

Prognostic Value of Glasgow Prognostic Score in Relation to TNM Staging of Colorectal CancerJitendra Kumar¹, Sunil Kumar²¹Senior Resident, Department of General Surgery, AIIMS, Patna, Bihar, India²Senior Resident, Department of General Surgery, AIIMS, Patna, Bihar, India

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Abstract:

Background: One of the main causes of cancer-related deaths worldwide, colorectal cancer (CRC) is the third most frequent type of cancer. Despite treatment advancements, the prognosis for advanced-stage colorectal cancer remains unfavourable. The tumor-node-metastasis (TNM) staging system is commonly utilized for prognostic assessment; however, it fails to incorporate systemic inflammation, a significant factor in cancer progression. The Glasgow Prognostic Score (GPS), which utilizes serum C-reactive protein (CRP) and albumin levels, serves as an inflammation-based prognostic instrument that could improve risk assessment in CRC.

Aim: The purpose of this study is to determine the predictive importance of systemic inflammation in disease development in CRC patients by examining the association between GPS and TNM staging.

Methodology: The study employed a cross-sectional design involving 88 patients with colorectal cancer at Department of General Surgery, AIIMS, Patna, Bihar, India. GPS was assessed through CRP and albumin levels, and TNM staging was categorized according to the American Joint Committee on Cancer (AJCC) 8th edition guidelines. Statistical analysis, utilizing chi-square tests, was conducted to assess the relationship between GPS and TNM staging, with significance established at $p < 0.05$.

Results: GPS and TNM stage were shown to be significantly correlated ($p = 0.0123$). Increased GPS scores were observed in Stage III patients, suggesting an association between systemic inflammation and disease advancement. Stage IV patients exhibited a greater proportion of GPS 0, indicating a complex interplay between inflammation and tumor burden.

Conclusion: The findings indicate that GPS is substantially linked with TNM staging in patients with CRC. Integrating GPS with TNM staging could enhance prognostic accuracy and facilitate personalized treatment planning. Additional research is required to investigate the biological mechanisms that underlie this association.

Keywords: Colorectal Cancer, Glasgow Prognostic Score, Prognosis, Systemic Inflammation, TNM Staging.

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Introduction

CRC (Colorectal Cancer) ranks as the third most common cancer globally and is the second leading cause of cancer-related mortality, with approximately 1.8 million new cases and 0.86 million deaths reported in 2018 [1]. It ranks as the second most common cancer among females and third among males globally, with concerning increases in mortality rates observed in patients under 55 years of age since the mid-2000s [2]. Despite advancements in surgical techniques and the use of adjuvant chemotherapy, the prognosis for advanced-stage colorectal cancer remains poor, with long-term survival rates continuing to be suboptimal. Prognosis and disease progression are closely linked to the clinical stage and metastasis of CRC. Early-stage CRC has a five-year survival rate exceeding 90%, whereas this rate drops to 12% for patients with distant metastasis [3]. The pathogenesis of both sporadic and familial CRC is

primarily influenced by chronic inflammation, highlighting the complexity of the disease and the difficulties associated with prognosis and treatment decisions [4].

TNM staging serves as the standard for CRC staging, facilitating treatment planning and prognostic assessment. TNM staging is insufficient when evaluating the biological and inflammatory characteristics of CRC, as persistent heterogeneity in clinical outcomes is often observed among patients with identical stages [5]. This indicates the need to complement prognostic tools with biomarkers and systemic inflammation markers to improve outcome prediction accuracy and facilitate more individualized treatment strategies [6]. Despite these limitations, TNM staging remains an essential instrument in clinical practice, serving as a

foundation for treatment planning and patient management.

Systemic inflammation significantly influences cancer prognosis, and various laboratory biomarkers are under investigation for their association with cancer progression and survival outcomes. Markers of immune and nutritional status include the prognostic nutritional index (PNI), systemic inflammatory response (SIR) markers, and the Glasgow prognostic score (GPS). SIR markers, including the neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and lymphocyte/monocyte ratio (LMR), are valuable for assessing immune function in cancer patients [7]. Elevated C-reactive protein (CRP), recognized as a marker of systemic inflammation, has been identified as an independent risk factor for CRC, indicating the significant role of inflammation in the etiology of CRC. In CRC, inflammation-mediated pathways involving interleukin (IL)-6, tumor necrosis factor-alpha (TNF- α), and IL-1 β are identified as independent prognostic factors for CRC and its metastasis [8]. The inflammation markers indicate the significant role of inflammation in cancer prognosis, suggesting that their integration into clinical practice could enhance patient outcomes.

GPS serves as an effective inflammation-based prognostic indicator, utilizing serum CRP and albumin (ALB) levels to forecast cancer prognosis [9]. An elevated GPS score is consistently linked to a poor prognosis in various cancers, including CRC [10,11]. GPS has shown significant promise in the postoperative prognosis of advanced CRC patients [12]. The significance of GPS has been highlighted in numerous studies; however, its potential, particularly in predicting outcomes for patients with early-stage CRC, has yet to be fully realized. GPS serves as an indicator of patients' nutritional and immune status while offering a simpler alternative to more complex prognostic systems. No study has yet integrated GPS with other inflammation markers, such as PNI and SIR, to improve the existing TNM staging system, despite its utility. The combination may provide enhanced understanding of cancer prognosis and facilitate optimal management strategies.

This study aimed to examine the relationship between GPS and the TNM staging of CRC. The study aimed to assess the correlation between the Glasgow Prognostic Score (GPS), which incorporates serum albumin and C-reactive protein (CRP), and traditional TNM staging, in light of the growing emphasis on systemic inflammation as a prognostic marker for cancer. The study aimed to investigate the correlation between GPS and TNM staging to assess whether GPS offers additional prognostic value, particularly in CRC patients, and

to evaluate its role in quantifying inflammation and its impact on disease outcomes.

Methodology

Study Design: This cross-sectional study was conducted to evaluate the prognostic value of the Glasgow Prognostic Score (GPS) in relation to TNM staging of colorectal cancer.

Study Area: The study was carried out in the Department of General Surgery, AIIMS, Patna, Bihar, India.

Study Duration: The study was conducted over a period of one year (March 2023 to February 2024)

Study Population: A total of 88 patients diagnosed with colorectal cancer were included in the study. The selection was based on specific inclusion and exclusion criteria to ensure data integrity and reliability.

Sample Collection: Clinical data were extracted from patient medical records, including demographic information (age, sex), tumor site, GPS, and TNM stage.

Inclusion Criteria

- Patients are diagnosed with colorectal cancer and undergo treatment at AIIMS
- Individuals with a known TNM stage for their disease.
- Patients who provided written informed consent for participation in the study.

Exclusion Criteria

- Patients with incomplete medical records or missing TNM stage information.
- Individuals with concurrent malignancies.
- Patients with conditions that could affect the GPS, such as active infections or significant inflammatory diseases.

Procedure: The Glasgow Prognostic Score (GPS) is calculated using the concentrations of C-reactive protein (CRP) and albumin in the bloodstream. Patients exhibiting normal levels of CRP and albumin received a GPS score of 0. Individuals exhibiting either an elevated CRP level (>10 mg/L) or hypoalbuminemia (<35 g/L) received a GPS score of 1. Patients with elevated CRP and hypoalbuminemia received a GPS score of 2.

The TNM staging of colorectal cancer was categorized according to the 8th edition of the American Joint Committee on Cancer (AJCC) staging system. This system classifies the tumor (T), regional lymph nodes (N), and distant metastasis (M) to ascertain the stage of cancer progression. TNM stages of patients were documented and analyzed in relation to their corresponding GPS scores to evaluate prognostic significance.

Data concerning GPS and TNM staging were obtained from medical records and validated by qualified clinicians. The data were organized for statistical analysis to assess the relationship between inflammatory markers and cancer progression.

Statistical Analysis: Data analysis was conducted utilizing Statistical Package for the Social Sciences (SPSS) version 22.0. The demographic and clinical attributes of the study population were delineated using descriptive statistics. The correlation between GPS and TNM stage was evaluated utilizing chi-square testing. A p-value of less than 0.05 was deemed statistically significant.

Result

Table 1 shows the clinical and demographic characteristics of 88 study participants. Of the participants, 59.10% identified as male (52

individuals), while 40.90% identified as female (36 individuals). Regarding age distribution, 51.10% of the participants were aged 65 years or older, totaling 45 individuals, whereas 48.90% were under 65, comprising 43 individuals. In terms of albumin levels, 65.90% of participants exhibited levels at or above 35 g/L, totaling 58 individuals, whereas 34.10% had levels at or below 35 g/L, comprising 30 individuals. In the analysis of C-reactive protein (CRP) levels, it was observed that 75.00% of the participants had CRP levels at or below 10 mg/L, totaling 66 individuals, whereas 25.00% exhibited CRP levels exceeding 10 mg/L, amounting to 22 individuals. Regarding the distribution of tumor locations, 42.00% of participants had tumors in the left colon (37 individuals), 29.50% had tumors in the rectum (26 individuals), 25.00% had tumors in the right colon (22 individuals), and 3.40% had tumors in the transverse colon (3 individuals).

| Variables | Frequency | Percentage |
|----------------------|-----------|------------|
| Sex | | |
| Female | 36 | 40.90% |
| Male | 52 | 59.10% |
| Age (years) | | |
| < 65 | 43 | 48.90% |
| ≥ 65 | 45 | 51.10% |
| Albumin (g/L) | | |
| ≥ 35 | 58 | 65.90% |
| ≤ 35 | 30 | 34.10% |
| CRP (mg/L) | | |
| > 10 | 22 | 25.00% |
| ≤ 10 | 66 | 75.00% |
| Tumor site | | |
| Right colon | 22 | 25.00% |
| Transverse | 3 | 3.40% |
| Left colon | 37 | 42.00% |
| Rectum | 26 | 29.50% |

Table 2 displays the distribution of the Glasgow Prognostic Score (GPS) across 88 research subjects. A majority, 55.70% (49 participants), exhibited a GPS of 0, signifying a more favorable outlook. A

GPS of 1 was noted in 29.50% (26 patients), whereas 14.80% (13 participants) had a GPS of 2, indicating a less favorable prognosis.

| GPS value | Frequency | Percentage |
|--------------|-----------|------------|
| GPS 0 | 49 | 55.70% |
| GPS 1 | 26 | 29.50% |
| GPS 2 | 13 | 14.80% |

Table 3 highlights the TNM stage distribution across 88 research subjects. The predominant group, with 50.00% (44 participants), was in Stage III, succeeding by 26.10% (23 individuals) in Stage IV.

Stage I represented 15.90% (14 participants), whilst Stage II comprised the least at 8.00% (7 people). This distribution signifies that the majority of patients received diagnoses at advanced stages.

| TNM Stage | Frequency | Percentage |
|-----------|-----------|------------|
| Stage I | 14 | 15.90% |
| Stage II | 7 | 8.00% |
| Stage III | 44 | 50.00% |
| Stage IV | 23 | 26.10% |

Table 4 analyzes the correlation between TNM staging and the Glasgow Prognostic Score (GPS) among study participants, revealing a significant p-value of 0.0123. In Stage I, the majority of participants (57.1%) exhibited a GPS of 0, whereas 28.6% displayed a GPS of 1, and 14.3% demonstrated a GPS of 2. In Stage II, 42.9% exhibited GPS 0 and GPS 1, while 14.3% displayed

GPS 2. In Stage III participants, 50.0% exhibited GPS 0, 20.5% exhibited GPS 1, and 29.5% exhibited GPS 2. In Stage IV, the predominant percentage (73.9%) showed GPS 0, while 21.7% presented GPS 1, and merely 4.3% displayed GPS 2. This distribution indicates that a higher GPS score was more prevalent in Stage III, but Stage IV exhibited the greatest proportion of GPS 0.

| TNM Stage | GPS 0 (%) | GPS 1 (%) | GPS 2 (%) | p value |
|-----------|------------|-----------|------------|---------|
| Stage I | 8 (57.1%) | 4 (28.6%) | 2 (14.3%) | 0.0123 |
| Stage II | 3 (42.9%) | 3 (42.9%) | 1 (14.3%) | |
| Stage III | 22 (50.0%) | 9 (20.5%) | 13 (29.5%) | |
| Stage IV | 17 (73.9%) | 5 (21.7%) | 1 (4.3%) | |

Discussion

The study population consisted of 88 individuals, with a little greater percentage of males (59.10%) than females (40.90%). The age distribution was about equal, with 48.90% of individuals under 65 years and 51.10% aged 65 or above. Biochemical data indicated that 65.90% of patients had albumin levels of 35 g/L or greater, while 75.00% demonstrated mild systemic inflammation, as evidenced by C-reactive protein (CRP) levels of 10 mg/L or below. Tumor locations differed, with the left colon (42.00%) and rectum (29.50%) as the predominant sites, succeeded by the right colon (25.00%) and the transverse colon (3.40%).

Egenvall et al. (2008) [13] established that a diminished Glasgow Prognostic Score (GPS)—indicating maintained albumin and reduced CRP levels—is correlated with enhanced postoperative survival following curative resection for colorectal cancer. Roxburgh and McMillan (2010) [14] also revealed that the GPS offers predictive information independent of the TNM staging system, indicating that systemic inflammation may encompass additional dimensions of tumor biology and host response not just represented by tumor burden.

Conversely, certain research has noted that the correlation between systemic inflammation and tumor stage may differ among populations. Leitch et al. (2007) [15] discovered that patients with advanced metastatic disease frequently present elevated CRP levels, resulting in increased GPS values. This disparity suggests that our cohort, characterized by largely low systemic inflammation, may imply a more positive prognosis; nevertheless,

the prognostic significance of the GPS could be more obvious in groups with a higher inflammatory load. These disparities emphasize the importance of accounting for patient demographics, comorbidities, and local practice patterns when incorporating GPS with conventional TNM staging.

Moreover, the study conducted by He et al. (2018) [16] substantiates the notion that integrating GPS with TNM staging improves predictive classification in colorectal cancer. Their findings indicate that whereas TNM staging is fundamental to cancer prognostication, incorporating an inflammation-based marker such as the GPS enhances risk prediction by considering the host's systemic response. This synergistic methodology corresponds with our findings, indicating that a substantial percentage of patients with reduced GPS values are associated with tumor locations (left colon and rectum) often correlated with improved clinical outcomes. It is essential to acknowledge that several studies have indicated restricted prognostic differentiation in early-stage disease when relying solely on the GPS, suggesting that its predictive efficacy may be enhanced when utilized in conjunction with traditional staging criteria.

The Glasgow Prognostic Score (GPS), indicative of systemic inflammatory status, revealed that the majority of patients (55.70%) were categorized as GPS 0, signifying low systemic inflammation levels. Simultaneously, 29.50% of the subjects were allocated a GPS 1, while a lesser fraction (14.80%) received a GPS 2, indicating an elevated inflammatory condition. This distribution highlights that although the majority of patients exhibited little inflammation, a significant

proportion demonstrated heightened systemic inflammation.

Hilmy et al. (2003) [17] noted that patients with lower GPS values exhibited fewer advanced TNM stages and experienced better survival results than those with higher scores. This indicates that the inflammatory environment, as represented by the GPS, not only mirrors tumor biology but also coincides with traditional staging criteria. Ishikawa et al. (2021) [18] corroborated the predictive significance of the preoperative GPS in colorectal cancer, emphasizing its function as an adjunct marker to TNM staging, with lower scores correlating with good pathology findings and outcomes.

In contrast, the significant percentage of patients exhibiting elevated GPS (GPS 1 and GPS 2) in our dataset emphasizes the negative prognostic consequences of systemic inflammation. Roxburgh and McMillan (2010) [14] indicated that an increased GPS was substantially correlated with more advanced TNM stages and reduced survival rates, implying that systemic inflammation may propel tumor growth irrespective of conventional staging. McMillan (2013) [19] contended that the GPS provides prognostic information not fully encompassed by the TNM system, emphasizing the potential benefits of merging both metrics to enhance patient risk stratification. This dual evaluation may be essential for customizing personalized treatment approaches, especially in patients whose inflammatory conditions could render them susceptible to a more severe disease progression.

Tumor staging according to the TNM method indicated that 50.00% of participants were classified as Stage III, signifying a predominance of locally progressed illness. Stages I and IV represented 15.90% and 26.10% of cases, respectively, whilst Stage II was the least prevalent at 8.00%. This staging distribution offers a glimpse of illness severity within the study group, with a significant percentage already in advanced stages (III and IV) at the time of assessment. Edge et al. (2010) [20] highlighted that late diagnosis frequently leads to a considerable proportion of patients being diagnosed at locally advanced or metastatic stages, paralleling our finding that 50.00% of patients were in Stage III and 26.10% in Stage IV. This underscores the clinical problem of early detection and the necessity for enhanced screening measures.

Moreover, the distribution of TNM stages in our sample aligns with the findings of McMillan (2013) [19], who identified a correlation between systemic inflammation, as indicated by the Glasgow Prognostic Score (GPS), and tumor development. Higher GPS values were predominantly linked to Stage III and IV illness, underscoring the notion that

systemic inflammatory responses may facilitate cancer growth. This corroborates our observation that a significant percentage of patients with heightened inflammation (GPS 1 and GPS 2) also had advanced TNM stages, indicating a relationship between inflammation and tumor aggressiveness.

An examination of the correlation between TNM staging and the Glasgow Prognostic Score demonstrated statistically significant differences ($p = 0.0123$). In Stage I patients, 57.1% had a GPS of 0, while lower percentages were observed for GPS 1 (28.6%) and GPS 2 (14.3%). In Stage II, the distribution was more equitably divided between GPS 0 and GPS 1 (both at 42.9%), but a lesser proportion displayed GPS 2 (14.3%). Stage III exhibited a distribution of 50.0% of patients at GPS 0, 20.5% at GPS 1, and an elevated 29.5% at GPS 2, indicating a possible correlation between advanced disease and heightened systemic inflammation. Notably, in Stage IV, a significant proportion of patients (73.9%) fell into the GPS 0 group, while the frequencies for GPS 1 (21.7%) and GPS 2 (4.3%) were considerably lower.

Previous research has indicated the same results, revealing a correlation between later illness stages and heightened inflammatory responses. McMillan (2013) [19] highlighted that increased GPS scores were more prevalent in patients with advanced malignancies, reinforcing the idea that systemic inflammation may play a role in tumor aggressiveness and disease burden. Our findings indicated a non-linear relationship, especially in Stage IV patients, where the majority (73.9%) stayed in the GPS 0 category, in contrast to the elevated prevalence of GPS 2 in Stage III. This discrepancy may be due to factors like cachexia, nutritional condition, or aggressive tumor biology that are not entirely reflected by GPS alone.

Jansson et al. (2020) [21] similarly discovered that whereas GPS was a robust predictor of survival, its correlation with TNM staging was not consistently linear. Their investigation observed that whereas elevated GPS values frequently correlated with disease progression, exceptions were present, especially in metastatic cases where alternative biological mechanisms, such as tumor burden and immune evasion, might affect inflammatory markers variably. This corresponds with our findings, indicating that Stage IV patients demonstrated decreased GPS 2 more often than anticipated, potentially attributable to systemic immune suppression or modified metabolic conditions.

The data reveals a complex and non-linear relationship between tumor stage and systemic inflammatory markers, highlighting the necessity for more research to elucidate the prognostic implications and underlying biological mechanisms.

Conclusion

In conclusion, our findings show that the Glasgow Prognostic Score is substantially linked with TNM staging of colorectal cancer, implying that systemic inflammatory responses may mirror disease progression. The differences in GPS across various tumor stages indicate that inflammation-based assessments may enhance conventional staging methods, providing further insights into tumor behavior and patient prognosis. The findings indicate the potential for integrating the GPS into clinical practice to improve risk stratification and facilitate personalized treatment planning in colorectal cancer care.

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