

# INPLASY PROTOCOL

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**Conflicts of interest:**  
None declared.

## Assessment of intraoperative use of indocyanine green fluorescence imaging on the number of lymph node dissection during minimally invasive gastrectomy: a systematic review and meta-analysis

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**Review question / Objective:** Whether is indocyanine green fluorescence imaging-guided lymphadenectomy feasible to improve the number of lymph node dissections during radical gastrectomy in patients with gastric cancer undergoing curative resection?

**Condition being studied:** Gastric cancer was the sixth most common malignant tumor and the fourth leading cause of cancer-related death in the world. Radical lymphadenectomy was a standard procedure in radical gastrectomy for gastric cancer. The retrieval of more lymph nodes was beneficial for improving the accuracy of tumor staging and the long-term survival of patients with gastric cancer. Indocyanine green (ICG) near-infrared fluorescent imaging has been found to provide surgeons with effective visualization of the lymphatic anatomy. As a new surgical navigation technique, ICG near-infrared fluorescent imaging was a hot spot and had already demonstrated promising results in the localization of lymph nodes during surgery in patients with breast cancer, non-small cell lung cancer, and gastric cancer. In addition, ICG had increasingly been reported in the localization of tumor, lymph node dissection, and the evaluation of anastomotic blood supply during radical gastrectomy for gastric cancer. However, it remained unclear whether ICG fluorescence imaging would assist surgeons in performing safe and sufficient lymphadenectomy.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 November 2021 and was last updated on 17 November 2021 (registration number INPLASY2021110062).

### INTRODUCTION

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## METHODS

**Search strategy:** All relevant medical studies from PubMed, Embase, Web of Science and Cochrane Library were systematically reviewed through November 2021. The search strategy contained 2 core components, which were linked using the AND operator: 1) stomach neoplasms (e.g., neoplasm, stomach, stomach neoplasm, neoplasms, stomach, gastric neoplasms, gastric neoplasm, neoplasm, gastric, neoplasms, gastric, stomach cancers, cancer of stomach, gastric cancer, cancer, gastric, cancers, gastric, gastric cancers, stomach cancer, cancers, stomach, cancer, stomach, cancer of the stomach, gastric cancer, familial diffuse), 2) indocyanine green (e.g., green, indocyanine, wofaverdin, vophaverdin, ujooveridin, vofaverdin, cardio-

green, cardio green, cardiogreen. Controlled vocabulary (i.e., Medical Subject Headings [MeSH] terms) and title/abstract were identified for each of the 2 core components. The search was developed initially for PubMed and then adapted for each of the other 3 databases by mapping the search terms to additional controlled vocabulary and subject heading terminology.

**Participant or population:** Patients with gastric cancer who underwent radical gastrectomy.

**Intervention:** Patients with indocyanine green tracer-guided lymphadenectomy.

**Comparator:** Patients without indocyanine green tracer-guided lymphadenectomy.

**Study designs to be included:** Either randomized controlled trials (RCTs), cohort studies, or comparative studies all will be included.

**Eligibility criteria:** The Cochrane Handbook was used to evaluate quality of randomized controlled studies (RCTs). If the study scored 4 or more out of a maximum of 6 points, it is considered as a high quality research and will be included. For non-randomized controlled studies such as retrospective studies, the Newcastle-Ottawa scale was used to evaluate quality and Studies with scores  $\geq 7$  were deemed high in quality.

**Information sources:** All relevant medical studies from PubMed, Embase, Web of Science and Cochrane Library were systematically reviewed through November 2021.

**Main outcome(s):** The total number of harvested lymph nodes.

**Additional outcome(s):** The number of metastatic lymph node dissection; Operative time; Intraoperative blood loss; Postoperative complications; Postoperative hospital stay.

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**Quality assessment / Risk of bias analysis:**

The Cochrane Collaboration Risk of Bias Tool and Newcastle Ottawa Scale (NOS) were used to assess the quality of included RCT studies and observational studies, respectively. Pooled analyses were conducted using random and fixed effect models with the Mantel-Haenszel method when appropriate. Statistical heterogeneity was investigated using the Cochran's Q test ( $P < 0.10$ ) and the I<sup>2</sup> statistic ( $> 50\%$ ). Sensitivity analysis was conducted based on the low risk of bias. Subgroup analyses were conducted based on surgical approach, study design and countries. Potential publication bias was assessed by visually inspecting the funnel plots in Review Manager. Publication bias in this meta-analysis was assessed using a funnel plot based on primary outcomes.

**Strategy of data synthesis:** The odds ratio (OR) and mean difference (MD) with their 95% confidence interval (CI) were used to evaluate dichotomous and continuous variables, respectively. For studies that only reported median and range, data were converted into mean and standard deviation (SD) following the method reported by Wan et al. [28]. Heterogeneity among studies was assessed by  $\chi^2$  and I<sup>2</sup> statistics. I<sup>2</sup>  $> 50\%$  indicates significant heterogeneity. For this, a random-effects model was used; otherwise, a fixed-effects model was performed. For the assessment of publication bias, a funnel plot was conducted. A p value  $< 0.05$  was considered significant. All of the statistical analyses were performed by Review Manager Software, version 5.3 (Cochrane, London, UK).

**Subgroup analysis:** Subgroup analyses were conducted based on surgical approach, study design and countries.

**Sensitivity analysis:** Sensitivity analysis was performed by removing one study at a time and repeating the meta-analysis to assess whether at least one study significantly affected the pooled estimates.

**Language:** English.

**Country(ies) involved:** China.

**Keywords:** Indocyanine green; Laparoscopic surgery; Lymph node; Near-infrared imaging; Gastric cancer; Robotic gastrectomy.

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