Serum Potassium Levels Predict Severity and Length of Hospital Stay in Patients with Group 2 Pulmonary Hypertension: A Clinical Study Postprint

Authors: Guo Yunting, Hou Xiaomin, Bai Jianying, Chang Mingyang, Zhao Xu, Sun Lin, Zheng Zhifa, Shi Yiwei, Qin Xiaojiang, Qin Xiaojiang

Date: 2023-07-05T00:00:00+00:00

Abstract

Background Pulmonary hypertension (PH) secondary to left heart disease (Group 2 PH) is characterized by difficult early diagnosis and high mortality. While potassium channel dysfunction is a hallmark of PH, epidemiological data remain unclear and the impact of potassium ions on pulmonary hypertension is not yet well understood.

Objective To investigate the relationship between serum potassium levels and myocardial markers, echocardiographic indices, and length of hospital stay in patients with Group 2 PH, to evaluate the predictive value of serum potassium levels for the severity of Group 2 PH, and to provide a theoretical basis for clinical diagnosis and treatment.

Methods The clinical data of 400 adult inpatients diagnosed with Group 2 PH at the First Hospital of Shanxi Medical University between January 2020 and December 2021 were retrospectively collected: (1) General information: gender, age, BMI, length of hospital stay, smoking status and smoking index (SI), and alcohol consumption history. (2) Underlying diseases (diabetes mellitus, hypertension). (3) Laboratory data: serum potassium, myocardial markers (procalcitonin, N-terminal pro-B-type natriuretic peptide, troponin I, troponin T, creatine kinase-MB), and echocardiographic indices (left atrial anteroposterior diameter, right ventricular anteroposterior diameter, right atrial area, left ventricular ejection fraction, fractional shortening, peak tricuspid regurgitation velocity, and pulmonary artery systolic pressure). Based on serum potassium levels, the included patients were divided into three groups: <3.5 mmol/L group (n=57), 3.5–5.5 mmol/L group (n=340), and >5.5 mmol/L group (n=3). Spearman rank correlation analysis was used to explore the correlation between serum

potassium levels and myocardial markers and echocardiographic indices; the Log-rank (Mantel-Cox) test was used to compare the discharge rates among patients with different potassium levels; and receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of serum potassium for the severity of Group 2 PH.

Results The levels of procalcitonin and N-terminal pro-B-type natriuretic peptide (NT-proBNP) in the >5.5 mmol/L group were higher than those in the <3.5 mmol/L group (P<0.05). Correlation analysis showed that serum potassium levels were positively correlated with NT-proBNP (rs=0.133), peak tricuspid regurgitation velocity (rs=0.017), and pulmonary artery systolic pressure (rs=0.126) (P<0.05). Serum potassium levels were further stratified into <3.5 mmol/L, 3.0–3.5 mmol/L, 4.0–4.9 mmol/L, 5.0–5.5 mmol/L, and >5.5 mmol/L to investigate the relationship between potassium levels and length of hospital stay. Log-rank (Mantel-Cox) test results demonstrated that, for Group 2 patients with hospital stays longer than the average, the cumulative hospitalization rates among patients with different potassium levels (<3.5 mmol/L, 3.5–3.9 mmol/L, 4.0–4.9 mmol/L, 5.0–5.5 mmol/L, >5.5 mmol/L) showed statistically significant differences (P=0.022). ROC curve analysis revealed that the diagnostic value of serum potassium for non-mild PH [area under the ROC curve (AUC) = 0.577, cutoff value = 3.91 mmol/L, sensitivity = 64.7%, specificity = 52.5%] was similar to that of NT-proBNP (AUC = 0.585, cutoff value = 1,070.69 pg/mL, sensitivity = 78.1%, specificity = 39.6%), indicating that serum potassium can effectively predict the severity of Group 2 PH.

Conclusion Serum potassium levels can predict the severity and length of hospital stay in patients with Group 2 PH, and intervention of potassium levels may represent a novel therapeutic approach for the prevention and treatment of PH.

Full Text

Prediction of Severity and Length of Hospital Stay in Patients with Group 2 Pulmonary Hypertension Based on Serum Potassium Level

GUO Yunting[1], HOU Xiaomin[2], BAI Jianying[1], CHANG Mingyang[1], ZHAO Xu[1], SUN Lin[1], ZHENG Zhifa[3], SHI Yiwei[4], QIN Xiaojiang[1]*

[1]School of Public Health, Shanxi Medical University, Taiyuan 030001, China
[2]School of Basic Medicine, Shanxi Medical University, Taiyuan 030001, China
[3]Department of Cardiovascular Surgery, Shanxi Bethune Hospital, Taiyuan 030001, China
[4]First Hospital of Shanxi Medical University, Taiyuan 030001, China

Corresponding author: QIN Xiaojiang, Professor; E-mail: sph@sxmu.edu.cn

Abstract

Background: Pulmonary hypertension (PH) is often caused by left heart disease (group 2 PH), which is difficult to diagnose early and carries a high mortality rate. Potassium channel dysfunction is a hallmark of PH; however, the epidemiological data of this condition remain unclear, and the effect of potassium ions on PH is not well understood.

Objective: To investigate the relationship between serum potassium levels and myocardial markers, echocardiographic indicators, and length of hospital stay in patients with group 2 PH, and to evaluate the predictive value of serum potassium levels for disease severity, thereby providing a theoretical basis for clinical diagnosis and treatment.

Methods: Clinical data were retrospectively collected from 400 adult inpatients diagnosed with group 2 PH at the First Hospital of Shanxi Medical University between January 2020 and December 2021. Data included: (1) general information: gender, age, BMI, length of hospital stay, smoking status, smoking index (SI), and alcohol consumption history; (2) comorbidities (diabetes, hypertension); and (3) laboratory data: serum potassium, myocardial markers (procalcitonin, N-terminal pro-B-type natriuretic peptide, troponin I, troponin T, creatine kinase-MB), and echocardiographic indicators (left atrial anteroposterior diameter, right ventricular anteroposterior diameter, right atrial area, left ventricular ejection fraction, fractional shortening, peak tricuspid regurgitation velocity, and pulmonary artery systolic pressure). Patients were divided into three groups based on serum potassium levels: <3.5 mmol/L (n=57), 3.5–5.5 mmol/L (n=340), and >5.5 mmol/L (n=3). Spearman rank correlation analysis was used to explore correlations between serum potassium levels and myocardial markers/echocardiographic indicators. The Log-rank (Mantel-Cox) test was used to compare discharge rates among patients with different potassium levels. Receiver operating characteristic (ROC) curves were constructed to evaluate the predictive value of serum potassium for group 2 PH severity.

Results: Patients in the >5.5 mmol/L group had significantly higher procalcitonin and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels compared to those in the <3.5 mmol/L group ($P<0.05$). Correlation analysis revealed that serum potassium level was positively correlated with NT-proBNP ($r=0.133$), peak tricuspid regurgitation velocity ($r=0.017$), and pulmonary artery systolic pressure ($r=0.126$) ($P<0.05$). To further investigate the relationship between potassium levels and hospital stay, serum potassium was reclassified into five categories: <3.5 mmol/L, 3.0–3.5 mmol/L, 4.0–4.9 mmol/L, 5.0–5.5 mmol/L, and >5.5 mmol/L. Log-rank (Mantel-Cox) test results showed that among group 2 PH patients with above-average hospitalization duration, cumulative hospitalization rates differed significantly across potassium level groups (<3.5 mmol/L, 3.5–3.9 mmol/L, 4.0–4.9 mmol/L, 5.0–5.5 mmol/L, >5.5 mmol/L) ($P=0.022$). ROC analysis demonstrated that the diagnostic value of serum potassium for non-mild PH (area under the curve [AUC]=0.577,

cutoff value=3.91 mmol/L, sensitivity=64.7%, specificity=52.5%) was similar to that of NT-proBNP (AUC=0.585, cutoff value=1,070.69 pg/mL, sensitivity=78.1%, specificity=39.6%), indicating that serum potassium can effectively predict group 2 PH severity.

Conclusion: Serum potassium level can predict both the severity and length of hospital stay in patients with group 2 PH. Intervening on serum potassium levels may represent a novel therapeutic approach for PH prevention and treatment.

Keywords: pulmonary arterial hypertension; serum potassium; echocardiography; hospital stay; predictive value

---

Introduction

Pulmonary hypertension (PH) refers to elevated pulmonary arterial pressure resulting from structural or functional changes in pulmonary vessels caused by various heterogeneous diseases and pathogenic mechanisms, which can progress to right heart failure and death [1-2]. Early diagnosis of PH is challenging [3], as clinical symptoms lack specificity, treatment is difficult and cannot achieve complete cure [4-5], and both disability and mortality rates are high, with a 5-year survival rate of only 57% [6]. The pathogenesis of PH is complex and remains incompletely understood. Research has shown that potassium channel dysfunction in pulmonary artery smooth muscle cells is a hallmark of PH [7], and that serum potassium levels are associated with heart failure [8-9], influencing the development and progression of PH.

At the 5th World Symposium on Pulmonary Hypertension, PH was classified into five groups, with PH due to left heart disease (group 2 PH) being the most common form [10]; however, its epidemiological data remain unclear. Serum potassium is a routine laboratory parameter that plays a crucial role in regulating vascular smooth muscle cell membrane potential, intracellular calcium concentration, and vascular tone [11]. Studies have demonstrated that potassium channel dysfunction in pulmonary artery smooth muscle cells is a marker of PH, and that serum potassium levels correlate with heart failure [7], affecting PH pathogenesis [8-9]. Currently, N-terminal pro-B-type natriuretic peptide (NT-proBNP) is an established biomarker for PH diagnosis [10], and length of hospital stay has become a major concern for both hospitals and patients. However, most studies on potassium in PH have focused on experimental mechanisms, with few population-based observational studies. It remains unclear whether serum potassium levels affect hospital stay duration in PH or can predict PH severity. Therefore, this retrospective case-control study investigates the relationship between serum potassium levels and severity/hospital stay in group 2 PH patients, evaluates the predictive value of potassium for PH severity, and explores whether this readily available metric can enable early diagnosis and severity assessment to provide a theoretical basis for clinical management.

Methods

1.1 Study Population This study utilized data from patients hospitalized at the First Hospital of Shanxi Medical University between January 2020 and December 2021 who received a first-time PH diagnosis. Based on inclusion and exclusion criteria, 400 patients were enrolled, including 144 with group 2 PH due to heart failure with reduced ejection fraction, 15 due to heart failure with preserved ejection fraction, 56 due to valvular heart disease, and 185 due to congenital/acquired cardiovascular diseases causing post-capillary PH.

Inclusion criteria: (1) Age 18–90 years; (2) Diagnosis of group 2 PH according to the Chinese Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension [1]; (3) Availability of serum potassium test results.

Exclusion criteria: (1) Pregnancy-related PH; (2) Malignant disease; (3) Comorbid pneumoconiosis or silicosis; (4) Other PH groups (arterial PH, PH due to lung disease and/or hypoxia, chronic thromboembolic PH and/or other pulmonary artery obstructions, PH with unclear and/or multifactorial mechanisms). The screening process is shown in [Figure 1: see original paper].

This study was approved by the Research Ethics Committee of the First Hospital of Shanxi Medical University (approval number: K-138), which granted a waiver of informed consent.

1.2 Data Collection Electronic medical records were reviewed at the time of first PH diagnosis and before any PH-specific treatment, collecting: (1) General information: gender, age, BMI, length of hospital stay, smoking status, smoking index (SI), and alcohol consumption history; (2) Comorbidities (diabetes, hypertension); (3) Laboratory data: serum potassium, myocardial markers (procalcitonin, NT-proBNP, troponin I, troponin T, creatine kinase-MB), and echocardiographic indicators (left atrial anteroposterior diameter, right ventricular anteroposterior diameter, right atrial area, left ventricular ejection fraction, fractional shortening, peak tricuspid regurgitation velocity, pulmonary artery systolic pressure). Myocardial markers reflect myocardial injury severity [12], and echocardiography can assess PH; both correlate with PH severity. (4) Definitions: Smoking was defined as $ $1 cigarette daily for $ $6 consecutive or cumulative months; alcohol consumption as $ $30 g ethanol weekly for $ $1 year [13]; SI = daily cigarettes $\times$ years smoked. Normal physiological serum potassium ranges from 3.5–5.5 mmol/L; >5.5 mmol/L indicates hyperkalemia, and <3.5 mmol/L indicates hypokalemia. PH severity was classified based on pulmonary artery systolic pressure (PASP) as mild (30 mmHg $\leq$ PASP $<$ 50 mmHg), moderate (50 mmHg $\leq$ PASP $<$ 70 mmHg), or severe (PASP $\geq$ 70 mmHg) [14]. For this study, PH severity was dichotomized into mild (30 mmHg $\leq$ PASP $<$ 50 mmHg) and non-mild (PASP $\geq$ 50 mmHg) to analyze the impact of potassium levels and their relationship with severity.

Patients were divided into three groups based on serum potassium: <3.5 mmol/L (n=57), 3.5–5.5 mmol/L (n=340), and >5.5 mmol/L (n=3).

1.3 Statistical Analysis Data were analyzed using SPSS 25.0. Non-normally distributed continuous variables are presented as median (Q1, Q3) and compared using nonparametric rank-sum tests. Categorical variables are expressed as percentages and compared using ^{2} tests. Spearman rank correlation analysis examined relationships between serum potassium and myocardial markers/echocardiographic indicators. The Log-rank (Mantel-Cox) test compared discharge rates across potassium groups. ROC curves were constructed to evaluate potassium's predictive value for group 2 PH severity. P<0.05 was considered statistically significant.

Results

2.1 Baseline Characteristics of Group 2 PH Patients Among the 400 enrolled PH patients, the median age was 70 years, median hospital stay was 11 days, 53.0% were male, 54.5% had hypertension, and median serum potassium was 4.01 mmol/L. Hypokalemia was present in 14.2% and hyperkalemia in 0.8%. Procalcitonin and NT-proBNP levels were elevated, right atrial area was enlarged, and PASP was high with a median of 53 mmHg. Results are shown in .

2.2 Characteristics of Group 2 PH Patients by Serum Potassium Level No significant differences were observed across potassium groups in gender, age, BMI, hospital stay, smoking index, smoking status, alcohol consumption, hypertension history, diabetes history, troponin I, troponin T, creatine kinase-MB, left atrial diameter, right ventricular diameter, right atrial area, left ventricular ejection fraction, fractional shortening, peak tricuspid regurgitation velocity, or PASP (P>0.05). However, procalcitonin and NT-proBNP levels in the >5.5 mmol/L group were significantly higher than in the <3.5 mmol/L group (P<0.05). See .

2.3 Correlation Between Serum Potassium Level and Myocardial Markers/Echocardiographic Indicators Serum potassium level was positively correlated with NT-proBNP (r =0.133), peak tricuspid regurgitation velocity (r =0.017), and PASP (r =0.126) (P<0.05). See .

2.4 Relationship Between Serum Potassium Level and Hospital Stay As serum potassium is a continuous variable, it was further categorized into five groups (<3.5 mmol/L, 3.0–3.5 mmol/L, 4.0–4.9 mmol/L, 5.0–5.5 mmol/L, >5.5 mmol/L) [15] to deeply examine its relationship with hospital stay. For group 2 PH patients with hospital stays exceeding the average, the Log-rank (Mantel-Cox) test revealed significant differences in cumulative hospitalization rates

across potassium groups (^{2}=11.49, P=0.0216). Among patients with potassium <5.5 mmol/L, cumulative discharge rates decreased as potassium levels increased. Patients with potassium 5.0–5.5 mmol/L had the longest hospital stays (median: 29 days), while those >5.5 mmol/L had the shortest (median: 15 days). See [Figure 2: see original paper].

2.5 Predictive Value of Potassium Levels for Non-Mild Group 2 PH NT-proBNP is an established PH biomarker [10]. ROC analysis showed that serum potassium had similar diagnostic value for non-mild PH (AUC=0.577, cutoff=3.91 mmol/L, sensitivity=64.7%, specificity=52.5%) as NT-proBNP (AUC=0.585, cutoff=1,070.69 pg/mL, sensitivity=78.1%, specificity=39.6%), effectively predicting group 2 PH severity with higher specificity than NT-proBNP. Results are shown in [Figure 3: see original paper] and .

Discussion

PH is a common cardiovascular disease, and echocardiography is currently the most important clinical tool for PH diagnosis and screening [16], with higher prevalence in individuals over 65 years [10]. The group 2 PH patients in this study had a median age around 70 years. NT-proBNP is a cardiac biomarker used to identify early myocardial dysfunction and is an established PH biomarker correlated with disease severity [17-18]. Procalcitonin is a commonly used biomarker that typically rises during bacterial infection or systemic inflammatory response [19]. Our findings that hyperkalemic patients had significantly higher NT-proBNP and procalcitonin than hypokalemic patients suggest that elevated potassium promotes inflammatory responses and exacerbates myocardial injury, advancing PH progression. The positive correlations between potassium and NT-proBNP, peak tricuspid regurgitation velocity, and PASP further indicate that hyperkalemia intensifies inflammation and myocardial damage, accelerates tricuspid regurgitation, and increases pulmonary artery pressure, promoting PH development.

Because serum potassium is continuous, we further categorized it into five groups (<3.5 mmol/L, 3.5–4.0 mmol/L, 4.0–4.9 mmol/L, 5.0–5.5 mmol/L, >5.5 mmol/L) to thoroughly investigate its relationship with hospital stay and avoid overlooking potential effects. Among patients with above-average hospital stays, we found significant differences in cumulative hospitalization rates across potassium groups. For potassium levels <5.5 mmol/L, cumulative discharge rates decreased as potassium increased, with 5.0–5.5 mmol/L patients having the longest stays (median: 29 days). Conversely, >5.5 mmol/L patients had the shortest stays (median: 15 days). This may be due to the small, unrepresentative hyperkalemia sample, patient transfers, early discharge, or treatment withdrawal. If these factors are excluded, moderate hyperkalemia might benefit group 2 PH treatment and recovery. Studies report that moderate hyperkalemia facilitates cardiac diastole and reduces myocardial oxygen consumption. Whether cardiac

damage from potassium follows an "n-shaped" pattern and whether this can be leveraged clinically to improve group 2 PH outcomes warrants further investigation. ROC analysis showed potassium's predictive value was comparable to NT-proBNP's, with much higher specificity, making it a useful predictor for group 2 PH. Potassium testing is convenient, rapid, and widely applicable, offering good clinical prospects.

In summary, serum potassium correlates with group 2 PH severity and can predict both disease severity and hospital stay duration. Intervening on serum potassium levels may represent a novel therapeutic approach for PH, giving new meaning to this routine metric and reminding us not to overlook conventional indicators. This provides a theoretical basis for clinical management. Since hospital stay is the most direct indicator of clinical efficacy and potassium is routinely measured, studying their relationship has practical significance for patients and clinicians. However, this was a retrospective single-center study with potential bias; further research with larger samples and improved methodology is needed to confirm potassium's role in PH.

References

[1] Chinese Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension (2021 Edition) [J]. National Medical Journal of China, 2021, 101(1): 11-51. DOI: 10.3760/cma.j.cn112137-20201112-03210.

[2] WANG Zengzhi, LIU Shuang. Progress in the treatment of pulmonary hypertension [J]. Chinese General Practice, 2007, 10(9): 752-756. DOI: 10.3969/j.issn.1007-9572.2007.09.034.

[3] CARPIO AM, GOERTZ A, KELLY C, et al. Unrecognized pulmonary arterial hypertension in hospitalized patients [J]. Int J Cardiovasc Imaging, 2021, 37(4): 1237-1243. DOI: 10.1007/s10554-020-02108-9.

[4] BORDENAVE J, TU L, SAVALE L, et al. Nouveau regard sur la physiopathologie de l'hypertension artérielle pulmonaire [J]. Revue Des Maladies Respir, 2019, 36(4): 433-437. DOI: 10.1016/j.rmr.2019.03.003.

[5] MARON BA, ABMAN SH, ELLIOTT CG, et al. Pulmonary hypertension: advances [J]. Am J Respir Crit Care Med, 2021, 203(12): 1472-1487. DOI: 10.1164/rccm.202012-4317so.

[6] CHEN Yunfang, WANG Sheng, QIAN Ziliang. Expression of HIF-1α and Nrf2 in lung tissue of cigarette smoke-induced pulmonary hypertension mouse model [J]. Journal of Jiangxi Normal University (Natural Science Edition), 2017, 41(2): 155-159. DOI: 10.16357/j.cnki.issn1000-5862.2017.02.07.

[7] SFAIROPOULOS D, ARSENIOU A, KORANTZOPOULOS P. Serum potassium and heart failure: association, causation, and clinical implications [J]. Heart Fail Rev, 2021, 26(3): 479-486. DOI: 10.1007/s10741-020-10039-9.

[8] BOUCHERAT O, CHABOT S, ANTIGNY F, et al. Potassium channels in pulmonary arterial hypertension [J]. Eur Respir J, 2015, 46(4): 1167-1177. DOI: 10.1183/13993003.00798-2014.

[9] BURG ED, REMILLARD CV, YUAN JXJ. Potassium channels in the regulation of pulmonary artery smooth muscle cell proliferation and apoptosis: pharmacotherapeutic implications [J]. Br J Pharmacol, 2008, 153(S1): S99-111. DOI: 10.1038/sj.bjp.0707635.

[10] GALIÈ N, HUMBERT M, VACHIERY JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): endorsed by: association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT) [J]. Eur Heart J, 2016, 37(1): 67-119. DOI: 10.1093/eurheartj/ehv317.

[11] SEVILLA-MONTERO J, LABROUSSE-ARIAS D, FERNÁNDEZ-PÉREZ C, et al. Cigarette smoke directly promotes pulmonary arterial remodeling and Kv7.4 channel dysfunction [J]. Am J Respir Crit Care Med, 2021, 203(10): 1290-1305. DOI: 10.1164/rccm.201911-2238OC.

[12] ABID S, MARCOS E, PARPALEIX A, et al. CCR2/CCR5-mediated macrophage-smooth muscle cell crosstalk in pulmonary hypertension [J]. Eur Respir J, 2019, 54(4): 1802308. DOI: 10.1183/13993003.02308-2018.

[13] AI Yi, ZHANG Qiao, PENG Nianchun, et al. Study on the correlation between serum TSH within normal reference range and bone mineral density in women aged 40 and above [J]. Guizhou Medical Journal, 2020, 44(8): 1179-1181. DOI: 10.3969/j.issn.1000-744X.2020.08.001.

[14] JANKOWICH M, MARON BA, CHOUDHARY G. Mildly elevated pulmonary artery systolic pressure on echocardiography: bridging the gap in current guidelines [J]. Lancet Respir Med, 2021, 9(10): 1185-1191. DOI: 10.1016/s2213-2600(21)00072-2.

[15] NAKHOUL GN, HUANG HQ, ARRIGAIN S, et al. Serum potassium, end-stage renal disease and mortality in chronic kidney disease [J]. Am J Nephrol, 2015, 41(6): 456-463. DOI: 10.1159/000437151.

[16] HOEPER MM, GHOFRANI HA, GRÜNIG E, et al. Pulmonary hypertension [J]. Deutsches Arzteblatt Int, 2017, 114(5): 73-84. DOI: 10.3238/arztebl.2017.0073.

[17] WANG H, LI Z, YIN M, et al. Combination of Acute Physiology and Chronic Health Evaluation II score, early lactate area, and N-terminal prohormone of brain natriuretic peptide levels as a predictor of mortality in geriatric patients with septic shock [J]. J Crit Care, 2015, 30(2): 304-309. DOI: 10.1016/j.jcrc.2014.11.013.

[18] SCHMITT W, RÜHS H, BURGHAUS R, et al. NT-proBNP qualifies as a surrogate for clinical end points in heart failure [J]. Clin Pharmacol Ther, 2021, 110(2): 498-507. DOI: 10.1002/cpt.2222.

[19] HAMADE B, HUANG DT. Procalcitonin [J]. Crit Care Clin, 2020, 36(1): 23-40. DOI: 10.1016/j.ccc.2019.08.003.

Author Contributions

GUO Yunting, QIN Xiaojiang, and HOU Xiaomin designed the study. BAI Jianying supervised the research and revised the manuscript. GUO Yunting, ZHAO Xu, and SUN Lin collected and verified data. GUO Yunting performed statistical analysis and drafted the manuscript. CHANG Mingyang, ZHENG Zhifa, and SHI Yiwei revised the manuscript.

Conflict of Interest Statement

The authors declare no conflicts of interest.

Funding: National Natural Science Foundation of China Youth Fund (81803282, 82204042); Shanxi Provincial Returned Overseas Students Fund (2020-087, 2020-075); Shanxi Provincial Science and Technology Activity Merit-based Funding for Returned Overseas Students Key Project (20220019); Shanxi Provincial Science and Technology Cooperation and Exchange Special Project Regional Cooperation Project (202204041101022); National Health Commission Key Laboratory of Pneumoconiosis Open Project (YKFKT006)

Received: February 19, 2023; **Revised:** May 19, 2023; **Accepted:** [Not provided]
Editor: CUI Sha

Note: Figure translations are in progress. See original paper for figures.