Deep Learning Predicts Mutations and Outcomes in Gastrointestinal Stromal Tumors

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Abstract

Gastrointestinal stromal tumor (GIST) is the most common gastrointestinal mesenchymal tumor, driven by tyrosine–protein kinase (KIT) and platelet-derived growth factor receptor A (PDGFRA) mutations. Specific variants, such as KIT exon 11 deletions, carry prognostic and therapeutic implications, whereas wild-type variants derive limited benefit from tyrosine kinase inhibitors. Given the limited reproducibility of established clinicopathologic risk models, deep learning (DL) applied to whole-slide images (WSI) emerged as a promising tool for molecular classification and prognostic assessment. We analyzed 8398 GIST cases from 21 centers in seven countries, including 7,238 with molecular data and 2,638 with clinical follow-up. DL models were trained on WSIs to predict mutations, treatment sensitivity, and recurrence-free survival (RFS). DL predicted mutational status in GIST from WSIs, with area under the curve of 0.87 for KIT and 0.96 for PDGFRA, and

high performance was observed for subtypes, including KIT exon 11 del–inss 557 to 558 (0.67) and PDGFRA exon 18 D842V (0.93). For therapeutic categories, performance reached 0.84 for avapritinib sensitivity and 0.81 for imatinib sensitivity. DL models predicted RFS, with hazard ratios of 8.44 in the overall cohort and 4.74 in patients receiving adjuvant therapy. Prognostic performance was comparable with pathology-based scores, with highest discrimination in the overall cohort and in patients without adjuvant therapy. DL applied to WSIs enables prediction of molecular alterations, treatment sensitivity, and RFS in GIST, performing comparably with established risk scores across international cohorts, providing a baseline for future multimodal predictors.

Significance: Deep learning on histology predicts KIT and PDGFRA mutations and stratifies recurrence-free survival in a large international cohort of gastrointestinal stromal tumors from multiple centers.