Paper 6

A NOVEL ALGORITHM TO PREDICT TREATMENT RESPONSE AFTER TOTAL NEOADJUVANT THERAPY FOR LOCALLY ADVANCED RECTAL CANCER

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Background

Patient selection for watch-and-wait (W/W) after total neoadjuvant therapy (TNT) for locally advanced rectal cancer remains challenging. We developed a predictive model for pathological complete response (pCR) after TNT to inform selection for W/W strategies.

Methods

A tabular foundation model was fine-tuned with ensemble learning in a cohort of adult patients with clinical stage II or III microsatellite stable rectal adenocarcinoma undergoing TNT and total mesorectal excision (TNT+TME) from 2018-2023 to predict pCR using pre-TNT, post-TNT and pre-TME variables. This model was externally validated in patients having TNT and W/W (TNT+W/W) to predict persistent clinical complete response (pcCR; the absence of local regrowth, distant metastases, or persistent near-cCR). Area under the receiver operator curve (AUROC), area under the precision-recall curve (AUPRC), and Brier score are reported with 95% confidence intervals (CI) from 1000 bootstrap resamples.

Results

Among 308 patients that underwent TNT+TME (median age 56; 40% female), the model predicted pCR with an AUROC 0.71 (95%CI 0.65-0.71), AUPRC 0.42 (95%CI 0.33-0.53), and was well calibrated with a Brier score of 0.17 (95%CI 0.15-0.20). External validation in a cohort of 83 patients that are being managed with TNT+W/W (median age 57; 37% female), the model predicted pcCR with an AUROC 0.71 (95%CI 0.57-0.82), AUPRC 0.90 (95%CI 0.84-0.96), and Brier score of 0.30 (95%CI 0.26-0.33), improving to 0.17 with recalibration.

Conclusion

This novel predictive model demonstrated good discrimination and calibration for pCR after TNT+TME with prognostic utility in TNT+W/W for pcCR after appropriate recalibration, supporting its use in W/W patient selection.

Figure: Ensemble TabPFN model evaluation plots depicting 10-fold cross validation performance of the model predicting pathological complete response (pCR) in the TNT+TME cohort (blue) and the model fully trained in the entire TNT+TME cohort, being applied to the TNT+W/W cohort to predict persistent clinical complete response (pcCR; orange); A) receiver operator curve for; B) precision-recall curve; C) calibration plot.