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Analysis of treatment-related adverse events and wound complications of surgical resection after neoadjuvant chemoimmunotherapy for non-small cell lung cancer

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Abstract

Neoadjuvant chemoimmunotherapy is becoming an increasingly important part of the management of lung cancer to facilitate surgical resection. This study aimed to summarize the treatment-related adverse events (TRAEs) and wound complications of neoadjuvant chemoimmunotherapy in non-small cell lung cancer (NSCLC). Eligible studies of neoadjuvant chemoimmunotherapy for NSCLC were identified from PubMed, Embase and Web of Science. The endpoints mainly included TRAEs and wound complications. Stata18 software was used for statistical analysis with $p < 0.05$ considered statistically significant. Twenty studies including a total of 1072 patients were eligible for this study. Among the patients who received neoadjuvant chemoimmunotherapy, the pooled prevalence of any grade TRAEs was 77% (95% confidence interval [CI] [0.64–0.86]), grade 1–2 TRAEs was 77% (95% CI [0.58–0.89]) and grade ≥3 TRAEs was 26% (95% CI [0.16–0.38]). Surgery-related complications rate was 22% (95% CI [0.14–0.33]). Among the wound complications, the pooled rate of air leakage was 10% (95% CI [0.04–0.23]), pulmonary/wound infection was 8% (95% CI [0.05–0.13]), bronchopleural fistula was 8% (95% CI [0.02–0.27]), bronchopulmonary haemorrhage was 3% (95% CI [0.01–0.05]), pneumonia was 5% (95% CI [0.02–0.10]), pulmonary embolism was 1% (95% CI [0.01–0.03]), pleural effusion was 7% (95% CI [0.03–0.14]) and chylothorax was 4% (95% CI [0.02–0.09]). Overall, neoadjuvant chemoimmunotherapy in NSCLC results a high incidence of grade 1–2 TRAEs but a low risk of increasing the incidence of ≥3 grade TRAEs and wound complications. These results need to be confirmed by more large-scale prospective randomized controlled trials and studies.

Yihang Li is the lead author.

KEYWORDS
chemoimmunotherapy, neoadjuvant therapy, NSCLC, TRAEs, wound complication

Key Messages

- This meta-analysis summarized the treatment-related adverse events (TRAEs), severe adverse events and wound complications of neoadjuvant chemoimmunotherapy among 20 studies including a total of 1072 patients with non-small cell lung cancer (NSCLC).
- This study assessed the incidence of TRAEs including any grade TRAEs, grade 1–2 TRAEs and ≥3 grade TRAEs during neoadjuvant treatment and perioperative surgery according to the Common Terminology Criteria for Adverse Events.
- The study analysed the occurrence of wound complications such as air leakage, wound infection, bronchopleural fistula, bronchopulmonary haemorrhage, pneumonia, pulmonary embolism, pleural effusion and chylothorax in patients who underwent surgery after neoadjuvant treatment in NSCLC.

1 | INTRODUCTION

Lung cancer starts when abnormal cells grow in an uncontrollable way in lungs. It is a significant public health concern, causing a considerable number of deaths globally. According to the 2022 global cancer statistics, lung cancer is the leading cause of cancer death in humans.[1] Non-small cell lung cancer (NSCLC) is the most common lung cancers (including lung adenocarcinoma and lung squamous cell carcinoma), which accounts for about 85% of all lung cancers and small-cell lung cancer (SCLC) accounts for the remaining 15%.[2] About 70% patients with NSCLC are diagnosed at an advanced stage and the 5-year survival rate is less than 18%.[3] Patients suitable for complete surgical resection have a high risk of disease recurrence, ranging from 25% to 70%.[4] Despite surgery plus cisplatin-based adjuvant chemotherapy, only 4%–8% patients have a 5-year survival benefit.[4]

Neoadjuvant therapy is accepted as a practice before surgery, revolutionizing the treatment in NSCLC, especially for chemoimmunotherapy. In recent years, some clinical trials have been developed to evaluate the use of neoadjuvant chemoimmunotherapy. Some of these trials reported that the main pathological response rate of neoadjuvant chemoimmunotherapy has been significantly improved, and even reached complete pathological response (pCR). A meta-analysis concluded that compared with neoadjuvant single-agent immunotherapy, neoadjuvant chemoimmunotherapy significantly improves pathological responses without increasing severe adverse events (SAEs) or surgical delay.[3] Meanwhile, Ge et al. conducted that neoadjuvant chemoimmunotherapy achieved more pathological relief in NSCLC but caused higher treatment-related adverse events (TRAEs) and postoperative complications than neoadjuvant immune checkpoint inhibitors (ICIs) only.[5]

Neoadjuvant chemoimmunotherapy brings a new era to surgical treatment for patients with NSCLC. The neoadjuvant chemoimmunotherapy has brought efficacy and survival benefits, but the TRAEs and wound complications have still not stated clearly. Here, we focused on neoadjuvant chemoimmunotherapy in NSCLC and analysed the TRAEs, grade ≥3 TRAEs, and wound complications after neoadjuvant chemoimmunotherapy, so as to provide a reference for clinicians in the subsequent treatment of NSCLC.

2 | METHODS

2.1 | Search strategy

PubMed, Embase and Web of Science were searched from 1 January 2020 to 31 December 2023 to identify eligible studies with a search query combining terms as follows: (lung cancer OR non-small cell lung cancer) AND (neoadjuvant) AND (Chemotherapy OR immunotherapy OR chemoimmunotherapy or immunochemotherapy) AND (surgery OR resection). We also searched the 'clinicaltrials.gov' to identify the clinical trials and the updated data of ongoing clinical trials of neoadjuvant chemoimmunotherapy in NSCLC from international congresses up to 31 December 2023.

2.2 | Inclusion and exclusion criteria

According to the population, intervention, comparison, outcome and study (PICOS) criteria, inclusion criteria

were listed as follows: (i) population: patients diagnosed with resectable NSCLC; (ii) intervention: neoadjuvant chemoimmunotherapy before surgical resection; (iii) comparison: no restriction on whether control groups or intervention measures were set up; (iv) outcome: the basic characteristics of the included population and the primary endpoints such as TRAEs and wound complications; (v) study design: non-randomized controlled trials (non-RCTs), cohort studies, RCTs, conference abstracts of clinical trials. Exclusion criteria were as follows: (i) treatment with chemotherapy or immunotherapy alone or chemotherapy combined with other therapies other than immunotherapy; (ii) studies that did not report the TRAEs and wound complications; (iii) duplicate articles.

2.3 | Data extraction

The relevant data were extracted from eligible studies: (i) The characteristics of studies (first author, years of publication, the stage of NSCLC, basic study design, National Clinical Trial [NCT] number and study phase). (ii) Patient characteristics (simple size, age, gender, proportion of squamous-cell carcinoma). (iii) Neoadjuvant treatment regimens. (iv) Endpoints: adverse reactions (incidence of any grade TRAEs, grade 1–2 TRAEs, grade ≥3 TRAEs and incidence of wound complications).

2.4 | Statistical analyses

Meta-analysis was performed utilizing Stata18 software. Since most of the included studies were single-arm clinical trials, we performed meta-analysis with single rate meta-analysis with random-effects model. The effect size was all the pooled prevalence proportions with 95% confidence intervals (CIs). I^2 was ≥50% or p value was ≥0.10 indicated that the test of homogenous was significant.

3 | RESULTS

3.1 | The characteristics of studies

The flowchart of literature search and study selection was summarized in Figure 1. After removing duplicate and ineligible articles, 20 studies and 1072 NSCLC patients were finally enrolled. Among all these studies, nine studies were non-RCTs,[6–14] nine studies were prospective studies[15–23] and two studies were RCTs.[24,25] In clinical trials and studies, the cycle of neoadjuvant therapy was

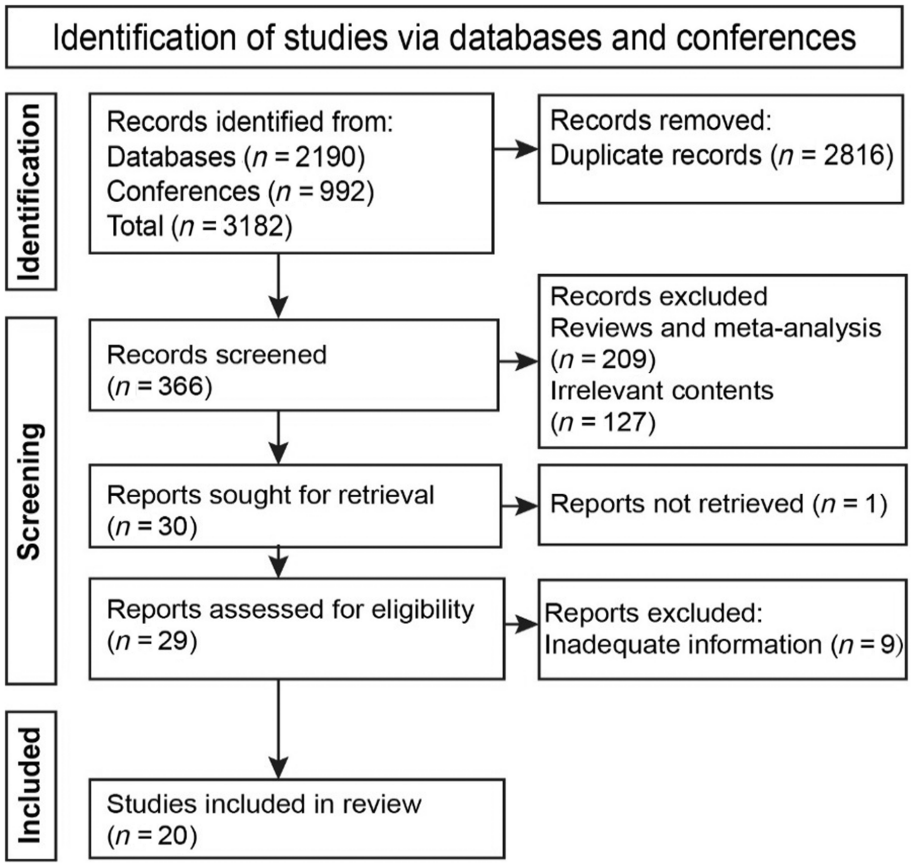

FIGURE 1 Flowchart of literature search and study selection.

between 2 and 4 cycles. The characteristics of included studies are presented in Table 1. This meta-analysis enrolled 1072 patients in NSCLC and 960 patients underwent surgery (Table 2). The median age was 63 years old. The proportion of males was 18%–96%, and squamous cell carcinoma ranged from 33% to 100%.

3.2 | The TRAEs of neoadjuvant chemoimmunotherapy

The TRAEs of neoadjuvant chemoimmunotherapy were presented in Figure 2 and summarized in Table 2. TRAEs and SAEs were evaluated according to the Common

TABLE 1 Studies characteristics of neoadjuvant chemoimmunotherapy in non-small cell lung cancer.

Study	Year	Stage	Neoadjuvant treatment regimen	Study design	NCT number	Study phase
Sun[6]	2023	IIIA/IIIB	2–3 circles of sintilimab + nab-paclitaxel + carboplatin	Single-centre, single-arm	NCT04326153	2
Shu[7]	2020	IB–IIIA	2–4 circles of atezolizumab + nab-paclitaxel + carboplatin	Multicentre, single-arm	NCT02716038	2
Provencio[8]	2020	IIIA	3 circles of nivolumab + paclitaxel + carboplatin	Multicentre, single-arm	NCT03081689	2
Zhang[9]	2022	IB–IIIA	2–4 circles of sintilimab + carboplatin + gemcitabine	Single-centre, single-arm	NR	2
Hou[10]	2022	II–IIIB	2–4 circles of toripalimab + platinum-paclitaxel	Single-centre, single-arm	NR	1
Zhao[11]	2021	IIIA or T3-4N2 IIIB	3 circles of toripalimab + carboplatin + pemetrexed/nab-paclitaxel	Single-centre, single-arm	NCT04304248	2
Zhu[12]	2022	II–III	2–4 circles of toripalimab + carboplatin	Single-centre, single-arm	NR	2
Rothschild[13]	2021	IIIA(N2)	3 circles of (cisplatin + docetaxel) + 2 circles of durvalumab	Multicentre, single-arm	NCT02572843	2
Yan[14]	2022	IIB–IIIB	2–4 circles of toripalimab + cisplatin-based chemotherapy	Single-centre, single-arm	NCT04606303	2
Hong[15]	2021	IIA–IIIC	2–4 cycles of neoadjuvant chemoimmunotherapy	Retrospective study	NR	NR
Wang[16]	2021	IIIA	2 circles of PD-1 inhibitors + albumin paclitaxel + carboplatin	Retrospective study	NR	NR
Fang[17]	2023	II–III	2 circles of PD-1 inhibitors + platinum	Retrospective study	NR	NR
Zhai[18]	2021	IIIA/IIIB	3 circles of nivolumab + paclitaxel + carboplatin	Retrospective study	NR	NR
Chen[19]	2022	IIIA/IIIB	4 cycles of pembrolizumab/2 cycles of Nivolumab + carboplatin + paclitaxel	Retrospective study	NR	NR
Chen[20]	2021	IIIA/IIIB	2 circles of pembrolizumab plus chemotherapy	Retrospective study	NR	NR
Shen[21]	2021	IIB–IIIB	2 circles of pembrolizumab + albumin-bound paclitaxel + carboplatin	Retrospective study	NR	NR
Tfayli[22]	2020	IB/II/IIIA	4 cycles of avelumab + 3 cycles of neoadjuvant chemotherapy	Retrospective study	NR	NR
Dai[23]	23	IB/IIIA/IIIB	2–4 cycles of neoadjuvant chemoimmunotherapy	Retrospective study	NR	NR
Forde[24]	2022	IB–IIIA	3 circles of nivolumab + platinum-based chemotherapy	Multicentre, randomized	NCT02998528	3
Provencio[25]	2022	IIIA	3 circles of nivolumab + paclitaxel + carboplatin	Multicentre, randomized	NCT03838159	2

Abbreviations: NCT, National Clinical Trial; NR, not reported.

TABLE 2 Patients characteristics and endpoints reported in studies.

Study	Sample size	Patients with resection	Median age (years)	Proportion of male (%)	Proportion of SCC (%)	Incidence of any grade TRAEs	Incidence of 1–2 grade TRAEs	Incidence of ≥ grade 3 TRAEs	Incidence of wound complications
Sun[6]	20	80% (16/20)	59.5 (34–71)	90% (18/20)	80% (16/20)	70% (14/20)	35% (7/20)	35% (7/20)	NR
Shu[7]	30	97% (29/30)	67 (62–74)	50% (15/30)	40% (12/30)	NR	NR	NR	NR
Provencio[8]	46	89% (41/46)	63 (58–70)	74% (34/46)	35% (16/46)	93% (43/46)	NR	30% (14/46)	29% (12/41)
Zhang[9]	50	60% (30/50)	64.84 ± 9.61	88% (44/50)	56% (28/50)	90% (45/50)	90% (45/50)	8% (4/50)	3% (1/30)
Hou[10]	11	100% (11/11)	63 (51–71)	91% (10/11)	82% (9/11)	45% (5/11)	NR	18% (2/11)	NR
Zhao[11]	33	91% (30/33)	61 (56–66)	18% (6/33)	55% (18/33)	NR	NR	18% (6/33)	NR
Zhu[12]	50	72% (36/50)	66 (57.8–68.0)	84% (42/50)	64% (32/50)	96% (48/50)	62% (31/50)	34% (17/50)	14% (5/36)
Rothschild[13]	67	82% (55/67)	61 (41–74)	52% (35/67)	33% (22/67)	100% (67/67)	NR	88% (59/67)	NR
Yan[14]	53	74% (39/53)	62 (45–76)	91% (48/53)	79% (42/53)	NR	94% (46/49)	31% (15/49)	NR
Hong[15]	25	100% (25/25)	62 (51–83)	92% (23/24)	76% (19/25)	52% (13/25)	NR	NR	52% (13/25)
Wang[16]	72	100% (72/72)	62.2 (42–76)	92% (66/72)	92% (66/72)	NR	NR	NR	NR
Fang[17]	211	100% (211/211)	64 (38–77)	93% (196/211)	82% (172/211)	46% (98/211)	NR	13% (13/98)	NR
Zhai[18]	46	98% (45/46)	63 (56–73)	57% (26/46)	59% (27/46)	NR	83% (38/46)	20% (9/46)	NR
Chen[19]	12	100% (12/12)	61 (55.25–66.75)	75% (9/12)	33% (4/12)	33% (4/12)	NR	NR	NR
Chen[20]	35	100% (35/35)	62.17 ± 5.99 (43–72)	83% (29/35)	75% (26/35)	NR	NR	3% (1/35)	NR
Shen[21]	37	100% (37/37)	62.8 (38–76)	95% (35/37)	100% (37/37)	70% (26/37)	NR	NR	NR
Tfayli[22]	15	73% (11/15)	65 (45–80)	47% (7/15)	13% (2/15)	NR	NR	27% (4/15)	NR
Dai[23]	23	100% (23/23)	63.2 ± 7.0	96% (22/23)	78% (18/23)	74% (17/23)	74% (17/23)	9% (2/23)	13% (3/23)
Forde[24]	179	83.2%% (149/179)	64 (41–82)	72% (128/179)	49% (87/179)	82% (145/179)	NR	NR	42% (62/149)
Provencio[25]	57	93% (53/57)	65 (58–70)	63% (36/57)	37% (21/57)	88% (50/57)	NR	19% (11/57)	NR

Abbreviation: NR, not reported.

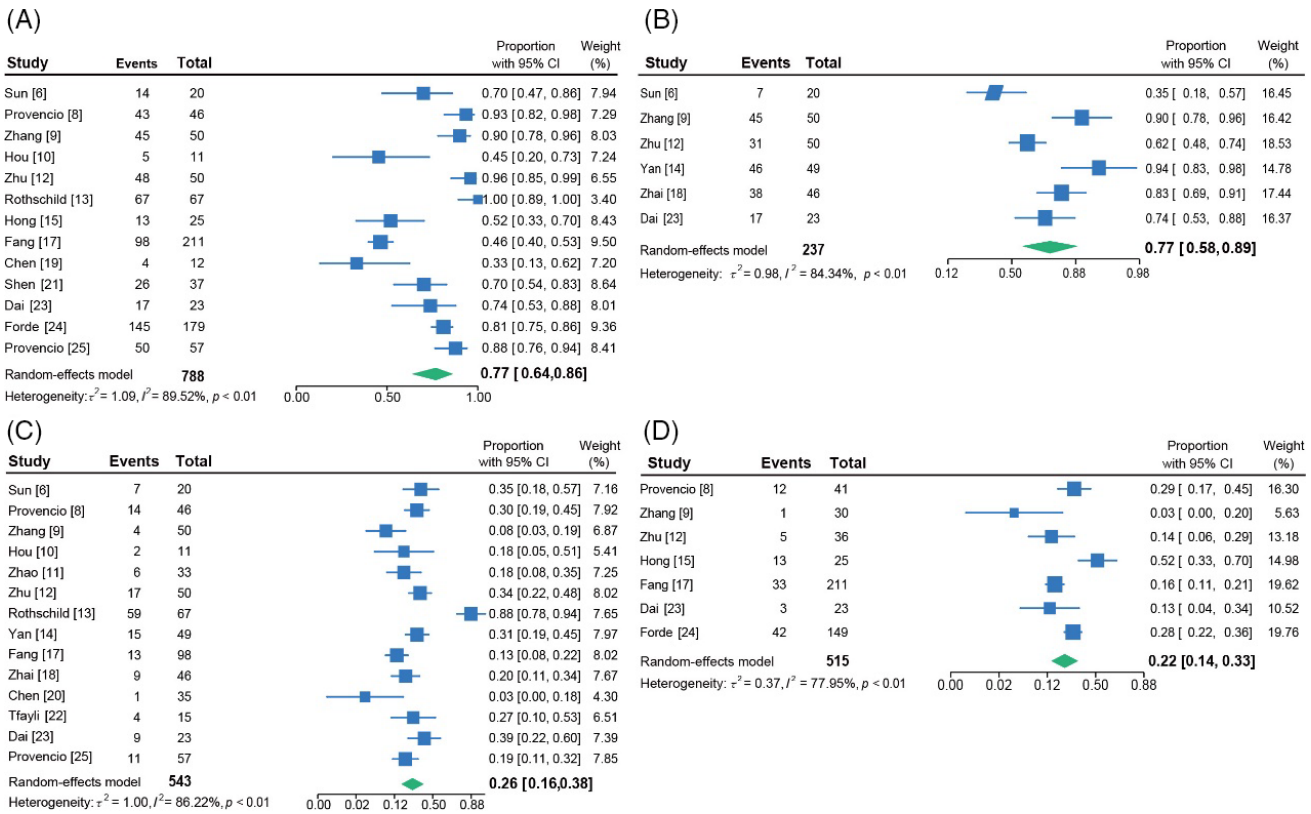

FIGURE 2 Forest plots of the treatment-related adverse events (TRAEs) of neoadjuvant chemoimmunotherapy. (A) The pooled any grade TRAEs rate; (B) the pooled rate of grade 1–2 TRAEs; (C) the pooled rate of grade ≥3 TRAEs. (D) The pooled incidence of surgical complications. CI, confidence interval.

Terminology Criteria for Adverse Events (CTCAE). SAEs were defined as grade 3–5 TRAEs. Thirteen studies provided the incidence of any grade TRAEs and the pooled TRAEs rate was 77% (95% CI [0.63–0.87], $I^2 = 90\%$, $p < 0.01$), ranging from 33% to 100% (Figure 2A). Five studies reported that the pooled rate of grade 1–2 TRAEs ranged from 35% to 94% with a pooled incidence of 77% (95% CI [0.55–0.91], $I^2 = 84\%$, $p < 0.01$) (Figure 2B). The pooled rate of grade ≥3 TRAEs was 25% (95% CI [0.15–0.38], $I^2 = 86\%$, $p < 0.01$; Figure 2C). Surgical complications were observed in 109 of 515 patients who underwent surgery and the pooled incidence of surgical complications was 23% (95% CI [0.14–0.35], $I^2 = 78\%$, $p < 0.01$), ranging from 3% to 52% (Figure 2D).

3.3 | Wound complications of neoadjuvant chemoimmunotherapy after surgery

The meta-analysed forest plots of wound complications are shown in Figure 3 and summarized in Table 3. Among all perioperative complications, the occurrence of wound complications can lead to serious adverse consequences and even death. We conducted a meta-analysis of wound complications including air leakage, pulmonary/wound infection, bronchopleural fistula, bronchopulmonary haemorrhage, pneumonia, pulmonary embolism, pleural effusion and chylothorax for these studies. The pooled rate of air leakage in six studies of 362 patients was 10% (95% CI [0.04–0.23], $I^2 = 81\%$, $p < 0.01$), ranging from 3% to 28% (Figure 3A). Seven studies provided that the pooled rate of pulmonary/wound infection, ranging from 0% to 14%, was observed in 17 of 254 patients (8%, 95% CI [0.05–0.13], $I^2 = 0\%$, $p = 0.51$) (Figure 3B). The pooled rate of bronchopleural fistula was 8% (95% CI [0.02–0.27], $I^2 = 0\%$, $p = 0.03$), ranging from 3% to 20% (Figure 3C). Among the 393 patients, the incidence of bronchopulmonary haemorrhage was 3% (95% CI [0.01–0.05], $I^2 = 0\%$, $p = 0.42$) (Figure 3D). The rate of pneumonia ranged from 1% to 20% with a pooled incidence of 5% (95% CI [0.02–0.10], $I^2 = 60\%$, $p = 0.02$) (Figure 3E). The pooled rate of pulmonary embolism, ranging from 1% to 3%, was observed in 5 of 423 patients (1%, 95% CI [0.01–0.03], $I^2 = 0\%$, $p = 0.66$) (Figure 3F). The pooled rate of pleural effusion was 7% (95% CI [0.03–0.14], $I^2 = 67\%$, $p = 0.05$) (Figure 3G), ranged from 3% to 11% and chylothorax

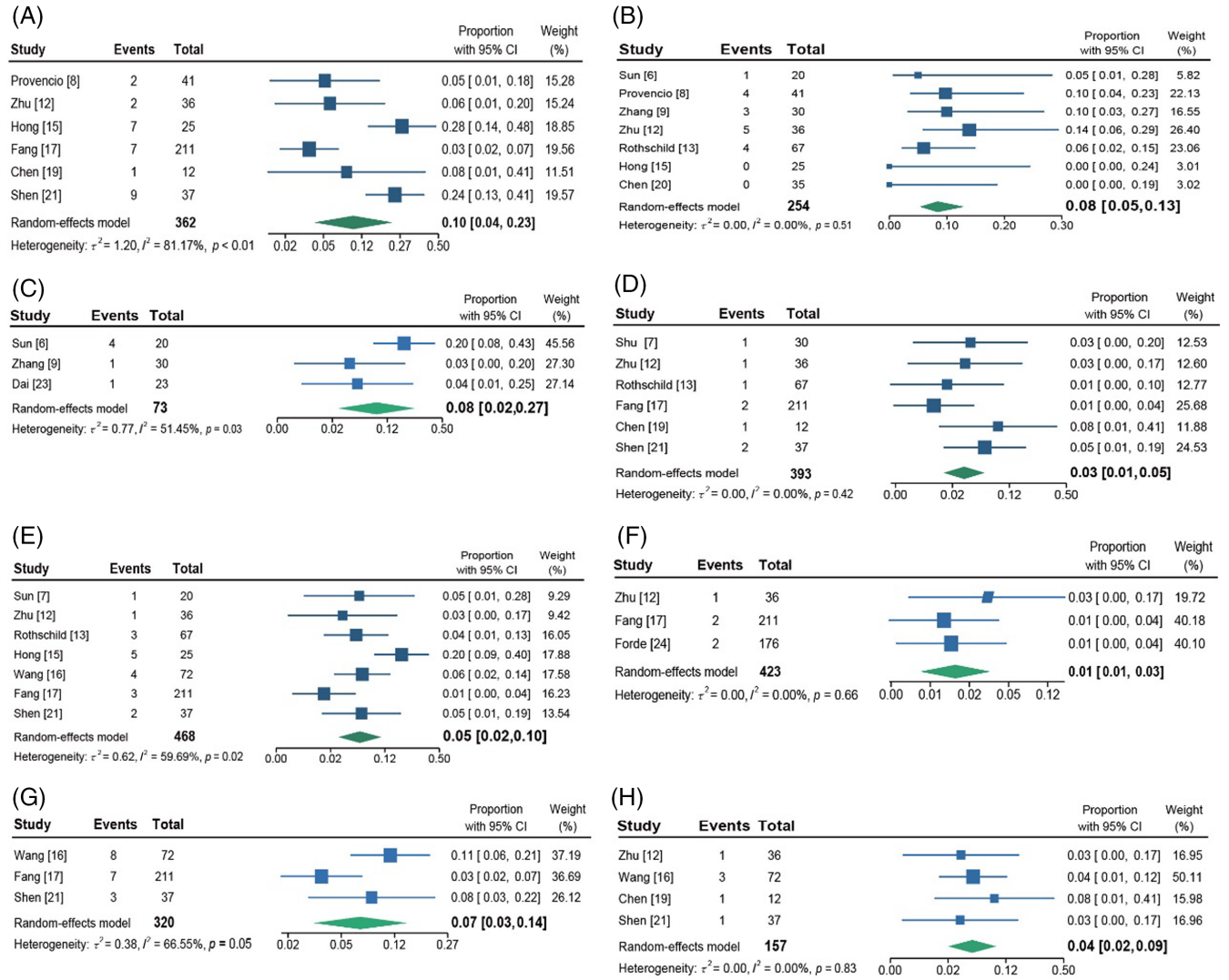

FIGURE 3 Forest plots of wound complications of neoadjuvant chemoimmunotherapy after surgery. (A) The pooled rate of air leakage; (B) the pooled rate of pulmonary/wound infection; (C) the pooled rate of bronchopleural fistula; (D) the pooled rate of bronchopulmonary haemorrhage; (E) the pooled rate of pneumonia; (F) the pooled rate of pulmonary embolism; (G) the pooled rate of pleural effusion; (H) the pooled rate of chylothorax.

pooled incidence was 4% (95% CI [0.02–0.09], $I^2 = 0\%$, $p = 0.83$) (Figure 3H), ranged from 3% to 8%.

4 | DISCUSSION

This study conducted a meta-analysis of 20 studies focusing on neoadjuvant chemoimmunotherapy in resectable NSCLC. The data showed that the treatment adverse events of grade 1–2 and ≥3 grade of chemoimmunotherapy were respectively 77% and 25%. The pooled incidence of surgical complications was 23%, ranging from 3% to 52%. Overall, neoadjuvant chemoimmunotherapy had acceptable adverse events in patients with NSCLC.

Neoadjuvant therapy has been seen as an approach, which could potentially improve survival in patients with NSCLC. In recent years, increasing number of clinical trials are exploring the efficacy and safety of neoadjuvant chemotherapy, ICIs or combination therapies such as chemoimmunotherapy and dual ICIs in NSCLC using different treatment regimens. In 2022, a meta-analysis published the results and reported the efficacy and safety of neoadjuvant immunotherapy in NSCLC.[5] Among a total of 358 patients in 13 studies, 157 (72%) patients who received chemoimmunotherapy showed a higher incidence of TRAEs, while 37 (26.4%) patients who received neoadjuvant ICIs only experienced TRAEs. Moreover, more postoperative complications were observed in the

TABLE 3 Summary of the meta-analysis results.

	Included studies	Events	Total	Proportion of 95% CI	Heterogeneity (I^2)	*p* Value
Any grade TRAEs	[6,8–10,12,13,15,17,19,21,23–25]	575	788	0.77 [0.64–0.86]	89.52%	<0.01
Grade 1–2 TRAEs	[6,9,12,14,18,23]	184	237	0.77 [0.58–0.89]	84.34%	<0.01
Grade ≥3 TRAEs	[6,8–14,17,18,20,22,23,25]	171	543	0.26 [0.16–0.38]	86.22%	<0.01
Surgical complications	[8,9,12,15,17,23,24]	109	515	0.22 [0.14–0.33]	77.95%	<0.01
Air leakage	[8,12,15,17,19,21]	28	362	0.10 [0.04–0.23]	81.17%	<0.01
Pulmonary/wound infection	[6,8,9,12,13,15,20]	17	254	0.08 [0.05–0.13]	0.00%	0.51
Bronchopleural fistula	[6,9,23]	6	73	0.08 [0.02–0.27]	51.45%	0.03
Bronchopulmonary haemorrhage	[7,12,13,17,19,21]	8	393	0.03 [0.01–0.05]	0.00%	0.42
Pneumonia	[7,12,13,15–17,21]	19	468	0.05 [0.02–0.10]	59.69%	0.02
Pulmonary embolism	[12,17,24]	5	423	0.01 [0.01–0.03]	0.00%	0.66
Pleural effusion	[16,17,21]	18	320	0.07 [0.03–0.14]	66.55%	0.05
Chylothorax	[12,16,19,21]	6	157	0.04 [0.02–0.09]	0.00%	0.83

Abbreviation: TRAEs, treatment-related adverse events.

neoadjuvant chemoimmunotherapy (18.9%, 35/185) group than neoadjuvant ICIs (11.9%, 15/140) group.[5] CheckMate 816 trial[24] demonstrated that the adverse events of any causes occurred in 92.6% of the patients in the chemoimmunotherapy group and in 97.2% of those in the chemotherapy-alone group and the incidence of grade 3 or 4 TRAEs was 33.5% and 36.9% in the respective groups. Wound complications occurred in 41.6% of the patients in the chemoimmunotherapy group and in 46.7% of those in the chemotherapy-alone group.[24] However, a trial reported that adverse events of any grade occurred during neoadjuvant treatment were 88% (50/57) in the chemoimmunotherapy group and 90% (26/29) in the chemotherapy-alone group and grade 3 or 4 adverse events that occurred were 19% (11/57) and 10% (3/29) in respective groups.[25] Notably, one patient from chemoimmunotherapy group died due to the wound complications 13 days after surgery.[25] A retrospective study reported that among three patients with wound complications, one patient who underwent surgery after chemoimmunotherapy died of bronchopleural fistula.[23] A phase 2 randomized NEOSTAR trial presented that Grade 3–5 TRAEs were reported in 13% (3/23) of patients treated with nivolumab and 10% (2/21) of patients treated with nivolumab + ipilimumab.[26] According to these trials, the occurrence of TRAEs and wound complications remains controversial and unclear.

Our study aimed to summarize the TRAEs and wound complications of neoadjuvant chemoimmunotherapy in NSCLC. We enrolled 20 studies including a total of 1072 patients for the meta-analysis. For patients who received neoadjuvant chemoimmunotherapy, the pooled prevalence of TRAEs (any grade) was 77% (95% CI [0.64–0.86]), grade 1–2 TRAEs was 77% (95% CI [0.58–0.89]) and grade ≥3 TRAEs was 26% (95% CI [0.16–0.38]). Surgery-related complications rate was 22% (95% CI [0.14–0.33]) in seven studies that provided postoperative complications. Based on these results, neoadjuvant chemoimmunotherapy in NSCLC leads a relatively high incidence of grade 1–2 TRAEs but low incidence of ≥3 grade TRAEs and wound complications. Inevitably, perioperative TRAEs and wound complications will have a serious impact on patients with NSCLC, affecting their survival and prognosis. Therefore, neoadjuvant chemoimmunotherapy regimens should be evaluated comprehensively for individual benefits and safety when applied to clinical practice.

The limitations of this study still existed. Firstly, most clinical studies of neoadjuvant chemoimmunotherapy are phase I/II small-sample non-randomized single-arm trials. Different chemotherapeutic regimens and ICIs led to a relative high heterogeneity, making subgroup analysis difficult to conduct. Secondly, the follow-up time of these studies was relatively short, resulting a limited data on adverse outcomes. Finally, the included studies provided incomplete data on the key endpoints including TRAEs and wound complications, and some have not reached the endpoint data. Thus, more large-scale, prospective and long-term follow-up studies are still needed.

5 | CONCLUSION

This meta-analysis demonstrated the TRAEs and wound complications of neoadjuvant chemoimmunotherapy. Compared with single-agent neoadjuvant immunotherapy or chemotherapy, neoadjuvant chemoimmunotherapy provide an impressive improvement in pathological response, but the risk of the SAEs or wound complications need to be further confirmed by more clinical trials. Our data support the potential application of neoadjuvant chemoimmunotherapy for resectable NSCLC. However, the effect on long term survival and recurrence has been not to be presented. There are many frequent TRAEs and wound complications related to chemoimmunotherapy which should be treated cautiously even though significance was not found in our study.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The data are available from the corresponding author upon reasonable request.

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