The value and limits of artificial intelligence in perioperative immunotherapy for gastric cancer

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PERIOPERATIVE IMMUNOTHERAPY HAS MADE PREOPERATIVE JUDGMENT MORE CONSEQUENTIAL

Perioperative immunotherapy has changed the practical problem in resectable gastric cancer. The question is no longer simply whether an immune checkpoint inhibitor can be added to chemotherapy. For surgeons and multidisciplinary teams, the harder task is to select patients, reassess treatment early enough, preserve the window for R0 resection with D2 lymphadenectomy (R0-D2 surgery), and adapt postoperative therapy after pathological information becomes available.

Recent evidence illustrates both opportunity and uncertainty. In DANTE, atezolizumab plus FLOT improved downstaging and pathological regression signals.[1] KEYNOTE-585 increased pathological complete response (pCR), but the relationship between short-term pathology and survival remained less straightforward.[2] MATTERHORN provided one of the clearest positive perioperative signals with durvalumab plus FLOT.[3] These findings support the promise of immunotherapy, but they do not justify uniform intensification for every resectable patient.

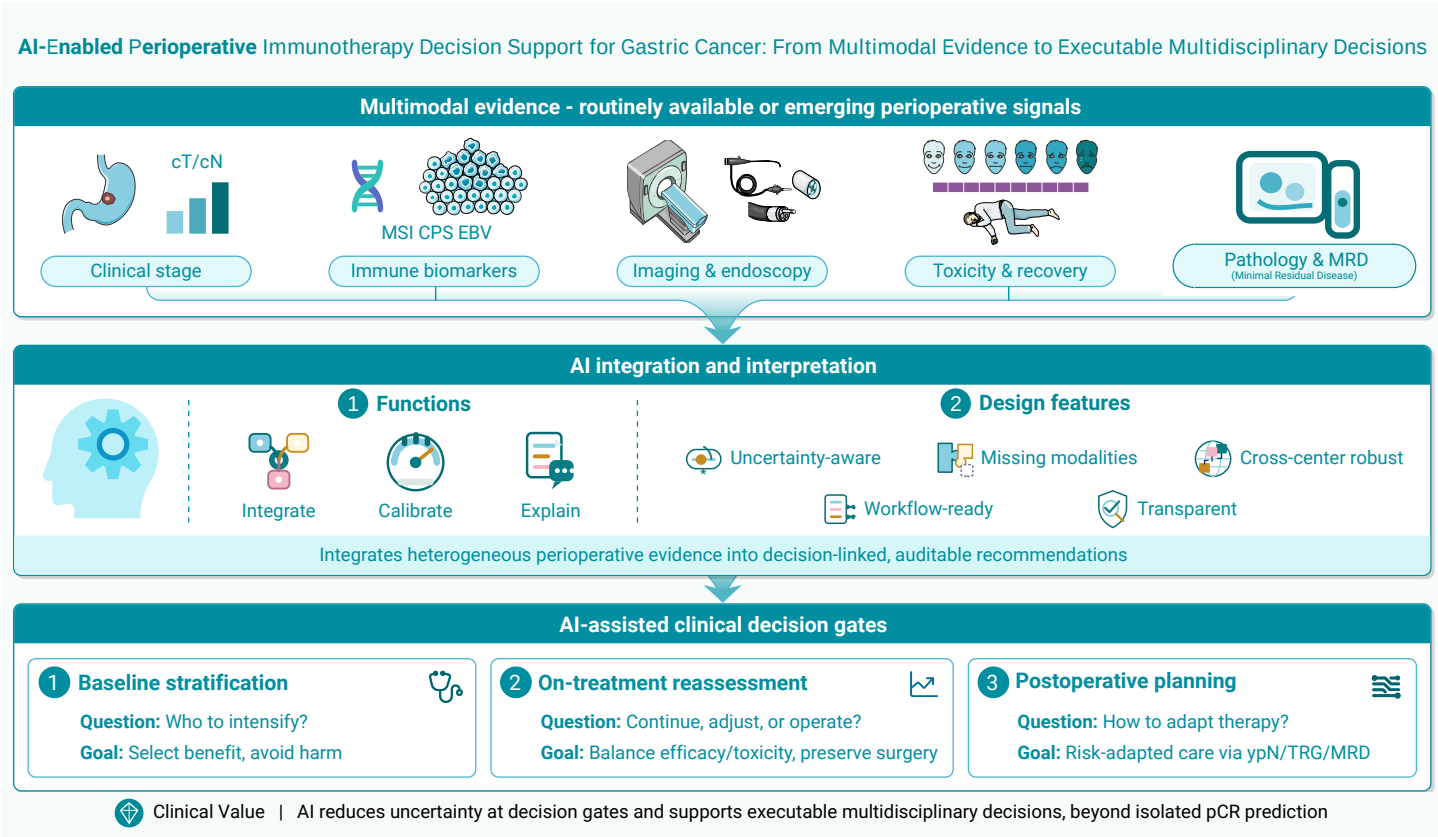

Figure 1. From multimodal evidence to executable multidisciplinary decisions: AI-enabled decision support for perioperative immunotherapy in gastric cancer Multimodal perioperative evidence is integrated through an AI interpretation layer to support three decision gates: baseline stratification, on-treatment reassessment, and postoperative planning. The framework emphasizes uncertainty reduction and executable multidisciplinary decisions rather than isolated pCR prediction. Abbreviations: AI, artificial intelligence; CPS, combined positive score; EBV, Epstein-Barr virus; MRD, minimal residual disease; MSI, microsatellite instability; pCR, pathological complete response; TRG, tumor regression grade; ypN, pathological nodal status after neoadjuvant therapy.

The clinical consequence is that perioperative immunotherapy shifts risk upstream. Intensification may benefit selected patients, but it can also create toxicity, ambiguous response interpretation, and potential delay before curative surgery. The essential problem is therefore not only prediction, but timing and coordination across the whole pathway.

Pathological response is useful, but it is not a complete surrogate for perioperative management. Radiological shrinkage, immune-related inflammation, fibrosis, residual nodal disease, operative findings, and recovery may point in different directions. A clinically useful framework must therefore connect biological response with surgical feasibility and postoperative risk, rather than treating pCR as the only meaningful target.

AI SHOULD SUPPORT THREE DECISIONS, NOT ONE ENDPOINT

Artificial intelligence (AI) may be useful when it reduces uncertainty at decision points where the pathway can diverge. Its value should not be defined

narrowly as predicting pCR with a higher area under the curve. A model that improves an offline endpoint but does not affect patient selection, reassessment timing, surgical planning, or postoperative treatment intensity is unlikely to matter clinically.

The first decision is baseline stratification. Before treatment starts, clinicians need to ask who is likely to benefit from preoperative immunotherapy and who may mainly be exposed to overtreatment. Microsatellite instability (MSI) or deficient mismatch repair (dMMR) status remains a biological anchor, but many patients fall outside a clearly defined high-benefit subgroup. A practical baseline judgment should integrate clinical tumor (cT) and clinical nodal (cN) stage, tumor burden, performance status, programmed death ligand 1 (PD-L1) combined positive score (CPS), Epstein-Barr virus (EBV) status, and emerging immune or molecular markers.

The second decision is on-treatment reassessment. Immunotherapy complicates response interpretation because tumor shrinkage, inflammation, fibrosis, toxicity, and residual viable tumor may not move in parallel. A single computed tomography (CT) measurement or one category according to the Response Evaluation Criteria in Solid Tumors (RECIST) is often insufficient for deciding whether to continue the regimen, modify treatment, or move to surgery. AI is better positioned when it integrates serial imaging, endoscopic change, laboratory trends, toxicity, and, when available, circulating tumor DNA.

The third decision is postoperative planning. A deep pathological response does not automatically mean that postoperative therapy can be omitted, and residual nodal disease or poor regression may still justify intensified follow-up or downstream treatment. Figure 1 summarizes these decision gates and the corresponding role of an AI decision-support layer.

For all three decisions, the output should be auditable. Clinicians should be able to see which signals support the recommendation, which signals conflict, how confident the model is, and whether a missing modality is important enough to obtain before making a decision. Without this interpretability, AI risks becoming another black box at a moment when perioperative teams need clearer evidence structure.

REQUIREMENTS FOR CLINICAL TRANSLATION

The most promising direction is multimodal decision support. Gastric cancer already generates multiple data streams, including contrast-enhanced CT, endoscopy, biopsy and surgical pathology, molecular biomarkers, routine laboratory tests, treatment exposure, toxicity, and recovery. Recent multimodal radiopathomics work illustrates that CT, digital pathology, and clinical variables can be assembled into interpretable models for immunotherapy-based treatment response and survival.[4] Such studies are important because they show feasibility, not because any single model is already ready for routine perioperative use.

Translation requires a stricter standard than retrospective discrimination. A useful AI system should be robust to missing or delayed inputs, because biopsy tissue, molecular testing, serial imaging, and ctDNA results often arrive at different times. Outputs must also be decision-linked. A model that predicts regression but does not indicate whether to intensify treatment, reassess earlier, or proceed to surgery may be academically interesting but clinically weak.

Prospective validation should therefore evaluate pathway-level outcomes: fewer ineffective escalations, fewer avoidable toxicities, preserved R0 resection opportunities, better alignment between postoperative risk and treatment intensity, and improved long-term outcomes. Reporting should also remain transparent and aligned with guidance for clinical prediction models using AI.[5] Clinicians must be able to understand which signals drive a recommendation, how uncertain the output is, and which missing data matter before deciding.

Implementation should be modest at first. AI could begin by flagging patients who need earlier multidisciplinary reassessment, identifying discordant response signals, or prompting discussion of surgical timing when toxicity accumulates. These functions are clinically meaningful because they fit existing workflow instead of asking teams to surrender judgment to an autonomous algorithm.

CONCLUSION

Perioperative immunotherapy has not simplified gastric cancer care; it has made preoperative judgment more important. AI can contribute if it helps clinicians connect patient selection, response monitoring, surgical timing, and postoperative adaptation into one executable pathway. Its future value will depend less on isolated predictive accuracy than on whether it reduces uncertainty where multidisciplinary decisions actually change patient care.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During preparation, the authors used ChatGPT (OpenAI) for language editing, condensation, figure layout, and formatting. The authors reviewed and edited all content and take full responsibility for the publication.

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AUTHOR CONTRIBUTIONS

Xin Xin drafted and revised the manuscript. Yan Li interpreted the literature and critically revised the text. Guoliang Zheng conceptualized the commentary, supervised clinical interpretation, and critically revised the manuscript. All authors contributed to the manuscript and approved the final version.

DECLARATION OF INTERESTS

The authors declare no competing interests.