

# Research Progress of Albumin-to-Alkaline Phosphatase Ratio (AAPR) in Digestive System Tumors

Xiaoyan Xue, Gefu Chi\*

Hospital of Inner Mongolia Medical University, Hohhot 010050, Inner Mongolia, China.

**How to cite this paper:** Xiaoyan Xue, Gefu Chi. (2026) Research Progress of Albumin-to-Alkaline Phosphatase Ratio (AAPR) in Digestive System Tumors. *International Journal of Clinical and Experimental Medicine Research*, 10(2), 134-138. DOI: 10.26855/ijcemr.2026.03.014

**Received:** January 31, 2026  
**Accepted:** February 28, 2026  
**Published:** March 31, 2026

\*Corresponding author: Gefu Chi, Hospital of Inner Mongolia Medical University, Hohhot 010050, Inner Mongolia, China.

## Abstract

Albumin-to-alkaline phosphatase ratio (AAPR), a composite biomarker based on routine biochemical indicators, integrates serum albumin (reflecting nutritional status and hepatic synthetic function) and alkaline phosphatase (indicating hepatobiliary damage and tumor invasion). First proposed by Chan et al. in 2015 for hepatocellular carcinoma prognosis, AAPR has demonstrated significant clinical value across digestive system malignancies. In hepatocellular carcinoma, AAPR > 0.40 predicts superior overall and recurrence-free survival. For cholangiocarcinoma, AAPR  $\geq$  0.41 correlates with improved 5-year survival rates (33.4% vs. 16.5%). In pancreatic cancer, AAPR  $\leq$  0.4 identifies patients with markedly shortened survival (6.4 vs. 9.3 months). Gastric and colorectal cancer studies confirm low AAPR as an independent predictor of poor prognosis (HR=2.49, 95% CI: 1.67-3.71). Additionally, AAPR < 0.50 significantly predicts worse outcomes in esophageal squamous cell carcinoma. Despite the advantages of convenience, low cost, and stability, AAPR faces limitations, including non-unified cutoff values and comorbidity interference. Future research should establish standardized thresholds, validate them through multi-center prospective studies, and expand applications in rare digestive tumors.

## Keywords

Albumin-to-alkaline phosphatase ratio (AAPR); digestive system tumors; prognostic biomarker; hepatocellular carcinoma; cholangiocarcinoma; pancreatic cancer; gastric cancer

## 1. Introduction

Biomarkers are important bridges connecting basic medicine and clinical medicine, providing objective evidence for early diagnosis, disease assessment, prognosis judgment, and therapeutic targets of diseases. Albumin (ALB) and alkaline phosphatase (ALP), as two of the most widely used routine biochemical detection indicators, respectively reflect the physiological and pathological status of the body from different dimensions. Moreover, their detection is convenient and cost-effective, suitable for primary medical institutions and large-scale population screening. ALB is a polypeptide chain produced by liver parenchymal cells, containing 585 amino acid residues in its molecular structure. The liver synthesizes approximately 9-12 grams daily, with a half-life of about 15-19 days in human plasma [1]. As one of the most abundant proteins in blood, it plays important roles in maintaining plasma osmotic pressure stability, transporting poorly water-soluble small molecular organic compounds and inorganic ions, ensuring communication between intracellular fluid, extracellular fluid, and tissue fluid, as well as anti-inflammatory and antioxidant effects [2-4]. Additionally, albumin has heparin-like activity and antiplatelet aggregation effects [5]. ALP is a hydrolyase widely present in human bone, liver, kidney, and intestine, mainly expressed on the cytoplasmic membrane of

human cells, forming glycoproteins combined with the membrane [6]. Under alkaline body fluid conditions, it can catalyze the hydrolysis of various phosphate monoesters [7]. Routine laboratory alkaline phosphatase detection is performed by measuring total alkaline phosphatase levels in serum [8]. Total ALP includes four isoenzymes: placental ALP, germ cell ALP, and intestinal ALP are tissue-specific ALPs, meaning they are only expressed in specific tissues under physiological conditions; while liver/bone/kidney ALP is non-tissue-specific ALP, therefore also present in blood [9-11], accounting for more than 90% of total alkaline phosphatase activity in blood [12]. Therefore, when the liver, bone, kidney, and other organs develop lesions, serum ALP levels usually appear higher than normal.

However, single biochemical indicators often only reflect a certain pathological link of disease, making it difficult to comprehensively assess the complex pathophysiological processes of diseases. Ratio-based biochemical indicators, by integrating two or more related indicators, can achieve a diagnostic efficacy of “1+1>2,” compensating for the shortcomings of single indicators. For example, the C-reactive protein to albumin ratio (CAR) comprehensively evaluates acute inflammatory response and nutritional consumption, being more accurate than single indicators [13], and superior to separate C-reactive protein or albumin in predicting disease severity and mortality [14-18]. The albumin-to-alkaline phosphatase ratio (AAPR) can comprehensively assess the inflammatory response, immunity, and nutritional status of the body. It was first proposed by Chan AW et al. in 2015 for predicting the prognosis of liver cancer [19]. With the steady growth of AAPR-related research, its research scope has expanded from initial hepatocellular carcinoma to cholangiocarcinoma, pancreatic cancer, lung cancer, nasopharyngeal carcinoma, and other solid tumors, and has been explored in liver diseases such as liver cirrhosis, liver fibrosis, and acute liver injury, as well as critical illnesses such as sepsis and acute respiratory distress syndrome. However, there are currently few systematic reviews summarizing the research progress of AAPR with different systemic tumors, so this article systematically searches AAPR-related Chinese and English literature and provides a systematic review of its applications in different systemic tumors.

## 1.1 Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is the 6th most common cancer globally and the 3rd leading cause of cancer death. China is a high-incidence area, with new cases accounting for more than 50% of global new cases annually [10]. AAPR was first proposed as a liver cancer prediction factor in 2015 [19]. With research progress, studies on AAPR in HCC prognosis have gradually increased [21, 22]. In a study including 188 HCC patients, it was pointed out that the AUC value of AAPR for predicting 1-year overall survival in liver cancer patients was 0.704, higher than other ratio indicators: aspartate aminotransferase-lymphocyte ratio (ALR) 0.697, lymphocyte-monocyte ratio (LMR) 0.677, and platelet-lymphocyte ratio (PLR) 0.693 [23]. In the study by Li Qun et al. [24] on hepatitis B-positive HCC, it was similarly shown that the cumulative incidence of 1-year, 3-year, and 5-year survival in the AAPR>0.40 group was 97.1%, 78.2%, and 67.3% respectively, significantly higher than the AAPR≤0.40 group (80.2%, 54.4%, and 40.1% respectively) ( $P<0.001$ ). AAPR can serve as an independent risk factor for overall survival and recurrence-free survival. In the study by Zhang Feng et al. [25], including 445 HCC patients, it was similarly shown that AAPR can serve as a predictor of tumor recurrence and prognosis in early HCC patients at initial treatment: patients with lower AAPR had significantly lower recurrence-free survival and overall survival than those with higher AAPR. AAPR was identified as an independent prognostic indicator, and its discriminative efficacy was superior to that of other liver function indicators. In advanced liver cancer patients who did not receive standard anti-cancer treatment, univariate and multivariate analysis confirmed that AAPR can also serve as a potential prognostic indicator (HR = 0.592,  $P = 0.007$ ) [26].

## 1.2 Cholangiocarcinoma

Cholangiocarcinoma (CCA) is a highly malignant tumor originating from the epithelium of the biliary system. In recent years, its global incidence and mortality have shown significant upward trends [27, 28]. As the second most common primary hepatobiliary malignancy after hepatocellular carcinoma, CCA is often diagnosed at middle or advanced stages due to its hidden anatomical location and lack of specific early symptoms [29]. Its prognosis and long-term survival have received extensive attention from scholars. AAPR has been found to have certain value in prognostic prediction for CCA. In the study by Li Hui et al. [30], AAPR showed superior predictive value for long-term survival in intrahepatic cholangiocarcinoma patients undergoing surgical treatment compared to combined albumin and bilirubin indicators. Meanwhile, Xiong Jianping et al. [31] pointed out that the overall 1-year, 3-year, and 5-year survival rates of the low AAPR group ( $<0.41$ ) were 70.2%, 38.0%, and 16.5% respectively, significantly lower than the high AAPR group ( $\geq 0.41$ ) (81.7%, 53.9%, and 33.4% respectively) ( $P<0.0001$ ). AAPR also has certain

predictive value in combined hepatocellular carcinoma and cholangiocarcinoma (cHCC-CCA) patients. In the retrospective study by Zhang Feng and Lu Shenxin et al. [32], it was pointed out that AAPR is a strong indicator of overall survival, superior to Child-Pugh (CP) score and albumin-bilirubin score (ALBI), and preoperative AAPR is an independent prognostic predictor for cHCC-CCA.

### 1.3 Pancreatic Cancer

Pancreatic cancer is the digestive tract tumor with the worst prognosis. It is difficult to diagnose early, with most cases discovered at advanced stages. Its prognosis is extremely poor, with a 5-year survival rate of less than 10% [33]. AAPR also has a certain predictive value in the prognosis of pancreatic cancer. In a cohort study including 419 unresectable pancreatic ductal adenocarcinoma patients receiving chemotherapy, it was pointed out that an AAPR of 0.4 was the optimal threshold for overall survival prediction. Patients with  $AAPR \leq 0.4$  had significantly shorter surgical cycles than those with  $AAPR > 0.4$  (6.4 months vs 9.3 months;  $P < 0.001$ ). AAPR can serve as an independent prognostic predictor for unresectable pancreatic ductal adenocarcinoma patients [34]. The study by Veysel Haksoyler et al. [35] similarly found that pre-treatment  $AAPR < 0.46$  is a novel independent indicator of overall survival in patients with unresectable locally advanced pancreatic carcinoma who ultimately received chemoradiotherapy. In the cohort study by Torre et al. [36], including 354 pancreatic cancer patients, it was pointed out that the 1-year, 2-year, and 3-year survival rates of the high-risk group with  $ARPR < 2.16$  ( $ARPR$  is the reciprocal of  $AAPR$ ) were all significantly higher than the low-risk group ( $ARPR > 2.16$ ).

### 1.4 Gastrointestinal Tumors

Gastric cancer and colorectal cancer are among the most common malignant tumors globally, ranking 5th and 3rd in global cancer incidence, accounting for 14.5% of new cancer cases. In terms of mortality, they rank 5th and 2nd, respectively, accounting for 16.1% of global cancer deaths, posing a significant burden on global health [37, 38]. With continuous advancement in research, treatment strategies for gastrointestinal tumors have also progressed, but overall survival outcomes remain unsatisfactory [39]. AAPR, as a low-cost and easily accessible indicator, can effectively predict survival prognosis in gastric cancer. Li Yuting et al. collected AAPR values from patients with distant metastatic gastric cancer and evaluated the prognostic efficacy of AAPR in metastatic GC patients using Kaplan-Meier methods and Cox proportional hazards regression models, concluding that  $AAPR \leq 0.48$  was significantly associated with bone ( $P < 0.05$ ) and liver metastasis ( $P < 0.05$ ), and patients with higher AAPR levels had better overall survival and progression-free survival. In the retrospective study by Arak et al. [42] on early colorectal cancer, it was similarly pointed out that in early colorectal cancer patients, the overall survival of the low AAPR group was worse than the high AAPR group, and the AAPR index showed significant prognostic value compared to NLR and PLR in the same patient cohort. A meta-analysis including 4 databases, 8 studies, and 2267 gastrointestinal cancer patients pointed out: comprehensive overall survival results from univariate and multivariate analysis showed that the death risk in the low AAPR group was significantly higher than the high AAPR group ( $HR = 2.49$ , 95% CI: 1.67 to 3.71,  $P < 0.001$ ,  $I^2 = 84.3\%$ ;  $HR = 2.59$ , 95% CI: 1.55 to 4.35,  $P < 0.001$ ,  $I^2 = 80.3\%$ ). For recurrence-free survival, univariate analysis showed worse outcomes in the low AAPR group ( $HR = 1.58$ , 95% CI: 1.18 to 2.13,  $P = 0.002$ ,  $I^2 = 0.0\%$ ). AAPR is expected to become a promising serological parameter for prognostic evaluation in gastrointestinal cancer patients.

### 1.5 Esophageal Cancer

Esophageal cancer ranks 7th in global cancer incidence and 6th in mortality. Esophageal squamous cell carcinoma is more common than esophageal adenocarcinoma, accounting for about 90% of all histological subtypes. Despite the continuous development of treatment plans for esophageal cancer, its 5-year survival rate remains between 10% and 20%. AAPR has been found to serve as a novel and promising prognostic biomarker for cancer patients undergoing esophagectomy. In a propensity score matching study, it was pointed out that esophageal squamous cell carcinoma patients with  $AAPR < 0.50$  had significantly lower overall survival (OS) and progression-free survival (PFS) than patients with  $AAPR \geq 0.50$  (log-rank  $P < 0.001$ ). This significant difference remained stable in propensity score matching analysis.

## 2. Summary

In summary, albumin-to-alkaline phosphatase ratio (AAPR), as a composite biomarker based on routine biochemical indicators, with advantages of convenient detection, low cost, and high stability, demonstrates diverse value in clinical

management of major digestive system tumors, including hepatocellular carcinoma, gastric cancer, colorectal cancer, pancreatic cancer, and cholangiocarcinoma. In differential diagnosis, it can effectively distinguish tumors from benign diseases, and its diagnostic efficacy is further improved when combined with traditional tumor markers; in prognostic prediction, low AAPR has been confirmed as an independent risk factor for poor survival in various digestive system tumor patients, providing a reliable basis for patient risk stratification; in treatment response evaluation, AAPR can effectively predict the efficacy and survival benefits of targeted therapy, immunotherapy, chemotherapy, and local treatment, providing references for individualized treatment plan formulation. The application characteristics of AAPR differ among different tumor types, with each having core advantages in specific areas, forming an application system covering the entire course management of digestive system tumors.

### 3. Limitations and Prospects

The clinical application of AAPR still has limitations, such as a lack of unified cutoff values, susceptibility to interference from comorbidities, insufficient high-quality prospective studies, and research gaps in rare tumors. Future research should focus on multi-center large-sample prospective validation to clarify optimal cutoff values for different tumor types, etiologies, and stages; explore combined application models of AAPR with novel biomarkers and imaging indicators to further improve diagnostic and therapeutic precision; expand research in special populations such as elderly patients and those with underlying diseases; establish dynamic monitoring systems to guide real-time adjustment of treatment plans; simultaneously fill research gaps in rare digestive system tumors such as small intestine cancer and neuroendocrine tumors, promoting AAPR to play a greater value in precision diagnosis and treatment of digestive system tumors.

### References

- [1] Nazha B, Moussaly E, Zaarour M, et al. Hypoalbuminemia in colorectal cancer prognosis: Nutritional marker or inflammatory surrogate? *World J Gastrointest Surg.* 2015;7:370-7.
- [2] Tuğç S, Cetinkaya A, Duman O. Spectroscopic investigations of the interactions of tramadol hydrochloride and 5-azacytidine drugs with human serum albumin and human hemoglobin proteins. *Photochem Photobiol B.* 2013;120:59-65.
- [3] Eckart A, Struja T, Kutz A, et al. Relationship of Nutritional Status, Inflammation, and Serum Albumin Levels During Acute Illness: A Prospective Study. *Am J Med.* 2020;133(6):713-22.
- [4] Seaton K. Albumin concentration controls cancer. *J Natl Med Assoc.* 2001;93:490-3.
- [5] Rozga J, Piątek T, Małkowski P. Human albumin: old, new, and emerging applications. *Ann Transplant.* 2013;18:205-17.
- [6] Zaher DM, El-Gamal MI, Omar HA, et al. Recent advances with alkaline phosphatase isoenzymes and their inhibitors. *Arch Pharm (Weinheim).* 2020;353:e2000017.
- [7] Orimo H. The mechanism of mineralization and the role of alkaline phosphatase in health and disease. *Nippon Med Sch.* 2010;77(1):4-12.
- [8] Wu XL. Changes and clinical significance of serum alkaline phosphatase in hyperthyroidism patients before and after treatment [dissertation]. Shanxi Medical University; 2023.
- [9] Lowe D, Sanvictores T, Zubair M, et al. Alkaline Phosphatase. In: *StatPearls.* Treasure Island (FL): StatPearls Publishing; 2023 Oct 29.
- [10] Magnusson P, Degerblad M, Sääf M, et al. Different responses of bone alkaline phosphatase isoforms during recombinant insulin-like growth factor-I (IGF-I) and during growth hormone therapy in adults with growth hormone deficiency. *J Bone Miner Res.* 1997;12(2):210-20.
- [11] Magnusson P, Sharp CA, Farley JR. Different distributions of human bone alkaline phosphatase isoforms in serum and bone tissue extracts. *Clin Chim Acta.* 2002;325(1-2):59-70.
- [12] Jiang Y, Li X, Walt DR. Single-Molecule Analysis Determines Isozymes of Human Alkaline Phosphatase in Serum. *Angew Chem Int Ed Engl.* 2020;59:18010-5.
- [13] Yang J, Chen Y, Wan J, et al. Prognostic value of the C-reactive protein to albumin ratio in patients with stroke: a meta-analysis. *Sci Rep.* 2025;15(1):21150.
- [14] Taş-Aygar G, Ataş H, Gönül M, et al. Importance of the C-Reactive Protein to Albumin Ratio in the Diagnosis and Prognosis of Mycosis Fungoides. *Dermatol Pract Concept.* 2024;14(2):e2024097.
- [15] Kocatürk M, Kocatürk Ö. Assessment of relationship between C-reactive protein to albumin ratio and 90-day mortality in patients with acute ischaemic stroke. *Neurol Neurochir Pol.* 2019;53(3):205-11.

- [16] Seringec Akkececi N, Yildirim Cetin G, Gogebakan H, et al. The C-Reactive Protein/Albumin Ratio and Complete Blood Count Parameters as Indicators of Disease Activity in Patients with Takayasu Arteritis. *Med Sci Monit.* 2019;25:1401-9.
- [17] Fu YJ, Li KZ, Bai JH, et al. C-reactive protein/albumin ratio is a prognostic indicator in Asians with pancreatic cancers: A meta-analysis. *Medicine (Baltimore).* 2019;98(48):e18219.
- [18] Kalyoncuoglu M, Durmus G. Relationship between C-reactive protein-to-albumin ratio and the extent of coronary artery disease in patients with non-ST-elevated myocardial infarction. *Coron Artery Dis.* 2020;31(2):130-6.
- [19] Chan AW, Kumada T, Toyoda H, et al. Albumin-to-Alkaline Phosphatase Ratio: A Novel Prognostic Index for Hepatocellular Carcinoma. *Dis Markers.* 2015;2015:564057.
- [20] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394-424.
- [21] Zhang X, Xin Y, Chen Y, et al. Prognostic effect of albumin-to-alkaline phosphatase ratio on patients with hepatocellular carcinoma: a systematic review and meta-analysis. *Sci Rep.* 2023;13(1):1808.
- [22] Li H, Wang L, Chen L, et al. Prognostic Value of Albumin-to-Alkaline Phosphatase Ratio in Hepatocellular Carcinoma Patients Treated with Liver Transplantation. *Cancer (Basel).* 2020;11(8):2171-80.
- [23] Yousif WI, Bakosh MF. Prognostic Impact of Initial Laboratory-based Scores for Hepatocellular Carcinoma Patients: A Retrospective Study. *Clin Exp Hepatol.* 2025;15(6):102604.
- [24] Li Q, Lyu Z, Wang L, et al. Albumin-to-Alkaline Phosphatase Ratio Associates with Good Prognosis of Hepatitis B Virus-Positive HCC Patients. *Onco Targets Ther.* 2020;13:2377-84.
- [25] Zhang F, Lu SX, Hu KS, et al. Albumin-to-alkaline phosphatase ratio as a predictor of tumor recurrence and prognosis in patients with early-stage hepatocellular carcinoma undergoing radiofrequency ablation as initial therapy. *Int J Hyperthermia.* 2021;38(1):1-10.
- [26] Cai X, Chen Z, Chen J, et al. Albumin-to-Alkaline Phosphatase Ratio as an Independent Prognostic Factor for Overall Survival of Advanced Hepatocellular Carcinoma Patients without Receiving Standard Anti-Cancer Therapies. *Cancer (Basel).* 2018;9(1):189-97.
- [27] Bertuccio P, Turati F, Carioli G, et al. Global trends and predictions in hepatocellular carcinoma mortality. *J Hepatol.* 2017;67(2):302-9.
- [28] Greten TF, Schwabe R, Bardeesy N, et al. Immunology and immunotherapy of cholangiocarcinoma. *Nat Rev Gastroenterol Hepatol.* 2023;20(6):349-65.
- [29] Ilyas SI, Gores GJ. Pathogenesis, diagnosis, and management of cholangiocarcinoma. *Gastroenterology.* 2013;145(6):1215-29.
- [30] Li H, Li J, Wang J, et al. Assessment of Liver Function for Evaluation of Long-Term Outcomes of Intrahepatic Cholangiocarcinoma: A Multi-Institutional Analysis of 620 Patients. *Front Oncol.* 2020;10:525.
- [31] Xiong JP, Long JY, Xu WY, et al. Albumin-to-alkaline phosphatase ratio: A novel prognostic index of overall survival in cholangiocarcinoma patients after surgery. *World J Gastrointest Oncol.* 2019;11(1):39-47.
- [32] Zhang F, Lu S, Tian M, et al. Albumin-to-Alkaline Phosphatase Ratio is an Independent Prognostic Indicator in Combined Hepatocellular and Cholangiocarcinoma. *Cancer (Basel).* 2020;11(17):5177-86.
- [33] Wenzel P, von Figura G. Diagnostik und Therapie des Pankreaskarzinoms [Diagnostics and therapy of pancreatic carcinoma]. *Dtsch Med Wochenschr.* 2021;146(4):246-52.
- [34] Zhang K, Dong S, Jing YH, et al. Albumin-to-alkaline phosphatase ratio serves as a prognostic indicator in unresectable pancreatic ductal adenocarcinoma: a propensity score matching analysis. *BMC Cancer.* 2020;20(1):541.
- [35] Haksoyler V, Topkan E. Prognostic Utility of Prechemoradiotherapy Albumin-to-Alkaline Phosphatase Ratio in Unresectable Locally Advanced Pancreatic Carcinoma Patients. *Gastroenterol Res Pract.* 2021;2021:6647145.
- [36] Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. *CA Cancer J Clin.* 2015;65(2):87-108.
- [37] Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2024;74(3):229-63.
- [38] Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. *CA Cancer J Clin.* 2025;75(1):10-45.
- [39] Ness RM, Llor X, Abbass MA, et al. NCCN Guidelines® Insights: Colorectal Cancer Screening, Version 1.2024. *J Natl Compr Canc Netw.* 2024;22(7):438-46.