



Decreased fluorescence latency and plateau intensity ratio as predictive markers of intraoperative hypoperfusion: quantitative indocyanine green perfusion analysis in colorectal cancer surgery

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Purpose: Intraoperative hypoperfusion is a major risk factor for postoperative anastomotic complications in colorectal surgery. Although most perfusion assessments emphasize arterial inflow, the roles of latency, sustained fluorescence, and venous outflow remain underexplored. This study aimed to identify quantitative indocyanine green (ICG) fluorescence parameters predictive of intraoperative hypoperfusion.

Methods: Eighty patients who underwent colorectal cancer resection between 2018 and 2022 were analyzed. Intraoperative perfusion was evaluated qualitatively using near-infrared ICG angiography and quantitatively through post hoc analysis of fluorescence time-intensity curves. Associations with hypoperfusion were assessed using group comparisons and receiver operating characteristic (ROC) analysis.

Results: Qualitative evaluation indicated hypoperfusion requiring intraoperative relocation of the anastomotic site in 12 patients (15%), with postoperative leakage in 1 patient (1.2%) despite revision of the anastomosis. Quantitative analysis showed that latency was significantly shorter in hypoperfused cases (5.5 seconds [interquartile range (IQR), 1.0–13.0 seconds] vs. 20.0 seconds [IQR, 6.8–27.0 seconds]; $P=0.003$), and the plateau intensity ratio (PIR; $F_{\text{plateau}}/F_{\text{max}}$) was markedly decreased (0.6 [IQR, 0.6–0.7] vs. 0.8 [IQR, 0.6–0.9]; $P=0.045$). The ROC analysis demonstrated good diagnostic performance for latency (area under the curve [AUC], 0.76; sensitivity, 33.3% [95% confidence interval (CI), 13.8–60.9]; specificity, 92.8% [95% CI, 84.1–96.9]; positive likelihood ratio, 4.6) and moderate accuracy for PIR (AUC, 0.68; sensitivity, 66.7% [95% CI, 39.1–86.2]; specificity, 68.1% [95% CI, 56.4–77.9]; positive likelihood ratio, 2.1).

Conclusion: Quantitative fluorescence analysis identified latency and PIR as complementary markers of perfusion dynamics. Whereas latency reflects early arterial inflow kinetics, PIR captures outflow characteristics related to microvascular and venous integrity. Combining these metrics may improve intraoperative detection of hypoperfusion and support data-driven decisions regarding anastomotic site selection.

Keywords: Perfusion; Colorectal surgery; Quantitative imaging; Fluorescence imaging; Indocyanine green

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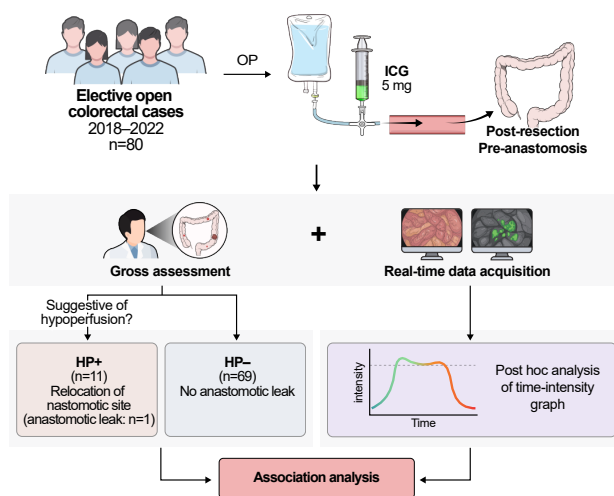
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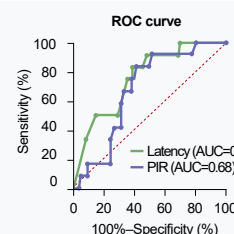
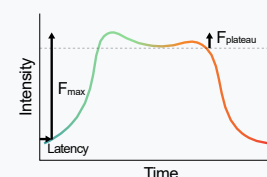
Graphical abstract

Decreased fluorescence latency and plateau intensity ratio as predictive markers of intraoperative hypoperfusion: quantitative indocyanine green perfusion analysis in colorectal cancer surgery**Purpose** To identify quantitative indocyanine green (ICG) fluorescence parameters that can effectively predict intraoperative hypoperfusion during colorectal cancer surgery**Methods****Results****Significant quantitative perfusion markers****Latency**Time to fluorescence onset
reflect arterial inflow

HP-	20 sec (IQR, 6.8–27 sec)
HP+	5.5 sec (IQR, 1–13 sec) $P < 0.01$

Plateau intensity ratio (PIR) $= F_{\text{plateau}} / F_{\text{max}}$
Related to microvascular
and venous integrity (outflow)

HP-	0.8 (IQR, 0.6–0.9)
HP+	0.6 (IQR, 0.6–0.7) $P < 0.05$

**Conclusion**

Combining latency and PIR may enhance intraoperative detection of hypoperfusion and support data-driven anastomotic decision-making

INTRODUCTION

Colorectal cancer is among the most prevalent malignancies of the gastrointestinal tract, and surgical resection remains the cornerstone of curative treatment. Anastomotic leakage (AL) is a frequent and severe postoperative complication after colorectal surgery and is associated with increased morbidity, mortality, length of hospitalization, and healthcare costs. Impaired perfusion at the anastomotic site is widely recognized as a major contributing factor to AL, underscoring the need for reliable intraoperative methods to assess bowel perfusion and thereby minimize the risk of AL [1].

Near-infrared fluorescence (NIRF) imaging with intravenous indocyanine green (ICG) provides real-time visualization of tissue perfusion and has been increasingly adopted in surgical practice. Although numerous studies support its feasibility and safety, standardized protocols for ICG dose, injection timing, and interpretation of fluorescence signals remain undefined. This variability contributes to heterogeneity in reported outcomes and limits the reproducibility and generalizability of ICG-guided approaches [2].

Evidence from both prospective and retrospective studies suggests that ICG angiography may reduce AL rates, although the results have been mixed. The PILLAR II study, which focused on left-sided hemicolectomy and anterior resection, reported an AL rate of 1.4% in 139 patients evaluated with ICG perfusion assessment [3]. Randomized trials by De Nardi et al. [4] and Alekseev et al. [5] demonstrated benefit only in selected patient subgroups or in low rectal anastomoses. Meta-analyses have reinforced the potential benefit of ICG-NIRF, particularly in high-risk patients, but substantial heterogeneity across studies remains [6].

Beyond visual assessment, quantitative analysis of fluorescence kinetics has emerged as a promising approach for reducing interobserver variability and improving objectivity in perfusion assessment. Parameters such as latency to fluorescence onset, time to maximum intensity, slope of the ingress curve, and outflow plateau characteristics provide a multiparametric characterization of perfusion dynamics and may predict AL risk more accurately than visual judgment alone [7–9]. Nevertheless, the clinical applicability of these quantitative metrics has not yet been fully validated.

Given these limitations, the present study sought to determine whether intraoperative ICG-NIRF perfusion assessment, using both visual interpretation and quantitative fluorescence metrics, can guide surgical decision-making regarding anastomotic site selection and reduce AL risk. Specifically, we analyzed whether modifications to the anastomotic level based on perfusion signals improved outcomes and assessed the predictive value of quantitative indices such as $F_{\text{plateau}}/F_{\text{max}}$, $T_{\text{plateau}}/T_{\text{max}}$, $F_{\text{plateau}}/T_{\text{plateau}}$, and $T_{1/2\text{max}}/T_{\text{max}}$.

METHODS

Ethics statement

The study protocol was approved by the Institutional Review Board of Scientific Research in Gdansk, Poland (No. NKBBN/94/2018 for the retrospective phase and No. NKBBN/944/2021 for the prospective phase). All patients included in the study were considered suitable candidates for surgery by a multidisciplinary oncologic board. Written informed consent for publication of the research details and clinical images was obtained from all patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Study setting

This study combined retrospective and prospective data collection: retrospective data, including fluorescence video recordings and clinical information, were collected between April 2018 and December 2021; and prospective data collection began in January 2022. All procedures were performed at the former Department of Surgical Oncology, University Clinical Center in Gdansk, Poland.

Study population

Eligible patients were aged ≥ 18 years, were of either sex, and had histologically confirmed colorectal cancer. Inclusion required adequate functional status, defined as a Karnofsky Performance Status of ≥ 80 and an Eastern Cooperative Oncology Group (ECOG) performance status grade of 0 or 1. Exclusion criteria were age < 18 years, pregnancy, hepatic or renal failure, known hypersensitivity to ICG or iodine-containing compounds, and active hematologic disorders. A total of 80 patients met these criteria and were included in the final analysis.

Surgical approach and imaging protocol

All surgical procedures followed the Enhanced Recovery After Surgery (ERAS) protocol. Patients underwent standardized open colorectal resection with intraoperative assessment of bowel perfusion.

NIRF imaging was performed using the Quest Spectrum system (Quest Medical Imaging), which is optimized for both open and minimally invasive surgery. The device provides simultaneous visible-light and NIRF visualization, using an excitation wavelength of 807 nm and capturing emission at approximately 822 nm. To improve image quality, ambient lighting was minimized, and the surgical field was illuminated with the system's integrated white-light source. The camera was mounted on a flexible arm 20 to 30 cm above the bowel, providing stable, hands-free, real-time imaging.

Fluorescence clips were recorded at 50 frames per second using the Quest Spectrum system. A standardized bolus of 5 mg ICG (5 mg/mL Verdyne, Carl Roth) was administered via a central venous catheter after colon transection and before creation of the anastomosis, followed by a 10-mL saline flush. Perfusion dynamics, including latency and time to maximum fluorescence, were observed at the bowel margins designated for anastomosis. Surgeons had continuous access to both white-light and NIRF images during intraoperative decision-making.

Hypoperfusion status was assessed intraoperatively before anastomosis creation by the same experienced colorectal surgeon. The assessment was based on ICG inflow time, duration of fluorescence persistence, and comparative perfusion of the proximal and distal bowel segments intended for anastomosis. Cases with delayed inflow, reduced fluorescence persistence, and visibly impaired perfusion of either bowel end were classified as hypoperfusion-positive (HP+).

Venous drainage was managed according to standard oncologic principles, with inferior mesenteric vein ligation performed as required to achieve adequate mobilization. Quantitative fluorescence analysis was therefore intended to capture the functional consequences of venous outflow adequacy at the anastomotic site rather than to evaluate the anatomical level of venous ligation per se.

Region of interest

All fluorescence recordings were analyzed post hoc using Quest ResearchTool ver. 4.7.2 (Quest Software). Three circular regions of interest (ROIs; diameter, approximately 20 pixels) were defined per frame using the integrated ROI tracker: (1) ROI 1, ischemic zone; (2) ROI 2, transitional/watershed zone; and (3) ROI 3, well-perfused reference.

The automated tracker compensated for tissue motion, and manual correction was applied if drift exceeded 1 pixel. The software generated time-intensity curves (arbitrary unit, AU) for each ROI (Figs. 1, 2). The system allowed simultaneous visualization of white-light, grayscale NIRF, and NIRF overlay views, which facilitated ROI selection and verification.

Quantitative analysis of colonic perfusion

Time-intensity curves derived from each ROI were analyzed to obtain quantitative perfusion metrics in accordance with previously described models of fluorescence kinetics [10]. Arterial inflow was assessed using maximum fluorescence intensity ($F_{\max}$), latency to onset (latency), time to maximum intensity ($T_{\max}$), and the maximal slope of the ingress curve ($\text{Slope}_{\max} = F_{\max}/T_{\max}$). Venous outflow and washout characteristics were characterized by plateau fluorescence intensity (F_{plateau}), plateau duration (T_{plateau}), the plateau time ratio (PTR; $T_{\text{plateau}}/T_{\max}$), which describes the relative duration of perfusion stabilization, and the plateau intensity ratio (PIR; $F_{\text{plateau}}/F_{\max}$), which quantifies the fraction of peak fluorescence sustained during the plateau phase. Additional derived parameters included the plateau slope ($\text{Slope}_{\text{plateau}} = F_{\text{plateau}}/T_{\text{plateau}}$), the time to half maximum intensity ($T_{1/2\max}$), and the relative time ratio (TR; $T_{1/2\max}/T_{\max}$). Together, these indices provided a multi-

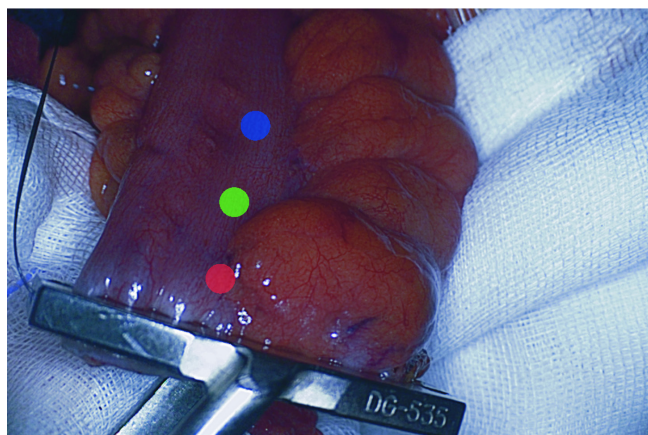


Fig. 1. Example of 3 circular regions of interest (ROIs) superimposed on every frame with the integrated ROI-tracker on the bowel loop. Red dot indicates ROI 1, the ischemic region; green dot indicates ROI 2, the transitional/watershed zone; and blue dot indicates ROI 3, the well-perfused reference.

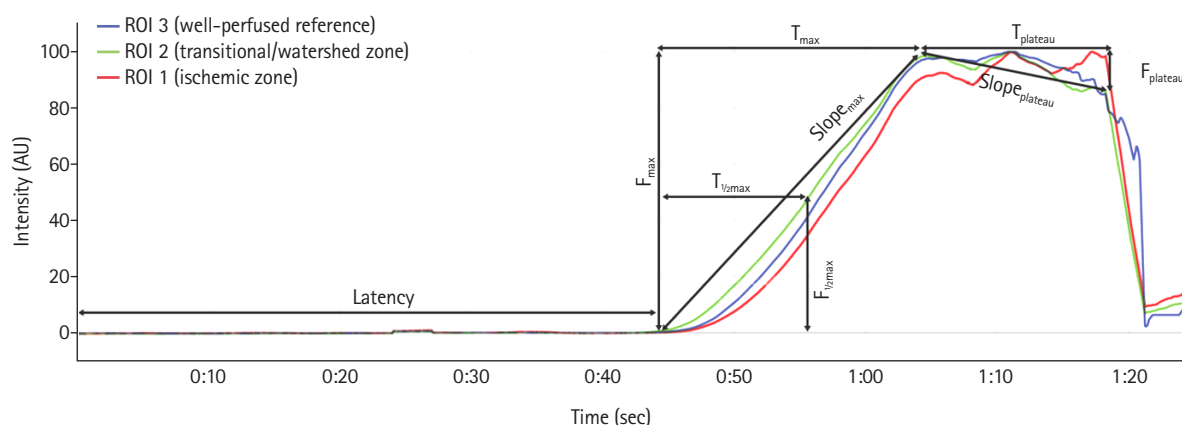


Fig. 2. Example of time-intensity curves for each region of interest (ROI). AU, arbitrary unit.

parametric characterization of arterial inflow and venous washout dynamics at the intended anastomotic site.

Statistical analysis

Sample size estimation was performed using G*Power ver. 3.1 (Heinrich Heine University Düsseldorf). Assuming a moderate effect size (Cohen $d = 0.7$), $\alpha = 0.05$, and 80% power, at least 68 patients (12 with significant hypoperfusion and 56 without hypoperfusion) were required. The final cohort of 80 patients, including 12 (15.0%) with intraoperative hypoperfusion prompting relocation of the anastomosis, exceeded this threshold and therefore provided sufficient statistical power.

Continuous variables were presented as mean $\pm$ standard deviation for normally distributed data or as median and interquartile range (IQR) for nonnormally distributed data. Categorical variables were expressed as frequencies and percentages. Normality was assessed using the Kolmogorov-Smirnov test.

Group comparisons between patients with and without intraoperative hypoperfusion suspected on the basis of qualitative inspection of the ICG signal were conducted using the independent-samples t-test or the Mann-Whitney U-test, depending on data distribution. Categorical variables were analyzed using the chi-square test or Fisher exact test, as appropriate. A two-sided P-value of < 0.05 was considered statistically significant, whereas results with $P < 0.1$ were interpreted as trends.

RESULTS

Study population

A total of 80 patients were included in the final analysis. Of these, 12 patients (15%) were included in the HP(+) group due to intraoperative hypoperfusion based on qualitative visual interpretation of the ICG signal, prompting relocation of the anastomotic site.

Among them, 1 patient (1.2%) developed postoperative AL within 30 days despite intraoperative revision of the anastomosis. The remaining 68 patients (85%) showed adequate perfusion on qualitative visual inspection of the ICG signal, required no modification of the anastomotic level, and were classified as the hypoperfusion-negative (HP-) group.

The mean age was comparable between groups, and the distribution of patients aged <70 and ≥70 years was also similar ($P=0.999$). Likewise, sex was not associated with intraoperative hypoperfusion; men comprised 75% of the HP+ group and 58.8% of the HP- group ($P=0.356$). Body mass index (BMI) was significantly associated with hypoperfusion. Patients with a BMI of <25 kg/m² were more frequently hypoperfused than those with a BMI of ≥25 kg/m² (66.7% vs. 33.3%, $P=0.017$). The prevalence of diabetes did not differ significantly between groups ($P=0.322$). No patient with type 1 diabetes developed hypoperfusion, whereas type 2 diabetes was more common in the HP+ group (33.3% vs. 19.1%). Smoking status was comparable between groups ($P=0.446$). Regarding surgical procedures, most patients underwent anterior resection, and the distribution of procedure types did not differ significantly between groups ($P=0.375$). No hypoperfusion was observed after right hemicolectomy, whereas left hemicolectomy and anterior resection showed similar hypoperfusion rates (Table 1).

Perfusion time-related factors

Among the time-dependent fluorescence parameters, latency was significantly shorter in the HP+ group than in the HP- group (5.5 seconds [IQR, 1.0–13.0 seconds] vs. 20.0 seconds [IQR, 6.8–27.0 seconds]; $P=0.003$), indicating earlier onset of the fluorescence signal in cases with intraoperative hypoperfusion (Fig. 3A). Other time-based variables, including $T_{\max}$ (16.5 seconds [IQR, 8.0–25.8 seconds] vs. 18.0 seconds [IQR, 9.0–31.5 seconds]; $P=0.821$), $T_{\frac{1}{2}\max}$ (7.0 seconds [IQR, 2.3–15.8 seconds] vs. 10.0 seconds [IQR, 3.5–13.5 seconds]; $P=0.543$), and T_{plateau} (17.0 seconds [IQR, 7.0–39.3 seconds] vs. 17.0 seconds [IQR, 11.0–26.0 seconds]; $P=0.770$), did not differ significantly between groups.

Similarly, the perfusion ratios TR (0.6 [IQR, 0.2–0.7] vs. 0.5 [IQR, 0.4–0.7]; $P=0.648$) and PTR (1.2 [IQR, 0.7–1.6] vs. 0.9 [IQR, 0.5–2.0]; $P=0.639$) did not differ significantly between groups. Overall, these findings suggest comparable inflow dynamics between groups despite the presence of localized hypoperfusion identified intraoperatively (Table 2).

Fluorescence intensity-related factors

Absolute intensity parameters, such as $F_{\max}$ (94.0 AU [IQR, 58.5–115.0 AU] vs. 100.0 AU [IQR, 57.5–100.0 AU]; $P=0.859$) and $\text{Slope}_{\max}$ (4.4 AU/sec [IQR, 3.7–6.6 AU/sec] vs. 4.4 AU/sec [IQR,

Table 1. Baseline demographic and clinical characteristics of patients stratified by hypoperfusion status (n = 80)

Characteristic	No. of patients (%)		P-value
	HP- group (n = 68)	HP+ group (n = 12)	
Age (yr)			0.999
< 70	29 (42.6)	5 (41.7)	
≥ 70	39 (57.4)	7 (58.3)	
Sex			0.356
Male	40 (58.8)	9 (75.0)	
Female	28 (41.2)	3 (25.0)	
Body mass index (kg/m ²)			0.017
< 25	19 (27.9)	8 (66.7)	
≥ 25	49 (72.1)	4 (33.3)	
Diabetes			0.322
No	48 (70.6)	8 (66.7)	
Type 1	7 (10.3)	0 (0)	
Type 2	13 (19.1)	4 (33.3)	
Smoking status			0.446
Never	41 (60.3)	8 (66.7)	
Former	11 (16.2)	3 (25.0)	
Current	16 (23.5)	1 (8.3)	
Surgery type			0.375
Anterior resection	26 (38.2)	5 (41.7)	
Anterior resection with ileostomy	11 (16.2)	2 (16.7)	
Right hemicolectomy	18 (26.5)	0 (0)	
Left hemicolectomy	13 (19.1)	5 (41.7)	

Hypoperfusion status was assessed intraoperatively using indocyanine green fluorescence before performing an anastomosis. P-values were calculated using the chi-square test or the Fisher exact test, as appropriate.

HP-, hypoperfusion-negative; HP+, hypoperfusion-positive.

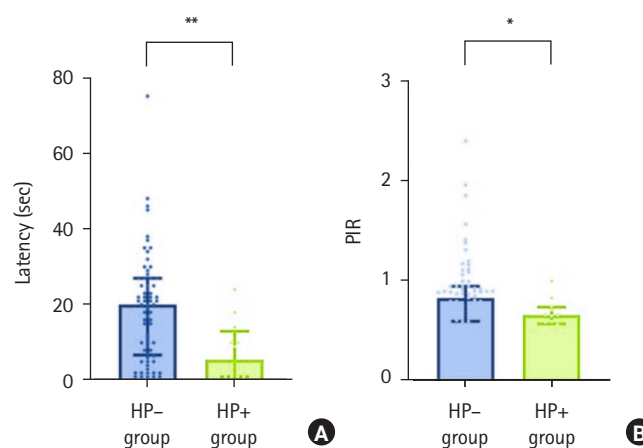


Fig. 3. Comparison of key perfusion parameters between hypoperfusion-negative (HP-) and hypoperfusion-positive (HP+) groups. (A) Latency was significantly shorter in the HP+ group ($P=0.003$), indicating faster fluorescence onset. (B) The plateau intensity ratio (PIR) was significantly lower in the HP+ group ($P=0.045$), suggesting impaired maintenance of perfusion despite initial inflow. Bars represent median values, and error bars represent interquartile ranges. * $P<0.05$, ** $P<0.01$.

Table 2. Comparison of quantitative indocyanine green fluorescence parameters between HP- and HP+ groups (n = 80)

Parameter	HP- group (n = 68)	HP+ group (n = 12)	P-value
Perfusion time-related			
Latency (sec)	20.0 (6.8–27.0)	5.5 (1.0–13.0)	0.003
T _{max} (sec)	18.0 (9.0–31.5)	16.5 (8.0–25.8)	0.821
T _{½max} (sec)	10.0 (3.5–13.5)	7.0 (2.3–15.8)	0.543
T _{plateau} (sec)	17.0 (11.0–26.0)	17.0 (7.0–39.3)	0.770
TR (T _{½max} /T _{max})	0.5 (0.4–0.7)	0.6 (0.2–0.7)	0.648
PTR (T _{plateau} /T _{max})	0.9 (0.5–2.0)	1.2 (0.7–1.6)	0.639
Fluorescence intensity-related			
F _{max} (AU)	100.0 (57.5–100.0)	94.0 (58.5–115.0)	0.859
F _{plateau} (AU)	70.0 (38.5–90.0)	51.5 (24.5–87.5)	0.390
Slope _{max} (F _{max} /T _{max}) (AU/sec)	4.4 (2.2–8.7)	4.4 (3.7–6.6)	0.593
Slope _{plateau} (F _{plateau} /T _{plateau}) (AU/sec)	3.3 (2.1–5.7)	2.8 (1.4–5.2)	0.500
PIR (F _{plateau} /F _{max})	0.8 (0.6–0.9)	0.6 (0.6–0.7)	0.045

Values are presented as median (interquartile range). Comparisons between groups were performed using the Mann-Whitney U-test.

HP-, hypoperfusion-negative; HP+, hypoperfusion-positive; T_{max}, time to maximum fluorescence intensity; T_{½max}, time to half maximum intensity; T_{plateau}, plateau duration; TR, time ratio; PTR, plateau time ratio; F_{max}, maximum fluorescence intensity; AU, arbitrary unit; PIR, plateau intensity ratio.

2.2–8.7 AU/sec]; $P = 0.593$), were similar between HP+ and HP- groups. However, perfusion indices describing sustained fluorescence, reflecting capillary filling and venous drainage, showed clearer separation between groups. Median F_{plateau} was lower in the HP+ group (51.5 AU [IQR, 24.5–87.5 AU] vs. 70.0 AU [IQR, 38.5–90.0 AU]; $P = 0.390$), and Slope_{plateau} was also lower (2.8 AU/sec [IQR, 1.4–5.2 AU/sec] vs. 3.3 AU/sec [IQR, 2.1–5.7 AU/sec]; $P = 0.500$), although neither difference reached statistical significance.

PIR showed the strongest discriminatory potential and was significantly lower in the HP+ group (0.6 [IQR, 0.6–0.7] vs. 0.8 [IQR, 0.6–0.9]; $P = 0.045$). This finding indicates that hypoperfused segments, despite reaching near-normal peak fluorescence, failed to maintain signal stability during the plateau phase, suggesting impaired venous clearance or reduced microvascular reserve (Table 2, Fig. 3B).

Analysis of perfusion markers

Among all quantitative fluorescence parameters, latency showed the best discriminatory performance for identifying intraoperative hypoperfusion, with an area under the receiver operating characteristic curve (AUC) of 0.76, indicating good diagnostic accuracy. The optimal threshold for latency (approximately 1.5 seconds) yielded a sensitivity of 33.3% (95% confidence interval [CI], 13.8–60.9) and a specificity of 92.8% (95% CI, 84.1–96.9), corresponding to a positive likelihood ratio of approximately 4.6 (Table 3, Fig. 4).

PIR showed moderate discriminatory ability for distinguishing hypoperfused (HP+) from normally perfused (HP-) segments,

with an AUC of 0.68. Using an optimal cutoff of approximately 0.68, PIR yielded a sensitivity of 66.7% (95% CI, 39.1–86.2) and a specificity of 68.1% (95% CI, 56.4–77.9), resulting in a positive likelihood ratio of approximately 2.1 (Table 3, Fig. 4).

DISCUSSION

This study evaluated both qualitative and quantitative intraoperative fluorescence perfusion assessment in colorectal cancer surgery and demonstrated that both early inflow dynamics and plateau-phase stability play distinct but complementary roles in identifying intraoperative hypoperfusion. Among all analyzed parameters, latency, representing the time from ICG injection to fluorescence onset, showed the strongest discriminatory performance, whereas the PIR provided additional insight into the maintenance of microvascular perfusion over time. Together, these findings underscore the clinical relevance of dynamic perfusion analysis beyond simple visual interpretation.

The shorter latency observed in the HP+ group may appear counterintuitive, because delayed inflow has traditionally been associated with ischemia. However, this phenomenon may reflect compensatory redistribution of perfusion or technical factors associated with superficial capillary hyperfluorescence in hypoperfused segments, resulting in earlier but less sustained fluorescence. Thus, early fluorescence onset does not necessarily indicate adequate tissue perfusion and may instead reflect superficial or transient inflow without sustained microvascular integrity, emphasizing the importance of interpreting latency in conjunction with plateau-based parameters such as PIR. Importantly, although in-

Table 3. ROC curve analysis of perfusion parameters

Parameter	Optimal cutoff ^a	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Positive LR	AUC	P-value
Latency (sec)	1.5	33.3 (13.8–60.9)	92.8 (84.1–96.9)	4.6	0.76	0.003
PIR	0.68	66.7 (39.1–86.2)	68.1 (56.4–77.9)	2.1	0.68	0.045

ROC, receiver operating characteristic; CI, confidence interval; LR, likelihood ratio; AUC, area under the curve; PIR, plateau intensity ratio.

^aDetermined using the Youden index.

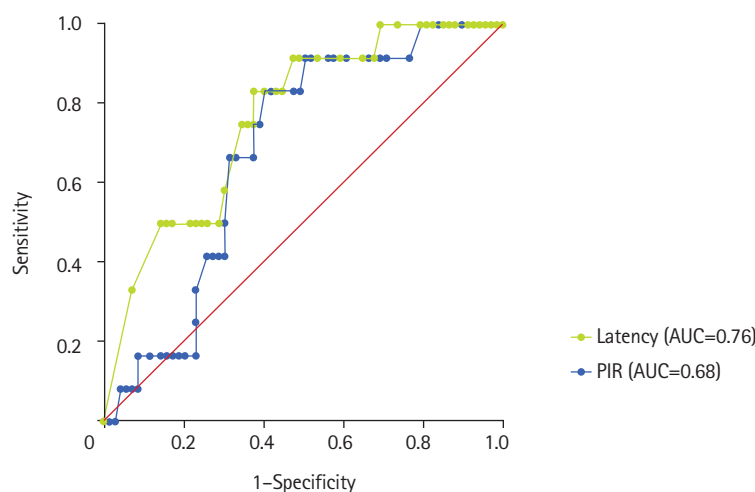


Fig. 4. Receiver operating characteristic curves for quantitative fluorescence perfusion parameters predicting intraoperative hypoperfusion. The latency parameter (green line) demonstrated the best diagnostic performance with an area under the curve (AUC) of 0.76, indicating good discriminatory ability between hypoperfused (hypoperfusion-positive) and normally perfused (hypoperfusion-negative) bowel segments. The plateau intensity ratio (PIR) showed moderate performance (AUC, 0.68), reflecting differences in sustained fluorescence intensity during the plateau phase. The diagonal line represents the line of no discrimination (AUC, 0.5).

flow parameters (latency, $T_{\max}$, and $\text{Slope}_{\max}$) describe arterial perfusion kinetics, their relationship to tissue viability is limited without corresponding assessment of venous outflow.

In this context, PIR, which quantifies the fraction of maximum fluorescence sustained during the plateau phase, emerged as the most physiologically meaningful indicator of adequate microcirculation. Despite preserved arterial inflow, hypoperfused bowel segments exhibited reduced PIR values, consistent with microvascular dysfunction that limited fluorescence maintenance through inadequate capillary perfusion or venous outflow [11]. Although vascular anatomy and ligation strategy may influence perfusion dynamics, intraoperative ICG fluorescence provides a direct tissue-level assessment that integrates arterial inflow, collateralization, and microcirculatory function, potentially reducing the impact of anatomical heterogeneity.

These findings are consistent with previous reports indicating that venous outflow and the capillary equilibrium phase, rather than initial arterial inflow, are critical determinants of anastomotic perfusion stability. Iwamoto et al. [7] identified delayed T_0 as a marker of increased leakage risk but noted that maximum-intensity parameters alone were not predictive, supporting our observation that static inflow metrics (such as $T_{1/2}$) provide limited

prognostic value. Likewise, Larsen et al. [12] highlighted substantial interobserver variability when perfusion assessment relied solely on visual inflow impressions, emphasizing the need for objective quantitative evaluation of the plateau phase. The present findings extend this understanding by demonstrating that even when peak inflow appears normal, reduced fluorescence stability, reflected by a lower PIR, may reveal subclinical hypoperfusion at the microvascular level.

From a physiological perspective, these results support the concept that anastomotic failure is not solely a consequence of impaired arterial supply but also reflects insufficient venous clearance and capillary homogeneity. Effective microvascular outflow is required to sustain oxygen exchange and prevent tissue congestion, both of which may be compromised when the plateau phase decays prematurely. Similar perfusion kinetics have been described in esophageal surgery, where well-perfused conduit regions show a balanced wash-in/washout pattern, whereas ischemic zones exhibit unstable fluorescence plateaus [13]. Applied to colorectal surgery, monitoring both the onset and stability of fluorescence may allow surgeons to detect subtle perfusion deficits before constructing the anastomosis.

Systemic hemodynamic variables such as mean arterial pres-

sure, vasopressor use, and hemoglobin concentration may influence fluorescence signal characteristics; however, these data were not uniformly available for multivariable adjustment. Future studies integrating synchronized anesthetic and perfusion data are warranted to clarify further the independent contribution of quantitative fluorescence metrics. Nevertheless, because ICG fluorescence reflects the net functional interaction between systemic hemodynamics and local microcirculatory regulation, it remains a clinically meaningful intraoperative endpoint.

From a practical standpoint, integrating quantitative fluorescence metrics such as latency and PIR could substantially enhance intraoperative decision-making. Real-time ICG analysis software can now automatically generate time-intensity curves, allowing surgeons to evaluate both inflow and plateau characteristics within seconds. The clinical value of quantitative ICG perfusion lies primarily in its capacity to guide real-time intraoperative decision-making. By identifying hypoperfusion before anastomosis construction, these metrics may allow surgeons to modify the anastomotic level or surgical strategy, potentially preventing postoperative complications. Accordingly, low leakage rates after such interventions should be interpreted as evidence of effective risk mitigation rather than as a sign of limited clinical relevance.

If future multicenter studies validate standardized threshold values, such as latency of < 1.5 seconds and PIR of < 0.68 as observed in our cohort, these metrics could serve as actionable indicators prompting revision of resection margins or consideration of a diverting stoma. Unlike qualitative fluorescence impressions, such data-driven thresholds offer reproducibility and objectivity suitable for integration into enhanced recovery pathways and emerging digital surgical platforms.

Limitations

This study has several limitations. First, although the sample size was adequately powered for the primary comparisons, it remains modest. Larger multicenter studies are needed to validate the generalizability of plateau-based indices. Second, technical factors such as camera positioning, movement, ambient light, and ICG dosing, although standardized in our protocol, may have influenced fluorescence kinetics. Third, although our findings strongly suggest that venous outflow is a key determinant of AL, perfusion is multifactorial and may also be affected by patient comorbidities, surgical technique, and anastomotic tension.

Conclusions

This study demonstrates that intraoperative quantitative fluorescence analysis can objectively characterize both arterial inflow and venous outflow dynamics at the anastomotic site. Although

latency provided the highest diagnostic accuracy for detecting intraoperative hypoperfusion, PIR emerged as the most physiologically relevant marker of sustained microvascular integrity. These findings support a comprehensive, multiphasic assessment of fluorescence perfusion that integrates both inflow and plateau parameters to improve intraoperative decision-making and reduce the risk of postoperative anastomotic failure.

ARTICLE INFORMATION

Conflict of interest

Luigi Marano is an editorial board member of this journal, but was not involved in the peer reviewer selection, evaluation, or decision process of this article. Ronald J. H. Borra is a medical consultant for Perfusion Tech. No other potential conflict of interest relevant to this article was reported.

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None.

Author contributions

Conceptualization: PDM; Data curation: PDM; Formal analysis: PDM; Investigation: PDM; Methodology: PDM, JC, LM; Supervision: PDM, KP, RJHB; Validation: PDM, KP, RJHB; Visualization: PDM, JC; Writing—original draft: PDM, JC, LM; Writing—review & editing: all authors. All authors read and approved the final manuscript.

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