Supplemental digital content to

Biomarkers improve diagnostics of sepsis in adult patients with suspected organ dysfunction based on the qSOFA score in the emergency department – results from the prospective observational LifePOC study

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LASSO regression

LASSO (least absolute shrinkage and selection operator) is a regression analysis method which performs variable selection in order to minimize the prediction error. This is achieved by imposing a constraint on the model parameters shrinking the regression coefficients towards zero, that is by forcing the sum of the absolute value of the regression coefficients to be less than a fixed value λ. Considering a linear regression with p potential predictors x_{ij} and outome values y_i for i=1,…,n and j=1,…,p the LASSO algorithm performs the minimization of

$\sum_{i=1}^{n}\left(y_i - \sum_{j=1}^{p} x_{ij}\beta_j\right)^2 + \lambda \sum_{j=1}^{p}|\beta_j|$, (Tibshirani, R. (2011))

For binary outcomes (sepsis, septic shock) a logit link function was applied in the model. Variables with a regression coefficient $ß_j$ of zero after shrinkage are excluded from the model. In this way the complexity of the model will be reduced, including only the variables that are predictive for the outcome variable. Reducing the number of variables in the final model also prevents the issue of overfitting. Traditional approaches like stepwise selection methods (e.g. backward elimination and forward selection procedures) are also capable of identifying a subset of relevant variables, however, the resulting final model depends on the order of the variables which are entered or removed. In LASSO regression all potential variables are entered simultaneously, which avoids this problem and therefore should be preferred for variable selection instead of conventional approaches. (Greenwood, C. J. (2020)).

Tibshirani, R. (2011): Regression Shrinkage and Selection via The Lasso: A Retrospective. Journal of the Royal Statistical Society Series B: Statistical Methodology, Volume 73, Issue 3, June 2011, 273–282.

Greenwood, C. J. et al. "A comparison of penalised regression methods for informing the selection of predictive markers." PloS one 15.11 (2020): e0242730.

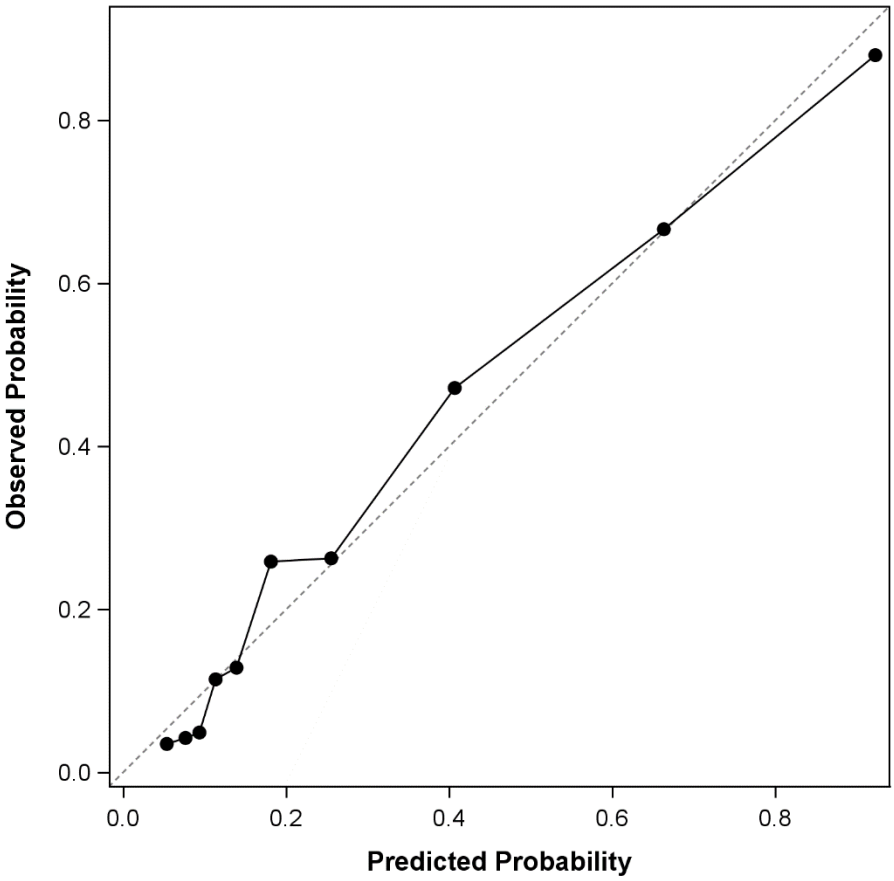
eTable 1: Conversion tables for imputation of respiratory SOFA score with SpO_2/FiO_2 ratios

Conversion table for calculating the oxygenation index

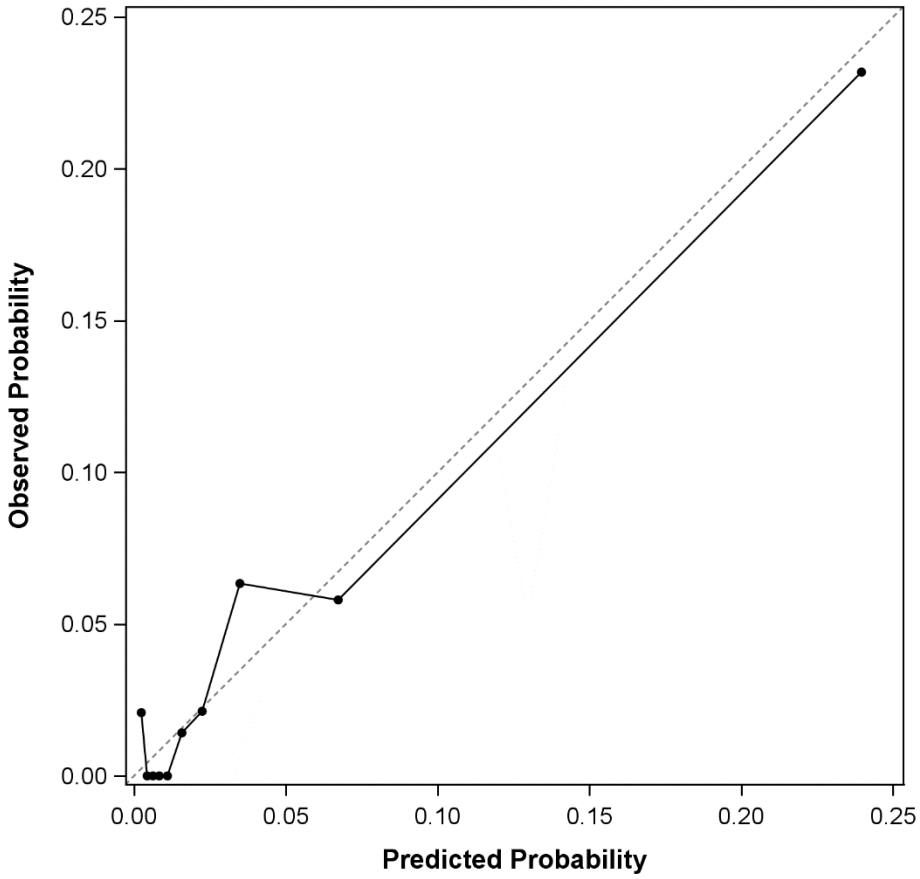
O_2 saturation conversion table	
SpO_2 (%)	**Calculated arterial PO_2 (mmHg)**
80	44
81	45
82	46
83	47
84	49
85	50
86	52
87	53
88	55
89	57
90	60
91	62
92	65
93	69
94	73
95	79
96	86
97	96
98	112
99	145

FiO_2 during oxygen therapy

Method	O_2-Flow	Estimated FiO_2
Nasal cannula	1	0,24
	2	0,28
	3	0,32
	4	0,36
	5	0,40
	6	0,44
Nasopharyngeal catheter	4	0,40
	5	0,50
	6	0,60
Facial mask	5	0,40
	6–7	0,50
	7–8	0,60
Facial mask with reservoir	6	0,60
	7	0,70
	8	0,80
	9	0,90
	10	0,95

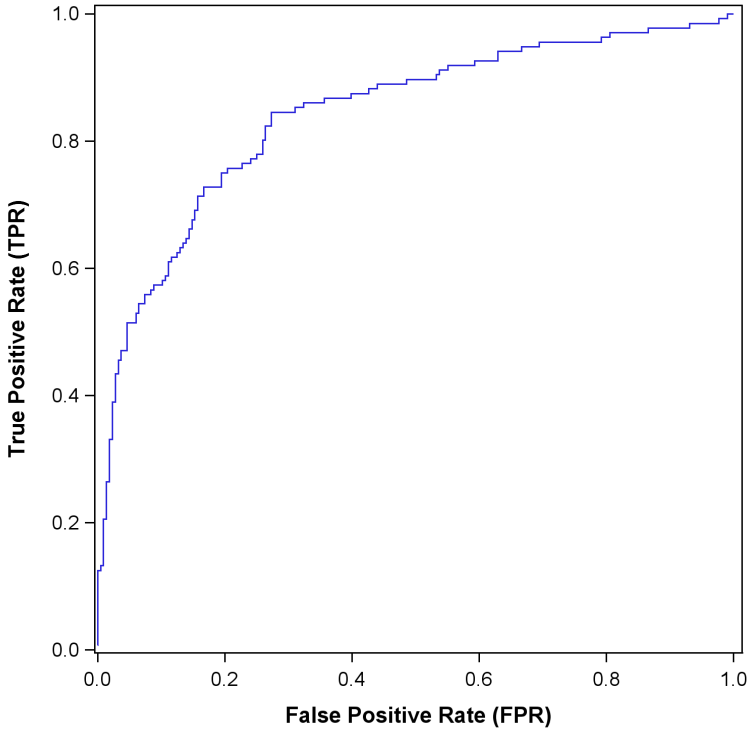


eFigure 1: Calibration of the model including PCT as a predictor of sepsis within 96h, comparison of predicted probabilities (deciles) and observed probabilities

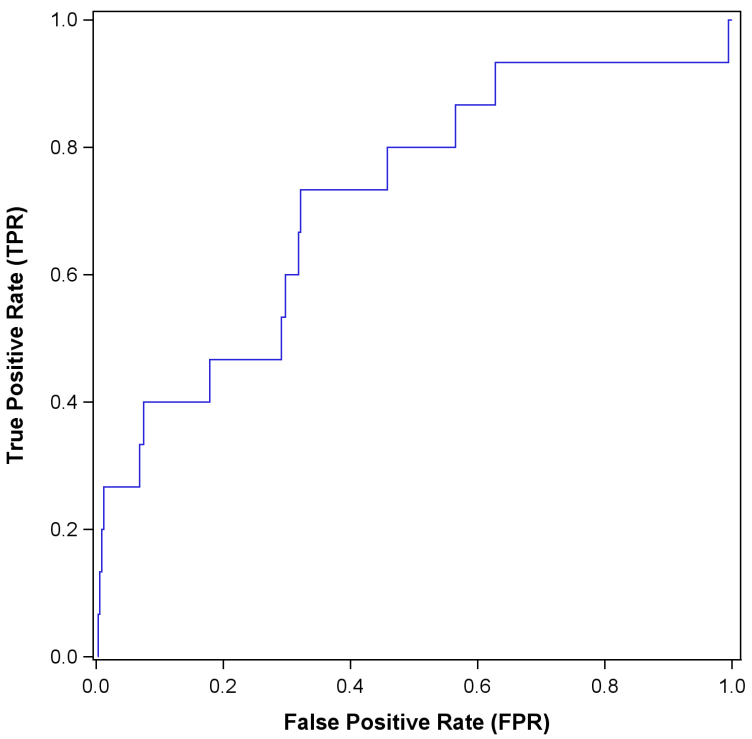


eFigure 2: Calibration of the model including PCT as a predictor of septic shock within 96h, comparison of predicted probabilities (deciles) and observed probabilities

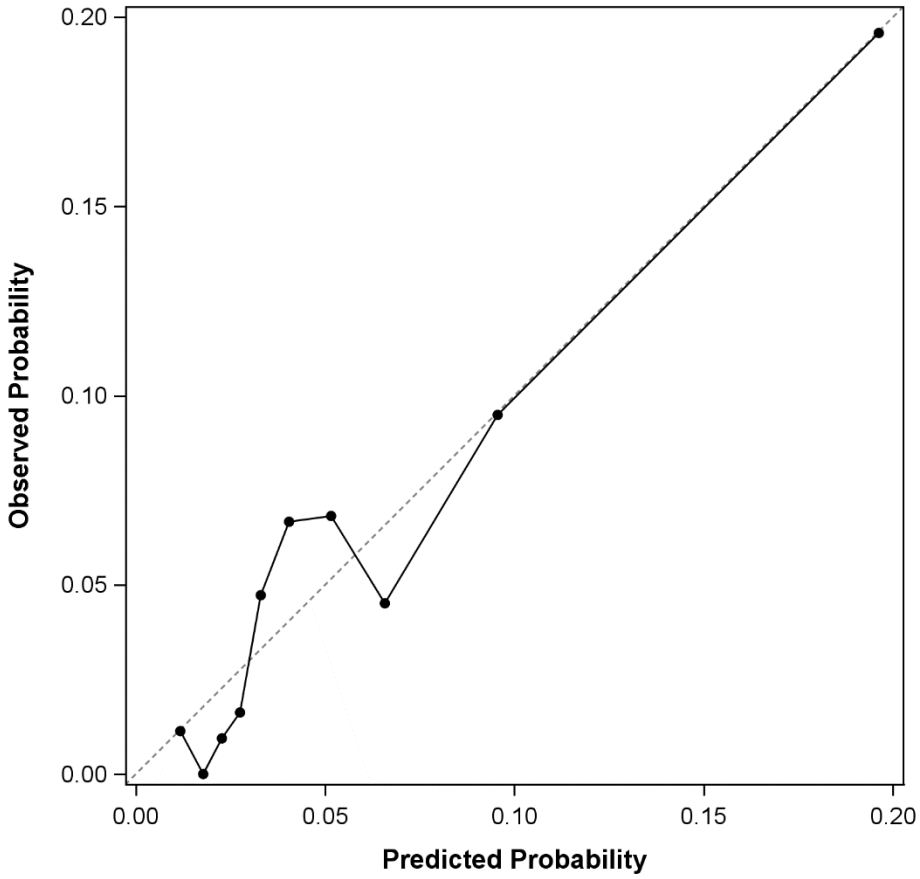
(A)



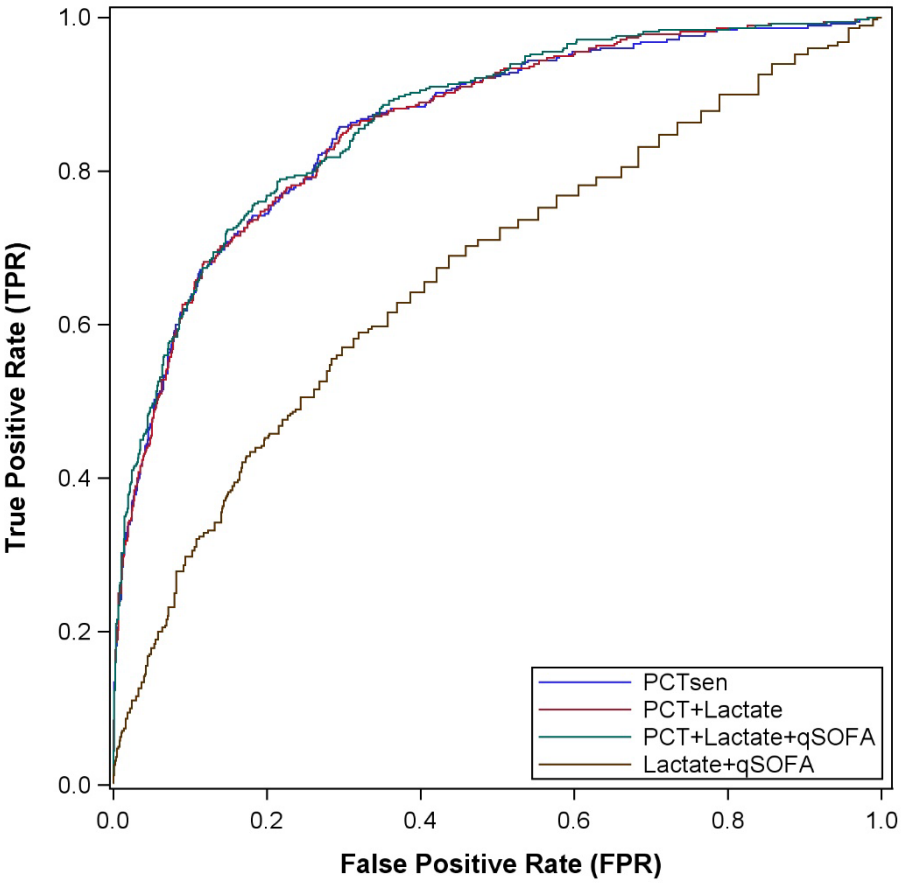
(B)



eFigure 3: Subgroup ROC analysis (immunocompromised patients). **(A)** AUC of PCT for the primary endpoint sepsis within 96h. **(B)** AUC of combined predictors PCT and proADM for the secondary endpoint septic shock 96h.



eFigure 4: Calibration of the model including PCT as a predictor of hospital admission, comparison of predicted probabilies (deciles) and observed probabilities



eFigure 5: ROC Analysis – AUC of PCT and/or Lactate to qSOFA for the primary endpoint sepsis within 96h