

INPLASY PROTOCOL

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None.

Prognostic Value of Lymph Node Yield on Long-term Survival in Colorectal Cancer Patients: A Systematic Review and Meta-analysis

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Review question / Objective: Whether increased lymph node yield improves overall survival and disease-free survival in patients with colorectal cancer undergoing curative resection or not, especially in those recipients of neoadjuvant therapy? Thus, this research had as PICO: P: patients with colorectal cancer; I: curative resection; C: high or low lymph node yield; O: overall survival and disease-free survival.

Condition being studied: It is estimated that colorectal cancer (CRC) incidence ranks second in women and third in men (Bray F. et. al., 2019). Notwithstanding the emergence of new therapies, surgical resection with adjuvant treatment is still the mainstream, especially for the locally advanced (Bromham N. et. al., 2020). Except for pTis, lymph node dissection is necessary in operation, in which, to ensure precision in staging, a minimum of 12 nodes is recommended, even sometimes as a judgement of surgery (Nelson H. et. al., 2001). Despite some disputations, particularly in different clinical stages, more evidence manifested that increased lymph node yield is also relevant to improved long-term survival in colorectal cancer (Nordholm-Carstensen A. et. al., 2020). In terms of rectal cancer of non-early stage, neoadjuvant treatment is proposed in clinical guidelines, which, to a certain extent, causes the decrease of lymph node yield. Hence, what arouses controversies is that increased lymph node yield remains necessary among recipients of neoadjuvant treatment. There have been several studies concerning the issue but with no consensus (McFadden C. et. al., 2013).

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 April 2020 and was last updated on 12 April 2020 (registration number INPLASY202040066).

INTRODUCTION

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METHODS

Participant or population: Studies that will include patients with a diagnosis of colorectal cancer undergoing curative resection.

Intervention: Curative resection including lymph node dissection.

Comparator: Patients with higher lymph node yield and lower lymph node yield.

Study designs to be included: Randomized controlled trials and observational studies (including respective and prospective cohort studies) will be included.

Eligibility criteria: The inclusion criteria are the following: (1) patients with curative resection due to colorectal cancer; and (2) investigation of the correlation between long-term survival (Overall survival or Disease-free survival) and lymph node yield.

Information sources: A systematic literature search will be conducted utilizing a combination of free-text terms and controlled vocabulary in 3 electronic databases: MEDLINE (Pubmed), EMBASE (OvidSP), and Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library. The search term will include "colorectal", "rectal", "cancer", "tumor", "lymph", "lymphadenectomy", "survival" and "recurrence", which will be used in combination with the Boolean operators "AND" or "OR". The search will be limited to human studies and English language publications.

Main outcome(s): Hazard ration between lymph node yield and overall survival.

Additional outcome(s): Hazard ration between lymph node yield and disease-free survival.

Quality assessment / Risk of bias analysis: Randomized controlled trials will be evaluated by the modified Jadad Rating Scale which included four metrics: method of randomization, concealment of allocation, number of patients lost to follow-up and corresponding reasons, and blinding. Non-randomized controlled trials will be assessed by the modified Newcastle Ottawa Scale (NOS) including three metrics: selection criteria for case and controls, comparability between groups, and ascertainment of outcome (case-control studies) or exposure (cohort studies). Publication bias will be evaluated via Egger regression test.

Strategy of data synthesis: The extraction of data will be performed by a standard form with the first author, country, year of publication, sample size, gender, age, tumor location, histology, pathological TNM stage, clinical-stage, neoadjuvant

treatment, follow-up period, lymph node yield, cut-off and hazard ratio. The studies that meet the inclusion criteria will have their data extracted by two reviewers, Y, J and Y, Ty. Any disagreement will be resolved, if necessary by a third author (S, Jj). Fixed- and random-effects models will be utilized to estimate the pooled hazard ratios with 95% confidence intervals. Highly heterogeneous groups of studies will be analyzed with the fixed-effects model, while less heterogeneous groups of studies will be analyzed with the fixed-effects model. Study heterogeneity will be determined using the I^2 statistic (in which numbers greater than 75% suggest considerable heterogeneity). The calculation of analysis will be performed by appropriate statistical software (STATA/SE12).

Subgroup analysis: Rectal cancer patients with or without neoadjuvant.

Sensibility analysis: If necessary, sensitivity analysis will be carried.

Country(ies) involved: China.

Keywords: Colorectal cancer; lymphadenectomy; survival; meta-analysis.

Dissemination plans: XXXX results of this systematic review will be disseminated through peer reviewed XXXXX.

Contributions of each author:

Author 1 - Project, search strategy, studies selection, data extraction and analysis, results description and article writing.

Author 2 - Selection of studies, data extraction and article writing.

Author 3 - Project and writing of article.

Author 4 - Project, revision of article.