e-ISSN: 2722-3558

Sriwijaya Journal of Surgery

[SJS]

https://sriwijayasurgery.com

High Improved Glasgow Prognostic Score (iGPS) Predicts Increased Postoperative Mortality in Stage I-III Colorectal Cancer: A Kaplan-Meier Survival Analysis

Gerry Armando[1]*, Efman Manawan[2], Theodorus[3]

[1]Residency Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

[2]Department of Digestive Surgery, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

[3]Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ARTICLE INFO

Keywords:
Colorectal cancer
Improved glasgow prognostic score
Mortality
Prognosis
Survival analysis

***Corresponding author:**
Gerry Armando

E-mail address:
armandomalau@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/sjs.v8i1.130

A B S T R A C T

Introduction: Colorectal cancer (CRC) represents a formidable cause of cancer-related mortality globally. Accurate prognostication that extends beyond conventional TNM staging is imperative for optimizing patient management. The Improved Glasgow Prognostic Score (iGPS), an inflammation-based biomarker derived from C-reactive protein (CRP) and albumin, has demonstrated considerable promise; however, its clinical utility has not been extensively validated in Southeast Asian populations. This study was therefore designed to investigate the association between preoperative iGPS and postoperative mortality among patients with non-metastatic CRC in an Indonesian tertiary care center. **Methods:** This study employed an ambispective cohort design, enrolling 33 patients with stage I-III CRC who underwent surgical resection at Dr. Mohammad Hoesin Hospital, Palembang. Preoperative serum CRP and albumin concentrations were utilized to calculate each patient's iGPS, which was then stratified into three risk categories: score 0 (low), 1 (medium), or 2 (high). The primary endpoint was all-cause postoperative mortality. The prognostic significance of iGPS in relation to survival was evaluated using the Kaplan-Meier method and log-rank test. **Results:** The patient cohort was predominantly composed of individuals aged ≥40 years (90.9%), with a median age of 59. Stage 3B was the most frequently observed pathological stage (39.4%). The overall mortality rate during the observational period was 57.6%. A robust association was identified between iGPS and survival outcomes. The survival probability for patients with iGPS 0 was 100%. Conversely, survival was substantially diminished in patients with iGPS 1 (33.3%) and iGPS 2 (42.1%). Kaplan-Meier analysis revealed a statistically significant divergence in survival distributions ($p < 0.05$), with higher iGPS scores correlating with markedly inferior survival. **Conclusion:** The preoperative iGPS is a potent and significant predictor of postoperative mortality in this Indonesian cohort of patients with non-metastatic CRC. Its utility as an accessible, cost-effective, and objective instrument for risk stratification is substantial. The integration of iGPS into routine clinical practice could enhance prognostic accuracy and aid in therapeutic decision-making.

1. Introduction

Colorectal cancer (CRC) constitutes a major global health challenge, ranking as the third most commonly diagnosed malignancy and the second leading cause of cancer-related mortality worldwide. In 2020, CRC accounted for over 1.9 million new cases and approximately 900,000 deaths, with projections portending a considerable escalation to 3.2 million new cases and 1.6 million deaths annually by the year 2040. This escalating burden is particularly pronounced in developing nations, including Indonesia, where CRC represents the third most prevalent malignancy. The geographic heterogeneity in CRC incidence and mortality is influenced by a confluence of factors, including lifestyle, diet, genetic predispositions, and the variable availability of

screening programs and advanced healthcare infrastructure.[1,2]

The current gold standard for CRC prognostication and therapeutic planning is the American Joint Committee on Cancer (AJCC) TNM (Tumor, Node, Metastasis) staging system.[5] This anatomical framework is indispensable for predicting patient outcomes and informing therapeutic strategies, most notably the application of adjuvant chemotherapy.[6] Nevertheless, the TNM system possesses well-recognized limitations. A significant degree of prognostic heterogeneity is observed among patients classified within the same TNM stage, a phenomenon especially evident in stage II and III disease.[7] The clinical course of patients can diverge substantially, underscoring that tumor biology and the host's systemic physiological response—factors not encapsulated by anatomical staging—exert a pivotal influence on clinical outcomes. This prognostic ambiguity has catalyzed a rigorous search for more nuanced, accessible, and biologically informative markers capable of supplementing the TNM system to refine risk stratification and facilitate the personalization of patient care.

A substantial body of evidence has now firmly established the role of the systemic inflammatory response (SIR) as a critical determinant of cancer progression and patient survival. Chronic inflammation is now considered a fundamental hallmark of cancer, contributing to nearly every phase of tumorigenesis, including proliferation, angiogenesis, invasion, and metastasis. The host's inflammatory reaction to a tumor is not merely a localized event but manifests systemically, a state that can be quantified through circulating biomarkers. Of these, C-reactive protein (CRP), an acute-phase reactant synthesized hepatically under the primary regulation of interleukin-6 (IL-6), has emerged as a robust and reliable indicator of systemic inflammation. Persistently elevated CRP levels in cancer patients are consistently correlated with greater tumor burden, more aggressive disease phenotypes, and consequently, a poorer prognosis across a wide spectrum of solid tumors, including CRC.[3,4]

Concurrently, the nutritional status of the cancer patient is intrinsically linked to both inflammation and clinical outcomes. Hypoalbuminemia is a frequent finding in patients with advanced cancer and serves as a powerful independent predictor of morbidity and mortality. Its prognostic significance is derived from its dual function as a surrogate for both malnutrition (cancer-associated cachexia) and the intensity of the SIR. Pro-inflammatory cytokines, such as IL-6 and TNF-α, actively suppress hepatic albumin synthesis. Thus, hypoalbuminemia reflects not only a deficient nutritional state but also the magnitude of the underlying inflammatory cascade, creating a pernicious cycle wherein inflammation exacerbates malnutrition, and malnutrition impairs the host's capacity to mount an effective anti-tumor immune response, further worsening the prognosis.[5,6]

Acknowledging the profound prognostic power of CRP and albumin, investigators have developed composite scoring systems to integrate these biomarkers into a single, clinically actionable tool. The genesis of this approach was the Glasgow Prognostic Score (GPS), introduced in 2003, which stratified patients based on the presence of elevated CRP (>10 mg/L) and/or hypoalbuminemia (<35 g/L). This was subsequently refined into the modified Glasgow Prognostic Score (mGPS), which prioritized inflammation by assigning a higher score only to patients exhibiting both abnormalities.[7,8]

This evolution culminated in the development of the Improved Glasgow Prognostic Score (iGPS), the focus of the present investigation. The iGPS was specifically engineered to provide a more granular and precise risk stratification for CRC patients by employing multiple, more sensitive cut-off thresholds for both CRP (≤2, >2-10, >10 mg/L) and albumin (≥39, 35-38.9, <35 g/L). This refined system aims to more accurately capture subtle variations in the host inflammatory-nutritional axis, particularly in patients with non-metastatic (Stage 0-III) disease. Initial validation studies have indicated that iGPS is a more

potent independent prognostic factor for both relapse-free and overall survival in comparison to its predecessors.[9,10]

Despite compelling evidence for the prognostic utility of inflammation-based scores, their validation has been predominantly concentrated in Western and East Asian populations. A conspicuous paucity of data exists for other regions, including Southeast Asia, where inherent differences in population genetics, diet, environmental factors, and healthcare systems could conceivably modulate the performance of such prognostic instruments. To our knowledge, no prior study has systematically investigated the clinical utility of the iGPS in an Indonesian population of CRC patients. This constitutes a critical evidence gap, as the clinical validity and utility of prognostic markers must be rigorously established in the specific populations for which their use is intended. The principal novelty of the present investigation is that it is the first to evaluate the prognostic accuracy of the preoperative iGPS within a cohort of Indonesian patients with non-metastatic CRC. By addressing this regional lacuna, this study aims to contribute crucial, locally relevant evidence on the performance of this simple, cost-effective, and objectively quantifiable biomarker-based score.

2. Methods

This investigation was structured as an ambispective cohort study with a survival analysis component. This design integrated the retrospective collection of baseline clinical and laboratory data from institutional medical records with a prospective follow-up to ascertain the primary endpoint. The study was executed at the Department of Digestive Surgery, Dr. Mohammad Hoesin General Hospital Palembang, South Sumatra, Indonesia. This institution functions as a national-level tertiary referral center, serving a large and demographically diverse patient population. The research was conducted over a six-month period, from November 2024 to April 2025, which encompassed patient enrollment, data acquisition, and final outcome assessment.

The study protocol adhered strictly to the ethical principles outlined in the Declaration of Helsinki. Prior to its initiation, formal ethical approval was obtained from the institutional review board of the Faculty of Medicine, Universitas Sriwijaya, and Dr. Mohammad Hoesin General Hospital. Anonymity and data confidentiality were maintained rigorously throughout the study. Written informed consent was obtained from all living participants or their legal next-of-kin during the prospective follow-up phase. Participants were fully apprised of the study's objectives and were assured of the voluntary nature of their participation and that all collected information would be utilized exclusively for research purposes.

The study population comprised all patients with a confirmed diagnosis of colorectal cancer admitted to the surgical ward of Dr. Mohammad Hoesin General Hospital during the study period who were candidates for surgical tumor resection. A non-probability, total sampling methodology was utilized, whereby all patients who satisfied the predefined eligibility criteria during the study timeframe were enrolled in the cohort. Inclusion criteria: Patients with a histopathologically confirmed diagnosis of primary colorectal adenocarcinoma; Patients with a definitive pathological stage of I, II, or III disease; Patients who were scheduled for, or had undergone, curative-intent surgical resection of the primary tumor; Availability of complete preoperative laboratory data for serum C-reactive protein (CRP) and albumin. Exclusion Criteria: Patients with a diagnosis of Stage IV (metastatic) colorectal cancer at presentation; Patients with active, severe infections or other acute inflammatory disorders at the time of blood sampling that could confound the biomarker results; Patients with severe, uncontrolled comorbidities that could independently influence prognosis, including uncontrolled diabetes mellitus, congestive heart failure not under routine management, recent stroke without therapeutic management, or chronic kidney disease requiring hemodialysis; Patients with incomplete medical records precluding the calculation of the iGPS. Following the application of these criteria,

a final cohort of 33 patients was deemed eligible for analysis.

Data were systematically collated from two sources: Secondary Data: Information was retrospectively extracted from institutional inpatient medical records. This included sociodemographic variables (age, sex, education level), clinical variables (final pathological TNM stage, adjuvant chemotherapy status), and preoperative laboratory values for serum CRP (mg/L) and albumin (g/L); Primary Data: The primary outcome variable, all-cause mortality, was ascertained prospectively at the conclusion of the follow-up period via a structured telephonic questionnaire administered to the patient or their next-of-kin.

The Improved Glasgow Prognostic Score (iGPS) algorithm provides a sophisticated method for risk stratification by translating two key biomarkers—C-reactive protein (CRP) and albumin—into a powerful, three-tiered clinical score. This refined system represents a significant advancement over previous inflammation-based scores by utilizing more sensitive and granular cut-off points.The algorithm identifies patients with the most favorable prognosis (iGPS Score 0) by applying stringent criteria that require both minimal systemic inflammation (CRP ≤2 mg/L) and optimal nutritional status (Albumin ≥39 g/L). This score signifies a state of systemic homeostasis, correlating with the best survival outcomes. Conversely, the algorithm gives primacy to severe malnutrition as the most critical indicator of a poor prognosis. Any patient presenting with significant hypoalbuminemia (Albumin <35 g/L) is automatically assigned the highest risk score (iGPS Score 2), reflecting a state of cancer-associated cachexia that is a powerful determinant of mortality. The intermediate iGPS Score 1 captures all other patients with mild-to-moderate disturbances in their inflammatory or nutritional status. This nuanced stratification allows for a more precise and clinically actionable assessment of patient risk.

All data were analyzed using the Statistical Package for Social Sciences (SPSS) software, version 27.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were compiled to delineate the baseline characteristics of the cohort. Categorical variables are presented as frequencies (n) and percentages (%). The normality of continuous variables was assessed using the Shapiro-Wilk test. As age was not normally distributed ($p<0.05$), it is reported as median with minimum and maximum values. Survival probabilities were estimated using the Kaplan-Meier method[46]. Differences between survival distributions for the iGPS groups were evaluated for statistical significance using the log-rank test. A two-sided p-value < 0.05 was considered statistically significant.

3. Results

The study cohort comprised 33 patients who met the established eligibility criteria. The data delineated in Table 1 provide a comprehensive sociodemographic and clinical snapshot of the 33-patient cohort, which is fundamental for contextualizing the study's primary findings on the prognostic utility of the Improved Glasgow Prognostic Score (iGPS). A thorough analysis of these baseline characteristics elucidates the specific patient population under investigation and highlights key factors that may influence the clinical presentation, management, and outcomes of colorectal cancer (CRC) within this specific Indonesian tertiary care setting.

The most salient demographic feature presented in Table 1 is the age distribution of the cohort. A striking 90.9% of the patients were aged 40 years or older at the time of diagnosis, with a median age of 59 years. This finding is profoundly consistent with the well-established global epidemiology of CRC, which overwhelmingly characterizes it as a disease of middle to late adulthood. The biological rationale for this age-dependent incidence is multifactorial, rooted in the "multi-hit" hypothesis of carcinogenesis. Over an individual's lifespan, the colonic epithelium is subjected to a cumulative burden of genetic and epigenetic insults from both endogenous metabolic processes and exogenous environmental exposures. This protracted timeline allows for the sequential acquisition of mutations in key tumor suppressor

genes (*APC*, *TP53*) and oncogenes (*KRAS*), which are necessary to drive the transformation of normal mucosa into malignant adenocarcinoma. The cohort's age profile, therefore, aligns perfectly with this canonical understanding of CRC pathogenesis and validates the study population as being representative of a typical CRC patient demographic. The near-complete absence of younger patients underscores that early-onset CRC, while a growing concern globally, remains a minority presentation in this specific clinical context.

The gender distribution within the cohort was nearly equal, comprising 17 males (51.5%) and 16 females (48.5%). This balanced representation suggests that there was no significant gender-based selection bias in patient enrollment. While larger epidemiological studies often report a slight male predominance in both the incidence and mortality of CRC—a disparity frequently attributed to a confluence of hormonal factors and lifestyle differences—the modest size of the present cohort precludes any definitive conclusions regarding gender-specific risk in this population. The observed equilibrium in gender serves to strengthen the study's internal validity, indicating that the prognostic findings related to iGPS are unlikely to be confounded by a disproportionate representation of one gender over the other.

Table 1. Baseline sociodemographic and clinical characteristics of the patient cohort (N=33).

Variable	Category	Frequency (n)	Percentage (%)
Age Group	<40 years	3	9.1
	≥40 years	30	90.9
Gender	Male	17	51.5
	Female	16	48.5
Education level	No Formal Schooling	1	3.0
	Elementary School	12	36.4
	Junior High School	8	24.2
	High School	9	27.3
	Diploma	1	3.0
	University Degree	2	6.1
Domicile	Palembang	5	15.2
	Outside Palembang	28	84.8

The distribution of patients according to the definitive pathological TNM stage is presented in Table 2. The data further reveal that the cohort is heavily weighted towards locally advanced CRC. The two most frequent stages were Stage 3B (39.4%) and Stage 2A (36.4%), which collectively account for over three-quarters (75.8%) of all patients. The clinical distinction between Stage II and Stage III disease is paramount: Stage III CRC, by definition, involves the metastatic spread of cancer cells to regional lymph nodes. Lymph node involvement is one of the most powerful independent predictors of distant recurrence and mortality in CRC. It signifies that the tumor has acquired the biological capacity to escape its primary site and travel through the lymphatic system, dramatically increasing the likelihood of subsequent systemic failure. The fact that nearly half the cohort (45.5%, combining stages 3B and 3C) presented with node-positive disease immediately classifies this population as being at high intrinsic risk for poor outcomes.

The substantial proportion of patients with Stage II disease (54.6% combining stages 2A, 2B, and 2C) is also highly significant. While technically node-negative, Stage II CRC is a notoriously heterogeneous category. It encompasses a wide spectrum of prognoses, from patients with tumors that barely penetrate the serosa (Stage IIA) to those with tumors that directly invade adjacent organs or cause perforation (Stage IIC). This clinical heterogeneity is a

primary driver for the search for non-anatomical biomarkers like the iGPS. The TNM system alone is often insufficient to distinguish which Stage II patients are at low risk of recurrence and can be safely managed with surgery alone, versus those who harbor micrometastatic disease and are at high risk, potentially warranting adjuvant chemotherapy.

Table 2. Distribution of patients by pathological tumour stage (N=33).

Pathological stage	Frequency (n)	Percentage (%)
II A	12	36.4
II B	4	12.1
II C	2	6.1
III B	13	39.4
III C	2	6.1
Total	**33**	**100**

Table 3 represents the analytical centerpiece of this investigation, providing a stark and quantitative demonstration of the association between the preoperative Improved Glasgow Prognostic Score (iGPS) and the primary study endpoint of postoperative mortality. The most profound and unambiguous finding within Table 3 lies in the iGPS 0 stratum. Although this group was the smallest, comprising only two patients (6.1% of the cohort), the outcome was absolute and unequivocal: zero deaths. This 100% survival rate is not merely a number; it is a powerful clinical and biological statement. It signifies that patients who present for major oncological surgery in a state of systemic homeostasis—characterized by minimal inflammation (CRP ≤2 mg/L) and optimal nutritional reserves (Albumin ≥39 g/L)—possess a remarkable degree of physiological resilience.

In stark contrast to the iGPS 0 group, the data for patients with an elevated score (iGPS 1 or 2) reveal a catastrophic decline in survival. When aggregated, these two strata encompass 31 patients, of whom 19 died during the observation period. This translates to an overall mortality rate of 61.3% for any patient exhibiting a preoperative iGPS greater than zero. The iGPS 1 (Medium-Risk) Stratum, comprising 12 patients, experienced 8 deaths, resulting in a staggering mortality rate of 66.7%. These are patients with an emerging or moderate degree of systemic inflammation and/or nutritional depletion. The data compellingly show that this "medium-risk" designation is, in absolute terms, a very high-risk state. The iGPS 2 (High-Risk) Stratum: This was the largest group in the cohort, with 19 patients (57.6%), further emphasizing the late-stage and poor baseline health of the population served by this tertiary center. Within this stratum, 11 patients died, for a mortality rate of 57.9%. This group is defined by significant hypoalbuminemia (<35 g/L), a robust surrogate for advanced cancer-associated cachexia and profound physiological depletion. An astute observer will note the seemingly counter-intuitive finding that the mortality percentage in the iGPS 1 group (66.7%) was slightly higher than in the iGPS 2 group (57.9%). It is imperative to interpret this finding with scientific caution and to avoid over-interrogation. This minor reversal is almost certainly a statistical artifact arising from the study's small sample size. With only 12 and 19 patients in these respective groups, the mortality percentages are highly sensitive to the outcome of a single patient and are susceptible to the random distribution of other unmeasured, poor prognostic factors (tumor grade, perineural invasion).

Table 3. Association between preoperative iGPS and postoperative mortality status (N=33).

iGPS category (Risk Stratum)	Survival Status: Alive (n)	Survival Status: Deceased (n)	Total (n, %)
Score 0 (Low Risk)	2	0	2 (6.1)
Score 1 (Medium Risk)	4	8	12 (36.4)
Score 2 (High Risk)	8	11	19 (57.6)
Total	14	19	33 (100.0)

The Kaplan-Meier survival analysis yielded a distinct and statistically significant stratification of patient survival based on the preoperative iGPS (Figure 1). The survival curve for patients with an iGPS of 0 demonstrated a 100% survival probability. Conversely, the survival curves for patients with iGPS scores of 1 and 2 exhibited a precipitous decline, indicating a substantially higher probability of mortality. The visual separation of the survival curve for the iGPS 0 group from those of the iGPS 1 and 2 groups was pronounced and sustained. The log-rank test confirmed that the differences among the three survival distributions were statistically significant ($p < 0.05$), providing robust evidence that the iGPS effectively discriminates between patient groups with vastly different survival prognoses.

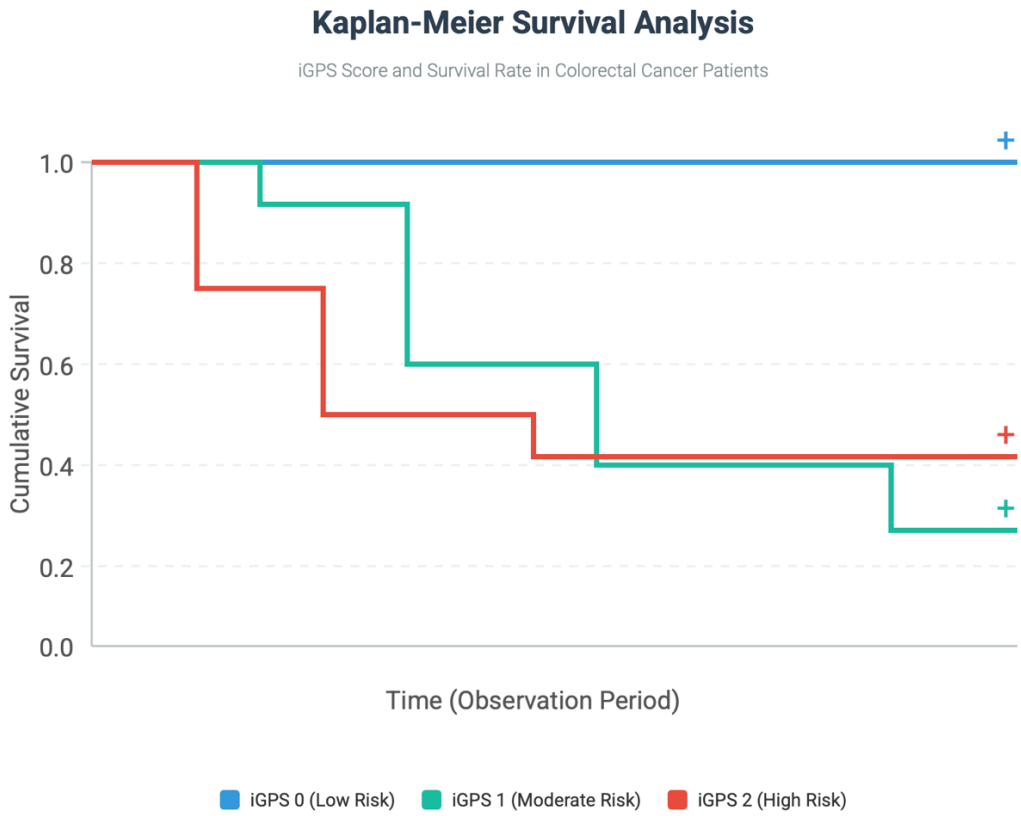

Figure 1. Kaplan Meier survival analysis.

4. Discussion

The present investigation was conceived to address a critical gap in the clinical literature: the validation of the Improved Glasgow Prognostic Score (iGPS) within a Southeast Asian, specifically Indonesian, cohort of patients with non-metastatic colorectal cancer (CRC). To our knowledge, this is the first study of its kind, offering novel insights into the performance of this

inflammation-based biomarker in a distinct demographic and healthcare context. The principal finding of our study is both unequivocal and profound: the preoperative iGPS, calculated from the routine and universally accessible measurements of C-reactive protein (CRP) and albumin, serves as a powerful and statistically significant predictor of postoperative mortality in this patient population. This conclusion is not merely an affirmation of a statistical association; it provides compelling evidence for the integration of a simple, cost-effective, and pathophysiologically-grounded tool into the clinical armamentarium for managing CRC. This discussion will endeavor to meticulously interpret these findings, explore the intricate biological mechanisms that bestow upon the iGPS its prognostic power, contextualize our results within the broader global literature, deliberate on the substantial clinical implications for patient care, and candidly address the study's inherent limitations while proposing a roadmap for future research directives.[11,12]

The core strength of the iGPS lies in its demonstrated ability to segregate patients into distinct prognostic strata with markedly different survival outcomes, a finding powerfully illustrated by both the tabular data and the Kaplan-Meier survival analysis. The interpretation of these strata provides a deep understanding of the score's clinical utility. The most striking result of this study is the perfect, 100% survival rate observed in the iGPS 0 cohort. While this group was the smallest in our study, comprising only 6.1% of the total cohort, the absolute nature of this outcome provides a vital prognostic anchor. The stringent criteria for achieving an iGPS of 0—requiring both a minimal systemic inflammatory response (CRP ≤2 mg/L) and an optimal nutritional status (Albumin ≥39 g/L) —effectively identify a unique subset of patients existing in a state of relative systemic homeostasis. From a pathophysiological perspective, these individuals have not yet succumbed to the profound systemic perturbations often incited by a malignancy. Their low CRP suggests a limited tumor-driven inflammatory cascade, which in turn implies a less aggressive tumor biology and a more competent host immune system, unhindered by the immunosuppressive effects of chronic inflammation. Simultaneously, their robust albumin levels indicate not only adequate nutritional reserves but also healthy hepatic function, free from the suppressive influence of inflammatory cytokines like IL-6.[13,14]

Consequently, these patients approach the physiological crucible of major oncological surgery with maximal resilience. They are better equipped to withstand the surgical stress, mount an effective wound-healing response, and maintain immunological surveillance against residual cancer cells. The perfect survival observed in this group is, therefore, the clinical manifestation of this preserved biological integrity. It validates the iGPS algorithm's ability to "select for" patients with the best possible prognosis, providing clinicians with a powerful tool for reassuring certain patients and for establishing a baseline against which the risk of other patients can be measured.

In stark and dramatic contrast to the iGPS 0 group, the survival outcomes for patients with any elevation in their score (iGPS 1 or 2) were uniformly poor. When these two high-risk strata are aggregated, they encompass 31 patients, of whom 19 (61.3%) were deceased by the end of the observation period. This finding illustrates a clear prognostic cliff; the transition from an iGPS of 0 to a score of 1 represents the crossing of a critical threshold, where the loss of systemic homeostasis precipitates a catastrophic decline in survival probability. The mortality rate within the iGPS 1 group was exceptionally high at 66.7%. This cohort represents a heterogeneous group of patients with either an emerging inflammatory response or a sub-optimal nutritional status. Their prognosis underscores that even a "moderate" deviation from homeostasis, as defined by the iGPS algorithm, is associated with a severe risk of mortality. These patients are already engaged in a systemic battle with their malignancy, and the substantial physiological insult of surgery appears to overwhelm their compromised reserves.[15,16]

The iGPS 2 group, defined by the overriding presence of significant hypoalbuminemia (<35 g/L), exhibited a similarly grim mortality rate of 57.9%. The fact that this was the largest stratum in our cohort (57.6% of all patients) is a crucial observation in itself, reflecting the advanced stage and poor baseline physiological status of the patients presenting to this tertiary referral center. These individuals are in a state of profound biological disadvantage, characterized by cancer-associated cachexia and significant systemic inflammation, rendering them extremely vulnerable to postoperative complications and disease progression.

A meticulous analysis reveals the seemingly paradoxical finding that the mortality percentage was slightly higher in the iGPS 1 group than in the iGPS 2 group. This observation, however, must be interpreted with extreme scientific caution and is almost certainly a statistical artifact of the study's small sample size. With only 12 and 19 patients in these respective strata, the percentages are highly volatile and can be disproportionately influenced by the outcome of one or two individuals. Furthermore, the random distribution of other unmeasured, powerful prognostic confounders—such as tumor grade, lymphovascular invasion, or specific comorbidities not captured by the exclusion criteria—could have, by chance, been more prevalent in the iGPS 1 group. Therefore, the clinically and scientifically robust conclusion is not to dwell on the minor statistical variance between the two high-risk groups, but to recognize the immense and undeniable prognostic chasm that separates a score of 0 (0% mortality) from any elevated score (over 60% mortality). This powerful, overarching trend is the central message of our findings. The prognostic power of the iGPS is not a mere statistical coincidence; it is deeply rooted in the fundamental biology of cancer progression. The score's elegance lies in its ability to simultaneously capture two intertwined pathophysiological axes that are now recognized as core determinants of patient outcomes: the host systemic inflammatory response (SIR) and the host nutritional status.[17]

Systemic inflammation is no longer considered an epiphenomenon but rather a key hallmark of cancer, actively promoting tumorigenesis and progression. Colorectal tumors are not inert masses; they are complex ecosystems that actively secrete a host of pro-inflammatory cytokines, chemokines, and growth factors into the systemic circulation. Among the most critical of these is Interleukin-6 (IL-6), which acts as a primary stimulant for the hepatic synthesis of acute-phase reactants, with C-reactive protein (CRP) being the most prominent and stable among them. An elevated serum CRP level is therefore an excellent and reliable surrogate marker for the intensity of the underlying tumor-driven, IL-6-mediated systemic inflammatory cascade.[18]

This systemic inflammation, in turn, fuels a vicious cycle of cancer progression through multiple mechanisms. Firstly, inflammatory cytokines directly promote tumor cell proliferation and survival by activating key signaling pathways like STAT3 and NF-κB. Secondly, they stimulate angiogenesis—the formation of new blood vessels—which is essential for providing tumors with the oxygen and nutrients required for growth and for creating conduits for metastasis. Thirdly, chronic inflammation fosters an immunosuppressive tumor microenvironment, hampering the ability of the host's own immune cells, such as T-lymphocytes, to recognize and eliminate cancer cells. Finally, inflammatory mediators can enhance the expression of enzymes like matrix metalloproteinases, which degrade the extracellular matrix and facilitate local invasion and distant metastasis. Thus, a high CRP level, as captured by the iGPS, is a direct reflection of a biologically aggressive tumor that has successfully hijacked the host's inflammatory machinery for its own benefit.[19]

Serum albumin, the other pillar of the iGPS, is a uniquely powerful prognostic marker due to its dual significance, reflecting both the patient's nutritional state and the intensity of the systemic inflammatory response. Its role as a marker of nutritional status is well-established. Progressing cancer often leads to anorexia and altered metabolism, culminating in

cancer-associated cachexia—a devastating syndrome of involuntary weight loss, muscle wasting, and profound weakness. Low serum albumin is a hallmark of this cachectic state, indicating depleted protein reserves and severe malnutrition.

However, hypoalbuminemia in cancer patients is not solely due to poor intake. It is also a direct consequence of the systemic inflammatory response itself. The same pro-inflammatory cytokines, particularly IL-6 and TNF-α, that drive up CRP levels concurrently act on the liver to suppress the synthesis of albumin, a process known as the negative acute-phase response. Therefore, a low albumin level is a composite signal of both nutritional depletion and high-grade inflammation. This duality makes it an exceptionally potent predictor of poor outcomes. A patient with hypoalbuminemia is physiologically compromised on two fronts: they lack the nutritional building blocks required for healing and immune function, and their body is simultaneously ravaged by a pro-tumorigenic inflammatory state. The iGPS algorithm astutely recognizes this by giving primacy to severe hypoalbuminemia (<35 g/L), assigning an automatic score of 2. This design feature is pathophysiologically sound, correctly identifying the state of advanced cachexia and inflammation as being so prognostically dire that it outweighs other considerations.[20]

Our findings, while novel for the Indonesian context, are strongly congruent with the broader international literature on inflammation-based prognostic scores. Our results, demonstrating a clear and significant survival stratification, provide crucial external validation for these findings in a genetically and environmentally distinct population. Similarly, large meta-analyses of the mGPS have consistently demonstrated that an elevated score confers a two- to three-fold increase in the risk of mortality in CRC patients, a finding that mirrors the dramatic survival drop we observed between the iGPS 0 and the elevated iGPS strata.

The true significance of our findings, however, must be interpreted through the lens of the regional healthcare context. As established by our cohort's characteristics, patients in this setting frequently present with locally advanced disease, with a striking 45.5% having node-positive Stage III cancer. This late-stage presentation, likely driven by the absence of widespread screening programs and other socio-demographic barriers, means that the patient population is inherently at a higher baseline risk than those in high-income countries where early detection is more common. In such a setting, the need for accurate, post-diagnosis risk stratification is not just important; it is paramount. The iGPS emerges as an ideal tool for this environment. It provides a means to further stratify risk within the large, heterogeneous groups of Stage II and III patients who constitute the bulk of the clinical workload. For clinicians in this setting, the iGPS offers a pragmatic solution to the challenge of managing a high-risk population, allowing for a more nuanced approach than is possible with TNM staging alone.

The preoperative calculation of iGPS can fundamentally alter a patient's management trajectory before they even enter the operating room. A high iGPS score serves as a clear "red flag," identifying a patient who is physiologically frail and at high risk for postoperative complications such as anastomotic leakage, surgical site infections, and prolonged hospitalization. This knowledge allows for proactive, personalized interventions. For instance, a patient with a high score could be a candidate for "prehabilitation"—a targeted, multidisciplinary program of intensive nutritional support, physical therapy, and potentially anti-inflammatory modulation aimed at improving their physiological reserve before surgery. This could transform them from a high-risk to a more acceptable-risk candidate, potentially improving both short-term surgical outcomes and long-term oncological survival.

Perhaps the most impactful application of iGPS lies in its potential to guide decisions regarding adjuvant chemotherapy. The management of Stage II CRC, in particular, is a well-known clinical dilemma. While adjuvant therapy is standard for most Stage III

patients, its benefit in Stage II is marginal and applies only to a small subset of high-risk individuals. The challenge lies in accurately identifying this subset. The iGPS offers a powerful, biologically-grounded tool to aid in this stratification. A Stage II patient with an iGPS of 0, for example, has an excellent prognosis and could likely be spared the toxicity of unnecessary chemotherapy. Conversely, a Stage II patient with a high iGPS has a prognosis more akin to a Stage III patient, and would be a strong candidate for receiving adjuvant therapy. By integrating iGPS with traditional high-risk pathological features, clinicians can make more informed and personalized decisions, maximizing benefit while minimizing harm. Finally, the iGPS provides a simple, objective metric that can greatly facilitate communication between clinicians, patients, and their families. Explaining complex prognostic information can be challenging. An easy-to-understand score can help patients grasp their situation more clearly and understand the rationale behind recommended treatment plans. This fosters a stronger therapeutic alliance and supports shared decision-making.

5. Conclusion

This investigation establishes that the preoperative Improved Glasgow Prognostic Score is a simple, potent, and significant predictor of postoperative mortality in Indonesian patients with non-metastatic colorectal cancer. The iGPS emerges as an invaluable, accessible, and cost-effective prognostic instrument. Its integration into routine clinical practice possesses the potential to substantially enhance risk stratification, inform therapeutic dialogues, and ultimately, improve the clinical management of colorectal cancer, particularly in resource-variable settings. Further large-scale validation is strongly warranted.

6. References

1. Ghosh A, Maitra S, Dasgupta P. Immune modulated Glasgow prognostic score as a predictor of toxicity profile and overall outcome in patients of head neck squamous cell carcinoma: a prospective single institutional study from eastern India. Clin Oncol (R Coll Radiol). 2024; 36(9): e360.
2. Li J, Yan K, Zhu P, Tang X, Yang Y, Gao R, et al. Prognostic value of Glasgow Prognostic Score and its modified scores on 5-year outcome in patients with coronary heart disease undergoing percutaneous coronary intervention. Heliyon. 2024; 10(18): e37317.
3. Endo S, Imai H, Shiono A, Hashimoto K, Miura Y, Okazaki S, et al. The Glasgow Prognostic Score as a predictor of survival after chemoradiotherapy for limited-disease small cell lung cancer. Oncology. 2025; 103(2): 83–93.
4. Shimomura K, Ogata T, Maeda A, Narita Y, Taniguchi H, Murotani K, et al. Investigation of the association between therapeutic effectiveness of anamorelin and Glasgow prognostic score in patients with cancer cachexia: a competing risk analysis. Invest New Drugs. 2025; 43(1): 118–25.
5. Yazdani A, Masum NH, Parveen R, Sazzad Hossain M, Hafizur Rahman Dipu M. Correlation between Glasgow prognostic score and tumor-node-metastasis staging in colorectal cancer. Int Surg J. 2025; 12(3): 279–83.
6. Chen J, Fu S, Yu J, Tang Q, Wu X, Luo S, et al. Modified Glasgow Prognostic Score as a marker for predicting outcomes in patients with either bladder or prostate cancer: a systematic review and meta-analysis. Oncology. 2025; 1–14.
7. Tian Z, Lin Y, Song Y, Zhang C, Wang Z. Comparison of the predictive value of neutrophil percentage-to-albumin ratio and modified Glasgow Prognostic Score for the risk of stroke-Associated Pneumonia among stroke patients. Int J Gen Med. 2025; 18: 1605–14.
8. Kokumai T, Aoki S, Nakagawa K, Iseki M, Sato H, Miura T, et al. High preoperative Glasgow

prognostic score increases a risk of hospital mortality in elderly patients with perihilar cholangiocarcinoma. J Hepatobiliary Pancreat Sci. 2025; 32(4): 298–310.
9. Ye H, Li M. Baseline (modified) Glasgow prognostic score as a predictor of therapeutic response to immune checkpoint inhibitors in solid tumors: a systematic review and meta-analysis. Oncol Lett. 2025; 29(4): 184.
10. Chen Y, Zhang B, Wang X, Chen Y, Anwar M, Fan J, et al. Prognostic value of preoperative modified Glasgow prognostic score in predicting overall survival in breast cancer patients: a retrospective cohort study. Oncol Lett. 2025; 29(4): 180.
11. Jiang L, Jin W. Prognostic value of Glasgow prognostic score in hematological malignancies: a systematic review and meta-analysis. Int J Hematol. 2025; 121(4): 450–61.
12. Karaduman A, Balaban İ, Biyiklı K, Keten MF, Kalkan S, Kahyaoglu M, et al. Relationship of the modified Glasgow Prognostic Score with peripheral artery disease severity and procedure success in patients who had undergone endovascular treatment. Vascular. 2025; 33(2): 410–8.
13. Liu R, Wang L, Ye J, Li X, Ma W, Xu X, et al. Preoperative glasgow prognostic score was an effective prognostic indicator in patients with biliary tract cancer. Front Immunol. 2025; 16: 1560944.
14. Victoria Juárez San Juan A, Juárez San Juan P, Artiles Armas M, Cano Contreras L, Beltrán Calero P, Jorge Ripper C, et al. Retrospective study on the Delta Shock Index associated with age and the Glasgow Coma Score (dSIAG) as a prognostic scale for mortality in polytrauma patients. Cir Esp (Engl Ed). 2025; (800111): 800111.
15. Numata K, Ono Y, Iguchi K, Uchiyama M, Asari M, Kazama K, et al. Prognostic significance of modified Glasgow Prognostic Score in patients undergoing FOLFOXIRI plus bevacizumab therapy for advanced or metastatic colorectal cancer. Oncology. 2025; 1–22.
16. Namiuchi S, Nochioka K, Ushigome R, Sunamura S, Tanita A, Ogata T, et al. Systemic inflammation-based Glasgow Prognostic Score as a prognostic indicator in chronic heart failure. Int J Cardiol Heart Vasc. 2025; 58(101660): 101660.
17. Ben Gal O, Doonan J, Lotfi N, McMahon S, Baker G, Cribb G, et al. The prognostic value of the modified Glasgow Prognostic Score in the management of patients with chondrosarcoma: a multicentre study. Bone Joint J. 2025; 107-B(6): 649–56.
18. Zhang L, Lin L, Ni J, Ling T, Huang L. Prognostic value of the pretreatment Glasgow prognostic score or modified Glasgow prognostic score in patients with advanced cancer receiving immune checkpoint inhibitors: a systematic review and meta-analysis. Oncol Lett. 2025; 30(1): 323.
19. Ishikawa S, Miyoshi N, Fujino S, Ogino T, Takahashi H, Uemura M, et al. Validation of the conventional Glasgow Prognostic Score and development of the improved Glasgow Prognostic Score in patients with stage 0-III colorectal cancer after curative resection. Ann Gastroenterol Surg. 2021; 5(3): 345–53.
20. Purwoyudho IGPS, Kamadjaja DB, Danudiningrat RMCP, Amir MS, Rizqiawan A, Mulyawan I, et al. The differences in expression of tumor marker KI-67 and proliferation cell nuclear antigen (PCNA) in ameloblastoma with histopathological subtypes follicular, plexiform, and mixed (follicular-plexiform). Eur J Dent. 2025.