Hindawi
Evidence-Based Complementary and Alternative Medicine
Volume 2023, Article ID 9846169, 1 page
https://doi.org/10.1155/2023/9846169

Retraction

Retracted: Study on Serum miR-204 Expression Levels in Patients with Severe Pneumonia and Patients with Primary Bronchial Lung Cancer and Its Diagnostic Value

Evidence-Based Complementary and Alternative Medicine

Received 20 June 2023; Accepted 20 June 2023; Published 21 June 2023

This article has been retracted by Hindawi following an investigation undertaken by the publisher [1]. This investigation has uncovered evidence of one or more of the following indicators of systematic manipulation of the publication process:

(1) Discrepancies in scope

(2) Discrepancies in the description of the research reported

(3) Discrepancies between the availability of data and the research described

(4) Inappropriate citations

(5) Incoherent, meaningless and/or irrelevant content included in the article

(6) Peer-review manipulation

The presence of these indicators undermines our confidence in the integrity of the article's content and we cannot, therefore, vouch for its reliability. Please note that this notice is intended solely to alert readers that the content of this article is unreliable. We have not investigated whether authors were aware of or involved in the systematic manipulation of the publication process.

Wiley and Hindawi regrets that the usual quality checks did not identify these issues before publication and have since put additional measures in place to safeguard research integrity.

We wish to credit our own Research Integrity and Research Publishing teams and anonymous and named external researchers and research integrity experts for contributing to this investigation.

The corresponding author, as the representative of all authors, has been given the opportunity to register their agreement or disagreement to this retraction. We have kept a record of any response received.

References

[1] W. Zheng, W. Huang, and X. Yu, "Study on Serum miR-204 Expression Levels in Patients with Severe Pneumonia and Patients with Primary Bronchial Lung Cancer and its Diagnostic Value," *Evidence-Based Complementary and Alternative Medicine*, vol. 2021, Article ID 6034413, 7 pages, 2021.

Hindawi
Evidence-Based Complementary and Alternative Medicine
Volume 2021, Article ID 6034413, 7 pages
https://doi.org/10.1155/2021/6034413

Research Article

Study on Serum miR-204 Expression Levels in Patients with Severe Pneumonia and Patients with Primary Bronchial Lung Cancer and Its Diagnostic Value

Wenhong Zheng,[1] Wei Huang,[2] and Xuchao Yu [3]

[1]*Danzhou People's Hospital, Internal Medicine-Oncology, Danzhou, Hainan 571700, China*
[2]*Hangzhou Xiaoshan District Hospital of Traditional Chinese Medicine, Department of Critical Medicine, Hangzhou, Zhejiang 310000, China*
[3]*Zhuji People's Hospital of Zhejiang Province, Department of Critical Medicine, Zhuji, Zhejiang 311800, China*

Correspondence should be addressed to Xuchao Yu; yuxuchao@163.com

Received 1 September 2021; Accepted 27 September 2021; Published 12 October 2021

Academic Editor: Songwen Tan

Objective. To analyze the expression and clinical significance of miR-204 in the serum of patients with severe pneumonia (SP) and primary bronchial lung cancer (LC). ***Methods.*** 65 SP patients and 43 primary bronchial LC patients who were treated in the hospital from January 2017 to December 2018 were randomly selected as the SP group and LC group. At the same time, healthy patients from the physical examination department of the hospital were selected. 65 cases were the control group. QRT-PCR detected serum miR-204 expression and compared the differences between groups. The pathological data of patients were collected, and the relationship between serum miR-204 and the patient's pathological data was compared; the area under the ROC curve and Kaplan–Meier curve were used to evaluate the diagnostic value of serum miR-204 for the two conditions and to explore the relationship between serum miR-204 and prognosis. *Results.* The serum miR-204 of the SP group was (0.43 ± 0.09), the serum miR-204 of the LC group was (0.40 ± 0.10), the serum miR-204 of the control group was (1.00 ± 0.09), and the miR-204 level of was significantly higher than that of the control group, and the difference between the groups was statistically significant ($P < 0.05$). There was no significant difference in serum miR-204 levels between the SP group and the LC group ($P > 0.05$). Serum miR-204 levels in SP patients with cumulative organs ≥3 were higher than those with cumulative organs <3, and the difference was statistically significant ($P < 0.001$). In the LC group, in patients with stage III to IV and low and undifferentiated patients, the level of miR-204 was higher than that of stage I~II and high and moderately differentiated patients, and the difference was statistically significant ($P < 0.001$). The level of miR-204 in the two groups of patients (0.89 ± 0.10, 0.83 ± 0.13) who died of illness was significantly higher than that of the surviving patients (1.00 ± 0.11, 1.00 ± 0.10), and the difference was statistically significant ($P < 0.05$); the survival rate of patients with high expression of miR-204 was higher than that of patients with low expression. The AUC of serum miR-204 level to SP and LC was 0.766 and 0.818, respectively. *Conclusion*. The level of miR-204 in the serum of SP patients and patients with primary bronchial LC was significantly lower than that of healthy people, and patients who died were lower than those who survived; the miR-204 in serum has a good diagnostic value for SP and LC and is related to the survival and prognosis of patients.

1. Introduction

Pneumonia is a common respiratory disease. According to the place where it is acquired, it can be divided into community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP); about 50,000 people die from pneumonia every year. 20%–60% of severe pneumonia (SP) patients require hospitalization due to the severity of the disease and the underlying disease or social factors [1, 2]. 10%–22% of inpatients who reach the diagnosis of SP need to be admitted to the intensive care unit (ICU) for treatment. The morbidity and mortality of SP are high. Despite the use

of antibiotics and emergency treatment measures, 44%–83% of patients still require mechanical ventilation when they are admitted to the ICU, and more than 50% of patients are complicated by septic shock, and the mortality rate is high [3]. SP is a type of pneumonia with severe disease, rapid progress, and poor prognosis. Although there are various treatment measures such as powerful anti-infective treatment and ventilator-assisted ventilation, SP has rapid changes in disease condition, complex inflammatory response, and multiple organ dysfunction syndrome (MODS), which is difficult to treat and expensive, and the prognosis is poor and the mortality rate is high [4, 5].

Primary bronchial lung cancer, referred to as lung cancer (LC), is a malignant tumor that occurs in the bronchial mucosal epithelium, which can grow into the bronchial lumen and/or adjacent lung tissue and can pass through lymphatic blood or transbronchial metastasis [6]. According to pathological characteristics, non-small-cell LC can be divided into squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma, and large-cell carcinoma. Among them, lung adenocarcinoma has the highest incidence, accounting for about 50% of all LC [7–9]. Surgical treatment is the first choice for early and midterm NSCLC. However, more than 80% of clinical patients who seek medical attention after the onset of symptoms are in the advanced stage and have lost the opportunity for surgery. In addition to surgery, treatments for NSCLC include chemotherapy, radiotherapy, and traditional Chinese medicine, but the prognosis is not ideal [10].

Since the biomarkers that have been used in clinical practice are not enough to provide a clear diagnosis basis for early disease, the early diagnosis and early treatment of SP and LC will be beneficial to prolong the overall survival of patients. miRNAs are RNAs with a length of 18–30 nt, which have a variety of important regulatory functions in cells. Each miRNA can have multiple target genes, and several miRNAs can also regulate the same gene. mRNA is a type of single-stranded ribonucleic acid that is transcribed from a strand of DNA as a template and carries genetic information that can guide protein synthesis [11]. In previous studies, it has been found that miR-204 can not only regulate the mRNA of target genes to play a role in diseases but also can be used as a biomarker for disease detection [12–14]. Therefore, this study aims to summarize the clinical characteristics of SP and primary bronchial LC, detect the serum miR-204 levels of both, and explore the diagnostic value of miR-204 expression levels for the disease, so as to provide a theoretical reference for the diagnosis and treatment of SP in the future.

2. Materials and Methods

2.1. General Information. 65 SP patients and 43 patients with primary bronchial LC who were treated in the hospital from January 2017 to December 2018 were randomly selected as the SP group and LC group, and 65 healthy people from the physical examination department of the hospital were selected as the control group. Neither SP patients nor primary bronchial LC patients had been treated. This study was approved by the ethics committee of our hospital, and the patient or close relatives signed an informed consent form for the study protocol.

2.2. Inclusion Criteria and Exclusion Criteria. SP: met the diagnostic criteria revised by the American Society of Infectious Diseases/American Thoracic Society (IDsA/ATs) in 2007 [15]: (1) main criteria: invasive mechanical ventilation was required; septic shock requires vasoconstrictor treatment; (2) secondary criteria: respiratory rate ≥30 times/min; oxygenation index ($Pa0_2/Fi0_2$) ≤ 250; multiple-lobe infiltration; disturbance of consciousness/disorientation; azotemia (BUN≥20 mg/d1); hemocytopenia (WBC<4.0×10^9/L); thrombocytopenia (platelets<10.0×10^9/L); hypothermia ($T < 36^{\circ}C$); low blood pressure, and strong fluid resuscitation was required. The diagnosis of severe community-acquired pneumonia that meets 1 major criterion or 3 minor criteria or more was established. The criteria for defining severe hospital-acquired pneumonia were as follows: (1) lived in the intensive care unit; (2) respiratory failure: mechanical ventilation was required or oxygen concentration of >35% was required to maintain arterial blood oxygen saturation >90%; (3) the condition progressed rapidly; X-ray showed cumulative multiple lung lobes or both lungs with infiltrating lesions and cavities; and (4) there was evidence of severe sepsis. Exclusion criteria: (1) SP patients under 18 years of age; (2) patients with severe immunosuppression (such as AIDS, blood disease, bone marrow suppression after chemotherapy, and after bone marrow transplantation); (3) those who lacked clinical data (such as medical advice and lack of examination results or inquiries); and (4) patients who were admitted to the hospital for a short period of time (within 48 h), did not cooperate with treatment, or are discharged automatically.

Primary bronchial LC: (1) the patient's personal data such as age, gender, tissue type, TNM staging, degree of tissue differentiation, and clinical pathological data were complete; (2) all postoperative pathological specimens of the patients were diagnosed as LC by pathologists; and (3) according to the WHO International Histological Classification Standards [16], the staging was carried out. Exclusion criteria: (1) patients with uncontrollable heart disease such as heart failure (congestive) and acute myocardial ischemia; (2) those who are pregnant and lactating; (3) those with uncontrollable liver and kidney function; (4) those who had received antitumor therapy (within 2 months); (5) people with mental illness; (6) people who were allergic to iodine or arsenic; (7) people with severe esophageal varices; and (8) people who did not cooperate with treatment or were discharged automatically.

2.3. Research Methods

2.3.1. Data and Sample Collection. Clinical data related to the patient's age, gender, and condition were collected, and the relevant data were entered. In the early morning of the next day of hospitalization, for all subjects, and the control group in the early morning of the physical examination, 3 ml

of fasting blood was drawn into a centrifuge tube and centrifuged at 3000 r/min at 4°C for 15 minutes, and then, the supernatant was transferred to a new centrifuge tube for storage and reserved in a −80 refrigerator.

2.3.2. qRT-PCR Detected the Level of Serum miR-204. The RNA extraction kit was used to extract serum RNA from all subjects, and the concentration of extracted RNA was determined. The RNA was reverse transcribed into cDNA using a reverse transcription kit, and then, qRT-PCR was used to detect the serum miR-204 level. The cycling conditions were 95°C 60 s; 95°C 30 s, 58°C 45 s, 72°C 30 s, and total 40 cycles, with U6 as the internal reference. The $2^{-\triangle\triangle Ct}$ method [$\triangle\triangle CT\ (n) = \triangle Ct\ (n) - \triangle Ct\ (1), \triangle Ct\ (n) = Ct$ target gene (n)−Ct internal reference gene (n)] was used to calculate the relative expression of serum miR-204, and the experimental operation was carried out in strict accordance with the reagent instructions. miR-204 forward primer sequence: 5′-GACGCTTTCCCTTTGTCATCCT-3′, reverse primer sequence: 5′-GTGCAGGGTCCGAGGTATTC-3'. U6 forward primer sequence: 5′-ATTGGAACGATACAGAGAAGATT-3′, reverse primer sequence: 5′-GGAACGCTTCACGAATTTG-3'.

2.3.3. Follow-Up Record. All patients are followed up by telephone or outpatient review, and their survival status is recorded. The deadline for follow-up is June 30, 2021. According to whether patients in all groups died during the follow-up period, patients with SP and primary bronchial LC were divided into a death group and survival group. The serum miR-204 levels of all patients were divided into a high-expression group and low-expression group according to their medians, and the relationship between serum miR-204 and the prognosis of the two conditions was explored.

2.4. Statistical Methods. SPSS 21.0 software was used for statistical analysis of all data. Measurement data conforming to normal distribution and uniform variance were expressed as mean ± standard deviation ($\overline{x} \pm s$), and a t-test was used for comparison between groups; The count data were expressed in terms of the number of cases and the rate (%), and the χ^2 test was used for comparison between groups; the receiver operating characteristic (ROC) curve was used to analyze the diagnostic value, and the area under the curve (AUC) was calculated; the Kaplan–Meier method was used to draw the survival curve, and the log-rank test was used for comparison between groups, and the difference was statistically significant with $P < 0.05$.

3. Results

3.1. Basic Information of the Research Object. The clinical data of the study subjects are shown in Table 1.

3.2. Serum miR-204 Levels of Subjects in Each Group. The serum miR-204 of the SP group was 0.43 ± 0.09, the serum miR-204 of the LC group was 0.40 ± 0.10, the serum miR-204 of the control group was 1.00 ± 0.09, and the miR-204 of the SP group and the LC group was significantly higher than that of the control group, and the difference between the groups was statistically significant ($P < 0.001$). There was no significant difference in serum miR-204 levels between the SP group and the LC group ($P > 0.05$), as shown in Figure 1.

3.3. The Relationship between Serum miR-204 Levels and the Pathological Data of the Subjects. In SP patients, the serum miR-204 level of patients with cumulative organs ≥3 was higher than that of patients with cumulative organs <3. The difference was statistically significant ($P < 0.001$). In the LC group, in patients with stage III to IV and low and undifferentiated patients, the level of miR-204 was higher than that of stage I~II and high and moderately differentiated patients, and the difference was statistically significant ($P < 0.001$), as shown in Tables 2 and 3.

3.4. The Diagnostic Value of Serum miR-204 Levels for SP and LC. The AUC of serum miR-204 level to SP was 0.766, and the AUC of serum miR-204 level to LC was 0.818, and the difference was statistically significant, as shown in Table 4 and Figure 2.

3.5. Analysis of Serum miR-204 Levels in Patients with Death and Survival SP and LC. In SP and LC patients, the serum miR-204 level of dead patients (0.89 ± 0.10, 0.83 ± 0.13) was significantly higher than that of surviving patients (1.00 ± 0.11, 1.00 ± 0.10), and the difference was statistically significant ($P < 0.05$), as shown in Figure 3.

3.6. The Relationship between Serum miR-204 Level and Patient Survival Prognosis. The median of serum miR-204 levels in SP patients was 0.45; therefore, >0.45 was high expression and ≤0.45 was low expression; the median of serum miR-204 levels in LC patients was 0.41; therefore, >0.41 was high expression and ≤0.41 was low expression; among them, the survival rate of patients with high serum miR-204 expression in SP patients was higher than that of patients with low serum miR-204 expression, and the difference was statistically significant (log-rank = 3.946, $P = 0.047$); patients with high serum miR-204 expression in LC patients survived. The rate is also higher than that of patients with low serum miR-204 expression, and the difference is statistically significant (log-rank = 4.197, $P = 0.041$), as shown in Figure 4.

4. Discussion

SP is one of the critical illnesses in respiratory medicine. It is often accompanied by respiratory failure, hemodynamic disorders, rapid progress, difficult-to-control infection, poor prognosis, easy to be complicated with multiple organ dysfunction syndrome, and high mortality [17]. SP has a variety of factors that cause inflammation of the trachea and alveoli. Inflammation causes the continuous release of

Table 1: Clinical data of study subjects (n, $\overline{x} \pm s$, %).

Factor	Control group ($n = 65$)	Severe pneumonia group ($n = 43$)	Lung cancer group ($n = 65$)
Age (years)	43.18 ± 7.65	58.14 ± 8.18	65.22.14 ± 7.24
Gender (male/female)	35/30	26/17	38/27
Number of days in hospital (d)	—	20.64 ± 10.26	25.74 ± 11.64
Involved organs (a)	—		—
≥3	—	19 (44.19%)	—
<3	—	24 (55.81%)	—
With chronic obstructive pulmonary disease	—		—
Yes	—	20 (46.51%)	—
No	—	23 (53.49%)	—
Mechanical ventilation	—		—
Yes	—	21 (48.84%)	—
No	—	22 (51.16%)	—
TNM staging	—	—	
I~II	—	—	50(76.92%)
III~IV	—	—	15(23.08%)
Tissue differentiation	—	—	
High and medium differentiation	—	—	16 (24.62%)
Low and undifferentiated	—	—	49 (75.38%)
Histological type	—	—	
Adenocarcinoma	—	—	36 (55.38%)
Squamous cell carcinoma	—	—	29 (44.62%)
Case fatality rate	—	58.14%	46.15%

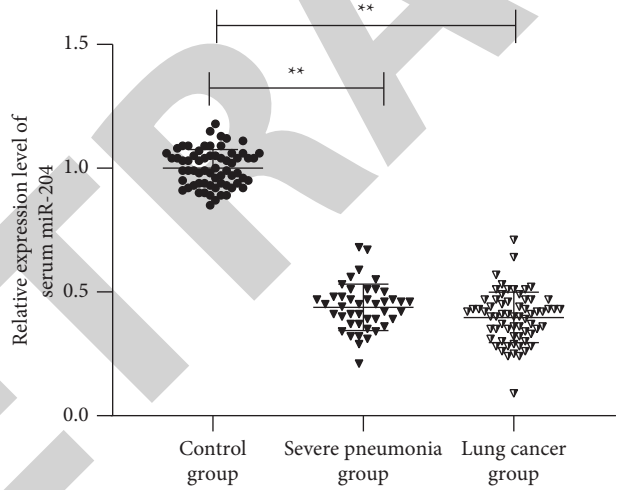

Figure 1: Serum miR-204 levels of subjects in each group. Note: compared with the control group, $^{**}P < 0.01$.

Table 2: The relationship between serum miR-204 levels and pathological data of patients with severe pneumonia (n, $\overline{x} \pm s$).

Factor	Serum miR-204	t value	P value
Involved organs (a)			
≥3	0.38 ± 0.13	4.035	<0.001
<3	0.51 ± 0.08		
With chronic obstructive pulmonary disease			
Yes	0.45 ± 0.11	0.721	0.475
No	0.43 ± 0.07		
Mechanical ventilation			
Yes	0.42 ± 0.11	1.991	0.053
No	0.35 ± 0.12		

inflammatory mediators in the lung tissue. The inflammatory mediators can enter the blood sequentially and cause other organs in the body, leading to systemic inflammatory response syndrome. On the other hand, the weakened immune function and the excessively strong endogenous anti-inflammatory response caused by infection lead to

Table 3: The relationship between serum miR-204 levels and pathological data of lung cancer patients (n, $\overline{x} \pm s$).

Factor	Serum miR-204	t value	P value
TNM staging			
I~II	0.44 ± 0.13	10.083	<0.001
III~IV	0.27 ± 0.05		
Tissue differentiation			
High and medium differentiation	0.52 ± 0.07	8.434	<0.001
Low and undifferentiated	0.36 ± 0.07		
Histological type			
Adenocarcinoma	0.40 ± 0.11	0.394	0.695
Squamous cell carcinoma	0.39 ± 0.09		

Table 4: The diagnostic value of serum miR-204 levels in severe pneumonia and lung cancer.

Disease	ROC	Std.	95%CI	P value
Severe pneumonia	0.766	0.051	0.666~0.865	<0.0001
Lung cancer	0.818	0.037	0.746~0.890	<0.0001

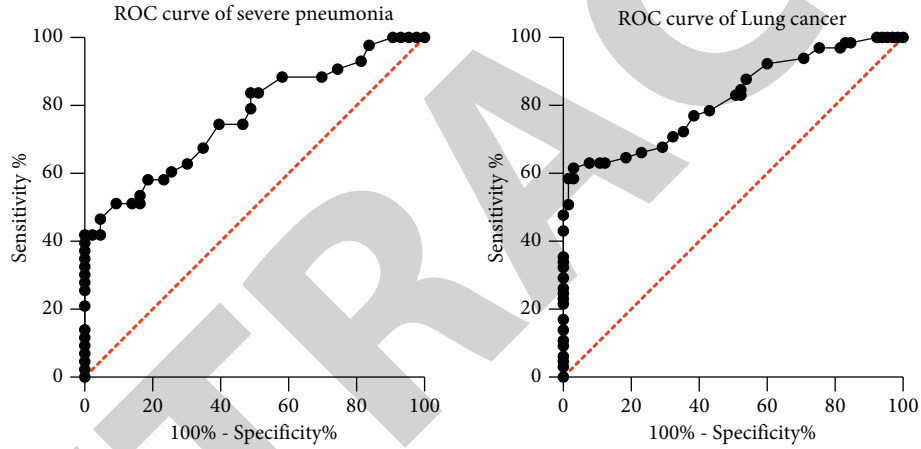

Figure 2: The diagnostic value of serum miR-204 levels in severe pneumonia and lung cancer.

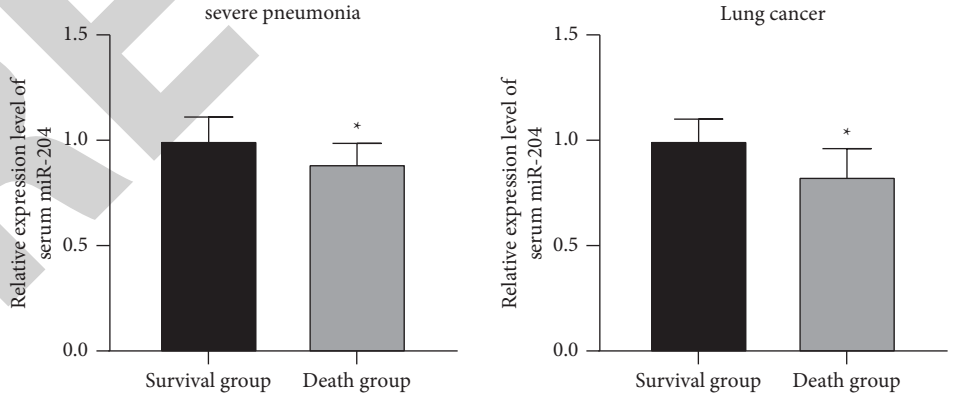

Figure 3: Serum miR-204 levels in patients with severe pneumonia and lung cancer in death and survival.

compensatory anti-inflammatory response syndrome. When the two are out of balance and the systemic inflammatory mediators are released in a cascade, it is easy to cause severe sepsis, septic shock, respiratory failure, and other complications [18, 19].

In addition to SP, the incidence of LC is also gradually increasing. LC is also one of the malignant tumors that seriously threaten human health, with a high fatality rate [20]. Studies have shown that abnormal changes in epigenetics and intracellular inheritance are the main factors that

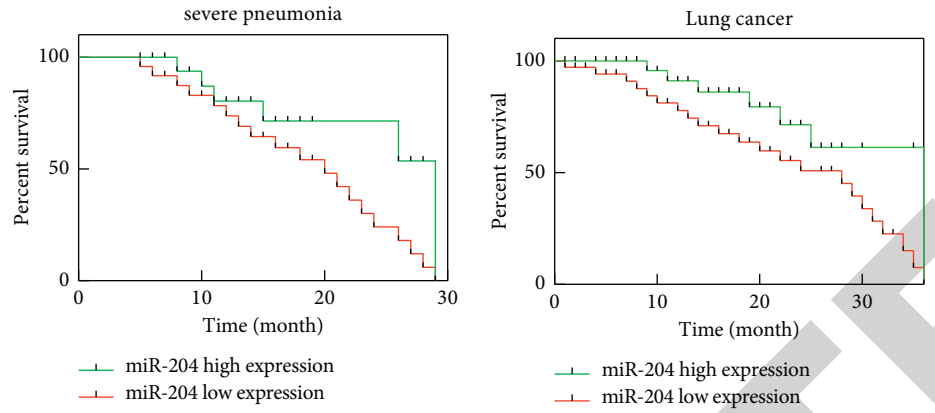

Figure 4: The relationship between serum miR-204 level and patient survival prognosis.

cause the production of human malignant tumor cells [21]. Epigenetic changes not only occur in the early stage of malignant tumors but also play an important role in the occurrence and development of tumors. With the development of molecular biology, the detection of biomarkers can provide an effective assessment of the prognosis of LC. The expression of miRNA is related to the growth, proliferation, migration, and other processes of tumor cells and affects the occurrence and prognosis of many diseases including tumors [22–24]. Many studies are limited to the clinical analysis of patients with SP and LC, while ignoring the importance of clinical diagnosis. Therefore, in this study, 65 patients treated with SP and 43 patients with primary bronchial LC were studied to detect the serum miR-204 level of both patients and to explore the diagnostic value of miR-204 expression level on the disease and the influence of pathological data and prognosis of patients.

The results of this study showed that the levels of miR-204 in the SP group and the LC group were significantly higher than those in the control group, while the difference in serum miR-204 levels between the two disease groups was not statistically significant. It suggests that miR-204 is low in the serum of SP and LC patients and miR-204 has an inhibitory effect on inflammation. In SP patients, the degree of inflammation is high, which may be due to the low level of miR-204 [25] and miR-204 is found in liver cancer [26], thyroid cancer [27], colon cancer [28], and other diseases, and can play an antitumor effect as a tumor suppressor. Therefore, a decrease in the level of miR-204 indicates that the body is in an abnormal state, which explains why the serum miR-204 level of patients in the SP group and the LC group is low. We analyzed the relationship between the serum miR-204 level and the pathological data of the two disease groups and found that the serum miR-204 level of patients with cumulative organs ≥3 in SP patients was higher than that in patients with cumulative organs <3; in the LC group, in patients with stages III to IV and in low and undifferentiated patients, the level of miR-204 was higher than that in stage I~II and high and moderately differentiated patients. It is suggested that the serum miR-204 level is related to the patient's pathological data. The lower the serum miR-204 expression, the more the accumulated organs in patients with pneumonia, the higher the stage of LC patients, and the lower the degree of differentiation. Therefore, we should focus on monitoring patients with low serum miR-204 expression.

Our study also compared the serum miR-204 of patients who survived and died in the two disease groups and found that the miR-204 levels of patients who died of illness in the two groups were significantly higher than those of surviving patients. We used Kaplan–Meier to draw a survival curve and found that the survival rate of patients with high miR-204 expression was higher than that of patients with low expression, and the AUC of serum miR-204 levels to SP and LC were 0.766 and 0.818, respectively. This is partly consistent with the expression in the work of Guo et al. [29].

In summary, the levels of miR-204 in the serum of SP patients and patients with primary bronchial LC were significantly lower than those of healthy people, and patients who died were lower than those who survived. The miR-204 in serum has good diagnostic value for SP and LC and is related to the pathology and survival prognosis of patients.

Data Availability

The data used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval

This study was approved by the ethics committee of Danzhou people's Hospital, Hangzhou Xiaoshan District Hospital of Traditional Chinese Medicine, and Zhuji People's Hospital of Zhejiang Province.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] B. Wahl, M. D. Knoll, A. Shet et al., "National, regional, and state-level pneumonia and severe pneumonia morbidity in children in India: modelled estimates for 2000 and 2015," *The*

Lancet Child & Adolescent Health, vol. 4, no. 9, pp. 678–687, 2020.

[2] C. Cillóniz, C. Dominedò, J. M. Pericàs, D. Rodriguez-Hurtado, and A. Torres, "Community-acquired pneumonia in critically ill very old patients: a growing problem," *European Respiratory Review*, vol. 29, no. 155, p. 190126, 2020.

[3] F. M. Russell, R. Reyburn, J. Chan et al., "Impact of the change in WHO's severe pneumonia case definition on hospitalized pneumonia epidemiology: case studies from six countries," *Bulletin of the World Health Organization*, vol. 97, no. 6, pp. 386–393, 2019.

[4] M. Iwasaki, J. Saito, H. Zhao, A. Sakamoto, K. Hirota, and D. Ma, "Inflammation triggered by SARS-CoV-2 and ACE2 augment drives multiple organ failure of severe COVID-19: molecular mechanisms and implications," *Inflammation*, vol. 44, no. 1, pp. 13–34, 2021.

[5] H. Zhang, D. Zhan, D. Chen et al., "Next-generation sequencing diagnosis of severe pneumonia from fulminant psittacosis with multiple organ failure: a case report and literature review," *Annals of Translational Medicine*, vol. 8, no. 6, p. 401, 2020.

[6] L. Gazourian, C. S. Durgana, D. Huntley et al., "Quantitative pectoralis muscle area is associated with the development of lung cancer in a large lung cancer screening cohort," *Lung*, vol. 198, no. 5, pp. 847–853, 2020.

[7] E. Zamarrón, E. Prats, E. Tejero et al., "Static lung hyperinflation is an independent risk factor for lung cancer in patients with chronic obstructive pulmonary disease," *Lung Cancer*, vol. 128, pp. 40–46, 2019.

[8] E. Pallari, M. Eriksson, A. Billhult et al., "Lung cancer research and its citation on clinical practice guidelines," *Lung Cancer*, vol. 154, pp. 44–50, 2021.

[9] T. Xu, X. Zhang, S. Zhang et al., "Imaging features and prognostic value of 18F-FDG PET/CT detection of soft-tissue metastasis from lung cancer: a retrospective study," *BMC Cancer*, vol. 20, no. 1, p. 596, 2020.

[10] B. Lan, Y. Wang, J. Wu, K. Wang, and P. Wang, "The predictive and prognostic effects of PD-L1 expression on TKI treatment and survival of EGFR-mutant NSCLC," *Medicine (Baltimore)*, vol. 100, no. 34, p. e27038, 2021.

[11] K. He, W.-X. Li, D. Guan et al., "Regulatory network reconstruction of five essential microRNAs for survival analysis in breast cancer by integrating miRNA and mRNA expression datasets," *Functional & Integrative Genomics*, vol. 19, no. 4, pp. 645–658, 2019.

[12] N. Wang, Y. Yang, G. Z. Jia et al., "Long non-coding RNA Down syndrome cell adhesion molecule-anti-sense 1 promotes gastric carcinoma cell proliferation and migration by regulating the miR-204/TPT1 axis," *Human & Experimental Toxicology*, vol. 9, p. 9603271211036037, 2021.

[13] A. Bereimipour, H. Najafi, E. S. Mirsane, S. Moradi, and L. Satarian, "Roles of miR-204 in retinal development and maintenance," *Experimental Cell Research*, vol. 406, no. 1, p. 112737, 2021.

[14] J.-w. Du, G.-q. Li, Y.-s. Li, and X.-g. Qiu, "Identification of prognostic biomarkers related to the tumor microenvironment in thyroid carcinoma," *Scientific Reports*, vol. 11, no. 1, p. 16239, 2021.

[15] H.-y. Li, Q. Guo, W.-d. Song et al., "Mortality among severe community-acquired pneumonia patients depends on combinations of 2007 IDSA/ATS minor criteria," *International Journal of Infectious Diseases*, vol. 38, pp. 141–145, 2015.

[16] X. Yang and D. Lin, "Changes of 2015 WHO Histological Classification of Lung Cancer and the Clinical Significance," *Zhongguo Fei Ai Za Zhi*, vol. 19, no. 6, pp. 332–336, 2016.

[17] Y. Zhou, L. Liu, and W. Gu, "Serum MMP-9 and SAA in the diagnosis of severe pneumonia caused by radiotherapy of esophageal cancer," *Evidence-based Complementary and Alternative Medicine eCAM*, vol. 2021, p. 6032546, 2021.

[18] E. N. Gitonga, J. Wang, S. Yu, N. Wu, and H. Shen, "Left ventricular dysfunction and reversible pulmonary hypertension secondary to severe pneumonia in a background of sepsis: a case report and review of the literature," *Annals of Palliative Medicine*, vol. 9, no. 5, pp. 3629–3642, 2020.

[19] X. Wang, J. Lan, R. Zhang, and X. Luo, "Successful treatment of severe pneumonia, pyopneumothorax with severe acute respiratory distress syndrome, and septic shock: a case report," *European Journal of Medical Research*, vol. 25, no. 1, p. 57, 2020.

[20] Y. Han, R. Ma, G. Cao et al., "Combined treatment of cinobufotalin and gefitinib exhibits potent efficacy against lung cancer," *Evidence-based Complementary and Alternative Medicine eCAM*, vol. 2021, p. 6612365, 2021.

[21] N. Eljabo, N. Nikolic, J. Carkic et al., "Genetic and epigenetic alterations in the tumour, tumour margins, and normal buccal mucosa of patients with oral cancer," *International Journal of Oral and Maxillofacial Surgery*, vol. 47, no. 8, pp. 976–982, 2018.

[22] A. Kandettu, R. Radhakrishnan, S. Chakrabarty, S. Sriharikrishnaa, and S. P. Kabekkodu, "The emerging role of miRNA clusters in breast cancer progression," *Biochimica et Biophysica Acta (BBA) - Reviews on Cancer*, no. 2, p. 188413, 1874.

[23] L. Chen, L. Heikkinen, C. Wang, Y. Yang, H. Sun, and G. Wong, "Trends in the development of miRNA bioinformatics tools," *Briefings in Bioinformatics*, vol. 20, no. 5, pp. 1836–1852, 2019.

[24] C. Q. Kong, X. C. Chen, G. H. Qiu et al., "Effects of miRNA-140 on the growth and clinical prognosis of SMMC-7721 hepatocellular carcinoma cell line," *BioMed Research International*, vol. 2021, p. 6638915, 2021.

[25] Y. Tu, E. Song, Z. Wang et al., "Melatonin attenuates oxidative stress and inflammation of Müller cells in diabetic retinopathy via activating the Sirt1 pathway," *Biomedicine & Pharmacotherapy*, vol. 137, p. 111274, 2021.

[26] X. Li, Y. Zhou, L. Yang et al., "LncRNA NEAT1 promotes autophagy via regulating miR-204/ATG3 and enhanced cell resistance to sorafenib in hepatocellular carcinoma," *Journal of Cellular Physiology*, vol. 235, no. 4, pp. 3402–3413, 2020.

[27] M. Ye, S. Dong, H. Hou, T. Zhang, and M. Shen, "Oncogenic role of long noncoding RNAMALAT1 in thyroid cancer progression through regulation of the miR-204/IGF2BP2/m6A-MYC signaling," *Molecular Therapy-Nucleic Acids*, vol. 23, pp. 1–12, 2020.

[28] C. Lu, T. Xie, X. Guo et al., "LncRNA DSCAM-AS1 promotes Colon cancer cells proliferation and migration via regulating the miR-204/SOX4 Axis," *Cancer Management and Research*, vol. 12, pp. 4347–4356, 2020.

[29] W. Guo, Y. Zhang, Y. Zhang et al., "Decreased expression of miR-204 in plasma is associated with a poor prognosis in patients with non-small cell lung cancer," *International Journal of Molecular Medicine*, vol. 36, no. 6, pp. 1720–1726, 2015.