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Comparison of arterial stiffness and ultrasound indices in patients with and without chronic obstructive pulmonary disease

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SUMMARY

OBJECTIVE: The purpose of this study was to compare arterial stiffness and ultrasound indices in patients with and without chronic obstructive pulmonary disease.

METHODS: In our retrospective study, 83 chronic obstructive pulmonary disease patients were assigned to the chronic obstructive pulmonary disease group and 80 healthy controls were enrolled. Pearson's correlation analysis software was used to analyze the correlation between arterial stiffness (including brachial ankle pulse wave velocity and ankle-brachial blood pressure index) and ultrasound index (including resistance index, pulsatility index, and intima-media thickness) at the carotid artery in chronic obstructive pulmonary disease patients.

RESULTS: The ultrasound resistance index and pulsatility index level of chronic obstructive pulmonary disease group were lower than those of control group ($t=6.326, 8.321, p<0.001$). Compared with the control group, the chronic obstructive pulmonary disease group had higher intima-media thickness, total plaque area, and number of plaques ($t=4.574, 7.493, 5.093, p<0.001$). The arterial stiffness and ankle-brachial blood pressure index level in the chronic obstructive pulmonary disease group were higher than those in the control group ($t=6.392, 5.109, p<0.001$). Moreover, arterial stiffness in patients with chronic obstructive pulmonary disease was negatively correlated with the ankle-brachial blood pressure index, resistance index, and pulsatility index levels ($p<0.05$), while it is positively correlated with intima-media thickness, total plaque area, and number of plaques ($p<0.05$).

CONCLUSION: Our results indicated that patients with chronic obstructive pulmonary disease have stiffer arteries compared with healthy control subjects; the ultrasound index could be used as an auxiliary indicator for clinical prediction of arterial stiffness, which is helpful to improve the accuracy of prediction and thus better guide clinical interventions in high-risk groups of chronic obstructive pulmonary disease in time.

KEYWORDS: Chronic disease. Chronic obstructive. Ultrasonography. Vascular stiffnesses.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a chronic respiratory disease characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities usually caused by high exposure to noxious particles or gases (usually tobacco smoke but also from environmental and occupational exposures) and influenced by host factors including abnormal lung development[1]. COPD can cause pulmonary hypertension, which can result in enlargement of the right ventricular and may develop to right heart failure, which seriously threaten the life of patients[2,3]. Cardiovascular disease is the most common chronic disease associated with COPD, a major cause of hospitalization, and also one of the leading causes of death[4]. Previous studies have shown that patients with COPD are at increased risk of atherosclerosis, and the mechanism may be related to hypoxemia and inflammation[5-7]. Arterial stiffness is highly relevant to cardiovascular disease and is an important arterial phenotype and an excellent indicator of cardiovascular morbidity and mortality. In clinical practice, measurements of arterial stiffness is currently one of the most commonly used methods to predict cardiovascular risk in patients with COPD[5,7,8]. Of note, early evaluation of arterial stiffness in patients with COPD is of great significance for the treatment and prognosis of the disease. Pulse wave velocity (PWV), defined as the ratio of the distance to transit time between two pressure waves recorded transcutaneous at two arterial sites, is a classic index to reflect arterial stiffness in clinical practice[8-10]. The occurrence of cardiovascular events is very dangerous, and early detection and early prevention play a particularly key role in such diseases. Although the monitoring of PWV has been very applicable in clinical practice, finding and combining with the detection of other early indicators of vascular diseases can only benefit the treatment of cardiovascular diseases. Ultrasound is a commonly used method for measuring arterial stiffness in clinic, but there are few reports on the relationship between other ultrasound indexes and arterial stiffness. Ultrasound, as a widely used clinical tool, might have

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its advantages in evaluating arterial stiffness in some clinical scenarios, especially when PWV was unavailable. The aim of the study was to compare and analyze the arterial stiffness in COPD patients and healthy people by ultrasonic indicators, find the correlation between COPD and arterial stiffness, and provide reference for better clinical prediction of the occurrence and development of COPD.

METHODS

Study design and patients

Consecutive 112 patients with COPD hospitalized in our hospital from August 2017 to August 2019 were retrospectively screened for eligibility. Inclusion criteria were as follows: ① patients meet the clinical diagnostic criteria of COPD[1]; ② patients with cough and progressive dyspnea; ③ patients with history of high exposure to toxic smoke or dust; and ④ patients agree to participate in the study and complete ultrasound and arterial hardness tests. Exclusion criteria were as follows: ① patients with hematological diseases or malignant tumors (n=7); ② patients with autoimmune diseases (e.g., systemic lupus erythematous and rheumatoid arthritis), diabetes, hypertension, or coronary heart disease (n=12); ③ patients with severe liver (bilirubin is two times higher than the normal upper limit, or transaminase was three times higher than the normal upper limit) or kidney dysfunction (hemodialysis, kidney transplantation, or serum creatinine ≥200 μmol/l) (n=4); and ④ patients with hyperlipidemia (total cholesterol ≥5.72 mmol/l or triglycerides ≥1.70 mmol/l) or hyperuricemia (uric acid ≥420 μmol/l) (n=6). In total, 83 patients were included as the COPD group. Meanwhile, 80 health subjects with normal pulmonary function, without history of COPD or other diseases included in the exclusion criteria, were selected as the control group. This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of our Hospital. Written informed consent was obtained from all participants.

Methods

Detection of carotid artery disease with ultrasound

① Detection method: All patients in both groups completed relevant examinations after admission. We explained the disease-related knowledge to patients and their families and informed patients of the importance and necessity of ultrasound examination to improve patients' cooperation. IU22 color Doppler ultrasound (manufacturer: Philips) was used for inspection, and the probe frequency was 2–10 MHz. During the examination, patients took the supine position and fully exposed the neck. The ultrasound probe was placed at the 2 cm position of the carotid artery bifurcation to complete the measurement of carotid artery intima-media thickness (IMT); resistance index (RI) and pulsatility index (PI) were two hemodynamic parameters calculated by flow velocity on ultrasound, which reflected vascular resistance. RI and PI were measured at the bifurcation of the carotid artery 1 cm near the heart and then determine the total plaque area and plaque number. The plaque area was calculated by the following formula: original lumen area — residual lumen area (Figure 1). To improve the accuracy of detection data and reduce the detection error, we measured each subject three times and averaged the results. ② Judgment method: according to the detection results of the two groups, IMT >1.2 mm indicated the patient has atherosclerotic plaque formation[11]. All ultrasound examinations were performed by ultrasound physicians in our hospital.

Measurement of arterial stiffness

① Detection method: BP-203III arterial stiffness tester (manufacturer: Omron) was used to detect brachial-ankle pulse wave velocity (baPWV) and ankle-brachial blood pressure index (ABI). During the test, the temperature in the control room was set at 22–25°C. All subjects wore thin clothes and took a lying posture. The test was started after resting for 5 min. Blood pressure and heart rate were measured first, followed by baPWV and ABI tests. Each case was measured twice and averaged[12]. ② Judgment method: baPWV ≥ 1400 cm/s indicated arterial stiffness; ABI > 1.4 indicated abnormal elevation[11].

Statistics

Statistical software SPSS version 20.0 was used to analyze the data. Normally distributed continuous variables were

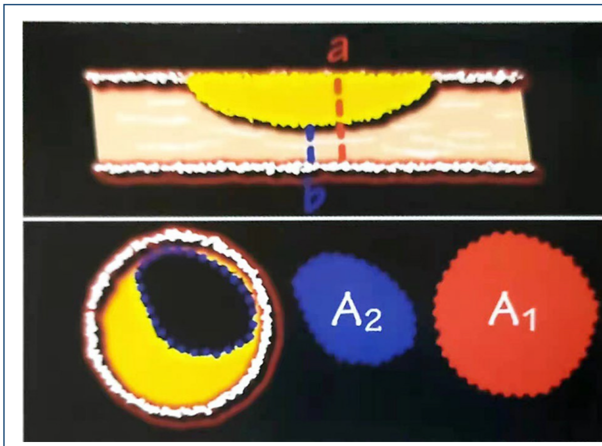

Figure 1. Measurement of patch area.

expressed as mean±standard deviation (SD), and categorical variables were expressed as percentage. An analysis of normality of the continuous variables was performed with the Kolmogorov-Smirnov test. The mean comparison between the two groups was performed by independent sample t-test; the count data were expressed in cases (%), and the comparison between groups was performed by χ^2. Pearson's correlation analysis was used for analyzing the correlation between arterial stiffness and ultrasound index in patients with COPD. The data were analyzed within the 95% confidence interval (CI95%) and p<0.05 was considered statistically significant.

RESULTS

Baseline characteristics of two groups

There were 46 males and 37 females in the COPD group, with an average age of 61.34±2.91 years and body mass index (BMI) of 22.41±2.15 kg/m^2. In the control group, there were 41 males and 39 females, with an average age of 61.87±3.04 years and BMI of 22.32±2.31 kg/m^2. There was no statistically significant difference in general data between the two groups (p>0.05) (Table 1).

Comparison of ultrasound examination results, arterial stiffness, and ABI between the two groups

The levels of RI and PI in the COPD group were lower than those in the control group (p<0.05); IMT level, total plaque area, and number of plaques in the COPD group were higher than those in the control group (p<0.05). The levels of baPWV and ABI in the COPD group were higher than those in the control group (p<0.05) (Table 1).

Correlation analysis of arterial stiffness and color doppler ultrasound index in patients with COPD

Pearson correlation analysis showed that the levels of baPWV and ABI were negatively correlated with RI and PI in patients with COPD (p<0.05), but positively correlated with IMT, total plaque area, and number of plaques (p<0.05) (Table 2).

DISCUSSION

In the present study, we compared arterial stiffness in patients with and without COPD and examined the relationship between ultrasound and arterial stiffness. The main findings can be summarized as follows: (1) compared with the control group, COPD patients had higher IMT, total plaque area, and number of plaques but lower ultrasound RI and PI; (2) the arterial stiffness and ABI level in the COPD group were higher than those in the control group; (3) arterial stiffness in patients with COPD was negatively correlated with the ABI, RI, and PI levels while it is positively correlated with IMT, total plaque area, and number of plaques.

Table 1. Comparison of basic characteristics and ultrasound results between the two groups.

Variables	COPD group (N=83)	Control group (N=80)	p-value
Basic characteristics			
Males, n	46	41	0.59
Age, year	61.34±2.91	61.87±3.04	0.87
BMI, kg/m^2	22.41±2.15	22.32±2.31	0.79
Current smoker, n	47	35	0.06
Current drinkers, n	42	38	0.75
Ultrasound results			
RI	0.62±0.14	0.81±0.22	<0.001
PI	2.61±0.38	2.95±0.36	<0.001
IMT, mm	1.36±0.13	0.94±0.10	<0.001
Total plague area, mm^2	19.75±2.19	5.84±1.32	<0.001
Plaque numbers, n	1.67±0.64	0.82±0.30	<0.001
BaPWV, cm/s	1585.49±14.36	1142.45±10.77	<0.001
ABI	1.63±0.24	1.12±0.16	<0.001

Values are mean±SD for continuous variables or n (%) for categorical variables.

Table 2. Correlation analysis of arterial stiffness and color Doppler ultrasound index in patients with chronic obstructive pulmonary disease.

Related factors	RI R value p-value	PI R value p-value	IMT R value p-value	Patch area R value p-value	Patch numbers R value p-value
baPWV	-0.693 (<0.001)	-0.721 (<0.001)	0.701 (<0.001)	0.668 (<0.001)	0.784 (<0.001)
ABI	-0.712 (<0.001)	-0.689 (<0.001)	0.667 (<0.001)	0.712 (<0.001)	0.722 (<0.001)

Chronic obstructive pulmonary disease is a common respiratory disease characterized by persistent airflow limitation. Its occurrence and development are closely related to the chronic inflammatory reaction caused by the exposure of airways and lungs to toxic substances. Cardiovascular disease is the most common complication in patients with COPD, and more patients die from cardiovascular disease than from respiratory disease[4,13-15]. Therefore, it is important to strengthen the early diagnosis of patients with COPD and timely take clinical intervention to reduce the incidence of COPD.

Arterial stiffness is a noninvasive examination commonly used in clinical prediction of carotid artery disease. Increased arterial stiffness is the early manifestation of arteriosclerosis, which can be effectively diagnosed by ultrasound. The measurement of arterial stiffness in high-risk groups of atherosclerosis can not only detect subclinical vascular structure changes in time but also guide clinical treatment. Previous studies have shown that arterial stiffness is associated with emphysema severity, cardiovascular disease risk, and severity and prognosis in patients with COPD[5,7,16-18]. In this study, we analyzed and compared the arterial stiffness in COPD patients and subjects without COPD by measuring PWV and ABI and detecting carotid artery disease with ultrasound. The results showed that the levels of RI and PI in the COPD group were lower than those in the control group ($p<0.05$); the IMT, total plaque area, and number of plaques in the COPD group were higher than those in the control group ($p<0.05$). The arterial stiffness and ABI level in the COPD group were higher than those in the control group ($p<0.05$), suggesting that the continuous development of COPD may lead to the increase in arterial stiffness and abnormal ultrasound examination.

At present, PWV is the main clinical method for arterial stiffness examination, with the advantages of simple operation, accurate results, and noninvasive, and is suitable for large-scale screening of asymptomatic population[19]. However, pulse wave propagation is affected by arterial stiffness. The greater the segmental arterial stiffness, the faster the PWV[20]. The detection of arterial stiffness is often affected by the nature and thickness of arterial wall. To reduce the influence of other related factors during the examination of arterial stiffness, we further analyzed the relationship between arterial stiffness and ultrasound results in patients with COPD. The results showed that arterial stiffness and ABI levels were negatively correlated with RI and PI levels ($p<0.05$) and positively correlated with IMT, total plaque area, and plaque number ($p<0.05$), suggesting that there was a correlation between arterial stiffness in patients with COPD and the results of ultrasound examination, which could be used as an auxiliary detection index of arterial stiffness.

Arterial stiffness has been increasingly recognized as a strong and independent predictor of cardiovascular events and all-cause mortality by a growing number of clinical and population-based studies[21,22]. Noninvasive arterial PWV, most commonly measured as carotid-femoral PWV (cfPMV), is a simple, robust, and reproducible parameter that is considered the "gold standard" for assessing arterial stiffness[23]. In practice, cfPWV can be calculated as the transit distance divided by the corresponding transit time, which can be reliably determined by Doppler ultrasound[24]. Arterial PWV measured with Doppler echocardiography has also been validated to have a fairly high correlation and agreement with invasive measurements[25]. Given its remarkable breadth, Doppler ultrasound has been recognized as a reliable method for noninvasive assessment of arterial stiffness.

The study has some limitations. First, this study is a single-center retrospective study, and the conclusions drawn need to be further confirmed by clinical studies with a larger sample size. Then, we did not collect all the information of the patients and could not conduct further logistic regression analysis due to the limitations of objective conditions. But we will discuss the problem in our follow-up research.

CONCLUSIONS

This study showed that arterial stiffness in patients with COPD was higher than that in people without COPD, and there is a correlation between arterial stiffness and ultrasonic index in COPD patients. Therefore, we speculated that ultrasonic index could be used as an auxiliary detection method for arterial stiffness to improve the accuracy of prediction of carotid artery lesions and better guide clinical treatment.

ETHICS APPROVAL AND INFORMED CONSENT

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Linxi Hospital of Kailuan General Hospital. Written informed consent was obtained from all participants.

AUTHORS' CONTRIBUTIONS

XHZ: Investigation and Methodology, Writing – original draft. **STZ:** Data curation. **QH:** Formal Analysis. **YQL:** Investigation and Methodology. **JNC:** Data curation. **PL:** Writing – review & editing.

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