

A pilot study of lymph node mapping with indocyanine green in robotic gastrectomy for gastric cancer

SAGE Open Medicine

Volume 5: 1–8

© The Author(s) 2017

Reprints and permissions:

sagepub.co.uk/journalsPermissions.nav

DOI: 10.1177/2050312117727444

journals.sagepub.com/home/smo

Yuan-Tzu Lan^{1,2}, Kuo-Hung Huang^{2,3,4}, Ping-Hsien Chen^{2,5},
Chien-An Liu^{2,6}, Su-Shun Lo^{2,7}, Chew-Wun Wu^{2,3}, Yi-Ming Shyr^{2,3}
and Wen-Liang Fang^{2,3}

Abstract

Objectives: Robotic gastrectomy has become increasingly popular in the treatment of gastric cancer, especially in Asian countries. The use of indocyanine green fluorescence has been reported in lymphatic mapping for gastric cancer in laparoscopic gastrectomy; however, there have been few reports regarding the use of indocyanine green in robotic gastrectomy.

Methods: From January 2011 to March 2016, a total of 79 patients underwent robotic gastrectomy for gastric cancer. Among them, intraoperative subserosal injection (n=9) or preoperative submucosal injection (n=5) of indocyanine green with near-infrared imaging was performed in 14 patients, and the other 65 patients underwent robotic gastrectomy without the use of indocyanine green.

Results: There was no significant difference in the operative time, total number of retrieved lymph nodes, operative blood loss, and postoperative hospital stay between the patients who underwent robotic gastrectomy with or without indocyanine green fluorescence. For each lymph node station, there was significantly more number of retrieved lymph nodes in the indocyanine green group than in the no-indocyanine green group at the greater curvature side of the low body (#4d) to the infrapyloric region (#6) of the stomach. Five of the 14 patients who received an indocyanine green injection for lymphatic mapping had lymph node metastasis, and metastatic lymph nodes were located in the lymph node stations as detected by indocyanine green fluorescence during surgery.

Conclusion: Indocyanine green fluorescence with near-infrared imaging is feasible and is a promising method of lymphatic mapping in robotic gastrectomy for gastric cancer. In future studies, larger patient numbers and long-term follow-up are required.

Keywords

Indocyanine green, robotic gastrectomy, near-infrared imaging, lymphatic mapping

Date received: 18 November 2016; accepted: 31 July 2017

Introduction

Minimally invasive surgery, including laparoscopic and robotic approaches, has become increasingly popular in the treatment of gastric cancer, especially in Asian countries. Some clinical trials comparing the surgical outcomes and prognosis between laparoscopic and open gastrectomy for advanced gastric cancer are ongoing.¹ However, lymph node metastasis (LNM) is one of the most important prognostic factors in gastric cancer.²

In our previous report, the frequency of LNM in early gastric cancer (T1) was 4.9% in cases with T1a lesions and 21.4% in cases with T1b lesions.³ For advanced gastric cancer, the frequency of LNM should be higher. As the desire increases for minimally invasive gastrectomy in advanced

¹Division of Colon & Rectal Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan

²National Yang-Ming University Hospital, Yilan City, Taiwan

³Division of General Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan

⁴Institute of Clinical Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan

⁵Endoscopy Center for Diagnosis and Treatment, Taipei Veterans General Hospital, Taipei, Taiwan

⁶Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan

⁷School of Medicine, National Yang-Ming University, Taipei, Taiwan

Corresponding author:

Wen-Liang Fang, Division of General Surgery, Department of Surgery, Taipei Veterans General Hospital, No. 201, Section 2, Shipai Road, Beitou District, Taipei City 11217, Taiwan.

Email: s821094@hotmail.com



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons

Attribution-NonCommercial 4.0 License (<http://www.creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

gastric cancer, there is a growing demand for an intraoperative guide for lymphadenectomy for surgeons. Indocyanine green (ICG) lymphatic mapping by sentinel node navigation surgery (SNNS) with infrared ray observation under laparoscopic view was reported to be an adequate method of lymph node (LN) dissection for gastric cancer.^{4–10} However, ICG lymphatic mapping is used for sentinel lymph node (SLN) navigation in early gastric cancer. It remains unknown whether ICG lymphatic mapping is useful in advanced gastric cancer as well.

To date, there have been few reports on the use of ICG for lymphatic mapping in robotic surgery for gastric cancer. In this article, we share our initial experience with intraoperative ICG lymphatic mapping during robotic surgery in gastric cancer and compare the surgical outcomes between patients who did not undergo ICG lymphatic mapping during robotic gastrectomy. Both early and advanced gastric cancers were enrolled in this study. The purpose of this study is to investigate whether ICG lymphangiography is helpful in robotic gastrectomy for both early and advanced gastric cancer, with regard to the number of retrieved LNs and the sensitivity of ICG lymphangiography.

Materials and methods

From January 2011 to March 2016, a total of 79 patients receiving robotic gastrectomy for gastric cancer were enrolled in this study. All the robotic gastrectomies were performed by a single experienced surgeon.

Surgical indication

The indication for robotic gastrectomy in the two groups at our hospital was gastric cancer with a clinical stage lower than T3N1M0. Patients who were suitable for endoscopic mucosal resection or endoscopic submucosal dissection were referred to gastrointestinal endoscopists. Patients who had a history of gastric surgery were excluded from the study.

All patients received gastrectomy with at least D1+ lymphadenectomy for early gastric cancer and D2 lymphadenectomy for advanced gastric cancer.

Surgical procedures

Under general anesthesia, each patient was placed in the reverse Trendelenburg position with the legs elevated approximately 15°. The setup of the robotic system was mentioned in our previous study.¹¹ Robotic surgery was conducted using a da Vinci Si Surgical system, and patients with ICG imaging were performed with a near-infrared (NIR) imaging system which was equipped in the da Vinci Si Surgical system.

ICG (Taiwan Sankyo Pharmaceutical Co., Ltd) in a volume of 10 mL (25 mg in total) was gently injected at four injection sites (0.6 mL in each injection site) around the

primary tumor. Approximately 1.5 mg of ICG was injected at each site. Intraoperative subserosal injection of ICG was performed in the initial nine patients, and preoperative submucosal injection of ICG the day before surgery was performed for the other five patients by the same gastroenterologist (Figure 1). We used a Chiba needle (18 gauge) for intraoperative subserosal injection around the tumor. After docking of the robotic arms, robotic gastrectomy with D2 LN dissection was initiated. Preoperative submucosal injection of ICG around the tumor was performed by a gastroenterologist during endoscopy the day before the operation.

Fluorescence imaging with the da Vinci Si system was used for the recent 14 patients. Compared with the ordinary light view during LN dissection, intraoperative NIR imaging with ICG fluorescence signals can enable the surgeons to visualize the channels of the lymphatic vessels and nodes (Figure 2).

This study was approved by the Institutional Review Board of Taipei Veterans General Hospital. Pathological stages were determined in accordance with the seventh edition of the classification guidelines issued by the American Joint Committee on Cancer.¹²

Statistical analysis

Statistical analysis was conducted using the IBM SPSS Statistics 22.0 software. Data are presented as mean ± standard deviation (SD). The independent Student's t-test was used for between-group comparisons of continuous variables, and chi-square tests were used for comparisons of categorical data. Values of *p* less than 0.05 were considered to be statistically significant.

Results

A total of 79 patients who underwent robotic surgery for gastric cancer were enrolled in this study. Among them, lymphatic mapping with ICG injection around the tumor was performed in 14 patients (17.7%). Among the 14 patients, 9 received an intraoperative subserosal injection of ICG, and five received a preoperative submucosal ICG injection by the same gastroenterologist during endoscopy the day before surgery.

In total, 7 of the 14 patients had stage IA lesions; two patients had stage IB lesions; one patient had stage IIA lesion; three patients had stage IIIA lesions; and one patient had a stage IIIC lesion. The median age of the patients was 70 years (range, 35–91), and the median body mass index (BMI) of the patients was 23.9 kg/m² (range, 16.7–31.4).

Table 1 shows the clinicopathological characteristics of the 14 patients. Five of them (35.7%) had LNM (Patient nos 1, 7, 9, 10, 12). Table 2 provides details of the metastatic LN stations. Patient no. 1 had a T2N3 (stage IIIA) lesion with LNM in LN stations #3 (2/4), #6 (6/8), #7 (12/13), #8a (2/4), and #9 (1/3) (Figure 3). Patient no. 7 had

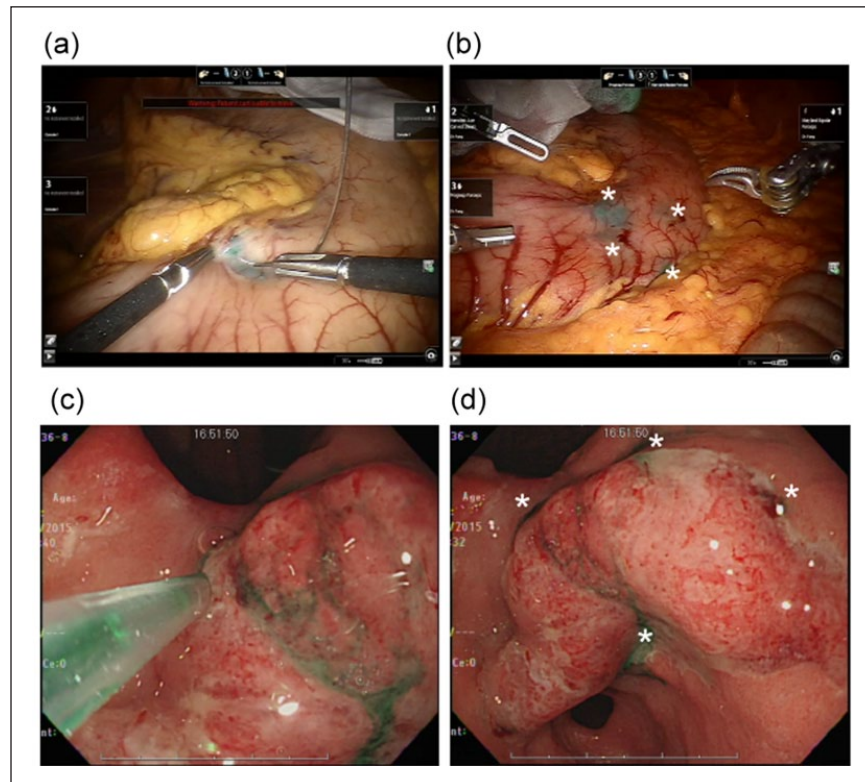


Figure 1. Injection of ICG at four sites around the tumor: (a) intraoperative subserosal injection of ICG around the tumor using a 18Fr. Chiba needle, (b) completion of intraoperative subserosal injection of ICG around the tumor, (c) preoperative submucosal injection of ICG over the border of the tumor under endoscopic view, and (d) completion of preoperative submucosal injection of ICG around the tumor under endoscopic view. The injection sites are marked with an asterisk.

a T4aN3a (stage IIIC) lesion with LNM in LN station #3 (2/6), #4d (1/3), #6 (2/5), and #8 (2/10). Patient no. 9 had a T4aN1 (stage IIIA) lesion with LNM in LN station #3 (2/7). Patient no. 10 had a T1aN1 lesion with LNM in LN station #7 (1/6). Patient no. 12 had a T2N3b (stage IIIA) lesion with LNM in LN station #3 (4/4), #7 (21/22), and #9 (1/5). All the metastatic LNs were found in the LN stations with ICG fluorescence signals.

The clinicopathological features and operative outcomes of robotic gastrectomy for gastric cancer are shown in Table 3. There was no significant difference between the ICG and non-ICG groups with respect to age, gender, tumor size (3.8 ± 1.7 vs 3.4 ± 1.6 cm), BMI, number of retrieved lymph nodes (RLNs) (35.8 ± 11.8 vs 30.0 ± 11.8), operative blood loss (79.2 ± 99.7 vs 78.3 ± 79.8 mL), pathological T and N categories, pathological TNM stage, and length of postoperative hospital stay (10.2 ± 3.6 vs 11.9 ± 12.8 days).

We further analyzed the number of RLNs in each LN station. We found that patients with ICG fluorescence had more number of RLNs over station #4d (7.5 ± 3.1 vs 5.0 ± 2.6 , $p=0.005$) and #6 (5.3 ± 3.3 vs 3.1 ± 2.7 , $p=0.016$) compared with those without ICG (Table 4).

There were more Billroth-I anastomoses in the ICG group. There were no significant differences in the surgical morbidity and mortality between the two groups. The only

surgical morbidity in the ICG group was esophagojejunostomy leakage with abscess formation. Conservative treatment with pigtail drainage with normal saline irrigation was performed, and the patient eventually recovered. The only surgical mortality in the non-ICG group was due to gastrojejunostomy leakage, followed by sepsis and acute renal failure.

Discussion

Our results showed that the clinicopathological features and operative outcomes were not significantly different between gastric cancer patients with or without ICG fluorescence during robotic gastrectomy. In the ICG group, the metastatic LNs were identified in the LN stations with ICG fluorescence signals both in early and advanced gastric cancer. Intraoperative NIR imaging with ICG is feasible, practical, and useful in lymphatic mapping during robotic gastrectomy for gastric cancer.

Our results showed no significant difference between patients who did and did not receive ICG with respect to the number of retrieved LNs and operative time. It was reported that ICG fluorescence may prolong the operative time due to the associated extensive LN dissection. The operative time may have been similar between the two groups because more

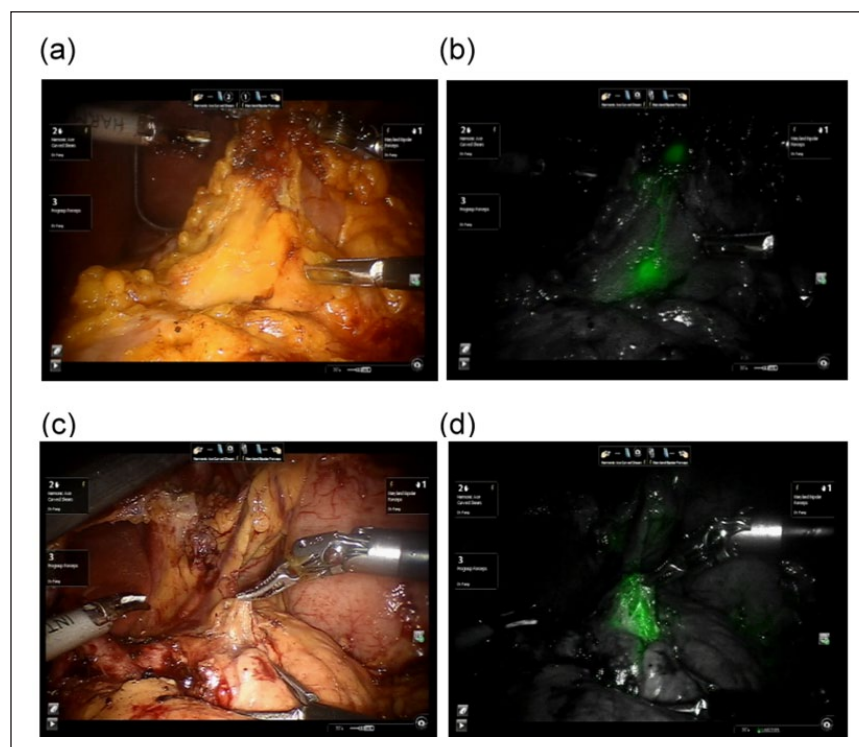


Figure 2. Images obtained during lymph node dissection with robotic gastrectomy for gastric cancer: (a) ordinary light imaging, (b) intraoperative NIR imaging with ICG fluorescence signals in the infrapyloric region, (c) ordinary light imaging, and (d) intraoperative NIR imaging with ICG fluorescence signals in the supra-pancreatic region. Intraoperative NIR imaging with ICG fluorescence signals enables the surgeons to visualize the entire length of the lymphatic vessels and nodes.

Table 1. The use of ICG during robotic gastrectomy in gastric cancer.

Patient no.	Age/sex	Tumor stage	Tumor location	Tumor size	Extent of gastrectomy	Number of LNM/RLN
1	64/F	T2N3b (IIIA)	Low body to angularis, PW	6×5 cm	RSG	31/45
2	77/M	T2N0 (IB)	Antrum, PW	3.5×3 cm	RSG	0/24
3	53/M	T1aN0 (IA)	Low body, AW	2×1 cm	RSG	0/37
4	66/M	T1bN0 (IA)	Angularis, LC	4.5×3.5 cm	RTG	0/32
5	53/M	T1aN0 (IA)	High body, GC	1.5×1 cm	RSG	0/32
6	73/F	T1aN0 (IA)	Midbody, PW	3×2 cm	RTG	0/34
7	84/M	T4aN3a (IIIC)	Angularis to antrum	5×3.5 cm	RSG	7/30
8	70/M	T1aN0 (IA)	Antrum, AW and LC	5×4 cm	RSG	0/26
9	66/M	T4aN1 (IIIA)	Low body, AW	1×1 cm	RSG	2/25
10	79/F	T1aN1 (IB)	Angularis, LC	7×7 cm	RSG	1/20
11	41/F	T1aN0 (IA)	Angularis, LC	3.5×3 cm	RSG	0/47
12	59/M	T2N3b (IIIA)	Angularis, LC	4×4 cm	RSG	26/50
13	56/F	T1aN0 (IA)	High body, PW	3×2 cm	RTG	0/61
14	81/M	T3N0 (IIA)	Antrum, LC	3×3 cm	RSG	0/36

ICG: indocyanine green; LNM: lymph node metastasis, RLN: retrieved lymph node; PW: posterior wall; RSG: radical subtotal gastrectomy; AW: anterior wall; LC: lesser curvature; RTG: radical total gastrectomy; GC: greater curvature.

Bilroth-I anastomoses were present in the ICG group compared with the non-ICG group (60% vs 13.6%). We used the intracorporeal delta-shaped method for Bilroth-I anastomosis, which is easier and takes less time than other reconstruction methods and is thought to be the main reason of

shortening the operation time and leads to no significant difference between the two groups. The other issue affecting the operation time is the learning curve. Although our previous report demonstrated the learning curve for robotic gastrectomy is 25 cases,¹¹ we acknowledge the fact that the

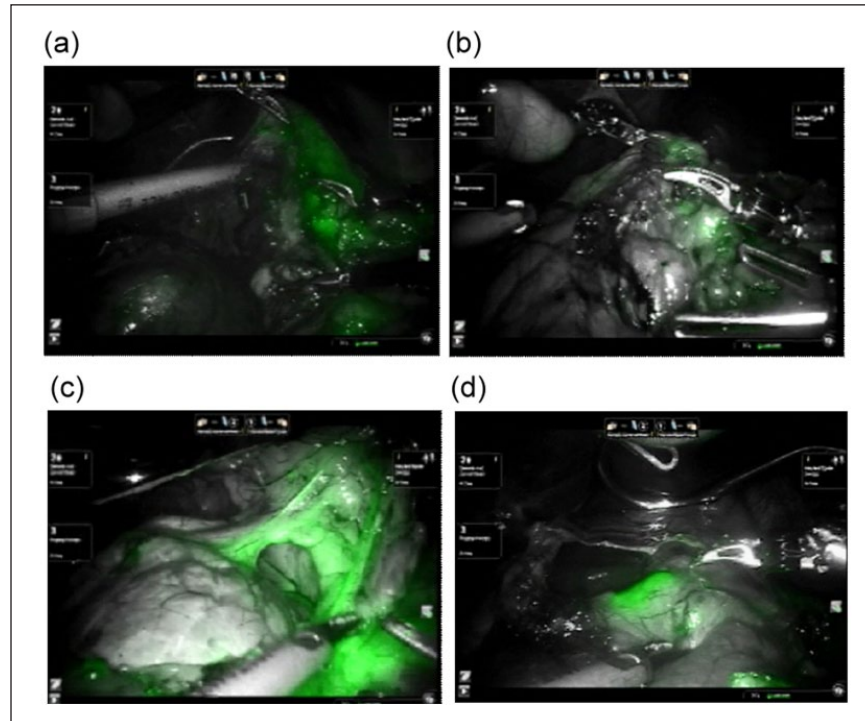


Figure 3. Detail of Patient no. 1 who had lymph node metastasis. The patient had a poorly differentiated adenocarcinoma from the posterior wall of the low body to the angularis of the stomach. The pathological stage was T2N3b (31/45), stage IIIA. Metastatic lymph nodes were located at station #3 (2/4), #6 (6/8), #7 (12/13), #9 (1/3), and #8a (2/4). All metastatic lymph nodes were included in the lymph node stations with ICG fluorescence signals: (a) #3, (b) #6, (c) #7 and #9, and (d) #8a.

Table 2. The lymph node stations of the four patients with lymph node metastasis.

Patient no.	The metastatic lymph node stations Number of MLN/RLN					
	#3	#4d	#6	#7	#8a	#9
1	2/4		6/8	12/13	2/4	1/3
7	2/6	1/3	2/5		2/10	
9	2/7					
10				1/6		
12	4/4			21/22		1/5

MLN: metastatic lymph node; RLN: retrieved lymph node.

operation time has been shortening after accumulating more cases. ICG fluorescence imaging for lymphangiography in gastric cancer is introduced to our institute in the later period since 2015. As a result, both Billroth-I reconstruction method and learning curve may shorten the operation time, which lead to similar operation time in the two groups. Moreover, because most of our patients underwent D2 LN dissection, the number of LN dissections may have been similar between the ICG and non-ICG groups. The relatively small number of the ICG cases in this study does not show significant difference of the total retrieved LN numbers compared with the non-ICG group, which might raise another question whether ICG is necessary if LN dissection is complete. The reason

might be the surgeon in this study performing robotic gastrectomy with or without ICG has overcome the learning curve, which makes no difference in the number of retrieved LN. However, due to the limited number of patients in the ICG group, we will enroll more patients in the future to investigate whether ICG fluorescence could increase the number of retrieved LN. The other question is whether ICG use is also helpful for patients undergoing laparoscopic or open gastrectomy. Future study comparing these three operative approaches with ICG lymphatic mapping might answer this question.

The methods of ICG injection include intraoperative subserosal and preoperative submucosal injections surrounding the tumor.^{4–10,13,14} In this study, we used a Chiba needle for the subserosal injection of ICG at the beginning of surgery for nine patients and a preoperative submucosal injection of ICG the day before surgery for five patients later. There were two cases of ICG leakage while injection. Although the leakage of ICG was minimized by the usage of gauze, it may spoil the view of near infrared. Besides, for early gastric cancer, it is also difficult to identify the location from the outside of the stomach without preoperative or intraoperative tumor localization. The above reasons are why we changed the method of ICG injection. In this study, the metastatic LNs were located in the LN stations observed with ICG fluorescence. We could not conclude 100% sensitivity of the ICG LN navigation because we did not distinguish each node

Table 3. Comparison of the clinicopathological differences and operative outcomes in robotic gastrectomy between gastric cancer patients with or without lymphatic mapping with ICG.

	ICG (n = 14)	Non-ICG (n = 65)	p value
Age (y/o)	66.0 ± 12.4	67.8 ± 15.6	0.684
Gender (M/F)	7/7	38/27	0.569
Tumor size (cm)	3.7 ± 1.7	3.4 ± 1.6	0.551
BMI (kg/m ²)	24.0 ± 4.1	24.4 ± 3.1	0.701
Resection extent			0.194
Subtotal/total gastrectomy	11/3	59/6	
Reconstruction method			<0.001
Billroth-I	9 (64.3)	9 (13.8)	
Billroth-II + Braun's procedure	2 (14.3)	0	
Roux-en-Y or uncut R-Y	3 (21.4)	56 (86.2)	
Extent of lymphadenectomy			0.582
<D2/D2	0/14	6/59	
Retrieved LN number	35.8 ± 11.4	30.0 ± 11.8	0.094
Pathological T category			0.197
T1/T2/T3/T4	8/3/1/2	47/7/9/2	
Pathological N category			0.141
N0/N1/N2/N3	8/2/1/3	43/7/12/3	
Pathological TNM stage			0.204
I/II/III	8/2/4	43/15/7	
Operative outcomes			
Operative time (min)	327.0 ± 79.7	349.8 ± 120.9	0.502
Operative blood loss (mL)	75.7 ± 96.7	78.3 ± 79.8	0.977
Postoperative hospital stay (day)	10.1 ± 3.5	11.9 ± 12.8	0.614
Surgical complication	1 (7.1)	8 (12.3)	1.000
Anastomosis leakage	1 (7.1)	2 (3.1)	0.448
Anastomosis stenosis	0	2 (3.1)	1.000
Intraabdominal abscess	1 (7.1)	0	0.177
Delayed gastric emptying	0	4 (6.2)	1.000
Intestinal obstruction	0	1 (1.5)	1.000
Surgical mortality	0	1 (1.5)	1.000

ICG: indocyanine green; BMI: body mass index; LN: lymph node.

Some patients had more than one complication.

Data were presented as mean ± standard deviation (SD) or n (%).

with or without ICG in the specimen. We can only know that the metastatic LNs are located in the LN station with ICG fluorescence observed during surgery. It is the limitation of our study, and we will distinguish the ICG fluorescence for each LN in the future study.

The optimal dosage of ICG injection varies in reported series.^{4–10,13,14} In our experience, we used 1.5 mg in each injection site, totally 6 mg of ICG injection. However, some patients had disseminated fluorescence signals in the omental and pancreatic surface. In order to obtain a better quality of fluorescence imaging, titration of the ICG dosage to 0.75 mg in each injection site (total 3 mg of ICG) is considered in the future. It is interesting that the determining factor of the image quality of the fluorescence imaging is the dosage of ICG injection, not the route of injection or duration between injection and surgery. For intraoperative subserosal injection, the period between ICG injection and starting of lymphadenectomy was 10–20 min; for submucosal injection by gastroenterologist the day before operation, the duration

was about one day. From our experience, there is no obvious difference in fluorescence imaging between subserosal or submucosal ICG injection for gastric cancer.

With our experience mentioned in the above two sentences, the criterion of success for the present pilot study is to continue this study with modification of the route and amount of ICG injection, which is submucosal injection of ICG with 0.75 mg for each of the four sites around the tumor the day before surgery.

There are some differences in the use of ICG fluorescence between laparoscopic and robotic surgery. The scope and associated equipment for near-infrared navigation are already included in the robotic system; additional laparoscope and associated equipment were required in laparoscopic surgery, which is still not available in our institute. Intraoperative lymphatic mapping with ICG during robotic gastrectomy allows the surgeons to easily change between three-dimensional (3D) ordinary light imaging and real-time NIR imaging by moving their fingers, enabling them to

Table 4. Comparison of the number of retrieved lymph node in each lymph node station.

Lymph node station	ICG (n = 14)	Non-ICG (n = 65)	p value
#1	1.5 ± 0.7	2.6 ± 3.2	0.639
#3	6.0 ± 3.1	6.4 ± 5.3	0.809
#4d	7.3 ± 3.1	5.0 ± 2.6	0.007
#5	2.2 ± 1.8	1.6 ± 2.1	0.410
#6	5.7 ± 3.5	3.1 ± 2.7	0.004
#7	6.6 ± 5.6	4.5 ± 3.2	0.066
#8a	4.0 ± 3.0	3.5 ± 2.7	0.551
#9	3.4 ± 3.3	2.5 ± 2.6	0.353
#11p	1.2 ± 1.0	1.7 ± 1.7	0.488
#12a ^a	1.0 ± 1.4	0.9 ± 1.2	0.890

ICG: indocyanine green.

^a#12a lymph node station is dissected for distal gastric cancer.

easily compare the NIR, and 3D images in a timely manner. The use of ICG fluorescence during robotic gastrectomy can help surgeons visualize residual LNs and achieve LN dissection as completely as possible. Although the number of RLN was similar between the patients with and without ICG fluorescence, we believe that the use of ICG fluorescence made the surgeons more confident and allowed them to more precisely perform LN dissections with the aid of the NIR system during robotic gastrectomy for gastric cancer.

The use of ICG fluorescence has been applied for early gastric cancer; however, our previous study demonstrated that the frequency of LNM can be 4% for T1a and 21% for T1b lesions.³ The other major controversy is the use of ICG fluorescence in lymphatic mapping in advanced gastric cancer. In our series, LNM was observed in five patients, including one T1a lesion, two T2 lesions, and two T4a lesions. Among the five patients, in addition to the LNs along the lesser curvature, the frequent stations of LNM included #6, #7, and #8a. Our results demonstrated that patients with ICG fluorescence had significantly more number of RLNs over the greater curvature side of low body to infrapyloric area (LN stations #4d and #6) compared with those without ICG. It was reported that the number of RLN was significant fewer in the infrapyloric area in laparoscopic gastrectomy than open gastrectomy.¹⁵ Subgroup analysis showed that only when the laparoscopic gastrectomy performed by experienced surgeons, the number of RLN over this area was similar in laparoscopic and open gastrectomy. The lymphatic and vascular drainage over infrapyloric area varies among patients,¹⁶ and frequent LNM around this area was observed in advanced gastric cancer over middle and lower third of the stomach.^{17,18} Patients with LNM in the infrapyloric region were more likely to developed LNM to the LNs along the splenic artery, the hepatoduodenal ligament, and even the posterior aspect of the pancreas.¹⁹ As a result, LNM over the infrapyloric area might serve as a prognostic factor in gastric cancer. Our results showed only difference in number of retrieved LNs between stations #4d and #6, which is possible due to the small sample size in the ICG group. More patient

enrollment would give us more information and might achieve statistical significance in the number of retrieved LNs in other stations. Because the frequency of LNM in advanced gastric cancer is relatively higher than that in early gastric cancer, precise and extensive LN dissection is important not only to obtain correct pathological N categories but also to achieve adequate cancer treatment. We suggest that ICG fluorescence can be performed in routine lymphatic mapping in robotic gastrectomy and even in laparoscopic gastrectomy and can serve as a good navigation tool for lymphatic mapping and enable surgeons to achieve extensive LN dissection in advanced gastric cancer.

We did not quantify the enrolled patient number prior to the study. In this study, a small sample size in the ICG group might cause false negative result, so-called type II error. Using a 95% confidence interval (CI) for the proportion of eligible patients with a margin of error of 0.05, a lower bound of this CI of 0.70, and an expected completion rate of 75% based on an educated guess, the required number of patients for the pilot study would be at least 75. As a result, we plan to enroll at least 75 patients in each group in the future.

Our study had certain limitations. First, this investigation is a retrospective study, and selection bias may exist. There is difference in some categories between the two groups. Second, the number of patients who underwent intraoperative lymphatic mapping with ICG was limited in this pilot study, and more patients need to be enrolled in future studies. Third, because we did not examine the fluorescence of each LN in the specimen with NIR imaging, we could not distinguish which LN is with or without fluorescence signal. In the future, we should examine the fluorescence signal of each LN and investigate the correlation between LNM and fluorescence signals.

Although a handful of reports about the ICG mapping in the robotic surgery were published, the benefit of such technique was demonstrated in the laparoscopic procedure, which might make our study lack of novelty. Currently, a prospective trial in Korea is in progress to compare the number of retrieved LNs in each nodal station after NIR fluorescence imaging during laparoscopic and robotic gastrectomy (NCT01926743). This method may help surgeons perform a more complete D1+ or D2 LN dissection. We believe that the above study will provide convincing results regarding the usefulness of ICG with NIR fluorescence in minimally invasive surgery.

In conclusion, our pilot study shows that intraoperative lymphatic mapping with ICG fluorescence during robotic surgery for gastric cancer is a feasible technique. A larger number of enrolled patients and long-term follow-up for survival analysis are required in future studies.

Acknowledgements

Y.-T.L., K.-H.H., P.-H.C., C.-A.L., S.-S.L., C.-W.W., Y.-M.S., and W.-L.F contributed in study concept and design. Y.-T.L., K.-H.H., and W.-L.F helped in acquisition of data. W.-L.F analyzed the data.

Y.-T.L., K.-H.H., and W.-L.F helped in analysis and interpretation. W.-L.F contributed in study supervision.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval for this study was obtained from the Institutional Review Board of Taipei Veterans General Hospital (2014-06-003BC).

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Written informed consent was obtained from all subjects before the study.

References

1. Son T, Kwon IG and Hyung WJ. Minimally invasive surgery for gastric cancer treatment: current status and future perspectives. *Gut Liver* 2014; 8(3): 229–236.
2. Fang WL, Huang KH, Chen JH, et al. Comparison of the survival difference between AJCC 6th and 7th editions for gastric cancer patients. *World J Surg* 2011; 35(12): 2723–2729.
3. Fang WL, Huang KH, Lan YT, et al. The risk factors of lymph node metastasis in early gastric cancer. *Pathol Oncol Res* 2015; 21(4): 941–946.
4. Ohdaira H, Nimura H, Mitsumori N, et al. Validity of modified gastrectomy combined with sentinel node navigation surgery for early gastric cancer. *Gastric Cancer* 2007; 10(2): 117–122.
5. Yano K, Nimura H, Mitsumori N, et al. The efficiency of micrometastasis by sentinel node navigation surgery using indocyanine green and infrared ray laparoscopy system for gastric cancer. *Gastric Cancer* 2012; 15(3): 287–291.
6. Kelder W, Nimura H, Takahashi N, et al. Sentinel node mapping with indocyanine green (ICG) and infrared ray detection in early gastric cancer: an accurate method that enables a limited lymphadenectomy. *Eur J Surg Oncol* 2010; 36(6): 552–558.
7. Tajima Y, Murakami M, Yamazaki K, et al. Sentinel node mapping guided by indocyanine green fluorescence imaging during laparoscopic surgery in gastric cancer. *Ann Surg Oncol* 2010; 17(7): 1787–1793.
8. Miyashiro I, Miyoshi N, Hiratsuka M, et al. Detection of sentinel node in gastric cancer surgery by indocyanine green fluorescence imaging: comparison with infrared imaging. *Ann Surg Oncol* 2008; 15(6): 1640–1643.
9. Kusano M, Tajima Y, Yamazaki K, et al. Sentinel node mapping guided by indocyanine green fluorescence imaging: a new method for sentinel node navigation surgery in gastrointestinal cancer. *Dig Surg* 2008; 25(2): 103–108.
10. Mitsumori N, Nimura H, Takahashi N, et al. Sentinel lymph node navigation surgery for early stage gastric cancer. *World J Gastroenterol* 2014; 20(19): 5685–5693.
11. Huang KH, Lan YT, Fang WL, et al. Initial experience of robotic gastrectomy and comparison with open and laparoscopic gastrectomy for gastric cancer. *J Gastrointest Surg* 2012; 16(7): 1303–1310.
12. Sobin L, Gospodarowicz M and Wittekind C (eds). *TNM classification of malignant tumours* (International Union Against Cancer (UICC)). 7th ed. New York: Wiley, 2009.
13. Miyashiro I, Hiratsuka M, Sasako M, et al; Gastric Cancer Surgical Study Group (GCSSG) in the Japan Clinical Oncology Group (JCOG). High false-negative proportion of intraoperative histological examination as a serious problem for clinical application of sentinel node biopsy for early gastric cancer: final results of the Japan Clinical Oncology Group multicenter trial JCOG0302. *Gastric Cancer* 2014; 17(2): 316–323.
14. Miyashiro I, Hiratsuka M, Kishi K, et al. Intraoperative diagnosis using sentinel node biopsy with indocyanine green dye in gastric cancer surgery: an institutional trial by experienced surgeons. *Ann Surg Oncol* 2013; 20(2): 542–546.
15. Ikeda O, Sakaguchi Y, Toh Y, et al. Evaluation of oncological adequacy of laparoscopic distal gastrectomy with special attention to lymph node dissection: a comparison with conventional open gastrectomy. *Hepatogastroenterology* 2012; 59(114): 627–632.
16. Cao LL, Huang CM, Lu J, et al. The impact of confluence types of the right gastroepiploic vein on No. 6 lymphadenectomy during laparoscopic radical gastrectomy. *Medicine* 2015; 94(33): e1383.
17. Wu CW, Hsieh MC, Tsay SH, et al. Adenocarcinoma of mid-stomach. Clinical and pathoanatomic relation to lymph node metastases. *J Clin Gastroenterol* 1994; 19(3): 259–263.
18. Zuo CH, Xie H, Liu J, et al. Characterization of lymph node metastasis and its clinical significance in the surgical treatment of gastric cancer. *Mol Clin Oncol* 2014; 2(5): 821–826.
19. Sawai K, Seiki K, Taniguchi H, et al. Rationalization of lymph node dissection for gastric cancer using small sized activated carbon particles adsorbing absolute ethanol. *Nihon Geka Gakkai Zasshi* 1989; 90(9): 1310–1313.