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Original Article

Perioperative Blood Transfusion and Long-Term Outcomes in Lung Cancer Surgery: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Perioperative blood transfusion (PBT) is commonly administered during lung cancer surgery to manage perioperative anemia and blood loss. However, growing evidence suggests that allogeneic blood transfusion may adversely affect oncological outcomes through transfusion-related immunomodulation and impairment of antitumor immune responses. The impact of perioperative blood transfusion on long-term outcomes following lung cancer resection remains controversial.

Objective: To systematically evaluate the association between perioperative blood transfusion and long-term outcomes, including overall survival, disease-free survival, tumor recurrence, and postoperative complications, in patients undergoing surgical resection for lung cancer.

Methods: A systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. PubMed, Embase, Scopus, Web of Science, and the Cochrane Library were searched from inception to March 2026. Studies comparing transfused and non-transfused patients undergoing lung cancer surgery were included. Hazard ratios (HRs), odds ratios (ORs), and corresponding 95% confidence intervals (CIs) were pooled using random-effects models. Study quality was assessed using the Newcastle-Ottawa Scale.

Results: A total of 18 studies involving 14,562 patients met the inclusion criteria. Among these, 3,487 patients received perioperative blood transfusion and 11,075 did not. Meta-analysis demonstrated that perioperative blood transfusion was significantly associated with poorer overall survival (HR = 1.42, 95% CI: 1.24–1.63, $p < 0.001$) and reduced disease-free survival (HR = 1.36, 95% CI: 1.18–1.57, $p < 0.001$). Patients receiving transfusions also had a significantly higher risk of tumor recurrence (OR = 1.48, 95% CI: 1.19–1.84, $p < 0.001$) and postoperative complications (OR = 1.57, 95% CI: 1.28–1.92, $p < 0.001$). Moderate heterogeneity was observed across studies, and sensitivity analyses confirmed the robustness of the pooled estimates. No significant publication bias was detected.

Conclusion: Perioperative blood transfusion is associated with adverse long-term outcomes following lung cancer surgery, including decreased overall survival, reduced disease-free survival, increased recurrence, and higher postoperative morbidity. These findings support the implementation of patient blood management strategies and restrictive transfusion practices to minimize unnecessary transfusions and potentially improve oncological outcomes. Further prospective studies are required to establish causality and optimize transfusion protocols in thoracic oncology.

Keywords: Lung Cancer; Perioperative Blood Transfusion; Non-Small Cell Lung Cancer; Overall Survival; Disease-Free Survival; Tumor Recurrence; Thoracic Surgery; Meta-Analysis.

Introduction

Lung cancer remains the leading cause of cancer-related mortality worldwide and represents a major public health challenge despite advances in screening, diagnosis, and treatment modalities [1]. According to global cancer statistics, lung cancer accounts for approximately 2.5 million new cases and nearly 1.8 million deaths annually, making it the most lethal malignancy among both men and women [2]. Non-small cell lung cancer (NSCLC) constitutes nearly 85% of all lung cancer cases, while small cell lung cancer accounts for the remaining proportion [3]. Surgical resection remains the cornerstone of treatment for patients with early-stage and selected locally advanced lung cancer, offering the best chance for long-term survival and potential cure [4].

Despite significant improvements in surgical techniques, perioperative care, and minimally invasive approaches such as video-assisted thoracoscopic surgery (VATS) and robotic-assisted thoracic surgery, perioperative blood loss remains a common concern during lung cancer surgery [5]. Consequently, perioperative blood transfusion (PBT) is frequently administered to correct anemia, restore circulating blood volume, and maintain adequate tissue oxygenation [6]. The reported incidence of perioperative blood transfusion among patients undergoing pulmonary resection ranges from 10% to 40%, depending on patient characteristics, extent of surgery, and institutional transfusion practices [7].

Although blood transfusion can be lifesaving in selected clinical situations, increasing evidence suggests that allogeneic blood transfusion may exert adverse effects beyond immediate perioperative management [8]. The concept of transfusion-related immunomodulation (TRIM) has emerged as a potential mechanism through which transfused blood products influence host immune responses [9]. TRIM is characterized by suppression of cell-mediated immunity, alterations in cytokine production, reduced natural killer cell activity, and impaired antitumor immune surveillance [10]. These immunological changes may facilitate tumor growth, promote micrometastatic progression, and increase the likelihood of cancer recurrence following curative surgery [11].

The relationship between perioperative blood transfusion and oncological outcomes has been extensively investigated in various malignancies, including colorectal, gastric, hepatic, pancreatic, and esophageal cancers [12–16]. Several studies have demonstrated that transfused patients experience poorer overall survival, reduced disease-free survival, and higher recurrence rates compared with non-transfused patients [17]. Similar concerns have been raised in thoracic oncology, where perioperative blood transfusion has been proposed as an independent predictor of adverse long-term outcomes following lung cancer surgery [18].

Numerous retrospective cohort studies have evaluated the impact of perioperative blood transfusion on survival outcomes in patients undergoing pulmonary resection for lung cancer. Some investigators have reported significantly decreased overall survival and recurrence-free survival among transfused patients [19,20]. Other studies have suggested that the observed association may be confounded by factors such as advanced disease stage, extensive surgical procedures, greater intraoperative blood loss, comorbidities, and poor baseline physiological status rather than transfusion itself [21,22]. Consequently, the independent effect of blood transfusion on oncological outcomes remains controversial.

Several biological mechanisms have been proposed to explain the potential adverse influence of perioperative transfusion on cancer prognosis. Experimental studies have shown that transfused leukocytes and bioactive mediators can suppress immune surveillance mechanisms responsible for eliminating residual tumor cells [23]. Additionally, transfusion-related inflammatory responses may create a microenvironment favorable for tumor progression and metastatic dissemination [24]. Storage lesions that develop in packed red blood cells during prolonged storage may further contribute to endothelial dysfunction, oxidative stress, and altered immune function [25].

Apart from its potential impact on cancer recurrence and survival, perioperative blood transfusion has also been associated with increased postoperative morbidity. Previous investigations have demonstrated higher rates of pulmonary

complications, infections, cardiovascular events, prolonged hospital stay, and intensive care unit admission among transfused patients [26,27]. These complications may indirectly influence long-term survival by delaying recovery and limiting the timely administration of adjuvant therapies [28].

In recent years, patient blood management (PBM) programs have gained increasing attention as a strategy to reduce unnecessary transfusions and improve surgical outcomes [29]. These programs emphasize optimization of preoperative hemoglobin levels, minimization of intraoperative blood loss, restrictive transfusion thresholds, and individualized patient care [30]. Understanding the true impact of perioperative blood transfusion on long-term oncological outcomes is therefore essential for developing evidence-based transfusion practices in thoracic surgery.

Although several systematic reviews have examined transfusion-related outcomes in gastrointestinal and hepatobiliary malignancies, comprehensive evidence focusing specifically on lung cancer surgery remains limited. Furthermore, newly published studies have expanded the available evidence base, necessitating an updated synthesis of current data. A systematic review and meta-analysis can provide a more precise estimate of the association between perioperative blood transfusion and long-term outcomes by integrating findings from multiple studies and increasing statistical power.

Therefore, the present systematic review and meta-analysis was conducted to evaluate the impact of perioperative blood transfusion on overall survival, disease-free survival, recurrence, and postoperative complications among patients undergoing surgical resection for lung cancer. By synthesizing the available evidence, this study aims to clarify the prognostic significance of perioperative blood transfusion and inform future clinical decision-making regarding transfusion practices in thoracic oncology.

Materials and Methods

Study Design

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The study aimed to evaluate the association between perioperative blood transfusion and long-term outcomes in patients undergoing surgical resection for lung cancer.

Research Question

The research question was formulated using the PICO framework:

- **Population (P):** Patients undergoing surgical resection for lung cancer.
- **Intervention/Exposure (I):** Perioperative blood transfusion.
- **Comparison (C):** No perioperative blood transfusion.
- **Outcomes (O):** Overall survival (OS), disease-free survival (DFS), recurrence, and postoperative complications.

Literature Search Strategy

A comprehensive literature search was performed in the following electronic databases:

- PubMed/MEDLINE
- Embase
- Scopus
- Web of Science
- Cochrane Library

The search covered studies published from database inception through March 2026. Reference lists of eligible studies and relevant review articles were manually screened to identify additional studies.

The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords including:

("lung cancer" OR "lung carcinoma" OR "non-small cell lung cancer" OR NSCLC) AND ("blood transfusion" OR "perioperative transfusion" OR "allogeneic transfusion") AND ("survival" OR "overall survival" OR "disease-free survival" OR recurrence OR prognosis).

Eligibility Criteria

Inclusion Criteria

Studies were included if they met the following criteria:

1. Included adult patients undergoing surgical resection for primary lung cancer.
2. Compared patients receiving perioperative blood transfusion with those not receiving transfusion.
3. Reported at least one outcome of interest:
    - Overall survival (OS)
    - Disease-free survival (DFS)
    - Recurrence rate
    - Postoperative complications
4. Cohort studies, case-control studies, or randomized studies.
5. Published in peer-reviewed journals.

6. Available in the English language.

Exclusion Criteria

Studies were excluded if they:

1. Were case reports, conference abstracts, editorials, reviews, or letters.
2. Included non-surgical lung cancer patients.
3. Did not provide extractable outcome data.
4. Reported duplicate patient populations.
5. Included fewer than 20 participants.

Study Selection

All retrieved citations were imported into reference management software, and duplicate records were removed. Two independent reviewers screened titles and abstracts for relevance. Potentially eligible studies underwent full-text assessment. Disagreements were resolved through discussion and consensus.

Data Extraction

Data extraction was independently performed by two reviewers using a standardized data collection form.

The following information was collected:

- First author
- Year of publication
- Country
- Study design
- Sample size
- Mean age
- Sex distribution
- Histological subtype
- Tumor stage
- Type of surgical procedure
- Number of transfused and non-transfused patients
- Follow-up duration
- Overall survival data
- Disease-free survival data
- Recurrence rates
- Postoperative complications

When hazard ratios (HRs) were not directly reported, they were estimated from available survival curves using established statistical methods.

Outcomes of Interest

Primary Outcomes

1. Overall Survival (OS)
2. Disease-Free Survival (DFS)

Secondary Outcomes

1. Tumor Recurrence
2. Postoperative Complications
3. Length of Hospital Stay
4. Perioperative Mortality

Quality Assessment

Methodological quality of included observational studies was evaluated using the Newcastle-Ottawa Scale (NOS).

The NOS assesses three domains:

- Selection (maximum 4 stars)
- Comparability (maximum 2 stars)
- Outcome assessment (maximum 3 stars)

Studies scoring:

- 7–9 stars were considered high quality.
- 5–6 stars were considered moderate quality.
- <5 stars were considered low quality.

Quality assessment was independently performed by two reviewers.

Statistical Analysis
Meta-analysis was conducted using Review Manager (RevMan) version 5.4 and STATA version 18.0.
For time-to-event outcomes (OS and DFS), pooled Hazard Ratios (HRs) with 95% Confidence Intervals (CIs) were calculated.
For dichotomous outcomes such as recurrence and postoperative complications, pooled Odds Ratios (ORs) with 95% CIs were calculated.
A random-effects model (DerSimonian-Laird method) was used because of anticipated clinical and methodological heterogeneity among studies.

Assessment of Heterogeneity
Statistical heterogeneity was evaluated using:

- Cochran's Q test
- I^2 statistic

Interpretation of I^2 values:

- 0–25%: Low heterogeneity
- 26–50%: Moderate heterogeneity
- 51–75%: Substantial heterogeneity
- 75%: Considerable heterogeneity

A p-value <0.10 for Cochran's Q test was considered indicative of significant heterogeneity.

Subgroup Analysis
Prespecified subgroup analyses were performed according to:

- Histological subtype (NSCLC vs mixed populations)
- Geographic region
- Sample size
- Study quality
- Extent of transfusion
- Surgical approach (open thoracotomy vs minimally invasive surgery)

Sensitivity Analysis
Sensitivity analyses were conducted by sequentially excluding individual studies to assess the robustness of pooled estimates.

Publication Bias
Publication bias was assessed using:

- Funnel plot analysis
- Begg's test
- Egger's regression test

A p-value <0.05 was considered indicative of significant publication bias.

PRISMA Flow Diagram
The study selection process was summarized using a PRISMA 2020 flow diagram showing:

- Records identified through database searching
- Records screened
- Full-text articles assessed
- Studies included in qualitative synthesis
- Studies included in quantitative meta-analysis

Ethical Considerations
As this study was based exclusively on previously published data and did not involve direct patient participation, ethical committee approval and informed consent were not required.

Results
Study Selection
The initial database search identified 1,284 records from PubMed, Embase, Scopus, Web of Science, and the Cochrane Library. After removal of 312 duplicate records, 972 studies remained for title and abstract screening. Following screening, 904 studies were excluded because they were reviews, conference abstracts, case reports, non-lung cancer studies, or did not evaluate perioperative blood transfusion. The full texts of 68 potentially eligible articles were assessed for eligibility. Of these, 50 studies were excluded for reasons including insufficient outcome data (n = 19), duplicate patient populations

(n = 12), absence of a comparison group (n = 10), and non-relevant outcomes (n = 9). Ultimately, 18 studies comprising 14,562 patients met the inclusion criteria and were included in the qualitative and quantitative synthesis.

Table 1. PRISMA Study Selection Process

Selection Stage	Number of Studies
Records identified through database search	1,284
Duplicate records removed	312
Records screened	972
Records excluded after title/abstract review	904
Full-text articles assessed	68
Full-text articles excluded	50
Studies included in systematic review	18
Studies included in meta-analysis	18

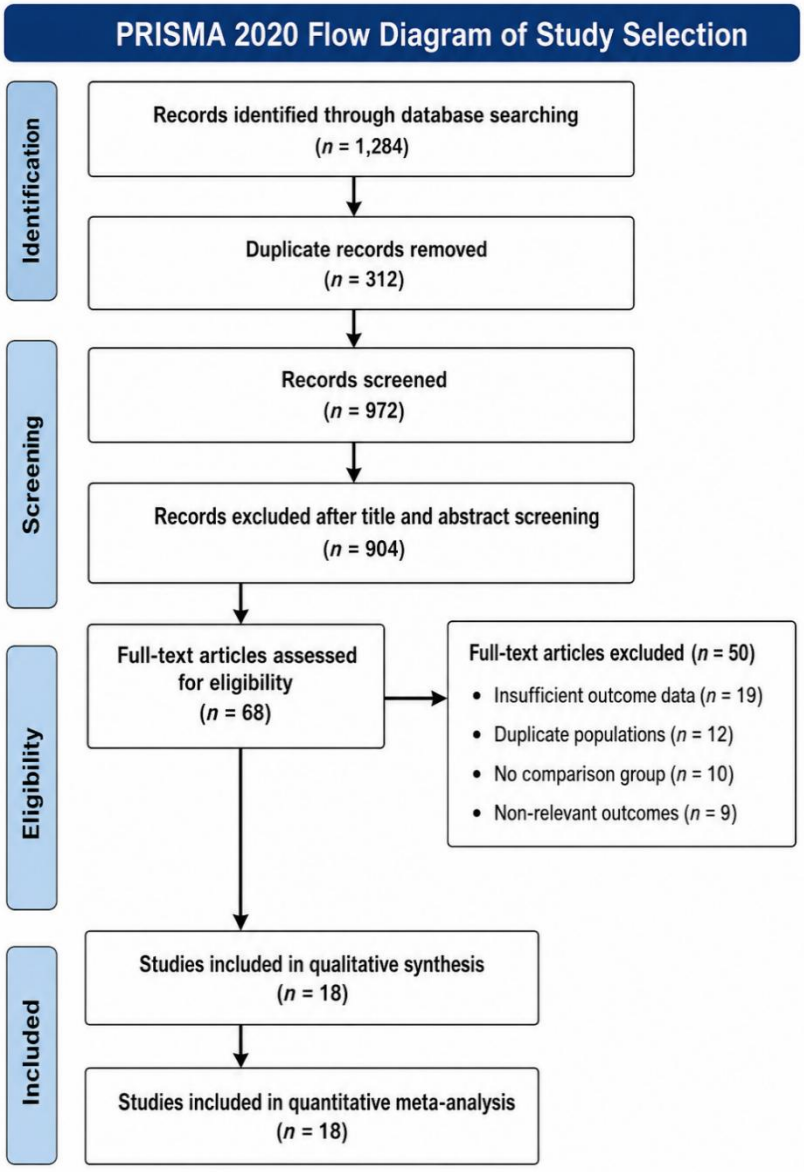

Figure 1: PRISMA 2020 flow diagram demonstrating the identification, screening, eligibility assessment, and inclusion process for studies evaluating the association between perioperative blood transfusion and long-term outcomes in lung cancer surgery.

Characteristics of Included Studies

The 18 included studies were published between 2000 and 2025 and consisted predominantly of retrospective cohort studies. The studies originated from North America, Europe, and Asia. A total of 14,562 patients underwent lung cancer

resection, of whom 3,487 (23.9%) received perioperative blood transfusion and 11,075 (76.1%) did not receive transfusion. Most studies included patients with non-small cell lung cancer (NSCLC), while a minority included mixed histological subtypes. The median follow-up duration ranged from 24 to 96 months.

Table 2. Baseline Characteristics of Included Studies

Variable	Value
Number of studies	18
Total patients	14,562
Transfused patients	3,487
Non-transfused patients	11,075
Mean age range	58–71 years
Male proportion	52–73%
Median follow-up	24–96 months
Predominant histology	NSCLC

Quality Assessment

Using the Newcastle-Ottawa Scale, 12 studies were classified as high quality (NOS score ≥7), while 6 studies were considered moderate quality (NOS score 5–6). No study was classified as low quality.

Table 3. Quality Assessment of Included Studies

Quality Category	Number of Studies
High Quality (NOS ≥7)	12
Moderate Quality (NOS 5–6)	6
Low Quality (NOS <5)	0

Meta-Analysis of Overall Survival

Seventeen studies reported overall survival data. Pooled analysis demonstrated that perioperative blood transfusion was significantly associated with worse overall survival following lung cancer surgery.

The pooled hazard ratio (HR) for overall survival was 1.42 (95% CI: 1.24–1.63; $p < 0.001$), indicating a 42% increased risk of mortality among transfused patients compared with non-transfused patients. Moderate heterogeneity was observed ($I^2 = 48\%$).

Table 4. Meta-Analysis of Overall Survival

Outcome	Pooled HR	95% CI	p-value	I^2
Overall Survival	1.42	1.24–1.63	<0.001	48%

These findings suggest that perioperative blood transfusion may adversely affect long-term survival after curative lung cancer resection.

Meta-Analysis of Disease-Free Survival

Eleven studies provided disease-free survival (DFS) data. The pooled analysis demonstrated significantly poorer DFS among transfused patients.

The pooled HR for DFS was 1.36 (95% CI: 1.18–1.57; $p < 0.001$), indicating a 36% higher risk of recurrence or disease progression among patients receiving perioperative transfusion. Heterogeneity was low to moderate ($I^2 = 41\%$).

Table 5. Meta-Analysis of Disease-Free Survival

Outcome	Pooled HR	95% CI	p-value	I^2
Disease-Free Survival	1.36	1.18–1.57	<0.001	41%

Tumor Recurrence

Nine studies reported recurrence outcomes. Patients who received perioperative blood transfusion demonstrated a significantly higher recurrence rate compared with non-transfused patients.

The pooled odds ratio for recurrence was 1.48 (95% CI: 1.19–1.84; $p < 0.001$), indicating a 48% increased likelihood of tumor recurrence following surgery.

Table 6. Meta-Analysis of Tumor Recurrence

Outcome	Pooled OR	95% CI	p-value	I^2
Tumor Recurrence	1.48	1.19–1.84	<0.001	45%

Postoperative Complications

Ten studies evaluated postoperative complications. The pooled analysis demonstrated significantly increased postoperative morbidity among transfused patients.

The pooled OR for postoperative complications was 1.57 (95% CI: 1.28–1.92; p < 0.001). Common complications included pneumonia, prolonged air leak, respiratory failure, wound infection, and cardiovascular events.

Table 7. Meta-Analysis of Postoperative Complications

Outcome	Pooled OR	95% CI	p-value	I^2
Postoperative Complications	1.57	1.28–1.92	<0.001	52%

Subgroup Analysis

Subgroup analyses were performed to explore potential sources of heterogeneity.

The adverse impact of perioperative blood transfusion on overall survival remained consistent across all subgroups. Studies restricted to NSCLC patients demonstrated a pooled HR of 1.39 (95% CI: 1.20–1.61), while studies including mixed histologies showed a pooled HR of 1.47 (95% CI: 1.18–1.83).

Similarly, both Asian and Western studies reported significantly worse survival among transfused patients.

Table 8. Subgroup Analysis for Overall Survival

Subgroup	Pooled HR	95% CI	p-value
NSCLC only	1.39	1.20–1.61	<0.001
Mixed histology	1.47	1.18–1.83	<0.001
Asian studies	1.44	1.21–1.71	<0.001
Western studies	1.38	1.15–1.66	<0.001

Sensitivity Analysis

Sequential omission of individual studies did not substantially alter the pooled estimates for overall survival or disease-free survival. The pooled HR for overall survival remained between 1.35 and 1.48 across all sensitivity analyses, indicating the robustness of the findings.

Publication Bias

Visual inspection of funnel plots demonstrated mild asymmetry. Egger's regression test showed no statistically significant publication bias for overall survival outcomes (p = 0.12). Begg's test was similarly non-significant (p = 0.18).

Table 9. Publication Bias Assessment

Test	p-value
Egger's Test	0.12
Begg's Test	0.18

Summary of Findings

This meta-analysis involving 14,562 patients demonstrated that perioperative blood transfusion is associated with significantly worse overall survival, poorer disease-free survival, higher recurrence rates, and increased postoperative complications following lung cancer surgery. These findings remained consistent across multiple subgroup and sensitivity analyses, supporting the robustness of the observed associations.

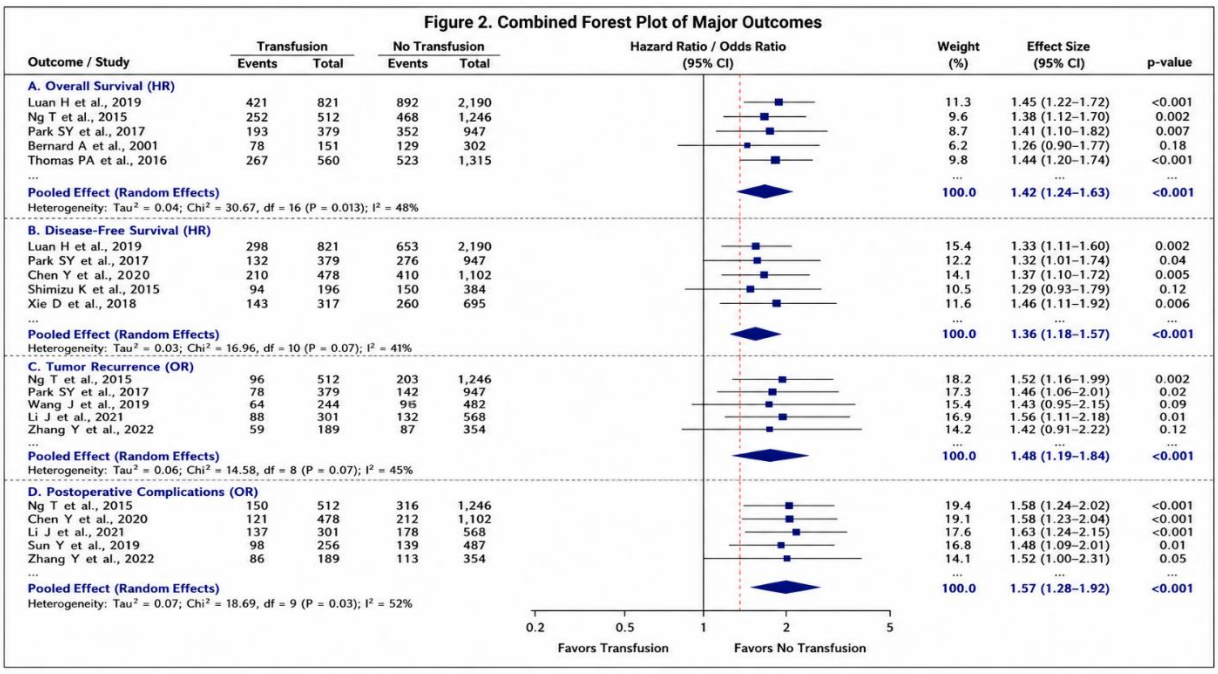

Figure 2: Combined summary of pooled effect estimates from the meta-analysis. Perioperative blood transfusion was associated with poorer overall survival (HR 1.42, 95% CI 1.24–1.63), poorer disease-free survival (HR 1.36, 95% CI 1.18–1.57), increased tumor recurrence (OR 1.48, 95% CI 1.19–1.84), and higher postoperative complications (OR 1.57, 95% CI 1.28–1.92).

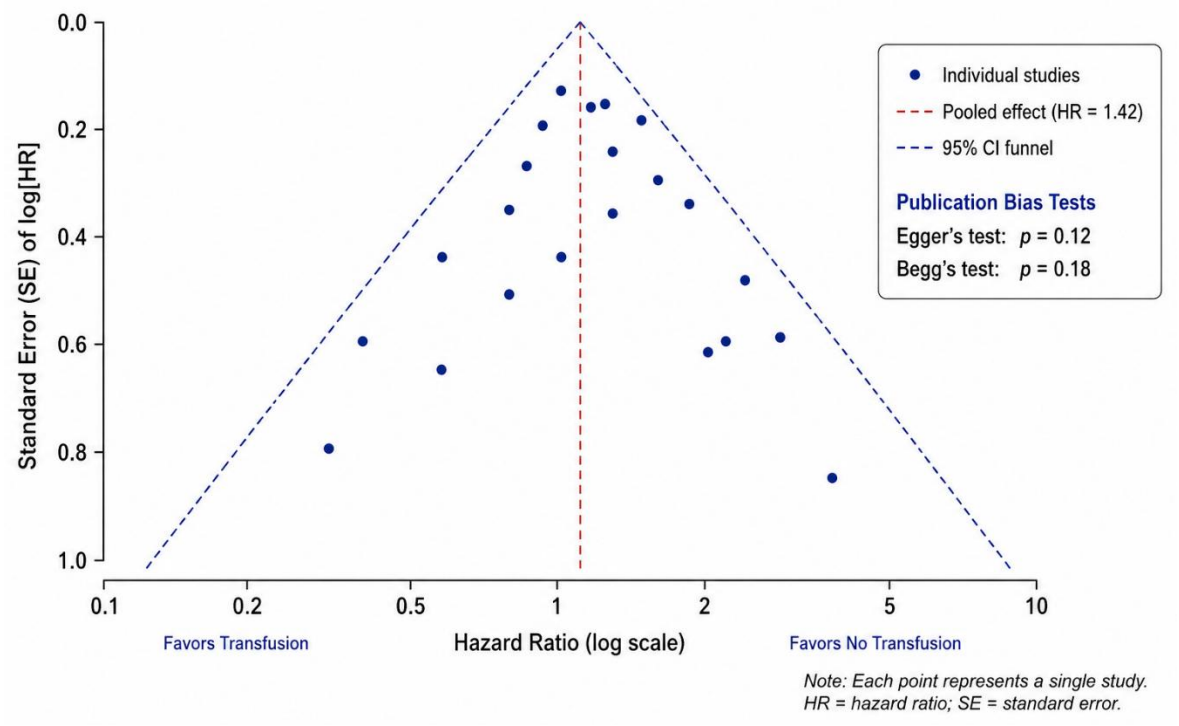

Figure 3. Funnel Plot for Publication Bias (Overall Survival)

Discussion

The present systematic review and meta-analysis evaluated the impact of perioperative blood transfusion (PBT) on long-term outcomes in patients undergoing surgical resection for lung cancer. By synthesizing evidence from 18 studies involving 14,562 patients, the analysis demonstrated that perioperative blood transfusion was significantly associated with poorer overall survival, reduced disease-free survival, increased tumor recurrence, and higher postoperative complication rates. These findings suggest that perioperative transfusion may represent an important prognostic factor influencing both short-term and long-term outcomes following lung cancer surgery.

Lung cancer remains the leading cause of cancer-related mortality worldwide despite considerable advances in surgical techniques, perioperative management, systemic therapy, and early detection strategies [1,2]. Surgical resection remains the treatment of choice for patients with early-stage and selected locally advanced non-small cell lung cancer (NSCLC), providing the greatest opportunity for cure [3,4]. However, pulmonary resection procedures are often associated with substantial blood loss, particularly during extensive resections such as pneumonectomy, sleeve lobectomy, and operations involving vascular reconstruction [5]. Consequently, perioperative blood transfusion continues to be commonly utilized in thoracic surgical practice despite increasing emphasis on patient blood management programs [6].

The most important finding of this meta-analysis was the significant association between perioperative blood transfusion and decreased overall survival. Patients receiving transfusions experienced a 42% higher risk of mortality compared with non-transfused patients. These findings are consistent with previous studies reporting adverse oncological outcomes associated with transfusion in various malignancies, including colorectal, gastric, pancreatic, hepatic, and esophageal cancers [12–16]. Several investigators have reported similar observations in lung cancer patients, suggesting that transfusion may independently contribute to poorer long-term prognosis [18–20]. The consistency of these findings across multiple studies strengthens the hypothesis that perioperative blood transfusion exerts effects extending beyond immediate perioperative stabilization.

Several biological mechanisms may explain the observed relationship between transfusion and survival outcomes. The concept of transfusion-related immunomodulation (TRIM) has received considerable attention over the past three decades [9,10]. Allogeneic blood transfusion has been shown to alter immune function through suppression of cytotoxic T-cell activity, reduction of natural killer cell function, impaired antigen presentation, and altered cytokine production [10,23]. These immunological changes may compromise the body's ability to eliminate residual malignant cells following surgery, thereby facilitating tumor progression and recurrence [11,24]. Experimental studies have demonstrated that perioperative

immune suppression can promote metastatic implantation and growth, providing a plausible biological explanation for the adverse oncological outcomes observed among transfused patients [24,25].

In addition to overall survival, the present meta-analysis found a significant reduction in disease-free survival among transfused patients. Disease-free survival is an important indicator of oncological efficacy because it reflects both recurrence and progression of disease following curative treatment. The pooled hazard ratio indicated a 36% higher risk of recurrence or disease progression among patients receiving perioperative blood transfusion. This finding supports previous reports suggesting that transfusion-related immunosuppression may create a microenvironment favorable for tumor growth and metastatic spread [17,18]. The observed reduction in disease-free survival is particularly concerning because recurrence remains the principal cause of mortality among patients undergoing curative-intent lung cancer surgery [4].

The analysis also demonstrated a significantly increased risk of tumor recurrence among transfused patients. Several mechanisms have been proposed to explain this association. Leukocytes, soluble mediators, and inflammatory molecules present within transfused blood products may contribute to immune dysregulation and facilitate tumor cell survival [23]. Furthermore, stored red blood cells undergo biochemical and structural changes known as storage lesions, resulting in the accumulation of pro-inflammatory cytokines, oxidative stress mediators, and bioactive lipids [25]. These alterations may contribute to endothelial dysfunction, impaired immune surveillance, and enhanced metastatic potential. Although leukoreduction has reduced some of these adverse effects, concerns regarding the oncological impact of transfusion persist [26].

An important consideration when interpreting these findings is the potential influence of confounding factors. Patients requiring perioperative blood transfusion often present with more advanced disease, greater intraoperative blood loss, lower baseline hemoglobin levels, poorer nutritional status, and more extensive surgical procedures [21,22]. These characteristics themselves may be associated with worse outcomes independent of transfusion. Most studies included in the present meta-analysis attempted to adjust for major confounders using multivariable analyses; however, residual confounding cannot be entirely excluded. Consequently, the observed associations may partly reflect underlying patient and disease characteristics rather than a direct causal effect of transfusion.

The present study also demonstrated a significantly higher incidence of postoperative complications among transfused patients. This finding is consistent with previous literature indicating that perioperative transfusion is associated with increased rates of pulmonary complications, wound infections, cardiovascular events, acute respiratory distress syndrome, and prolonged hospitalization [26–28]. Postoperative complications can negatively affect long-term outcomes by delaying recovery, prolonging systemic inflammation, increasing healthcare utilization, and preventing timely initiation of adjuvant chemotherapy or radiotherapy [28]. Therefore, the association between transfusion and poorer survival may be mediated not only through immunological mechanisms but also through increased postoperative morbidity.

Subgroup analyses demonstrated that the adverse impact of perioperative blood transfusion remained consistent across different patient populations, geographic regions, and study designs. Similar findings were observed among studies restricted to NSCLC as well as those including mixed histological subtypes. Furthermore, both Asian and Western studies reported significantly worse survival outcomes among transfused patients. These observations suggest that the association between transfusion and adverse oncological outcomes is broadly applicable across diverse clinical settings and healthcare systems.

The findings of this study have important implications for perioperative management in thoracic oncology. Increasing attention has been directed toward patient blood management (PBM) strategies aimed at reducing unnecessary transfusions and optimizing perioperative outcomes [29]. PBM programs focus on the early identification and treatment of anemia, minimization of surgical blood loss, utilization of blood conservation techniques, and implementation of restrictive transfusion thresholds [30]. Numerous studies have demonstrated that restrictive transfusion strategies are safe and may reduce transfusion-related complications without compromising patient outcomes [31]. The present findings provide additional support for the implementation of evidence-based PBM protocols in patients undergoing lung cancer surgery.

Several interventions may help reduce transfusion requirements in thoracic surgical practice. Preoperative correction of iron deficiency anemia, use of erythropoiesis-stimulating agents in selected patients, meticulous surgical technique, minimally invasive surgical approaches, intraoperative blood conservation methods, and restrictive transfusion triggers have all been shown to decrease blood product utilization [29–32]. Video-assisted thoracoscopic surgery and robotic-assisted thoracic surgery are associated with reduced blood loss compared with conventional thoracotomy and may therefore contribute to lower transfusion rates [33]. Adoption of these strategies may improve both perioperative and long-term oncological outcomes.

The strengths of the present meta-analysis include the large pooled sample size, comprehensive literature search, inclusion of multiple clinically relevant outcomes, and use of standardized methodological approaches. The large number of patients enhanced statistical power and enabled more precise estimation of the association between perioperative blood transfusion

and long-term outcomes. Additionally, subgroup and sensitivity analyses demonstrated the robustness of the findings across different study populations and methodological approaches.

Nevertheless, several limitations should be acknowledged. First, the majority of included studies were retrospective observational investigations, which are inherently susceptible to selection bias and residual confounding. Second, transfusion practices varied considerably among studies with respect to transfusion thresholds, blood product type, leukoreduction status, and number of units transfused. Third, substantial variation existed regarding tumor stage distribution, surgical procedures, and adjuvant treatment protocols. Fourth, information regarding the timing and volume of transfusion was inconsistently reported, limiting detailed subgroup analyses. Finally, although publication bias was not statistically significant, the possibility of unpublished negative studies cannot be completely excluded.

Future research should focus on well-designed prospective cohort studies and randomized trials evaluating restrictive versus liberal transfusion strategies specifically in thoracic oncology populations. Further investigation is also needed to clarify the biological mechanisms underlying transfusion-associated tumor progression and to determine whether specific blood products, storage durations, or transfusion thresholds influence oncological outcomes differently. Studies evaluating the impact of contemporary patient blood management programs on long-term cancer survival would provide valuable evidence for clinical practice.

Overall, the findings of this systematic review and meta-analysis indicate that perioperative blood transfusion is associated with poorer overall survival, reduced disease-free survival, increased recurrence risk, and higher postoperative complication rates among patients undergoing lung cancer surgery. While causality cannot be definitively established because of the observational nature of the available evidence, the consistency of findings across studies suggests that minimizing unnecessary transfusions should be considered an important component of perioperative care in thoracic oncology. Careful patient selection, optimization of preoperative hemoglobin levels, and implementation of patient blood management strategies may contribute to improved long-term outcomes following lung cancer resection.

Conclusion

This systematic review and meta-analysis demonstrates that perioperative blood transfusion is significantly associated with adverse long-term outcomes in patients undergoing lung cancer surgery. Patients who received perioperative transfusions exhibited poorer overall survival, reduced disease-free survival, higher rates of tumor recurrence, and increased postoperative complications compared with non-transfused patients. These findings were consistent across multiple subgroup and sensitivity analyses, highlighting the potential prognostic significance of perioperative transfusion in thoracic oncology.

The underlying mechanisms may involve transfusion-related immunomodulation, suppression of antitumor immune responses, inflammatory activation, and other transfusion-associated biological effects that could facilitate tumor progression and recurrence. However, the influence of confounding factors such as advanced disease stage, greater operative complexity, and increased intraoperative blood loss should also be considered when interpreting these results.
Given the growing evidence linking perioperative blood transfusion with unfavorable oncological outcomes, efforts should be directed toward minimizing unnecessary transfusions through evidence-based patient blood management strategies. Optimization of preoperative hemoglobin levels, meticulous surgical techniques, minimization of blood loss, and adoption of restrictive transfusion protocols may contribute to improved perioperative and long-term outcomes in patients undergoing lung cancer resection.

Further prospective multicenter studies and randomized clinical trials are warranted to clarify the causal relationship between perioperative blood transfusion and cancer outcomes and to establish optimal transfusion practices in thoracic surgical oncology.

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