

Significance of Serum Lactate Dehydrogenase-to-Albumin Ratio as a Prognostic Marker in Patients with Colon Cancer: A Prospective Cohort Study

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Abstract

Background

Colon cancer remains a major cause of cancer-related morbidity and mortality worldwide. Prognostic biomarkers capable of identifying high-risk patients are essential for individualized treatment planning. The lactate dehydrogenase-to-albumin ratio (LAR), combining a marker of tumor metabolism and systemic inflammation with a marker of nutritional status, has emerged as a promising prognostic indicator.

Aim

To evaluate the prognostic significance of preoperative serum lactate dehydrogenase-to-albumin ratio in patients undergoing surgery for colon cancer.

Methods

A prospective observational study was conducted in the Department of General Surgery, IGIMS Patna, over two years. Seventy-two patients with histopathologically confirmed colon cancer undergoing curative surgery were included. Preoperative serum LDH and albumin levels were measured, and LAR was calculated. Patients were categorized into low-LAR and high-LAR groups using a cut-off value of 4.9. Associations between LAR and clinicopathological characteristics, postoperative outcomes, recurrence, and one-year survival were analyzed.

Results

Thirty patients (41.7%) had high LAR values. Advanced TNM stage, lymph node positivity, elevated CEA levels, and postoperative recurrence were significantly more frequent in the high-LAR group ($p < 0.05$). One-year disease-free survival was significantly lower among patients with elevated LAR (63.3% vs. 90.5%; $p = 0.002$).

Conclusion

Preoperative LAR is a simple, cost-effective, and reliable prognostic biomarker in colon cancer. Elevated LAR is associated with advanced disease, increased recurrence, and poorer survival outcomes.

Recommendations

Further multicenter studies with larger sample sizes and longer follow-up are recommended to validate the prognostic significance and optimal cut-off value of LAR.

Future research should assess whether LAR provides independent prognostic information beyond established clinicopathological factors.

Keywords: Colon cancer, Lactate dehydrogenase, Albumin, Lactate dehydrogenase-to-albumin ratio, Prognosis, Biomarker.

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Introduction

Colon cancer continues to be a major healthcare burden and is one of the main causes of cancer-related mortality worldwide. Disease recurrence and mortality are still high despite advancements in targeted medicines, chemotherapy, and surgical methods. Therefore, risk classification and customised treatment planning depend on accurate prognostic assessment.(1). Tumor-node-metastasis (TNM) staging has historically been used to assess the prognosis of colon cancer. Patients with similar stages frequently have differing outcomes, even though TNM staging is still the mainstay of clinical decision-making. As a result, finding new biomarkers that can increase prognosis accuracy has received more attention.(2).

Systemic inflammation and nutritional condition have a significant impact on the course of cancer. Inflammatory cells, cytokines, and metabolic mediators that support tumour growth, invasion, and metastasis make up the tumour microenvironment. These biological processes may be reflected in biomarkers, which could offer useful prognostic data. One important enzyme in anaerobic glycolysis is lactate dehydrogenase (LDH). Increased tumour metabolism, hypoxia, angiogenesis, and aggressive biological behaviour are all reflected in elevated serum LDH levels. Poor outcomes in several cancers, including colorectal cancer, have been linked to elevated LDH levels.(3).

An accepted measure of inflammatory and nutritional state is serum albumin. Reduced survival among cancer patients, higher surgical complications, and compromised immunity have all been associated with hypoalbuminemia. Systemic inflammatory reactions that affect the course of cancer are also reflected in albumin levels. Tumour metabolic activity and host nutritional status are integrated into a single indicator called the lactate dehydrogenase-to-albumin ratio (LAR). The prognostic importance of LAR in colorectal cancer has been shown in recent research, indicating that it may have a role in predicting survival and recurrence.(4). The current study was conducted to assess the predictive relevance of preoperative LAR among patients receiving surgery for colon cancer at a tertiary care facility, given the paucity of Indian data on this biomarker.

Materials and methods

Study design and setting

This prospective cohort study was conducted in the Department of General Surgery, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India. The study included patients with histopathologically confirmed colon cancer who underwent planned curative surgical resection.

Participants

Patients aged 18–75 years with histopathologically confirmed colon cancer who were planned for curative surgical resection were eligible for inclusion. Patients who had received neoadjuvant chemotherapy or radiotherapy, had recurrent colon cancer, autoimmune disorders, chronic liver disease, or a history of blood transfusion before surgery were excluded. A total of 72 eligible patients were included in the final analysis.

Sample Size and Sampling

A total of 72 patients were included in the study

Data collection

Demographic and clinical characteristics were recorded for all participants. Tumor-related characteristics, including tumor location and TNM stage, were documented. Preoperative serum lactate dehydrogenase (LDH) and albumin levels were measured, and the lactate dehydrogenase-to-albumin ratio (LAR) was calculated. Serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) levels were also recorded. Histopathological findings, including lymph node involvement, lymphovascular invasion, and tumor differentiation, were documented. Patients were followed postoperatively for recurrence and disease-free survival.

Lar classification

The LAR was calculated from the preoperative serum LDH and albumin values. Patients were categorized into low-LAR and high-LAR groups using a cut-off value of 4.9. In the final cohort, 42 patients were classified into the low-LAR group and 30 into the high-LAR group.

Bias

Potential sources of selection and information bias were addressed by applying predefined inclusion and exclusion criteria and collecting demographic, biochemical, clinicopathological, and follow-up information systematically. However, because this was a single-center observational study with a relatively small sample size, residual selection bias and confounding cannot be completely excluded.

Ethical considerations

The study was approved by IGIMS, Patna. Written informed consent was obtained from all participants before enrollment.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 26.0. Continuous variables were presented as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. Differences between the low-LAR and high-LAR groups were assessed using the independent-samples t-test for continuous variables and the chi-square test for categorical variables, as appropriate. Kaplan–Meier analysis was performed to assess disease-free survival. A two-sided **p-value** <0.05 was considered statistically significant.

Results

Study participants

A total of 72 patients with histopathologically confirmed colon cancer who underwent planned curative surgery were

included in the final analysis. Of these, 42 patients (58.3%) were classified into the low-LAR group and 30 patients (41.7%) into the high-LAR group.

Baseline characteristics

The mean age was 54.8 ± 10.2 years in the low-LAR group and 57.3 ± 11.1 years in the high-LAR group, with no statistically significant difference between the groups ($p=0.318$). The low-LAR group included 24 males and 18 females, whereas the high-LAR group included 19 males and 11 females ($p=0.641$). Elevated CEA levels were observed in 11 patients in the low-LAR group and 18 patients in the high-LAR group, with a statistically significant difference between the groups ($p=0.008$).

Table 1. Baseline characteristics

Variable	Low LAR (n=42)	High LAR (n=30)	p-value
Mean Age (years)	54.8 ± 10.2	57.3 ± 11.1	0.318
Male	24	19	0.641
Female	18	11	
Elevated CEA	11	18	0.008*

Association of LAR With TNM Stage

The distribution of TNM stages differed significantly between the low-LAR and high-LAR groups ($p=0.004$). In the low-LAR group, 10 patients had stage I disease, 18 had stage II, 11 had stage III, and 3 had stage IV disease. In the high-LAR group, 2 patients had stage I disease, 8 had stage II, 14 had stage III, and 6 had stage IV disease.

Table 2. Association of LAR with TNM Stage

TNM Stage	Low LAR	High LAR	p-value
Stage I	10	2	
Stage II	18	8	
Stage III	11	14	
Stage IV	3	6	0.004*

Histopathological characteristics

Lymph node positivity was present in 13 patients in the low-LAR group and 19 patients in the high-LAR group ($p=0.011$). Lymphovascular invasion was observed in 8 and 15 patients, respectively ($p=0.006$). Poor tumor differentiation was reported in 4 patients in the low-LAR group and 10 patients in the high-LAR group ($p=0.021$).

Table 3. Histopathological features

Parameter	Low LAR	High LAR	p-value
Node Positive	13	19	0.011*
Lymphovascular Invasion	8	15	0.006*
Poor Differentiation	4	10	0.021*

Follow-up Outcomes

During follow-up, recurrence was observed in 4 patients (9.5%) in the low-LAR group and 11 patients (36.7%) in the high-LAR group ($p=0.003$). Disease-free survival at one year was reported in 38 patients (90.5%) in the low-LAR group and 19 patients (63.3%) in the high-LAR group, with a statistically significant difference between the groups ($p=0.002$).

Table 4. Follow-up Outcomes

Outcome	Low LAR	High LAR	p-value
Recurrence	4	11	0.003*
Disease-Free Survival	38 (90.5%)	19 (63.3%)	0.002*

Discussion

The present prospective observational study evaluated the prognostic significance of preoperative serum lactate dehydrogenase-to-albumin ratio (LAR) in 72 patients with histopathologically confirmed colon cancer undergoing surgical resection. Of these, 42 patients (58.3%) were categorized into the low-LAR group and 30 (41.7%) into the high-LAR group. The mean age was 54.8 ± 10.2 years in the low-LAR group and 57.3 ± 11.1 years in the high-LAR group, with no statistically significant difference between the groups ($p=0.318$). Similarly, the sex distribution was comparable ($p=0.641$). The principal findings demonstrated that elevated preoperative LAR was significantly associated with advanced TNM stage, elevated carcinoembryonic antigen (CEA) levels, lymph node positivity, lymphovascular invasion, poor tumor differentiation, increased postoperative recurrence, and reduced disease-free survival. These findings suggest that LAR may have potential utility as an additional prognostic marker in patients with colon cancer.

The prognostic significance of LAR may be explained by the biological characteristics of its two components. Lactate dehydrogenase (LDH) is involved in cellular glycolysis and may reflect increased tumor metabolic activity, hypoxia, and aggressive tumor behavior. Conversely, serum albumin is an indicator of nutritional status and systemic inflammatory activity. Reduced albumin concentrations may be associated with malnutrition, inflammation, and impaired host responses. Therefore, an elevated LAR may reflect the combined effects of tumor-related metabolic alterations and systemic inflammatory or nutritional disturbances. Previous studies have also reported associations between elevated LAR and unfavorable outcomes in patients with malignancies (5,6).

Regarding tumor stage, the present study demonstrated a significant association between elevated LAR and advanced TNM stage (Table 2). Stage III and IV disease was observed in 20 patients (66.7%) in the high-LAR group compared with 14 patients (33.3%) in the low-LAR group ($p=0.004$). This finding suggests that elevated LAR may be associated with greater disease burden and more advanced tumor

characteristics. Similar observations have been reported in previous studies evaluating LAR in colorectal cancer, supporting its potential role in prognostic assessment (7).

The present study also demonstrated significant associations between elevated LAR and unfavorable histopathological characteristics (Table 3). Lymph node positivity was observed in 19 patients in the high-LAR group compared with 13 patients in the low-LAR group ($p=0.011$). Similarly, lymphovascular invasion was more frequent in the high-LAR group (15 vs. 8 patients; $p=0.006$), as was poor tumor differentiation (10 vs. 4 patients; $p=0.021$). These findings indicate that elevated LAR is associated with pathological features commonly linked to adverse oncological outcomes. Previous studies have similarly investigated the relationship between LAR and clinicopathological characteristics in colorectal cancer (8).

Furthermore, elevated serum CEA levels were significantly more frequent in the high-LAR group than in the low-LAR group (18 vs. 11 patients; $p=0.008$), as shown in Table 1. CEA is an established tumor marker used in the clinical assessment and postoperative surveillance of colorectal cancer. The observed association between elevated CEA and LAR suggests that LAR may provide additional information regarding tumor-related biological activity. However, further studies are required to determine whether LAR offers independent prognostic information beyond established tumor markers and clinicopathological parameters.

One of the clinically relevant findings of the present study was the association between elevated LAR and postoperative recurrence (Table 4). Recurrence occurred in 11 patients (36.7%) in the high-LAR group compared with four patients (9.5%) in the low-LAR group ($p=0.003$). Furthermore, one-year disease-free survival was significantly lower in the high-LAR group than in the low-LAR group (63.3% vs. 90.5%; $p=0.002$). These findings suggest that elevated preoperative LAR may be associated with an increased risk of recurrence and unfavorable postoperative outcomes. Previous studies have also reported an association between elevated LAR and adverse oncological outcomes, supporting its potential role in prognostic risk stratification (9).

The observed associations may be explained by the combined influence of tumor metabolism, systemic inflammation, and nutritional status. Increased LDH levels may reflect enhanced glycolytic activity and tumor hypoxia, whereas reduced albumin concentrations may indicate systemic inflammation or impaired nutritional status. Together, these alterations may characterize patients with more advanced disease and unfavorable clinical outcomes. However, the observational nature of the present study does not establish a causal relationship between elevated LAR and disease progression.

The findings also suggest that LAR may have potential clinical applicability because LDH and albumin are routinely measured biochemical parameters that are relatively inexpensive and widely available. Incorporating LAR into preoperative assessment may provide additional information alongside TNM staging, CEA levels, and histopathological findings. Nevertheless, the present findings do not establish that LAR independently predicts recurrence or survival, and its use as a standalone prognostic tool cannot currently be recommended. Larger studies with multivariable adjustment and external validation are required to determine its incremental prognostic value (10,11).

Generalizability

The findings of the present study may apply to adult patients with histopathologically confirmed colon cancer undergoing surgical treatment in tertiary-care settings. However, the study was conducted at a single tertiary-care institution and included a relatively small sample size, which may limit its generalizability to broader populations. Differences in patient characteristics, tumor stage, treatment approaches, nutritional status, and laboratory measurement methods may influence LAR values and their association with clinical outcomes. Therefore, multicenter studies involving diverse patient populations are required to establish the external validity of these findings.

Limitations

The present study has several limitations. First, the single-center design may have introduced selection bias and limited the generalizability of the findings. Second, the relatively small sample size may have reduced statistical precision and limited the ability to detect smaller associations. Third, the observational design does not establish causality, and residual confounding from factors such as nutritional status, systemic inflammation, comorbidities, and treatment-related differences cannot be excluded. Furthermore, the absence of reported multivariable adjustment limits conclusions regarding the independent prognostic value of LAR. Finally, the limited follow-up period restricts the assessment of long-term

recurrence and overall survival. These limitations should be considered when interpreting the findings.

Recommendations

Further multicenter studies with larger sample sizes and longer follow-up are recommended to validate the prognostic significance and optimal cut-off value of LAR. Future research should assess whether LAR provides independent prognostic information beyond established clinicopathological factors.

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List of abbreviations

CA 19-9	Carbohydrate antigen 19-9
CEA	Carcinoembryonic antigen
DFS	Disease-free survival
IGIMS	Indira Gandhi Institute of Medical Sciences
LAR	Lactate dehydrogenase-to-albumin ratio
LDH	Lactate dehydrogenase
SPSS	Statistical Package for the Social Sciences
TNM	Tumor-node-metastasis

Conflict of interest

The authors declare that they have no conflicts of interest.

Source of funding

The study received no external funding.

Data availability

The datasets generated and analyzed during the present study are not publicly available due to participant confidentiality but may be made available from the corresponding author upon reasonable request, subject to institutional and ethical approval.

Author contributions

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