MOOSE Checklist

Title: **Head-to-head Comparison Between FOLFIRINOX and Gemcitabine Plus Nab-paclitaxel in the Neoadjuvant Chemotherapy of Localized Pancreatic Cancer: A Systematic Review and Meta-analysis.**

Criteria		Brief description of how the criteria were handled in the meta-analysis
Reporting of background should include		
√	Problem definition	Neoadjuvant chemotherapy treatment is an effective weapon that enables the radical resection pancreatic cancer and eradicates occult cancer. However, which neoadjuvant regimen harbours the utmost clinical benefits remains controversial.
√	Hypothesis statement	Neoadjuvant FOLFIRINOX provided more survival benefits over GA in localized pancreatic cancer.
√	Description of study outcomes	The primary outcome was the overall survival of patients. The secondary outcome comprised PNI, LVSI, R0 status, postoperative complications and resection rate.
√	Type of exposure or intervention used	Neoadjuvant FOLFIRINOX versus GA
√	Type of study designs used	We included eight prospective cohort studies.
√	Study population	Patients with localized pancreatic cancer.
Reporting of search strategy should include		
√	Qualifications of searchers	Two independent searchers are experienced in this area and have published several meta-analyses in many famous SCI journals.
√	Search strategy, including time period included in the synthesis and keywords	Till 11th September 2020
√	Databases and registries searched	PubMed, EMBASE, Cochrane and Web of Science
√	Search software used, name and version, including special features	We did not employ a search software. EndNote was used to merge retrieved citations and eliminate duplications.
√	Use of hand searching	We hand-searched bibliographies of retrieved papers for additional references.
√	List of citations located and those excluded, including justifications	Details of the literature search process are outlined in the flow chart. The citation list is available upon request.
√	Method of addressing articles published in languages other than English	We placed no restrictions on language; local scientists fluent in the original language of the article were contacted for translation.
√	Method of handling abstracts and unpublished studies	We contacted a few authors for unpublished studies on the association.
	Description of any contact with authors	Not applicable.

Reporting of methods should include		
√	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Detailed inclusion and exclusion criteria are described in the methods section.
√	Rationale for the selection and coding of data	Data extracted from each of the studies were relevant to the population characteristics, study design, exposure, outcome, and possible effect modifiers of the association.
√	Assessment of confounding	We performed a subgroup analysis including studies adjusted for confounders.
√	Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Two independent authors assessed study quality according to NOS score.
√	Assessment of heterogeneity	Heterogeneity of the studies was explored using Cochrane's Q test of heterogeneity and the I^2 statistic that provides the relative amount of variance of the summary effect due to the between-study heterogeneity.
√	Description of statistical methods in sufficient detail to be replicated	The procedures for meta-analyses, sensitivity analyses, meta-regression and assessment of publication bias are detailed in the methods.
√	Provision of appropriate tables and graphics	We included 1 flow chart, 1 summary table, 1 forest plot of all studies, 1 forest plot to examine effect modification by age, 3 forest plots for 1- to 3-year survival rate and 5 forest plots for perioperative parameters.
Reporting of results should include		
√	Graph summarizing individual study estimates and overall estimate	Figure 2
√	Table giving descriptive information for each study included	Table 1
	Results of sensitivity testing	Data not shown.
√	Indication of statistical uncertainty of findings	The 95% confidence intervals were presented with all summary estimates, I^2 values and results of sensitivity analyses.
Reporting of discussion should include		
√	Quantitative assessment of bias	Statistically, heterogeneity between studies was minor in most models of our study. For models with obvious heterogeneity, we performed sensitivity analysis (leave-one-out analysis) to assess whether the obvious heterogeneity came from some specific study. If so, we

		further evaluated the methodological heterogeneity between this study and counterparts and excluded it when necessary. In most cases, sensitivity analysis did not distinguish the culprit for significant heterogeneity (data not shown). Then, we applied the random effect model to compute the pooled effect value with a conservatively extended confidence interval.
√	Justification for exclusion	Studies were excluded from the present meta-analysis if they met the following criteria: (1) studies focused on metastatic pancreatic cancer; (2) patients preoperatively received regimens other than FOLFIRINOX or GA or patients postoperatively received FOLFIRINOX or GA without neoadjuvant treatment; (3) studies lacked adequate data to compare the difference of efficacy between FOLFIRINOX and GA for the overall survival of pancreatic cancer; (4) studies were review articles, notes, case reports and animal studies.
√	Assessment of quality of included studies	The NOS was applied to evaluate the quality of included studies. The score of each study varied from 5 to 8, which means the overall design of these studies was acceptable in spite of some flaws.
Reporting of conclusions should include		
√	Consideration of alternative explanations for observed results	The present study has some limitations to declare. First, almost all the included studies were retrospective, which may introduce some unexpected bias. Even though Perri et al used a prospectively maintained database, the authors admitted that it was still a retrospective and single-institution design. Second, the comparability of baseline characteristics was not well-controlled in some studies. For example, patients were universally younger in the FOLFIRINOX cohort than in the GA cohort. Although the unbiased subgroup analysis showed a conclusion similar to that of the whole population analysis, more prospective and baseline-matched studies are expected.
√	Generalization of the conclusions	In conclusion, the results of our meta-analysis suggest that FOLFIRINOX is non-inferior to GA in patients who are FOLFIRINOCX capable.
√	Guidelines for future research	Future studies are encouraged to explore the optimized dosage and chemotherapy cycles of FOLFIRINOX in the NCT of pancreatic cancer.
√	Disclosure of funding source	No separate funding was necessary for the undertaking of this systematic review.

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