INPLASY PROTOCOL

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None declared.

Selection strategy of cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy in peritoneal metastasis patients of gastric cancer, with consideration to peritoneal cancer index (PCI) and completeness of cytoreduction (CC) sorce. A single-center experience and meta-analysis

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Review question / Objective: **The present study aimed to explore the effect of peritoneal cancer index (PCI) and completeness of cytoreduction (CC) on survival in peritoneal metastases (PM) patients of Gastric cancer (GC) and to identify the optimal indication of CRS+HIPEC. - Population (P): patients with histologically confirmed PM and/or positive peritoneal cytology of GC. - Intervention (I): patients undergoing complete CRS and HIPEC with curative intent; patients with low PCI. - Comparison (C): patients undergoing incomplete CRS and HIPEC with curative intent; patients with high PCI. - Outcomes (O): median overall survival(OS), 1-, 2, 3-, and 5-year survival rates of patients. - Study design (S): both controlled and Single arm trials.**
Condition being studied: **Gastric cancer (GC) patients frequently develop peritoneal metastases (PM) with a poor longterm prognosis. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) may be an effective treatment option, but there has always been controversy. The tumor burden and completeness of cytoreduction have been considerated as crucial factors affecting outcome of GCPM patients. Therefore, strict case screening and complete CRS may be the key to the benefit of patients.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 May 2022 and was last updated on 09 May 2022 (registration number INPLASY202250053).

INTRODUCTION

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METHODS

Participant or population: Inclusion: Both patients with visible peritoneal carcinoma nodule (macroscopic disease) and those with isolated positive cytology (microscopic disease) have been included. Only patients with histopathological confirmed PM of GC who complete treatments including CRS and HIPEC were included in the present study.Exclusion: patients with any other distant metastases (e.g., liver, lung, and brain) or receiving intraperitoneal chemotherapy other than HIPEC (e.g., normothermic intraperitoneal chemoth -erapy) were excluded.

Intervention: Patients undergoing complete CRS and HIPEC with curative intent; patients with low PCI.

Comparator: Patients undergoing incomplete CRS and HIPEC with curative intent; patients with high PCI.

Study designs to be included: Both controlled and Single arm trials.

Eligibility criteria: We only included studies reporting gastric cancer patients who developed peritoneal metastases and/or positive peritoneal cytology and treated with CRS+HIPEC in the context of chemotherapy. Exclusion criteria for articles are as follows: (1) Population consisting of mixed patients with any other distant metastases (e.g., lung ,bone , and liver), (2) Studies with missing both PCI and CC documentations, (3) Intervention consisting of only HIPEC without CRS or CRS without HIPEC or CRS with other types of intraperitoneal chemotherapy, (4) Reviews, letters, editorials, meta analysis and abstracts (5) non clinical studies.

Information sources: The PubMed, FMRS, and Cochrane library databases were systematically searched without time restrictions (up to March 1, 2022)

Main outcome(s): The main outcomes of this study were median overall survival (OS), 1-, 2- and 3-Year survival rate of patients. OS was defined as the time between CRS+HIPEC and the date of death by any cause or the last follow-up of the patient. The effect measures for the main outcomes were Relative risk and 95% confidence interval.

Additional outcome(s): Long-term survival of patients: 5-year survival. The effect measures for the additional outcome were Relative risk and 95% confidence interval.

Quality assessment / Risk of bias analysis: We assessed the risk of bias in randomized controlled studies (RCT) using the Cochrane Collaboration's tool for assessing risk of bias. In RCTs, seven items have been considered relevant. Excluding highly biased RCTs: items whose quality standard wer completely not met (high-risk)≥1, or items whose quality standard were completely met (low-risk)≤1. Traffic light charts were created to graphically display the results of deviation risk assessment. The Methodological index for non-randomized studies (MINORS) was

used to assessed the risk of bias for non-randomized studies. By assessing 12 indexes (8 for non-comparative and additional 4 for comparative studies) herefthe total scores were calculated by summing the values attributed as follows: not reported (zero point), reported but insufficient (one point), reported and sufficient (two point). The ideal global score would be 16 for the non-comparative studies and 24 for the comparative studies. We consided the cutoff of high quality article was 12 points for non-comparative studies and 20 points for comparative studies in the present study. Two reviewers applied Cochrane Collaboration's tool and MINORS for assessing risk of bias respectively, and then resolve all conflicts through discussion.

Strategy of data synthesis: For the meta-analysis, statistical analysis was conducted in Review Manager (RevMan) (Version5.4.1 Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2021). To the continuous variables, the weighted mean difference (WMD) were used as the effect analysis statistics. Correspondingly, the dichotomous data were combined by calculating the relative risk (RR). The point estimates and 95% CI of each effect were given. To account for clinical heterogeneity, we used the random-effects based on DerSimonian-Laird methods or fixed-effects model based on Inverse-variance methods. The heterogeneity of the included literature was evaluated by I2 value, where below 50% was considered subtle heterogeneity, the influence of heterogeneity could be ignored. A p value below 0.05 was considered to be significant. Funnel plot was drawn to describe the potential publication bias.

Subgroup analysis: Patients with PCI≤6 vs. patients with PCI>7; Patients undergoing complete CRS vs. patients undergoing incomplete.

Sensitivity analysis: A sensitivity analysis to test for robustness of the pooled estimates was further performed by comparison with estimates generated after the sequential exclusion of individual studies.

Language: English.

Country(ies) involved: China.

Keywords: Gastric cancer; Peritoneal metastases; CRS; HIPEC; Meta-analysis.

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