Systematic Review and Meta-Analysis

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Thoracic perfusion of lobaplatin combined with endostar for treating malignant pleural effusions

A meta-analysis and systematic review

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Abstract

Introduction: Lobaplatin is a new platinum-based cytotoxic chemotherapeutic agent. Endostar is an endogenous angiogenic inhibitor with implicated anti-tumor activity. This study was to investigate the efficacy and safety of thoracic perfusion of lobaplatin combined with endostar in the treatment of malignant pleural effusions (MPE).

Methods: We searched the databases of Pubmed, the Cochrane Library, Embase, WanFang Data, and CNKI to select the studies regarding the efficacy and safety of lobaplatin combined with endostar to treat MPE. A total of 10[3–12] randomized controlled trials with 651 patients were included.

Results: The objective response rate ($P < .001$, odds ratio = 4.08) and disease control rate ($P < .001$, odds ratio = 3.69) of lobaplatin combined with endostar were significantly higher than lobaplatin alone. In addition, lobaplatin combined with endostar remarkably promoted the quality of life of patients ($P < .001$, odds ratio = 3.93) compared with lobaplatin alone. Lobaplatin combined with endostar also promoted the quality of life of patients ($P < .05$, odds ratio = 2.56) compared with cisplatin combined with endostar. At the same time, the leukopenia rate ($P < .05$, odds ratio = .40) and the incidence of nausea and vomiting ($P < .05$, odds ratio = .38) of lobaplatin combined with endostar were significantly lower than that of cisplatin combined with endostar.

Conclusions: The efficacy of lobaplatin combined with endostar was superior to lobaplatin alone. The safety was higher than cisplatin combined with endostar through thoracic perfusion in treating MPE, which indicated that lobaplatin combined with endostar could be the effective agent for controlling MPE.

Abbreviations: AEs = adverse effects, CI = confidence interval, DCR = disease control rate, MPE = malignant pleural effusions, OR = odds ratio, ORR = objective response rate, QOL = quality of life, RCTs = randomized controlled trials.

Keywords: endostar, lobaplatin, malignant pleural effusions, meta-analysis, MPE

1. Introduction

Malignant pleural effusions (MPE) is caused by pleura malignant tumor. Malignant tumors from another site involving the pleura also lead to the accumulation of pleural effusions. Almost all malignant tumors can invade the pleura and cause MPE. Lung cancer is one of the most common causes, accounting for about one-third of MPE.[1] Patients with MPE often suffer from anemia, shortness of breath, dry cough, and chest pain, which have a serious negative impact on the quality of life.[2] Lobaplatin and cisplatin are commonly used for pleural chemotherapy which is the most common clinical treatment for MPE. Endostar, as a molecular targeted anti-tumor drug developed independently in China, is widely used in the treatment of lung cancer and other malignant tumors. In recent years, some studies have especially investigated the clinical effect and the safety of thoracic perfusion of lobaplatin combined with endostar in treating MPE. Here, we performed a meta-analysis and systematic review to assess the clinical benefit of lobaplatin combined with endostar in treating MPE.

2. Methods

2.1. Search strategies

We searched and identified relevant randomized controlled trials (RCTs) from the databases of Pubmed, the Cochrane Library, Embase, WanFang Data, and CNKI (from the establishment time of the database to April 2022). We adopted various MeSH terms and keywords that related to MPE,

Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research.

The authors have no conflict of interests to disclose.

The datasets generated and/or analyzed during the current study are publicly available.

The meta-analysis and systematic review is based on published data, ethical approval is not a requirement.

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lobaplatin, and endostar as follows: "malignant pleural effusions", "MPE", "lobaplatin", "endostar", "endostatin", and "recombinant human endostatin". Take the Cochrane Library as an example, its search strategy is shown in Figure 1. In addition, if we found useful information that was intimately associated with endostar in the reference lists of those studies, we should further look for additional studies and identified them.

2.2. Criteria that studies were included and excluded

2.2.1. Inclusion criteria. Randomized controlled trials; patients must be diagnosed with MPE; patients must be given drugs through thoracic perfusion; experimental group: lobaplatin combined with endostar; control group: lobaplatin alone or cisplatin combined with endostar.

2.2.2. Exclusion criteria. Non-randomized controlled trials; review, case report, or meta-analysis; studying on animals, not humans; unable to extract data.

2.3. Identification of literature

Two independent investigators reviewed study titles and abstracts. The studies that satisfied the inclusion criteria were retrieved for full-text assessment. Trials selected for detailed analysis were analyzed by 2 investigators, and disagreements were resolved by a third investigator.

2.4. Collection of study variables

The data that we extracted included: publication date of literature; the number of patients of each RCT; the clinical characteristics of data; the ways of clinical intervention; objective response rate (ORR), disease control rate (DCR), quality of life (QOL), and adverse effects (AEs).

2.5. Quality assessment of included RCTs

We used the evaluation criteria shaped by the Cochrane Handbook (Version 5.0.1) to assess the included trials, which included: methods to a random group of patients; how to perform an adequate setting blinding; how to perform an adequate allocation and conceal the sequence; a description of intention to treat. Eventually, the quality of trials was divided into 3 levels: low risk, unclear risk, and high risk.

2.6. Statistical methods and analysis

We used Stata 17.0 software for statistical analysis. The odds ratio (OR) with 95% confidence interval (CI) was major statistical data that were applied to explore the difference in efficacy. The overall effect was calculated by Z-scores and P values <.05 were considered to be statistically significant. The identification of homogeneity of studies was calculated by the λ^2 statistic and was quantified with the I^2 statistic. In our study, we adopted random effects model to perform meta-analysis. To assess the bias of the literature, we omitted each study from the estimated pool to analyze the influence of each study on the overall effect. In addition, Egger's test, and Begg's test were performed to assess publication bias.

#1 endostar
#2 endostatin
#3 recombinant human endostatin
#4 #1 OR #2 OR #3
#5 lobaplatin
#6 malignant pleural effusion
#7 MPE
#8 #6 OR #7
#9 #4 AND #5 AND #8

Figure 1. The search strategy of the Cochrane Library.

3. Results

3.1. Study selection process

We identified 879 studies, of which 10[3–12] were included in our analysis. Seven RCTs[3–9] studied the comparison of lobaplatin combined with endostar with lobaplatin alone. Three RCTs[10–12] studied the comparison between lobaplatin combined with endostar with cisplatin combined with endostar. All studies involved a total of 651 patients with malignant pleural effusions. The selection process is shown in Figure 2.

3.2. Characteristics and quality of study design

The characteristics of the studies are shown in Table 1 and Table 2. All 10 RCTs referred to randomized methods and all data were complete. The quality of each study design is shown in Table 3.

3.3. Analysis results

3.3.1. Objective response rate. Lobaplatin combined with endostar versus lobaplatin alone: We identified 7[3–9] RCTs pertaining to ORR comparison. The odds ratio of random effects was 4.08 (95% CI, 2.69–6.20; Z = 6.58, P < .001), which indicated that the ORR of lobaplatin combined with endostar was significantly higher than that of lobaplatin alone. Among these 7 studies, we did not observe evidence of heterogeneity (Chi² = 2.18, df = 6 (P = .90); I^2 = 0%) (Fig. 3).

Lobaplatin combined with endostar versus cisplatin combined with endostar: Three[8–10] trials met the inclusion criteria. The odds ratio of random effects was 1.60 (95% CI, .82–3.13; Z = 1.31, P = .17), which indicated that the ORR of lobaplatin combined with endostar was similar to cisplatin combined with endostar. Among these 3 studies, we did not observe evidence of heterogeneity (Chi² = .83, df = 2 (P = .66); I^2 = 0%) (Fig. 4).

3.3.2. Disease control rate. Lobaplatin combined with endostar versus lobaplatin alone: We identified 6[3,4,6–9] RCTs pertaining to DCR comparison. The odds ratio of random effects was 3.69 (95% CI, 1.76–7.73; Z = 3.46, P < .001) and did not imply the existence of heterogeneity (Chi² = 4.56, df = 5 (P = .47); I^2 = 0%), which indicated that the DCR of lobaplatin combined with endostar was significantly higher than that of lobaplatin alone (Fig. 5).

Lobaplatin combined with endostar versus cisplatin combined with endostar: Three[8–10] trials met the inclusion criteria compared to the DCR. The odds ratio of random effects was 1.50 (95% CI, .55 to 4.15; Z = .79, P = .43) and did not imply the existence of heterogeneity (Chi² = .01, df = 2 (P = .99); I^2 = 0%), which indicated that the DCR of lobaplatin combined with endostar was similar to cisplatin combined with endostar (Fig. 6).

3.3.3. Quality of life. Lobaplatin combined with endostar versus lobaplatin alone: Five[3,5–8] studies investigated the changes of QOL after treatment. Lobaplatin combined with endostar had a higher symptom improvement rate than lobaplatin alone (odds ratio=3.93, 95% CI, 2.37–6.52; Z = 5.30, P < .001). Among these 5 studies, we did not observe evidence of heterogeneity (Chi² = .72, df = 4 (P < .948); I² = 0%) (Fig. 7).

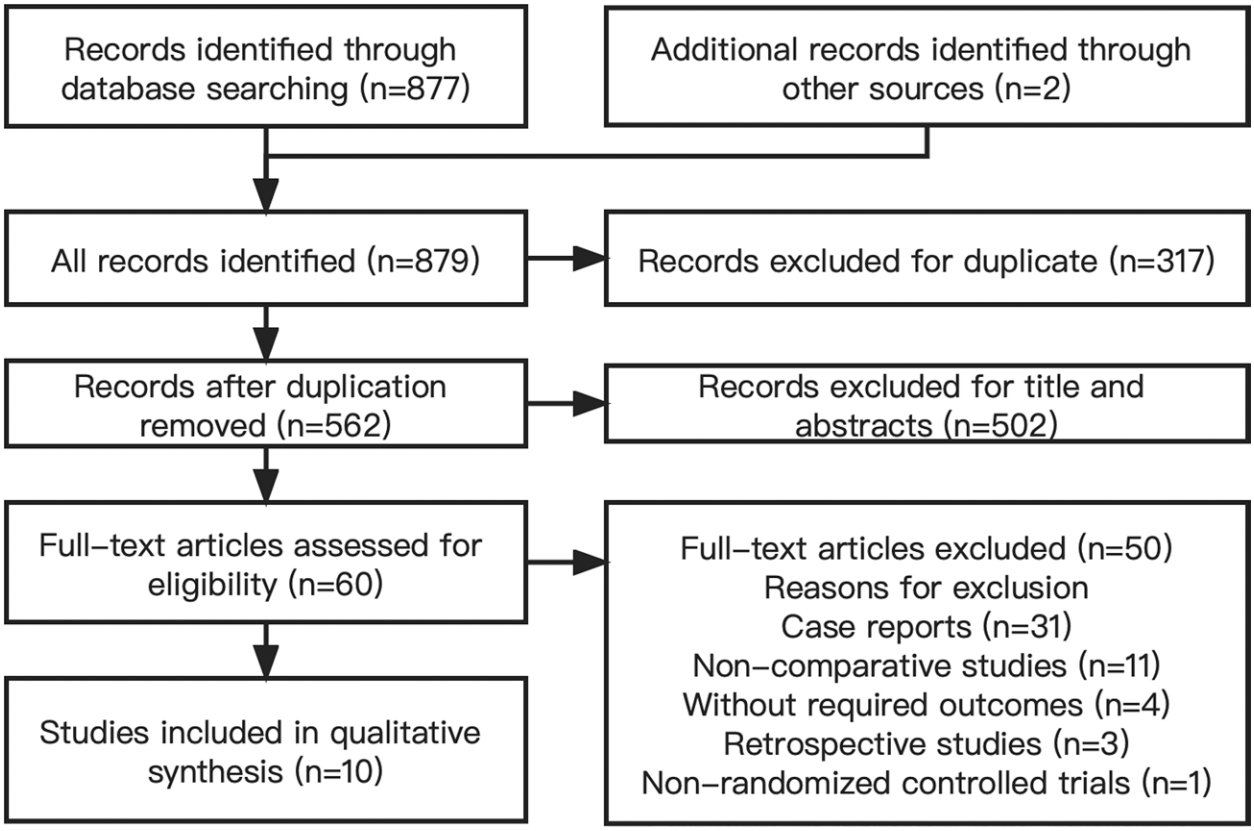

Figure 2. The study selection process.

Table 1

Data analysis of included studies.

Study	Type	N	Sources of tumor (N)				Quality of life	Endpoint
			Lung/Pleura	Breast	Esophagus	Others		
Wen et al (2014)[3]	RCT	60	45	9	6	–	KPS	ORR, DCR, QOL, AEs
Chen et al (2017)[4]	RCT	88	88	–	–	–	–	ORR, DCR, AEs
Li et al (2016)[5]	RCT	100	Unavailable				KPS	ORR, QOL, AEs
Yin et al (2020)[6]	RCT	60	45	5	4	6	KPS	ORR, DCR, QOL, AEs
Shi et al (2016)[7]	RCT	42	42	–	–	–	KPS	ORR, DCR, QOL
Ji et al (2020)[8]	RCT	60	Unavailable				KPS	ORR, DCR, QOL, AEs
Chen et al (2021)[9]	RCT	60	60	–	–	–	–	ORR, DCR, AEs
Du et al (2017)[10]	RCT	58	48	3	4	3	KPS	ORR, DCR, QOL, AEs
Wen et al (2018)[11]	RCT	60	Unavailable				KPS	ORR, DCR, QOL, AEs
Cao et al (2012)[12]	RCT	63	63	–	–	–	KPS	ORR, DCR, QOL, AEs

AEs = adverse effects, DCR = disease control rate, KPS = karnofsky physical status score, N = numbers of patients, ORR = objective response rate, QOL = quality of life.

Lobaplatin combined with endostar versus cisplatin combined with endostar: Three[8–10] studies investigated the changes of QOL after treatment. Lobaplatin combined with endostar had a higher symptom improvement rate than cisplatin combined with endostar (odds ratio=2.56, 95% CI, 1.26–5.17; Z = 2.61, $P < .05$). Among these 3 studies, we did not observe the evidence of heterogeneity (Chi² = 2.31, df = 2 ($P = .32$); I² = 13.2%) (Fig. 8).

3.3.4. Adverse effects. As shown in Table 4 and Table 5, 9 [3–6,8–12] studies compared the adverse effects, which presented four common AEs including leukopenia, thrombocytopenia, nausea/vomiting, and fatigue. The meta-analysis shows that the incidence of adverse effects of lobaplatin combined with endostar was similar to lobaplatin alone (Table 4). The incidences of leukopenia and nausea/vomiting in lobaplatin combined with endostar group were lower in cisplatin combined with endostar group (Table 5).

3.4. Assessment of publication bias

The Begg's test ($z = .63$, Pr>|z| =.59) and the Egger test ($t = .04$, P>|t|= .97) suggesting that publication bias did not have an impact on the results. All evidence showed that no publication bias existed in these included studies (Fig. 9).

4. Discussion

Malignant pleural effusions are a common complication of advanced lung cancer and other malignant tumors of the chest, which can lead to intractable cough, chest pain, and

Table 2

Assessment of administration of included studies.

Study	Trial group	Control group	Interventions		Treatment cycle	Termination of treatment
	(N)	(N)	Lobaplatin combined with endostar	Lobaplatin OR cisplatin combined with endostar		
Wen et al (2014)[3]	30	30	Lobaplatin 30 mg/m^2, 1/week Endostar 30 mg, 1/week	Lobaplatin 30 mg/m^2, 1/week	7–10 d/cycle 4 cycles	>4 Cycles, or pleural Effusion disappeared
Chen et al (2017)[4]	44	44	Lobaplatin 30 mg, 1/2weeks Endostar 30 mg, 1/2weeks	Lobaplatin 30 mg, 1/2weeks	2 weeks/cycle 2 cycles	>4 Weeks, or pleural Effusion disappeared
Li et al (2016)[5]	50	50	Lobaplatin 50 mg, 1/week Endostar 30 mg, 1/week	Lobaplatin 50 mg, 1/week	1 week/cycle 3 cycles	>3 Weeks, or pleural Effusion disappeared
Yin et al (2020)[6]	30	30	Lobaplatin 40 mg, 1/week Endostar 60 mg, 2/week	Lobaplatin 40 mg, 1/week	1 week/cycle 2 cycles	>2 Weeks, or pleural effusion disappeared
Shi et al (2016)[7]	21	21	Lobaplatin 30 mg/m^2, 1/3weeks Endostar 30 mg, 2/week	Lobaplatin 30 mg/m^2, 1/3weeks	1 week/cycle 3 cycles	>3 Weeks, or pleural Effusion disappeared
Ji et al (2020)[8]	30	30	Lobaplatin 30 mg/m^2, 2/week Endostar 60 mg, 3/week	Lobaplatin 30 mg/m^2, 1/week	4 weeks/cycle 2 cycles	>2 Cycles, or pleural Effusion disappeared
Chen et al (2021)[9]	30	30	Lobaplatin 30 mg/m^2, 1/week Endostar 30 mg, 1/week	Lobaplatin 30 mg/m^2, 2/week	1 week/cycle 4 cycles	>4 Weeks, or pleural Effusion disappeared
Du et al (2017)[10]	29	29	Lobaplatin 30 mg/m^2, 1/week Endostar 30 mg, 1/week	Cisplatin 30 mg/m^2, 1/week Endostar 30 mg, 1/week	1 week/cycle 4 cycles	>4 Weeks, or pleural Effusion disappeared
Wen et al (2018)[11]	30	30	Lobaplatin 30 mg/m^2, 1/week Endostar 30 mg, 1/week	Cisplatin 30 mg/m^2, 1/week Endostar 30 mg, 1/week	1 week/cycle 4 cycles	>4 Weeks, or pleural Effusion disappeared
Cao et al (2012)[12]	32	31	Lobaplatin 30 mg, 1/week Endostar 30 mg, 1/week	Cisplatin 30 mg, 1/week Endostar 30 mg, 1/week	1week/cycle 4 cycles	>2 Weeks, or pleural Effusion disappeared

d = day, N = numbers of patients.

Table 3

Design quality of included trials.

Study	Region	Sequence generation	Allocation concealment	Blind	Outcome data	Selective outcome reporting	Other sources of bias	Intention to treat	Risk of bias
Wen et al (2014)[3]	Single center	Unclear	Clear	Unclear	Yes	No	Clear	Yes	Unclear
Chen et al (2017)[4]	Single center	Random number table	Unclear	Unclear	Yes	No	Clear	Yes	Unclear
Li et al (2016)[5]	Single center	Random number table	Sufficient	Unclear	Yes	No	Clear	Yes	Low
Yin et al (2020)[6]	Single center	Unclear	Unclear	Unclear	Yes	No	Clear	Yes	Unclear
Shi et al (2016)[7]	Single center	Random number table	Unclear	Unclear	Yes	No	Clear	Yes	Low
Ji et al (2020)[8]	Single center	Unclear	Sufficient	Unclear	Yes	No	Clear	Yes	Unclear
Chen et al (2021)[9]	Single center	Random number table	Insufficient	Unclear	Yes	No	Clear	Yes	Unclear
Du et al (2017)[10]	Single center	Random number table	Unclear	Unclear	Yes	No	Clear	Yes	Unclear
Wen et al (2018)[11]	Single center	Random number table	Unclear	Unclear	Yes	No	Clear	Yes	Low
Cao et al (2012)[12]	Single center	Unclear	Unclear	Unclear	Yes	No	Clear	Yes	Unclear

progressively worsening dyspnea, all of which seriously affect patients' quality of life. Treatment of malignant pleural effusions by repeated extraction of pleural fluid often leads to loss of protein, the formation of cachexia, and patient death.[12] On the one hand, some studies have suggested that the causes of the development of malignant pleural effusion are the destruction of the balance between production and absorption. On the other hand, it is related to immunity and factors inducing vascular permeability, such as T lymphocyte subsets, immunoglobulin, VEGF, and matrix metalloproteinase.[13,14] Therefore, we would inhibit the development of malignant pleural effusion, and improve the treatment efficacy and prognosis by intervening the above factors. The local treatment is the primary current mode of administration for patients with MPE, including closed thoracic drainage, chemical pleurodesis, and thoracic perfusion of antineoplastic agents.[15] Intrathoracic chemotherapy can directly kill tumor cells, but local chemotherapy often leads to complications such as extensive pleural fibrosis, adhesions, or drug resistance.[16] It is crucial to select appropriate drugs for the treatment of malignant pleural effusion.

So far, several studies have reported on the advantages and security of lobaplatin combined with endostar through thoracic perfusion for treating MPE. We searched 10 RCTs and found that lobaplatin combined with endostar had better ORR and DCR benefits compared with lobaplatin alone (odds ratio = 4.08; 3.90 respectively) for treating MPE. In addition to the cure of the primary disease, the improvement of QOL is an important indicator of disease control, especially for malignant tumors. Our meta-analysis showed that lobaplatin combined with endostar remarkably improved the QOL compared to lobaplatin alone or cisplatin combined with endostar (odds ratio = 3.93; 2.56 respectively). We found that hematological toxicity and digestive reactions are the most common adverse reactions. Through further analysis, we noticed that the incidences of leukopenia and nausea/vomiting in the group of lobaplatin combined with endostar were lower than that of cisplatin combined with endostar (odds ratio = .40; .38 respectively).

Endostar is an endogenous angiogenic inhibitor. Endostar inhibits endothelial cell migration, represses the neovascularization of new tumors, blocks the nutrient supply of tumor cells, and thus suppresses tumor proliferation and metastasis.[17] In addition, endostar also reduces the production of effusions by decreasing the permeability of tumor neovascularization and decreasing the chances of protein and red blood cells entering

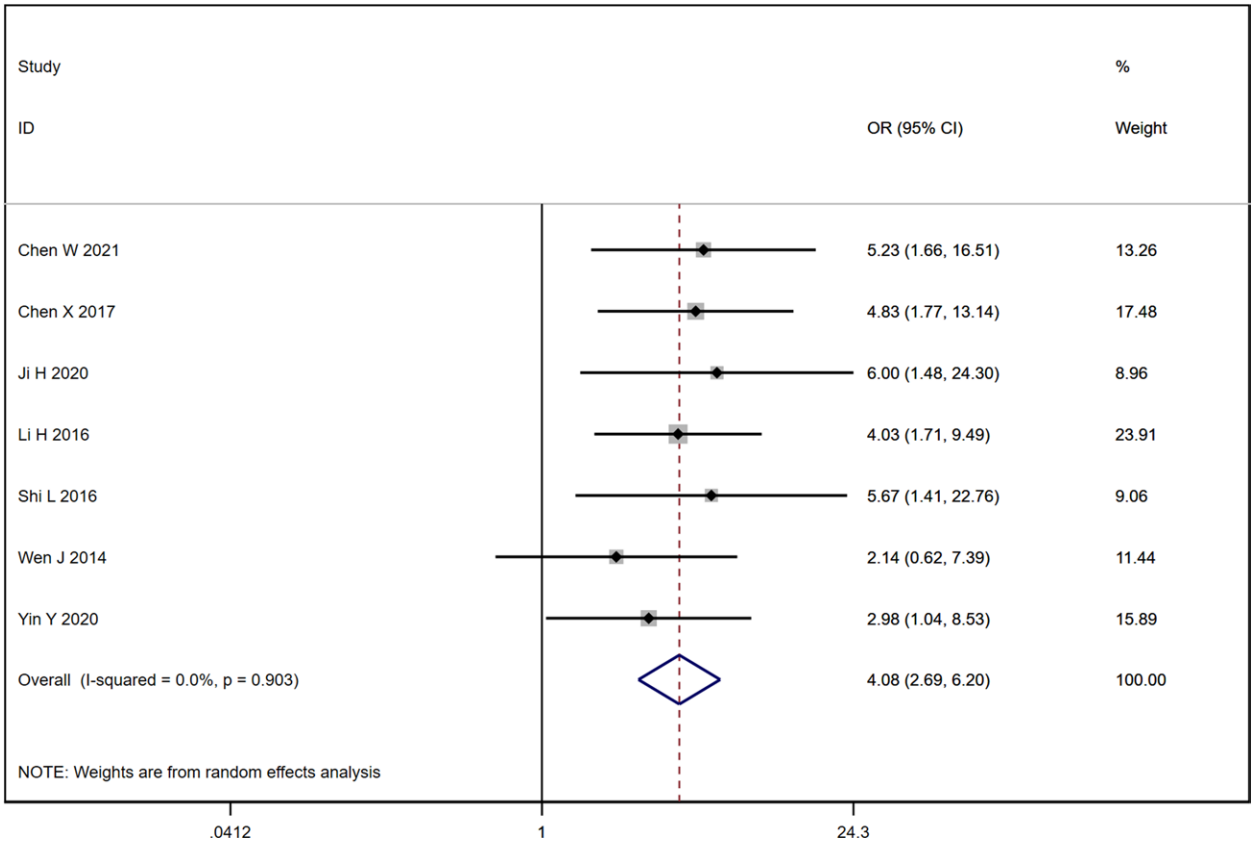

Figure 3. Comparison of ORR between lobaplatin combined with endostar versus lobaplatin alone. CI = confidence interval, OR = odds ratio, ORR = objective response rate.

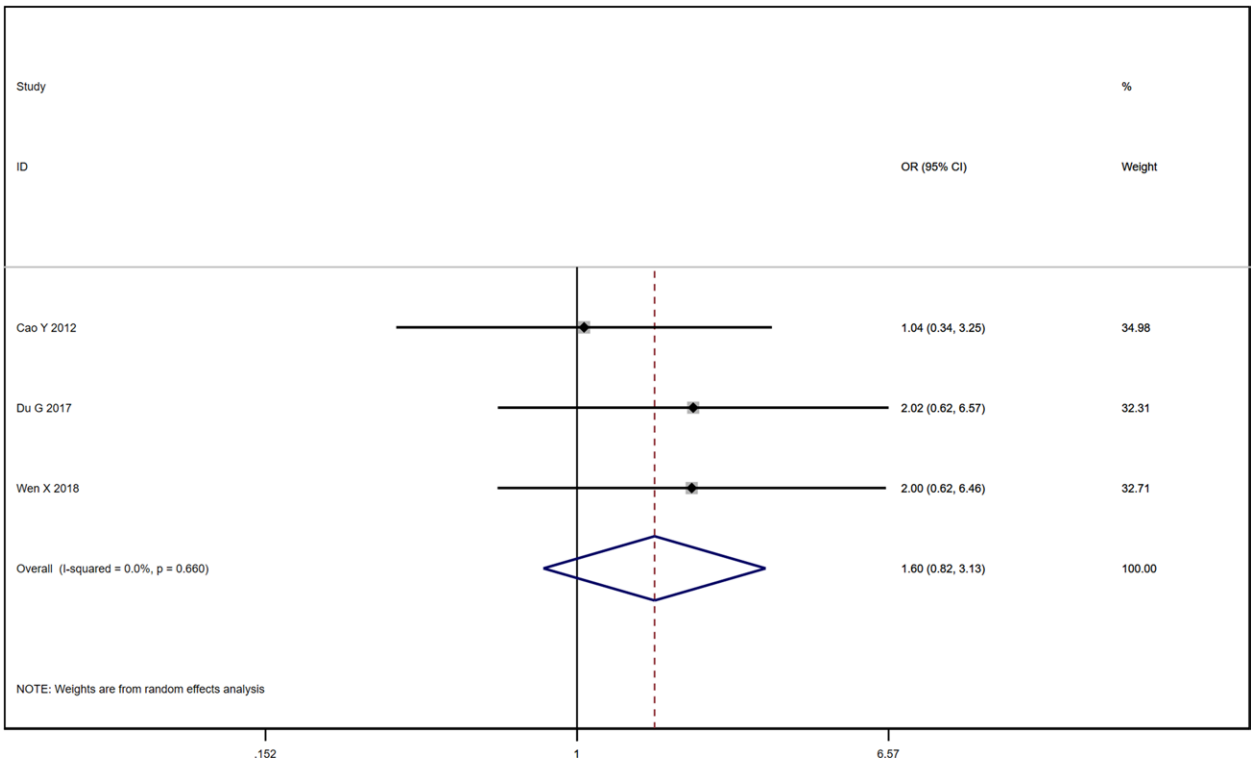

Figure 4. Comparison of ORR between lobaplatin combined with endostar versus cisplatin combined with endostar. CI = confidence interval, OR = odds ratio, ORR = objective response rate.

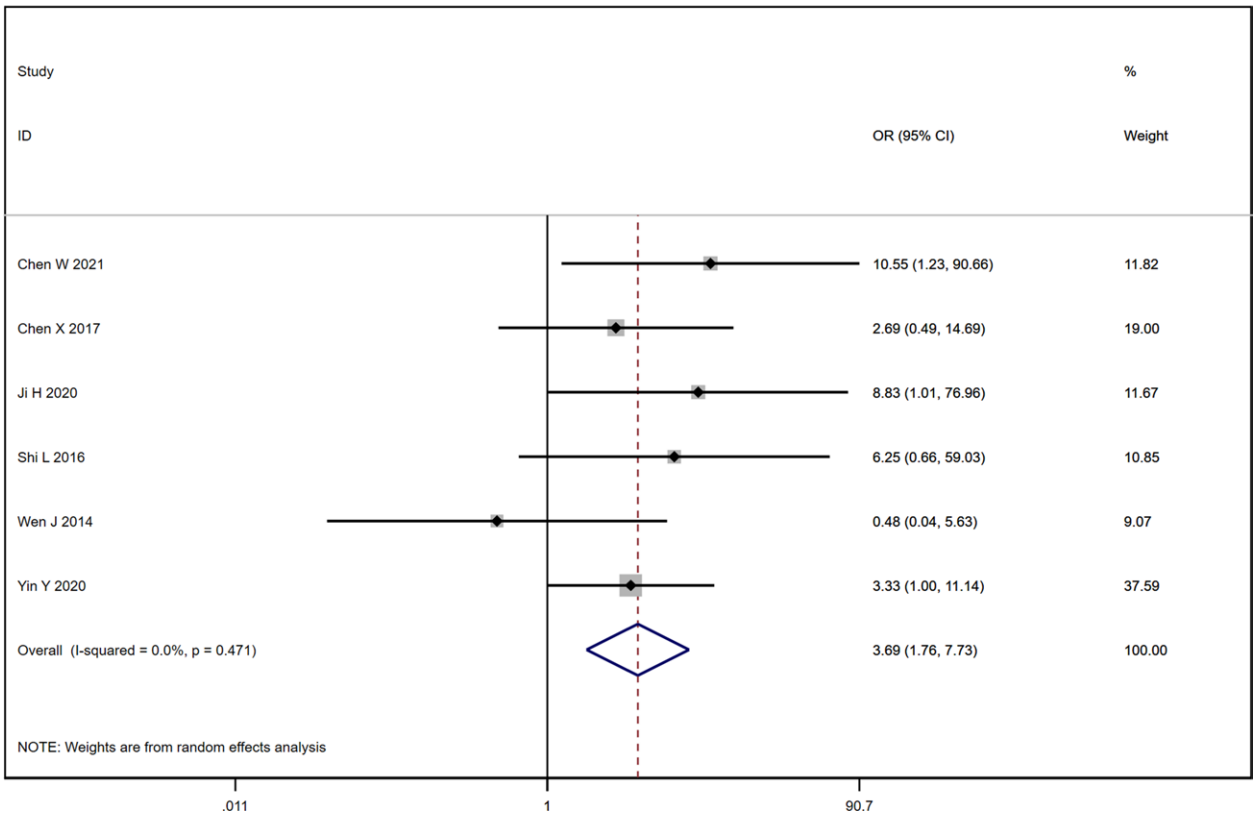

Figure 5. Comparison of DCR between lobaplatin combined with endostar versus lobaplatin alone. CI = confidence interval, OR = odds ratio, DCR, disease control rate.

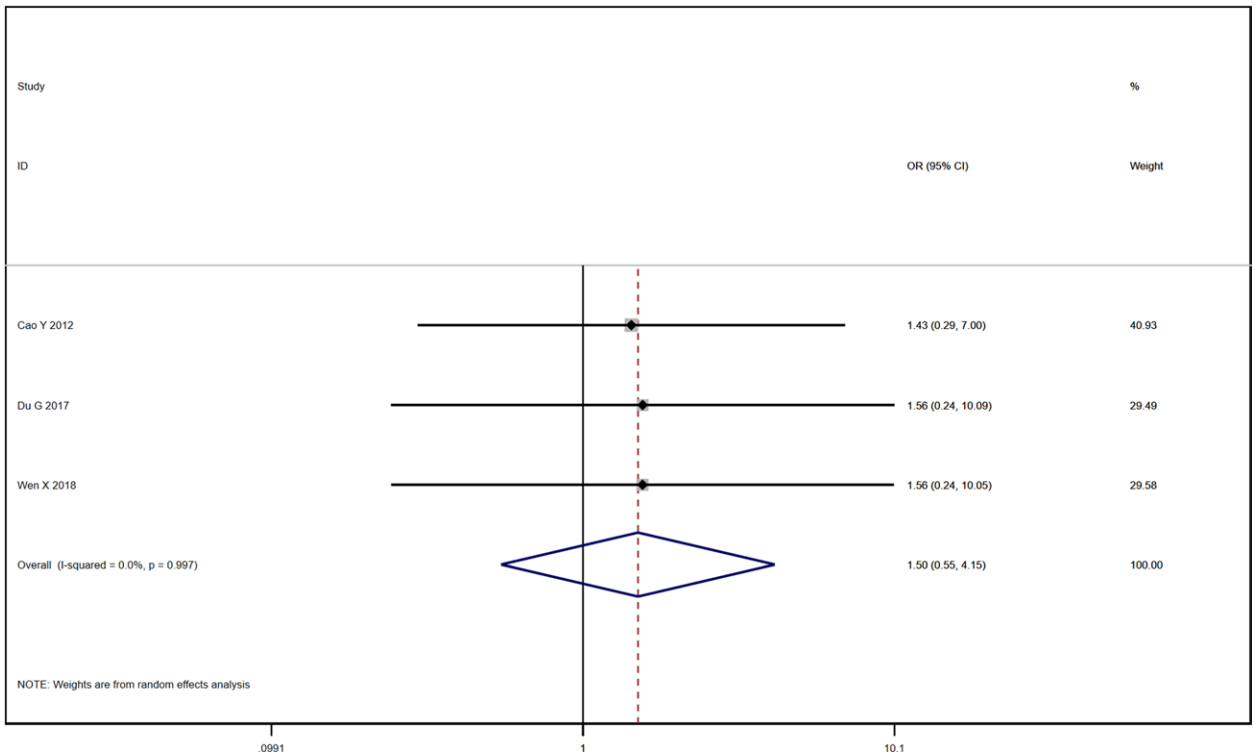

Figure 6. Comparison of DCR between lobaplatin combined with endostar versus cisplatin combined with endostar. CI = confidence interval, OR = odds ratio, DCR, disease control rate.

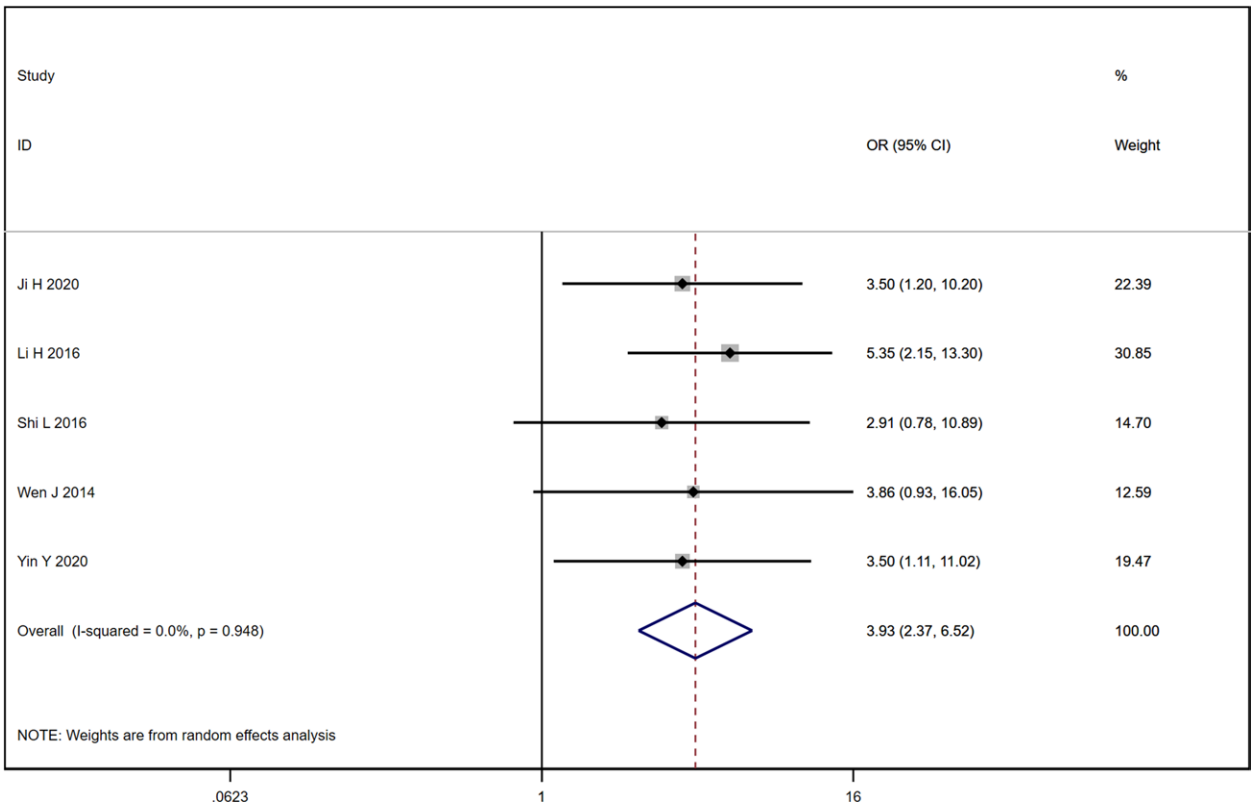

Figure 7. Comparison of QOL between lobaplatin combined with endostar versus lobaplatin alone. CI = confidence interval, OR = odds ratio, QOL, quality of life.

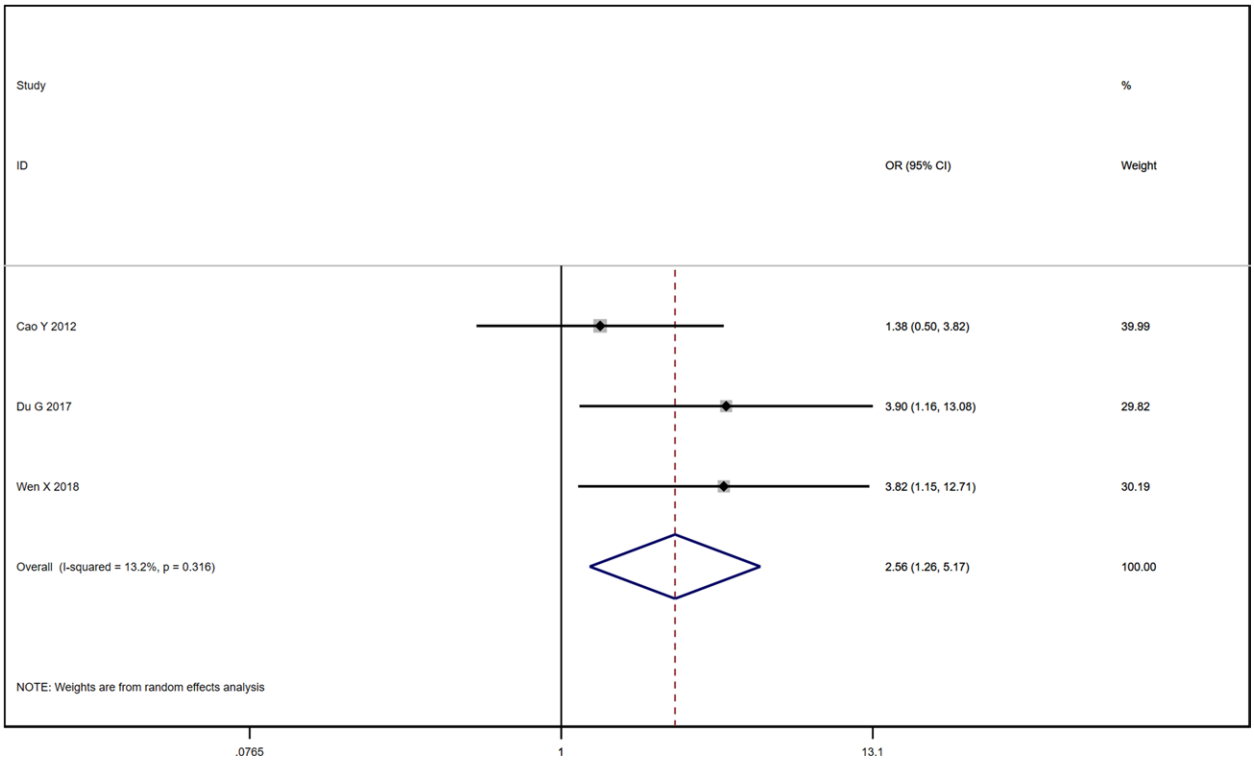

Figure 8. Comparison of QOL between lobaplatin combined with endostar versus cisplatin combined with endostar. CI = confidence interval, OR = odds ratio, QOL, quality of life.

Table 4

Comparison of adverse events between lobaplatin combined with endostar versus lobaplatin alone.

	Leukopenia (%)		Thrombocytopenia (%)		Nausea/Vomiting (%)		Fatigue (%)	
Study	**Trial group**	**Control group**	**Trial group**	**Control group**	**Trial group**	**Control group**	**Trial group**	**Control group**
Wen (2014)[3]	10 (33.33)	8 (26.67)	10 (33.33)	12 (40.00)	6 (20.00)	4 (13.33)	4 (13.33)	3 (10.00)
Chen (2017)[4]	–	–		–	6 (13.64)	5 (11.36)	2 (4.55)	4 (9.09)
Li (2016)[5]	–	–	–	–	5 (10.00)	7 (14.00)	–	–
Yin (2020)[6]	10 (33.33)	8 (26.67)	10 (33.33)	12 (40.00)	11 (36.67)	9 (30.00)	13 (43.33)	10 (33.33)
Shi (2016)[7]	–	–	–	–	–	–	–	–
Ji (2020)[8]	14 (46.67)	16 (53.33)	15 (50.00)	14 (46.67)	18 (60.00)	18 (60.00)	17 (56.67)	14 (46.67)
Chen (2021)[9]	–	–	–	–	2 (6.67)	1 (3.33)	1 (3.33)	2 (6.67)
Meta-analysis	OR = 1.10, 95% CI [.59–2.05], *P* = .75		OR = .87, 95% CI [.48–1.58], *P* = .65		OR = 1.14, 95% CI [.68–1.91], *P* = .61		OR = 1.47, 95% CI [.81, 2.69], *P* = .21	

Table 5

Comparison of adverse events between lobaplatin combined with endostar versus cisplatin combined with endostar.

	Leukopenia (%)		Thrombocytopenia (%)		Nausea/Vomiting (%)		Fatigue (%)	
Study	**Trial group**	**Control group**	**Trial group**	**Control group**	**Trial group**	**Control group**	**Trial group**	**Control group**
Du (2017)[10]	6 (20.69)	11 (37.93)	10 (34.48)	12 (41.38)	5 (17.24)	14 (48.28)	5 (17.24)	7 (24.14)
Wen (2018)[11]	7 (23.33)	12 (40.00)	11 (36.67)	13 (43.33)	6 (20.00)	15 (50.00)	6 (20.00)	8 (26.67)
Cao (2012)[12]	20 (62.50)	26 (83.87)	18 (56.25)	19 (61.29)	15 (46.88)	16 (51.61)	–	–
Meta-analysis	OR = .40, 95% CI [.21–.78], *P* = .007		OR = .77, 95% CI [.43–1.40], *P* = .40		OR = .38, 95% CI [.16–.90], *P* = .027		OR = .67, 95% CI [.28, 1.62], *P* = .376	

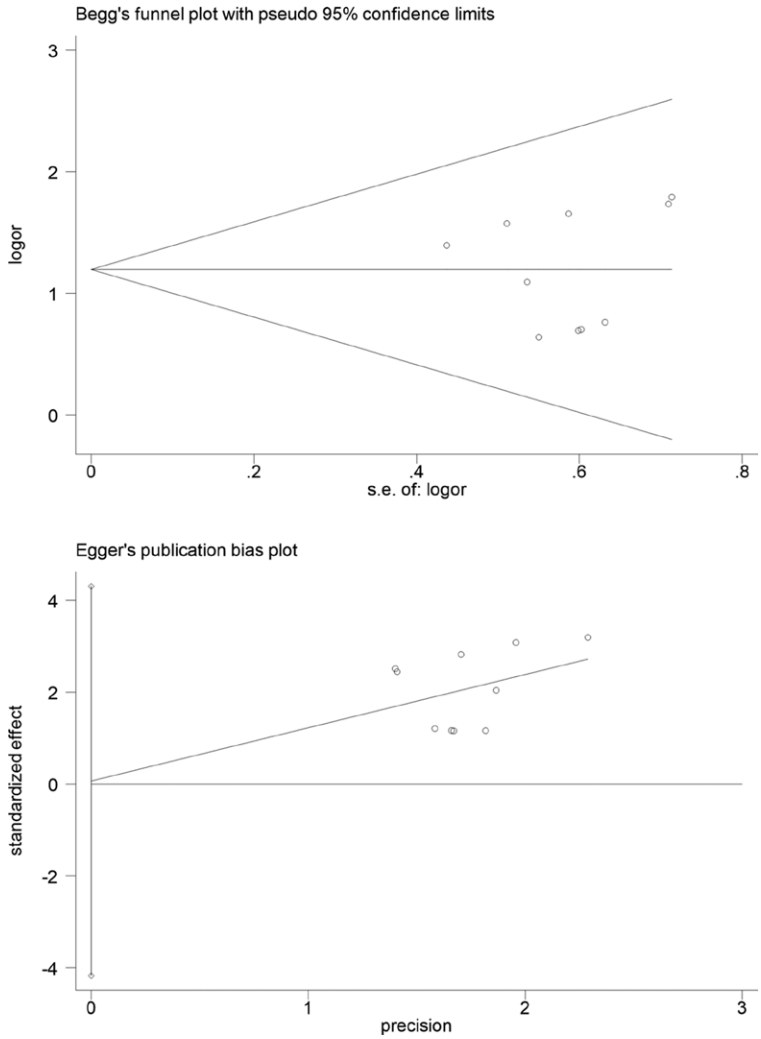

Figure 9. Assessment of publication bias. Begg's test and Egger's test did not imply a publication bias.

the chest cavity.[18,19] Compared with lobaplatin alone, the combination of lobaplatin and endostar improves the effectiveness of MPE treatment by killing tumor cells, inhibiting angiogenesis, and reducing effusion.

As a platinum-based chemotherapy drug, lobaplatin has a similar anti-tumor mechanism to cisplatin. Our study indicated that the efficacy of lobaplatin combined with endostar was similar to cisplatin combined with endostar in treating MPE. But patients treated with lobaplatin and endostar had higher quality of life and lower incidence of adverse effects. Compared with cisplatin, lobaplatin has higher solubility in water, higher pleural permeability, and less nephrotoxicity, digestive tract toxicity, and neurotoxicity. So lobaplatin is more suitable for thoracic perfusion therapy.

The detection of heterogeneity is essential to meta-analysis because it will affect the pooled statistical efficacy. We included ten randomized controlled trials in this study. We carefully assessed the included studies and found that these studies had good clinical homogeneity. However, there are some deficiencies in the included trials. Some studies lack perfect trial designs such as allocation, concealment, and blind. In addition, some sample sizes are too small. Despite those, these studies still propose a credible suggestion that lobaplatin combined with endostar is a new choice for treating MPE with good effectiveness and safety.

5. Conclusion

Thoracic perfusion of lobaplatin combined with endostar has a better benefit of ORR and DCR in treating MPE and improves the QOL of MPE patients, compared with lobaplatin alone. Compared to cisplatin combined with endostar, lobaplatin combined with endostar not only reduces the incidence of adverse effects but also improves the QOL of patients. Because the included studies and sample size are limited, the findings need to be further debated. Therefore, we expect more rigorous randomized controlled trials to confirm the efficacy and safety of lobaplatin combined with endostar in the treatment of malignant pleural effusion.

Author contributions

Conception and design: Wei Wang and Cheng-Qian Wang.
Collection and assembly of data: Cheng-Qian Wang, Fei-yu Liu.
Data analysis and interpretation: Cheng-Qian Wang, Fei-yu Liu, Wei Wang.
Manuscript writing and revising: Cheng-Qian Wang, Fei-yu Liu, Wei Wang.
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References

[1] Wu Y, Xu L, Wang X, et al. Diagnostic value of medical thoracoscopy in malignant pleural effusion. BMC Pulm Med. 2017;17:109.
[2] Azzopardi M, Thomas R, Muruganandan S, et al. Protocol of the Australasian Malignant Pleural Effusion-2 (AMPLE-2) trial: a multicentral randomized study of aggressive versus symptom-guided drainage via indwelling pleural catheters. BMJ Open. 2016;6:e011480.
[3] Wen J, Ge W, Li G, et al. Clinical observation of intrapleural infusion of Endostar combined with lobaplatin in the treatment of malignant pleural effusion. Biomed Eng Clin Med. 2011;18:540–3.
[4] Chen X, Chen J. Clinical observation of lobaplatin combined with Endostar in the treatment of lung cancer complicated with malignant pleural effusion. Proceedings of the Digital Chinese Medicine Section of the International Society for Digital Medicine 2017:895.
[5] Li H, Cai S, Zhao G, et al. Clinical effect of recombinant human endostatin injection combined with lobaplatin in the treatment of malignant pleural effusion. Chin J Front Med Sci. 2016;8:42–5.
[6] Yin Y, Zhou H, Yang J, et al. Effect observation and prognosis analysis of recombinant human endostatin combined with lobaplatin in the treatment of malignant pleural effusion. Eval Anal Drug-Use Hospitals China. 2020;20:804–7.
[7] Shi L, Bai Y, Yang W. Efficacy of Endostar combined with Lobaplatin in the treatment of malignant pleural effusion in non-small cell lung cancer. World Latest Med Information. 2016;16:153–4.
[8] Ji H, Wei F, Zhou D, et al. Clinical effect of endostar combined with lobaplatin in the treatment of malignant pleural effusion. Electronic J Pract Gynecol Endocrinol. 2020;7:186–8.
[9] Chen W. Analysis of the efficacy and adverse reactions of lobaplatin combined with Endostar by pleural infusion in the treatment of non-small cell lung cancer complicated with malignant pleural effusion. Qinghai Med J. 2021;51:8–10.
[10] Du G, Jiang L, Zhou J, et al. Clinical observation on the treatment of malignant pleural effusion by pleural infusion of lobaplatin combined with Endostar. Chin J Oncol Prevent Treatment. 2017;9:152–4.
[11] Wen X. Clinical study of intrapleural infusion of lobaplatin combined with Endostar in the treatment of non-small cell lung cancer with malignant pleural effusion. Int J Respiration. 2018;38:1694–7.
[12] Cao Y, Zhao G, Huang Y. Clinical study of intrapleural infusion of lobaplatin combined with recombinant human endostatin in the treatment of malignant pleural effusion of lung cancer. J Dali Univ. 2012;11:41–3.
[13] Davidson B, Konstantinovsky S, Nielsen S, et al. Altered expression of metastasis-associated and regulatory molecules in effusions from breast cancer patients: a novel model for tumor progression. Clin Cancer Res. 2004;10:7335–46.
[14] Hooper CE, Elvers KT, Welsh GI, et al. VEGF and sVEGFR-1 in malignant pleural effusions: association with survival and pleurodesis outcomes. Lung Cancer. 2012;77:443–9.
[15] Du N, Li X, Li F, et al. Intrapleural combination therapy with bevacizumab and cisplatin for non-small cell lung cancer- mediated malignant pleural effusion. Oncol Rep. 2013;29:2332–40.
[16] Tamiya M, Tamiya A, Yasue T, et al. Vascular endothelial growth factor in plasma and pleural effusion is a biomarker for outcome after bevacizumab plus carboplatin-paclitaxel treatment for non-small cell lung cancer with malignant pleural effusion. Anticancer Res. 2016;36:2939–44.
[17] Huang C, Wang X, Wang J, et al. Incidence and clinical implication of tumor cavitation in patients with advanced non-small cell lung cancer induced by Endostar, an angiogenesis inhibitor. Thoracic Cancer. 2014;5:438–46.
[18] Fang S, Zhang H, Hu H, et al. Effect of Endostar combined with angiopoietin-2 inhibitor on malignant pleural effusion in mice. Med Oncol. 2015;32:410.
[19] Liang R, Xie H, Lin Y, et al. Intraperitoneal perfusion therapy of endostar combined with platinum chemotherapy for malignant serous effusions: a meta-analysis. Asian Pacific J Cancer Prevent. 2015;16:8637–44.