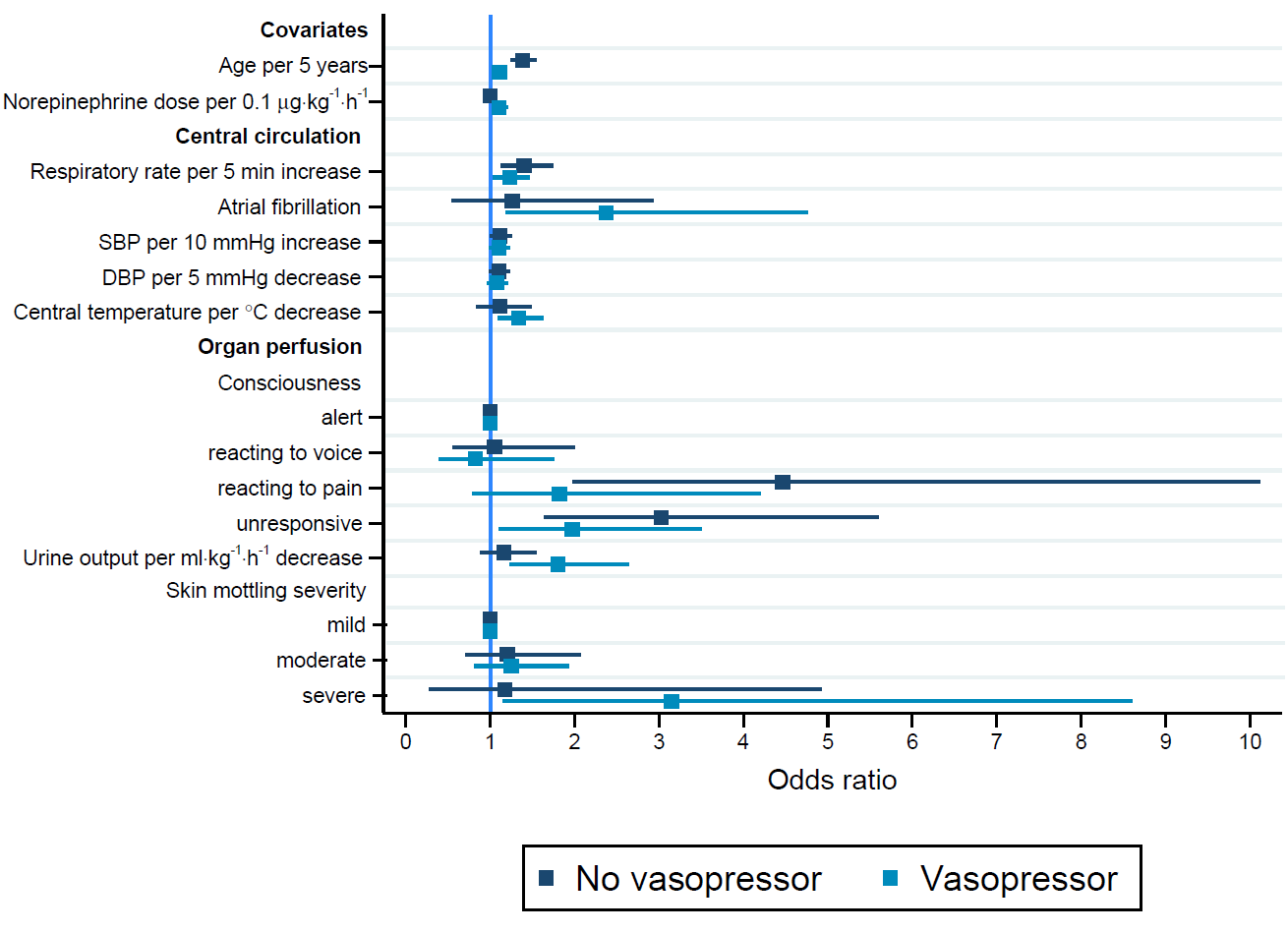


Figure description. The ‘No vasopressor’ model included 547 patients of whom 115 died. Pseudo R2=0.16. Hosmer-Lemeshow goodness-of-fit test χ2 10.19; p=0.42. AUC = 0.77 (95% CI 0.72-0.82). The ‘Vasopressor’ model included 528 patients of whom 183 died. Pseudo R2=0.11. Hosmer-Lemeshow goodness-of-fit test χ2 2.00; p=1.00. AUC = 0.73 (95% CI 0.68-0.77). Mottling was scored according to Ait-Oufella et al. [19]. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure.

#### eTable 9. Statistically significant predictors of 90-day mortality in patient subgroups

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Odds ratio** | **95% confidence interval** | **P-value** | **Independent contribution %** |
| *Subgroup analysis 1* |  |  | | |
| **No vasopressor** |  | **n = 547; 115 died** | | |
| Age in years | 1.07 | 1.05 - 1.10 | <0.001 | 79.0 |
| Respiratory rate | 1.06 | 1.02 - 1.11 | 0.004 | 7.5 |
| AVPU |  |  |  |  |
| Alert (A) |  | Reference |  | 13.5 |
| Reactive to voice (V) | 1.02 | 0.55 - 1.90 | 0.95 |  |
| Reactive to pain (P) | 4.07 | 1.86 - 8.90 | <0.001 |  |
| Unresponsive (U) | 2.70 | 1.51 - 4.83 | 0.001 |  |
| **Vasopressor** |  | **n = 528; 183 died** | | |
| Age in years | 1.02 | 1.01 - 1.04 | 0.008 | 14.7 |
| Respiratory rate per minute | 1.04 | 1.00 - 1.07 | 0.026 | 7.2 |
| Atrial fibrillation | 2.13 | 1.07 - 4.22 | 0.031 | 8.9 |
| Central temperature per °C decrease | 1.30 | 1.07 - 1.59 | 0.010 | 13.7 |
| AVPU |  |  |  |  |
| Alert (A) | 1.00 | Reference |  | 14.1 |
| Reactive to voice (V) | 0.87 | 0.41 - 1.83 | 0.71 |  |
| Reactive to pain (P) | 1.85 | 0.81 - 4.26 | 0.15 |  |
| Unresponsive (U) | 2.02 | 1.16 - 3.52 | 0.013 |  |
| Urine output per µg∙kg-1∙h-1 decrease | 1.83 | 1.29 - 2.62 | 0.001 | 26.2 |
| Skin mottling severity |  |  |  |  |
| Mild (0-1) | 1.00 | Reference |  | 15.3 |
| Moderate (2-3) | 1.30 | 0.85 - 2.01 | 0.23 |  |
| Severe (4-5) | 3.31 | 1.21 - 9.05 | 0.020 |  |
| *Subgroup analysis 2* |  |  |  |  |
| ***Septic shock*** |  |  |  | *n = 147; 58 died* |
| Age in years | 1.04 | 1.01 - 1.07 | 0.005 | 52.7 |
| Skin mottling over the knee | 3.22 | 1.31 - 7.94 | 0.011 | 47.3 |
| ***Acute liver failure or post OLT*** | *Too few events*  *Too few events*  *Too few events* | |  | *n = 54; 15 died* |
| ***Cardiac arrest*** |  | *n = 96; 36 died* |
| ***CNS pathologies*** |  | *n = 142; 39 died* |
| ***Heart failure*** | *Too few events* | |  | *n = 63; 25 died* |

The ‘Septic shock’ model included 147 patients of whom 58 died. Pseudo R2=0.12. Hosmer-Lemeshow goodness-of-fit test χ2 6.64; p=0.759. Area under the receiver-operating curve = 0.69 (95% CI 0.60-0.77). Abbreviations: OR, odds ratio; CI, confidence interval; CNS, central nervous system; OLT, orthotopic liver transplantation.