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Albumin-to-alkaline phosphatase ratio as a prognostic biomarker in gastrointestinal cancer: clinical potential and research imperatives

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Dear Editor,

We read with interest the recent systematic review and meta-analysis by Zhu *et al*[1] evaluating the prognostic significance of the albumin-to-alkaline phosphatase ratio (AAPR) in gastrointestinal (GI) cancers. Their synthesis of eight high-quality retrospective cohort studies (n = 2267) demonstrated that low pretreatment AAPR was consistently associated with inferior overall survival (OS) in both univariate (HR 2.49, 95% CI 1.67–3.71) and multivariate (HR 2.59, 95% CI 1.55–4.35) analyses, with confirmatory robustness on subgroup assessments.

To ensure the transparency and rigor of our idea, this study adheres to the TITAN 2025 Guideline Checklist[2]. This checklist provides a standardized framework for the application of artificial intelligence in oncology research, emphasizing data compliance, human oversight, and ethical considerations to uphold scientific integrity across study design, data analysis, and model development. The detailed information of TITAN Guidelines 2025 is indicated in Supplemental Digital Content Table S1, available at: http://links.lww.com/JS9/F49.

In GI oncology, accurate preoperative prognostication is essential for individualized treatment planning. While tumor-node-metastasis (TNM) staging remains the gold standard, it inadequately reflects the host systemic condition and tumor biology[3]. Recent interest has grown in the AAPR, a composite biomarker derived from routine blood tests, as a prognostic tool in several malignancies[4,5]. AAPR – calculated as albumin divided by alkaline phosphatase – integrates two readily available biochemical indices. As albumin reflects nutritional and inflammatory status[6]. Li *et al* found that AAPR can serve as a novel risk stratification tool to refine prognostic prediction for surgical non-small-cell lung cancer[7]. Furthermore, Tian *et al* found that AAPR may be a prognostic indicator in solid cancers[8], the ratio plausibly captures a composite of patient resilience and disease aggressiveness.

From a surgical oncology perspective, such a marker offers appeal. First, both components are part of standard preoperative profiles, making the test cost-neutral and universally available. Second, it could be incorporated into preoperative decision-making, perioperative risk stratification, and patient counselling. Notably, in Zhu *et al*'s analysis, the negative OS impact of low AAPR persisted across gastric and colorectal cancers, as well as in both surgical and non-surgical treatment groups.

Recurrence-free survival results, however, were less conclusive: while statistically significant in pooled univariate analyses (HR 1.58, 95% CI 1.18–2.13), multivariate adjustment negated the association (HR 1.54, 95% CI 0.84–2.83). This attenuation may reflect the dominance of tumor stage, nodal status, and resection margins over biochemical indices in recurrence prediction.

Nevertheless, some caveats should guide interpretation. The reported studies were retrospective, predominantly from China and Turkey, with variable and non-standardized AAPR cut-off values (0.37–0.70). High heterogeneity (I^2 > 80% for OS) underlines the need for harmonization in assay methods and threshold determination. Moreover, laboratory parameters can be influenced by non-malignant comorbidities – such as chronic liver disease or bone pathology – which were variably adjusted for.

Several research priorities emerge. First, prospective multicenter validation across diverse ethnicities is essential, ideally with pre-specified, standardized AAPR thresholds derived from ROC-curve optimization in large training cohorts. Second, integration into multi-parameter prognostic nomograms alongside TNM stage, molecular markers, and patient-reported outcomes may refine prognostication. Third, exploring dynamic changes in AAPR – rather than a single preoperative value – could assess temporal correlations with treatment response and survival.

If validated, AAPR could serve as a trigger for prehabilitation strategies. Nutritional support and targeted interventions to modulate systemic inflammation preoperatively may not only improve surgical resilience but could potentially shift a patient's AAPR into a more favorable range, though interventional

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evidence is currently lacking. We believe this biomarker, given its negligible cost and global accessibility, is worthy of further study, particularly within prospective surgical oncology trials.

Ethical approval

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Consent

Not applicable.

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Conflicts of interest disclosure

The authors affirm that they have no financial or personal conflicts of interest that could have influenced or appeared to influence the work reported in this paper.

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Data availability statement

The data included in the study are available from the corresponding author upon reasonable request.

Declaration of whether any AI was used in the research and manuscript development

In accordance with the TITAN 2025 Guideline Checklist (https://premierscience.com/pjs-25-950/), we declare that generative AI tools (ChatGPT 4.0) were solely used for language polishing, including grammatical correction and sentence structure refinement. All scientific content, data interpretation, and conclusions remain the sole responsibility of the authors, with no AI involvement in substantive revisions.

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