

Surgical difficulty and factors associated with conversion to thoracotomy after neoadjuvant chemoimmunotherapy for non-small cell lung cancer: a single- center retrospective study

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Abstract

Background: Neoadjuvant chemoimmunotherapy can produce substantial tumor regression in resectable or potentially resectable non-small cell lung cancer (NSCLC), but treatment-related inflammation, fibrosis, and hilar adhesions may increase technical surgical difficulty.

Methods: We retrospectively analyzed 101 patients with NSCLC who underwent surgery after neoadjuvant chemoimmunotherapy at a single center. Thirty-four patients completed video-assisted thoracoscopic surgery (VATS) and 67 underwent conversion to thoracotomy.

Results: In the principal Firth penalized multivariable analysis, cT3-4 disease (OR 34.33, 95% CI 7.84–150.22), pulmonary artery relationship grade (OR 2.03 per grade, 95% CI 1.09–3.79), and bronchial relationship grade (OR 3.25 per grade, 95% CI 1.35–7.82) were associated with conversion. The cT3-4 estimate should be interpreted cautiously because of sparse non-conversion observations. Pulmonary artery and bronchial grades were also associated with longer operative time. Conversion was associated with longer operative time, greater blood loss, and longer chest tube duration, whereas no statistically significant differences were observed in R0 resection or pulmonary complication rates.

Conclusions: Higher clinical T stage and more complex pulmonary artery and bronchial relationships on CT were associated with conversion and technical surgical difficulty after neoadjuvant chemoimmunotherapy. Preoperative assessment of local tumor extent and hilar anatomy may assist operative planning; conversion should be interpreted as a potential intraoperative safety strategy rather than automatically as failure of minimally invasive surgery.

Background

Neoadjuvant immune checkpoint inhibition combined with chemotherapy has become an important component of multidisciplinary treatment for resectable and potentially resectable NSCLC [1]. Although this approach can produce radiological tumor regression, downstaging, major pathological response, and pathological complete response, tumor shrinkage does not necessarily translate into technically easier surgery.

After neoadjuvant immunotherapy, inflammatory reaction, fibrosis, nodal changes, and dense hilar adhesions may obscure normal anatomical planes and complicate dissection of the pulmonary artery and bronchus [2–7]. Therefore, a smaller post-treatment tumor may still be associated with substantial intraoperative complexity.

Conversion from a minimally invasive approach to thoracotomy is one clinically apparent manifestation of surgical difficulty, but it should not be equated with surgical failure [2, 6, 8–10]. Some difficult procedures can still be completed minimally invasively despite prolonged operative time, increased blood loss, or complex bronchovascular dissection. We therefore considered surgical difficulty as a multidimensional construct.

The primary objective of this study was to identify clinical and preoperative CT characteristics associated with conversion to thoracotomy after neoadjuvant chemoimmunotherapy for NSCLC. Secondary objectives were to characterize surgical difficulty using operative time, blood loss, transfusion, and complex resection, and to compare perioperative and short-term surgical outcomes between completed minimally invasive surgery and conversion.

Methods

Study design and patients

This was a single-center retrospective observational study conducted at the Affiliated Hospital of Zunyi Medical University between January 2022 and March 2026. A total of 607 patients with NSCLC were initially screened. Patients were eligible for the present analysis if they had pathologically confirmed NSCLC, received 2–4 cycles of neoadjuvant chemoimmunotherapy, subsequently underwent surgical resection through an initially attempted video-assisted thoracoscopic surgery (VATS) approach, and had evaluable preoperative chest CT imaging and complete clinical data. Patients were excluded if they did not receive neoadjuvant chemoimmunotherapy ($n = 189$), did not undergo surgical resection ($n = 120$), had incomplete clinical data ($n = 150$), or had unavailable or non-evaluable CT imaging ($n = 47$). The final analysis included 101 patients, of whom 34 completed VATS and 67 underwent intraoperative conversion to thoracotomy (Fig. 1). Clinical T and N categories and clinical stage were determined according to the 8th edition of the AJCC TNM classification. Reporting was guided by the STROBE recommendations for observational studies [11].

The study protocol was approved by the Ethics Committee of the Affiliated Hospital of Zunyi Medical University (approval No. KLL-2026-117). The requirement for individual informed consent was waived because of the retrospective nature of the study.

All patients initially underwent VATS; no robotic-assisted thoracic surgery (RATS) procedures were included. Conversion to thoracotomy was defined as an intraoperative transition from the initially attempted VATS approach to open thoracotomy because difficult hilar dissection prevented continued minimally invasive dissection from being considered technically feasible or safe. Operative-record review confirmed that all 67 conversion cases met this definition and that no planned thoracotomy cases were included. The final decision to convert was made by the operating surgeon according to intraoperative technical feasibility and safety. All procedures were performed by three thoracic surgeons with more than 10 years of operative experience.

Clinical and imaging variables

Clinical variables included age, sex, BMI, smoking history, ECOG performance status, pathological subtype, maximum tumor diameter, clinical T and N categories, clinical stage, neoadjuvant treatment cycles, treatment-to-surgery interval, LDH (U/L), NLR, and SII. Neoadjuvant chemoimmunotherapy

consisted of a PD-1 inhibitor (tislectumab, sintilimab, or toripalimab) combined with paclitaxel and carboplatin. Overall, 18 patients received 2 cycles, 73 received 3 cycles, and 10 received 4 cycles before surgery.

Preoperative chest CT images were reconstructed at 1-mm slice thickness using standard soft-tissue reconstruction. Multiplanar reconstruction (MPR) was available during image review. Two radiologists from the Department of Radiology independently reviewed the CT examinations while blinded to the final conversion outcome. Reader 1 was an associate chief physician and Reader 2 was a chief physician. Each reader independently assessed tumor location, hilar fat-plane obliteration, pulmonary artery relationship, bronchial relationship, conglomerated/fused lymph nodes, and hilar/mediastinal fibrosis. Discrepancies were resolved by consensus, and the consensus assessment was used for the primary analysis.

The pulmonary artery relationship was graded using a four-level semiquantitative system: grade 0, no obvious contact; grade 1, tumor or lymph node contact with the pulmonary artery $\leq 90^\circ$ without deformation; grade 2, contact $> 90^\circ$ and $\leq 180^\circ$ with or without mild distortion; and grade 3, contact $> 180^\circ$, encasement, narrowing, or deformation. Bronchial relationship was graded as grade 0, no obvious involvement; grade 1, contact or adjacency; and grade 2, invasion, stenosis, or obstruction. Interobserver agreement was calculated using the original independent ratings recorded by each reader before any discussion or consensus procedure. Weighted Cohen's kappa with 95% confidence intervals was used for ordinal pulmonary artery, bronchial, and fibrosis grades; Cohen's kappa was used for binary assessments. One indeterminate bronchial assessment was excluded from the bronchial agreement analysis. Consensus scores were used for the primary clinical analyses.

Outcomes

The primary outcome was conversion to thoracotomy. Secondary measures of surgical difficulty were operative time, intraoperative blood loss, transfusion, complex resection, and pulmonary vascular reconstruction. Operative time and estimated blood loss were taken from the operative record. Complex resection was defined as sleeve resection, pneumonectomy, or bilobectomy. Pulmonary vascular reconstruction was analyzed separately because it could overlap with these resection categories and could not be added directly to the complex-resection count without double counting. R0 status was based on the recorded pathological margin assessment. Postoperative pulmonary complications, chest tube duration, hospital stay, and reoperation were obtained from the clinical record. The database recorded 30/90-day mortality as a combined short-term mortality indicator; therefore, it was analyzed as a combined endpoint. These outcomes were considered perioperative and short-term surgical/pathological outcomes rather than long-term oncological outcomes.

Statistical analysis

Continuous variables were summarized as median (IQR) and compared using the Mann-Whitney U test as appropriate. Categorical variables were summarized as n (%) and compared using chi-square or Fisher exact tests. Univariable logistic regression was initially used to examine factors associated with conversion. Because cT3–4 status showed near-complete separation, Firth penalized logistic regression [12] was used as the principal multivariable model to reduce small-sample and separation-related bias. The prespecified multivariable model included cT3–4 status, pulmonary artery grade, bronchial grade, and fibrosis grade. Odds ratios (ORs), 95% confidence intervals (CIs), and two-sided P values were reported. Multicollinearity among the included covariates was assessed using variance inflation factors (VIFs). Conventional maximum-likelihood multivariable logistic regression and L1-penalized (LASSO) logistic regression [13] were additionally performed as sensitivity analyses to assess the robustness and stability of the findings. Missing data were handled using complete-case analysis; no imputation was performed. Variables with unavailable assessments were analyzed using available cases, and the corresponding denominators are reported where applicable. Multivariable logistic regression analyses were performed using complete cases for all included variables. Two patients with cNx were excluded from analyses requiring cN2 + classification, and one indeterminate bronchial assessment was excluded from analyses requiring an ordinal bronchial grade.

Operative time and blood loss were analyzed as continuous measures of surgical difficulty using multivariable regression with heteroscedasticity-robust standard errors. ROC and calibration analyses were retained only as exploratory supplementary descriptions of apparent model discrimination and calibration and were not used to establish or validate a clinical prediction model. Additional sensitivity analyses evaluated the interaction between treatment-to-surgery interval (TTI) and fibrosis grade, as well as pathological nodal downstaging (ypN0) among patients with baseline cN2 disease. Sparse outcomes such as R0 failure, reoperation, and short-term mortality were not subjected to conventional adjusted logistic models. $P < 0.05$ was considered statistically significant.

Results

Patient characteristics and conversion rate

Among the 101 patients included in the final analysis, 34 (33.7%) completed minimally invasive surgery and 67 (66.3%) underwent conversion to thoracotomy. Most patients received three cycles of neoadjuvant chemoimmunotherapy (73/101, 72.3%); 18 (17.8%) received two cycles and 10 (9.9%) received four cycles. Patients who required conversion had larger tumors and a substantially greater proportion of cT3-4 disease. Detailed baseline and preoperative characteristics are summarized in Table 1.

CT anatomical characteristics and surgical difficulty

Interobserver agreement was excellent for pulmonary artery relationship grading (weighted kappa = 1.00, 95% CI 1.00–1.00; n = 101) and bronchial relationship grading (weighted kappa = 1.00, 95% CI 1.00–1.00; n = 100). Fibrosis grading showed moderate agreement (weighted kappa = 0.55, 95% CI 0.37–0.72; n = 101).

Conversion rates increased with greater pulmonary artery and bronchial involvement on CT. Pulmonary artery grades 0, 1, 2, and 3 were associated with conversion rates of approximately 40.0%, 60.0%, 76.0%, and 88.5%, respectively. Bronchial grades 0, 1, and 2 were associated with conversion rates of approximately 45.0%, 71.0%, and 89.7%, respectively. These findings support a graded relationship between central anatomical complexity and conversion (Fig. 2).

The relationship between CT anatomy and surgical difficulty was not limited to conversion. Increasing pulmonary artery grade and bronchial grade were independently associated with longer operative time (standardized beta approximately 0.27, $P = 0.005$ and 0.26, $P = 0.020$, respectively) (Fig. 3). Associations with intraoperative blood loss were less consistent.

Factors associated with conversion

In univariable analysis, tumor size was associated with conversion (OR 1.95 per 1-cm increase, 95% CI 1.36–2.81; $P < 0.001$), and cT3-4 disease showed a strong association (OR 32.94, 95% CI 8.87–122.25; $P < 0.001$).

In the principal Firth penalized multivariable logistic regression model (complete-case n = 100), cT3-4 disease was strongly associated with conversion (OR 34.33, 95% CI 7.84–150.22; $P < 0.001$). Each one-grade increase in pulmonary artery relationship was associated with higher odds of conversion (OR 2.03, 95% CI 1.09–3.79; $P = 0.026$), as was each one-grade increase in bronchial relationship (OR 3.25, 95% CI 1.35–7.82; $P = 0.008$) (Fig. 4). Fibrosis grade was not independently associated with conversion (OR 0.61, 95% CI 0.25–1.47; $P = 0.270$). The cT3-4 estimate should be interpreted cautiously because only three patients with cT3-4 disease completed VATS, resulting in sparse observations in the non-conversion group.

In the conventional maximum-likelihood logistic regression sensitivity analysis using the same four covariates, the findings remained directionally consistent: cT3-4 disease (OR 51.82, 95% CI 10.10–265.89; $P < 0.001$), pulmonary artery grade (OR 2.18, 95% CI 1.12–4.24; $P = 0.022$), bronchial grade (OR 3.70, 95% CI 1.45–9.43; $P = 0.006$), and fibrosis grade (OR 0.57, 95% CI 0.22–1.46; $P = 0.243$). VIFs were low (1.13 for cT3-4, 1.20 for pulmonary artery grade, 1.32 for bronchial grade, and 1.19 for fibrosis grade), arguing against clinically important multicollinearity. LASSO sensitivity analysis likewise retained cT3-4, pulmonary artery grade, and bronchial grade, whereas fibrosis was shrunk to zero.

Perioperative and short-term surgical outcomes

Median operative time was 205.0 minutes (IQR 172.5–230.0) in the conversion group compared with 140.0 minutes (IQR 120.0–167.5) in the completed minimally invasive group ($P < 0.001$). Median blood loss was 150.0 mL (IQR 100.0–200.0) versus 50.0 mL (IQR 27.5–95.0), respectively ($P < 0.001$). Chest tube duration was also longer after conversion: 6.0 days (IQR 5.5–8.0) versus 4.0 days (IQR 3.2–5.0), $P < 0.001$.

Hospital stay did not differ significantly (14.0 vs 12.5 days; $P = 0.133$). Transfusion rates were 10.4% versus 5.9% ($P = 0.714$). Complex resection, defined as sleeve resection, pneumonectomy, or bilobectomy, occurred in 23 of 67 patients (34.3%) in the conversion group and 8 of 34 patients (23.5%) in the completed minimally invasive group ($P = 0.362$). Pulmonary vascular reconstruction was performed in 7 of 67 patients (10.4%) in the conversion group and 3 of 34 patients (8.8%) in the completed minimally invasive group (Fisher exact $P = 1.000$). R0 resection (95.5% vs 100%; $P = 0.549$) and pulmonary complications (10.4% vs 14.7%; $P = 0.532$) were not significantly different between groups. Reoperation occurred in neither group, and one 30/90-day death occurred in the conversion group.

Discussion

The principal finding of this study was that surgical complexity after neoadjuvant chemoimmunotherapy was associated with both overall local tumor extent and CT-defined hilar anatomy. cT3-4 disease was the strongest factor associated with conversion, while pulmonary artery and bronchial involvement provided additional independent information.

The strong association between cT3-4 disease and conversion should nevertheless be interpreted cautiously because of sparse observations in the non-conversion group. Conversion occurred in 51 of 54 patients with cT3-4 disease, leaving only three patients who completed VATS. We therefore used Firth penalized logistic regression as the principal multivariable approach to reduce separation-related and small-sample bias. Although the resulting OR remained large (34.33, 95% CI 7.84–150.22), the wide confidence interval indicates substantial uncertainty regarding the precise magnitude of the association. The finding should therefore be interpreted as evidence of a strong association rather than as a precise individual risk estimate. The conventional maximum-likelihood logistic regression sensitivity analysis produced a larger estimate but showed the same direction of association.

The pulmonary artery and bronchial findings are clinically plausible because safe minimally invasive anatomical resection depends on adequate exposure, mobilization, and control of these structures. Their association with operative duration further supports the concept that these CT characteristics reflect technical difficulty beyond the binary decision to convert.

Not all CT characteristics were equally informative. Fibrosis grade was not independently associated with conversion. Because fibrosis may mature over time after treatment, we examined TTI as a potential effect modifier. Median TTI was 25 days; fibrosis grade was not significantly associated with conversion in either the ≤ 25 -day or > 25 -day subgroup, and the fibrosis-by-TTI interaction was not significant ($P =$

0.731). Thus, the negative fibrosis result was not explained by a detectable TTI-dependent effect in this cohort. CT after neoadjuvant treatment likely represents a mixture of residual tumor, inflammation, fibrosis, and nodal response, and qualitative fibrosis may not correspond directly to the density of surgical adhesions.

An inverse univariable association between cN2 + status and conversion was observed but should not be interpreted as a protective effect. To explore whether nodal response might explain this finding, we examined pathological nodal downstaging among patients with baseline cN2 disease. Among 65 cN2 patients with evaluable ypN status, conversion occurred in 23 of 38 patients who achieved ypN0 and 14 of 27 patients with residual ypN-positive disease; this difference was not significant ($P = 0.612$). Therefore, ypN downstaging did not explain the inverse univariable cN2 association, which is more plausibly related to selection, staging structure, or residual confounding.

The conversion rate of 66.3% is high and requires careful interpretation. Operative-record review confirmed that all 67 cases represented true intraoperative conversion from an initially attempted minimally invasive approach because of difficult hilar dissection; no planned thoracotomy cases were included. The high rate therefore reflects this selected single-center cohort, which contained a high proportion of locally advanced tumors, and should not be interpreted as an expected conversion rate or benchmark for other institutions. All procedures were performed by three thoracic surgeons with more than 10 years of operative experience. Nevertheless, surgeon-specific thresholds for conversion, technical preference, and perceived vascular risk remain potential sources of residual confounding. Recent multicenter and pooled evidence has likewise shown substantial heterogeneity in minimally invasive surgical use and conversion rates after neoadjuvant immune-based therapy, reflecting differences in patient selection, disease extent, and surgical practice [10, 14, 15].

Longer operative time and greater blood loss in the conversion group should be interpreted cautiously because these differences may partly reflect consequences of the conversion procedure itself rather than solely representing pre-existing surgical complexity. Therefore, these perioperative differences were considered complementary measures of operative difficulty and should not be interpreted as independent evidence that conversion itself caused worse surgical outcomes. Conversion should not automatically be regarded as failure. In difficult cases, timely conversion may be an appropriate safety decision when normal planes are lost or pulmonary vascular control is uncertain. The absence of statistically significant differences in R0 resection, pulmonary complications, reoperation, or mortality should not be interpreted as proof of equivalence because these adverse outcomes were sparse.

This study is limited by its retrospective single-center design, modest sample size, high proportion of locally advanced tumors, surgeon-dependent conversion thresholds, and absence of external validation. Although all conversion cases were verified by operative-record review, the threshold for conversion remains influenced by surgeon judgment and institutional practice. The CT grading system was study-specific and should be regarded as an exploratory anatomical assessment framework rather than a validated prediction tool; external validation is required. Pulmonary vascular reconstruction was

available as a group-level variable but may overlap with sleeve resection, pneumonectomy, or bilobectomy and was therefore analyzed separately rather than incorporated into the complex-resection composite. Length of stay may also be influenced by center-specific discharge practices, rehabilitation pathways, insurance settlement, or other administrative factors. Finally, long-term oncological outcomes were not the focus of the present analysis, and the available data were insufficient for robust conclusions regarding disease-free or overall survival.

Conclusions

Among patients undergoing surgery for NSCLC after neoadjuvant chemoimmunotherapy, cT3-4 disease and greater pulmonary artery and bronchial involvement on preoperative CT were associated with conversion to thoracotomy. Pulmonary artery and bronchial CT grades were also associated with prolonged operative time, indicating that these anatomical characteristics reflect technical surgical difficulty beyond conversion alone. Conversion should be interpreted as a potential intraoperative safety strategy rather than automatically as failure of minimally invasive surgery.

Abbreviations

AJCC: American Joint Committee on Cancer

BMI: Body mass index

CI: Confidence interval

CT: Computed tomography

ECOG: Eastern Cooperative Oncology Group

IQR: Interquartile range

LASSO: Least absolute shrinkage and selection operator

LDH: Lactate dehydrogenase

MPR: Multiplanar reconstruction

NLR: Neutrophil-to-lymphocyte ratio

NSCLC: Non-small cell lung cancer

OR: Odds ratio

RATS: Robot-assisted thoracic surgery

ROC: Receiver operating characteristic

SII: Systemic immune-inflammation index

TTI: Treatment-to-surgery interval

VATS: Video-assisted thoracoscopic surgery

VIF: Variance inflation factor

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of the Affiliated Hospital of Zunyi Medical University (approval No. KLL-2026-117). The requirement for individual informed consent was waived by the ethics committee because of the retrospective nature of the study.

Clinical trial number: not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are not publicly available because they contain individual clinical data but are available from the corresponding author on reasonable request and subject to appropriate institutional and ethical approval.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Guicheng Pan conceived and designed the study, performed the data analysis, and drafted the manuscript. Lingling Geng, Qian Luo, Pan Chen, and Jiajie Zhou collected the clinical cases and organized the study data. Lv Sun and Xianli Luo reviewed and evaluated the CT images. Junliang Ma, Anping Chen, and Wendong Qu performed the surgical procedures and critically revised the manuscript. Yongxiang Song supervised the study and served as the corresponding author. All authors reviewed and approved the final manuscript.

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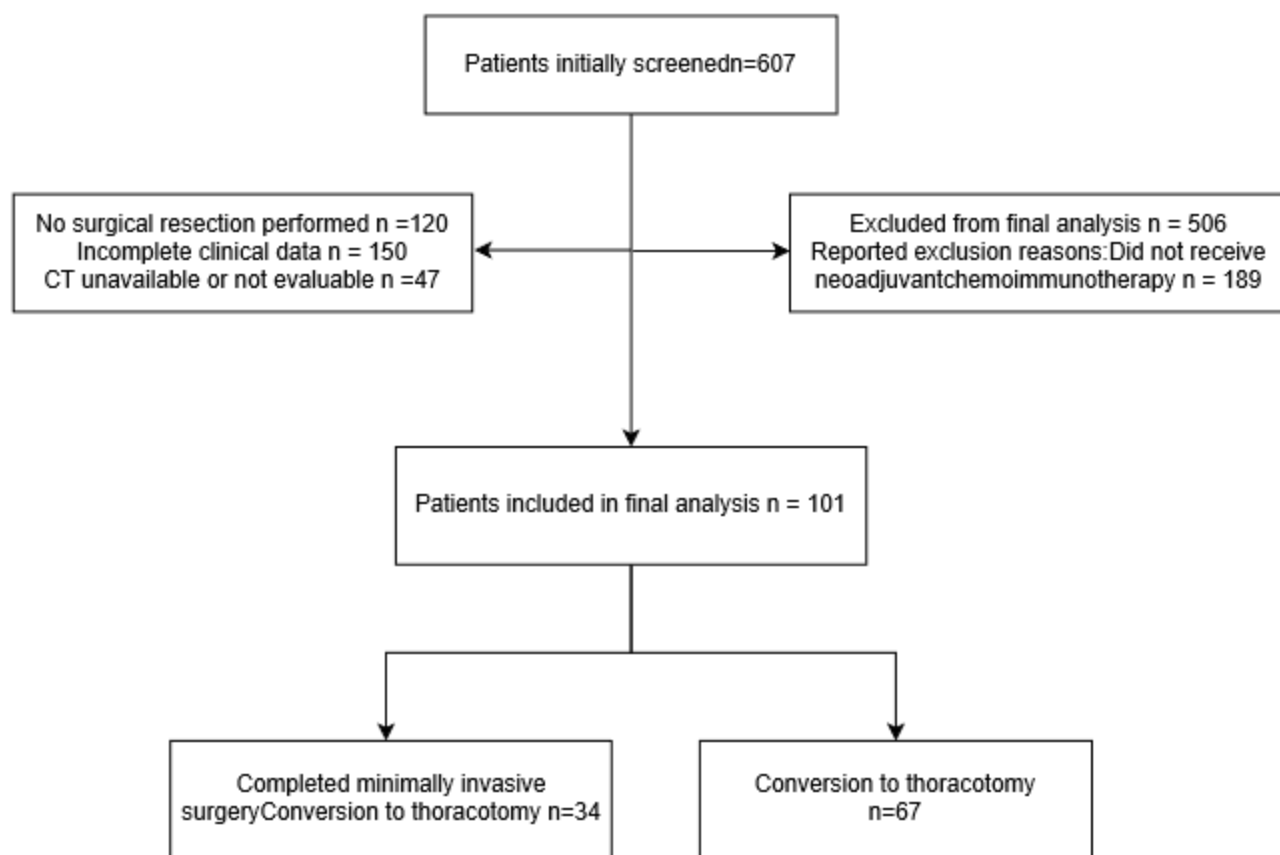
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Tables

Tables 1 to 4 are available in the supplementary files section.

Figures



NSCLC patients undergoing surgery after neoadjuvant chemoimmunotherapy

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Figure 1

Patient selection flow diagram.

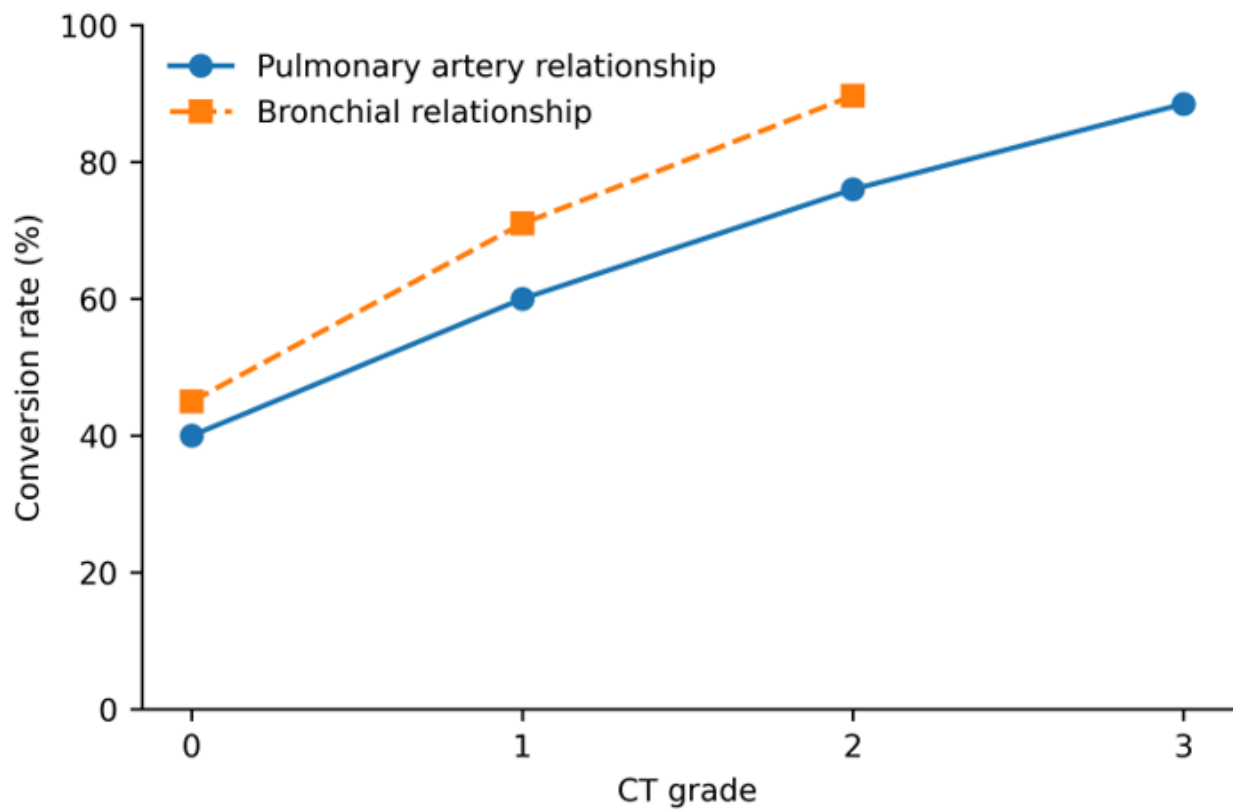


Figure 2

Preoperative pulmonary artery and bronchial CT grades and observed conversion rate.

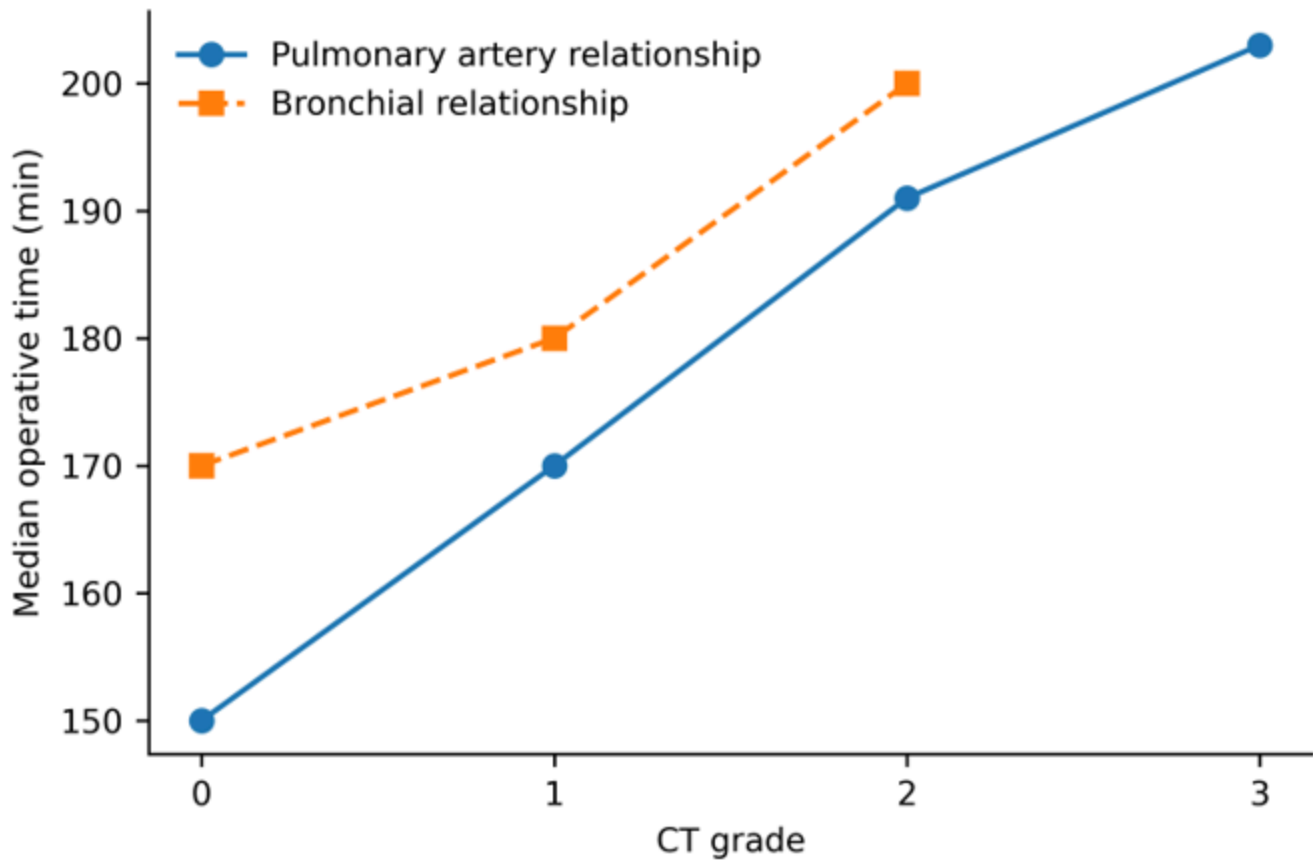


Figure 3

Relationship between CT anatomical grade and operative time.

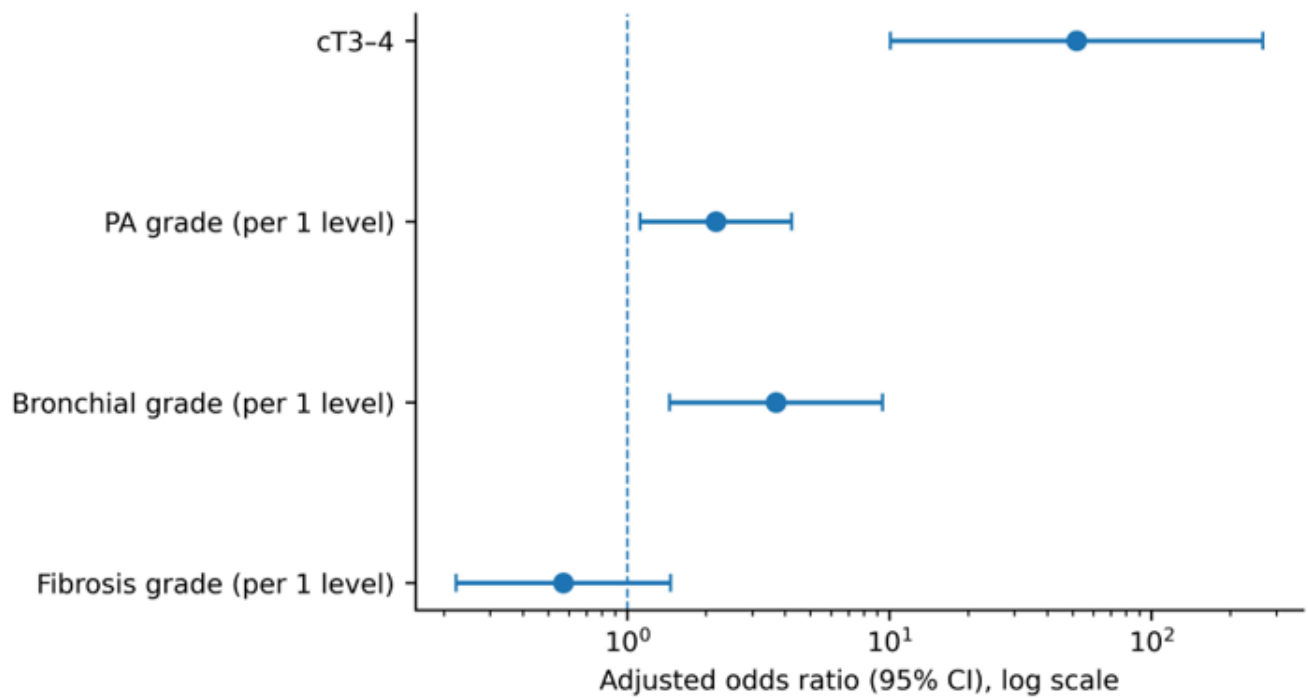


Figure 4

Multivariable logistic regression for conversion to thoracotomy.

Supplementary Files

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