**Supplementary Text**

**Abbreviations**

CLABSI: central line-associated bloodstream infection

LCBI: laboratory confirmed bloodstream infection

MPC score: Michigan peripherally inserted central catheter-associated bloodstream infections score

PBSI: Peripherally inserted central venous catheter-associated bloodstream infection

PICC: Peripherally inserted central venous catheter

**Supplementary Methods**

This report follows a framework proposed to enhance the interpretation of external validation studies1 and conforms to the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) statement.2

*PICC catheterization*

Dedicated vascular access nurses performed PICC catheterization using a 60-cm, 4-Fr single-lumen catheter (Groshong; Becton, Dickinson and Company, Franklin Lakes, NJ) or a 55-cm, 5-Fr double- or triple-lumen catheter (Power PICC; Becton, Dickinson and Company, Franklin Lakes, NJ) at the request of the physicians in charge. Catheterization was performed under maximal sterile barrier precautions with ultrasound guidance according to the standard procedure guidelines. The puncture site was strictly disinfected with 2% chlorhexidine. The catheter tip was placed in the optimal part of the superior vena cava, which was confirmed by fluoroscopy or chest radiography. Post-PICC placement care followed a standardized clinical care protocol for PICCs, which were stabilized using a catheter stabilization device (StatLock; Becton, Dickinson and Company, Franklin Lakes, NJ) and dressed in sterile film. Routine disinfection of the puncture site and dressing change was performed weekly and more frequently if needed. All patients were followed up until the PICC was removed or developed PBSI.

*Predictors*

Predictors of PBSI (points assigned by the score3) included (1) past/present history of hematological malignancy vs. none (3 points); (2) CLBSI history within 3 months of PICC insertion vs. none (2 points); (3) active cancer with receipt of chemotherapy (2 points); (4) multi-lumen PICC vs. single-lumen PICC (2 points); (5) presence of another CVC upon PICC placement vs. none (1 point); and (6) receipt of TPN through the PICC vs. none (1 point). All predictors were extracted from the hospital PICC database, except for two items, namely CLBSI history and presence of another CVC upon PICC placement, the data for which were retrospectively collected by the first author from the microbiology database and medical records. No data were missing.

*Outcome*

Following the National Healthcare Safety Network (NHSN) Laboratory Confirmed Bloodstream Infection (LCBI) Checklist,4 PBSIs were defined as blood stream infections that satisfied the LCBI-2 criterion. Specifically, the LCBI-2 criterion required that all of the following three conditions be present: (1) ≥1 index clinical signs/symptoms—fever (>38.0 ℃), chills, or hypotension; (2) organism(s) identified in the blood being unrelated to an infection at another site; and (3) detection of an identical NHSN-defined common commensal through culture from multiple blood specimens collected on separate occasions. The first author, not blinded to the MPC score, assessed the linked microbiology data to confirm all PBCI events.

*Sample size*

Despite targeting a minimum sample size of 100 events, our available cohort had only 89 events, meagerly satisfying a smaller threshold of >50, for which experts recommend more events approaching 100.5

*Statistical analysis*

All variables were descriptively analyzed as means and standard deviations (SDs) or medians and interquartile ranges (IQRs) depending on their distribution or as numbers and percentages. We estimated the 95% confidence intervals (CIs) of proportions using the standard method.

This study followed the recommended framework for external validation of a Cox prognostic model.6 The Harrell’s *C*-statistic7 and Gönen and Heller’s *K* statistic8 were used as measures of concordance, whereas the Royston–Sauerbrei *D* statistic (*R2D*)9 was used as a measure of variation. To visualize the extent of discrimination, the proportion of observed PBSIs were plotted using the Kaplan–Meier method.

To examine calibration, we estimated the regression coefficient of the linear predictor (i.e., linear combination of a set of coefficients and predictive variables) on the original MPC score in the Cox model as the calibration slope and assessed its model fit.6 To visualize the calibration, the following two approaches were performed: First, the model-derived predicted mean event curves 3,10 were visually compared to the Kaplan–Meier curves for the observed events. We fitted a Weibull proportional hazards model using the reported CLABSI rates at days 6, 10, 21, and 28 of PICC placement in the original cohort3 to obtain the predicted mean event curves. Standard linear regression was used to approximate the slope and intercept for the log baseline cumulative hazard function,10 with which the baseline survival model was obtained as log(−log(S0(t))) = −5.322 + 1.025 × log(t). Second, we constructed the standard calibration plots, which were presented at 10, 21, and 28 days after PICC placement.

To update the original MPC score, the baseline hazard function11 was recalibrated using the Royston–Parmar flexible parametric survival models.12 We specified 2 (selected among 1 to 5) degrees of freedom for the restricted cubic spline based on the lowest Akaike information criterion/Bayesian information criterion (AIC/BIC), and selected the generalized Weibull proportional hazards model on the log cumulative hazard based on the comparable AIC/BIC across the alternative flexible parametric models (i.e., generalized proportional hazard, loglogistic, and probit-scaled Royston-Parmer models).12 Through this approach, we obtained the baseline survival model as log(−log(S0(t))) = −3.916 + 1.684 × log(t) + 0.416 × *z*, where *z* was the basis function created for the restricted cubic spline for log time.12

Thereafter, we visually compared the updated predicted mean event curves with the Kaplan–Meier curves. Additionally, the standard calibration plots were constructed.

To compare among strategies based on the original or updated MPC score and among default management strategies (i.e., some interventions to prevent PBSIs for all and no intervention for all), decision curve analysis was conducted.13 We estimated the difference between the proportion of “true positives” (i.e., appropriate implementation of interventions for patients who developed PBSI) and the proportion of “false positives” (i.e., unnecessary implementation of interventions for patients who did not develop PBSI) as the net benefit, weighted by the odds of provider and/or patient preference regarding whether or not to implement the interventions.14

Our main analysis used the original MPC score and grouped patients into seven risk categories according to the total points (i.e., 0, 1, 2, 3, 4, 5, and ≥6 points).3 During sensitivity analyses, the linear predictor with the originally reported coefficients was used to calculate the prognostic index, which was used to categorize patients into five equal-sized risk groups. To depict the predicted mean event curves, we *post-hoc* selected five values (i.e., 0, 1, 2, 3, and 4) from the prognostic index based on the distribution of the observed values. Planned subgroup analyses according to admitted departments were not performed due to the limited PBSI events.

All statistical analyses were performed using Stata SE version 17.1 (Stata Corp, College Station, TX, USA). To obtain cluster-robust standard errors during repeated observations, a clustered sandwich estimator was used. All analyses used two-tailed P values with the level of significance set at <0.05.

**Supplementary Tables**

**Supplementary Table 1.** Confirmed pathogens causing peripherally inserted central catheter-associated bloodstream infections

|  |  |
| --- | --- |
| Pathogen | Number of Infections (*n*=89) (%) |
| **Gram-positive bacteria** | 60 (67.4) |
| Methicillin-resistant *Staphylococcus aureus* | 10 (11.2) |
| Methicillin-susceptible *Staphylococcus aureus* | 3 (0.3) |
| Coagulase-negative staphylococci | 44 (49.4) |
| *Enterococcus* species | 3 (0.3) |
| **Gram-negative bacteria** | 14 (15.7) |
| *Escherichia coli* | 5 (5.6) |
| *Klebsiella pneumoniae* | 4 (4.5) |
| *Acinetobacter* species | 1 (1.1) |
| *Pseudomonas aeruginosa* | 4 (4.5) |
| **Candida species** | 15 (16.9) |

**Supplementary Table 2.** Discrimination measures and hazard ratios between risk groups.

|  |  |  |  |
| --- | --- | --- | --- |
| Original MPC scoreEstimates followed by 95% CI | P-value | Prognostic index based on the original linear predictorEstimates followed by 95% CI | P value |
| Calibration slope | 1.16 | 1.02 to 1.32 | 0.024 | Calibration slope | 1.50 | 1.17 to 1.93 | 0.001 |
| Model Misspecification Chi2 | 5.13 |  | <0.001 | Model Misspecification Chi2 | 29.6 |  | <0.001 |
| Harrell *C*-index | 0.608 | 0.543 to 0.673 |  | Harrell *C*-index | 0.610 | 0.542 to 0.678 |  |
| Gonen & Heller *K* | 0.544 | 0.507 to 0.580 |  | Gonen & Heller *K* | 0.569 | 0.520 to 0.614 |  |
| Explained variation, R2*D* | 0.039 | 0.003 to 0.108 |  | Explained variation, R2*D* | 0.052 | 0.007 to 0.130 |  |
| Log-rank test, Chi2 | 11.66 |  | 0.11 | Log**-**rank test, Chi2 | 14.5 |  | 0.006 |
|  |  |  |  |  |  |  |  |
| Risk groups (*n*) | HRs | 95% CI |  | Quintiles (*n*) | HRs | 95%CI |  |
| 0 points (332) | – | – |  | Q1 (292) | – | – |  |
| 1 point (642) | 2.65 | 1.29 to 5.45 |  | Q2 (292) | 3.03 | 1.27 to 7.18 |  |
| 2 points (296) | 2.82 | 1.24 to 6.37 |  | Q3 (292) | 2.80 | 1.15 to 6.82 |  |
| 3 points (109) | 3.18 | 1.24 to 8.13 |  | Q4 (292) | 2.21 | 0.87 to 5.64 |  |
| 4 points (43) | 3.48 | 1.14 to 10.7 |  | Q5 (291) | 3.94 | 1.66 to 9.35 |  |
| 5 points (32) | 1.52 | 0.31 to 7.51 |  |  |  |  |  |
| ≥6 points (5) | 4.61 | 0.94 to 22.5 |  |  |  |  |  |

CI, confidence interval; HR, hazard ratio; PI, prognostic index; Q, quartile

**Supplementary Figures**



**Supplementary Figure 1.** Distribution of the MPC scores (left) and prognostic indexes calculated using the linear predictor (right).

MPC score, Michigan peripherally inserted central catheter-associated bloodstream infections score; PBSI, peripherally inserted central catheter-associated bloodstream infection.



**Supplementary Figure 2.** Calibration plots of the original MPC score.

Calibration plots with 95% confidence intervals (indicated in green open circles with vertical lines) of the original MPC score applied in the validation cohort. The dashed diagonal line represents perfect calibration. A smooth calibration line with locally weighted scatterplot smoothing was shown in red. Plots shown are at 10, 21, and 28 days (A, B, and C, respectively) after peripherally inserted central catheter placement.

MPC score, Michigan peripherally inserted central catheter-associated bloodstream infections score; PBSI, peripherally inserted central catheter-associated bloodstream infection.



**Supplementary Figure 3.** Calibration plots of the updated MPC score.

Calibration plots with 95% confidence intervals (indicated in green open circles with vertical lines) and the spike plot for events (indicated in red; 1 = PBSI development; 0 = no PBSI development) of the updated MPC score applied in the validation cohort. The dashed diagonal line represents perfect calibration. Plots shown are at 10, 21, 28, and 70 days (A, B, C, and D, respectively) after peripherally inserted central catheter placement.

MPC score, Michigan peripherally inserted central catheter-associated bloodstream infections score; PBSI, peripherally inserted central catheter-associated bloodstream infection.



**Supplementary Figure 4.** Decision curve analysis.

The plotted lines denote intervention for none (assuming no PBSI event for all; solid red line), intervention for all (assuming a PBSI development for all; solid dark green line), and the original (solid brown line) and updated (solid navy line) MPC score model-guided interventions. The preferred strategy is the model with the highest net benefit at any given threshold probability (the corresponding odds in the parenthesis). Plots shown are at 10, 21, 28, and 70 days (A, B, C, and D, respectively) after peripherally inserted central catheter placement.

MPC score, Michigan peripherally inserted central catheter-associated bloodstream infections score; PBSI, peripherally inserted central catheter-associated bloodstream infection.



**Supplementary Figure 5.** Observed and predicted PBSI event curves.

Kaplan-Meier plots for the observed PBSI events (left panel) and predicted mean event curves for the PI calculated with the linear predictor of the updated MPC score (right panel). The curves are color-coded per the 1st to 5th quintile groups (mean calculated PI for each group in the parenthesis).

MPC score, Michigan peripherally inserted central catheter-associated bloodstream infections score; PBSI, peripherally inserted central catheter-associated bloodstream infection; PI, prognostic index



**Supplementary Figure 6.** Calibration plots of the PI calculated using the updated MPC score.

Calibration plots with 95% confidence intervals (indicated in green open circles with vertical lines) and the spike plot for events (indicated in red; 1 = PBSI development; 0 = no PBSI development) of the PI calculated using the linear predictor of the updated MPC score applied in the validation cohort. The dashed diagonal line represents perfect calibration. Plots shown are at 10 days, 21 days, 28 days, and 70 days after peripherally inserted central catheter.

MPC score, Michigan peripherally inserted central catheter-associated bloodstream infections score; PBSI, peripherally inserted central catheter-associated bloodstream infection; PI, prognostic index



**Supplementary Figure 7.** Decision curve analysis.

The plotted lines denote intervention for none (assuming no PBSI event for all; solid red line), intervention for all (assuming a PBSI development for all; solid dark green line), and the updated (solid navy line) MPC score model-guided intervention. The PIs calculated using the linear predictor of the updated MPC score were used instead of the MPC scores. The preferred strategy is the model with the highest net benefit at any given threshold probability (the corresponding odds in the parenthesis). Plots shown are at 10 days, 21 days, 28 days, and 70 days after peripherally inserted central catheter.

MPC score, Michigan peripherally inserted central catheter-associated bloodstream infections score; PBSI, peripherally inserted central catheter-associated bloodstream infection; PI, prognostic index

**Supplementary Appendix**

1. Debray TP, Vergouwe Y, Koffijberg H, Nieboer D, Steyerberg EW, Moons KG. A new framework to enhance the interpretation of external validation studies of clinical prediction models. *J Clin Epidemiol.* 2015;68(3):279-289.

2. Collins GS, Reitsma JB, Altman DG, Moons KGM. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD Statement. *BMC Medicine.* 2015;13(1):1.

3. Herc E, Patel P, Washer LL, Conlon A, Flanders SA, Chopra V. A Model to Predict Central-Line-Associated Bloodstream Infection Among Patients With Peripherally Inserted Central Catheters: The MPC Score. *Infect Control Hosp Epidemiol.* 2017;38(10):1155-1166.

4. National Healthcare Safety Network (NHSN). Bloodstream Infection (BSI) Events. 2021. <https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc_clabscurrent.pdf>. Published Jan 2021. Accessed August 19, 2021.

5. Collins GS, Ogundimu EO, Altman DG. Sample size considerations for the external validation of a multivariable prognostic model: a resampling study. *Statistics in Medicine.* 2016;35(2):214-226.

6. Royston P, Altman DG. External validation of a Cox prognostic model: principles and methods. *BMC Med Res Methodol.* 2013;13:33.

7. Harrell FE, Jr, Califf RM, Pryor DB, Lee KL, Rosati RA. Evaluating the Yield of Medical Tests. *JAMA.* 1982;247(18):2543-2546.

8. Gönen M, Heller G. Concordance probability and discriminatory power in proportional hazards regression. *Biometrika.* 2005;92(4):965-970.

9. Royston P, Sauerbrei W. A new measure of prognostic separation in survival data. *Stat Med.* 2004;23(5):723-748.

10. van Houwelingen HC. Validation, calibration, revision and combination of prognostic survival models. *Stat Med.* 2000;19(24):3401-3415.

11. Steyerberg EW. *Clinical Prediction Models: A Practical Approach to Development, Validation, and Updating.* Springer International Publishing; 2019.

12. Royston P, Lambert PC. *Flexible Parametric Survival Analysis Using Stata: Beyond the Cox Model.* Stata Press; 2011.

13. Vickers AJ, Elkin EB. Decision curve analysis: a novel method for evaluating prediction models. *Med Decis Making.* 2006;26(6):565-574.

14. Vickers AJ, Van Calster B, Steyerberg EW. Net benefit approaches to the evaluation of prediction models, molecular markers, and diagnostic tests. *Bmj.* 2016;352:i6.