# INPLASY PROTOCOL

To cite: Jin et al. The impact of preoperative sarcopenia on survival prognosis of patients with neoadjuvant therapy for esophageal cancer: a systematic review and meta-analysis. Inplasy protocol 202050057. doi: 10.37766/inplasy2020.5.0057

Received: 14 May 2020

Published: 14 May 2020

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Support: No.

Review Stage at time of this submission: Data analysis.

Conflicts of interest: No.

# The impact of preoperative sarcopenia on survival prognosis of patients with neoadjuvant therapy for esophageal cancer: a systematic review and meta-analysis

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Review question / Objective: To evaluate the effect of preoperative diagnosis of sarcopenia on survival and prognosis of patients with neoadjuvant therapy for esophageal cancer.

Condition being studied: Esophageal cancer(EC) is a common and often fatal cancer that it is the sixth leading cause of cancer-related deaths worldwide, although recent progress in surgical and postoperative management techniques has improved treatment outcomes, the prognosis of EC is still unsatisfactory. Sarcopenia is a progressive and generalized skeletal muscle disorder involving the accelerated loss of muscle mass and function that is linked to increased adverse outcomes including falls, functional decline, frailty, and mortality. Over the last few years, an increasing number of studies have been conducted on effects of preoperative sarcopenia for the prognosis of EC patients undergoing neoadjuvant therapy; however, their conclusions have been inconsistent. Therefore, we will discuss the further effect of neoadjuvant therapy on the prognosis of preoperative diagnosis of sarcopenia in EC patients.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 May 2020 and was last updated on 14 May 2020 (registration number INPLASY202050057).

### **INTRODUCTION**

Review question / Objective: To evaluate the effect of preoperative diagnosis of sarcopenia on survival and prognosis of patients with neoadjuvant therapy for esophageal cancer. Condition being studied: Esophageal cancer(EC) is a common and often fatal cancer that it is the sixth leading cause of cancer-related deaths worldwide, although recent progress in surgical and postoperative management techniques has improved treatment outcomes, the

prognosis of EC is still unsatisfactory. Sarcopenia is a progressive and generalized skeletal muscle disorder involving the accelerated loss of muscle mass and function that is linked to increased adverse outcomes including falls, functional decline, frailty, and mortality. Over the last few years, an increasing number of studies have been conducted on effects of preoperative sarcopenia for the prognosis of EC patients undergoing neoadjuvant therapy; however, their conclusions have been inconsistent. Therefore, we will discuss the further effect of neoadjuvant therapy on the prognosis of preoperative diagnosis of sarcopenia in EC patients.

### **METHODS**

Search strategy: (esophageal neoplasms OR esophagus neoplasm OR cancer of esophagus OR esophagus cancer OR esophageal cancer) AND (sarcopenia OR sarcopenic OR skeletal muscle depletion OR muscle index OR muscle mass) AND (esophagectomy OR surgery or surgical OR resection) AND (neoadjuvant therapy OR neoadjuvant treatment OR neoadjuvant chemoradiotherapy OR neoadjuvant chemotherapy OR neoadjuvant radiotherapy OR preoperative chemotherapy OR preoperative radiotherapy preoperative chemoradiotherapy OR preoperative therapy).

Participant or population: The adult of esophageal cancer patients who be diagnosised preoperative sarcopenia.

Intervention: neoadjuvant therapy(including neoadjuvant chemotherapy, neoadjuvant radiotherapy and neoadjuvant chemoradiotherapy).

Comparator: Patients without preoperative sarcopenia.

Study designs to be included: Cohort study and prospective study.

Eligibility criteria: (1) patients with other digestive tract cancers or include partial

esophageal cancer patients. (2) letters, case reports, reviews or preclinical studies; (3) The data referred to in the literature are incomplete (4) nonhuman studies; (5) studies not published in English.

**Information sources:** We comprehensively searched the following databases for relevant studies up to Mar 8, 2020: PubMed, Embase, the Cochrane library and Web of Science. The following information was extracted from these studies: first author's name, year of publication, country of the patients, research type, number of patients, patients age, follow-up time, diagnosis time of sarcopenia. Partial studies did not provide sufficient data, the researchers described the results only by providing Kaplan-Meier survival curve. If it's not mentioned we can extract data by using Enguage digitizer (measure the corresponding survival rate value from the Kaplan-Meier survival curves).

Main outcome(s): Over survival (OS) and disease free survival (DFS).

Quality assessment / Risk of bias analysis: According to the searching strategies, two authors independently searched relevant researches and screened literature by their titles and abstracts. After the initial screening, these articles satisfied the inclusion criteria evaluated with full texts for final inclusion. In this process, the third author would resolve the discrepancy. Two authors collected data form involved literature and compared outcome data independently. The quality of studies would be evaluated by the Newcastle-Ottawa Scale (NOS)[17]. Three factors were used for evaluation: (1) patient selection; (2) comparability of research groups; (3) assessment of outcome. This quality assessment scale had a maximum score of 9, studies with scores ≥ 7 were considered to be high quality.

Strategy of data synthesis: Random effects models would be applied if significant heterogeneity was identified by P 50%, otherwise fixed effects models were utilized. We performed a subgroup analysis

according to the time of diagnosis of sarcopenia and patients age, and ubiquitous bias was presented by Funnel plots and assessed by Eggers test and Begg test.

Subgroup analysis: The subgroup analysis will include factors like age and sarcopenia diagnosis time (include pre-neoadjuvant group and after neoadjuvant therapy group).

Sensibility analysis: There was no sensitivity analysis due to low heterogeneity.

Language: English.

Country(ies) involved: China.

Keywords: esophageal cancer, esophagectomy; meta-analysis; prognosis; sarcopenia; neoadjuvant therapy.

### Contributions of each author:

Author 1 - Shengbo Jin.

Author 2 - Xue Jing.

Author 3 - Zibin Tian.

Author 4 - Tao Mao.