MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2019; 25: 8482-8491
DOI: 10.12659/MSM.917075

Received: 2019.04.19
Accepted: 2019.07.02
Published: 2019.11.11

A Retrospective Case-Control Study on the Chest Wall and Lung Characteristics in Patients with Primary Spontaneous Pneumothorax

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

AE **Haibo Huang***
AE **Xiaonu Peng**
BC **Hongwei Zhang**
CD **Wenjun Li**
CDF **Chaoyang Wang**

Department of Thoracic Surgery, The Affiliated Yantai Yuhuangding Hospital of Qingdao University, Yantai, Shandong, P.R. China

* Haibo Huang and Xiaonu Peng contributed equally to this work

Corresponding Authors: Chaoyang Wang, e-mail: hongyi982713372@yeah.net and Wenjun Li, e-mail: liwenjun90808@163.com

Source of support: Wu Jieping Foundation Clinical Special Scientific Research Project (32027301901)

Background: Primary spontaneous pneumothorax (PSP) is reported to be more common in young men who are thin and tall. This retrospective study aimed to analyze the clinical and chest wall characteristics associated with PSP.

Material/Methods: Between January 2008 to December 2017, the clinical and imaging data of 99 patients at first presentation with PSP were compared with 82 age-matched healthy controls. Computed tomography (CT) imaging was used to measure the anteroposterior and transverse diameters of the chest at four levels, including the aortic arch, tracheal bifurcation, right inferior pulmonary vein, and lower sternal edge. Chest deformity was calculated as the ratio of the transverse diameter of the hemithorax divided by anteroposterior diameter. Lung volume and average lung density of 32 cases with PSP were measured and compared with 10 patients without PSP. Intrapleural pressure of 43 cases PSP who were treated with a closed chest drain was measured and compared with 39 patients with mediastinal tumor who underwent thoracoscopic surgery.

Results: Patients with PSP showed a normal age distribution with a median of 17–18 years. The patients with PSP had significantly reduced anteroposterior and transverse diameters of the chest when compared with controls at four levels on CT ($p<0.01$). The lung volumes in patients with PSP were significantly reduced when compared with the controls ($p<0.05$), as were the minimum intrapleural pressure and pressure difference ($p<0.05$).

Conclusions: The findings support that chest wall dimensions may be associated with lung development, which are contributing factors in PSP.

MeSH Keywords: **Human Characteristics • Pneumothorax • Thoracic Diseases**

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/917075

3382 8 4 30

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Background

Pneumothorax, or the presence of air in the pleural space, was a term first used by Itard in 1803, who believed that it was mainly caused by the tuberculosis of the lung apex [1]. In cases that were not associated with lung disease, the term simple pneumothorax was used [1]. In 1932, Kjaergard first defined primary spontaneous pneumothorax (PSP) [2].

PSP is most common in previously healthy male adolescents. In the US, the reported incidence in men is between 7.4–18 per 100,000 population per year, and is between 1.2–6 per 100,000 population per year in women [3]. Patients with PSP are usually previously healthy without underlying lung disease, but bullae, subpleural blebs, and apical emphysematous-like change (ELC) are common with a prevalence of 90% of cases that undergo surgery and are found in up to 80% of cases on computed tomography (CT) imaging of the chest [4,5]. Therefore, it has been assumed that the rupture of pleural bullae and subpleural blebs are the main causes of PSP. There have been several hypotheses regarding the mechanism of their formation, including distal airway obstruction and inflammation caused by smoking [6–11], pleural porosity [6,12,13], deficiency in lung elastic fibers [14], ischemia of the lung apex [15,16], and increased negative intrapleural pressure [17]. However, these hypotheses can only partly explain the characteristics of patients with PSP who present clinically.

Currently, no hypothesis can fully explain the mechanism and pathogenesis of PSP, but there are several common characteristics. The epidemiology of PSP has shown that it mainly occurs in male patients aged between 14–25 years, and is rarely found after the age of 30 years and has been rarely reported after the age of 40 years [18]. A reduced anteroposterior diameter of the chest wall and the ectomorphic habitus is common in patients with PSP [18]. Surgery for PSP includes bullectomy, which can have a high recurrence rate [19,20]. However, bullectomy combined with pleurodesis can significantly reduce the recurrence rate of PSP, but a residual apical space is usually found on chest X-ray after bullectomy [19,20]. Several previous studies have shown that episodes of PSP could be associated with changes in atmospheric pressure and even with loud music [19,20].

Therefore, this retrospective study aimed to analyze the clinical and chest wall characteristics associated with PSP and compared healthy controls and patients with thoracic disease.

Material and Methods

Selection of patients and controls

Approval for this study was obtained from the Ethics Committee of Yuhuangding Hospital, Qingdao University. Retrospective data from the medical records of patients with PSP and controls were recorded from January 2008 to December 2017. There were complete records for 652 cases that met the study inclusion criteria, and included 138 cases that were first presentation of PSP and 514 cases that were cases of recurrent PSP. The control group included 82 healthy individuals aged between 15–31 years that included 53 men and 29 women, who had undergone chest imaging, including chest computed tomography (CT) for complaints of chest pain or other symptoms but did not have a diagnosis of pneumothorax.

In patients who had a first presentation with PSP, there were five cases treated by simple observation, 13 cases were treated with thoracentesis, 139 cases were treated with closed chest drainage, and 495 cases were treated with thoracoscopic surgery. The retrospective review identified 107 cases with a smoking history and 545 cases who were non-smokers, 350 cases were diagnosed as left-sided pneumothorax, 271 cases were right-sided pneumothorax, and 31 cases had bilateral pneumothorax.

In patients with recurrent PSP, 119 cases were treated by simple observation, 103 cases were treated by thoracentesis, and 292 cases were treated with closed chest drainage. There were no cases of recurrence after thoracoscopic surgery or pleurodesis.

There were 99 cases with a first presentation with PSP that underwent chest CT examination following chest drainage, which confirmed no air leak and full lung expansion seen on chest X-ray. Chest deformity was calculated as the ratio of the transverse diameter of the hemithorax divided by the anteroposterior diameter.

In the 99 cases of PSP, 32 cases underwent three-dimensional chest CT, which was used for further reconstruction and used to analyze lung volume and average lung density. There were 10 cases with hyperhidrosis that had undergone a three-dimensional chest CT from January 2008 to December 2017 in our department, who were aged between 16–30 years, including four men and six women. These patients were included as a control group for the analysis of lung volume and average lung density.

From January 2017, the Thopaz Digital chest drainage system (Medela AG, Baar, Zug, Switzerland) was used in our department. We collected the data of intrapleural pressures, which were stored in the digital system. There were 43 cases of PSP who were treated with closed chest drainage after the first presentation and 39 cases of mediastinum tumor who were

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

treated with thoracoscopic surgery were enrolled in this study. The age of the patients with mediastinal tumor was from 16–31 years. The gender distribution was 21 men and 18 women.

Analysis of physical characteristics

There were 652 cases that underwent an analysis of the physical characteristics. The height and bodyweight of all patients were measured. The body mass index (BMI) was calculated as bodyweight (kg) divided by the square of the height (m^2). Because it was difficult to obtain the height and bodyweight data of large numbers of normal healthy people, we used data from previous studies on the physical development of adolescents aged 16–18 years in our city [21,22]. Therefore, in this study, we compared the height, bodyweight, and BMI of patients from 16–18 years with the control.

Comparison of the anteroposterior diameter of the chest wall, or chest flattening

The method previously reported by Murakawa et al. [18] was used to calculate chest deformity as the ratio of the transverse diameter of the hemithorax divided by the anteroposterior diameter of the same hemithorax. The transverse diameter and anteroposterior diameter were both obtained by measurement of the CT image using the Picture Archiving and Communications System (PACS) software (GE Healthcare Life Sciences, Logan, UT, USA). The anteroposterior and transverse diameters of the hemithorax on both sides were measured at the predetermined levels of the aortic arch, tracheal bifurcation, right inferior pulmonary vein, and lower edge of the sternum on chest CT. In measuring transverse diameter, we used the longest distance from the center of the vertebra to the chest wall. In measuring anteroposterior diameter, we used the longest distance from the anterior chest wall to the posterior chest wall. The comparison of chest flattening was performed on the same level and same side.

To avoid the influence of other deformities of the chest wall, patients with the appearance of funnel chest, pigeon chest, and a history of severe rib fracture were excluded from this study. To avoid the influence of tension of pneumothorax on the morphometric measurements of the chest wall, all the measurements were conducted after closed chest drainage. All scans were performed using a same single spiral 64-slice CT scanner system, the Sensation 64 (Siemens Medical Solutions, Forcheim, Germany), with settings of 120 kVp and mAs based on body size with a rotation time of 0.5 sec. The methods used are shown in Figure 1.

Measurement of lung volume and average lung density

Measurement of lung volume and average lung density were performed using Philips IntelliSpace Portal PACS software (Philips Healthcare, Andover, MA, USA), according to a previously reported method [23]. Three-dimensional reconstruction was performed using this software to determine the lung volume and average lung density when compared with air. As shown in Figure 2, the average and standard error of the mean of the volume and average density were used for further analysis.

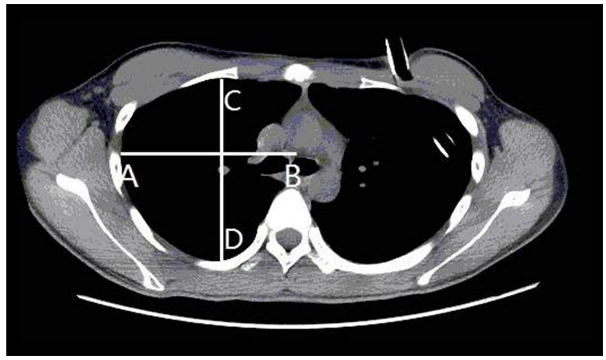

Figure 1. Computed tomography (CT) imaging of the chest wall shows the method of calculation of chest deformity in cases of primary spontaneous pneumothorax (PSP) and controls. Computed tomography (CT) imaging was used to measure the transverse diameter (AB) and anteroposterior diameter (CD) of the chest. Chest deformity was calculated as the ratio of the transverse diameter of the hemithorax divided by anteroposterior diameter (AB/CD). This figure shows the measurements at the level of the tracheal bifurcation.

Figure 2. The method of measurement of lung volume and average lung density in cases of primary spontaneous pneumothorax (PSP) and controls. The arrow shows the results of the lung volume and average lung density, which were automatically calculated using the imaging software.

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 1. Comparison of body physique between patients with primary spontaneous pneumothorax (PSP) who initially presented between 16–18 years with the normal healthy controls between 16–18 years (* P<0.05).

Age	Variables	First episode of PSP	Healthy control	P-value
16 (M)	Height (m)	1.73±0.18	1.72±0.06	0.15
	Weight (Kg)	58.87±11.12	63.93±10.56	0.06
	BMI (Kg/m^2)	19.67±1.51	21.61±1.23	0.04*
17 (M)	Height (m)	1.74±0.23	1.72±0.05	0.09
	Weight (Kg)	59.28±12.03	63.96±10.42	0.13
	BMI (Kg/m^2)	19.58±0.99	21.62±1.18	0.04*
18 (M)	Height (m)	1.73±0.19	1.71±0.06	0.34
	Weight (Kg)	59.73±11.91	62.06±10.34	0.28
	BMI (Kg/m^2)	19.46±1.23	21.22±1.12	0.05*
16 (F)	Height (m)	1.64±0.04	1.61±0.05	0.09
	Weight (Kg)	50.76±8.01	53.18±7.31	0.17
	BMI (Kg/m^2)	18.87±1.20	20.52±0.96	0.03*
17 (F)	Height (m)	1.65±0.01	1.59±0.05	0.06
	Weight (Kg)	51.06±6.82	51.79±7.50	0.48
	BMI (Kg/m^2)	18.75±1.15	20.49±1.37	0.02*
18 (F)	Height (m)	1.65±0.13	1.60±0.05	0.07
	Weight (Kg)	51.34±7.49	52.30±7.2	0.27
	BMI (Kg/m^2)	18.86±1.23	20.43±1.83	0.03*

BMI – body mass index.

Measurement of intrapleural pressure

Measurement of the intrapleural pressure was performed as previously described [24], using the Thopaz Digital Chest Drainage System (Medela Healthcare, Manchester, UK). The data stored on the intrapleural pressure were downloaded and analyzed using Thopaz computer software (Medela Healthcare, Manchester, UK). To avoid the possible adhesion caused by longer drainage, the data were obtained on the first day after the chest drain was sited. When the chest drain was sited, no air leakage was present for more than 3 hours, and full lung expansion was confirmed by chest X-ray. The digital system used allowed for continuous multiple measurements every 2 minutes during airflow, measuring maximum and minimum intrapleural pressures using microelectronic mechanical sensor technology. The average of the minimum and maximum intrapleural pressure and the pressure difference were analyzed. All patients had a single chest tube, and the tubes were made from the same material and were the same size. All chest drain tubes were sited in the seventh intercostal space in the mid-axillary line.

To exclude the influence of depth of breathing on the measurements, body temperature, heart rate, respiratory rate, and numerical rating scale [25] of the two groups were also recorded and compared. A nurse from our department recorded all the measurements and clinical data from the medical records. During the measurements, the nurses and the patients were unaware of the assignment of the study groups.

Statistical analysis

Data were analyzed using SPSS version 19.0 software (IBM SPSS Inc., Armonk, NY, USA). All data were expressed as the mean ± standard error from the mean (SEM). Because that measurements of the lung density and intrapleural pressure were both negative, their absolute values were used for the statistical analysis. Comparison of the numerical data between the groups was analyzed using a t-test, and comparison of categorical data between groups was analyzed using the chi-squared (χ^2) test or Fisher's exact test, when the number of cases was less than five. A P-value <0.05 was considered to be statistically significant.

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

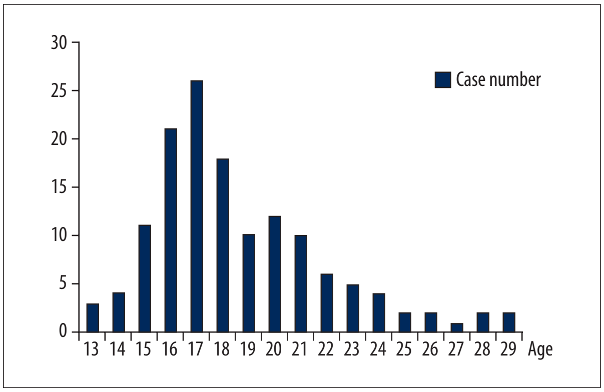

Figure 3. The age distribution of cases of primary spontaneous pneumothorax (PSP) on initial presentation.

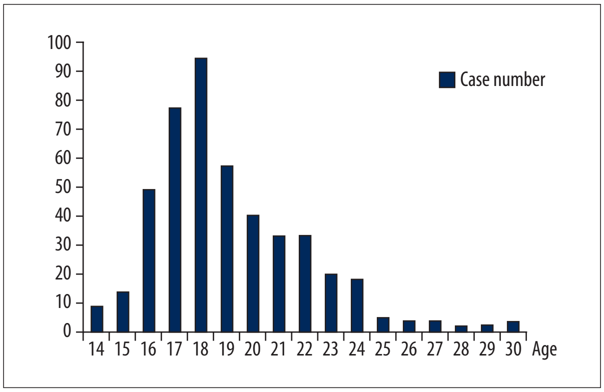

Figure 4. The age distribution of recurrent primary spontaneous pneumothorax (PSP).

Table 2. Comparison of body physique between the patients with recurrent primary spontaneous pneumothorax (PSP) aged between 16–18 years with the normal healthy controls aged 16–18 years.

Age	Variables	First episode of PSP	Healthy control	P-value
16 (M)	Height (m)	1.74±0.05	1.72±0.06	0.13
	Weight (Kg)	58.12±10.45	63.93±10.56	0.25
	BMI (Kg/m^2)	19.19±1.71	21.61±1.23	0.03*
17 (F)	Height (m)	1.74±0.56	1.72±0.05	0.08
	Weight (Kg)	59.13±11.27	63.96±10.42	0.12
	BMI (Kg/m^2)	19.53±0.71	21.62±1.18	0.04*
18 (M)	Height (m)	1.74±0.08	1.71±0.06	0.17
	Weight (Kg)	59.69±10.93	62.06±10.34	0.21
	BMI (Kg/m^2)	19.72±1.03	21.22±1.12	0.04*
16 (F)	Height (m)	1.64±0.06	1.61±0.05	0.07
	Weight (Kg)	50.17±10.23	53.18±7.31	0.11
	BMI (Kg/m^2)	18.65±0.83	20.52±0.96	0.03*
17 (F)	Height (m)	1.65±0.03	1.59±0.05	0.05*
	Weight (Kg)	51.11±5.98	51.79±7.50	0.39
	BMI (Kg/m^2)	18.77±1.15	20.49±1.37	0.03*
18 (F)	Height (m)	1.65±0.27	1.60±0.05	0.06
	Weight (Kg)	51.91±9.37	52.30±7.2	0.36
	BMI (Kg/m^2)	19.07±1.04	20.43±1.83	0.05*

BMI – body mass index.

Results

Physical characteristics of patients at first presentation with primary spontaneous pneumothorax (PSP)

Among 138 cases with the first presentation of PSP, there were 125 men and 13 women, 64 cases of left-sided pneumothorax, 68 cases of right-sided pneumothorax, and six cases of bilateral pneumothorax (Table 1). The age range was 13–30 years, and the age distribution was shown in Figure 3. There was a normal age distribution with a peak incidence at 17 years. Comparison of the body physique between patients with a first episode of PSP aged 16–18 years with the normal healthy controls from 16–18 years, the height of the patients with PSP was greater than the controls, but this difference did not reach statistical significance. The bodyweight of the patients with PSP was lower than the controls, but this difference did not reach statistical significance. The body mass index (BMI)

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 3. The common characteristics of the 99 cases of primary spontaneous pneumothorax (PSP) who were treated with chest drainage on initial presentation and 82 healthy adolescents.

	PSP	Control	P-value
Case number	99	82	
Age	17.25±4.58	18.61±5.16	0.06
Gender			0.07
Male	76	53	
Female	23	29	
Height (m)	1.75±0.16	1.73±0.19	0.44
Weight (Kg)	54.67±12.68	58.91±17.27	0.06
Smoking history			0.08
Yes	13	19	
No	86	63	

of the patients with PSP was significantly lower than the controls ($p<0.05$). The results were showed in Table 1.

Physical characteristics of patients with recurrent PSP

Among 514 cases of recurrence PSP, there were 462 men and 52 women, 286 cases of left-sided pneumothorax, 203 cases of right-sided pneumothorax, and 25 cases of bilateral pneumothorax (Table 2). The age range was 14–38 years and the age distribution was showed in Figure 4. There was a normal age distribution and the peak incidence was at 18 years. Comparison of the body physique between the patients with recurrent PSP aged16–18 years with the normal healthy controls aged 16–18 years, the height of patients with recurrent PSP was greater than the controls, but this difference did not reach statistical significance. The bodyweight of patients with recurrent PSP was lower than the controls but did not reach statistical significance. The BMI of patients with recurrent PSP was significantly lower than the controls ($p<0.05$). The results were shown in Table 2.

Measurement of chest flatness, or reduced anteroposterior diameter

Table 3 showed the common characteristics between the 99 cases with the first presentation of PSP that underwent treatment with a chest drain and 82 healthy adolescents. There was no significant difference in age, gender, height, bodyweight, and smoking history between the two groups. Reduced anteroposterior diameter, or flattening, of the left side and right side of the chest, at the level of the aortic arch level, the tracheal bifurcation, the right inferior pulmonary vein, and the level of the lower sternal edge were compared (Table 4). Both left-sided and right-sided flattening of the chest in patients with PSP was significantly greater than that of the controls ($p<0.01$).

Measurement of lung volume and average lung density

As shown in Table 5, the patient characteristics, including age, height, weight, and smoking habit, showed no significant difference between 32 cases with PSP and the 10 control cases with hyperhidrosis. Lung volume of men was greater than that of women. The two groups were divided into two, according to gender (Table 6). The lung volume in both male and female patients with PSP was significantly less than for controls ($p<0.05$). There was no significant difference in the average lung density between patients with PSP and the controls or between men and women.

Measurement of intrapleural pressure

Table 7 showed that the body temperature, heart rate, respiratory rate, and numerical rating scale (NRS) were not significantly different between the 43 cases of PSP who were treated with closed chest drainage after initial presentation, and the 39 patients who had a mediastinal tumor who were treated thoracoscopic surgery (Table 8). The patients were subdivided by gender (Table 8). The minimum intrapleural pressure and the pressure difference between patients with PSP and the controls were significantly different ($p<0.05$). However, the maximum intrapleural pressure and the pressure difference between patients with PSP and the controls were not significantly different.

Discussion

The mechanism and pathogenesis of primary spontaneous pneumothorax (PSP) remain unclear, but inflammation caused by smoking that obstructs the distal airway has been proposed [6–11,26]. However, this hypothesis cannot explain the

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 4. The results of chest measurements in 99 cases at first presentation with primary spontaneous pneumothorax (PSP) treated with chest drainage chest drainage and 82 healthy adolescent controls (* P<0.05).

	PSP (left)	Control (left)	P-value
Case number	99	82	
Aortic arch level	1.059±0.021	1.090±0.024	0.0000*
Tracheal bifurcation level	1.148±0.023	1.171±0.019	0.0000*
Right inferior pulmonary vein level	1.268±0.013	1.273±0.011	0.006*
Lower sternal edge level	1.169±0.019	1.178±0.018	0.001*
	PSP (right)	**Control (right)**	**P-value**
Case number	99	82	
Aortic arch level	1.068±0.022	1.082±0.023	0.0000*
Tracheal bifurcation level	1.152±0.023	1.162±0.027	0.007*
Right inferior pulmonary vein level	1.277±0.015	1.285±0.017	0.0009*
Lower sternal edge level	1.172±0.023	1.183±0.025	0.002*

Table 5. The characteristics in 32 patients with primary spontaneous pneumothorax (PSP) and 10 control cases with lung volume and average lung density measurements (* P<0.05).

	PSP	Control	P value
Case number	32	10	
Age	17.51±4.62	19.09±4.73	0.35
Gender			0.002
Male	28	4	
Female	4	6	
Height (m)	1.74±0.28	1.72±0.17	0.83
Weight (Kg)	53.91±11.73	61.27±16.54	0.13
Smoking history			0.18
Yes	5	4	
No	27	6	

Table 6. The results of lung volume and average lung density measurement in 32 cases with primary spontaneous pneumothorax (PSP) and 10 controls (* P<0.05).

	PSP (male)	Control (male)	P-value
Case number	28	4	
Lung volume (mL)	4813±905	5942±1601	0.04*
Average lung density (HU)	836±58	807±61	0.35
	PSP (female)	**Control (female)**	**P-value**
Case number	4	6	
Lung volume (mL)	3318±965	4689±826	0.04*
Average lung density (HU)	849±63	817±59	0.43

HU – Hounsfield unit.

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 7. The common characteristics and body habitus at the time of measurement between 43 cases of primary spontaneous pneumothorax (PSP) treated with closed chest drainage after initial presentation and 39 patients with mediastinum tumor treated with thoracoscopic surgery (* P<0.05).

	PSP	Control	P-value
Case number	43	39	
Age	17.12±4.23	19.09.5±5.17	0.06
Gender			
Male	39	21	
Female	4	18	
Height (m)	1.73±0.17	1.70±0.14	0.39
Weight (Kg)	53.17±14.09	59.13±15.28	0.06
Smoking history			0.75
Yes	5	6	
No	38	33	
Heart rate	89.23±15.49	90.38±14.26	0.72
Body temperature	36.8±0.43	36.6±0.57	0.08
Respiratory rate	16.06±1.69	15.43±1.43	0.07
NRS			0.72
0–3	38	36	
4–6	5	3	
7–10	0	0	

NRS – Numerical rating scale.

Table 8. The results of intrapleural pressure measurement between 43 cases of primary spontaneous pneumothorax (PSP) treated with closed chest drainage on first presentation and 39 cases of mediastinum tumor who were treated with thoracoscopic surgery (* P<0.05).

	PSP (Male)	Control (Male)	P-value
Case number	39	21	
Minimum absolute value (cmH_2O)	16.23±3.71	13.53±3.56	0.008*
Maximum absolute value (cmH_2O)	5.59±0.46	5.38±0.52	0.11
Pressure difference (cmH_2O)	10.02±1.74	8.91±1.92	0.03*
	PSP (Female)	**Control (Female)**	**P value**
Case number	4	18	
Minimum absolute value (cmH_2O)	14.96±3.01	9.87±3.09	0.03*
Maximum absolute value (cmH_2O)	5.76±0.35	5.27±0.41	0.08
Pressure difference (cmH_2O)	9.13±0.97	5.26±1.08	0.0004*

pathogenesis of PSP in patients who have never smoked or without bullae. It is difficult to explain why bullae, subpleural blebs, and apical emphysematous-like change (ELC) are usually found in the lung apex and why there is a high recurrence rate after bullectomy. In the present study, nearly 80% of patients with PSP were 16–25 years old, and were mainly high school or college students, and only 5% were smokers.

The hypothesis of pleural porosity proposes that PSP is a disease that is associated with diffuse pathological changes of the

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

pleura [6,12,13]. The mechanism of pleural porosity is unclear, and this hypothesis is only applicable to cases of PSP without bullae or blebs and is unsupported by the pathological findings in cases of PSP, and is not widely accepted. The hypothesis of deficiency in lung elastic fibers in PSP supports that this should be regarded as a congenital disease with proteinase deficiency or as a type of connective tissue disease [14]. Lack of elastic fibers in the lung may result in enlargement of the alveolar spaces and the formation of bullae or blebs [14]. The hypothesis of apex ischemia as a cause of PSP includes a decreased blood supply to the lung apex due to the effects of gravity and the formation of pleural bullae or blebs that result in pneumothorax [15,16].

Previously published studies have shown that some cases of PSP are familial [27]. Studies that have used gene assays based on polymerase chain reaction (PCR) and breakpoint analysis have shown that the germline mutations rate of the FLCN gene was increased in patients with familial primary spontaneous pneumothorax (FPSP) [27]. However, patients with FPSP form only a small part of the population with PSP, and most have no family history of the condition. In this study, we found that the age distribution of patients with a first presentation of with recurrence of PSP showed a normal age distribution with a peak age of 17–18 years, which is an important time during adolescent development. This finding supported the view that the increased incidence of PSP was associated with the adolescent growth phase and the associated changes in body development.

Another hypothesis for the pathogenesis of PSP is that a tall and thin, or ectomorphic physiognomy, is associated with increased negative intrapleural pressures, resulting in bullae and blebs [17]. The findings of the present study showed that the bodyweight of patients with PSP was lower than the normal healthy control and their height was higher than the normal healthy controls, but the differences did not reach statistical significance. However, the body mass index (BMI) of patients with PSP was significantly lower than the normal healthy controls. These findings are consistent with those from previous studies, which supports the role of physical development during late adolescence and the imbalance in growth in the development of PSP. However, in the study by Fujino et al., they compared body development in terms of bodyweight and height, but did not compare lung development of patients with PSP [28]. According to the lung development theory, only approximately 15% of alveoli are formed before birth, and lung growth depends on the growth of the ribcage [28]. Therefore, during respiration in patients with a normal habitus, the intrathoracic pressure is always negative.

Because it is difficult to evaluate and compare lung development directly, we studied this indirectly by comparison of the lung volume and average lung density using three-dimensional chest computed tomography (CT) imaging. Before chest CT imaging, patients usually need to take and hold a deep breath. Therefore, the results of lung volume and average lung density measurement will be influenced by the volume of the breath. The lung volume is directly proportional to the volume of a deep breath, whereas the average lung density is inversely proportional to the air volume of a deep breath. In the present study, we found that the lung volume in patients with PSP was significantly lower than in the controls, but the average lung density between patients with PSP and the controls showed no significant difference.

Previous studies have reported a role for intrapleural negative pressure in the pathogenesis of PSP, but previous studies have not measured and compared the intrapleural pressure between patients with PSP and normal controls. Because it is difficult to measure intrapleural pressure during the respiration cycle by non-invasive methods, we measured the intrapleural pressure using the closed chest drainage system. The results showed that the minimum intrapleural pressure and the pressure difference in patients with PSP were significantly different when compared with the controls, which supported the hypothesis of Fujino et al. [28].

Following surgery for PSP, if there is no air leak from the chest drain tube, a chest X-ray for commonly shows residual space in the apical thoracic cavity, which has been a common reason for partial apical lung resection [29]. However, in surgical procedures that include partial lung resection or lobectomy, in which the volume of lung resection is much larger, there is not usually a residual space of the apical thoracic cavity. From the findings of the present study, delayed lung development may explain the presence of overexpansion of the lung after partial resection of the lung apex. A further study has shown that negative intrathoracic pressure during surgery can lead to expansion of blebs and bullae [30].

This study had several limitations. First, this study was conducted in a single center, which may have resulted in selection bias of the patients and controls. Also, invasive methods of measurement, including the measurement of the intrapleural pressure, could not be performed in the healthy control group. This study was retrospective and relied on the quality and availability of data in the patient medical records, and future prospective randomized controlled studies are needed. The mechanism and pathogenesis of PSP appear to be complex, and following this preliminary study, further studies are needed to investigate the underlying factors that lead to PSP.

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Conclusions

This retrospective study aimed to analyze the clinical and chest wall characteristics associated with primary spontaneous pneumothorax (PSP). The findings supported that the pathogenesis of PSP was associated with an imbalance between height and lung development, and was associated with a reduced lung volume and body mass index (BMI), and increased chest flattening or reduced anteroposterior diameter, resulting in increased negative intrapleural pressure, especially in the apical thoracic cavity. Increased intrapleural pressure plays an important role in the formation of bullae, subpleural blebs, and apical emphysematous-like change (ELC).

Conflict of interest

None.

References:

1. Laennec RTH: Trait de l'auscultation mediate et des maladies des poumons et du coeur. Tome Second. Paris, 1819 [in French]
2. Kjaergard H: Spontaneous pneumothorax in the apparently healthy. Acta Med Scand (Suppl.), 1932; 43: 1–159
3. Melton LJ, Hepper NGG, Offord KP: Incidence of spontaneous pneumothorax in Olmsted County, Minnesota: 1050–74. Am Rev Respir Dis, 1979; 120: 1379–82
4. Donahue DM, Wright CD, Viale G et al: Resection of pulmonary blebs and pleurodesis for spontaneous pneumothorax. Chest, 1993; 104: 1767–69
5. Lesur O, Delorme N, Frogamet JM et al: Computed tomography in the aetiological assessment of idiopathic spontaneous pneumothorax. Chest, 1990; 98: 341–47
6. Ohata M, Suzuki H: Pathogenesis of spontaneous pneumothorax. With special reference to the ultratsructure of emphysematous bullae. Chest, 1980; 77: 771–76
7. Hatz RA, Kaps MF, Meimerakis G et al: Long-term results after video-assisted thoracoscopic surgery for first-time and recurrent spontaneous pneumothorax. Ann Thorac Surg, 2000; 70: 253–57
8. Korner H, Andersen KS, Stangeland L et al: Surgical treatment of spontaneous pneumothorax by wedge resection without pleurodesis or pleurectomy. Eur J Cardiothorac Surg, 1996; 10: 656–59
9. Loubani M, Lynch V: Video-assisted thoracoscopic bullectomy and acromycin pleurodesis: An effective treatment for spontaneous pneumothorax. Respir Med, 2000; 94: 888–90
10. Horio H, Nomori H, Kobayashi R et al: Impact of additional pleurodesis in video-assisted thoracoscopic bullectomy for primary spontaneous pneumothorax. Surg Endosc, 2002; 16: 630–34
11. Schramel F, Meyer CJ, Postmus PE: Inflammation as a cause of spontaneous pneumothorax and emphysema-like changes: Results of bronchoalveolar lavage. Eur Respir J, 1995; 8(Suppl. 19): 397S
12. Radomsky J, Becker HP, Hartel W: [Pleural porosity in idiopathic spontaneous pneumothorax.] Pneumologie, 1989; 43: 250–53 [in German]
13. Masshof W, Hofer W: [Pathology of so-called idiopathic spontaneous pneumothorax.] Dtsch Med Wochenschr, 1973; 98: 801–5 [in German]
14. Morrison PJ, Lowry RC, Nevin NC: Familial primary spontaneous pneumothorax consistent with true autosomal dominant inheritance. Thorax, 1998; 53: 151–52
15. Withers JN, Fishback ME, Kiehl PV et al: Spontaneous pneumothorax. Suggested etiology and comparison of treatment methods. Am J Surg, 1964; 108: 772–76
16. Kawajami Y, Irie T, Kawashima K: Stature, lung height, and spontaneous pneumothorax. Respiration, 1982; 43: 35–40
17. Fujino S, Inoue S, Tezuka N et al: Physical development of surgically treated patients with primary spontaneous pneumothorax. Chest, 1999; 116: 899–902
18. Saita K, Murakawa T, Kawano H et al: Chest wall deformity found in patients with primary spontaneous pneumothorax. Asian Cardiovasc Thorac Ann, 2013; 21(5): 582–87
19. Bulajich B, Subotich D, Mandarich D et al: Influence of atmospheric pressure, outdoor temperature, and weather phases on the onset of spontaneous pneumothorax. Ann Epidemiol, 2005; 15(3): 185–90
20. Noppen M, Verbanck S, Harvey J et al: Music: A new cause of primary spontaneous pneumothorax. Thorax, 2004; 59(8): 722–24
21. Sun M, Cong M, Lin D et al: [The comparison and analysis of body development in YanTai city adolescence.] Maternal and Children Health Care of China, 2007; 22(22): 3105–6 [in Chinese]
22. Wang Z, Guo Y, Qi C et al: [The trend analysis of the body mass index of the adolescence in YanTai city from 1985 to 2010.] Chinese Journal of School Health, 2014; 35(4): 607–10 [in Chinese]
23. Yamashiro T, Matsuoka S, Bartholmai BJ et al: Collapsibility of lung volume by paired inspiratory and expiratory CT scans: Correlations with lung function and mean lung density. Acad Radiol, 2010; 17(4): 489–95
24. Refai M, Brunelli A, Varela G et al: The values of intrapleural pressure before the removal of chest tube in non-complicated pulmonary lobectomies. Eur J Cardiothorac Surg, 2012; 41(4): 831–33
25. Downie WW, Leatham PA, Rhind VM et al: Studies with pain rating scales. Ann Rheum Dis, 1978; 37(4): 378–81
26. Cottin V, Streichenberger N, Gamondès JP et al: Respiratory bronchiolitis in smokers with spontaneous pneumothorax. Eur Respir J, 1998; 12(3): 702–4
27. Ding Y, Zhu C, Zou W et al: FLCN intragenic deletions in Chinese familial primary spontaneous pneumothorax. Am J Med Genet A, 2015; 167(5): 1125–33
28. ad hoc Statement Committee, American Thoracic Society: Mechanisms and limits of induced postnatal lung growth. Am J Respir Crit Care Med, 2004; 170(3): 319–43
29. Gaunt A, Martin-Ucar AE, Beggs L et al: Residual apical space following surgery for pneumothorax increases the risk of recurrence. Eur J Cardiothorac Surg, 2008; 34(1): 169–73
30. Kawachi R, Takei H, Koshi-Ishi Y, Goya T: Novel method for bulla detection with video-assisted thoracoscopic surgery in patients with spontaneous pneumothorax. Eur J Cardiothorac Surg, 2008; 34: 212–13

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]