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Clinical effect and standardization of indocyanine green angiography in the laparoscopic colorectal surgery

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Anastomotic complications occur after 5% to 20% of operations for rectosigmoid colon cancer. The intestinal perfusion status at the anastomotic site is an important modifiable risk factor, and surgeons should carefully evaluate and optimize the perfusion at the intended site of anastomosis. Indocyanine green (ICG) angiography is a simple noninvasive perfusion assessment modality. The use of ICG angiography is rapidly spreading in the field of colorectal surgery. However, there is debate on its contribution to reducing anastomotic complications. In this review, we discuss the clinical utility and the standardization of ICG angiography. ICG angiography can unequivocally reveal unfavorable perfusion zones and provide quantitative parameters to predict the risk of hypoperfusion-related anastomotic complications. Many studies have demonstrated the clinical utility of ICG angiography for reducing anastomotic complications. Recently, two multicenter randomized clinical trials reported that ICG angiography did not significantly reduce the incidence of anastomotic leakage. Most previous studies have been small-scale single-center studies, and there is no standardized ICG angiography protocol to date. Additionally, ICG angiography evaluations have mostly relied on surgeons' subjective judgment. For these reasons, it is necessary to establish a standardized ICG angiography protocol and develop a quantitative analysis protocol for the objective assessment. In conclusion, ICG angiography could be useful for detecting poorly perfused colorectal segments to prevent anastomotic leakage after colorectal surgery. An optimized and standardized ICG angiography protocol should be established to improve the reliability of perfusion assessments. In the future, artificial intelligence-based quantitative analyses could be used to easily assess colonic perfusion status.

Keywords: Indocyanine green, Angiography, Quantitative light-induced fluorescence, Anastomotic leak, Colorectal surgery

INTRODUCTION

Colorectal cancer is one of the commonest gastrointestinal tumors. The rectosigmoid colon is the most common location for colon cancer. Anastomotic complications occur after approximately 5% to 20% of anterior resections for rectosigmoid colon cancer [1]. Risk factors associated with anastomotic complications vary considerably, but they include the tension of anastomosis, perfusion status, distance of the anastomosis from the anal verge, preoperative chemoradiation, smoking, advanced stage, difficult

total mesorectal excision, male patient, stapler characteristics, anemia, and nutrition [2]. Most of these variables are unmodifiable patient-related risk factors. However, there are some modifiable risk factors that are gradually becoming possible to overcome with technological advances. Intestinal perfusion status has become a modifiable risk factor, and surgeons can evaluate and select anastomosis sites with optimal perfusion to perform safe colorectal anastomoses [3].

Ligation of the inferior mesenteric artery (IMA) has been considered an essential step for oncological dissection of the rectosigmoid colon. Several studies have reported that IMA ligation may cause hypoperfusion of the left-sided colon [4,5]. Almost half of anastomotic leaks are suspected to be associated with hypoperfusion. Subjective assessments have been used to evaluate blood flow in the gastrointestinal tract. This might have limited diagnostic accuracy dependent on the surgeon's experience. Indocyanine green (ICG) angiography is a simple, noninvasive method that is carried out using a near-infrared (NIR) camera system. Currently, ICG angiography is rapidly gaining adoption in colorectal surgery. The clinical utility of ICG angiography for reducing anastomotic complications is under scientific investigation through several multicenter randomized clinical trials [6,7]. The expectations and interests of ICG angiography among surgeons are continually increasing. However, since ICG angiography has been carried out with various protocols, standardization is required [8,9]. In this review, we discuss the clinical utility and standardization of ICG angiography for colonic perfusion assessment.

MAIN SUBJECTS

Prolonged debate about inferior mesenteric artery ligation and hypoperfusion

IMA ligation in rectosigmoid colon cancer surgery is commonly performed for sufficient D3 lymph node dissection and tension-free anastomosis through sufficient proximal colon lengthening. However, it may increase the risk of damage to the autonomic nerve plexus of the IMA root and ischemia of the left-sided colon. To overcome this risk, some surgeons perform low ligation of the IMA to preserve the left colic artery [10]. This procedure requires a high level of surgical expertise for vascular branch dissection. However, D3 lymph node dissection cannot be performed as an en bloc resection, and controversy remains over oncological safety for low IMA ligation even though these two procedures have not been shown to significantly affect oncologic outcomes [11]. The IMA could be a mesenteric anchoring point in the cases of short sigmoid colons and advanced rectosigmoid colon cancer. Therefore, high ligation is inevitably selected to obtain sufficient redundancy of the proximal colonic segment.

When performing colorectal surgery, anastomotic complications are the most difficult hurdles faced by surgeons and patients. The large intestine has a different blood flow supply system on the right and left-sided colon. The marginal arterial arcade of the right and left-sided colon might be connected near the splenic flexure, forming a collateral circulation between the superior mesenteric artery (SMA) and the IMA. The lower rectum is supplied with blood flow by the middle and lower rectal arteries branching from the internal iliac artery. Therefore, even when IMA ligation accompanies anterior resection, blood flow in the left colon can be maintained by the SMA. However, an anatomical cadaver study reported that in 20% of individuals, linkage of the marginal arcade forming the collateral circulation might be insufficient [12].

Hypoperfusion of the left side of the colon is a well-known phenomenon associated with IMA ligation. We reported on marginal arterial pressures measured through mesenteric artery cannulation, particularly looking at changes in colonic mesenteric artery pressure before and after the IMA ligation; we measured marginal arterial pressure before and after IMA clamping. In more than 10% of rectosigmoid cancer patients, marginal arterial pressure was significantly decreased by more than 30% [4]. Therefore, colonic hypoperfusion might be a rare but real event, potentially leading to ischemic colitis in some patients with poor collateral circulation. To prevent hypoperfusion-related anastomotic complications, this 10% of high-risk patients with ischemic changes must be identified.

Experienced surgeons have traditionally practiced observing intestinal color, arterial pulsation, and colonic peristalsis, or bleeding at the cutting edge of the mesenteric artery. These subjective evaluations could be considered good clinical assessments by experienced surgeons. However, the accuracy and reliability of subjective evaluations could have a wide spectrum depending on surgical experience [13]. Accordingly, an objective and quantitative technique is needed to improve the accuracy and reliability of bowel perfusion status evaluations. Such an evaluation method should be noninvasive and easy to apply, and the results could be interpreted intuitively in real time by the surgeon. Additionally, the diagnostic technique used should be able to be safely applied to the patient for measuring colonic perfusion [14].

There are a variety of methods for evaluating blood flow. Arterial pressure can be measured through arterial cannulation via connections to blood pressure monitoring equipment in the operating room. [4,15]. Color Doppler ultrasonography is a safe, noninvasive procedure, which has the advantage of allowing repeated and safe evaluation of perfusion status in real time. However, there are technical limitations for evaluating very small blood vessels within 1–2 mm of the colonic wall [16]. Computed tomography (CT) angiography can be used for assessing the mesenteric arterial structure. CT resolution has been gradually

improving and now permits the evaluation of the arterial circuit using three-dimensional reconstruction. However, CT angiography has a limited resolution for visualization of the collateral marginal artery connection with very small vascular diameters of less than 1 mm at the splenic flexure [4].

Therefore, a simple and noninvasive assessment method is needed for obtaining high-resolution images in real time for daily practice in the era of minimally invasive surgery.

Indocyanine green angiography and anastomotic leakage

ICG is a fluorescent agent that was approved by the U.S. Food and Drug Administration in 1956. To date, it is the only fluorescent substance that can be administered to humans for clinical practice. Although ICG-related side effects are rare, allergic reactions may occur, particularly when a patient has a history of CT contrast allergy. ICG solutions contain a trace amount of iodine, which is a component of CT contrast solution [17]. Therefore, it is necessary to review a patient's allergy history before performing ICG angiography; it is also important to monitor for allergic reactions during the examination.

ICG becomes fluorescent at around 800 nm, which is within the NIR wavelength range. NIR spectroscopy was developed to detect ICG fluorescence, and it is possible to use this technology to visualize ICG in blood samples. This function is mainly used to evaluate the reserve liver function before liver transplantation or liver resection [18]. However, the equipment used for this investigation is still so large that the collected venous blood should be measured in a special laboratory for ICG concentration measurement. Since ICG binds to proteins, such as albumin and globulins in the blood, extravasation does not occur easily, which is useful for evaluating blood flow. ICG was first applied to cardiac function evaluation and ophthalmoscopic angiography. In the surgical field, a handheld NIR camera was developed to evaluate blood flow by detecting fluorescence from intravascular ICG. Recently, a laparoscopic NIR camera has been developed, making ICG angiography available for use in minimally invasive surgery [19]. With ICG angiography, a surgeon can directly observe the intestinal perfusion status with a fluorescence image. Changes in the fluorescence intensity (FI) are viewed along the path of blood flow to the target organ. Fluorescence images can be expressed in green, cyan, or blue on a black-and-white background, depending on the NIR camera system [20]. A fluorescence image can also be expressed as an overlay on the same image of a white light view.

ICG angiography can be used to unequivocally reveal unfavorable perfusion zones and obtain quantitative parameters to predict the risk of complications associated with hypoperfusion. Transection line changes have been reported in 5% to 20% of patients with unfavorable perfusion segments identified by ICG

angiography. At our institution, the anastomotic complication rate reached nearly 10% before we instituted ICG angiography, and it rapidly decreased to 1% to 2% after we started evaluating colonic perfusion [3]. Many studies have demonstrated the clinical utility of ICG angiography for reducing anastomotic complications (Table 1) [3,5–7,13,14,19,21–41].

However, two multicenter randomized clinical trials reported that ICG angiography did not significantly reduce the incidence of anastomotic leakage [6,7]. Nevertheless, a meta-analysis determined that there were significantly fewer anastomotic complications in patients who underwent ICG angiography in the included studies (Table 2) [42–49]. One of the reasons for these contradictory results is that quantitative analysis and optimal standardized protocols are still lacking for ICG angiography. Most of the existing evidence has been obtained from small-scale, single-center studies, and the ICG angiography protocol has not been standardized. Additionally, the evaluation of ICG angiography has mostly relied on the subjective judgment of the surgeon, and few studies have applied quantitative analyses. For these reasons, it is necessary to establish a standardized ICG angiography protocol and develop a quantitative analysis protocol for objectively assessing FI.

Standardization of indocyanine green angiography protocol

To date, various NIR devices and different angiography protocols have been applied at different institutions. Therefore, to compare and analyze image data from multiple institutions, we need to establish a standardized ICG angiography protocol to improve efficacy and accuracy. Additionally, qualitative perfusion parameters could improve the accuracy of a surgeon's subjective judgment. The ability to detect changes in FI is a breakthrough in fluorescence imaging that allows tissue perfusion to be easily visualized [3]. However, in ICG angiography, FI is greatly affected by the external environment. Other quantitative parameters based on FI also depend on external conditions. For example, one study found the maximal FI level and increasing slope to vary significantly, influenced by various conditional factors, including perfusion status [9]. FI scale can be changed because it is quite sensitive to external environmental conditions.

We previously applied various external conditions to obtain the best fluorescence images for several years. From these experiences, we found the optimal external environmental conditions for maximizing FI [9]. The distance between the camera and tissue was one of the most important determinants of brightness. In current ICG cameras for laparoscopy, the brightness changes sharply according to the distance when it is closer than 4 to 5 cm; when it is further than 4 to 5 cm, the brightness becomes relatively stable, which reduces the quality of evaluation of FI chang-

Table 1. Characteristics of studies and ICG angiography to reduce anastomotic leak

Study	Year	Study design	No. (ICG/control)	Type of surgery	ICG dose	NIR light source	NIR system	Quantitative parameter	Transection line change (%)	Anastomotic leak (%)	p value
Jafari et al. [6]	2021	Multicenter RCT (PILLAR III)	178/169	Laparoscopic LAR	5–10 mg	Laser	PINPOINT (Stryker)/SPY Elite (LifeCell)	NA	NA	9.0/9.6	0.37
De Nardi et al. [7]	2020	Multicenter RCT	118/122	Laparoscopic AR or LAR	0.3 mg/kg	Xenon	D-light P (Karl Storz)	NA	11	4.9/8.5	NS
Park et al. [14]	2020	Prospective study	65/-	Laparoscopic LAR	0.2 mg/kg	Laser	1588 AIM (Stryker)	ICG pattern, T1/2, TR, slope	10.3	4/-	NA
Alekseev et al. [21]	2020	Single-center RCT	187/190	Laparoscopic AR or LAR	0.2 mg/kg	Xenon	D-light P (Karl Storz)	NA	19.3	9.1/16.3	0.04
Wojcik et al. [22]	2020	Prospective case-matched study	42/42	Laparoscopic AR or LAR	0.1 mg/kg	Laser	FLUOBEAM (Fluoptics)/PINPOINT (Stryker)	NA	10.9	2.4/16.7	0.026
Morales-Conde et al. [23]	2020	Prospective study	192/-	Colorectal Surgery	15 mg	Xenon/laser	IMAGE1 S (Karl Storz)/1588 AIM (Stryker)	NA	18.2	2.6/-	NS
Watanabe et al. [24]	2020	Multicenter PSM cohort study	211/211	Laparoscopic LAR	0.25 mg/kg	Xenon/laser	D-light P (Karl Storz)/1588 AIM (Stryker)	NA	5.7	4.7/10.4	0.042
Benčurik et al. [25]	2020	Prospective study	100/100	Laparoscopic or robotic LAR	0.2 mg/kg	Xenon/laser	SPIES (Karl Storz)/Firefly (Intuitive)	NA	15	9/19	0.042
Bonadio et al. [26]	2020	Prospective study	33/33	Laparoscopic LAR	0.2 mg/kg	Xenon	SPIES (Karl Storz)	NA	18.2	6/21.2	0.15
Hasegawa et al. [27]	2020	Retrospective, cohort study	141/279	Laparoscopic LAR	5 mg	Xenon	IMAGE1 S (Karl Storz)	NA	NA	2.8/13.6	0.001
Otero-Piñeiro et al. [28]	2020	Retrospective comparative study	80/204	TaTME	2.5 mg/mL	Laser	PINPOINT (Novadaq)	NA	28.7	2.5/11.3	0.02
Ishii et al. [29]	2020	Retrospective study	87/87	Laparoscopic and Robotic LAR	5 mg	Laser	1588 AIM (Stryker)	NA	3.1	3.4/11.5	0.044
Son et al. [3]	2019	Prospective study	86/-	Laparoscopic LAR	0.25 mg/kg	Xenon	IMAGE1 S (Karl Storz)	Tmax, T1/2, TR, slope	8.1	4.7/-	NA
Wada et al. [30]	2019	Retrospective PSM study	34/34	Laparoscopic LAR	5 mg	Xenon	PDE (Hamamatsu Photonics)	NA	27.1	8.8/14.7	0.71
Ogino et al. [31]	2019	Prospective study	74/-	Colorectal Surgery	5 mg	Xenon	PDE (Hamamatsu Photonics)	NA	8.1	1.4/-	NA
Chang et al. [32]	2019	Prospective, observational study	110/-	Colorectal Surgery	5 mg	Laser	SPY Elite (Novadaq)	NA	30.9	5.5/-	NA
van den Bos et al. [33]	2019	Clinical pilot study	30/-	Colorectal surgery	0.2 mg/kg	Xenon/laser	D-light P (Karl Storz)/Firefly (Intuitive)	Target-to-background ratio	20	16/-	NA
Ris et al. [34]	2018	Multicenter phase II trial	504/1,173	Colorectal surgery	7.5 mg	Laser	PINPOINT (Novadaq)	NA	5.8	2.4/5.8	0.009

Table 1. Continued

Study	Year	Study design	No. (ICG/control)	Type of surgery	ICG dose	NIR light source	NIR system	Quantitative parameter	Transection line change (%)	Anastomotic leak (%)	p value
Mizrahi et al. [35]	2018	Comparative cohort study	30/30	Laparoscopic LAR	0.1–0.3 mg/kg	Laser	PINPOINT (Novadaq)	NA	13.3	0/6.7	0.492
Kim et al. [36]	2017	Retrospective study	310/347	Robotic LAR	10 mg	Laser	Firefly (Intuitive)	NA	15.5	0.6/5.2	NA
Boni et al. [13]	2017	Case-matched study	42/38	Laparoscopic LAR	0.2 mg/kg	Xenon	IMAGE1 (Karl Storz)	NA	4.7	0/5.3	NS
Jafari et al. [37]	2015	Multicenter phase II (PILLAR II)	139/-	Laparoscopic LAR	3.75–7.5 mg	Laser	PINPOINT (Novadaq)	NA	7.9	1.4/-	NA
Watanabe et al. [5]	2015	Prospective study	119/-	Colorectal surgery	0.5 mg/kg	Xenon	Olympus NIR camera (Olympus)	NA	NA	5.9/-	NA
Kin et al. [38]	2015	Retrospective study	173/173	Colorectal surgery	3 mg	Laser	SPY imaging system (Novadaq)	NA	4.6	7.5/6.4	0.67
Kim et al. [39]	2015	Prospective cohort study	123/313	Robotic LAR	10 mg	Laser	Firefly (Intuitive)	NA	10.6	0.8/5.4	0.031
Ris et al. [40]	2014	Prospective study	30/-	Colorectal surgery	2.5 mg/kg	Laser	PINPOINT (Novadaq)	NA	10	0/-	NA
Jafari et al. [41]	2013	Retrospective case-control study	16/22	Robotic LAR	6–8 mg	Laser	Firefly (Intuitive)	NA	19	6.2/18.2	NA
Kudszus et al. [19]	2010	Retrospective study	201/201	Laparoscopic LAR	0.2–0.5 mg/kg	Laser	IC view (Pulsion)	NA	16.4	3.5/7.5	NA

ICG, indocyanine green; NIR, near-infrared; RCT, randomized clinical trial; PSM, propensity score matching; AR, anterior resection; LAR, low anterior resection; TaTME, transanal total mesorectal excision; TR, perfusion time ratio; NA, non-accessible; NS, non-specific.
Stryker, Kalamazoo, MI, USA; LifeCell, Branchburg, NJ, USA; Karl Storz, Tuttlingen, Germany; Fluoptics, Grenoble, France; Intuitive, Sunnyvale, CA, USA; Novadaq, Mississauga, ON, Canada; Hamamatsu Photonics, Hamamatsu, Japan; Olympus, Tokyo, Japan; Pulsion, Glasgow, UK.

Table 2. Meta-analysis for clinical effects of ICG angiography to reduce anastomotic leak

Study	Year	No. of enrolled study	No. (ICG/control)	Type of surgery	Anasto-motic leak (%)	Odds ratio	95% CI	*p* value
Zhang and Che [42]	2021	29	2,354/3,522	AR and LAR	3.2/9.2	0.39	0.30–0.50	<0.00001
Arezzo et al. [43]	2020	9	862/468	Colorectal surgery	4.2/11.3	0.34	0.22–0.53	<0.001
Liu et al. [44]	2020	13	1,806/2,231	Colorectal surgery	3.8/7.8	0.4	0.33–0.59	<0.00001
Lin et al. [45]	2020	11	1,364/1,773	Colorectal surgery	2.9/30.8	0.31	0.21–0.44	<0.0001
Chan et al. [46]	2020	20	2,220/3,278	Colorectal surgery	3.7/8.6	0.46	0.31–0.62	<0.00001
Rausa et al. [47]	2019	11	555/1,768	Colorectal surgery	3.6/6.0	0.44	0.14–0.87	<0.05
Shen et al. [48]	2018	4	569/608	Laparoscopic and robotic LAR	1.8/6.4	0.27	0.13–0.53	<0.0002
Blanco-Colino et al. [49]	2018	5	555/747	Colorectal surgery	1.1/6.1	0.51	0.23–1.13	0.10

ICG, indocyanine green; AR, anterior resection; LAR, low anterior resection; CI, confidence interval.

es. Therefore, with laparoscopic ICG cameras, it is expected that the optimal fluorescence image can be obtained by measuring fluorescence at a distance of 4 to 5 cm. Additionally, it is helpful to obtain a fluorescence image of good quality by performing ICG angiography in the abdominal cavity or in as dark an environment as possible by turning off all room lights when capturing images from outside the abdominal cavity. Moreover, using a laser rather than a xenon lamp as a fluorescence emission source is advantageous for obtaining a fluorescence image of higher resolution and quality. Even with ICG laparoscopy using xenon lamps, the ICG-specific image mode can improve the quality of fluorescence images through image processing methods, such as red color inversion. Under these premises, when the conditions for fluorescence imaging are satisfied, we will be able to evaluate the colonic perfusion status using quantitative parameters, such as ascending slope or maximum FI.

FI and persisting duration are affected by the dilution concentration and dose of the intravenous ICG injection. In our previous study for ICG angiography, a typical dilution concentration of 2.5 mg/mL was prepared, and an intravenous dose of 0.25 mg/kg was applied according to the patient's weight. In early ICG cameras using xenon lamps, blue fluorescence was visualized, so there was a resolution limitation in which the difference between the background and the blue color tone was not clear, so the appropriate ICG dose was set at 0.25 mg/kg. The initial ICG study of our research team also applied a dose of 0.2 to 0.25 mg/kg using a laparoscopic NIR camera with a xenon lamp. As the fluorescence emission source for the laparoscopic camera is a laser, and with improvements in fluorescence imaging resolution, research on the optimal ICG dosage is required for repetitive ICG angiography. Optimized ICG angiography should be able to show a definite FI change. If necessary, repeated ICG angiography could be performed without disturbances from remnant fluorescence in the tissues. Therefore, the optimal ICG

dose should also be rapidly cleared by the liver, facilitating repeat ICG angiography. We conducted a study to find the optimal ICG capacity for quantitative fluorescence analysis using a laser NIR camera and compared the fluorescence images between standard (0.2 mg/kg) and experimental (0.01–0.05 mg/kg) dosage groups. In our recent study, sufficient quantitative perfusion evaluation was possible even with a low dose of 0.02 mg/kg, which is ten times lower than the conventional dose of 0.2 mg/kg (unpublished data).

Quantitative perfusion analysis

After 10 to 30 seconds of intravenous ICG injection, fluorescence begins to appear in the colon wall. It is possible to evaluate perfusion status by changing FI to ensure that the perfusion is well preserved to the planned transection line.

A time-fluorescence graph could be displayed by measuring changes in FI, allowing evaluation of various quantitative parameters. In the measurement of FI, the basic quantitative factors are the maximal level of FI (F_{max}) and the interval to FI_{max} (T_{max}). Time scales include latency time (the initial fluorescence onset time), the interval to half of FI_{max} ($T_{1/2max}$), and perfusion time ratio (TR). The ascending slope can reflect arterial flow conditions and can be calculated considering both FI and time scale (Fig. 1). Since the perfusion status of the small intestine can be used as a criterion for a good FI level, the perfusion status can also be evaluated by calculating the FI ratio of the small intestine and colon [30].

Among these variables, many studies have explored $T_{1/2max}$. In cases of insufficient blood flow, $T_{1/2max}$ delays have been reported in a number of digestive organs, such as the small intestine and large intestine. We found that $T_{1/2max}$ and TR can reflect blood flow conditions well [3]. In particular, $T_{1/2max}$ has the highest sensitivity for predicting anastomotic complications, and TR is

analyzed as a variable with high specificity. Therefore, we proposed a step-by-step flow chart to improve diagnostic accuracy. At first, $T_{1/2max}$ can be used to screen for patients at risk of insufficient perfusion; second, TR can be used to predict the risk of anastomotic complications [3].

Based on the tissue perfusion status information, the surgeon will be able to perform safer colonic anastomoses by clearly identifying colonic segments with excellent blood flow. In particular, such quantitative perfusion evaluation would be of great help to a novice surgeon who lacks experience in subjective evaluation of tissue perfusion [50]. ICG angiography allows the surgeon to
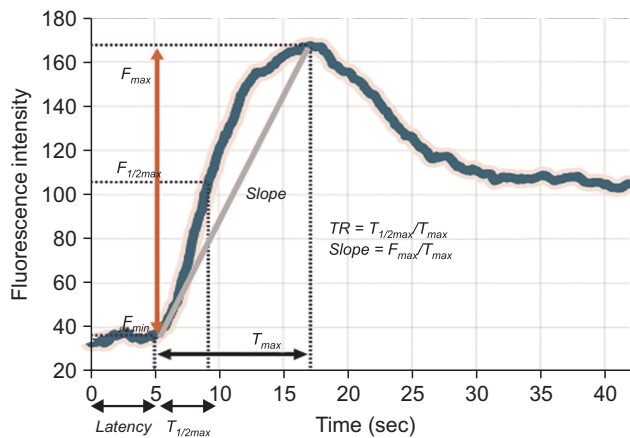

Fig. 1. Quantitative parameters based on the time-fluorescence of indocyanine green angiography. This graph could be displayed by measuring changes in the fluorescence intensity (FI), allowing evaluation of various quantitative parameters. In the measurement of FI, the basic quantitative factors are the maximal level of FI (F_{max}) and the interval to FI_{max} (T_{max}). Time scales include latency time (the initial fluorescence onset time), the interval to half of FI_{max} ($T_{1/2max}$), and perfusion time ratio (TR). The ascending slope can reflect arterial flow conditions and can be calculated considering both FI and time scale. Adapted from Ahn et al. [9], according to the Creative Commons License.

intuitively estimate tissue perfusion in real time. Eventually, ICG angiography may facilitate a reduction in anastomotic complications associated with poor colonic perfusion.

For this, a safe and reliable ICG angiography protocol must be established. Additionally, it is necessary to develop and verify accurate analytical indicators for predicting the risk of complications and quantitatively evaluating the state of tissue microperfusion in real time.

Experienced surgeons can empirically assess tissue perfusion without ICG angiography, but surgical beginners do not. However, manual evaluation by novice surgeons is subject to error. Accurate evaluation requires many years of practice to obtain sufficient experience. On the other hand, artificial intelligence (AI) can evaluate tissue perfusion with the highest accuracy via learning using numerous ICG angiography videos. The processed information can then be used to supplement the surgeon's judgment.

In the fluorescence graph used for quantitative analysis, a nonideal pattern may be observed due to the various blood flow pathways of the vascular structures and collateral circulation. In such a case, the quantitative parameter would be incorrectly recorded. This could be a hidden pitfall potentially leading to interpretation errors in perfusion evaluation. Additionally, environmental factors of ICG angiography such as NIR illuminance and lighting outside the shooting distance can affect the perfusion evaluation. Quantitative analysis has this limitation, but AI can be used to overcome it. AI, which has learned both patterns and various environmental factors, has superior analysis performance and stability relative to quantitative analysis. Real-time AI analysis can be used to quickly evaluate the state of the tissue microcirculation so that analysis results can be checked right in the operating room. The results can be expressed visually through a color map overlying the surgical field (Fig. 2). When the limited data for machine learning is solved in the future, it is expected that this will play an important role as a reliable assistant in the operating room [14].
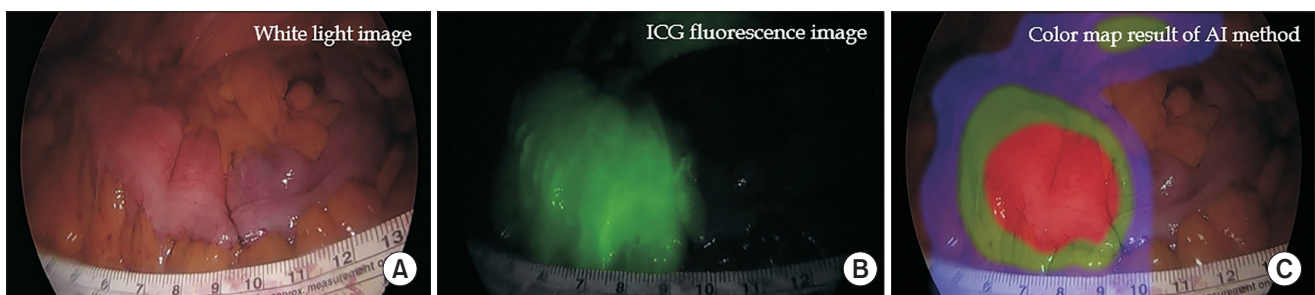
Fig. 2. Colonic perfusion images. (A) White light image, (B) indocyanine green (ICG) fluorescence image, and (C) color map result of artificial intelligence (AI) analysis of ICG pattern. Real-time AI-based quantitative analysis can be used to evaluate the tissue microcirculation and express visually through a color map overlying the surgical field. The visual information can help the surgeons assess the perfusion status during laparoscopic surgery. Adapted from Park et al. [14], according to the Creative Commons License.

PERSPECTIVES

Currently, various fluorescence imaging devices, fluorescent drugs, hyperspectral image, and laser speckle contrast imaging systems are being rapidly developed. ICG fluorescence images can be obtained more delicately through the second window using a wavelength of 1,000 nm or more. This can increase the resolution of ICG fluorescence images and improve transmittance to achieve deeper penetration of fluorescence [51]. In addition to ICG, various fluorescent materials are currently being developed for clinical applications. Fluorescence imaging of the urinary system, as well as the biliary tract, can be performed using the different metabolic pathways applicable to fluorescent drugs [52]. Additionally, window fluorescence drugs have been developed for tissue-specific fluorescence imaging in the laboratory.

Aside from ICG angiography, tissue perfusion status and oxygen saturation levels can be determined using hyperspectral imaging or laser speckle contrast imaging. This new imaging technique will be able to noninvasively evaluate *in vivo* physiological states using the physical properties of light without fluorescent drugs, such as ICG. A tissue-specific imaging technology has also been developed for reflecting the physiological characteristics of tissues [53].

We are fortunate to be able to stand in the middle of a revolutionary era of fluorescence surgical technology and surgical navigation systems. Currently, surgeons have a new imaging device at their disposal, with which they can easily and safely apply ICG angiography in the operating room. By evaluating tissue microcirculation in real time, tissues with poor blood flow can be accurately identified. The risk factors of hypoperfusion can be predicted intraoperatively, and postoperative complications can be prevented. These advanced imaging technologies will improve the safety of colorectal surgery, which will eventually bring medical and economic benefits to doctors, patients, and health care systems. We believe that this seemingly small step in the operating room could prove to be a giant leap toward preventing anastomotic complications for colorectal cancer patients.

CONCLUSION

ICG angiography could be useful for detecting poorly perfused colonic segments and preventing anastomotic leakage after colorectal surgery. An optimal standardized ICG angiography protocol should be established to facilitate the implementation of reliable multicenter clinical trials to confirm the clinical benefits of ICG angiography. In the future, we envision AI-based quantitative analysis software being used to assess colonic perfusion during laparoscopic or robotic colorectal surgery.

NOTES

Authors' contributions

Conceptualization: GMS
Formal Analysis: GMS, HMA, SHP
Investigation: GMS
Methodology: GMS, SHP, IYL, KRB
Writing–Original Draft: GMS, HMA, SML, SHP
Writing–Review & Editing: GMS
All authors read and approved the final manuscript.

Conflict of interest

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