Pathologic Response and Surgical Outcomes of Neoadjuvant Immunochemotherapy in Locally Advanced NSCLC: A Single-Center, Retrospective Study

KAILEI WANG
Guangdong Medical University
LINHUI WANG
Department of Thoracic Surgery, Yuebei People's Hospital, Guangdong Medical University
RENPING WAN
Department of Thoracic Surgery, Yuebei People's Hospital, Guangdong Medical University
HUIYONG CHEN
chy03022021@163.com

Guangdong Medical University

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Abstract

The present study aimed to observe the efficacy and safety of neoadjuvant immunocombination chemotherapy (nICT) in patients with locally advanced resectable non-small cell lung cancer (NSCLC). Patients who received nICT combined with chemotherapy followed by radical surgery at Yuebei People's Hospital, Guangdong Medical University, from November 2020 to November 2024, were enrolled in the present study. The primary endpoint was major pathological response (MPR), while secondary endpoints included pathological complete response (pCR), R0 resection rate and safety outcomes. A total of 48 patients with NSCLC receiving nICT were enrolled, consisting of 41 males and 7 females, aged 41–73 years. All patients successfully completed surgery without delay. The pCR rate was 25.0% [12/48; 95% confidence interval (CI), 13.6–39.6%], the MPR rate was 41.7% (20/48; 95% CI, 27.6–56.8%) and the R0 resection rate was 97.9% (47/48; 95% CI, 88.9–99.9%). There were no operative deaths; however, one case was converted to thoracotomy due to intraoperative bleeding. Patients exhibited favorable safety profiles during both the nICT and post-operative period. Collectively, findings of the present study demonstrated that nICT for locally advanced NSCLC exhibits favorable efficacy and safety profiles. Although the single-arm design precludes direct comparative analyses, the observed response rates were superior to historical control data; therefore, randomized controlled trials are warranted to further validate these results.

Introduction

Lung cancer remains one of the most aggressive malignancies. According to the latest global cancer statistics (GLOBOCAN 2022), it ranks first in incidence with approximately 2.48 million new cases annually, and first in mortality, causing an estimated 1.82 million deaths each year. This stark disparity between incidence and mortality underscores its aggressive nature and the significant challenges it poses to public health worldwide (1). At present, non-small cell lung cancer (NSCLC) is the predominant histological subtype. For resectable NSCLC cases, surgical resection is considered the primary treatment modality; however, surgery alone is associated with substantial risks of recurrence and metastasis (2). While chemotherapy has been widely adopted as a standard pre-operative approach, the impact on long-term survival remains limited (3). Comparative studies demonstrated that neoadjuvant chemoradiotherapy (nCRT) does not significantly improve survival compared with chemotherapy alone followed by surgery (4). Therefore, further investigations that explore more effective adjuvant strategies to improve surgical outcomes, reduce post-operative recurrence and increase five-year survival rates are required. The introduction of immune checkpoint inhibitors (ICIs) has transformed treatment approaches for advanced and recurrent NSCLC, demonstrating high levels of efficacy, particularly in advanced-stage disease (5). These breakthroughs have provided a strong rationale for incorporating ICIs into neoadjuvant strategies. The CheckMate-816 trial (6) highlighted that a combination of immunotherapy with chemotherapy significantly improved pathological complete response (pCR) rates, major pathological response (MPR) and event-free survival compared with chemotherapy alone. Previous studies corroborated the favorable safety and tolerability profiles of neoadjuvant immunocombination chemotherapy (nICT) in NSCLC (7-9). Moreover, the KEYNOTE-671

study revealed that nICT not only achieved superior pathological responses, but also exhibited lower rates of grade 3-4 adverse events compared with chemotherapy alone, with the majority of toxicities being mild in severity (grade 1-2) (10).

Results of a previous study indicated that nICT induced significant pathological regression without increasing surgical risks or severe adverse events, indicative of a potential therapeutic advancement (11). Therefore, to further evaluate the potential real-world clinical value, the present study retrospectively analyzed post-operative outcomes in patients with NSCLC who received nICT followed by surgery. Primary endpoints included MPR (≤10% viable tumor cells), pCR (0% viable tumor cells) and treatment-related adverse events. Through comprehensive assessment of the aforementioned parameters, the present study aimed to provide robust clinical evidence regarding the efficacy and safety of this combined modality approach.

Materials and methods

Patients. In total, 48 patients with NSCLC who underwent nICT followed by radical surgery from November 2020 to November 2024 at Yuebei People's Hospital of Guangdong Medical University were retrospectively analyzed. The inclusion criteria were as follows: i) Pathological examination to confirm the diagnosis of NSCLC prior to receiving nICT; ii) clinical staging of T1N + M0 ~ T3-4N0-2/M0 (Stage II-IIIB), according to the 8th edition of the TNM staging system for NSCLC of the American Joint Committee on Cancer (AJCC; 2018) (12); and iii) no history of any antitumor therapy following diagnosis until nICT. Patients were excluded according to the following criteria: i) Age < 18 years or > 80 years; ii) the presence of other malignant tumors; iii) a history of intra-abdominal surgery or intrathoracic surgery; iv) the presence of immune system defects or autoimmune diseases; v) previous immunosuppressive therapy; vi) abnormal function of the liver, kidneys, bone marrow or organic damage of other organs; vii) abnormal cardiopulmonary function or inability to tolerate surgery; viii) notable signs of infection prior to treatment; ix) a lack of radical surgical resection following nICT; and x) incomplete data.

All patients received nICT combination treatment with a treatment cycle of 21 days. Chemotherapeutic drugs were included once in three cycles and included albumin bound paclitaxel (single dose, 260 mg/m^2 D1), docetaxel (75 mg/m^2 D1), pemetrexed (500 mg/m^2 D1) or gemcitabine (1,000 mg/m^2 D1, D8). Patients may have also been treated with carboplatin [single dose, AUC (mg/ml/min) x (creatinine clearance (ml/min) + 25); D1], cisplatinum complexes (single dose, 75 mg/m^2) or an immunotherapy regimen (PD-1 or PD-L1 inhibitor, such as sindilizumab 200 mg Q3W, tirilizumab 200 mg Q3W, karelizumab 200 mg or PD-L1 monoclonal antibody 200 mg Q3W, SHR-1316). Treatment selection guidelines were as follows: Patients with squamous cell carcinoma received albumin-bound paclitaxel plus platinum-based therapy; patients with non-squamous adenocarcinoma without driver mutations received pemetrexed plus platinum-based therapy; patients who were contraindicated for paclitaxel received docetaxel plus platinum-based therapy; and patients contraindicated for paclitaxel received docetaxel plus platinum-based therapy. Gemcitabine plus platinum-based therapy was only indicated in the following two scenarios: i) Previous exposure to albumin-bound paclitaxel, docetaxel or pemetrexed

that resulted in grade ≥ 3 allergic reactions or severe neurotoxicity; and ii) concurrent moderate-to-severe renal impairment (eGFR 30–49 ml/min) requiring avoidance of cisplatin. The selection of PD-1/PD-L1 inhibitors was based on the medical insurance reimbursement directory and the economic capacity of the patient. For example, patients with medical insurance were treated with sintilimab or tislelizumab, and those who did not have medical insurance were treated with camrelizumab or the PD-L1 antibody, SHR-1316. Notably, nICT varied from two to five cycles. Blood was collected prior to and following each cycle for cytological and biochemical analysis. After the 2nd and 4th cycles of nICT, routine blood tests, liver and renal functions, tumor markers, nail function, cardiac enzymes, magnetic resonance imaging (MRI)/computed tomography (CT) scanning of the head, CT scanning of the chest and upper abdomen, electrocardiograms and pulmonary function tests were performed to rule out contraindications to surgery. Subsequently, surgery was performed. Surgical approaches were discussed and decided by the department and the operation was performed by an appropriately qualified physician.

Prior to nICT, and following the 2nd and 4th cycles of treatment, patients were examined. Notably, if patients received three cycles of treatment, they were examined following the end of the treatment. Examinations included hematological analysis and imaging, such as CT scans of the chest and abdomen, and MRI. Efficacy and adverse reactions were analyzed using the RECIST 1.1 and NCICTAE grading standards, respectively, and complete remission (CR) and adverse reactions were recorded. CR was defined as the complete disappearance of all lesions and the normalization of tumor markers. Partial response (PR) was defined as the disappearance of all measurable target lesions and the normalization of tumor markers when compared with the baseline. Moreover, PR was also defined as a reduction of ≥ 30% in the diameter of all measurable target lesions compared with baseline, indicative of disease improvement. Stable disease (SD) was defined as a reduction of < 30% in the sum of target lesion diameters and an increase of ≤ 20% in the diameter of the target lesions compared with baseline, suggesting that the disease had not worsened or improved significantly. According to the Expert Consensus on Pathological Evaluation of the Efficacy of nICT for NSCLC, pCR referred to the absence of live tumor cells in the tumor bed and lymph nodes following nICT. MPR was defined as ≤ 10% residual live tumor cells in the tumor bed regardless of the status of lymph nodes following nICT. This was considered successful treatment.

In the present study, the primary endpoint was MPR rate. Secondary endpoints included pCR rate and objective response rate (ORR), defined as the percentage of PR + CR. In addition, secondary endpoints included disease control rate (DCR), defined as the percentage of CR + PR + SD, and the safety of surgery following nICT.

Statistical analysis. Statistical analysis was performed using SPSS (version, 27.0; IBM Corp.) and R 4.3.2 software, with two-sided Student's t-tests and $\alpha = 0.05$. Quantitative data were initially compared using Shapiro-Wilk normality tests. Data that met the criteria for normal distribution were expressed as the mean ± standard deviation, while those that did not were expressed as the median and interquartile range. Categorical data were expressed as frequencies (%) and reported with 95% CIs following the Clopper-Pearson method. The primary endpoint; namely, MPR; and secondary endpoints; namely, pCR,

R0 resection rate, ORR and DCR, were all reported as proportions with 95% CIs. Categorical variables were compared using Pearson's χ^2 test, Yates' correction or Fisher's exact test. Continuous variables were analyzed using Student's t-tests or Mann-Whitney U tests. Missing data were described but not included in comparisons. $P < 0.05$ was considered to indicate a statistically significant difference.

Table 1
Clinical characteristics of patients included in the present study.

Characteristic	n (%)
Age, years	
<60	20 (41.7)
≥60	28 (58.3)
Sex	
Male	41 (85.4)
Female	7 (14.6)
Smoking history	
Yes	23 (47.9)
No	25 (52.1)
Pathological type	
Squamous cell carcinoma	32 (66.7)
Adenocarcinoma	11 (22.9)
Other	5 (10.4)
Tumor site	
Right lung	32 (66.7)
Left lung	16 (33.3)
T-stage	
cT1	4 (8.3)
cT2	12 (25.0)
cT3	19 (39.6)
cT4	13 (27.1)
N-stage	
N0	2 (4.2)
N1	12 (25.0)
N2	33 (68.8)
N3	1 (2.1)
Clinical staging	

Characteristic	n (%)
II	6 (12.5)
III	40 (83.3)
IV	2 (4.2)
Post-operative treatment	
Yes	44 (91.7)
No	4 (8.3)
Neoadjuvant combination immunotherapy regimen	
Albumin-paclitaxel combination regimen	21 (43.8)
Docetaxel combination regimen	15 (31.2)
Pemetrexed combination regimen	10 (20.8)
Gemcitabine combination	2 (4.2)
Number of treatment cycles	
<3 cycles	19 (39.6)
≥3 cycles	29 (60.4)
Continuation of treatment following surgery	
Yes	44 (91.7)
No	4 (8.3)

Table 2
Use of chemotherapeutic agents with PD-1/PD-L1 immune checkpoint inhibitors.

Chemotherapy	Immunotherapy			
	Sindilizumab, n	Tirilizumab, n	Karelizumab, n	PD-L1 monoclonal antibody, SHR-1316, n
Albumin-bound Paclitaxel + platinum	11	3	3	4
Docetaxel + platinum	6	4	5	0
Pemetrexed + platinum	2	4	2	2
Gemcitabine + platinum	2	0	0	0
The numerical values in the table represent the number of patients who received the corresponding drug treatments.				

Table 3
Efficacy analysis of neoadjuvant treatment and surgery in patients.

Characteristic	95% CI	
Imaging expression following neoadjuvant treatment		
CR	0.0-7.4%	0 (0.0)
PR	58.2–84.7%	35 (72.9)
SD	13.6–39.6%	12 (25.0)
PD	0.1–11.1%	1 (2.1)
ORR	58.2–84.7%	72.9
DCR	88.9–99.9%	97.9
Post-operative T-stage		
0 stage	12.0-37.3%	11 (22.9)
cT1	20.4–48.4%	16 (33.3)
Ct2	17.0-44.1%	14 (29.2)
cT3	3.5–22.7%	5 (10.4)
cT4	0.5–14.3%	2 (4.2)
Post-operative N stage		
pN0 stage	58.2–84.7%	35 (72.9)
pN1 stage	4.7–25.2%	6 (12.5)
pN2 stage	6.1–27.8%	7 (14.6)
Pathological expression		
PCR	13.6–39.6%	12 (25.0)
pT0/TisN + M0	0.1–11.1%	1 (2.1)
MPR	27.6–56.8%	15 (31.3)
No-MPR	43.2–72.4%	20 (41.7)
All percentage-based endpoints were reported with 95% CI calculated using the exact Clopper-Pearson method.		

Table 4
Subgroup analysis of patient baseline information using MPR and no-MPR.

Characteristic	Total, n	MPR 27, n	no-MPR 21, n	P-value
Age, years				0.863
<60	20	10	9	
≥60	28	17	12	
Sex				0.015
Male	41	26	15	
Female	7	1	6	
Smoking history				0.230
Yes	23	15	8	
No	25	12	13	
Pathological type				0.008
Squamous cell carcinoma	32	23	9	
Adenocarcinoma	11	3	8	
Other	5	1	4	
Tumor site				0.537
Right lung	32	17	15	
Left lung	16	10	6	
T-stage				0.271
cT1	4	2	2	
cT2	12	4	8	
cT3	19	13	6	
cT4	13	8	5	
N-stage				0.552
N0	2	1	1	
N1	12	5	7	
N2	33	20	13	
N3	1	1	0	

Characteristic	Total, n	MPR 27, n	no-MPR 21, n	P-value
Clinical staging				0.235
II	6	3	3	
III	40	24	16	
IV	2	0	2	
Post-operative treatment				0.430
Yes	44	24	20	
No	4	3	1	
Neoadjuvant combination immunotherapy regimen				0.279
Albumin-paclitaxel combination regimen	21	14	7	
Docetaxel combination regimen	15	9	6	
Pemetrexed combination regimen	10	3	7	
Gemcitabine combination	2	1	1	
Number of treatment cycles				0.853
<3 cycles	19	11	8	
≥3 cycles	29	16	13	
All values were derived from Chi-squared/Fisher's exact tests (categorical variables) or Mann-Whitney U tests (continuous variables).				

Table 5
Post-operative data obtained from all patients.

Characteristic	
Operative time (min)	225.7 (150–345)
Intraoperative bleeding (mL)	135.2 (20 – 1,800)
Surgical procedure	
Thoracoscopic	46 (95.3)
Thoracoscopic intermediate open	2 (4.7)
Post-operative hospitalization(d)	6.3 (3–16)
R0 resection rate	47 (97.9)
Post-operative complications	22
Pleural effusion	14 (63.6)
Pneumonia	2 (9.1)
Pneumothorax or pneumothorax	2 (9.1)
Intraoperative bleeding	1 (4.5)
Pulmonary atelectasis	1 (4.5)

Table 6
Adverse reactions in neoadjuvant patients

Adverse reactions	Total	G1 -G2	G3 -G4
Hypoproteinemia	30	30 (62.5)	0 (0.0)
Anemia	22	21 (43.8)	1 (2.1)
Elevated transaminases	14	14 (29.2)	0 (0.0)
Loss of appetite	12	12 (25.0)	0 (0.0)
Nausea	9	9 (18.8)	0 (0.0)
Vomiting	6	6 (12.5)	0 (0.0)
Neutropenia	6	5 (10.4)	1 (2.1)
Abnormal thyroid function	2	2 (4.2)	0 (0.0)
Itchy skin	2	2 (4.2)	0 (0.0)
Cardiotoxicity	1	1 (2.1)	0 (0.0)
Elevated blood glucose	2	2 (4.2)	0 (0.0)
Capillary hyperplasia	2	2 (4.2)	0 (0.0)

Results

A total of 48 patients met the inclusion and exclusion criteria and were enrolled in the present study. Among them, 41 patients were male and 7 were female, with ages ranging from 41.0 to 73.0 years (mean 60.9 ± 7.2 years). A total of 23 patients were smokers and 25 were non-smokers. According to the histological analysis, 32 patients exhibited squamous cell carcinoma and 16 presented with adenocarcinoma, while less common subtypes included mixed adenosquamous carcinoma (1 case), lymphoepithelioma-like carcinoma (3 cases) and mucoepidermoid carcinoma (1 case). Regarding clinical stage, 6 patients presented with Stage II disease, 40 presented with Stage III disease, and 2 presented with Stage IV disease with isolated organ metastasis.

A total of 44 patients received further post-operative treatment. Among them, 21 patients received an albumin-paclitaxel-based regimen, 15 received a docetaxel-based regimen, 10 received a pemetrexed-based regimen and 2 patients received a gemcitabine-based regimen. In total, 20 patients received two cycles of neoadjuvant therapy and 2 patients received three cycles. In terms of nICT, 20 patients received two cycles, 2 patients received three cycles and 3 patients received five cycles. Baseline patient characteristics are summarized in Table 1.

PD-L1 expression levels were unavailable for 31 patients, as standardized PD-L1 22C3/SP263 assays were not routinely performed at Yuebei People's Hospital of Guangdong Medical University between

2020 and 2021. In total, 17 patients presented with PD-L1 tumor proportion score (TPS) results that were obtained from preoperative biopsy specimens (Dako 22C3 antibody; positivity threshold ≥ 1%). The use of ICIs and chemotherapy drugs is displayed in Table 2.

All 48 patients with NSCLC completed nICT. According to RECIST 1.1 criteria, following two to five cycles of treatment, 35 patients achieved a PR and 12 exhibited SD, resulting in an ORR of 72.9% and a DCR of 97.9%. Post-operative pathological assessment revealed that 25.0% of patients (12/48; 95% CI, 13.2–39.6%) achieved pCR (pT0/TisN0), with an additional 2.1% (1/48; 95% CI, 0.1–11.1%) achieving pT0/TisN + M0. MPR was observed in 41.7% of patients (20/48; 95% CI, 27.6–56.8%; Table 3). Radiological response demonstrated no association with MPR in the resected specimens. Pathological response was not associated with sex, histological subtype, clinical stage or smoking history (Table 4).

All 48 patients underwent surgical treatment with thoracoscopic radical resection of lung cancer, and 2 patients required conversion to intermediate open surgery. The R0 resection rate was 97.9% (47/48; 95% CI, 88.9–99.9%). The mean operative time was 225.7 min, and mean intraoperative blood loss was 135.2 ml. Pleural effusion was the most common post-operative complication (14/48; 63.6%), followed by pneumonia (2/48; 4.2%; Table 5).

The majority of adverse events during nICT were grade 1–2. In total, 2 patients experienced grade ≥ 3 events. Chemotherapy-associated toxicities, including hematological, hepatic and gastrointestinal adverse events, were common but predominantly grade 1–2. Grade 3–4 events included anemia in 1 patient (1/48; 2.1%) and neutropenia in 1 patient (1/48; 2.1%). Immune-associated adverse events included pruritus (2/48; 4.2%), thyroid dysfunction (2/48; 4.2%), hyperglycemia (2/48; 4.2%), capillary hyperplasia (2/48; 4.2%) and cardiotoxicity (1/48; 2.1%). Notably, all immune-associated adverse events were grade 1–2, and no grade 5 adverse events were observed. Detailed adverse event data are presented in Table 6.

Discussion

Chemotherapy, as a systemic treatment modality, effectively targets free-floating cancer cells throughout the body and is suitable for patients with NSCLC at all stages. In advanced cases, chemotherapy may alleviate symptoms and prolong survival. Results of previous studies (13–14) demonstrated its central role in the treatment of NSCLC. Chemotherapy provides clear clinical benefits through reducing tumour burden, increasing the likelihood of successful surgical resection and extending overall survival. However, while cytotoxic agents target malignant cells, they also inevitably damage healthy cells, resulting in various adverse reactions.

Results of a previous study demonstrated that immunotherapy alone, such as the use of PD-1 inhibitors, may be effective in selected patients, particularly those with high PD-L1 expression (TPS ≥ 50%). However, the ORR remains limited at 20–40%, and efficacy is markedly reduced in individuals with oncogenic driver mutations, such as Epidermal Growth Factor Receptor(EGFR)mutations or Anaplastic Lymphoma Kinase (ALK) fusions (15). Results of a previous study further indicated that nICT is

significantly more effective than immunotherapy alone (16). Thus, the development of nICT has emerged as a potential pre-operative treatment strategy, offering an opportunity to improve surgical conditions and long-term outcomes in lung cancer.

The enhanced efficacy of nICT is attributable to the synergistic mechanisms of chemotherapy and immunotherapy. Platinum-based and taxane-based agents induce immunogenic tumour cell death, releasing damage-associated molecular patterns, such as CALR, HMGB1 and ATP, which promote dendritic cell-mediated antigen presentation. Concurrently, the lymphopenia-regeneration window induced by chemotherapy increases infiltration of CD8 + T cells, while PD-1 blockade prevents T-cell exhaustion, strengthening anti-tumour immunity through a 'prime-boost' cycle. Moreover, chemotherapy reduces immune-suppressive cell populations, such as Regulatory T cells (Tregs) and Myeloid-Derived Suppressor Cells (MDSCs), while combination immunotherapy fosters M1 macrophage polarization. These mechanisms collectively reshape the tumour microenvironment from an immune-suppressive to an immune-permissive state, resulting in higher pCR rates (17–19). Such biological synergy explains the superior pathological responses observed with nICT compared with chemotherapy alone. Consequently, nICT has become a widely accepted standard treatment for NSCLC, particularly for tumours lacking driver gene mutations (20).

A total of 48 patients with advanced NSCLC were enrolled in the present study. The pCR rate following nICT was 25.0%, the MPR rate reached 41.7% and the overall stage-reduction rate was 87.5%. The post-operative R0 resection rate was 97.1%. The immunochemotherapy agents used in the present study included sindilizumab, tirilizumab, karelizumab and the PD-L1 monoclonal antibody, SHR-1316. Given the limited sample size, safety and efficacy were analyzed across the entire cohort rather than by individual drug type.

Results of the present study aligned with results of previous studies. A multi-center Phase II study (21) evaluating camrelizumab plus chemotherapy compared with chemotherapy alone in resectable Stage IIIA/IIIB (T3N2) NSCLC reported an MPR rate of 32.6% and a pCR rate of 65.1% in the combination group. Similarly, the RATIONALE-315 trial (22) demonstrated an MPR rate of 56.2% and a pCR rate of 40.7% with tirilizumab plus chemotherapy, which was substantially higher than placebo. Although response rates varied across studies, all findings confirmed that nICT yields consistently high MPR and pCR rates. These data support further refinement and optimization of this treatment strategy.

In the present study, 93.8% of patients presented with clinical N1-2 disease at baseline. Following nICT, only 27.1% remained N+, while 72.9% achieved ypT0/Tis, indicating substantial downstaging of metastatic lymph nodes. For patients with locally advanced NSCLC and nodal disease, nICT may offer superior therapeutic benefits compared with chemotherapy alone. In addition, the ORR was significantly higher than the MPR rate, a trend also observed in previous studies, such as CheckMate-816 (ORR 36% vs. MPR 24%) and NADIM (23) (ORR 71% vs. MPR 63%). Potential explanations may be the presence of immune-associated delayed responses, in which dense lymphocyte infiltration and fibrosis produce radiologic findings suggestive of residual tumour despite extensive pathological necrosis (pCR/MPR).

Moreover, these results may be explained by tumour heterogeneity, with differential responses across primary and nodal sites, or differences between RECIST size-based assessments and pathological viability criteria.

The neoSCORE trial (24) observed a 14.5% improvement in MPR following three cycles of nICT compared with two cycles, with optimal tolerability. However, the CheckMate 77T trial (8) demonstrated no significant differences in pCR or MPR between patients who completed four cycles and those who received fewer cycles. In the present study, patients receiving three cycles exhibited higher MPR rates than those receiving fewer (< 3 cycles, 10.4%; ≥3 cycles, 31.3%), while the pCR rate remained 12.5%. Overall, these results suggested that three to four cycles of nICT may optimize pathological response without compromising surgical feasibility.

Phase III trials (23, 25–26) revealed that higher PD-L1 expression was associated with improved pathological response, although benefits were observed across all expression levels. However, results obtained from the present real-world cohort did not reflect this association. PD-L1 positivity was not an independent predictor of pathological response, likely due to the absence of PD-L1 testing in 57.4% of patients, primarily due to cost constraints.

Zhang *et al* (27) compared outcomes between patients receiving nICT and those receiving chemotherapy alone. Surgical resection rates were comparable, while R0 resection rates were numerically higher in the nICT group. No significant differences were observed in surgical timing, complication rates or operative complexity. In the present study, the R0 resection rate (97.9%) exceeded those reported in NADIM (89 vs. 79%) and CheckMate-816 (94 vs. 85%). The mean operative duration was 225.7 min, and mean intraoperative blood loss was 135.2 ml. The conversion-to-thoracotomy rate (4.2%) aligned with literature values for nICT (3–8%) (28–29). The most common post-operative complication was pleural effusion (14/48; 63.6%), which was higher than a previous study that included chemotherapy cohorts (40–50%) (30). However, all cases were Clavien-Dindo grade I and required no invasive intervention. These results may reflect heightened inflammatory responses associated with immunotherapy. Collectively, these findings indicated that nICT followed by surgical resection is safe and feasible in NSCLC and does not increase peri-operative risk.

Results of a previous study (31) reported grade ≥ 3 adverse event rates of 65.8% for chemotherapy and 16.5% for immunotherapy. By contrast, the majority of adverse events in the present study were grade 1–2, with only 2 patients experiencing grade ≥ 3 events. Chemotherapy-associated hematotoxicity, hepatotoxicity and gastrointestinal adverse events were common, but these were predominantly mild in severity. Grade 3–4 toxicities included anaemia (2.1%) and neutropenia (2.1%). Immune-associated adverse events, including pruritus, thyroid dysfunction, hyperglycemia, capillary hyperplasia and cardiotoxicity, were all grade 1–2. Notably, no treatment-associated deaths occurred. Results of a previous systematic review and meta-analysis (32) comparing post-operative adverse events between nICT and chemotherapy alone highlighted no significant differences, indicating similar overall safety

profiles. These data supported nICT as a safe and feasible neoadjuvant strategy for locally advanced NSCLC.

Notably, the present study exhibited numerous limitations. The single-center, non-randomized design may have introduced selection bias due to geographical and institutional constraints. However, bias was minimized through consecutively enrolling all patients meeting AJCC 8th edition staging criteria and excluding individuals with prior treatments. Notably, pathological response rates observed in the present study align with the results of previous studies, supporting the broader applicability of the results of the present study.

Declarations

Ethics approval and consent to participate

The present study was reviewed and approved by the Medical Ethics Committee of Yuebei People's Hospital affiliated with Guangdong Medical University (approval no. YBSKY-2025-141-001).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

KW contributed to the conception, design and writing of the manuscript. LW and RW were responsible for data extraction and analysis. The first draft of the manuscript was written by KW. HC supervised the study, contributed to the research design and data interpretation, and critically revised the manuscript for intellectual content. KW and HC confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

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Data Availability

The data generated in the present study may be requested from the corresponding author.

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