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Review Article

Construction and evaluation of a predictive model for radiation-induced lung injury in lung cancer: a meta-analysis

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Abstract: Objective: To construct and evaluate a predictive model for radiation-induced lung injury (RILI) in lung cancer patients based on a meta-analysis of observational studies. Methods: A systematic search was conducted across various databases to identify observational studies on the prevalence and risk factors of RILI in lung cancer from the inception of each database up until June 2024. Meta-analysis was performed using Review Manager 5.3 software to calculate the latest prevalence data and pooled risk values for significant risk factors associated with RILI. A logistic regression model was developed using the natural logarithmic transformation of the combined risk values. External validation was performed with 180 lung cancer patients who underwent radiotherapy at Yinzhou Affiliated Hospital from July 2023 to June 2024. The predictive performance of the model was assessed using the area under the receiver operating characteristic (ROC) curve (AUC), and clinical practicability was evaluated by decision curve analysis. Results: A total of 27 studies were included in the analysis. The meta-analysis revealed that the prevalence of RILI in lung cancer patients was 33.0% (95% confidence interval [CI]: 23.0%-42.0%). Key risk factors identified for RILI included age, mean lung dose (MLD), volume of the lung receiving P20 Gray (V20), chronic obstructive pulmonary disease (COPD), radiotherapy dose, and volume of normal lung spared from irradiation at doses > 5 Gy (AVS5). The combined odds ratios (ORs) for these factors were 2.42 (95% CI: 1.08, 5.43) for age, 1.31 (95% CI: 1.16, 1.48) for MLD, and 1.64 (95% CI: 1.02, 2.64) for V20, among others. The resulting predictive model was: Logit(P) = -0.955 + 0.884X1 + 0.270X2 + 0.495X3 + 1.688X4 + 1.147X5 - 1.966X6, where X1, X2, X3, X4, X5, and X6 represent age, MLD, V20, COPD, radiotherapy dose, and AVS5, respectively. The model's AUC was 0.875 (95% CI: 0.799-0.951), with a sensitivity of 83.3% and specificity of 91.7%. Conclusion: Age, MLD, V20, COPD, radiotherapy dose, and AVS5 are significant risk factors for RILI in lung cancer patients. The constructed predictive model based on these factors demonstrates strong performance, with good evaluation results, making it useful for clinical risk assessment and management.

Keywords: Meta-analysis, lung cancer, radioactivity, lung injury, risk factors, predictive model

Introduction

Lung cancer is a major global health threat, and radiotherapy is a crucial treatment modality for this condition [1]. However, radiation-induced lung injury (RILI) is a common and serious complication during lung cancer radiotherapy. It not only affects patients' quality of life but can also limit the radiotherapy dose and efficacy, potentially endangering patients' lives [2, 3]. Currently, predicting RILI in clinical practice presents significant challenges. The lack of accurate and reliable prediction methods makes it difficult for physicians to balance treatment effectiveness and complication risks when planning radiotherapy [4].

Meta-analysis is a powerful tool that can integrate results from multiple independent studies, enhancing statistical power and the reliability of conclusions [5]. Developing an effective predictive model for RILI in lung cancer may help identify high-risk patients early, enabling personalized adjustments to radiation doses

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and treatment strategies or the implementation of preventive drug interventions, ultimately improving treatment outcome [6]. Identifying independent risk factors for RILI and constructing a risk prediction model are urgentpriorities. While numerous studies [7, 8] have investigated the risk factors for RILI in lung cancer, there are discrepancies in the risk factors identified across studies, and many studies suffer from small sample size, which reduces the predictive power of their models and limits the ability to accurately identify high-risk patients.

This study aims to conduct an evidence-based evaluation of existing research on the risk factors for RILI in lung cancer. A meta-analysis was used to calculate the combined risk values of each factor. The identified predictive variables were then used to construct a logistic regression model and assess its predictive efficacy.

Materials and methods

Literature search

This study has been registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42024586813). We selected the following databases for our search: PubMed, Web of Science, Embase, Scopus, IEEE Xplore, Cochrane Library, EBSCO Information Services (EIS) host (EBSCOhost), etc. The search terms used included “lung cancer”, “radiation-induced lung injury”, “morbidity”, “prevalence”, “epidemiology”, “incidence”, “risk factors”, and “influence factors”. Two researchers performed the search using a combination of subject and free terms to capture both prospective and retrospective studies evaluating the risk factors of radiation-induced lung injury in lung cancer. The time frame for the search extends from the establishment of each database to June 2024, and only full-text literature published in English was included for evaluation. Additionally, the reference lists of qualified studies and relevant reviews were examined to ensure comprehensive coverage. After completing the search, the two researchers cross-checked the results. Any discrepancies were resolved through discussion. The search strategy used was: (((lung cancer[Title/Abstract]) AND (radiation-induced lung injury[Title/Abstract])) AND (Morbidity[Title/Abstract])) OR (Prevalence[Title/Abstract]) OR (Epidemiology [Title/Abstract]) OR (Incidence[Title/Abstract]) OR (risk factors[Title/Abstract]) OR (influence factor[Title/Abstract]).

Study screening and inclusion criteria

The search results were imported into Endnote literature management software to create a citation database. Two researchers independently screened the studies based on the inclusion and exclusion criteria. After completing the screening, the results were cross-checked, and any disagreements were submitted to a third senior researcher for arbitration.

Inclusion criteria: (1) Studies involving lung cancer patients undergoing radiotherapy and reporting RILI. (2) Studies providing sufficient data for analyzing risk factors. (3) Retrospective or prospective studies. (4) Studies involving adult lung cancer patients. (5) Studies clearly diagnosing RILI according to relevant criteria.

Exclusion criteria: (1) Duplicate publications. (2) Basic research studies. (3) Review articles. (4) Studies without a control group. (5) Studies from which data could not be converted into odds ratios (OR) and 95% confidence intervals (CI).

Data extraction and quality evaluation

Min Peng and Zhiwei Sun used a standardized data extraction form developed by the research group to extract the following information from eligible studies: first author’s name, publication year, sample size, study type, incidence of RILI (2015-2024), risk factors, and associated data (such as OR, 95% CI, contingency table data). After data extraction, the results were cross-checked by the researchers. Any discrepancies were resolved by consulting a third senior researcher. Based on the extracted information, two researchers independently evaluated the quality of the studies using the Newcastle-Ottawa Scale (NOS) [9]. Any disagreements in the quality assessment were also referred to a third senior researcher for arbitration.

Meta-analysis

Meta-analysis was conducted using Review Manager 5.3 software to determine the risk factors for RILI in lung cancer through data aggregation. Since this was a combined analysis of risk factors, the OR and the correspond-

ing 95% CI [10] were used as the effect size. First, the clinical and methodological similarities of the included studies were assessed, followed by an evaluation of statistical heterogeneity between the studies using both qualitative and quantitative methods. The evaluation indicators included the Q-test and I^2 test. If the results showed $P > 0.1$ and $I^2 < 50\%$, the fixed-effects model (FEM) was used for data aggregation; otherwise, the random-effects model (REM) was applied.

Sensitivity analysis and publication bias evaluation

After the meta-analysis, a sensitivity analysis was performed to assess the robustness of the results. In this analysis, the statistical approach was modified by alternating between the FEM and REM to check for any significant changes in the pooled effect size. Concurrently, publication bias was evaluated using Begg's and Egger's tests. *P*-value less than 0.05, suggested possible publication bias.

Prediction model construction

A logistic regression model was constructed based on data from prospective or retrospective studies to calculate the OR of risk factors and evaluate their contribution to the occurrence of specific diseases. This model was used to predict disease risk. In this study, meta-analysis was first used to calculate the combined risk value for each risk factor (as predictor variables) for RILI in lung cancer. Then, a logistic regression model was developed based on the natural logarithmic transformation of the combined risk. This approach accumulates the sample size from existing studies, overcoming limitations such as small sample sizes in individual studies, thus ensuring the scientific validity, reliability, and accuracy of the model's predictions.

The theoretical predictive model was expressed as:

$$Logit(P) = Ln\left(\frac{P}{1 - P}\right) = \alpha + \beta 1X1 + \beta 2X2 + \ldots + \beta iXi + \ldots \beta nn$$

The risk probability of RILI in lung cancer can be calculated by the following formula:

$$P = \frac{e^{\alpha} + \beta 1X1 + \beta 2X2 + \ldots + \beta iXi + \ldots \beta nXn}{1 + e^{\alpha + \beta 1X1 + \beta 2X2 + \ldots + \beta iXi + \ldots \beta nXn}}$$

In the above formula, "X1, X2,..., Xi,..., Xn" represent the risk factors. The regression coefficient of each factor βi is the natural logarithm value of the combined risk. The formula for calculating βi is:

$$\beta i = Ln(ORi)$$

As shown in the theoretical model, the constant term α can be calculated as follows:

$$\alpha = Ln\left(\frac{Poj}{1 - Poj}\right) - \beta 1\bar{X}1 + \beta 2\bar{X}2 + \ldots + \beta i\bar{X}i + \ldots \beta n\bar{X}n$$

In this equation, P0 is the prevalence rate. X1, X2,..., Xi,..., Xn represent the average values of the risk factors in the population (i.e., the average exposure rate). These values can be estimated based on the prevalence and incidence of RILI in a specific area. However, obtaining the average exposure rate in practice can be challenging. Therefore, it is generally recommended not to adjust the constant term. Instead, it is calculated directly as:

$$\alpha = Ln\left(\frac{Poj}{1 - Poj}\right)$$

While simplifying the calculation of the constant term increases the model's practicality, if the prevalence of risk factors in the target population is high, or if the risk factors carry significant risk, the resulting disease risk may be overestimated.

Clinical validation of the model

Lung cancer patients undergoing radiotherapy were selected for external validation. Patient screening and identification: Lung cancer patients who received radiotherapy at Yinzhou Affiliated Hospital from July 2023 to June 2024 were specifically chosen as the research subjects. Using the hospital's electronic medical record system, patients were screened based on admission dates and diagnostic records to identify those meeting the criteria for the study period and disease type. A total of 180 patients were selected. Data sources: Clinical data were primarily sourced from the electronic medical record system, which included patients' basic information, disease diagnoses, treatment procedures, and examination and test results.

Statistical analysis

Meta-analysis was performed using Review Manager 5.3 software. The combined OR was

Table 1. Basic characteristics of studies

Serial number	Radiation-induced lung injury types	Follow-up time [mean (range) months]	Age Mean years	Gender (male * female)	n/N	Reported risk factors	NOS
[11]	RRP	-	69	-	15/80	-	7
[12]	≥ 2 grade RILI	1	-	79*41	34/120	-	6
[13]	≥ 2 grade RILI	1 years	73.5	15*5	9/21	-	7
[14]	≥ 2 grade RILI	2 years	67	108*34	29/142	-	9
[15]	Grade 2 RP	Two years	79	39*24	2/63	-	7
[16]	RILT	2 years	73	70*20	19/90	-	7
[17]	Acute pneumonia	Median 16	73	58*52	55/110	-	7
[18]	Local lung fbrosis	36	73	58*52	36/110	-	8
[19]	Acute G1 RILD	≤ 90 days	75	61*45	72/106	-	8
[20]	ILAs	≥ 6 months	61	85*10	15/95	-	7
[21]	RP	26.6 (10.8-37.6)	76	14*2	12/16	-	7
[22]	RP	1 year	67	81*6	64/87	-	8
[23]	Severe RILT	9 (6-114)	67.75	53*1	22/54	K	6
[24]	RILT	≥ 6 months	60.59	79*47	45/126	DEFJK	6
[25]	≥ 3 grade RILI	Within 1 to 3 months	60	116*35	36/151	ACDK	7
[26]	≥ grade 3 RP	-	-	-	12/95	L	8
[27]	≥ 2 grade RILI	-	58	193*58	140/251	A	7
[28]	≥ 2 grade RILI	12.3 (6.1-52.0)	61	75*8	25/83	I	7
[29]	≥ 2 grade RILI	Median 545 days	56	137*24	51/161	A	7
[30]	Clinically significant pneumonitis	4.5 years	65	82*27	17/109	ACH	8
[31]	≥ 2 grade RILI	-	68	328*110	122/438	C	8
[32]	Grade 2-3 pulmonary toxicity	30.9 (6.7-56.7)	71.7	50*10	9/60	AB	6
[33]	RP	-	32 to 78	72*8	13/93	EGH	7
[34]	Acute ARP	12 weeks	70	37*10	11/47	BFM	7
[35]	≥ 2 grade RP	6	-	263*106	146/369	BJ	8
[36]	RP	6	59	81*9	90/96	B	9
[37]	≥ G3 grade RP	≥ 5	63	109*13	14/174	BCI	7

n is the number of people with radiation-induced lung injury, and N is the total number of included patients. RILI: radiation-induced lung injury; RILT: radiation-induced lung toxicity; RILD: radiation-induced liver disease; ILAs: interstitial lung abnormalities; RP: radiation pneumonitis; RF: radiation fibrosis; RRP: radiation recall pneumonitis; ARP: acute radiation pneumonitis; ILAs: interstitial lung abnormalities; G: RTOG grade. A: mean lung dose (MLD); B: Age; C: volume of the lung receiving P20 Gray (V20); D: radiotherapy dose; E: chronic obstructive pulmonary disease (COPD); F: smoke; G: forced expiratory volume in one second (FEV1) or FEV1/forced vital capacity (FVC); H: normal-tissue toxicity probability (NTCP); I: absolute volume of normal lung spared from irradiation at a dose > 5 Gy (AVS5); J: planning target volume; K: neutrophil to lymphocyte ratio (NLR); L: radiological ILAs; M: administration of induction gemcitabine. NOS: Newcastle Ottawa Scale.

used to determine the overall risk level. Additionally, if the OR was approximately 1, this indicated that the risk factor has minimal impact, and such factors were excluded from the risk prediction model. External validation: The model's predictive performance was evaluated using the area under the receiver operating characteristic curve (AUC), sensitivity, and specificity.

Results

Literature search results

Fourteen studies [11-29] published between 2015 and 2024 reported the incidence of RILI in lung cancer. A total of 1,363 cases were included, with 351 cases of RILI (25.75%). Studies [23-29] and others [30-37] reported risk factors and OR (with 95% CI) for RILI in lung cancer. The basic characteristics and NOS scores of each study are shown in **Table 1**, and the screening process is shown in **Figure 1**.

Radiotherapy for lung cancer

Radiotherapy techniques for lung cancer: Three-dimensional conformal radiotherapy (3D-CRT): Approximately 6% of the included studies utilized 3D-CRT. This technique constructs the three-dimensional shape of the tumor using computed tomography (CT) and

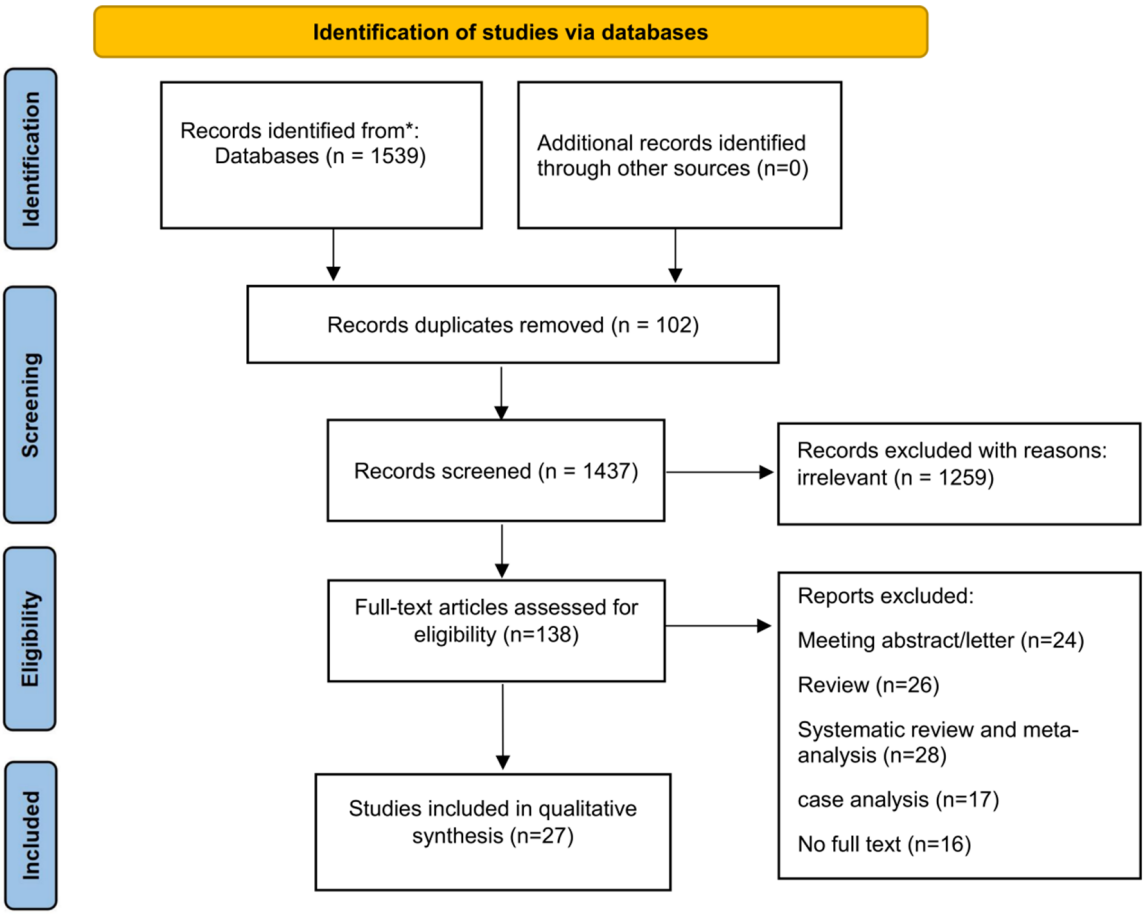

Figure 1. The screening process.

adjusts the angles and shapes of the radiation beams so that the high-dose radiation area coincides with the tumor's target volume, minimizing radiation exposure to surrounding healthy tissues.

Intensity-modulated radiotherapy (IMRT): Around 5% of the studies employed IMRT. This method modulates the intensity of radiation beams based on 3D-CRT, creating a more uniform dose distribution within the tumor while better protecting critical organs, such as the heart and spinal cord, from radiation damage.

Drug therapy for lung cancer: Cisplatin: Approximately 63% of the studies combined cisplatin with other drugs. Cisplatin is typically administered via intravenous injection, with the dose calculated based on the patient's body surface area. In combination chemotherapy regimens, a common dose is 75-100 mg/m^2, with treatments administered every 3-4 weeks. It is frequently combined with drugs such as paclitaxel and gemcitabine for lung cancer treatment. Its mechanism of action involves binding to DNA, disrupting the DNA structure of cancer cells, and preventing their replication and proliferation. However, due to the variety of research sources, the exact number of studies involving cisplatin was not recorded in the original data.

Carboplatin: Approximately 60% of the studies involved carboplatin. Like cisplatin, carboplatin is administered intravenously, with the dose typically calculated using the Calvert formula (based on factors such as glomerular filtration rate). In lung cancer treatment, it is often combined with other chemotherapeutic agents, such as pemetrexed for non-small cell lung cancer. Its anti-tumor effect is primarily due to DNA cross-linking, similar to cisplatin.

Pemetrexed: Primarily used for non-small cell lung cancer, especially lung adenocarcinoma,

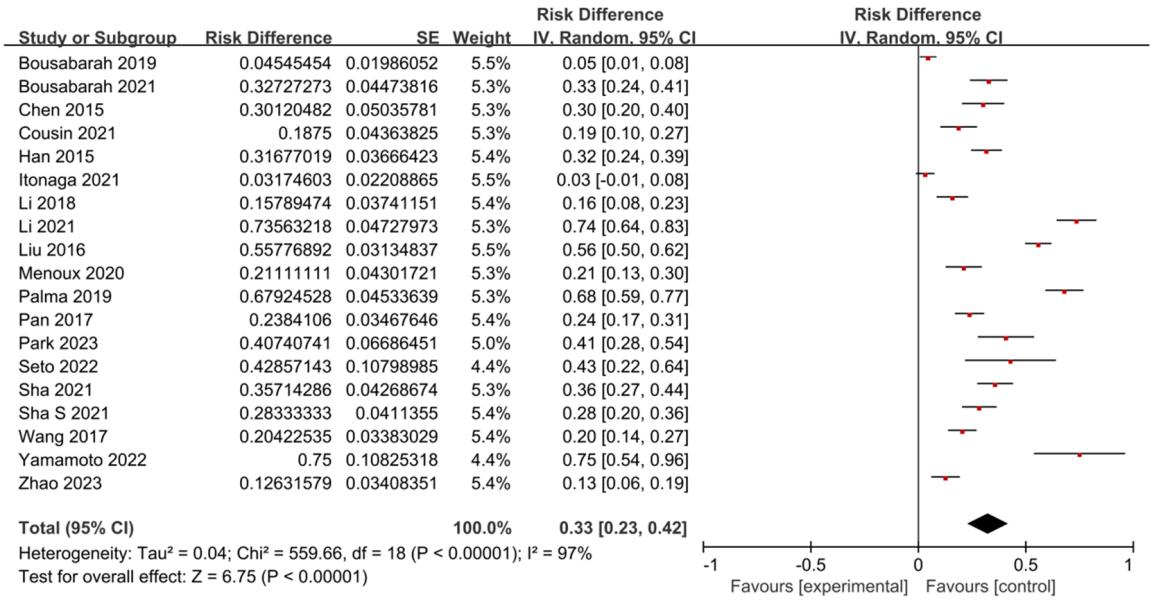

Figure 2. Forest plot of meta-analysis of prevalence of radiation-induced lung injury in lung cancer.

pemetrexed was used in approximately 20% of the studies. It is administered intravenously and is often combined with platinum-based drugs in regimens like AP (pemetrexed + cisplatin). The usual dose is 500 mg/m^2, with a treatment cycle every 3 weeks. Pemetrexed works by inhibiting cell growth through interference with the folate metabolic pathway in cancer cells. Due to issues with the original data, the exact number of studies using pemetrexed could not be determined.

Gemcitabine: Used in the treatment of non-small cell lung cancer, approximately 8% of the studies included gemcitabine. Administered by intravenous infusion, it can be used alone or in combination with other drugs, such as in the GP regimen (gemcitabine + cisplatin). When used alone, the dose is typically 1000-1250 mg/m^2 with a 3-week treatment cycle. Gemcitabine inhibits cancer cell growth by incorporating into DNA and interfering with DNA synthesis. The exact number of studies involving gemcitabine is difficult to determine.

However, some studies did not specify the treatment methods for lung cancer.

Meta-analysis of the prevalence of RILI in lung cancer

The heterogeneity test yielded I^2 = 98%, P < 0.001, indicating significant heterogeneity among the studies. The REM was used for the meta-analysis. The overall prevalence of RILI in lung cancer was 33.0% (95% CI: 23.0%-42.0%) (**Figure 2**).

Meta-analysis of risk factors for RILI in lung cancer

Meta-analysis was performed on risk factors reported in more than three studies. Five studies reported that age is a risk factor for RILI in lung cancer. Seven studies identified the mean lung dose (MLD) as a risk factor, and four studies reported that the volume of the lung receiving P20 Gray (V20) is a risk factor. All analyses used the REM to combine odds ratios (ORs). The combined ORs for age, MLD, and V20 were 2.42 (95% CI: 1.08, 5.43), 1.31 (95% CI: 1.16, 1.48), and 1.64 (95% CI: 1.02, 2.64), respectively. All P values were less than 0.05 (**Figure 3**).

Two studies each reported that normal-tissue toxicity probability (NTCP), neutrophil-to-lymphocyte ratio (NLR), smoking, chronic obstructive pulmonary disease (COPD), radiotherapy dose, and the absolute volume of normal lung spared from irradiation at a dose > 5 Gy (AVS5) are risk factors for RILI in lung cancer. The combined ORs for NTCP, NLR, and smoking were 3.70 (95% CI: 0.25, 54.69), 1.46 (95% CI: 0.11, 19.67), and 0.71 (95% CI: 0.04, 11.44), respec-

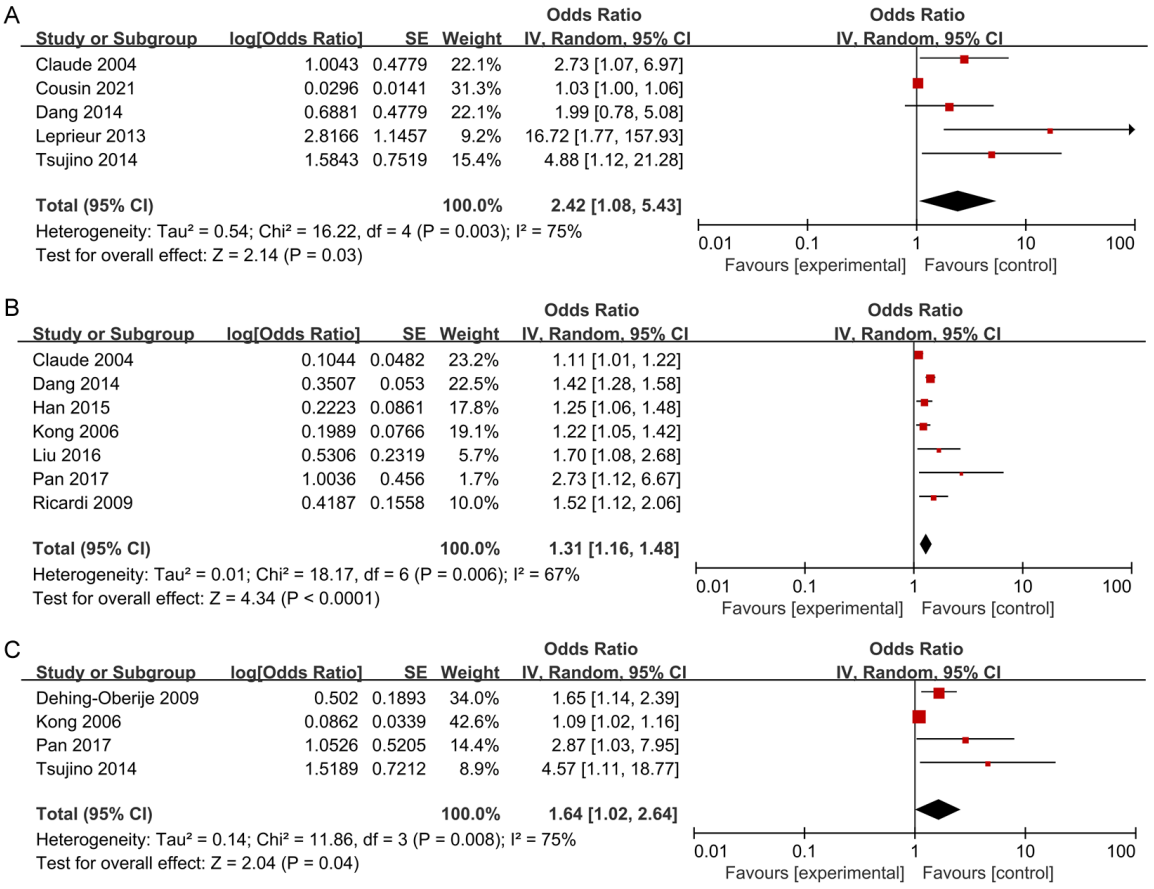

Figure 3. Forest plot of meta-analysis of combined ORs of age, mean lung dose, and volume of the lung receiving P20 Gray. A. Age; B. Mean lung dose (MLD); C. Volume of the lung receiving P20 Gray (V20).

tively, with all *P* values greater than 0.05. The combined ORs for COPD, radiotherapy dose, and AVS5 re 5.41 (95% CI: 1.86, 15.74), 3.15 (95% CI: 1.92, 5.17), and 0.14 (95% CI: 0.03, 0.71), respectively, with all *P* values less than 0.05 (**Figure 4**).

Sensitivity analysis and publication bias assessment

The pooled analysis models of the significant risk factors for RILI were switched to examine the sensitivity of the meta-analysis results. The results showed no significant differences between the FEM and REM for risk factors like age, MLD, V20, COPD, radiotherapy dose, and AVS5, indicating that the results had relatively good stability (**Figures 5** and **6**). Begg's rank correlation and Egger's regression tests were used to assess publication bias. The results showed no significant publication bias in the studies (Begg's test: Z = 0.057, *P* = 0.814; Egger's test: t = 4.232, *P* = 0.592).

Results of prediction model construction

Based on the meta-analysis results and the selection criteria for comprehensive risk factors, a risk prediction model was constructed using the combined results of independent risk factors (age, MLD, V20, radiotherapy dose, and AVS5): Logit(P) = -0.955 + 0.884X1 + 0.270X2 + 0.495X3 + 1.688X4 + 1.147X5 - 1.966X6. In the prediction model, X1, X2, X3, X4, X5, and X6 represent age, MLD, V20, COPD, radiotherapy dose, and AVS5 respectively (**Table 2**).

Model validation

Among the 180 lung cancer patients, 36 cases (20%) had RILI. According to the model, an estimated 42 cases of RILI may occur among the 180 patients. The ROC curve was plotted based

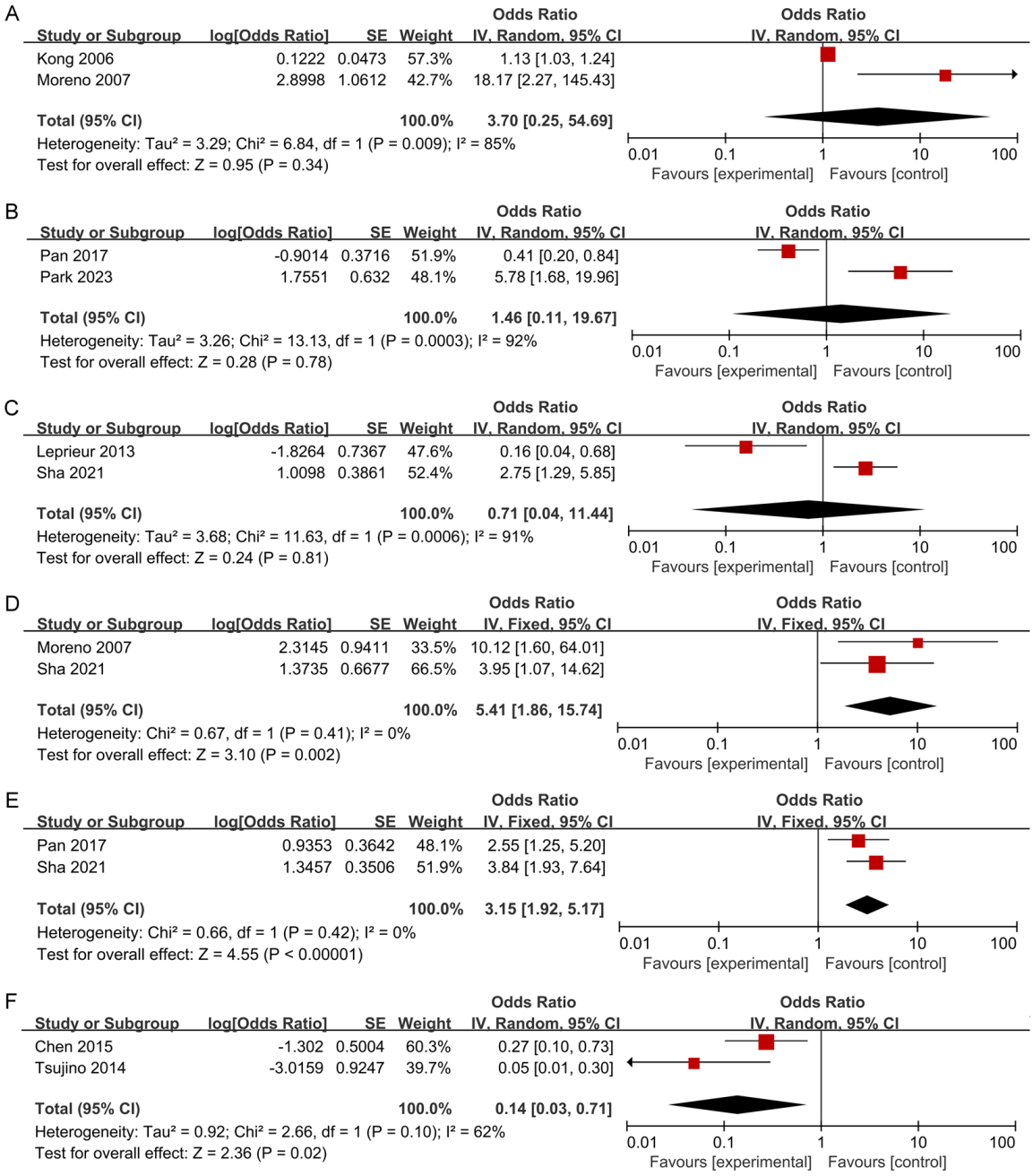

Figure 4. Forest plot of meta-analysis of combined odds ratios of other indicators. A. Normal-tissue toxicity probability (NTCP); B. Neutrophil-to-lymphocyte ratio (NLR); C. Smoke; D. Chronic obstructive pulmonary disease (COPD); E. Radiotherapy dose; F. Absolute volume of normal lung spared from irradiation at a dose > 5 Gy (AVS5).

on the model's evaluation results. The validation results were as follows: AUC = 0.875 (95% CI: 0.799-0.951), sensitivity = 83.3%, and specificity = 91.7% (**Figure 7**).

Discussion

RILI is a serious complication following radiotherapy for lung cancer. The mechanisms underlying its occurrence are complex and involve multiple factors. Currently, there is no accurate method for predicting RILI in clinical practice, making it difficult to identify high-risk patients in advance and implement preventive measures. This study aims to determine the prevalence and risk factors of RILI in lung cancer patients through meta-analysis and construct a

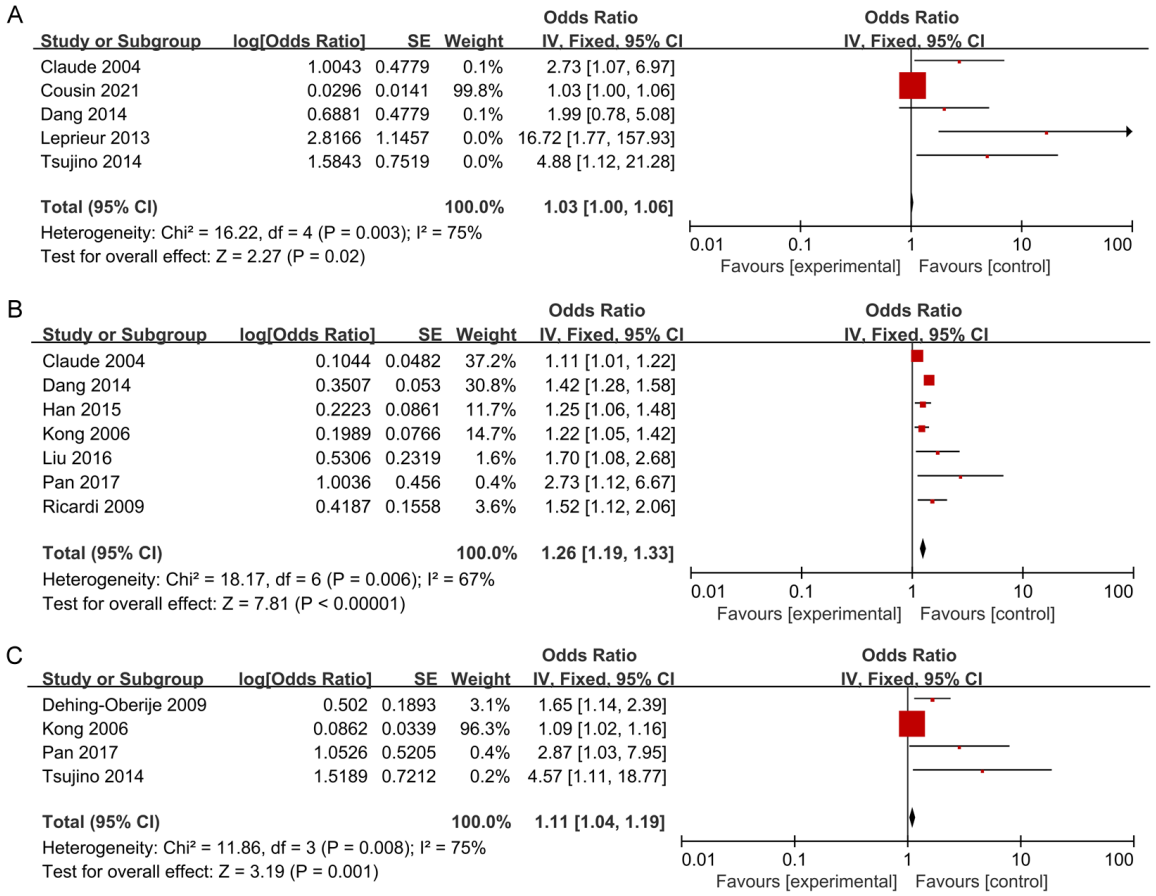

Figure 5. Sensitivity analysis of the impact of age, mean lung dose, and volume of the lung receiving P20 Gray. A. Age; B. Mean lung dose (MLD); C. Volume of the lung receiving P20 Gray (V20).

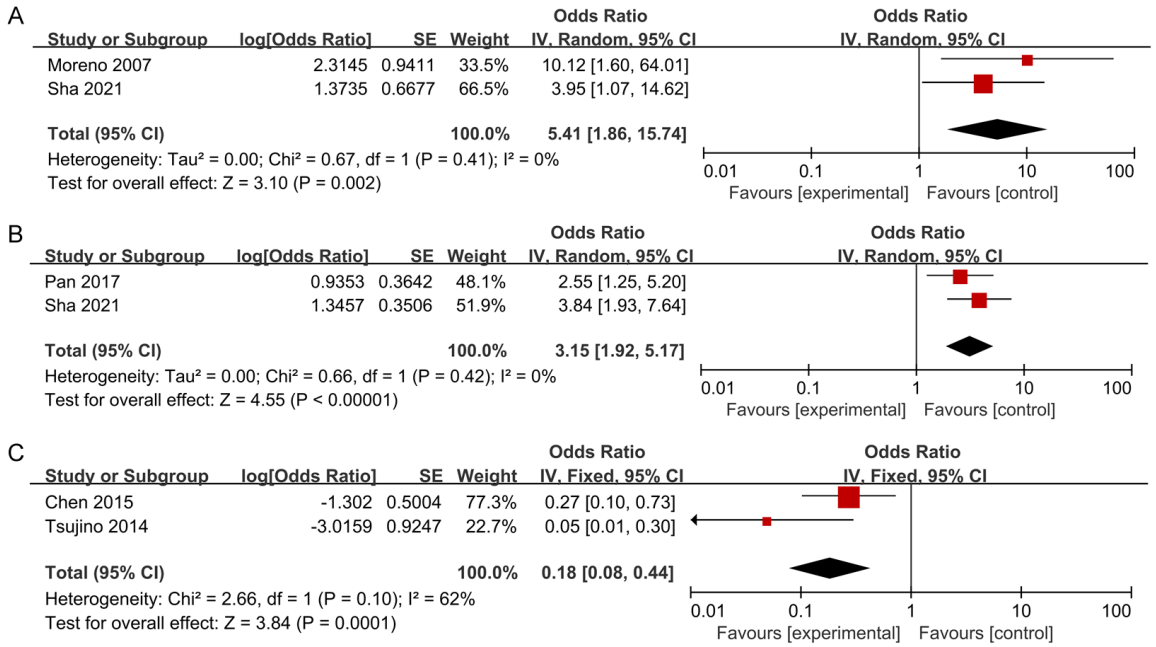

Figure 6. Sensitivity analysis of the impact of chronic obstructive pulmonary disease, radiotherapy dose, and absolute volume of normal lung spared from irradiation at a dose > 5 Gy. A. Chronic obstructive pulmonary disease (COPD); B. Radiotherapy dose; C. Volume of normal lung spared from irradiation at a dose > 5 Gy (AVS5).

Table 2. Construction indicators for predictive models

X	Pooled OR	β
Age	2.42	0.884
MLD	1.31	0.270
V20	1.64	0.495
COPD	5.41	1.688
Radiotherapy dose	3.15	1.147
AVS5	0.14	-1.966

MLD: mean lung dose; V20: volume of the lung receiving P20 Gray; COPD: chronic obstructive pulmonary disease; AVS5: volume of normal lung spared from irradiation at a dose > 5 Gy; OR: odds ratio.

risk predictive model to provide a decision-making basis for clinicians.

The meta-analysis found that the prevalence of RILI in lung cancer patients was 33.0%. This relatively high prevalence indicates that clinicians should prioritize the prevention and management of RILI when treating lung cancer with radiotherapy. RILI primarily results from a series of pathophysiologic changes caused by the lung's exposure to ionizing radiation [38]. Studies have shown that factors such as age, MLD, V20, COPD, radiotherapy dose, and AVS5 are significantly associated with RILI.

Age is a risk factor for RILI in lung cancer. As people age, physical function declines, and the tolerance to radiotherapy decreases, making elderly patients more susceptible to RILI [39]. Therefore, for older lung cancer patients, lung function should be closely monitored during radiotherapy, and preventive measures should be taken promptly. MLD refers to the average dose received by the entire lung during radiotherapy. A higher MLD leads to greater radiation damage to lung tissue, thereby increasing the risk of RILI. The main manifestation of MLD-induced lung injury is lung toxicity, particularly in the low-function areas of the irradiated lung, which may lead to a higher toxicity rate [40]. During radiotherapy planning, efforts should be made to minimize MLD to reduce the risk of RILI.

V20 refers to the percentage of lung volume receiving a dose of 20 Gy or more relative to the total lung volume. A higher V20 means that a larger portion of lung tissue is irradiated with a high dose, which increases the likelihood of

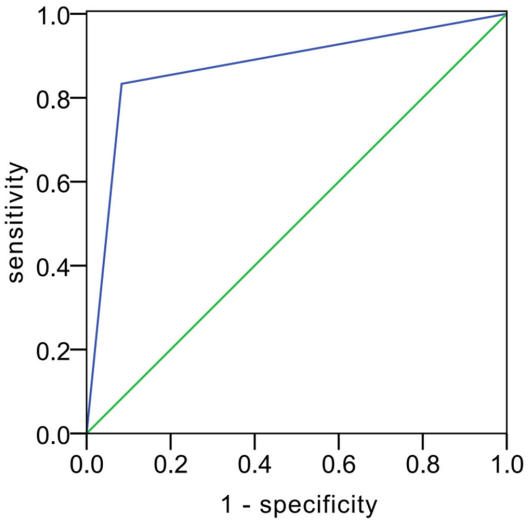

Figure 7. Receiver operator characteristic curve of model validation.

RILI [41]. In radiotherapy planning, V20 should be kept within a reasonable range to minimize the risk of RILI. COPD may also be a risk factor for RILI in lung cancer due to several reasons. First, lung function is already impaired in COPD patients, with chronic inflammation and structural damage present in the lung tissue [42]. This reduced lung function makes the tissue more susceptible to radiation-induced damage. Second, COPD patients are often in a continuous inflammatory state, which can be exacerbated by radiotherapy, leading to further lung tissue damage [43].

The relationship between radiotherapy dose and RILI is more direct. High-dose radiation directly damages lung tissue, destroys cell structures, triggers inflammatory responses, and disrupts tissue repair processes, thus increasing the risk of RILI [44, 45]. The role of AVS5 as a risk factor can be explained by the amount of lung tissue spared from high radiation doses. A small AVS5 indicates that more normal lung tissue is exposed to higher doses of radiation, increasing the likelihood of RILI [46, 47]. Conversely, a larger AVS5 protects more lung tissue, thereby reducing the risk of injury.

It is important to note that the mechanisms of RILI in lung cancer are complex, involving interactions between multiple factors. Further research is needed to understand these mechanisms fully.

Based on the risk factors identified through meta-analysis, we developed a risk prediction model. The model incorporates three key factors: age, MLD, and V20, to calculate the likelihood of patients developing RILI. The model shows strong discriminative ability, with an AUC of 0.875. Both the sensitivity and specificity of the model are high, indicating robust performance in identifying patients at risk of RILI.

This predictive model enables clinicians to assess patient risk before radiotherapy for lung cancer and identify those at high risk for RILI. For high-risk patients, more proactive preventive measures can be implemented, such as adjusting radiotherapy doses, optimizing treatment plans, and prescribing preventive medications to reduce the risk of RILI. Based on the risk assessment, personalized treatment plans can be devised. For example, low-risk patients may receive standard radiotherapy protocols, while high-risk patients might benefit from reduced radiotherapy doses or the addition of other therapeutic approaches to minimize RILI risk. During radiotherapy, the model can also be used for dynamic monitoring of patients, allowing for timely adjustment to the treatment plan.

The model holds significant promise for clinical application. It can be integrated into electronic medical record systems, facilitating daily use by clinicians. Moreover, multi-center studies are needed to further validate and optimize the model, enhancing its accuracy and reliability. Additionally, incorporating other biological markers and clinical factors could help build a more comprehensive prediction model for RILI in lung cancer patients.

However, this study has certain limitations. This study included a limited number of relevant studies for meta-analysis, which may introduce selection bias. Additionally, the quality of the included studies varied, which could affect the reliability of the meta-analysis results. Furthermore, only three risk factors - age, MLD, and V20 - were identified in this study, and other risk factors for RILI may still be undiscovered. The interactions between these risk factors also warrant further investigation. Finally, the predictive model developed in this study needs validation across different populations to assess its universality and reliability. Future research should include more studies to improve result reliability and explore additional risk factors, such as gene polymorphisms and inflammatory markers, to construct a more comprehensive predictive model.

In conclusion, based on meta-analysis, this study developed a predictive model for RILI in lung cancer. It identified age, MLD, V20, COPD, radiotherapy dose, and AVS5 as significant risk factors for RILI and constructed a risk prediction model. This model demonstrates high AUC, sensitivity, and specificity, providing clinicians with an essential tool for predicting the risk of RILI in lung cancer patients. By identifying high-risk patients early, personalized treatment plans can be developed to reduce RILI incidence.

Disclosure of conflict of interest

None.

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