


RESEARCH HIGHLIGHT

A safe and effective surgical navigation technique in laparoscopic radical gastrectomy: Indocyanine green-mediated near-infrared fluorescent imaging

Yan Qian^{1,2}  | Shirong Cai^{1,2}¹Division of Gastrointestinal Surgery Center, the First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong 510080, P. R. China²Gastric Cancer Center, Sun Yat-sen University, Guangzhou, Guangdong 510080, P. R. China**Correspondence**Shirong Cai; Division of Gastrointestinal Surgery Center, the First Affiliated Hospital of Sun Yat-sen University, Guangzhou 510080, Guangdong, China.
Email: caishirong@yeah.net

In the past decades, gastric cancer (GC) is one of the most common cancers and causes of cancer-related deaths worldwide [1]. China has the highest incidence of GC [2] and accounts for more than 40% of all new GC cases in the world [3]. Radical lymphadenectomy serves as an important role in the staging and definitive management of GC [4, 5]. At present, laparoscopic radical gastrectomy has been shown to significantly improve the accuracy of tumor staging and long-term survival of GC patients [6]. The retrieval of more lymph nodes (LNs) via lymphadenectomy is a current requirement for laparoscopic radical gastrectomy [5]. Lymphadenectomy is usually performed according to the experience of surgeons. However, it is a substantial challenge for surgeons to efficiently and accurately acquire enough LNs without increasing the risk of complications as the vascular and lymphatic anatomy of stomach is extremely complex. Therefore, surgeons are looking for more accurate strategies to perform adequate lymphadenectomy under laparoscopic guidance.

In recent years, surgical navigation techniques have proven to be effective in the localization of sentinel LNs in cancer patients [6]. One of the widely studied surgical navigation techniques in cancer surgery is indocyanine green (ICG)-mediated near-infrared (NIR) fluorescent imaging. It has already demonstrated promising results in the localization of LNs during surgery in many types of cancers [7, 8]. As ICG

has better tissue penetration than other dyes and NIR imaging can more accurately identify LNs than visible light imaging [9, 10], ICG fluorescence imaging-guided laparoscopic radical gastrectomy has become a hot spot in GC treatment [11]. However, the findings regarding the actual benefits of using ICG for GC lymphadenectomy in previous studies is controversial [12, 13]. Additionally, almost all of these previous studies were retrospective studies with small sample size and were only focused on the evaluation of evaluated sentinel LNs and anastomotic blood flow [14, 15]. Therefore, it was necessary to conduct large-scale randomized clinical trials to evaluate the safety and effectiveness of ICG-guided LN dissection during laparoscopic radical gastrectomy in GC patients.

In a study recently published in *JAMA Surgery*, titled “Safety and Efficacy of Indocyanine Green Tracer-Guided Lymph Node Dissection during Laparoscopic Radical Gastrectomy in Patients with Gastric Cancer: A Randomized Clinical Trial”, Chen *et al.* [16] enrolled 258 resectable GC patients in a prospective randomized clinical trial to evaluate the safety and efficacy of ICG-mediated NIR fluorescent imaging during laparoscopic D2 lymphadenectomy. In this study, the patients were randomly assigned to ICG group ($n = 129$; underwent ICG-mediated NIR fluorescent imaging-guided laparoscopic gastrectomy) or non-ICG group ($n = 129$; underwent conventional laparoscopic gastrectomy). The mean

List of Abbreviations: GC, gastric cancer; ICG, indocyanine green; LN, lymph node; NIR, near-infrared.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *Cancer Communications* published by John Wiley & Sons Australia, Ltd. on behalf of Sun Yat-sen University Cancer Center

number of positive LNs retrieved in the non-ICG group was significantly lower than that in the ICG group (42.0 vs. 50.5 LNs; $P < 0.001$). Similarly, within the scope of D2 lymphadenectomy, the mean total number of LNs retrieved in the non-ICG group was significantly lower than that in the ICG group (41.7 vs. 49.6 LNs; $P < 0.001$). In contrast, the LN noncompliance rate of the non-ICG group was significantly greater than that of the ICG group (57.4% vs. 31.8%; $P < 0.001$). Within 30 days after surgery, no significant difference was observed in the incidence of surgery-related complications between the ICG and non-ICG groups (15.5% vs. 16.3%; $P = 0.86$). These observations indicated that ICG-mediated NIR fluorescent imaging could noticeably improve the efficacy of lymphadenectomy during laparoscopic radical gastrectomy safely.

Compared with previous studies, this clinical trial additionally enrolled a large number of GC patients with stage cT1-cT4a disease and the authors conducted an in-depth analysis using multiple parameters including the number of LNs retrieved within the scope of D2 lymphadenectomy, the total number of LNs retrieved, the LN noncompliance rate, the incidence of surgery-related complications. They could thereby accurately assess the safety and efficacy of ICG-mediated NIR fluorescent imaging-guided laparoscopic gastrectomy and showed its important role in guiding the choice of surgical navigation technology and accurate staging. Furthermore, since this prospective randomized clinical trial strictly followed the randomized clinical trial standards in patient selection, it avoided the selection bias and makes the general data comparable. Most importantly, it also developed the methods about the standard use of ICG.

This clinical trial has several limitations. First, the data were only collected from a single center and the long-term follow-up data were not available. Second, only 56.3% of metastatic LNs were detected via fluorescence, indicating that there may be a great risk of false-negative results when ICG-mediated NIR fluorescent imaging is used to detect metastatic LNs. These false-negative results may have been owing to the infiltration of a large number of cancer cells in LNs or the obstruction of lymphatic vessels. Third, further analyses according to the tumor location were not performed; which may have led to uneven stratification of individual variables.

Despite the limitations mentioned above, this prospective randomized clinical trial by Chen *et al.* showed more accuracy in evaluating the efficacy and perioperative safety of ICG-mediated NIR fluorescent imaging during laparoscopic D2 lymphadenectomy, compared to previous studies. The findings can promote the standardization of NIR imaging in laparoscopic resection of GC and lays the foundation for the application of ICG imaging in the radical resection of GC.

DECLARATIONS

AUTHORS' CONTRIBUTIONS

The author read and approved the final manuscript.

ACKNOWLEDGMENTS

Not applicable.

COMPETING INTERESTS

The author declares no competing interests.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

FUNDING

Not applicable.

ORCID

Yan Qian  <https://orcid.org/0000-0002-5391-2869>

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin.* 2019;69(1):7-34.
2. Feng RM, Zong YN, Cao SM, Xu RH. Current cancer situation in China: good or bad news from the 2018 Global Cancer Statistics? *Cancer Commun.* 2019;39(1):22.
3. Gao K, Wu J. National trend of gastric cancer mortality in China (2003-2015): a population-based study. *Cancer Commun.* 2019;39(1):24.
4. Ozer I, Bostanci EB, Ulas M, Ozogul Y, Akoglu M. Changing Trends in Gastric Cancer Surgery. *Balkan Medical Journal.* 2017;34(1):10-20.
5. Wang FH, Shen L, Li J, Zhou ZW, Liang H, Zhang XT, et al. The Chinese Society of Clinical Oncology (CSCO): clinical guidelines for the diagnosis and treatment of gastric cancer. *Cancer Commun.* 2019;39(1):10.
6. Kiyokawa T, Fukagawa T. Recent trends from the results of clinical trials on gastric cancer surgery. *Cancer Commun.* 2019;39(1):11.
7. Vahrmeijer AL, Hutteman M, van der Vorst JR, van de Velde CJ, Frangioni JV. Image-guided cancer surgery using near-infrared fluorescence. *Nat Rev Clin Oncol.* 2013;10(9):507-18.
8. Valente SA, Al-Hilli Z, Radford DM, Yanda C, Tu C, Grobmyer SR. Near Infrared Fluorescent Lymph Node Mapping with Indocyanine Green in Breast Cancer Patients: A Prospective Trial. *J Am Coll Surg.* 2019;228(4):672-8.
9. Gioux S, Choi HS, Frangioni JV. Image-guided surgery using invisible near-infrared light: fundamentals of clinical translation. *Mol Imaging.* 2010;9(5):237-55.

10. Schaafsma BE, Mieog JS, Hutteman M, van der Vorst JR, Kuppen PJ, Lowik CW, et al. The clinical use of indocyanine green as a near-infrared fluorescent contrast agent for image-guided oncologic surgery. *J Surg Oncol*. 2011;104(3):323-32.
11. Desiderio J, Trastulli S, Gemini A, Di Nardo D, Palazzini G, Parisi A et al. Fluorescence image-guided lymphadenectomy using indocyanine green and near infrared technology in robotic gastrectomy. *Chinese Journal of Cancer Research*. 2018;30(5):568-70.
12. Kim TH, Kong SH, Park JH, Son YG, Huh YJ, Suh YS et al. Assessment of the Completeness of Lymph Node Dissection Using Near-infrared Imaging with Indocyanine Green in Laparoscopic Gastrectomy for Gastric Cancer. *Journal of Gastric Cancer*. 2018;18(2):161-71.
13. Tajima Y, Murakami M, Yamazaki K, Masuda Y, Kato M, Sato A et al. Sentinel node mapping guided by indocyanine green fluorescence imaging during laparoscopic surgery in gastric cancer. *Ann Surg Oncol*. 2010;17(7):1787-93.
14. Yano K, Nimura H, Mitsumori N, Takahashi N, Kashiwagi H, Yanaga K. 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):287-91.
15. Tajima Y, Yamazaki K, Masuda Y, Kato M, Yasuda D, Aoki T et al. Sentinel node mapping guided by indocyanine green fluorescence imaging in gastric cancer. *Ann Surg*. 2009;249(1):58-62.
16. Chen QY, Xie JW, Zhong Q, Wang JB, Lin JX, Lu J et al. Safety and Efficacy of Indocyanine Green Tracer-Guided Lymph Node Dissection During Laparoscopic Radical Gastrectomy in Patients With Gastric Cancer: A Randomized Clinical Trial. *JAMA Surgery*. 2020. <https://doi.org/10.1001/jamasurg.2019.6033>.

How to cite this article: Qian Y, Cai S. A safe and effective surgical navigation technique in laparoscopic radical gastrectomy: Indocyanine green-mediated near-infrared fluorescent imaging. *Cancer Communications*. 2020;40:270–272. <https://doi.org/10.1002/cac2.12033>