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REVIEW ARTICLE

Efficacy and safety of oxaliplatin-based regimen versus cisplatin-based regimen in the treatment of gastric cancer: a meta-analysis of randomized controlled trials

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Abstract

Background Cisplatin played an important role in the treatment of gastric cancer (GC). Oxaliplatin has been shown to be at least as effective as cisplatin for GC, with less toxicity and a better tolerability profile. We performed a meta-analysis to compare the efficacy and safety of oxaliplatin-based regimen versus cisplatin-based regimen in the treatment of GC.

Methods Databases of CNKI, CBM, VIP, Wanfang, PubMed, Embase, Cochrane Library were searched for eligible literatures from their establishments to November 2018. Randomized controlled trials that compared the efficacy and safety of oxaliplatin-based regimen with that of cisplatin-based regimen in the treatment of GC were included. Statistical analyses were calculated using RevMan 5.3 software.

Results Seven randomized controlled trials including 2297 patients were included. Compared with cisplatin-based regimen intervention in GC, oxaliplatin-based regimen treatment was able to significantly improve the partial response rate (OR = 1.26, 95% CI 1.07–1.49; $p = 0.007$), disease progression rate (OR = 0.41, 95% CI 0.25–0.66; $p = 0.0002$) and 1-year survival (OR = 1.25, 95% CI 1.00–1.56; $p = 0.05$). The toxicities of hematopoietic system were significantly higher in cisplatin-based regimen group (OR = 0.6, 95% CI 0.46–0.79; $p = 0.0002$), while oxaliplatin-based regimen group had higher neurosensory toxicity (OR = 2.21, 95% CI 1.52–3.21; $p < 0.0001$), In addition, gastrointestinal toxicity was similar between the two groups (OR = 1.01, 95% CI 0.5–2.01; $p = 0.27$).

Conclusions Compared with cisplatin-based regimen, oxaliplatin-based regimen treatment has an obvious advantage in patients with GC with acceptable tolerance.

Keywords Gastric cancer · Oxaliplatin · Cisplatin · Chemotherapy

Introduction

Gastric cancer (GC) is ranked as the fourth highest in incidence and is the second most common cause of death from malignant tumors [1]. In each year, almost 996,000 people are diagnosed with GC and among which 738,000 are dead globally [2]. Unfortunately, the early diagnosis rate of GC is very low and the majority of patients lose the chance of undergoing surgery [3]. This results in only having the choice of either palliative chemotherapy or symptomatic support treatment.

In 1989, neoadjuvant chemotherapy was first applied to treat GC by Wilke et al. and the results suggested that neoadjuvant chemotherapy improved the chance of radical resection in patients with GC [4]. Adjuvant therapy also played a pivotal role in the prevention of recurrence and progression in GC. The famous CLASSIC trial demonstrated that patients with GC who received both surgery and chemotherapy were shown to have a higher 3-year disease-free survival rate [5]. In addition, a meta-analysis including 17 randomized controlled trials showed that adjuvant chemotherapy can significantly improve overall survival (HR = 0.82; 95% CI 0.76–0.90; $p < 0.001$) and disease-free survival (HR = 0.82; 95% C: 0.75–0.90; $p < 0.001$) compared with surgery alone in patients with advanced GC [6]. Nowadays, systemic chemotherapy is widely accepted as palliative

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treatment for patients with advanced GC, leading to objective responses, improvement of quality of life, and survival time [7].

Platinum-based drugs are widely used in anti-tumor treatment of various cancers by binding to tumor cell DNA chains and interfering with their replication [8]. As a platinum drug, cisplatin plays an important role in the treatment of advanced gastric cancer. Patients with advanced gastric cancer were treated with S-1 plus cisplatin as the first-line treatment presenting markedly longer median overall survival (OS) and progression-free survival (PFS) than those treated with S-1 alone [9]. In addition, oxaliplatin is a third-generation cisplatin analog with a 1,2-diaminocyclohexane (DACH) that also has an obviously inhibitive effect on locally advanced or metastatic gastric cancer [6]. Popov et al. [10] have reported that leucovorin (LV) with 5-fluorouracil (5-FU) for 2 days plus oxaliplatin (LV5–FU2–oxaliplatin) regimen may be substituted for LV5–FU2–cisplatin regimen with favorable safety and efficacy profile in GC patients. A randomized phase III study (the G-SOX trial) demonstrated that S-1 and oxaliplatin (SOX) combination therapy was noninferior to S-1 and cisplatin combination therapy [11]. Therefore, our paper aims to compare oxaliplatin-based regimen with cisplatin-based regimen in the treatment of GC in terms of meta-analysis to provide a suitable treatment option for patients diagnosed with GC.

Methods

Literature search

Electronic databases (CNKI, CBM, VIP, Wanfang, PUBMED, EMBASE and Cochrane Controlled Trials Register) were searched from inception till November 2018 to identify studies that provided information on the issue of oxaliplatin- or cisplatin-based regimen in the treatment of GC. Free text terms combined with MeSH (Medical Subject Headings) terms were used for the subject search. Search terms used were "gastric cancer*" or "stomach cancer*", "gastric neoplasm*" or "stomach neoplasm*", "oxaliplatin" or "cisplatin". Additional studies were performed by manually reviewing the references of included studies and relevant review articles to further identify other potentially relevant studies.

Inclusion and exclusion criteria

Two reviewers (Gong-chen Wang and Zhao-yuan Fu) independently assessed every retrieved study for inclusion. The inclusion criteria were as follows: (1) the included studies were randomized controlled trials that were conducted on the treatment of GC with oxaliplatin- or cisplatin-based regimen. (2) The participants included must be ≥ 18 years and should have histologically or cytologically confirmed GC. (3) The participants included should have adequate function of major organs (including cardiac, hepatic, bone marrow and renal function); and not previously treated for disease with any regimen of chemotherapy or radiotherapy. Exclusion criteria were: (1) language other than English; (2) case reports and reviews.

Data extraction

Data collection and analysis were performed according to a standard Cochrane protocol [12]. The same two reviewers independently reviewed eligible studies for study characteristics and clinical relevance. All disagreements were resolved by an independent third reviewer (Zhi-ming Zhang). If feasible, the data were extracted. The following information was extracted onto standardized data collection forms: author, trial title and year of publication, study design, length of follow up, number of participants and their basic characteristics.

Outcome definition

Grade 3–4 toxicity was defined as severe, life-threatening or disabling adverse events according to NCI Common Terminology Criteria for Adverse Events version 3.0 (CTCAE) [13] with cases that the severity of nausea/vomiting and diarrhea are upper separate 6 and 7 episodes in 24 h or patients have the life-threatening consequences; the severity degree of anemia as hemoglobin ranged from 65–80 g/L for grade 3 or lower for grade 4, while the severity of thrombocytopenia as plate ranged from $25 \sim 50 \times 10^9$/L for grade 3 or lower for grade 4; the severity of neutropenia is counted as the absolute neutrophil count $< 1.0 \times 10^9$/L.

Assessment of methodological quality of included studies

All studies that met the selection criteria were evaluated for methodological quality to assess the risk of bias for each outcome. This assessment was performed independently by two reviewers using the Cochrane Collaboration's risk of bias tool as described in the Cochrane Handbook for Systematic Reviews of Interventions [14]. If there were any disagreements in the assessment of studies, we would have had a discussion. The outcome measures were assessed in the following domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data addressed, selective reporting, and other bias. The results of the meta-analysis are interpreted in terms of the findings regarding the risk of bias.

Statistical analysis

We anticipated heterogeneity among included studies due to the variety of methods of analysis, lag exposures, or patient population. In this meta-analysis, RevMan 5.2 software, developed by the Cochrane Collaboration, was used to analyze the data. Enumeration data and measurement data were carried out for statistical efficacy analysis using odds ratio (OR), mean and standard deviation (SD), respectively. Statistical heterogeneity among the included studies was examined using the χ^2 test and the I^2 statistic. The heterogeneity was considered minimal when $I^2 < 25\%$; moderate, when $25\% < I^2 < 50\%$; and substantial, when $I^2 \geq 50\%$. If there was no statistically significant heterogeneity in a given set of data, the fixed effects model was used for meta-analysis. If the results of trials showed heterogeneity, the random effects model was used. If heterogeneity among the groups is too large, the descriptive analysis was used. P values ≤ 0.05 were considered statistically significant. A funnel plot was applied to detect publication bias in the meta-analysis.

Results

Studies selection

Our initial search strategy yielded 185 potentially relevant articles. After elimination of duplicates or irrelevant papers, 30 articles were included and reviewed for their titles, abstracts and the full text examinations. Among them, 22 articles were excluded from the final assessment for the following reasons: letter to editorials ($n = 10$), uncontrolled case series ($n = 8$), conference abstracts ($n = 4$), subgroup analysis ($n = 1$). Seven randomized clinical trials (Korea = 1, China = 2, UK = 1, Japan = 1, German = 1, Serbia = 1) were eventually eligible for the final meta-analysis [10, 11, 15–19] involving a total of 2297 patients of whom 1144 underwent oxaliplatin-based regimen and 1153 underwent cisplatin-based regimen. Figure 1 presents the PRISMA statement of search results.

The details of the risk of bias assessment of included studies are summarized in Fig. 2. In terms of the adequate randomization sequence, all studies were assessed as low risk. However, most of the relative information in the studies was not available, such as allocation concealment and blinding of participants and personnel, as well as blinding of outcome assessment. Nevertheless, the overall methodological quality was generally fair.

Characteristics of eligible studies

The included studies were published between 2008 and 2016 with the number of the enrolled patients ranging from 43 to 1002. Five studies used adequate random allocation sequences [10, 11, 15–17]. While the exactly randomization methods of the other studies were unclear, since there was only a statement of "allocation had been randomized" in their papers. Information about allocation concealment was not mentioned in any of the studies, since it was impossible to perform blinding due to the nature of the two different chemotherapy regimens. The characteristics of the included studies are presented in Table 1.

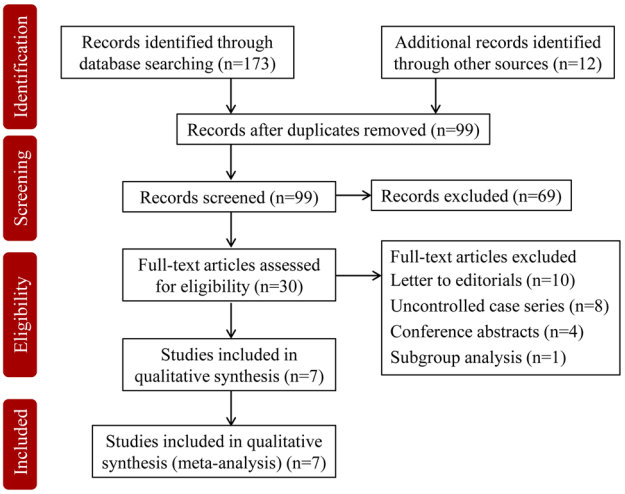

Fig. 1 The PRISMA statement of search results

Outcome of meta-analysis

Partial response rate

Seven studies including 2297 patients reported the partial response rate [10, 11, 15–19]. The fixed effect model was used and the pooled analysis suggested that when comparing with cisplatin-based regimen treatment group, oxaliplatin-based regimen treatment was associated with a significantly increased partial response rate (OR = 1.26, 95% CI 1.07–1.49; $p = 0.007$), with low heterogeneity among the studies ($I^2 = 40\%$; heterogeneity $p = 0.12$; Fig. 3).

Disease stability rate

Four studies involving 1095 patients evaluated the disease stability rate [10, 11, 15, 16, 18] and no heterogeneity among them was observed ($p = 0.69$, $I^2 = 0\%$). The fixed effect model was used with no significant difference of disease stability rate between the two groups (OR = 1.05, 95% CI 0.81–1.36; $p = 0.7$) (Fig. 4).

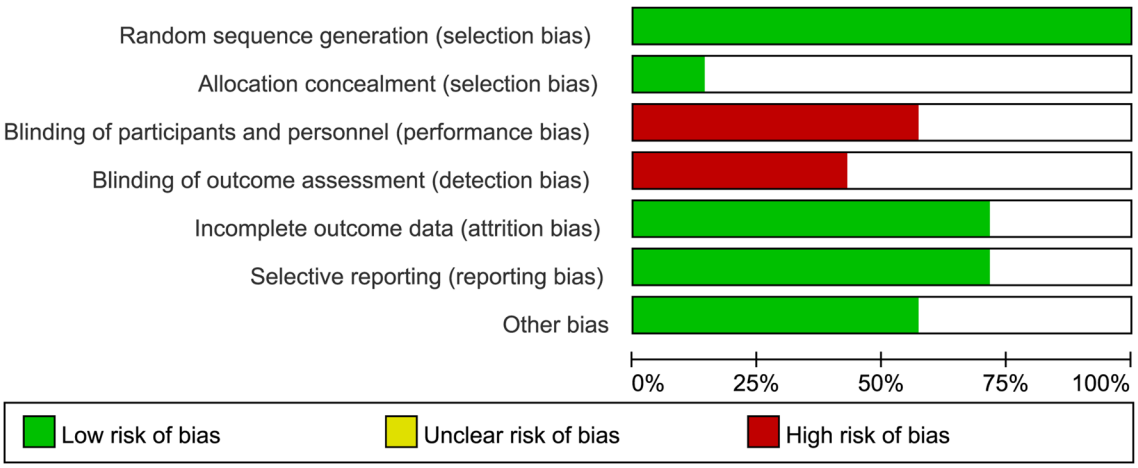

Fig. 2 Risk of bias summary of the included study. Low risk = bias, if present, is unlikely to alter the results seriously, unclear risk = bias raises some doubt about the results, high risk = bias may alter the results seriously

Disease progression rate

Three studies containing 410 patients evaluated the disease progression rate [10, 15, 16, 18] A meta-analysis showed that oxaliplatin-based regimen treatment substantially improved disease progression rate compared with the cisplatin-based regimen treatment (OR = 0.41, 95% CI 0.25–0.66; $p = 0.0002$), with no heterogeneity among the studies ($I^2 = 0\%$; $p = 0.51$; Fig. 5).

1-Year survival rate

Three studies including 1263 patients reported the 1-year survival rate [16–18]. Compared with the cisplatin-based regimen treatment, oxaliplatin-based regimen treatment was associated with a significant increase of 1-year survival rate (OR = 1.25, 95% CI 1.00–1.56; $p = 0.05$), with low heterogeneity among the studies ($I^2 = 28\%$; $p = 0.25$; Fig. 6).

Grade 3–4 gastrointestinal toxicity

Four trials on 1883 patients evaluated the grade 3–4 gastrointestinal toxicity rate [11, 15–17] Among them, significant heterogeneity was observed ($p < 0.0001$, $I^2 = 80\%$). The random effect model was used and the result showed no significant difference between the two groups (OR = 1.01, 95% CI 0.5–2.01; $p = 0.27$) (Fig. 7). Subgroup analysis showed no significant difference in the incidences of nausea or vomiting (OR = 0.58, 95% CI 0.31–1.08; $p = 0.09$) and diarrhea (OR = 174, 95% CI 0.64–4.71; $p = 0.27$) between the two groups.

Grade 3–4 hematopoietic system toxicity

Four studies containing 1883 patients evaluated the grade 3–4 hematopoietic system toxicity rate [11, 15–17] and significant heterogeneity among them was observed ($p = 0.006$, $I^2 = 58\%$). The random model was used and the incidences of grade 3–4 hematopoietic system toxicity in cisplatin-based regimen treatment group were significant higher than the oxaliplatin-based regimen treatment group (OR = 0.6, 95% CI 0.46–0.79; $p = 0.0002$) (Fig. 8). Subgroup analysis showed that the rate of anemia (OR = 0.49, 95% CI 0.33–0.74; $p = 0.0005$) and neutropenia (OR = 0.50, 95% CI 0.34–0.73; $p = 0.0003$) in cisplatin-based regimen treatment group was significantly higher than that in oxaliplatin-based regimen treatment group, whereas the incidences of thrombocytopenia (OR = 0.98, 95% CI 0.68–1.42; $p = 0.93$) were similar.

Grade 3–4 peripheral neurotoxicity

Four studies including 1883 patients reported the grade 3 – 4 peripheral neurotoxicity rate [11, 15–17] and significant heterogeneity was observed among them ($p = 0.02$, $I^2 = 71\%$). The random effect model was used and the incidences of peripheral neurotoxicity were significantly higher in oxaliplatin-based regimen treatment group than cisplatin-based regimen treatment group (OR = 2.21, 95% CI 1.52–3.21; $p < 0.0001$) (Fig. 9).

Publication bias assessment

Begg's funnel plot was performed to assess the publication bias of literatures. The shape of the funnel plot did not reveal any evidence of obvious asymmetry. The finding suggested

Table 1 Characteristics of the included studies

Study	Population	Patients		Sex		Age	TNM stage	Pathological type	Treatment cycle	Treatment regimens
		Oxaliplatin group	Cisplatin group	Male	Female					
Wang et al. 2008 [19]	China	103	97	–	–	28–71	IV	Adenocarcinoma	> 4	FOLFOX4, FP
Li et al. 2014 [18]	China	22	21	23	20	–	IV	Adenocarcinoma	3	FOLFOX4, FLP
Kim et al. 2014 [15]	Korea	39	38	54	23	35–74	III IV	Adenocarcinoma	3	DO DP
Yamada et al. 2015 [11]	Japan	343	342	447	208	21–85	IV	Adenocarcinoma	6	SOX CS
Al-Batran et al. 2008 [16]	German	112	106	143	75	27–86	III IV	Adenocarcinoma	6	FLO FLP
Cunnigham et al. 2008 [17]	UK	489	513	785	217	22–83	III IV	Adenocarcinoma	6	EOF ECF
Popov et al. 2008 [10]	Serbia	36	36	24	26	–	II	Adenocarcinoma	8	FOLFOX4, FLP

FOLFOX4/OLF Oxaliplatin + fluorouracil + calcium folinate, *DO/DOF* docetaxel + oxaliplatin (+ fluorouracil), *SOX* oxaliplatin + tiggio, *XELOX* oxaliplatin + capecitabine, *EOF* oxaliplatin + epirubicin + fluorouracil, *PLF* cisplatin + fluorouracil + calcium folinate, *DCF* cisplatin + docetaxel + fluorouracil, *SP/CS* cisplatin + tiggio, *XP* cisplatin + capecitabine, *DP* cisplatin + docetaxel, *ECF* cisplatin + epirubicin + fluorouracil, – not mentioned

that there was no publication biases likely affecting the results of the meta-analysis (Fig. 10).

Discussion

A total of 2297 GC patients from 7 studies were eventually included in the present meta-analysis to quantitatively assess the efficacy of oxaliplatin or cisplatin-based regimen in the treatment of GC. With the assessment of the bias risk and the quality, all the included studies were proven to be high quality and had good results. Finally, our research showed that:

1. Compared with cisplatin-based regimen, oxaliplatin-based regimen could significantly improve partial response rate (OR = 1.26, 95% CI 1.07–1.49; $p = 0.007$), reduce disease progression rate (OR = 0.41, 95%CI: 0.25–0.66; $p = 0.0002$), while, no obvious difference was observed in terms of disease stability rate.
2. On the long-term effect, oxaliplatin-based group was superior than cisplatin-based group in 1-year survival rate (OR = 1.25, 95% CI 1.00–1.56; $p = 0.05$).
3. The incidence of 3–4 grades toxicity was evaluated in three categories. In terms of grade 3–4 gastrointestinal toxicity, there was no significant difference in the occurrence rate of nausea or vomiting ($p = 0.09$) and diarrhea ($p = 0.27$) between the oxaliplatin-based regimen and the cisplatin-based regimen. In hematological toxicity, the rate of anemia ($p = 0.0005$) and neutropenia ($p = 0.0003$) in the cisplatin-based regimen was significantly higher than that in oxaliplatin-based regimen, whereas incidences of thrombocytopenia ($p = 0.93$) were similar. However, the peripheral nerve damage was significantly higher in oxaliplatin group than that in cisplatin group ($p < 0.0001$).

Oxaliplatin is the third generation of chemotherapeutic agents after cisplatin and carboplatin. It was indicated that oxaliplatin also played a very important role in the treatment of cancer. In 1996, Machover et al. carried out two consecutive phase II trials of oxaliplatin for treatment of advanced colorectal carcinoma. Results showed that the overall response rate of two trials was 10% (95% CI 0.046–0.16). The most common toxicity was peripheral nerve damage, and the incidences of grade 3 and 4 levels of toxicity in study I were 23% and 8%, in study II were 14% and 4%; fewer patients experienced gastrointestinal toxicity and bone marrow suppression [20]. Another study reported the efficiency of FOLFOX (oxaliplatin and 5-FU/leucovorin) regimen in advanced colorectal cancer, 32 patients with more than 2 lesions were included in the study. The results indicated that complete response, partial response and stable disease were

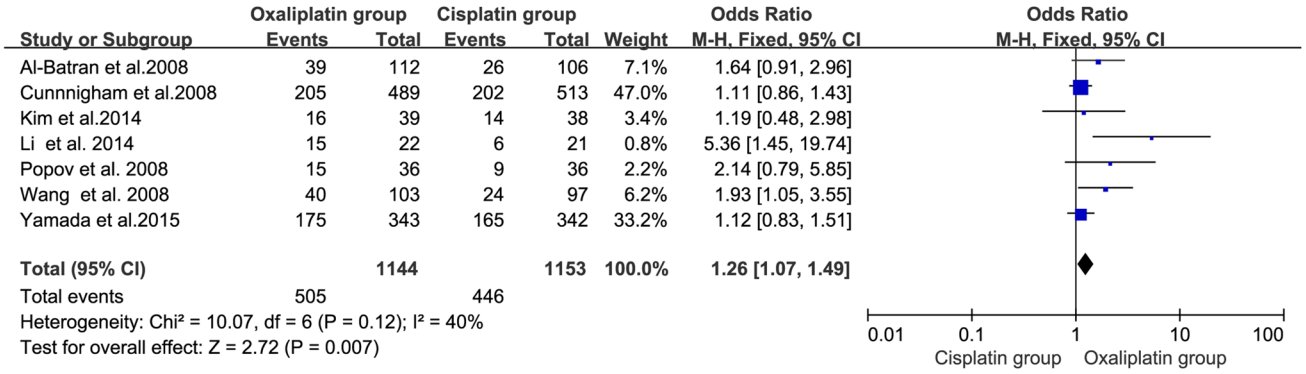

Fig. 3 Meta-analysis results of oxaliplatin-based regimen treatment on partial response rate as compared with cisplatin-based regimen treatment

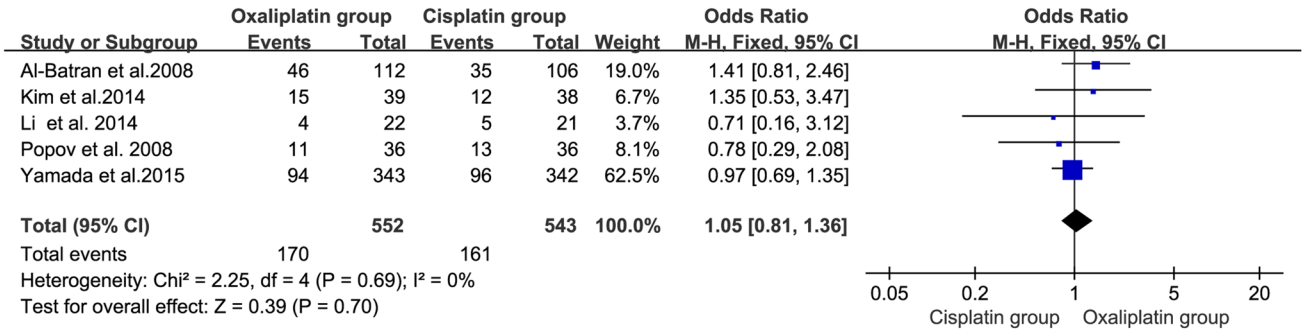

Fig. 4 Meta-analysis results of oxaliplatin-based regimen treatment on disease stability rate as compared with cisplatin-based regimen treatment

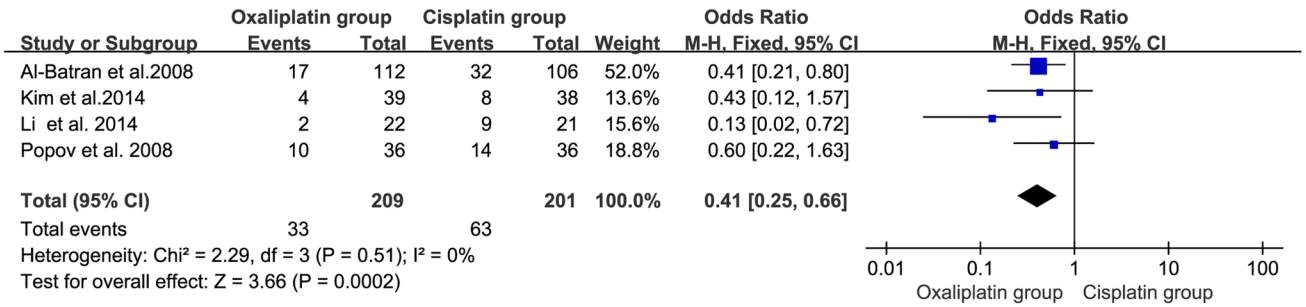

Fig. 5 Meta-analysis results of oxaliplatin-based regimen treatment on disease progression rate as compared with cisplatin-based regimen treatment

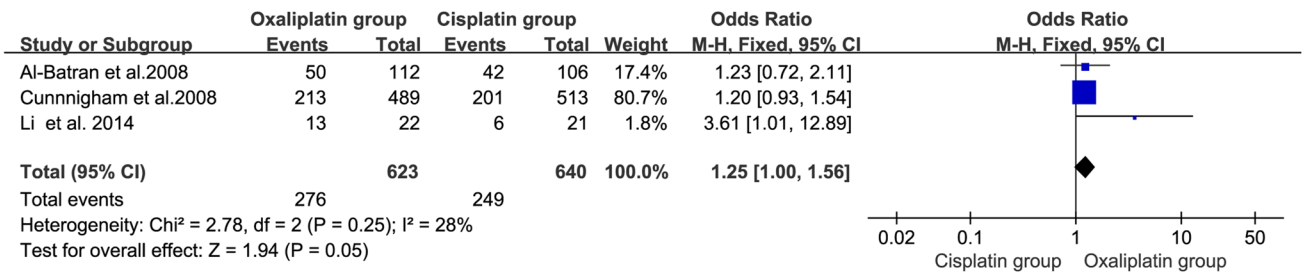

Fig. 6 Meta-analysis results of oxaliplatin-based regimen treatment on 1-year survival rate as compared with cisplatin-based regimen treatment

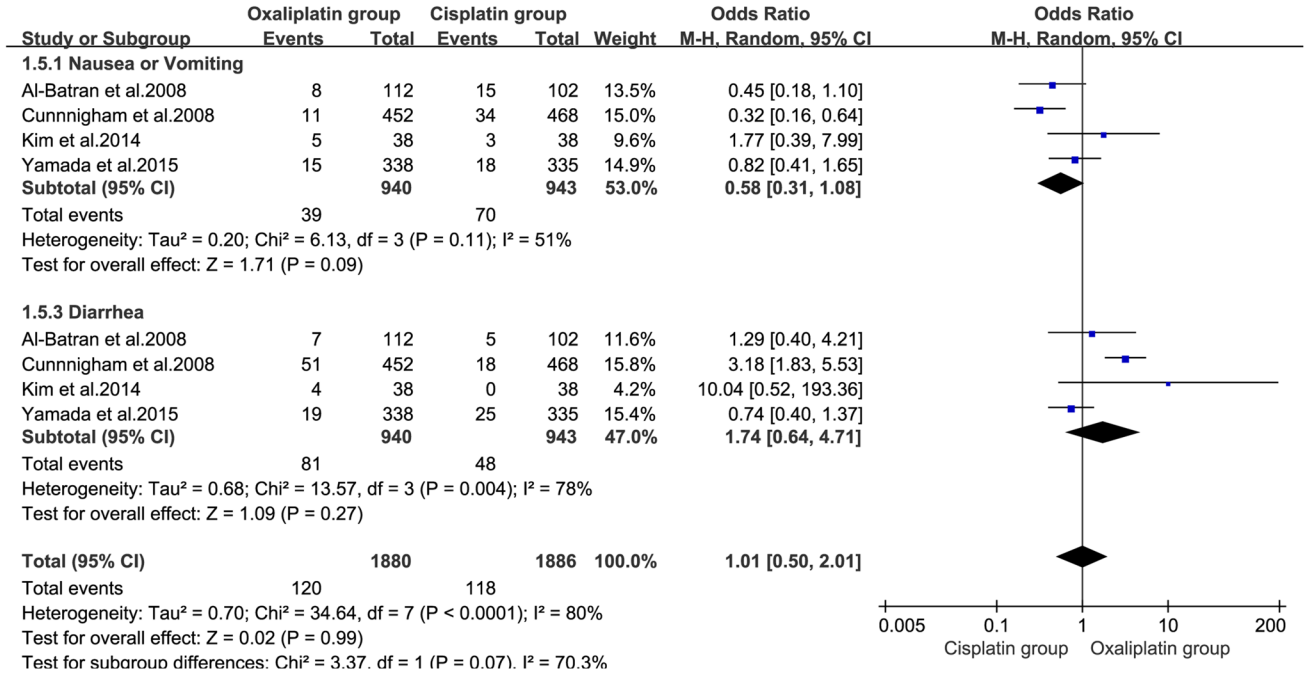

Fig. 7 Meta-analysis results of oxaliplatin-based regimen treatment on grade 3–4 gastrointestinal toxicity as compared with cisplatin-based regimen treatment

6.2%, 28% and 41%, separately. After 1 year follow-up, the survival rate was 72%, grade 3–4 nerve damage appeared in about 50% of patients [21]. These reports have revealed that oxaliplatin could significantly improve the short-term efficacy of patients with colon cancer, but the emergence of neurotoxicity should n'ot be ignored, as the main performance was peripheral sensory nerve abnormalities, such as "socks levy" and so on. In 2007, the famous NSABPC-07 trial compared the efficacy and neurotoxicity of FULV (fluorouracil, leucovorin) regimen with FOLFOX regimen in 2492 patients with colon cancer. The results showed that neurotoxicity in FOLFOX group was significantly higher than that in FULV group ($p < 0.0001$) after 18 months of follow-up. Meanwhile, a higher proportion of hand-foot paresthesia (26% vs. 2.6%), and fatigue (27.4% vs. 16.2%) were observed in the FOLFOX group. After 18 months of treatment, hand paresthesia disappeared in most of patients, but the foot paresthesia still existed. However, regarding the long-term efficacy, the 2-year survival rate in FOLFOX group exceeded FULV regimen by nearly 10% [22].

Although lots of studies confirmed the efficiency of oxaliplatin, neurotoxicity occurred in a considerable number of patients. Based on this, a number of scholars tried a variety of ways to explore how to minimize the adverse reactions caused by oxaliplatin, summed up the results, mainly in the following ways:

(1) Dose adjustment: Studies have found that when the cumulative dose of oxaliplatin reached 750–850 mg/m^2, the rate of grade 3 neurotoxicity was 15%, and up to 50% after a total dose of 1170 mg/m^2 [23]. MOSAIC trial showed that the neurotoxicity could be reversible and controllable; in the course of oxaliplatin treatment, the cumulative concentration should be lower than its toxic threshold, so that the incidence of nerve damage could be reduced [24].

(2) Stop-and-go fashion: The previous description suggested that the nerve damage would gradually disappear after withdrawal. OPTIMOX test proposed a chemotherapy regimen of 6 cycles of FOLFOX6 regimen with 12 cycles of irinotecan combined 5-FU-6 cycles of FOLFOX7 regimen, and the promotion of this chemotherapy strategy has significantly reduced the accumulation of oxaliplatin in body [25].

(3) Glutathione: In 2002, Cascinu et al. evaluated the role of glutathione in colorectal cancer patients receiving chemotherapy which contained oxaliplatin. 53 patients were divided into glutathione group and placebo group. Toxicity was evaluated in 4 cycles (the accumulation of oxaliplatin was about 400 mg/m^2), 8 cycles (800 mg/m^2) and 12 cycles (1200 mg/m^2); the patients with neurotoxicity in two groups were 7 vs. 11, 2 vs. 11 ($p = 0.003$), 3 vs. 8 ($p = 0.004$), respectively. In addition, the neurological function test found that gastrocnemius muscle sensation was significantly reduced in placebo group [26].

(4) Calcium and magnesium combination: In 2004, Gamelin L et al. performed a retrospective analysis of FOLFOX regimen in 161 patients with colorectal cancer, among which, 96 patients received calcium gluconate and

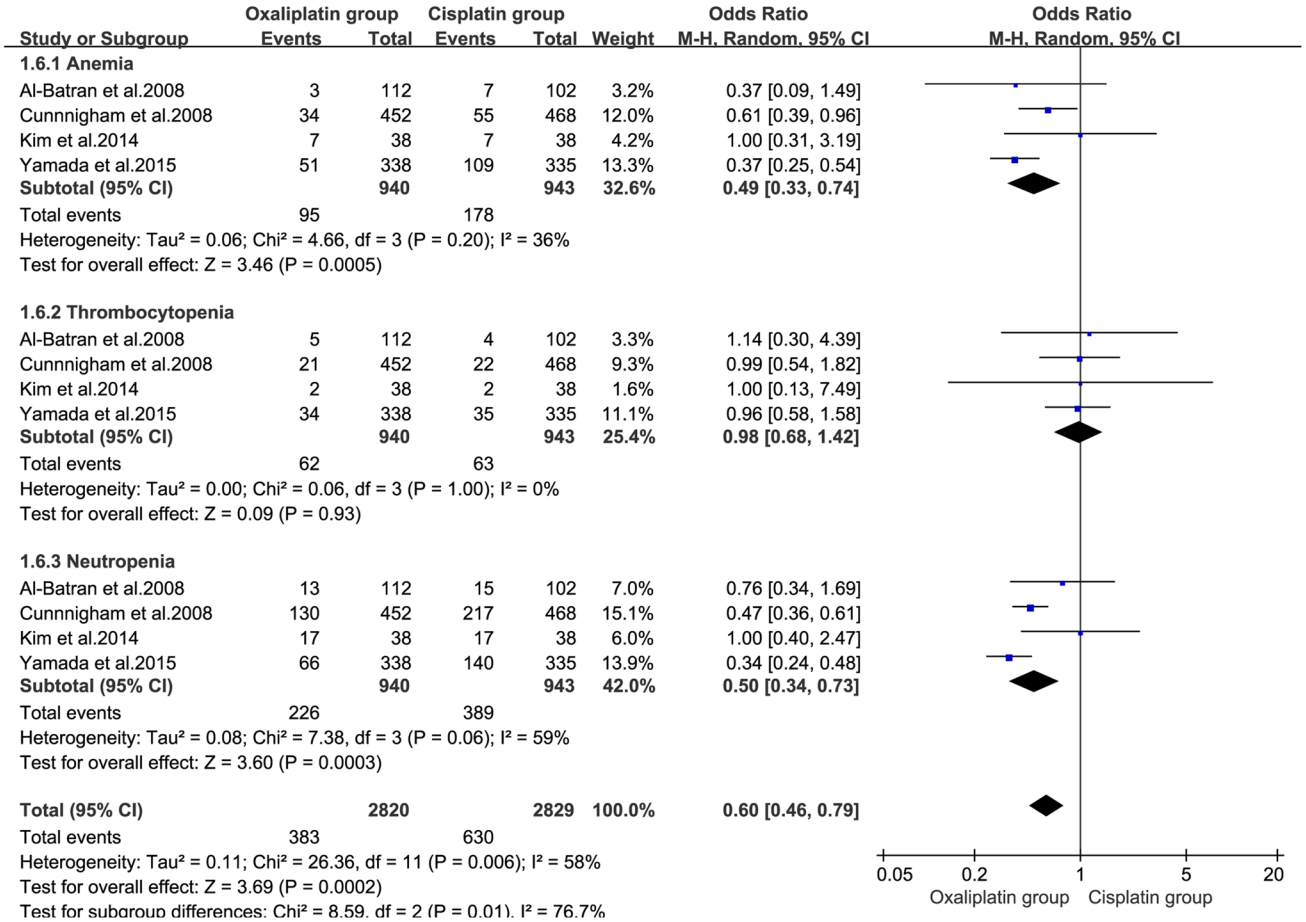

Fig. 8 Meta-analysis results of oxaliplatin-based regimen treatment on grade 3–4 hematopoietic system toxicity as compared with cisplatin-based regimen treatment

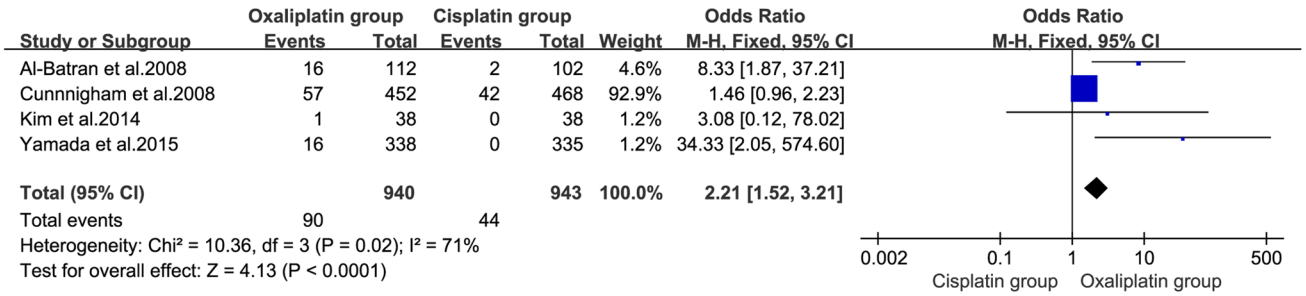

Fig. 9 Meta-analysis results of oxaliplatin-based regimen treatment on grade 3–4 peripheral neurotoxicity as compared with cisplatin-based regimen treatment

magnesium sulfate (group A), while the other 65 did not (group B). The results showed that only 4% patients in group A stopped chemotherapy because of neurotoxicity; Meanwhile, the proportion was 31% in group B ($P=0.000003$). Distal nerve sensory abnormalities in the two groups was 7% and 26% ($p=0.001$). The incidence of neurotoxicity of the two groups was 45% and 20% ($p=0.003$), the response rate was similar [27]. This study showed that calcium and magnesium combined could significantly reduce the toxicity of oxaliplatin.

(5) Lipoic acid: Many studies have shown that lipoic acid has achieved satisfactory results in terms of improving the physical and autonomic neuropathy caused by diabetes [28, 29]. Researchers tried to improve neurological damage caused by oxaliplatin. In a trial, 15 patients with colorectal cancer received chemotherapy (oxaliplatin

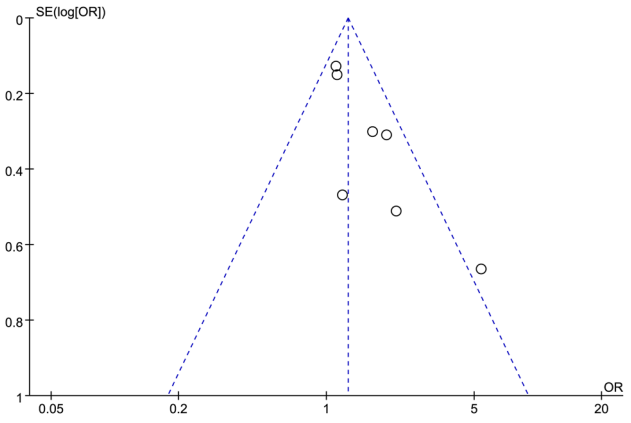

Fig. 10 Funnel plot detailing publication bias of the literatures

combined with raltitrexed). After 6 cycles of chemotherapy, 15 patients experienced neurotoxicity, then they received lipoic acid treatment. Six months later, neurotoxicity was relieved in 8 patients [30]. The results suggested that lipoic acid could be a choice to improve the neurotoxicity of oxaliplatin.

Our results suggested that the efficiency of oxaliplatin-based regimen was superior to cisplatin-based regimen in the treatment of GC. Compared with cisplatin-based regimen, oxaliplatin has achieved both short- and long-term efficacy. In terms of efficacy, the study seems to suggest that oxaliplatin can replace cisplatin. However, some potential limitations needed to be pointed out: (1) Although the basic characteristics of the two groups were well balanced, some differences still existed, such as age, sex, nationality, tumor location, disease stage, surgery type and TNM classification. In addition, different chemotherapy regimens and drugs were used in the patients. It is worth noting that although not mentioned in any of the included studies, the nutritional status and postoperative surgical complications in the two groups may also be different. All of these differences may have a potential effect on the results. (2) Potential publication bias may exist in this meta-analysis, our meta-analysis was restricted to publications in English language, without some potential eligible studies in other languages included, which probably led to bias. (3) The results of this meta-analysis were based on studies with relatively small sample sizes and, therefore, should be interpreted cautiously. More well-designed and large-scale randomized controlled clinical trials should be conducted for further study on the comparison of adjuvant chemoradiotherapy with chemotherapy in GC.

In conclusion, our meta-analysis suggested that oxaliplatin-based regimen had a significant advantage in treatment of GC compared with cisplatin-based regimen. Further prospective studies with different adjuvant approaches are needed to strengthen our findings.

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Compliance with ethical standards

Conflict of interest The authors declare that they had no conflict of interest in preparing this article.

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