

**Synchronous Surgery Combined Preoperative Chemotherapy Benefits Patients Suffering Pancreatic Ductal Adenocarcinoma with Liver Metastases: A Systematic Review and Meta-analysis**

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**ADMINISTRATIVE INFORMATION****Support** - No financial support.**Review Stage at time of this submission** - Data analysis.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2024100064

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 October 2024 and was last updated on 15 October 2024.

**INTRODUCTION**

**Review question / Objective** P: PDAC patients with hepatic metastases. I: Synchronous resection of the primary and metastatic tumors plus preoperative chemotherapy. C: Synchronous resection of the primary and metastatic tumors without chemotherapy. O: Overall survival.

**Condition being studied** Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive malignant digestive system tumors, and surgical resection is taken as the only curative therapy. However, more than half of the patients are unable to have the opportunity to undergo surgery because of distant metastases. The most common site of metastasis is the liver, which accounts for approximately 80% of PDAC cases with distant metastases, and palliative chemotherapy seem to be the only option. Historically, resection of recurrent or metastatic pancreatic cancer seemed to be inconceivable. However, in recent years, pancreatectomy

combined with synchronous or metachronous metastasectomy has been considered for selected patients with UR-M PDAC. Moreover, synchronous resection the primary and metastatic tumors has gained wide acceptance as a curative treatment in colorectal cancer and pancreatic neuroendocrine tumor patients with liver metastases. Hence, the aim of our study is to evaluate the clinical value of surgical resection of PDAC with synchronous metastases and to confirm the prognostic factors of PDAC patients with simultaneous liver metastasis.

**METHODS**

**Search strategy** (((pancreatic neoplasms[MeSH Terms]) OR (((Pancreatic[Title/Abstract]) OR (pancreas[Title/Abstract]))) AND ((adenocarcinoma[Title/Abstract]) OR (carcinoma[Title/Abstract]) OR (cancer[Title/Abstract]) OR (neoplasm\*[Title/Abstract]) OR (tumor[Title/Abstract]))) AND (((((((metastasis[Title/Abstract]) OR (metastases[Title/Abstract])) OR (metastatic[Title/Abstract])) OR (M1[Title/Abstract]))

OR (oligometastasis[Title/Abstract]) OR (oligometastatic[Title/Abstract]) OR (oligometastases[Title/Abstract]) OR (stage IV[Title/Abstract]) AND ((((((resection[Title/Abstract]) OR (resections[Title/Abstract]) OR (surgery[Title/Abstract]) OR (operation[Title/Abstract]) OR (operations[Title/Abstract]) OR (hepatectomy[Title/Abstract]) OR (hepatectomies[Title/Abstract])).

**Participant or population** Patients are diagnosed with PDAC with synchronous liver metastases.

**Intervention** PDAC patients with liver metastases underwent simultaneous resection of primary and metastatic tumor with preoperative chemotherapy.

**Comparator** PDAC patients with liver metastases underwent simultaneous resection of primary and metastatic tumor without preoperative chemotherapy.

**Study designs to be included** Retrospective studies.

**Eligibility criteria** Inclusion criteria: (1) all patients were diagnosed with PDAC with synchronous liver metastases; (2) primary tumor and metastases were simultaneously resected with or without preoperative chemotherapy; (3) survival data can be collected in the literature; (4) Newcastle-Ottawa Quality Assessment Scale (NOS) score  $\geq 6$ .

The exclusion criteria were as follows: (1) neuroendocrine tumor and other pathological types; (2) metachronous liver metastasis; (3) studies with incomplete survival data; (4) abstracts, case reports, editorials, letters, systematic reviews, and comments; (5) studies that enrolled the overlapped or same population; and (6) duplicate studies.

**Information sources** The PubMed, Embase, and Cochrane Library databases were searched for eligible articles.

**Main outcome(s)** Overall survival, median survival time, HR with 95%CI.

**Additional outcome(s)** OR.

**Quality assessment / Risk of bias analysis** Newcastle-Ottawa Quality Assessment Scale.

**Strategy of data synthesis** The heterogeneity of the pooled effect was assessed using Cochran's Q test and the Higgins  $I^2$  statistic. Q test pvalue 50% was considered significant heterogeneity, and a random-effect model was applied to estimate the

pooled HR. While heterogeneity was not significant (Q test p value  $> 0.1$  or  $I^2 < 50\%$ ), a fixed-effect model was used.

**Subgroup analysis** No subgroup analysis.

**Sensitivity analysis** Sensitivity analysis was applied to reduce and explain heterogeneity among the studies. Whether omitting any individual studies had significant effect on the pooled HR.

**Country(ies) involved** China.

**Keywords** pancreatic ductal adenocarcinoma, liver metastases, synchronous resection, chemotherapy, meta-analysis.

#### Contributions of each author

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