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Effect of Amifostine on Patients with Lung Cancer Treated with Radiotherapy or Concomitant Chemoradiotherapy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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【**Abstract**】 **Objective** Amifostine is clinically used as a chemical radioprotector. Nevertheless, its efficacy as a radioprotector remains controversial. **Methods** PubMed, Cochrane Central Register of Controlled Trials, EMBASE, China National Knowledge Infrastructure, and the references of the published results of trials on the efficacy of amifostine in patients with lung cancer and who received radiotherapy or concomitant chemoradiotherapy were searched. The pooled radiation protection efficacy, treatment response, and side effects of amifostine were calculated using RevMan software. **Results** Twelve randomized controlled trials involving 1000 patients with lung cancer were ultimately analyzed. Results of meta-analysis revealed that the use of amifostine reduced the risk of acute esophageal toxicity(RR, 0.56; 95%*CI*, 0.39-0.81; *P*=0.002) and pulmonary toxicity(RR, 0.42; 95%*CI*, 0.25-0.70; *P*=0.001). Subgroup analysis also demonstrated that the risk of acute esophageal toxicity and pulmonary toxicity significantly reduced in patients who received chemoradiation concurrent with amifostine or radiation only. Pooled data showed that the use of amifostine did not significantly decrease the risk of late pulmonary toxicity(RR, 0.74; 95%*CI*, 0.45-1.19; *P*=0.210). Moreover, subgroup analysis demonstrated that the risk oflate pulmonary toxicity did not significantly decrease in patients who received chemoradiotherapy concomitant with amifostine(RR, 0.84; 95%*CI*, 0.48-1.46; *P*=0.540). Amifostine did not exert tumor-protective effects in partial response(RR,0.98; 95%*CI*, 0.83-1.15; *P*=0.800) but improved complete response(RR, 1.50; 95%*CI*, 1.03-2.18; *P*=0.030), although publication bias was observed through Egger′s test(*P*=0.000). Moreover, amifostine had no effect on one-year overall survival (RR, 0.94; 95%*CI*, 0.81-1.09; *P*=0.400) and two-year overall survival(RR, 1.06; 95%*CI*, 0.81-1.39; *P*=0.680) rates. The incidence of neutropenia, a hematologic side effect of amifostine, was not significantly different(RR, 1.02; 95%*CI*, 0.61-1.71; *P*=0.940) between the amifostine and control group. The use of amifostine, however, significantly decreased the incidence of thrombocytopenia(RR, 0.45; 95%*CI*, 0.21-0.94; *P*=0.030). The most common amifostine-related side effects were nausea, vomiting, and hypotension with average incidence rates of 11%, 14%, and 24%, respectively. **Conclusions** This systematic review showed that the concurrent administration of amifostine with radiotherapy to patients with lung cancer significantly reduced the risks of acute esophageal toxicity and acute pulmonary toxicity and decreased the incidence of thrombocytopenia without tumor-protecting effects. In addition, the toxicities of amifostine were generally controllable through clinical treatment or resting.

【Key words】 Amifostine; Lung neoplasms; Radiotherapy; Concomitant chemoradiotherapy; Meta-analysis

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Radiotherapy has a crucial role in the treatment of non-small cell lung cancer[1]. However, esophageal toxicity and pulmonary toxicity are common toxic side effects of radiotherapy and usually interrupt its planned course[2]. Acute esophageal toxicity during the course of treatment can disrupt normal activities, such as swallowing, drinking, and eating, of patients. Pulmonary toxicity causes coughing, aggravates sputum production, and induces posterior sternal pain. Thus, esophageal and pulmonary toxicities cause the life quality of patients to deteriorate.

Numerous drugs with the potential to protect normal tissues from intensive radiotherapy and/or chemotherapy while exerting the optimal therapeutic effect have been investigated over the past several decades. Amifostine is an organic thiophosphate prodrug that is dephosphorylated in vivo into its active moiety, WR-1065(5); it has been developed to selectively protect normal tissues against the toxic effects of radiotherapy and/or chemotherapy by scavenging free radicals[3]. Some randomized controlled trials(RCTs) have demonstrated that amifostine could reduce the risk of esophageal toxicity and pulmonary toxicity in patients with lung cancer and receiving radiation or concomitant chemoradiotherapy[4-5]. However, some RCTs have shown that amifostine cannot reduce radiation toxicities[6-7]. Some investigators have even suggested that amifostine can reduce the therapeutic effects of radiation or chemotherapy by exerting tumor-protective effects[8].

Thus far, however, the radiotherapy and/or chemotherapy protection efficacy of amifostine lacks adequate statistical support. We performed this systematic review and meta-analysis to confirm whether amifostine can reduce the risk of radiotherapy and/or chemotherapy toxicities and to evaluate its therapeutic efficacy in lung cancer.

1 METHODS

1.1 Search strategy

The procedure for study selection is shown in Fig.1. The electronic databases PubMed, Cochrane Central Register of Controlled Trials, EMBASE, and China National Knowledge Infrastructure were comprehensively searched for articles that were published over the period of January 1, 2000 to December 31, 2016. The following search terms were used: "lung cancer", "WR2721" and "amifostine". Search languages were limited to English and Chinese. All references of relevant articles were scanned for additional articles.

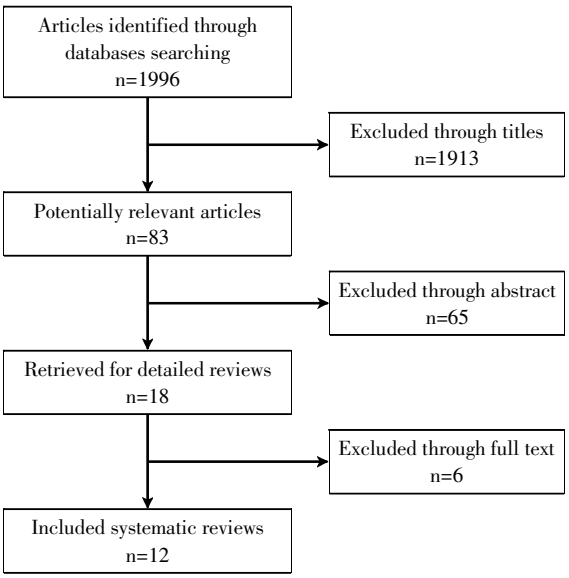

Fig.1 Literature-screening process

1.2 Selection criteria

Details regarding the patients' eligibility criteria, treatment methods, and outcomes of the relevant trials were extracted by two reviewers(Huanan Wang and Feng Wang) and then checked by the third reviewer (Yonghan Wang) in accordance with the Cochrane Handbook for systematic reviews(version 5.1.0)[9]. The

patient population was limited to patients with lung cancer. The intervention was radiotherapy or chemoradiotherapy plus amifostine, and the control intervention was radiotherapy or chemoradiotherapy. Outcomes were restricted to esophageal toxicity, pulmonary toxicity, response rate, overall survival rate, hematological toxicity, and amifostine-related side effects. RCTs that included patients with lung cancer and other kinds of tumors were also included in the meta-analysis. However, data were extracted only for patients with lung cancer.

1.3 Data extraction and quality assessment

Data were independently extracted by two reviewers (Huanan Wang and Yonghan Wang) from all included RCTs. Another investigator (Feng Wang) was consulted to resolve any disagreements. The general characteristics (name of the first author, year of publication, number of patients, stages, chemoradiation regimens, and amifostine dosage), outcomes(esophageal toxicity, pulmonary toxicity, response rate, overall survival rate, hematological toxicity, and amifostine-related side effects) were extracted. The methodological qualities of the trials were assessed by the same investigators (Huanan Wang and Yonghan Wang) in accordance with the Cochrane Reviews Handbook 5.1.0. Allocation concealment, binding of participants and personnel, random sequence generation, binding of outcome assessment, incomplete data outcome, and selective reporting received special attention during the trial inclusion procedure given that these factors represent the quality of the RCT[9].

1.4 Statistical analysis

All analyses were performed strictly with Review Manager (RevMan 5.3, provided by The Cochrane Collaboration). Dichotomous data were calculated as the risk ratio (RR) with 95% confidence interval (*CI*). The null hypothesis was considered as no association(RR=1) between amifostine use and the incidence of chemoradiation toxicity or the tumor response rate. RR<1 indicated that amifostine positively affected the outcome. The statistical heterogeneity of the results across trials was assessed through χ^2 test[10], and inconsistency was calculated through I^2 test[11]. If heterogeneity was present (χ^2, P<0.05, or I^2>50%), data were pooled through the random-effect method(Dersimonian-Laird method). Subgroup analysis was conducted for further evaluation. The fixed-effect method was used if significant heterogeneity was absent. Egger′s tests were used for each effect size to evaluate possible publication bias as described by Egger[12].

2 RESULTS

2.1 Included trials and characteristics(Table 1)

For the entire patient population, 1996 articles were retrieved through the initial search. After reviewing titles and abstracts, 1778 articles were removed. The full texts of the remaining 12 articles were reviewed for inclusion in the meta-analysis. All twelve trials were RCTs and published in English or Chinese[4–7, 13–20] in the period of 2000 to 2016. The included RCTs involved 1000 patients(604 and 563 in each treatment arm).

Methodological quality was evaluated with a seven-question instrument described in the Cochrane Reviews Handbook 5.1.0. Generally, the 12includedtrials were considered to be at moderate risk of bias. Although randomization was performed in all 12 trials, only two articles mentioned allocation concealment[16, 18]. In addition, all 12 trials performed an adequate sequence generation[4–7,13–20]. Only one trial described blinding patients and physicians or evaluators. The outcome of methodological quality for each trial is presented in Fig.2.

2.2 Acute esophageal toxicity

Of the 12 trials, nine[4, 6–7, 13, 15–19] trials evaluated acute esophageal toxicity with evident heterogeneity between studies(I^2=84%) (Fig.3). The meta-analysis was performed using the random-effect model(Dersimonian-Laird method). Pooled analysis showed that the use of amifostine reduced acute esophageal toxicity by 44% (RR, 0.56; 95%*CI*, 0.39–0.81; P=0.002). Egger′s test revealed that publication bias was absent(P =0.206). Subgroup analysis indicated that the use of amifostine significantly reduced acute esophageal toxicity in patients receiving concurrent chemoradiation(RR, 0.67; 95%*CI*, 0.49–0.93; P=0.020) and radiation only(RR,

Table 1 General characteristics of included radomized controlled trials

Trials	No. of patients Ami/Control	Stage included	Daily ami (dose)	Administration	Concomitant chemotherapy	Radiotherapy
Zhao (2014)[5]	69/68	Ⅲ, Ⅳ	200 mg/m^2	Ⅳ, 30 min before RT, q.d		54–66 Gy, 2 Gy/fraction, 5 fractions/week
Lin (2013)[13]	21/23	Ⅱ, Ⅲ	300 mg/m^2	Ⅳ, 15–30 min before RT, q.d		54 Gy, 1.8 Gy/fraction, 5 fractions weekly
Liu (2015)[4]	25/25	Ⅲ	300 mg/m^2	Ⅳ, 30 min before RT, q.d	DDP (50 mg/m^2) + E (50 mg/m^2) daily for the first 4 weeks of RT. DDP (50 mg/m^2) + E(50 mg/m^2)/ DDP(50 mg/m^2) + V(50 mg/m^2)/ C(50 mg/m^2) + P(50 mg/m^2) daily for the second 4 weeks of RT	66 Gy, 16.5 Gy/week
Li (2010)[14]	55/53	Ⅱ, Ⅲ, Ⅳ	200 mg/m^2	Ⅳ, 30 min before RT, q.d		54–66 Gy, 2 Gy/fraction, 5 fractions/week
Weng (2007)[15]	30/30	Ⅲ	300 mg/m^2	Ⅳ, 30 min before RT, q.d	P (135 mg/m^2) days: 1 + DDP (50 mg/m^2) days:1–3	50–60 Gy, 2 Gy/fraction, 5 fractions/week
Movsas (2005)[6]	114/115	Ⅲ	500 mg, 4 times/ week	Ⅳ, 15–30 min before RT q.d, on RT-only days; 180 min before RT q.d, on CT + RT days	P(225 mg/m^2) + C(AUC6) days: 1, 22; P(50mg/m^2) + C (AUC2) days: 43, 50, 57, 64, 71, 78	69.6 Gy, 1.2 Gy bid, 5 days/week
Komaki (2004)[16]	31/31	Ⅱ, Ⅲ	500 mg, 2 times/ week	Ⅳ, 20–30 min before CT q.d, days: 1, 8, 29, 36; 60–90 min before first fraction RT; 30–60 min before RT q.d, days: 2, 9, 30, 37	E(50mg/m^2)days: 1–10, 29–38 DDP(50mg/m^2)days: 1, 8, 29, 36	69.6 Gy, 1.2 Gy bid, 5 days/week
Leong (2003)[17]	30/30	Ⅲ	740 mg/m^2	Ⅳ, 30 min before CT q.d	P(175 mg/m^2) + C (AUC6) days: 1, 22; P(60 mg/m^2) days: 43, 50, 57, 64, 71, 78	60–66 Gy, 2 Gy fraction, 5 fractions/week
Antonadou (2003)[18]	36/32	Ⅲ	300 mg/m^2	Ⅳ, 15 min before RT and before CT on CT days q.d	P(60 mg/m^2) / C(AUC2) weekly before RT	55–60 Gy, 2 Gy fraction, 5 fractions/week
Senzer (2002)[7]	24/25	Ⅲ	500 mg/ 200 mg q.d	Ⅳ, 500 mg, 15–30 min weekly before CT; 200 mg/m^2, 15–30 min before RT (including the day of CT) q.d	P(50 mg/m^2) + C(AUC^2) weekly + G(1000 mg/m^2) days: 22, 29, 36+ DDP(80 mg/m^2) days: 29 before RT	64.8 Gy, 36 fractions over 7.5 weeks
Antonadou (2001)[19]	44/53	Ⅲ	340 mg/m^2	Ⅳ, 15 min before RT q.d		55–60 Gy, 2 Gy fraction, 5 fractions/week
Koukourakis (2001)[20]	19/17	Ⅲ	500 mg	IH, 20 min before RT q.d		64 Gy, 2 Gy/fraction, 5 fractions/week

Notes: Ami=amifostine; IV=intravenous injection; IH=subcutaneously injected; RT=radiotherapy; C=carboplatin; G=gemcitabine; V=vinorelbine; DDP=cisplatin; P=paclitaxel; E=etoposide; AUC=area under the curve; qd=daily; bid=twice daily.

0.20; 95%*CI*, 0.05–0.80; *P*=0.020)(Table 2).

2.3 Acute pulmonary toxicity

Nine articles[4–7, 13–14, 16, 18–19] reported the number of patients who developed acute pulmonary toxicity in both treatment arms. Heterogeneity was observed among trials. Pooled analysis with the random-effect model demonstrated that amifostine reduced all grades ofacute pulmonary toxicity in patients with lung cancer (RR, 0.42; 95%*CI*, 0.25–0.70; *P*=0.001)(Fig.4). Egger′s test revealed the absence of publication bias (*P*=0.244). Subgroup analysis revealed that the use of amifostine significantly reduced acute pulmonary toxicity in patients treated with concurrent chemoradiation(RR, 0.44; 95%*CI*, 0.21–0.95; *P*=0.040) and radiation only (RR, 0.38; 95% *CI*, 0.25–0.58; *P*<0.001)(Table 2).

2.4 Late pulmonary toxicity

Late pulmonary toxicity was reported in three trials[6, 18–19] with heterogeneity among studies (I^2=59%). Meta-analysis showed that the risk (RR, 0.74; 95%*CI*, 0.45–1.19; *P*=0.210) of late pulmonary toxicity was not significantly lower in the amifostine group than that in the control treatment (Fig.5). Publication bias was not observed by Egger′s test (*P*=0.052). Subgroup analysis also showed that the use of amifostine did not reduce

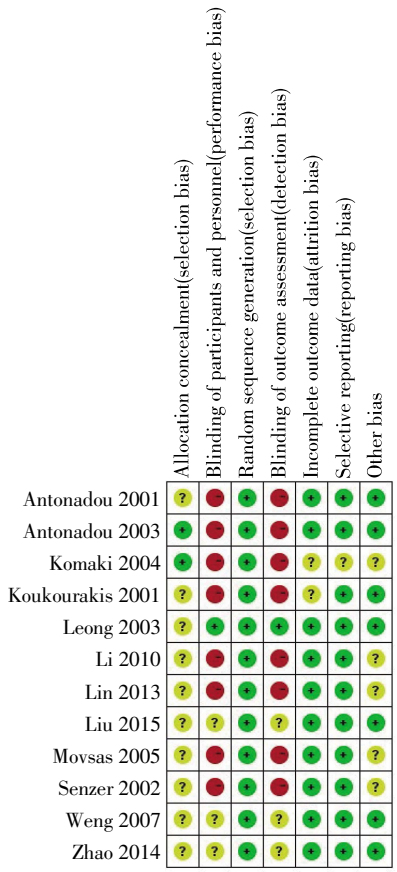

Fig.2 Risk of bias summary. The authors' judgments for each risk of bias item. + is "low risk"; – is "high risk"; ? is "unclear".

the risk of pulmonary toxicity in lung cancer patients treated with concurrent chemoradiation (RR, 0.84; 95% *CI*, 0.48–1.46; *P*=0.540) (Table 2).

2.5 Hematological toxicity

Data on hematological toxicity, including neutropenia and thrombocytopenia, were extracted from five articles[6, 15–18]. Studies involving neutropenia exhibited heterogeneity (I^2=74%). However, studies involving thrombocytopenia were not heterogeneous(I^2=0%). Meta-analysis showed that the incidences of neutropenia (RR, 1.02; 95% *CI*, 0.61–1.71; *P*=0.940) in the amifostine and control groups were not significantly different. Egger's test revealed no publication bias in this subset analysis(*P*=0.182). The use of amifostine significantly reduced the incidence of thrombocytopenia(RR, 0.45; 95%*CI*, 0.21–0.94; *P*=0.030)(Fig.6).

2.6 Treatment response

Nine articles provided response rates[4–6, 13, 15, 17–20]. No statistical heterogeneity among studies was found in both complete(I^2=0%) and partial(I^2=0%) response analysis. The pooled RR estimate for partial response was 0.98(95%*CI*, 0.83–1.15; *P*=0.800) (Fig.6), which was not statistically significant. Publication bias was not observed through Egger's test(*P*=0.138). The pooled RR estimate for the complete response was 1.50(95%*CI*, 1.03–2.18; *P*=0.030) and was statistically significant (Fig.7). However, publication bias was observed through Egger's test (*P*=0.000).

2.7 Overall survival

Three articles reported overall survival rates[6, 16–17]. No statistical heterogeneity among studies was found in both one-year overall survival(I^2=0%) and two-year overall survival(I^2=0%) analysis. The pooled RR estimate for the one-year overall survival was 0.94(95% *CI*, 0.81–1.09; *P*=0.400). Publication bias was not observed through Egger's test(*P*=0.555). The pooled RR estimate for two-year overall survival was 1.06(95%*CI*, 0.81–1.39; *P*=0.680) (Fig.8). Publication bias was not observed through Egger's test(*P*=0.732). Neither one-

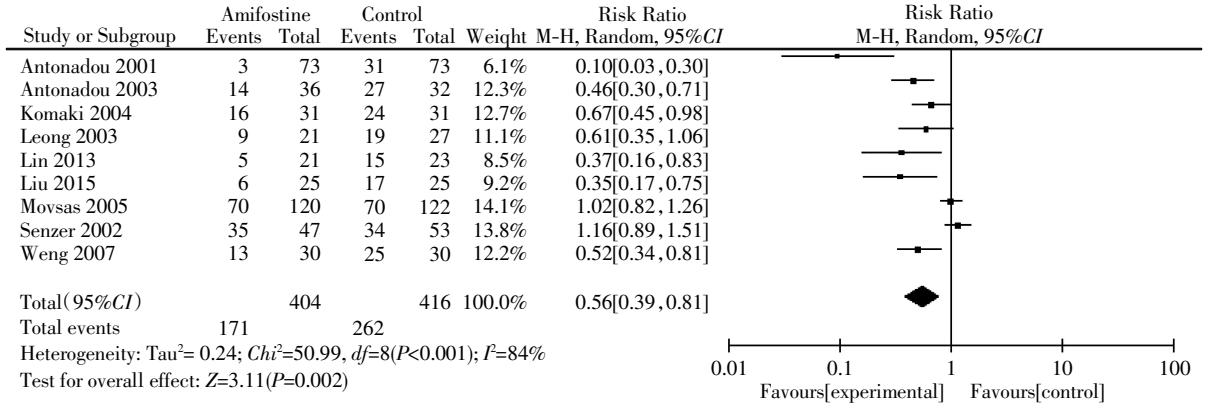

Fig.3 Forest plot of acute esophageal toxicity(all grades) in patients with lung cancer who received radiotherapy or concomitant chemoradiation

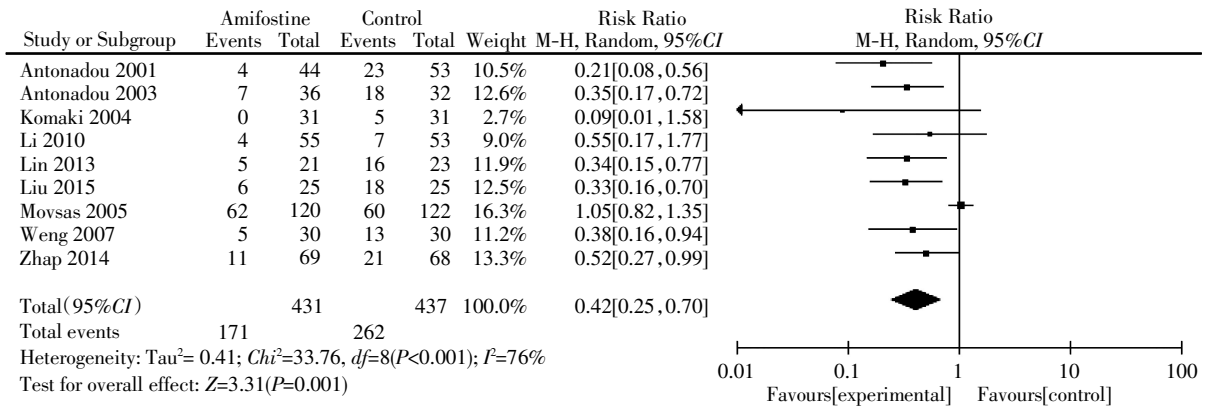

Fig.4 Forest plot of acute pulmonary toxicity (all grades) in patients with lung cancer who received radiotherapy or concomitant chemoradiation

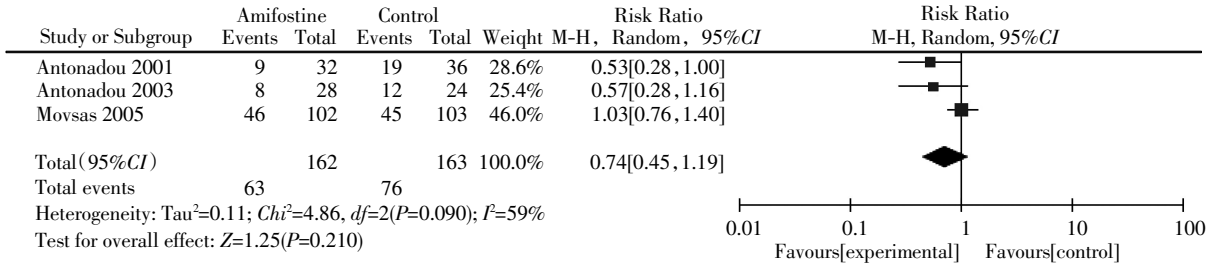

Fig.5 Forest plot of late pulmonary toxicity in patients with lung cancer who received radiotherapy or concomitant chemoradiation

Table 2 Subgroup analysis of radiation-induced side effects in accordance with treatment strategy

Subgroup	Acute esophageal		*P*	Acute pulmonary		*P*	Late pulmonary		*P*
	RR	95%*CI*		RR	95%*CI*		RR	95%*CI*	
Chemoradiation	0.67	0.49–0.93	0.020	0.44	0.21–0.95	0.040	0.84	0.48–1.46	0.540
Radiation only	0.20	0.05–0.80	0.020	0.38	0.25–0.58	0.001			

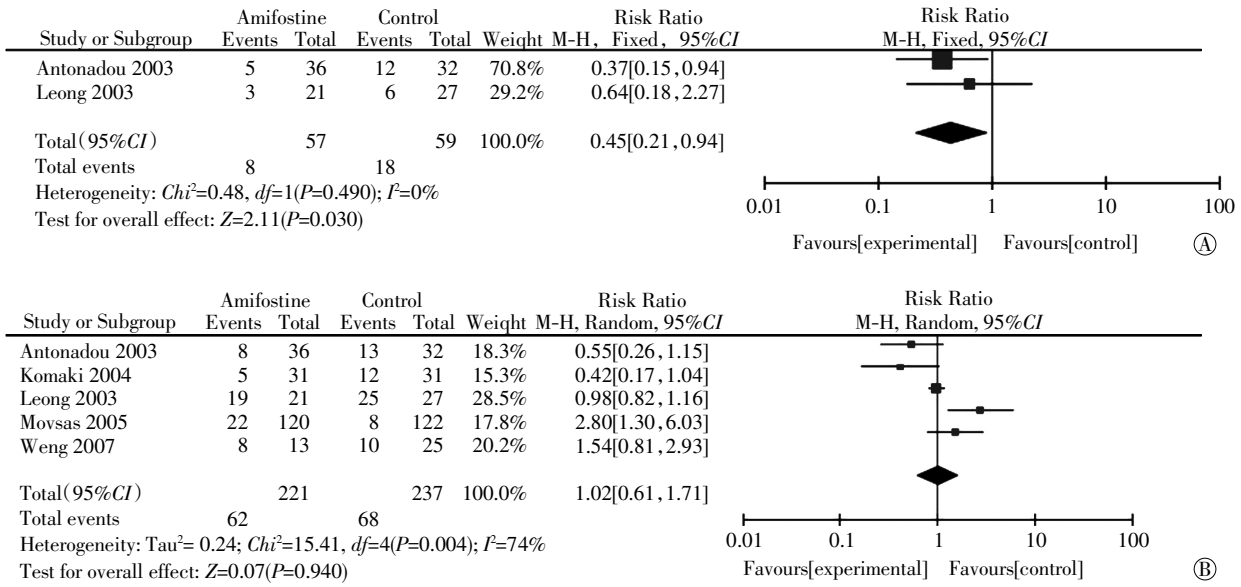

Fig.6 Forest plot of hematological toxicity in patients with lung cancer who received radiotherapy or concomitant chemoradiation(A: thrombocytopenia; B: neutropenia)

year overall survival nor two-year overall survival reached statistical significance (Fig.8).

2.8 Side effects of amifostine

Six studies[14–19] described amifostine toxicity. The

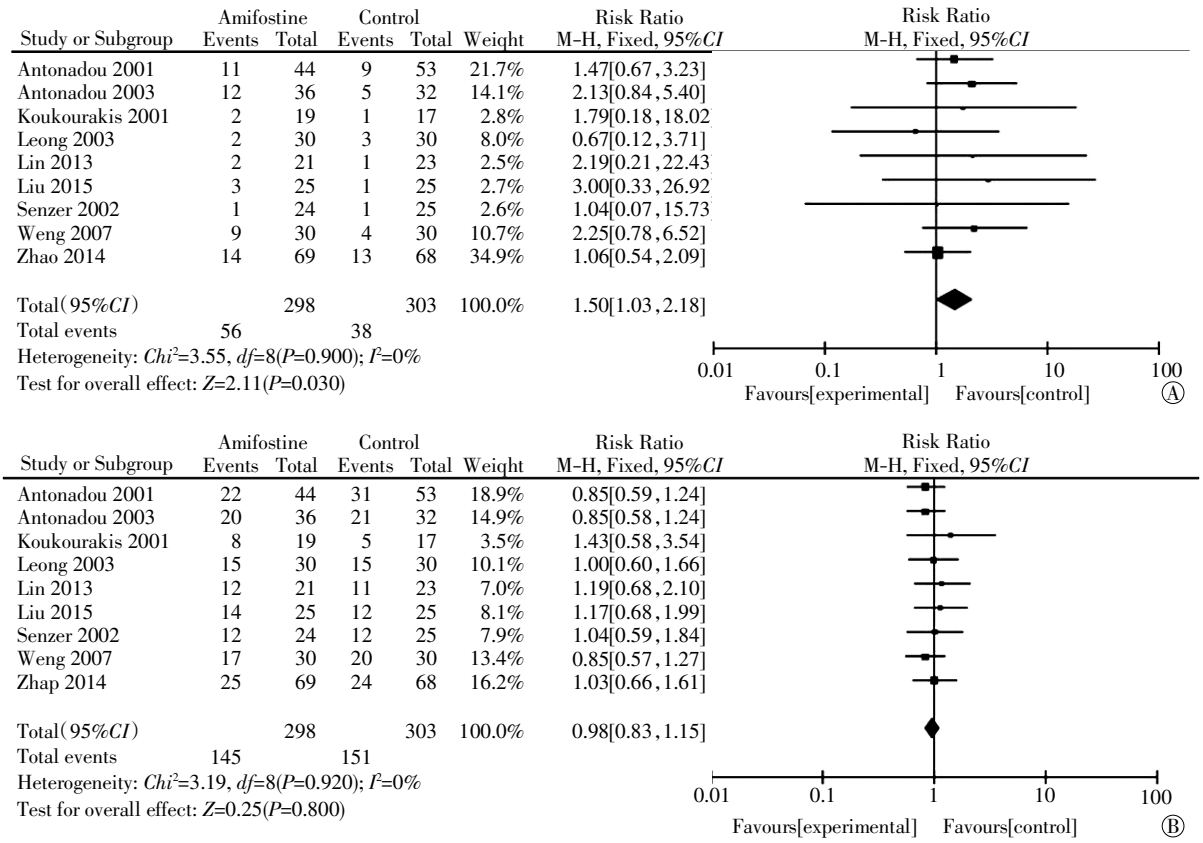

Fig.7 Forest plot of treatment response in patients with lung cancer who received radiotherapy or concomitant chemoradiation(A: Complete response; B: Partial response)

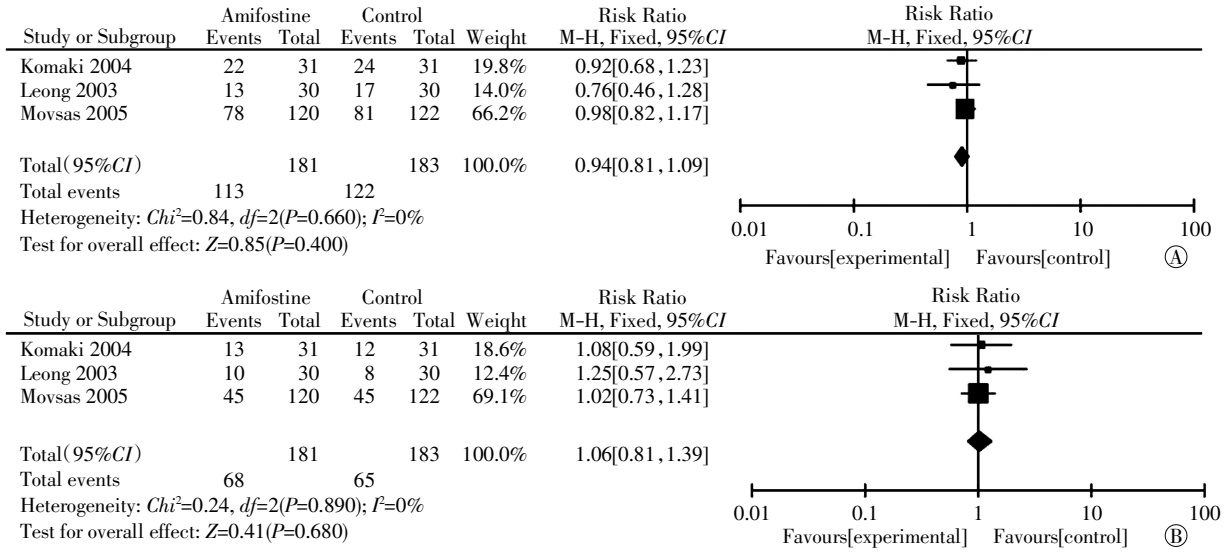

Fig.8 Forest plot of treatment response in patients with lung cancer who received radiotherapy or concomitant chemoradiation (A: one-year overall survival; B: two-year overall survival)

most common amifostine-related side effects included nausea, vomiting, and transient hypotension with average incidence rates of 11%, 14%, and 24%, respectively. However, amifostine toxicity can be controlled through clinical treatment or resting.

3 DISCUSSION

In 2016, lung cancer became the leading cause of cancer-related deaths worldwide and accounted for more than 21% of all cancer-related deaths. Most lung cancer

cases are diagnosed at advanced stages[21] and thus could not be treated through surgery. Chemotherapy with radiotherapy may be the most effective treatment strategy against lung cancer[22]. However, patients inevitably experience serious radiation-related toxicities, such as esophageal toxicity and pulmonary toxicity, as they receive increasing radiotherapy doses. In the 1950s, amifostine, a thiol-containing radioprotector, was initially developed as part of the nuclear warfare program. The cytoprotective mechanism of amifostine is complicated and involves free-radical scavenging, DNA protection and repair acceleration, and cellular hypoxia induction[23]. The US Food and Drug Administration has approved the use of amifostine as a cytoprotector in cisplatin chemotherapy and radiation-induced xerostomia[23]. However, whether amifostine can attenuate the severity of radiation-related toxicity without exerting tumor-protective effects remains controversial. Thus, we performed this systematic review and meta-analysis to compile inconsistent evidence for the assessment of the true clinical efficacy of this drug.

In this meta-analysis, we found that use of amifostine significantly reduced radiation-induced acute esophageal toxicity(P=0.002) and acute pulmonary toxicity(P=0.001). Subgroup analysis showed that the use of amifostine significantly reduced acute esophageal toxicity(P=0.020) and acute pulmonary toxicity (P<0.001) in patients receiving concurrent chemoradiation(P=0.020) and radiation only(P=0.020) (Table 2). However, the use of amifostine did not reduce late ulmonary toxicity(P=0.210). Subgroup analysis demonstrated that patients receiving concomitant chemoradiation do not derive benefit from amifostine in terms of reduced late pulmonary toxicity. Thus, amifostine can reduce acute esophageal toxicity and pulmonary toxicity in patients receiving concomitant chemoradiation and radiation only but cannot reduce late pulmonaryin patients receiving concomitant chemoradiation.

A major controversy for the clinical use of amifostine is its potential tumor-protective effect. Several pharmacological experiments have indicated that amifostine may exert a protective effect on tumor tissues by a lower degree than on normal tissues[8]. Some RCTs have shown that amifostine does not significantly influence treatment response[5, 17]. However, considering the realities of RCTs and clinical practice, absolutely negating the tumor-protective effects of amifostineis difficult. Therefore, we performed a meta-analysis to obtain an objective result from repeatedly inconsistent trials. We found no statistically significant difference in partial response(P=0.800) between the two treatment arms. Although we found that amifostine improved complete response(P=0.030), we observed publication bias through Egger′s test(P=0.000). Moreover, we did not find a statistically significant difference in one-year overall survival(P=0.400) and two-yeary overall survival (P=0.680). Therefore, we concluded that amifostine does not exert tumor-protective effects in radiation therapy.

Another controversial issue about amifostine is its related toxicities. The most common side effects of this drug include nausea, vomiting, or transient hypotension with incidences of 2%–70%[14–19]. Our study showed that the average incidences of nausea, vomiting, and hypotension are 11%, 14% and 24% respectively. However, amifostine toxicity can be controlled through clinical treatment or resting.

The results of this meta-analysis were based on published RCTs and not on the data of individual patients. Our results should therefore be interpreted with caution. Save for the result of complete response, no evidence of publication bias was observed through Egger′s test. Nevertheless, given the small number of trials and possible existence of unpublished studies, publication bias may be difficult to exclude completely.

Similar reviews of amifostine have been published in the past. Compared with previous studies, we included more updated RCTs in our study. We retrieved 1996 articles involving the entire patient population from the initial search. We ultimately analyzed 12 RCTs involving 1000 patients with lung cancer. The full texts ofall 12 trials were published in English or Chinese and were published in the period of 2000 to 2016. We then

performed a subgroup analysis of radiation-induced side effects in accordance with treatment strategy. Therefore, our meta-analysis may be more comprehensive and credible than previous meta-analyses given that we included a higher number of patients and we conducted subgroup analysis for further evaluation.

In conclusion, this systematic review demonstrated that the concurrent administration of amifostine with radiotherapy to patients with lung cancer significantly reduces acute esophageal toxicity, pulmonary toxicity, and thrombocytopenia without exerting any tumor-protective effects. Amifostine-related toxicities can be controlled through clinical treatment or resting. We should weigh the beneficial effects of the reduction in radiation-induced toxicities against the adverse effects of amifostine-related toxicities in accordance with individual treatment strategy. Our results indicated that amifostine has a continuously expanding role inradiation therapy. Well-designed RCTs are essential for exploring the potential benefits of amifostine in the future.

Conflict of interest The authors declare no conflicts of interest.

Authors contribution statement Treatment methods, and outcomes of the relevant trials were extracted by Huanan Wang and Feng Wang and checked by Yonghan Wang. Huanan Wang and Yonghan Wang extracted the data and assessed the methodological qualities of the trials from all included RCTs. Feng Wang was consulted to resolve any disagreements.

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《走近神秘的核医学——“核”协诊疗》出版发行

本书由上海市医学会核医学专科分会牵头编写，是一本核医学科普读物，从多方位、多角度介绍核医学相关知识，解答疑问，内容深入浅出，体现了科学性、通俗性和实用性。

全书分为“读经典”和“问名医”两部分。“读经典”由核医学资深专家、学科带头人用最通俗的语言、最生动的故事，讲述核医学独有的魅力；“问名医”收集了在核医学就诊的患者和家属最常见的疑问，由核医学科专家详细解答，涵盖了 PET/CT 应用、SPECT/CT 应用、甲状腺疾病、骨关节疾病等诊疗中的注意事项、方案选择，甚至包括疗程中的护理细节。本书旨在帮助大众读者了解核医学这门新兴学科，帮助患者安全、顺利的完成核医学检查和治疗。

本书由吕中伟教授、赵晋华教授主编，余飞教授、邢岩教授副主编，集合了 60 余位来自上海核医学专家和核医学科普委员的共同智慧，秉承健康科普教育的优良传统，全面普及核医学知识，使大众了解核医学的实用价值。

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（赵晋华　乔文礼）