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Real-Time Fluorescence Vessel Navigation Using Indocyanine Green During Laparoscopic Colorectal Cancer Surgery

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Abstract. *Background/Aim: Indocyanine green (ICG) fluorescence technique is known to help visualize blood vessels. The efficacy of real-time fluorescence vessel navigation (FVN) using ICG for ligation of the inferior mesenteric vein (IMV) and left colic artery (LCA) during laparoscopic left colorectal cancer surgery was investigated. Patients and Methods: Participants were 59 patients who underwent laparoscopic left colorectal cancer surgery from February 2017 to November 2018, and were divided into groups: i) with FVN (FVN+, n=21) and ii) without FVN (FVN–, n=38). Groups were compared for the time it took to ligate their IMV and LCA. Results: The results are expressed as median values. The time to ligate the IMV and LCA was significantly shorter for FVN+ (230 seconds; range 126-346) than for FVN– (417.5 seconds; range 137-1327) (p<0.001). Conclusion: Real-time FVN using ICG shortened the times for IMV and LCA ligation. This was enabled by clear visualization of the direction of the bloodstream flow inside the vessels. This technique simplifies vessel ligation and safer laparoscopic surgery for left colorectal cancer.*

Indocyanine green (ICG) fluorescence methods are gradually being applied in colorectal cancer surgery, as they allow for a better intraoperative imaging diagnosis (1). The use of ICG helps evaluate intestinal blood flow of anastomoses to avoid leakage (2-7), as well as intestinal lymph flow (8). For the intestinal blood flow evaluation of the anastomosis, ICG is administered intravenously, with arteries first showing fluorescence, followed by veins (2-7). In left colorectal cancer surgery, lymph node dissection requires ligation of the inferior mesenteric artery (IMA). Furthermore, the inferior mesenteric vein (IMV) and the left colic artery (LCA) are ligated in the line of division of the mesentery. By intravenous injection of ICG, the directions of blood flow of the IMV and LCA can be visualized (Figures 1-3). This study evaluated whether real-time fluorescence vessel navigation (FVN) can shorten the time required for safe ligation of the IMV and LCA.

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Key Words: Indocyanine green fluorescence, vessel navigation, colorectal cancer.

Patients and Methods

Participants in this study comprised 59 patients who underwent laparoscopic left colorectal cancer surgery by a single surgeon between February 2017 and November 2018. They were divided into two groups: i) those with FVN aid (FVN+, n=21); and ii) those without FVN (FVN–, n=38). Real-time FVN using ICG was applied for patients who provided consent to participate in this study from January 2018 (FVN+). The two groups were compared in terms of time to ligate the IMV and LCA, surgical outcomes and patient characteristics. The time to ligate the IMV and LCA was measured using information on the video clips of the surgical procedures.

To standardize the preparation of the surgical field for ligation of the IMV and LCA, the stump of the transected IMA was grasped with one pair of forceps (right hand) and the mesentery of the sigmoid colon with a second pair of forceps (left hand).

The time to vessel ligation was measured between the standardized preparation of the surgical site and the transection of the IMV and LCA. When IMV and LCA were running closely at the level of the root of IMA, they were clipped and stitched together. Otherwise, they were clipped and stitched individually.

In the FVN+ group, fluorescent imaging was performed using either the VISERA ELITE2 system (Olympus, Tokyo, Japan) or the 1588 AIM camera system (Stryker, Kalamazoo, Michigan, USA), following intravenous injection of ICG at 0.1 mg/kg. In the FVN+ group, the time required for the observation of fluorescent imaging was included in the time it took to ligate the IMV and LCA.

Additionally, the same comparison was performed for patients with a higher body mass index (BMI >22 kg/m^2) (Figure 4), based on the Japanese Society for the Study of Obesity (9), which defines the Standard BMI as 22 kg/m^2.

The results are expressed as median values (+range). This study was approved by the Research Ethics Committee of the University School of Medicine (approval number: 29-049).

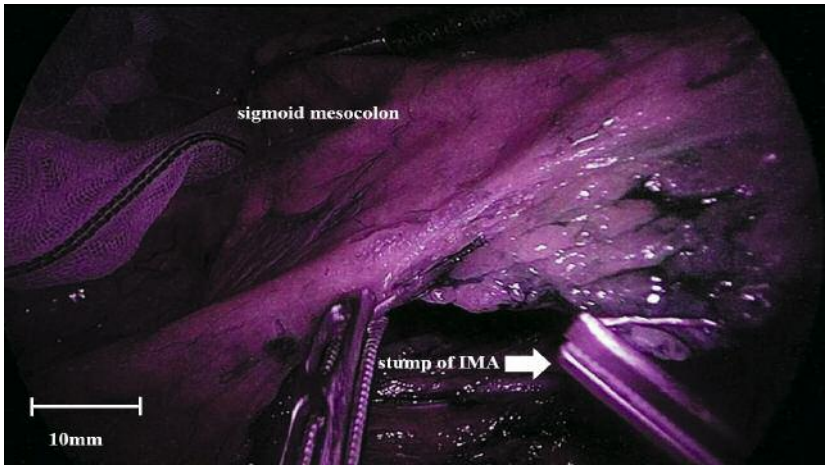

Figure 1. *Intraoperative photo before ICG injection. This photo shows the sigmoid mesocolon following ligation of the inferior mesenteric artery (IMA) (thick arrow), before ICG injection in indocyanine green (ICG) fluorescent mode.*

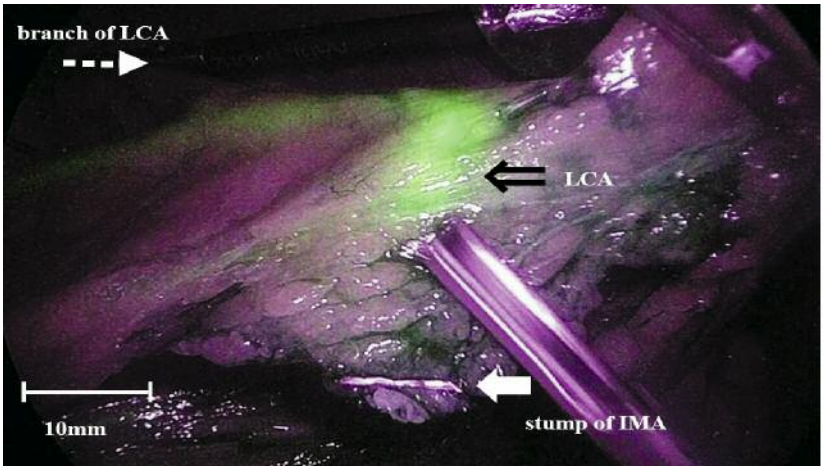

Figure 2. *Intraoperative photo after ICG injection. Plain white arrow is stump of IMA. With intravenous injection of indocyanine green (ICG), the left colic artery (LCA) (open black arrow) and a branch from the LCA (dashed arrow) first show fluorescence in the blood from the middle colic artery.*

Results

The mean age was 69.5 (35-93) years for FNV- patients and 71 (47-87) years for FNV+ patients. The male:female ratios for each group were 24:14 and 13:8, respectively, and the mean BMI was 20.95 (16.24-25.29) *versus* 22.60 (17.34-27.09) kg/m^2, respectively. No significant differences were seen between the FNV– and FNV+ groups. Location of cancer (descending colon, sigmoid colon, or rectum) was 0:4:17 for FVN+ and 1:13:24 for FVN–, showing no significant difference (p=0.4023). There were no significant differences between the two groups with age, sex, BMI, or location of the cancer. The time to ligate the IMV and LCA was 230 (126-346) seconds for FVN+ compared to. 417.5 (137-1327) seconds for FVN–, showing significant difference (p<0.0001) (Figure 5). Neither group showed adverse events, such as vessel injury or complications related to ICG injection.

In the high-BMI group (BMI>22 kg/m^2), the time to ligate the IMV and LCA was significantly shorter for FVN+ [n=12, 264 (126-346) sec] than for FVN– [n=12, 576.5 (189-1327) sec, p<0.0014].

Postoperative hospital stay was 21 (11-48) days for FVN+ compared to 15.0 (9-94) days for FVN–, showing no significant difference. Post-operative complications (Clavien-Dindo grades III or over (10) occurred in 4 cases (19%) in the FVN+ group (paralytic ileus in 2 and anastomotic

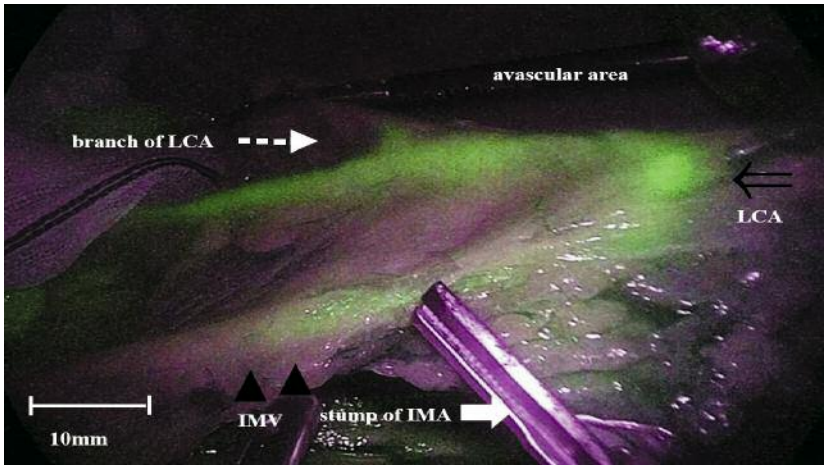

Figure 3. *Intraoperative photo after ICG injection-2. Subsequent to left colic artery (LCA, open black arrow) fluorescence, the inferior mesenteric vein (IMV, black arrowheads) becomes fluorescent. A branch from the LCA (dashed arrow) is clearly identified.*

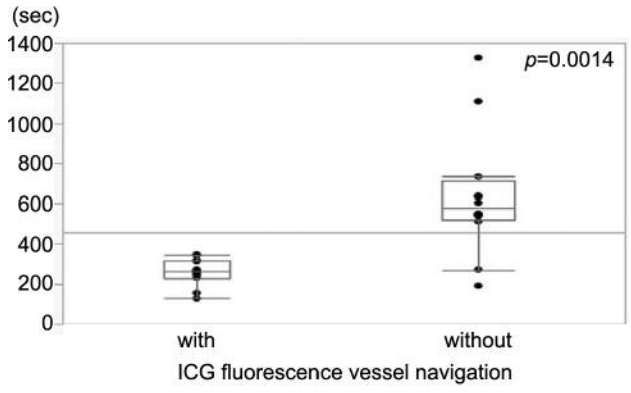

Figure 4. *Time to vessel ligation in the high-BMI group (BMI >22.0 kg/m^2). The time to ligate IMV and LCA was 264 (126-346) seconds for FVN+ versus 576.5 (189-1327) seconds for FVN–, demonstrating a significantly shorter time in the FVN+ group (p=0.0014).*

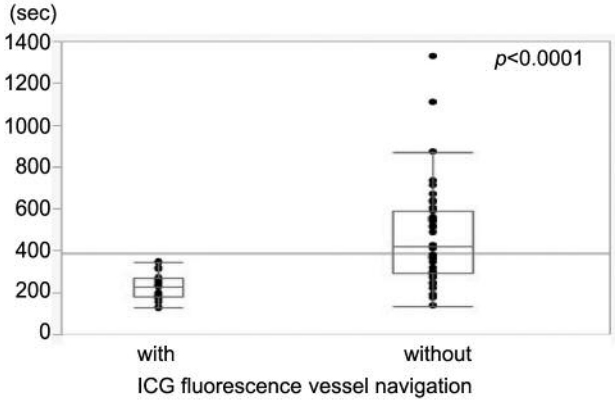

Figure 5. *Time to vessel ligation with and without fluorescence vessel navigation (FVN). Time to ligate the IMV and LCA was 230 (126-346) seconds for FVN+ versus 417.5 (137-1327) seconds for FVN–, demonstrating a significantly shorter time in the FVN+ group (p<0.0001).*

leakage in 2 cases) compared to 2 cases (5%) in the FVN– group (leakage and intra-abdominal abscess in one case each.

Discussion

The ICG fluorescence technique is known to help visualize blood vessels and flow during cranial nerve surgery and reconstructive surgery (11, 12). In digestive surgery, few reports have described the identification of vessels using ICG fluorescence techniques, such as identification of the infrapyloric artery during gastric cancer surgery (13). To our knowledge, ICG FVN for colorectal cancer surgery has not been reported. Using ordinary light, ligation of the IMV and LCA is easy in cases where vessels can be seen through the mesentery with little fat, but difficult in cases with large amounts of visceral fat. In such cases, branches of vessels are indistinct and under high risk of injury. Under such circumstances, tedious dissection of fat and exposure of blood vessels without injury are thus required. Real-time FVN using ICG can shorten the time to ligate the IMV and LCA, as it allows clear visualization of the blood flow direction inside the vessels, by making blood visible with fluorescence without prior fat dissection and vessel exposure. Clipping and transection of vessels can, thus, be performed speedily with minimal dissection of the mesentery.

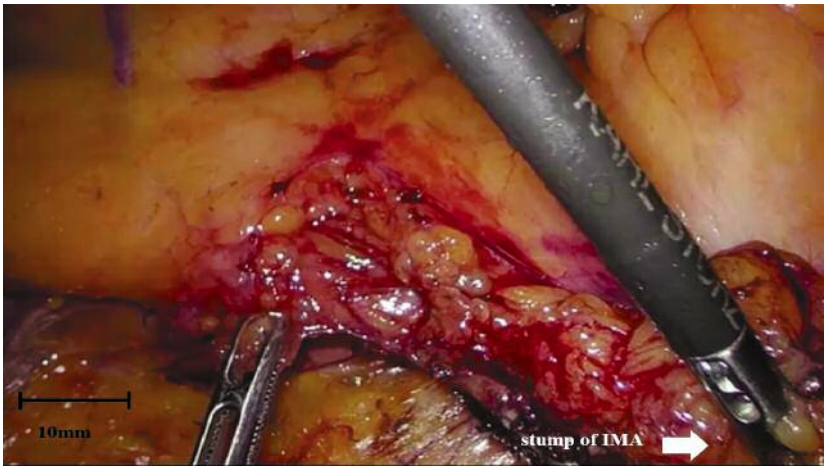

Figure 6. *Intraoperative photo of an obese patient before indocyanine green (ICG) injection. Directions of the vessel before ICG injection are not clear.*

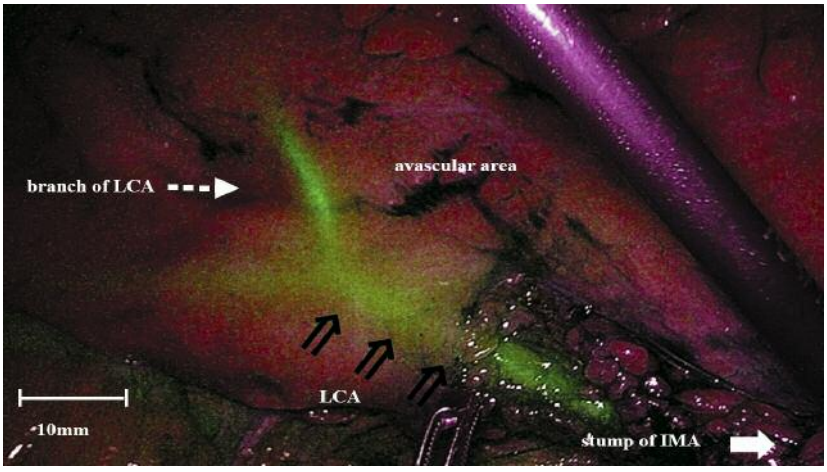

Figure 7. *Intraoperative photo of an obese patient using fluorescence vessel navigation (FVN). Plain white arrow is stump of IMA. FVN allowed clear visualization of the direction of the left colic artery (LCA, open black arrow) and a branch from the LCA (dashed arrow).*

Furthermore, even in high BMI cases, this technique allows for clear visualization of the directions of the blood flow of the vessels (Figures 6 and 7), even if fluorescent vessels may not appear as clearly in high BMI cases. This can happen because the avascular regions of the mesentery in these high BMI cases that do not have fluorescence become distinct, allowing for quick and safe dissection of the mesentery around vessels. Therefore, for high BMI cases, this technique is expected to expedite ligation of the IMV and LCA. In open surgery, vessels can be identified by palpation based on arterial pulsation in the mesentery. However, laparoscopic surgery cannot depend on tactile sensation and is performed visually. Therefore, this technique can potentially simplify vessel ligation and division of the mesentery for safer laparoscopic left colorectal cancer surgery. Although expert surgeons may not necessarily need this technique, a clear benefit for surgeons that are not yet expert is that it may help improve the safety of their operation. Moreover, this technique may help to ease the operation for patients with high BMI.

The limitation of this study was its retrospective design, the small number of patients at a single institution and possibly a selection bias.

Conflicts of Interest

The Authors declare that they have no competing interests.

Authors' Contributions

SR made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data. KS was involved with drafting the manuscript or revising it critically for important intellectual content. TK, MI, TU, TO and KE have discussed about this study. KY gave final approval of the version to be published.

All Authors read and approved the final manuscript.

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