



Lymphadenectomy Guided by Indocyanine-Green (ICG) in Colorectal Cancer: A Pilot Study

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Abstract

Background: The Indocyanine Green (ICG) lymphography has the advantage of offering a good visualization of the lymphatic channels but there are problems in order to identify the lymphatic nodes. Intraoperative fluorescence ICG navigation also aims for detection of aberrant lymphatic drainage outside of the planned resection. Our objective with this study is to rate the use of the intraoperative lymphogram in cases of elective colorectal surgery to evaluate if there were changes in the surgical attitude regarding the performance of lymphadenectomy.

Methods: Indocyanine green was injected into the submucosal layer around the tumor at 2 points (2 cm proximal and distal from the tumor) with a 23-gauge localized injection before lymph node dissection and the lymph flow was observed using a near-infrared camera system observed after 1,3 and 5 minutes after injection. A complete mesocolic excision with central vascular ligation was performed in all cases and an additional lymphadenectomy was realized including the region where the lymph flow was fluorescently observed.

Results: The application of ICG was carried out in 10 selected patients with cT3-N0 colon cancer. In brief, it was observed that 20% of patients obtained additional lymph nodes after the expansion of the surgical plan; moreover in 10% affected lymph nodes were spotted after the expansion of the surgical plan.

Conclusion: Intraoperative real-time visualization of the lymph flow using indocyanine green fluorescence imaging during laparoscopic colon cancer surgery is feasible and a helpful technique for lymph node mapping which may lead to intraoperative changes in lymphadenectomy. Further studies with prospective clinical series will be necessary to know the role of this technique in colorectal cancer.

Keywords: Fluorescence; Colorectal cancer; Lymphadenectomy; Indocyanine green; Laparoscopy

Introduction

Lymph node status is one of the key prognostic factors in patients with colorectal cancer, and remains the most important selection criteria for adjuvant chemotherapy. It is believed that at least 30% of node negative patients will suffer disease recurrence within the first 5 years after surgery. This may be due to under staging of lymph node status. These missed node metastases are either isolated tumor cells or micro-metastases, which may be not accurately diagnosed with current standard processing and H&E staining. Some studies even identify up to 33% of patients with upstaging who underwent adjuvant chemotherapy without evidence of lymph node metastases in conventional studies. The risk of missing small tumor cell metastases has been minimized with immunohistochemistry and multi-level sectioning of lymph nodes. As these procedures can be expensive and time consuming, sentinel lymph node mapping is used in some procedures, by identifying the node with the highest probability of having tumoral infiltrates [1-3]. Sentinel lymph node mapping is widely used for staging of breast cancer and melanoma; with injection of colloid Tc99 and Isosulfan Blue (IB), which has also been used alone or in combination for sentinel lymph node biopsy in colorectal cancer. However, Indocyanine Green (ICG) fluorescence guidance is a new technical approach to this issue, with promising results as it is not influenced by body mass index or lymphatic invasion. The ICG lymphography has the advantage of offering a good visualization of the lymphatic channels but there are problems in order to identify the lymphatic nodes. Intraoperative fluorescence ICG navigation also aims for detection of aberrant lymphatic drainage outside of the planned resection [4]. Our objective with this study is to rate the use of the intraoperative lymphogram in cases of elective colorectal surgery to evaluate if there were changes in the surgical

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Table 1: Clinical cases with the planned lymphadenectomy, the added lymphadenectomy and the number of nodes outside the primary planned resection and the affected ones.

	Lymphadenectomy (Expected)	ICG -Lymphography	Lymphadenectomy (Realized)	Nodes Outside [*]	Nodes Affected ^{**}
Ascending Colon	Right Ileocolic Vessels	Right Ileocolic Vessels	Right Ileocolic Vessels	0	NA
Ascending Colon	Right Ileocolic Vessels	Right Ileocolic Vessels	Right Ileocolic Vessels	0	NA
Hepatic Flexure	Right Ileocolic Vessels + Right Branch Middlecolic Vessels	Right Branch Middlecolic Vessels	Right Ileocolic Vessels + Right Branch Middlecolic Vessels	0	NA
Transverse Colon	Right Ileocolic Vessels + Right Branch Middlecolic Vessels	Right Branch Middlecolic Vessels	Right Ileocolic Vessels + Right Branch Middlecolic Vessels	0	NA
Transverse Colon	Right Ileocolic Vessels + Right Branch Middlecolic Vessels	Right And Left Branch Middlecolic Vessels	Right Ileocolic And Middlecolic Vessels	5	0
Transverse Colon	Right Ileocolic Vessels + Right Branch Middlecolic Vessels	Right And Left Branch Middlecolic Vessels	Right Ileocolic And Middlecolic Vessels	7	1
Esplenic Flexure	Left Colic Vessels + Left Branch Middlecolic Vessels	Left Branch Middlecolic Vessels	Left Colic Vessels + Left Branch Middlecolic Vessels	0	NA
Esplenic Flexure	Left Colic Vessels + Left Branch Middlecolic Vessels	Left Branch Middle Colic Vessels	Left Colic Vessels + Left Branch Middle Colic Vessels	0	NA
Sigmoid Colon	Inferior Mesenteric Vessels	Inferior Mesenteric Vessels	Inferior Mesenteric Vessels	0	NA
Sigmoid Colon	Inferior Mesenteric Vessels	Inferior Mesenteric Vessels	Inferior Mesenteric Vessels + Paraaortic Excision	0	NA

^{*}Additional lymph nodes after the ampliation of the surgical plan

^{**}Affected lymph nodes after the ampliation of the surgical plan

attitude regarding the performance of lymphadenectomy.

Methods

A stock solution of the ICG dye was prepared by dissolving 25 mg of powdered ICG in 10.0 ml of sterilized water; 2.0 ml of the suspension was used for bowel injection and 8.0 ml for intravenous perfusion. It is important that the dye solution should not be stored longer than 8 hrs and should be protected from light. Indocyanine green was injected into the subserosal layer around the tumor at 2 points (2 cm proximal and distal from the tumor) with a 23-gauge localized injection before lymph node dissection and the lymph flow was observed using a near-infrared camera system observed after 1,3 and 5 minutes after injection (Spies™ filter, from Karl Storz, Germany). A complete mesocolic excision with central vascular ligation was performed in all cases and an additional lymphadenectomy was realized including the region where the lymph flow was fluorescently observed. A laparoscopic approach was used with Karl-Storz Spies processor for ICG laparoscopic identification. Laparoscopy was performed with four ports, 30° optic and rigid instruments. The ICG injection was performed with a solution of 25 mg of ICG pulsion™ with 10 ml of sterile water. After the injection, the lymphography was registered and the investigators looked for the lymphatic nodes at the mesenteric artery. Following the marking of the ICG, the expansion of the surgical plan in terms of the lymphadenectomy procedure, was made in those cases only when necessary. The expected, fluorescence guided and realized lymphadenectomy were reported. The lymph node status was collected paying attention to the number of nodes outside the primary planned resection and the affected ones. The remaining 8.0 ml of ICG solution were employed for the study of correct vascular supply in the proximal and distal colon when the anastomosis was performed in order to minimize the anastomotic leak.

Results

The application of ICG was carried out in 10 selected patients with cT3-N0 colon cancer, this method being applied in the following specific cases: two cases of ascending colon cancer, one case of hepatic flexure, three cases of transverse colon, two of splenic flexure and two of sigmoid colon. In the cases with right ascending colon cancer the surgery was not enlarged in any case. In right transverse colon cancer

the surgery was enlarged to the left branch of the middle colic vessels in 66% of cases. In cases with location of the tumor in the splenic flexure there were no changes in the planned surgery. In a case of sigmoid cancer (50%) an extended para-aortic excision was made added to the lymphadenectomy of the inferior mesenteric artery. In brief, it was observed that 20% of patients obtained additional lymph nodes after the expansion of the surgical plan; moreover in 10% affected lymph nodes were spotted after the expansion of the surgical plan. The Table 1 summarizes the 10 procedures performed as well as the lymphadenectomy performed before and after the use of ICG.

Discussion and Conclusion

Our study is a prospective pilot study with a short clinical series that collects data from patients undergoing laparoscopic surgery with cT3-N0 colorectal cancer. This study has assessed the rate of additional lymph nodes found at the fluorescence guided lymphadenectomy and the rate of tumor infiltration in those lymph nodes. In the future we may be able to select those patients with higher risk of early recurrence and establish a method of lymphatic mapping to lower the rate of such recurrences and adequate adjuvant treatment to a more accurate staging of the disease. Intraoperative real-time visualization of the lymph flow using indocyanine green fluorescence imaging during laparoscopic colon cancer surgery is feasible and a helpful technique for lymph node mapping which may lead to intraoperative changes in lymphadenectomy [5,6]. And if such is the case, the resection of possibly affected lymph nodes would not be included in the lymphadenectomy corresponding to the drainage of colon that the cancer presents, without the use of this technique. In sentinel node navigation surgery for colorectal cancer, in contrast to radio colloid, blue dye, or both, which were difficult to use, ICG Fluorescence Imaging (FI) has advantages including high sensitivity, better lymph vessel transitivity, and no need for radiation. In addition, ICG-FI is capable of assessing not only lymph nodes but also the lymph flow in real time. This leads to a new field of investigation and innovation in the surgery of colorectal cancer.

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