A machine learning-derived, blood count based algorithm improves prediction of sepsis

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Overview

Sepsis Prediction and Clinical Decision Support

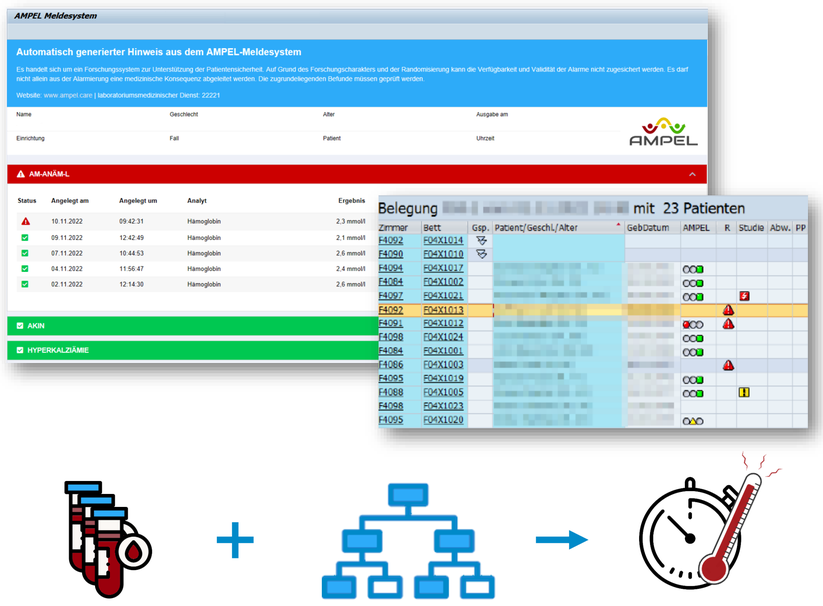


Figure 1: Integration of sepsis early detection into the Clinical Decision Support System "AMPEL"

Introduction

Delay in diagnosing sepsis results in potentially preventable deaths. Mainly due to their complexity or limited applicability, machine learning models to predict sepsis have not yet become part of clinical routines. For this reason, we created a machine learning model that only requires complete blood count (CBC) diagnostics.

Methods

Non-intensive care unit (non-ICU) data from a German tertiary care centre were collected from January 2014 to December 2021. Patient age, sex, and CBC parameters (haemoglobin, platelets, mean corpuscular volume, white and red blood cells) were utilised to train a boosted random forest, which predicts sepsis with ICU admission. Two external validations were conducted using data from the Greifswald University Hospital and the Medical Information Mart for Intensive Care IV database (MIMIC-IV). Using a subset of laboratory data including also procalcitonin, an analogous model was trained with procalcitonin as an additional feature.

Results

After exclusion, 1,381,358 laboratory requests (2016 from sepsis cases) were available. The derived CBC model shows an area under the receiver operating characteristic (AUROC) of 0.872 [CI: 0.857–0.887] for predicting sepsis. External validations show AUROCs of 0.805 [CI: 0.787–0.824] for the Greifswald University Hospital and 0.845 [CI: 0.837–0.852] for MIMIC-IV. The model including procalcitonin revealed a significantly higher performance [AUROC: 0.857; CI: 0.836–0.877] than procalcitonin alone [AUROC: 0.790; CI: 0.759–0.821; p<0.001]. Thus, the CBC model can facilitate early sepsis prediction in non-ICU patients with high robustness in external validations

Clinical Validation in Emergency Department

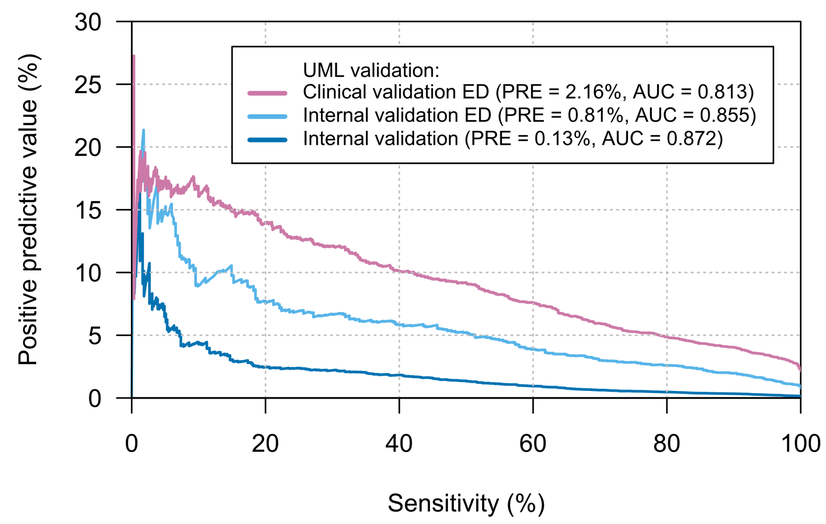


Figure 2: The positive predictive value in dependence of sensitivity for different cohorts.

UML: University of Leipzig Medical Centre; ED: emergency department; PRE: prevalence; AUC: area under the receiver operating characteristic

Validation & Comparison to WBC and PCT

Validation Datasets

Characteristic	Overall	UMLT	UMLV	UMG	MIMIC-IV
General					
N (control cases)	1,421,497	527,038 (37.1)	180,157 (12.7)	157,680 (11.1)	556,622 (39.2)
N (sepsis cases)	4,911	1,488 (30.3)	472 (9.6)	438 (8.9)	2,513 (51.2)
- Age	68 (58 – 79)	67 (57 – 76)	68 (59 – 78)	69 (58 – 78)	69 (58 – 81)
- Male	2,961 (60.3)	938 (63.0)	310 (65.7)	278 (63.5)	1,435 (57.1)
- Female	1,950 (39.7)	550 (37.0)	162 (34.3)	160 (36.5)	1,078 (42.9)
Sepsis Laboratory Diagnostics					
HGB [mmol/l]	6.8 (5.5 – 7.9)	7.1 (5.6 – 8.3)	6.8 (5.5 – 8.4)	6.9 (5.6 – 8.1)	6.6 (5.5 – 7.6)
MCV [fl]	91.0 (86.0 – 96.8)	88.6 (84.2 – 93.5)	90.1 (85.3 – 95.9)	90.7 (86.3 – 96.3)	93.0 (88.0 – 98.0)
PLT [Gpt/l]	199.0 (123.2 – 290.0)	194.5 (113.0 – 287.0)	204.0 (125.2 – 292.0)	193.5 (106.0 – 275.2)	201.0 (131.0 – 294.0)
RBC [Tpt/l]	3.7 (3.0 – 4.3)	3.9 (3.1 – 4.5)	3.7 (2.9 – 4.5)	3.8 (3.0 – 4.4)	3.6 (3.0 – 4.2)
WBC [Gpt/l]	12.9 (8.2 – 18.6)	13.1 (7.8 – 18.8)	12.7 (8.3 – 18.0)	12.1 (7.7 – 17.7)	13.0 (8.5 – 18.8)

Table 1: Baseline characteristics of all datasets

n (%) or Median (IQR); UMLT: University of Leipzig Medical Center (Training Set); UMLV: University of Leipzig Medical Center (Validation Set); UMG: University Medicine Greifswald; MIMIC: Medical Information Mart for Intensive Care IV database; HGB: haemoglobin; MCV: mean corpuscular volume; PLT: platelets; RBC: red blood count; WBC: white blood count.

AUROC: External Validation & Procalcitonin Comparison

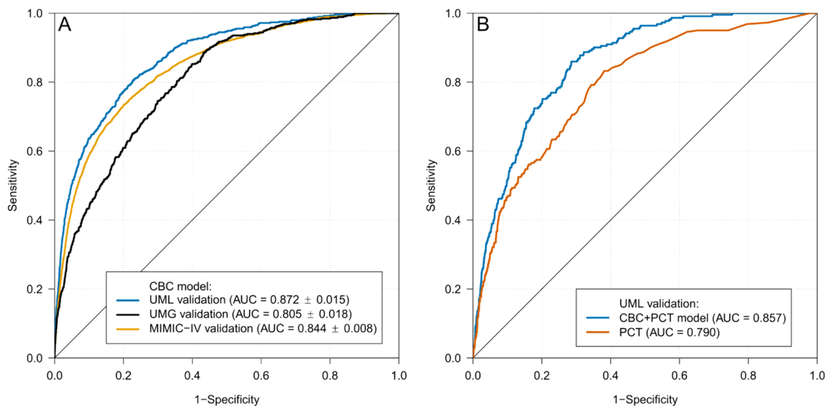


Figure 3: ROC Curves of the CBC Model for Internal and External Validation Data and the Comparison of the CBC Model Including PCT as Feature to PCT Alone

ROC: receiver operating characteristic; AUC: area under the receiver operating characteristic CBC: complete blood count; UML: University Medicine Leipzig; UMG: University Medicine Greifswald; MIMIC-IV: Medical Information Mart for Intensive Care IV database; PCT: procalcitonin

To evaluate the performance of the CBC model in comparison to the sepsis biomarker PCT, data from 17,898 cases with 24,125 simultaneous measurements of CBC and PCT, including 425 sepsis cases with 425 measurements, could be extracted from the UMLT dataset. The difference between both predictors is statistically significant (p<0.001, DeLong test).

White Blood Count Comparison

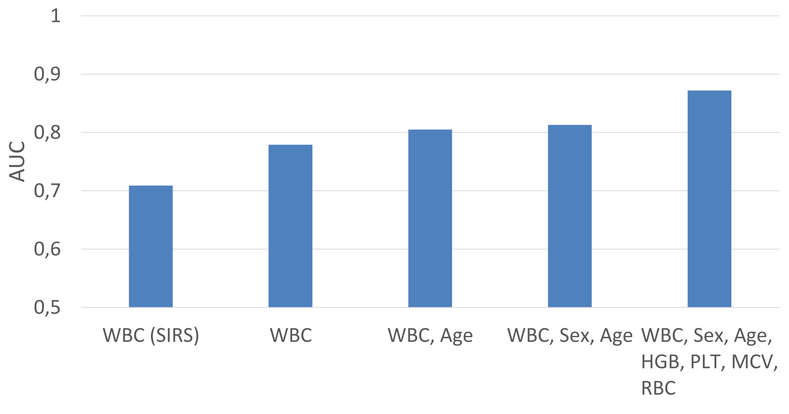


Figure 4: Comparison of AUCs of the SIRS WBC Classification and CBC Models with Different Features

AUC: area under the receiver operating characteristic; SIRS: systemic inflammatory response syndrome; CBC: complete blood count; WBC: white blood count; HGB: haemoglobin; PLT: platelets; MCV: mean corpuscular volume; RBC: red blood count

Due to the non-linear indicator WBC – where both very low and high values can indicate inflammation – we refrained from conducting logistic regression. Instead, we chose to use the same random forest method as in the training of the CBC model.

Importance of Laboratory Parameters[1]

White Blood Count Influence on Sepsis Classification

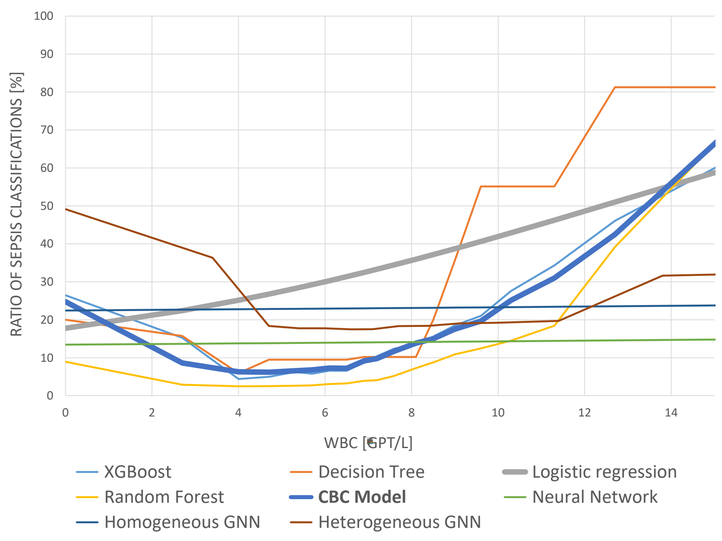


Figure 5: Feature Variation Graph for White Blood Count

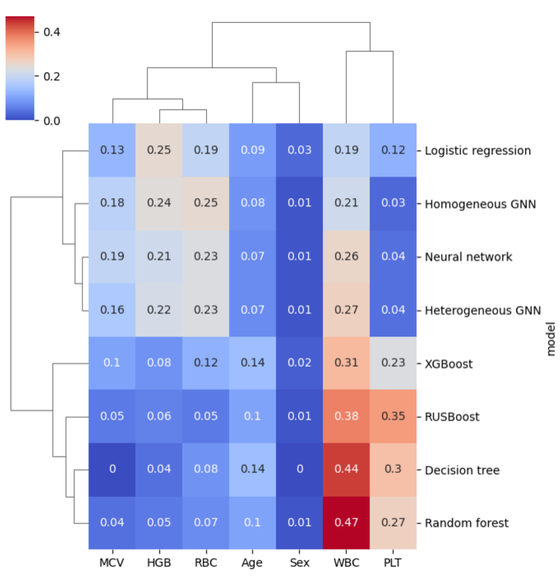
The graph illustrates the proportion of sepsis classifications relative to all classifications generated by various machine learning models. Tree-based algorithms tend to classify data points with extremely low or high white blood count (WBC) counts as sepsis cases, whereas non-tree-based algorithms (e.g. logistic regression) fail to identify this particular pattern. Notably, non-tree-based heterogeneous Graph Neural Networks (GNNs) stand out as an exception. The performance of GNNs will be further discussed in the work by Walke et al[1].

Figure 6: Heatmap of Feature Importance

A synthetic dataset was generated by creating 20 variations for each feature from the minimum value to the maximum value of the features' original values. Combining each feature variation a dataset with $2*20^6$ synthetic complete blood counts was used to score feature importance. High values and red colors display high importance.

[1]Daniel Walke; Daniel Steinbach; Sebastian Gibb; Thorsten Kaiser; Gunter Saake; Paul C. Ahrens; David Broneske; Robert Heyer: Edges are all you need: Potential of Medical Time Series Analysis with Graph Neural Networks. [in submission]

Feature Importance



Preprint: „Applying Machine Learning to Blood Count Data Predicts Sepsis with ICU Admission"
Paul C. Ahrens, Daniel Steinbach, Maria Schmidt, Martin Federbusch, Lara Heuft, Christoph Lübbert, Matthias Nauck, Matthias Gründling, Berend Isermann, Sebastian Gibb, Thorsten Kaiser; medRxiv 2022.10.21.22281348; https://doi.org/10.1101/2022.10.21.22281348

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