Supplementary material

Manuscript No. 125117

Development and internal validation of a disease-free survival model after radical resection of pT4 colorectal adenocarcinoma

Supplementary Table 1 Parameters for individual risk prediction

Term	Coefficient	Centering mean
ln(CA19-9 + 1)	0.122032085	2.412347192
Female vs male	0.309278188	0.425000000
ASA III or higher vs ASA I-II	0.472620314	0.165909091
Preoperative bowel obstruction: yes vs no	0.423322077	0.054545455
Poor vs moderate/well differentiation	0.386837988	0.170454545
Lymphovascular invasion: positive vs negative	0.249850024	0.368181818
pN1 vs pN0	0.565960386	0.406818182
pN2 vs pN0	0.696416405	0.240909091

Binary terms are coded 1 when present and 0 otherwise; both pN indicators are 0 for pN0. ln denotes the natural logarithm.

LP = sum[coefficient × (value - centering mean)]. DFS event risk at time t = 1 - S0(t)^exp(LP), where S0(36) = 0.780891353187 and S0(60) = 0.617542894398. Time is measured in months.

Supplementary Table 2 Apparent calibration at 36 and 60 months

Months	Quantity	Estimate	95%CI
36	Calibration intercept	0.077	-0.339 to 0.522
36	Calibration slope	1.064	0.736 to 1.417
60	Calibration intercept	0.290	-0.049 to 0.751
60	Calibration slope	1.339	0.893 to 1.947

IPCW complementary-log-log recalibration jointly estimated intercept and slope (ideal: 0 and 1); 95% confidence intervals used 1000 bootstrap resamples with predictions fixed. IPCW: Inverse probability of censoring weighting. AUCs and decision curves used inverse-probability-of-censoring weights based on Kaplan-Meier estimates of the censoring distribution. AUC confidence intervals used 1000 resamples with predictions fixed and censoring weights re-estimated.

Supplementary Table 3 Proportional hazards diagnostics

Final term	Rank transformed Schoenfeld test P
ln(CA19-9 + 1)	0.945
Female vs male	0.321
ASA III or higher vs ASA I-II	0.051
Preoperative bowel obstruction: yes vs no	0.302
Poor vs moderate/well differentiation	0.733
Lymphovascular invasion: positive vs negative	0.009
pN1 vs pN0	0.346
pN2 vs pN0	0.965

P values are from term-specific rank-transformed Schoenfeld tests.

Supplementary Table 4 Selection stability of the final model terms

Final model term	Selection frequency
ln(CA19-9 + 1)	86.8%
Female vs male	63.8%
ASA III or higher vs ASA I-II	83.2%
Preoperative bowel obstruction: yes vs no	59.4%
Poor vs moderate/well differentiation	72.0%
Lymphovascular invasion: positive vs negative	74.2%
pN1 vs pN0	56.0%
pN2 vs pN0	83.2%

Selection frequencies were calculated from 500 bootstrap LASSO fits at the fixed original penalty (0.0511788955).

Supplementary Table 5 Paired differences in model discrimination

Comparison	Measure	Difference	95%CI
Proposed model minus TNM-only comparator	C-index	0.061	0.026 to 0.096
	AUC 36 months	0.083	0.035 to 0.133
	AUC 60 months	0.175	0.113 to 0.238
Proposed model minus model without pN2	C-index	0.016	-0.006 to 0.039
	AUC 36 months	0.005	-0.024 to 0.037
	AUC 60 months	-0.012	-0.050 to 0.030

Differences and 95% confidence intervals used 1000 paired bootstrap resamples with predictions fixed. The TNM-only comparator includes pT4 subtype and pN stage. Omitting the pN2 indicator groups pN2 with pN0 as the reference in the diagnostic refit. AUC: Area under the receiver operating characteristic curve.