Value of miR-21 and miR-141 in Evaluating the Efficacy and Prognosis of Thoracoscopic Lobectomy for Early-Stage Lung Cancer in the Elderly

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Abstract: The effectiveness and prognosis of thoracoscopic lobectomy in sennior individuals with early-stage cancer were evaluated by assessing the value of microRNAs (miR)-21 and miR-141. A total of 116 sennior individuals with early-stage cancer were divided into two cohorts based on the surgical effect: the observation cohort (effective) and the control cohort (ineffective). Moreover, 80 healthy individuals who underwent medical examination were selected as the comparison cohort B. The levels of serum miR-141serum miR-21 and were assessed in all participants. The comparison revealed that the highest levels of these two serum biomarkers were observed in control cohort A, followed by the observation cohort, and the lowest levels were found in control cohort B (P<0.05). The receiver operating characteristic curve (ROC) analysis showed that the area under the curve for individual assessment of miR-141 and miR-21 in predicting efficacy and prognosis were 0.838 and 0.740, respectively. The sensitivity and specificity for miR-21 were 85.3% and 76.2%, respectively, while for miR-141, they were 53.7% and 85.1%, respectively. These findings suggest that serum miR-21 and serum miR-141 are closely associated with postoperative efficacy and prognosis in individuals with early-stage cancer. Both miR-141 and miR-21 can serve as biomarkers for evaluating effectiveness and prognosis.

Keywords: MicroRNA-21; MicroRNA-14; Early-stage Lung Cancer; Thoracoscopic Lobectomy; Efficacy; Prognosis

1. Introduction

Lung cancer in its early stages is characterized by the absence of local lymphatic metastasis, distant metastasis, or invasion of adjacent tissues. The tumor radius is relatively small, and surgical treatment can be selected in the early stage. After treatment, the survival period is longer and the prognosis is better [1]. The clinical symptoms of early-stage lung cancer are relatively weak, and individuals may not even feel any discomfort. For sennior individuals, their bodies are in the process of gradual aging, their organs and system capabilities are weaker, and tumor progression is slower than that of young people. Even if lung cancer develops Corresponding symptoms of lung cancer may not appear in the late stage, seriously affecting later treatment and prognosis [2]. Therefore, for the sennior, early detection of effective indicators to help diagnose lung cancer is of great meaning to individuals' physical and mental health, later treatment, and prognosis assessment. Studies have shown that miR-21 and miR-141 are abnormally expressed in sennior individuals with colorectal cancer, prostate cancer, etc., and play an important role in cancer tissue proliferation, metastasis, invasion, etc[3]. However, there are few studies on the evaluation of the efficacy and prognosis of miR-21 and miR-141 in sennior individuals with early-stage lung cancer after thoracoscopic lobectomy. For this reason, this study selected individuals admitted to our hospital from January 2020 to July 2022. 116 sennior individuals with early-stage lung cancer and 80 healthy subjects who underwent physical examination at the same time were used as research subjects. The contents of serum miR-21 and miR-141 were detected, and the relationship between miR-21, miR-141, and sennior individuals with early-stage lung cancer who underwent thoracoscopy were analyzed. The relationship between efficacy and prognosis after lobectomy can provide valuable predictive biomarkers for early

diagnosis and prognosis of sennior individuals with lung cancer.

2. General Information and Methods

2.1 General Information

We recruited 116 sennior individuals diagnosed with early-stage lung cancer who stayed at our facility from January 2020 to July 2022. Each individual underwent a thoracoscopic lobectomy. Based on the surgical results, we divided the individuals into two cohorts: those who did not respond to the surgery (defined as persistent or worsening postoperative symptoms) and those who responded to the surgery (marked by improved or stable symptoms). 95 individuals with effective postoperative treatment were set as the observation cohort, and 21 individuals with ineffective postoperative treatment were set as control cohort A. Inclusion criteria: (1) All meet the "Chinese Expert Consensus on Lung Cancer Screening and Management" [4] diagnostic criteria for early-stage lung cancer in middle-aged and sennior people; (2) All meet the indications for thoracoscopic lobectomy; (3) Clinical and imaging data are Complete persons; (4) Those aged ⩾65 years old. Exclusion criteria: (1) People with malignant tumors other than lung cancer; (2) People with heart, lung, kidney, and other organ diseases; (3) People who refuse to cooperate with treatment and are unconscious; (4) People with a history of radiotherapy and chemotherapy By. In addition, 80 healthy individuals who underwent physical examinations within the same timeframe were chosen as control cohort B. Those individuals under the age of 65 with detrimental behaviors like alcohol abuse and hypertension were excluded. The observation cohort consisted of 57 males and 38 females, aged 66-78 years old, with an average age of (72.45 ± 5.12) years and a weight range of 56-72 kg, with an average weight of (62.56 ± 4.54) kg. Among the participants, there were 51 cases of squamous cell carcinoma and 44 cases of adenocarcinoma.

Control cohort A comprised 13 males and 8 females, aged 67-78 years old, with an average age of (72.81 ± 5.13) years and a weight range of 56-72 kg, with an average weight of (62.63 ± 4.76) kg. In this cohort, there were 11 cases of squamous cell carcinoma and 10 cases of adenocarcinoma.

Control cohort B included 48 males and 32 females, aged 66-77 years old, with an average age of (72.02 ± 5.78) years and a weight range of 56-73 kg, with an average weight of (62.88 ± 4.81) kg. The baseline data of the three study cohorts showed no statistically meaningful contrasts and can be compared (P>0.05).

2.2 Testing Instruments and Kits

RT-PCR instrument and qPCR kit (Shanghai Yisheng Biotechnology Co., Ltd.), Trizol reagent (Shanghai Lianmai Bioengineering Co., Ltd.), reverse transcriptase kit (Shanghai Ruishi Biotechnology Co., Ltd.).

2.3 Method

Three days after surgery, 3-5 milliliters of fasting peripheral venous blood were collected from the observation cohort and control cohort A. In addition, during the routine physical examination, 3 to 5 milliliters of fasting peripheral venous blood were obtained from control cohort B. Subsequently, the blood sample was centrifuged at a speed of 2000 revolutions per minute for 15 minutes, and the resulting transparent liquid was stored in a -20 ° C freezer for future analysis. Total RNA was isolated using Trizol technology and then transcribed into cDNA using qPCR assay kit. Then, a reverse transcriptase kit was used to reverse-transcribe cDNA into DNA. U6 serves as an internal reference gene. Using DNA as a template, RT-PCR was used to detect serum levels of miR-21 and miR-141. The specific operation was carried out according to the instructions provided together with the kit.

2.4 Statistical Method

All recorded data were analyzed using SPSS 19.0 statistical software. Count data were presented as percentages "%". The comparison between data was conducted using the χ^2 test. Measurement data were presented as mean ± standard deviation ( ). The t-test was employed for data comparison. The receiver operating characteristic (ROC) curve was utilized to assess the sensitivity and specificity of serum miR-21 and miR-141 as indicators for evaluating the effectiveness and prognosis of thoracoscopic lobectomy in individuals with

early-stage lung cancer. A significance level of P<0.05 indicates a statistically meaningful contrast.

3. Findings

3.1 Comparison of Serum Levels of miR-21 and miR-141 Among Three Cohorts of Individuals

Table 1 shows that the serum degrees of miR-21 and miR-141 in the observation cohort and control cohort A were higher than those in the control cohort B (P<0.05). The serum levels of miR-21 and miR-141 in the observation cohort were lower than those in the control cohort A (P<0.05).

Table 1 Comparison of Serum miR-21 and miR-141 Levels Among Three Cohorts of Individuals ($\bar{x} \pm s$)

Group	miR-21	miR-141
Observation cohort (n=95)	1.32±0.12[ab]	1.34±0.14[ab]
Control cohort A (n=21)	1.56±0.23[a]	1.56±0.23[a]
Control cohort B (n=80)	1.12±0.11	1.22±0.12
F	24.504	16.906
P	<0.001	<0.001

Note: a means compared with control cohort B, P<0.05; b means compared with control cohort A, P<0.05.

Table 2 Diagnostic Value of Serum miR-21 and miR-141 on the Efficacy and Prognosis of Sennior Individuals with Early-stage Lung Cancer after Thoracoscopic Lobectomy

Index	AUC	95% Confidence interval	P	SE	Sensitivity	Specificity
miR-21	0.838	0.779~0.898	0.000	0.030	85.3	76.2
miR-141	0.740	0.670~0.810	0.000	0.036	53.7	85.1

3.2 The Diagnostic Value of Serum miR-21 and miR-141 on the Efficacy and Prognosis of Sennior Individuals with Early-stage Lung Cancer after Thoracoscopic Lobectomy

The ROC curve showed that the AUCs of miR-21 and miR-141 in predicting postoperative efficacy and prognosis were 0.838 and 0.740, respectively, with sensitivities of 85.3% and 53.7%, and specificities of 76.2% and 85.1%, respectively. See Table 2 and Figure 1.

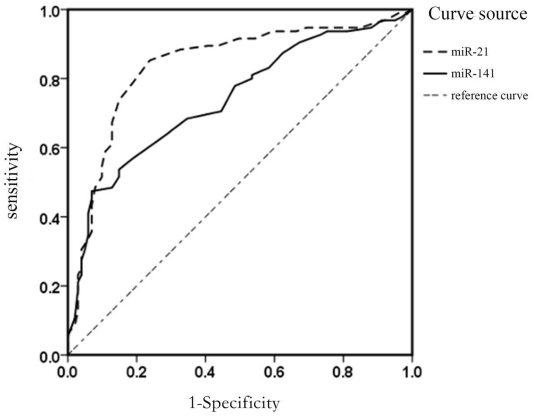

Figure 1. ROC Curve Chart

4. Discussion

Lung cancer is a malignant tumor originating in the lungs, trachea, and bronchi. The global morbidity and mortality rates are in a rapid increase stage, seriously endangering human life and health [5]. The pathogenesis of lung cancer is complex and has not yet been fully clarified, but researchers have found that lung cancer is closely related to factors such as environmental pollution, smoking, and occupational exposure. It is more likely to occur in people with genetic and genetic changes, long-term exposure to air pollution or exposure to carcinogens, and smoking. and other cohorts [6-7]. The symptoms of early-stage lung cancer are not obvious. When relevant clinical symptoms appear, it means that the disease has reached a certain degree of severity. It is easy to miss the best opportunity for treatment, resulting in poor prognosis and increased mortality. Clinically, minimally invasive surgery for lung cancer is mainly performed through thoracoscopic surgery. Although it has a certain effect, recurrence may still occur [8]. Especially the sennior. Some scholars have found that about 2/3 of clinical lung cancer individuals are middle-aged and sennior people. Therefore, the sennior are not only a high-risk cohort for lung cancer, but also pose huge challenges to treatment due to their weak physical constitution, poor immunity and other problems. It seriously affects the life, health and prognosis of individuals [9]. Lung cancer metastasis and invasion are one of the

important factors that affect the treatment effect and prognosis of individuals. Therefore, finding an effective indicator that can predict whether the tumor will metastasize and invade is of great meaning for early tumor diagnosis, efficacy evaluation, and prognosis evaluation in sennior individuals. In recent times, there has been a surge of interest in the study of microRNA. These small RNA molecules exhibit aberrant expression patterns in the serum and tumor tissues of individuals diagnosed with various malignant tumors, including prostate cancer and breast cancer. By modulating the expression of target genes, microRNAs play a pivotal role in the initiation, progression, and metastasis of tumors. Consequently, they indirectly impact the treatment outcomes and prognosis of individuals afflicted with cancer. [10-12].

Studies have found [13] that miR-21 plays a certain role in predicting the disease development and treatment outcomes of individuals with ovarian cancer and gastric cancer. Hao Wentao et al. [14] found that the level of miR-21 in the plasma of individuals with serous ovarian cancer was higher than that of individuals with benign epithelial ovarian cancer. Different tumor stages and different degrees of tumor differentiation have contrasts in miR-21 levels. The research results of Shen Zilong et al. [15] showed that there is abnormal expression of miR-21 in the lesion tissue of children with osteosarcoma, which is related to tumor development and metastasis and can be used as an independent risk factor for the onset of disease. The findings of this investigation indicate that sennior individuals with early-stage lung cancer who have undergone effective surgery exhibit lower levels of serum miR-21 compared to those who have experienced ineffective surgery ($P<0.05$). This suggests the involvement of serum miR-21 in the development and progression of lung cancer, as well as its relevance to surgical outcomes in this population. Notably, there is a higher expression of miR-21 in individuals with poor surgical efficacy. Furthermore, the ROC curve analysis revealed an AUC of 0.838, with a sensitivity of 85.3% and a specificity of 76.2%, underscoring the utility of serum miR-21 monitoring in prognostic evaluation for sennior individuals with early-stage lung cancer.

Foreign studies have confirmed that miR-141 is abnormally expressed in individuals with malignant tumors such as nasopharyngeal cancer and prostate cancer, and can prevent the metastasis and invasion of cancer cells through various pathways. Wang Xuelin et al. [16] found that serum miR-141 has a certain correlation with tumor stage, degree of lymphatic metastasis and prognosis in sennior lung cancer individuals, and individuals with high serum miR-141 expression have a lower survival rate. In a study conducted by Ma Ling et al. [17], it was discovered that miR-141 expression levels in tumor tissues of individuals with non-small cell carcinoma were elevated compared to adjacent tissues. Furthermore, this microRNA played a significant role in suppressing tumor cell proliferation, metastasis, and invasion. The findings of Ma's research indicate that the serum levels of miR-141 were higher in elderly individuals with early-stage lung cancer who responded well to surgery, as well as in those who did not respond effectively to surgery, in comparison to the degrees observed in healthy individuals undergoing physical examinations. Notably, miR-141 levels were lower in elderly individuals with early-stage lung cancer who responded well to surgery compared to those who did not respond effectively to surgery ($P < 0.05$). This shows that serum miR-141 has certain predictive value in the evaluation of efficacy and prognosis after thoracoscopic lobectomy in sennior individuals with early-stage lung cancer. It can help diagnose the development process of cancer cells and provide beneficial value for early clinical prevention and improvement of prognosis. Liu Hongyun et al. [18] found that after individuals with lung cancer underwent minimally invasive thoracoscopic surgery, the expression of serum miR-141 and miR-21 in individuals with tumor recurrence was higher than that in individuals without recurrence.The expression of miR-141 and miR-21 was found to be elevated in individuals with recurrence compared to those without recurrence, as determined by ROC curve analysis. The joint detection of postoperative cancer recurrence demonstrated an AUC of 0.896, a sensitivity of 80.00%, and a specificity of 85.54%, indicating a higher predictive value. Furthermore, the ROC curve analysis in this study revealed that serum miR-141 and miR-21 had AUCs of 0.838 and 0.740, respectively,

for diagnosing the postoperative efficacy and prognosis of sennior individuals with early-stage lung cancer. The sensitivity and specificity for miR-141 were 85.3% and 76.2%, while for miR-21, they were 53.7% and 85.1%, respectively. These findings suggest that both tests can aid in evaluating the postoperative efficacy and prognosis of sennior individuals with early-stage lung cancer.

5. Conclusion

The study explored the expression of miR-21 and miR-141 in sennior individuals with early-stage lung cancer and their predictive value for postoperative efficacy and prognosis. By analyzing the data of 116 sennior early-stage lung cancer individuals and 80 healthy controls, it was found that serum levels of miR-21 and miR-141 were meaningfully lower in individuals who responded to surgery than in those who did not respond to surgery, and were meaningfully different from those in healthy controls. This indicates that miR-21 and miR-141 can be used as valuable biomarkers to evaluate the surgical efficacy and prognosis of sennior individuals with early-stage lung cancer, providing important information for early diagnosis and treatment.

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