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Meta-analysis of c-Myc gene expression in prognosis of elderly patients with NSCLC underwent surgery and chemoradiotherapy

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► ***Review article***

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ABSTRACT

Background*:** This paper is conducted to analysis the effects of c-Myc gene expression on surgical intervention and outlook of elderly sufferers with Non-Small Cell Lung Cancer (NSCLC) through meta-analysis. ***Materials and Methods: Through searching the key words "small cell lung cancer, c-Myc" on China National Knowledge Internet (CNKI) and other platforms, the literature meeting the inclusion criteria was screened. Finally, a total of 14 relevant studies were included. Statistical methods were used to analyze the data, including calculation of standard deviation and 95% confidence interval, and for analysis, the fixed effects model was utilized. ***Results:*** Meta-analysis of untreated and healthy groups showed that serum c-Myc mRNA expression in untreated group is remarkably superior to healthy group (standard deviation -1.64, 95% confidence interval -1.85 to -1.45, P<0.001). In addition, serum c-Myc mRNA expression levels in elderly sufferers with NSCLC are remarkably superior to younger group (standard deviation 1.45, 95% confidence interval 1.15 to 1.74, P<0.001). In addition, serum c-Myc mRNA expression in the non-smoking group is remarkably superior to smoking group (OR=-1.78, 95% CI -1.95 to -1.60, P<0.001). ***Conclusions:*** Serum c-Myc mRNA expression levels in elderly NSCLC suffers are superior to healthy groups, which were related to age and smoking behavior. This finding is significant for the early screening, diagnosis and prognosis assessment of NSCLC, providing a basis for further research on the role of c-Myc gene in elderly NSCLC.

INTRODUCTION

One of the lung cancers is Non-Small Cell Lung Cancer (NSCLC), with a particularly high incidence among the elderly. Although surgery is one of the main treatments for NSCLC, elderly patients are often less effective and prognostic than younger patients due to age-related physiological changes and potential comorbidities. *c-Myc* gene is an important regulatory gene, which is involved in a variety of cellular biological activities. In tumors, the formation, incidence, and prognosis of tumors are all correlated tightly with aberrant *c-Myc* gene expression. However, there is a lack of comprehensive analysis of *c-Myc* gene expression on the surgical management and outlook for elderly NSCLC suffers. This study aims to evaluate *c-Myc* gene expression's function in the surgical treatment and prognosis of elderly NSCLC through meta-analysis comprehensively, providing essential reference value for research and clinical practice in this field.

Currently, there are many studies on the surgical management of elderly NSCLC. Wang M believed that non-small cell carcinoma mostly occurs in elderly people over 60 years old, and the combined treatment of chemotherapy and radiotherapy for NSCLC was mostly applied in patients, and the surgical treatment was not effective [1]. However, Stamatelopoulos [2] believed that it was appropriate to remove cancer in older persons, and the recurrence rate and mortality of patients after cancer resection have been decreasing in recent years. The studies showed that the stage of disease and the occurrence of cardiopulmonary complications were the main factors determining the prognosis [2]. Alexander *et al.* argued that surgery with a thoracoscopic camera was a better option than traditional thoracotomy for older NSCLC patients with early operative conditions. It can not only cure surgery, but also effectively reduce surgical complications and improve prognosis [3]. The study of Reck *et al.* showed that serum miRNA-130a and miRNA-143 expression levels were highly predictive of prognosis in NSCLC patients receiving surgery and chemotherapy [4]. According to Mimae *et al.*, dissection of lymph nodes was the standard treatment for early NSCLC, and wedge resection was considered a compromise. It is suggested that cuneiform resection may be an alternative to lobectomy or segmental resection combined with lymph node dissection for patients over 80 with NSCLC [5]. de Ruiter *et al.* proposed a strategy of

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stereotactic radiotherapy for NSCLC patients who could not be excised. The discussion was conducted through retrospective studies, and the results showed that stereotactic radiotherapy was increasingly popular among octogenarians and young patients [6]. Tantraworasin *et al*. discussed the short - and long-term surgical outcomes of NSCLC sufferers over 70 through a retrospective analysis. Studies found that in-hospital mortality and complex postoperative complications during pneumonectomy were acceptable for NSCLC patients over 70 years of age [7]. The above studies could find that there were currently two perspectives on the surgical treatment of NSCLC in the elderly. On the one hand, NSCLC surgery in the elderly was a good method to treat NSCLC. On the other hand, some scholars believed that the surgical treatment of NSCLC in the elderly was not effective.

Existing researches show that the expression of *c-Myc* gene in NSCLC may be related to the outcome and prognosis of surgical treatment in elderly patients. Jänne *et al.* demonstrated that MYH9 inactivates the AKT/*c-Myc* axis, thereby inhibiting the expression of BCL-2 like protein 1. Meanwhile, it promoted the expression of BH3 interaction domain death agonist protein and apoptosis regulator BAX, and activated caspase 3 and casPASE 9 [8]. Li *et al*. demonstrated that Abemaciclib significantly inhibited the proliferation, invasion, migration and cell cycle process of NSCLC. By inhibiting CDK4/6, it down-regulated the expression of *c-Myc*, ASCL1, YAP1 and NEUROD1 proteins, and also enhanced the PD-L1's expression [9]. Drilon *et al*. showed that the expression level of serum exosome *c-Myc* mRNA in lung cancer group was remarkably superior to benign and healthy group (P<0.001). There is no remarkable difference in the expression level of serum exosome *c -Myc* mRNA in NSCLC patients with different gender, age, tumor diameter, pathological type and differentiation [10]. According to Sunpaweravong Patrapim, increased chromosome 17 copy number or amplification of the HER2 gene was seen in the malignancies of 41.7% of patients with *c-Myc* positivity. Lower overall survival was linked to HER2 gene amplification, more copies of chromosome 17, and greater expression of *c-Myc* [11]. Ren *et al*. suggested that depletion of circRHOT1 induced apoptosis and cell cycle arrest in NSCLC cells in vitro, while significantly reducing *c-Myc* mRNA and protein expression in NSCLC cells. This study showed that circRHOT1 performed epigenetic enhancement of *c-Myc* expression by recruiting KAT5, thereby preventing the development of NSCLC [12]. Li *et al.* found that resveratrol was a favored natural antioxidant in the field of anticancer, which could inhibit the vitality of human small - cell lung cancer H446 cells through the *c-Myc* pathway, and promote cell apoptosis. This study also demonstrated the positive role of gene expression of *c-Myc* in the treatment of NSCLC [13].

In addition to its role in the cellular proliferation and survival of cancer cells, *c-Myc* gene expression has significant implications for radiation and chemotherapy treatments. The *c-Myc* gene has been shown to modulate the sensitivity of cancer cells to both radiation and chemotherapy by influencing DNA repair mechanisms and apoptotic pathways [9]. High *c-Myc* expression can enhance the efficacy of chemotherapy agents by increasing cancer cell proliferation and subsequently making them more susceptible to the cytotoxic effects of these drugs. Similarly, *c-Myc* overexpression has been associated with increased radiosensitivity, as it can impair the ability of cancer cells to repair DNA damage induced by radiation. Understanding the interaction between *c-Myc* gene expression and these treatment modalities is crucial for optimizing therapeutic strategies and improving the prognosis for elderly NSCLC patients.

Compared with previous studies, this paper adopted meta-analysis to evaluate the *c-Myc* gene's function in the surgical treatment and prognosis of elderly NSCLC. By collecting and analyzing data from multiple independent studies, this paper is able to obtain more accurate and reliable conclusions. This comprehensive assessment can provide an understanding of the correlation between *c-Myc* gene expression and NSCLC in the elderly and more reliable evidences for future research.

MATERIALS AND METHOD

Criteria for inclusion and exclusion

Literature search

Several major medical literature databases, including CNKI, Wanfang, PubMed, MEDLINE and Embase, were selected to ensure that the relevant literature was as comprehensive as possible. Keywords that were relevant to the study topic were selected, including "older adults", "non-small cell lung cancer", "surgical treatment," "prognosis" and "*c-Myc* gene." These keywords cover study subjects, disease types, treatment methods, prognostic outcomes and related genes. Using appropriate logical operators (such as AND, OR) to combine keywords in the literature retrieval platform, a search strategy with high sensitivity and specificity is constructed. For example, (" elderly "OR" elderly patients ") AND "non -small cell lung cancer" AND "surgical treatment" AND "prognosis" AND "*c-Myc* gene ".

Criteria for inclusion and exclusion

Inclusion criteria: - NSCLC patients made up the study's participants. - Including clinical studies, prospective studies, randomized controlled trials (RCTS), etc. - The study reported the *c-Myc* gene expression level in NSCLC patients. - The study

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involved the surgical management of elderly people with NSCLC, including lobectomy and lung wedge resection.

Exclusion criteria: -Review, only summary literature and case reports; - Animal, cell or other experimental mode;- Lack of control group; - Subjects taking multiple drugs meanwhile; - Only the antigen phenotype or characteristic is reported, but the corresponding genetic variation is not reported; - With other malignant tumors.

Quality evaluation

Two researchers evaluated the value of each paper. But when the two subjects disagreed, the other subject would re-evaluate to reach a final conclusion. The diagnostic meta-analysis was conducted according to QUADAS-2 criteria. The applicability and risk of bias of diagnostic studies will be evaluated from four aspects: patient screening (2), indicator validation (2), reference criteria (2), process and time limit (1).

Data extraction

After eliminating duplicates, the retrieved papers were screened by two independent researchers in terms of title and abstract according to existing input and output criteria. These references were then filtered based on them. After consulting with other researchers and reaching a consensus, the uncertain results were extracted for a second time. The extracted data included: (1) Research characteristics: Initial author's name, publication date, and nation; (2) Samples' Characteristics: *c-Myc* gene expression; (3) Test the physical and chemical properties of the sample. (4) Relevant data required for meta-analysis: 2x2 data tables, such as sensitivity (SEN) and specificity (SPE), were extracted for diagnostic meta-analysis. The prognostic indexes and 95% CI of the two groups were compared by Meta method.

Statistical Methods

RevMan5.3 was applied to conduct the meta-analysis, and descriptive analysis was performed on the results that could not be performed. The Odds ratio (OR) and its 95%CI (95% CI) were used as statistical indicators for the double-graded variables. The results of each included study were tested for differences, and the inverted funnel plot was used to assess the publishing bias.

Heterogeneity analysis

Different literature data, different indicators and different regions may produce different heterogeneity. Therefore, the experiment conducted a heterogeneity analysis of these different studies to determine whether the results of these different studies can be merged. An acceptable statistical difference was represented with $P>0.1$ and $I^2<50\%$. At this time, to aggregate the data, the fixed effects model (FE) was utilized. If $P<0.1$ and $I^2>50\%$, there was a statistical difference. This paper uses the random effects model (RE) to test these differences. The OR values reported in the literature were combined to calculate their effect combination values and 95% CI. The data were combined and analyzed according to $\alpha=0.1$ level and Z-test was performed.

Subgroup analysis

In the case of statistically significant differences, the error of data extraction should be eliminated first, and then the cause of differences should be verified by subgroup analysis. On this basis, sensitivity analysis was combined to find the cause of the difference, and detailed statistical explanation was carried out. If the source of the difference cannot be identified, it was converted to an RE model, or descriptive analysis was used.

Sensitivity analysis

The studies that have an impact on the overall analysis results were included one by one. The stability and reliability of the Meta were judged by observing the impact of these excluded studies on the combined effect size. The commonly used treatment methods include: modifying the inclusion criteria of the literature and eliminating the studies with low quality. If the difference between the two data sets was not obvious when analyzed again, it indicated that the results are robust and reliable. People often use funnel plots to analyze publication bias. If the model has good symmetry, then the publication bias of the model will be small.

RESULTS

Results of literature inclusion and quality evaluation

In this paper, the key words "small cell lung cancer, *c-Myc*, etc." were searched on CNKI and other platforms, and 475 items in total were collected. 214 articles were de-duplicated, 161 abstracts were read, and reviews, in vitro studies, and retrospective analyses were preliminarily screened. The 45 literatures included after preliminary screening were reviewed in full, 12 that did not meet the efficacy criteria, 19 that were not genotyped, 6 that were excluded from meta-analysis, and finally 14 related studies were included, which is shown in figure 1.

The included 14 articles all mentioned the relationship between *c-Myc* expression and NSCLC. Among them, the difference in *c-Myc* expression between patients with and without non-small cell carcinoma was discussed in 10 research; 5 literatures mentioned the variation in *c-Myc* expression in different age groups, and 7 literatures mentioned the variation in *c-Myc* expression in whether or not smoking. In figure 2, the QUADAS-2 was used to score all included trials.

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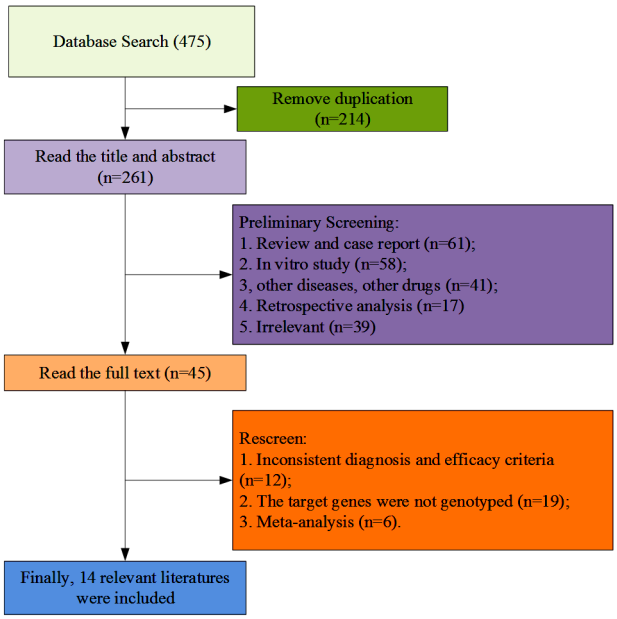


Figure 1. Flowchart for literature screening.

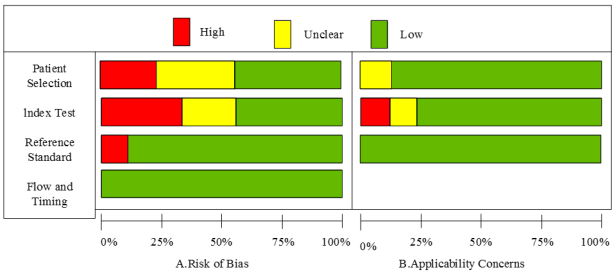


Figure 2. QUADAS-2 scoring.

Lung cancer incidence is correlated with the expression of serum c-Myc mRNA

Of the included studies, 10 articles reported differences in serum c-myc mRNA expression between untreated and healthy controls. The 10 literatures included in Total patients covered in table 1 were 868, with 436 in the untreated group and 432 in the healthy group. It was showed that all studies had good homogeneity, and the homogeneity test's P-value was 0.36, I2 was 9%. The comprehensive results showed that the serum c-myc mRNA expression in the untreated group was remarkably superior to the healthy group, with a standard deviation of -1.64 and 95% confidence interval of (-1.85, -1.45), and there was a discernible and substantial deviation (P<0.001).

Table 1. Results of fixed effect model analysis of serum c-Myc mRNA expression.

	Untreated group	Health group	OR
Summary (95%CI)	436	432	-1.64[-1.85, -1.45]
Heterogeneity test	Chi^2=4.39	Df=4(p=0.36)	I^2=9%
Total effect test	Z=24.91(p<0.001)		

Note: "OR": Ratio, the ratio of exposed population to unexposed population in the case group and control group. "CI": Confidence interval; "Chi^2": chi square test value; "Df": degrees of freedom; "I^2": Information gain rate; "Z": Differences in sample mean values.

The forest plot represents the effect size of each study and its 95% confidence interval in a plane cartesian coordinate system, centered on an invalid line perpendicular to the X-axis (usually X=0), with several line segments parallel to the X-axis. The prismatic squares in the figure represent the effect size and reliability of the combination of multiple studies. The random forest plot in figure 3(a) showed that 95% of CI horizontal lines fall to the left and do not intersect invalid lines. Therefore, the expression of serum c-myc mRNA in the untreated group was remarkably better than the healthy group. The funnel plot was mainly used to observe whether there were various biases in the results of meta-analysis. The funnel-plot analysis in figure 3(b) showed that the 10 included articles did not present any measurable publication bias.

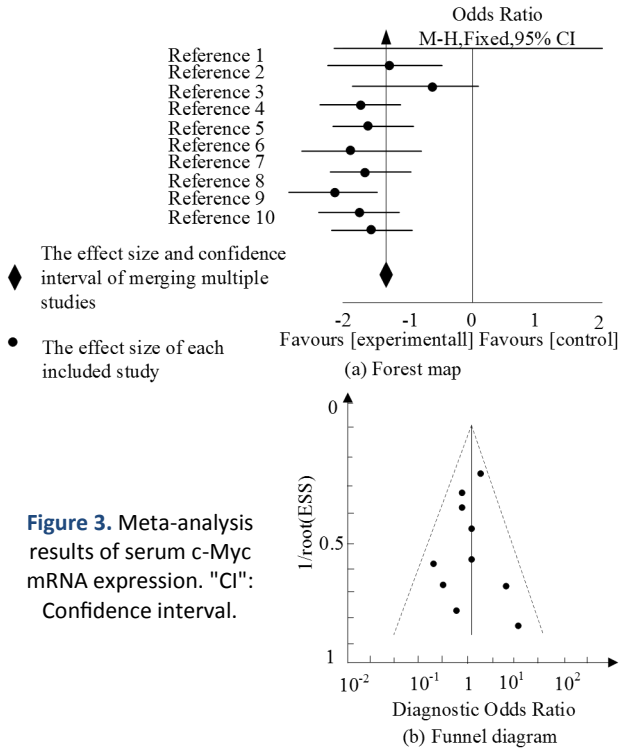


Figure 3. Meta-analysis results of serum c-Myc mRNA expression. "CI": Confidence interval.

Differences in serum c-Myc mRNA expression among different age groups

To study the correlation between serum *c-Myc* mRNA expression level and age of lung cancer patients, this study included 5 literatures that mentioned the difference of *c-Myc* mRNA expression at different ages, and divided NSCLC patients who had not received treatment into ≥60 years old group (elderly group) and less than 60 years old group (young group) according to age. As shown in table 2 and figure 4, five literatures contained a total of 513 patients. The elderly group had 261 instances, whereas the new group had 252 cases. It is showed that the standard deviation of each study was 1.45, 95% confidence interval was (1.15, 1.74), and there was a discernible and substantial deviation (P<0.001). Statistically, the Spearman correlation coefficient of the five diagnostic studies was -0.143, and the P-value was 0.760, indicating high

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inter-group heterogeneity. On this basis, subgroup analysis was performed by sample size, cancer classification, etc., to determine the differences between different samples. The overall sensitivity of the sample size difference was 0.83(95% confidence interval 0.77~0.88), and I2=0. The specificity was 0.74 (95% confidence interval: 0.76~0.87), and I2=0. The results of subgroup analysis showed that the heterogeneity was probably due to the sample size variation. Studies with high sample size were more likely to find significant differences in serum *c-Myc* mRNA expression among different age groups.

Table 2. Results of fixed effect model analysis of age difference in c-Myc mRNA expression.

	Older age group	Younger age group	OR
Summary (95%CI)	261	252	1.45[1.15, 1.74]
Heterogeneity test	Chi^2=3.15	Df=5(p=0.41)	I^2=13%
Total effect test	Z=12.41(p<0.001)		

Note: "OR": Ratio, the ratio of exposed population to unexposed population in the case group and control group. "CI": Confidence interval; "Chi^2": chi square test value; "Df": degrees of freedom; "I^2": Information gain rate; "Z": Differences in sample mean values.

The forest map in figure 4 showed that the horizontal line of 95% CI falls to the right of the null line and does not intersect with the null line, suggesting that the expression level of serum *c-Myc* mRNA in the elderly group was significantly different from that in the younger group.

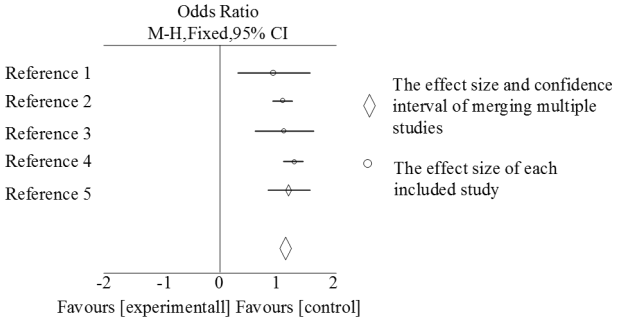


Figure 4. Comparison of c-myc mRNA expression by age using a forest plot. "CI": Confidence interval.

Serum c-Myc mRNA expression was significantly correlated with smoking

A number of relevant studies have mentioned the relationship of serum *c-Myc* mRNA expression and smoking behavior. To determine if smoking and serum *c-Myc* mRNA levels are related, this study included 7 articles that mentioned the difference of *c-Myc* mRNA expression in whether smoking or not. 685 patients were included in a total of 7 literatures. In the smoking group, there were 487 instances, whereas there were only 198 cases in the non-smoking group. Meta-analysis showed that each study was homogeneous. For heterogeneity test, Chi2=8.32, df=6, P=0.22,f=28%. The combined results [OR=-1.78,95% CI (-1.95,-1.60)] showed a statistically significant difference between two groups (P<0.001), indicating that serum *c-Myc* mRNA expression in the smoking group was remarkably superior to the non-smoking group.

Table 3. Results of fixed effect model analysis on whether c-Myc mRNA expression is different from smoking.

	Smoking group	Non-smoking group	OR
Summary (95%CI)	487	198	-1.78[-1.95,-1.60]
Heterogeneity test	Chi^2=8.32	Df=6(p=0.22)	F=28%
Total effect test	Z=19.69(p<0.001)		

Note: "OR": Ratio ratio, the ratio of exposed population to unexposed population in the case group and control group. "CI": Confidence interval.

The forest plot in figure 5 showed that 95% of CI horizontal lines fall to the left and do not intersect invalid lines. In conclusion, the expression of serum c -myc mRNA in the smoking group was remarkably better than the non-smoking group.

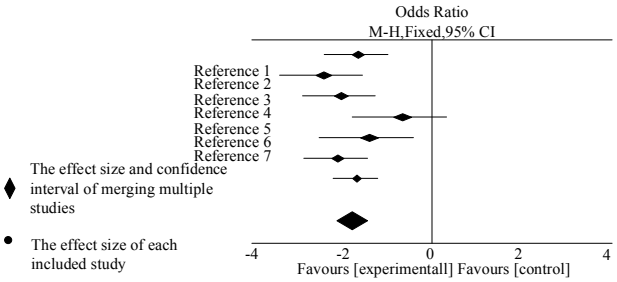


Figure 5. Forest map of the difference between c-myc mRNA expression and smoking. "CI": Confidence interval.

ROC curve of c-Myc gene expression

After quantitative synthesis of 14 studies, the AUC was 0.8543, indicating that *c-Myc* gene expression had a certain accuracy in surgical treatment and prognosis of adult NSCLC.

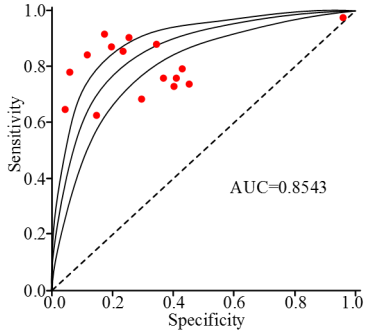


Figure 6. ROC curve of c-Myc gene expression.

DISCUSSION

Most incidences of lung cancer are of the non-small cell kind (NSCLC) [14]. According to China's cancer statistics, lung cancer is the leading cause of death, which highlights the importance of early screening and diagnosis of lung cancer [15]. Surgical treatment of NSCLC in old people is a common treatment that aims to achieve therapeutic goals by surgically removing tumor tissue. Surgical therapy of NSCLC in the elderly is indicated for the same reasons as in the young, mainly considering the clinical stage of tumor, surgical feasibility and overall health status of patients [16]. Typically, surgery is

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performed on early stage NSCLC (stage I and II) as well as certain high-risk stage IIIA patients.

The detection of serum markers has a broad application prospect in cancer. Serum marker detection owns the advantages of simple operation, low cost, little harm to the body, easy access to samples and continuous monitoring. However, traditional serum markers, such as CEA, NSH, CA-199 and tissue polypeptide antigen, have poor sensitivity and specificity in the early screening and prognosis assessment of lung cancer, and can only be used for diagnosis, limiting their accuracy and efficiency. Recently, liquid biopsy has become an effective method for early diagnosis and prognosis assessment of cancer [17]. Circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and tumor-derived exosomes in the blood have become the focus of research. In particular, with regard to exosomes, they are a class of extracellular vesicles that carry abundant proteins, nucleic acids, and metabolites and are stable in the blood. Exosomes shows great potential in the early diagnosis, prognosis assessment, and targeted therapy of cancer. As an important regulatory gene, the *c-Myc* gene is crucial in the initiation and progression of lung cancer. The proliferation, metastasis, invasion, and treatment resistance of tumor cells are all tightly correlated with aberrant *c-Myc* expression. Therefore, screening, diagnosis, and prognosis of NSCLC may all benefit from the identification of the serum marker *c-Myc*. Through the detection of *c-Myc* in serum, the molecular level monitoring of patients with NSCLC can be realized. This detection method is non-invasive, reproducible and easy to obtain samples, which can provide essential information for early diagnosis and prognosis assessment. In addition, the detection of *c-Myc* is also expected to become the guiding basis for individualized treatment and targeted therapy of lung cancer, providing patients with more accurate and effective treatment programs.

To explore the value of *c-Myc* mRNA in early detection of lung cancer, the results of the meta-analysis of 10 literatures included in this study showed that all studies had good homogeneity, and the P-value of heterogeneity test was 0.36. It was shown that the expression of serum *c-Myc* mRNA in the treatment group was superior to the healthy group. The standard deviation was -1.64 and the 95% confidence interval was (-1.85, -1.45), with a significant deviation (P<0.001). *c-Myc* is an important cell proliferation-related gene that is overexpressed in tumor cells, which is similar to the research results in Yuan's study [18]. In this study, in patients with untreated NSCLC, the proliferative activity of tumor cells was generally higher, leading to elevated levels of *c-Myc* expression. This may be because untreated tumor cells continue to grow and spread, expressing more *c-Myc* mRNA. Cell cycle progression is assisted by *c-Myc*, an important regulator of the cell cycle. In NSCLC, tumor cells in the untreated group often have cell cycle disorders and lose their normal cell cycle regulation mechanisms. This may lead to over-activation of *c-Myc* gene, resulting in a significant increase in serum *c-Myc* mRNA expression level in the untreated group, and a similar conclusion was reached in Patrapim *et al.* study [19]. There is an inflammatory response, including the tumor cell's own inflammatory response and tumor-associated immune cell infiltration. These inflammatory responses might lead to increased *c-Myc* gene expression by activating multiple signaling pathways, such as NF-κB. Therefore, in patients with untreated NSCLC, serum *c-Myc* mRNA expression levels may be elevated, reflecting the presence of a tumor-associated inflammatory state.

The risk of developing lung cancer increases with age. The results of meta-analysis of 5 included literatures showed that the standard deviation of each study was 1.45, and the 95% confidence interval was (1.15, 1.74), with statistically significant differences (P<0.001). It was showed that the average relative expression level of *c-Myc* mRNA in the elderly group was remarkably superior to the lower age group. According to the American Cancer Society, the typical age of a person diagnosed with lung cancer is 70 [20-21]. The source of heterogeneity was the number of samples. The average relative expression level of *c-Myc* mRNA in the high age group was remarkably superior to the low age group in the large-sample studies. With age, the function of the immune system gradually declines, which is known as immune aging. The regulatory gene *c-Myc* is essential for cell division and immune system function. In the elderly, immune aging may lead to increased expression levels of *c-Myc* in response to compensatory demands caused by decreased immune function. The transcription factor *c-Myc* has a significant function in controlling the cell cycle. The cell cycle regulation mechanism may be disturbed in the elderly, resulting in abnormal cell proliferation and differentiation. This may lead to over-activation and increased expression of the *c-Myc* gene, causing *c -Myc* mRNA to be expressed somewhat more strongly in the older population. People in higher age groups may have experienced longer periods of environmental exposure, such as long-term smoking, air pollution, etc. These environmental exposures can lead to DNA damage and cell mutations that activate the expression of the *c-Myc* gene. In addition, cells may have accumulated multiple types of damage during their life cycle. Such as DNA damage and incomplete repair, it is likely to lead to abnormal expression of *c-Myc*.

Smoking greatly increases the risk of developing lung cancer. The meta-analysis showed that the heterogeneity test Chi2=8.32, df=6, P=0.22,f=28%. The combined results [OR=-1.78,95% CI (-1.95,

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-1.60)] showed a statistically significant difference between the two groups (P<0.001), indicating that serum *c-Myc* mRNA expression in the smoking group was remarkably superior to the non-smoking group. Some studies have compared the expression of *c-Myc* mRNA in serum exosomes from smokers and non-smokers with NSCLC. The expression level of *c-Myc* mRNA in serum exosomes of the smoking population was 0.095671. The expression level of *c-Myc* mRNA in serum exosomes of non-smoking patients was 0.050523. They were quite different from one another (P<0.05) [21]. These results indicated that smoking could cause abnormally high expression of *c-Myc*, and carried *c-Myc* mRNA into the blood in the form of exosome, causing lung cancer. It has been reported that tobacco smoke extract can up-regulate the expression of CCAT1 and *c-Myc* and down-regulate the expression of let-7c in human airway epithelial cells. In HBE, the expression of *c-Myc* decreased significantly. Chromatin immunoprecipitation (ChIP) experiment showed that *c-Myc* was up-regulated under tobacco smoke stimulation, and combined with CCAT1 promoter to promote transcriptional activation of c-myc gene. These results all confirmed that the expression of serum *c-Myc* mRNA in the smoking group was remarkably superior to the non-smoking group, but its specific mechanism needs to be further explored.

The *c-Myc* gene, known for its role in cell proliferation, apoptosis, and metabolism, is often dysregulated in various cancers, making its expression a critical biomarker to monitor during treatment. In patients receiving chemotherapy, assessing *c-Myc* expression can provide insights into the tumor's response to the treatment, as high *c-Myc* levels often correlate with aggressive tumor behavior and resistance to certain chemotherapeutic agents. In radiotherapy, evaluating *c-Myc* can help predict radiosensitivity and the likelihood of treatment success, as c-myc overexpression has been linked to increased radioresistance. For surgical patients, particularly those undergoing resection of solid tumors, *c-Myc* assessment could aid in determining the likelihood of residual microscopic disease and the potential need for adjuvant therapies. Therefore, monitoring c-myc expression is particularly beneficial for patients undergoing chemotherapy and radiotherapy, as it can guide treatment adjustments and predict outcomes, though it also has relevance in the surgical context for comprehensive treatment planning.

CONCLUSION

In summary, the results of the meta-analysis in this study highlighted the essential role of c-Myc gene in elderly NSCLC. Among them, the significant increase of serum c-Myc mRNA expression level was directly related to the onset of NSCLC, age, and smoking behavior. These findings had important clinical significance to guide the early screening, individualized treatment and prognosis assessment of elderly NSCLC.

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