



Fate of spontaneous pneumothorax from middle to old age: how to overcome an irritating recurrence?

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Background: The causes and treatment of pneumothorax in older patients are different from those in younger patients. However, studies on this topic are limited thus; pneumothorax in older patients is often inadequately managed. The purpose of this research was to investigate the characteristics of pneumothorax in patients over 45 years old, understand patterns of management and factors of recurrence, and propose reasonable guidelines for the treatment of older patients.

Methods: Of 438 consecutive patients with spontaneous pneumothorax between 2013 and 2017, 120 patients were enrolled and divided into two groups: (I) 45–64 years and (II) ≥ 65 years. Basic demographics, treatment modality, and patterns of surgery/recurrence were described. Clinical variables were compared between groups, and risk factors of recurrence were analyzed using logistic regression.

Results: The study population was divided into group A (younger, $n=61$) and B (older, $n=59$). Chest tube drainage was the most common procedure for both groups and chemical pleurodesis was applied more often in B (27% vs. 11%, $P=0.03$). The length of hospital stay was longer in B (8.8 vs. 5.9 days, $P<0.01$) but complications and recurrence rate did not differ between groups ($P=0.09$ and 0.93). The choice of procedures in recurrent pneumothorax was different ($P=0.02$). Specifically, invasive procedures such as surgery occurred more often in A, but non-invasive procedures occurred more often in B. Multivariate analysis revealed that bullae/blebs (odds ratio=5.57) and emphysema (odds ratio=3.83) showed a positive association with recurrence whereas surgery (odds ratio=0.11) was negative.

Conclusions: Radiological findings of emphysema or bullae/blebs are risk factors for recurrence of pneumothorax in elderly patients. Surgery in selected patients is an effective method for decreasing the recurrence rate.

Keywords: Pneumothorax; the elderly; surgery; recurrence

Submitted Apr 26, 2019. Accepted for publication Sep 27, 2019.

doi: 10.21037/jtd.2019.10.30

View this article at: <http://dx.doi.org/10.21037/jtd.2019.10.30>

Introduction

Pneumothorax is a benign disease, but sometimes intractable and irritating due to frequent recurrence (1,2). Previous studies for risk factors of recurrence have focused on younger patients, usually under 45 years old (3,4). However, the age distribution of pneumothorax shows a double peak: one in younger patients and the other in the elderly group (5). The typical pneumothorax of the former peak is a primary spontaneous pneumothorax (PSP), whereas that of the latter is a usually secondary spontaneous pneumothorax (SSP) related to pulmonary disease (6). Since the causes of pneumothorax are different between the two groups, the causes of recurrence are thought to be different as well. However, there are limited studies relating to the cause of recurrence in elderly patients.

Moreover, the management of pneumothorax in older patients is not easy. In contrast, the treatment pathway of younger patients is simple. Oxygen therapy or chest tube drainage can be performed on a case-by-case basis, and surgery can be applied on recurrence. However, it is difficult to apply the same principles to older patients. In this group, cardiopulmonary function is sometimes compromised and there may be many obstacles related to treatment and surgery, in particular (7). Therefore, bedside management, such as chemical pleurodesis, is often chosen as a primary treatment for them but its superiority is not clear (8). Although guidelines have been established, the evidence is still insufficient and the treatment modality is often chosen on the basis of the clinician's own experience.

The purpose of this study was to investigate the characteristics of pneumothorax in elderly patients, find patterns of management and risk factors for recurrence, and propose reasonable treatment guidelines for older patients.

Methods

Study design and population

This is a retrospective study using the medical records of 120 patients who had undergone pneumothorax management between March 2013 and February 2017 at a university-based tertiary hospital in Cheongju, South Korea. The follow-up period lasted until June 2018. Patient eligibility criteria included the following: spontaneous pneumothorax patients over 45 years of age, diagnosed by thoracic surgery specialists (D Kim, SW Kim, JM Hong), whose pneumothorax was managed under the same policy. The exclusion criteria were as follows: (I) patients with

traumatic or iatrogenic pneumothorax; (II) patients with spontaneous pneumothorax who were under 45 years old; (III) patients who were admitted to the intensive care unit or had fatal diseases, such as lung malignancy or necrotizing pneumonia, which may have confounded clinical outcomes. The study group was divided into two groups: group A (45–64 years old) and group B (≥ 65 years old). As PSP in patients under 45 years old may involve a different disease entity than pneumothorax in older patients, these younger patients were excluded from the study. Therefore, patients aged 45–64 years were operationally defined as the younger group (group A) and those aged over 64 years were the older group (group B).

Variables and primary outcomes

Demographic information, including gender, age, and medical history, particularly of pneumothorax and its management, were investigated. Radiological findings were summarized from the official report of the chest computed tomography (CT) made by radiology specialists. If there was no official CT report, we omitted the patient's results, rather than obtain a *de novo* reading of the CT, in order to minimize selection bias. Clinical outcomes were: patient's hospital stay (duration from the time of admission to discharge), complications (from the day of admission to a month after discharge), and recurrence of pneumothorax (considered the primary outcome; defined as the re-development of pneumothorax that was the primary cause of re-admission and subsequently requiring management). All data were collected and compared between the two groups. This study was reviewed and approved by the Institutional Review Board (IRB) of Chungbuk National University Hospital (2018-04-005).

Management of pneumothorax

All patients were diagnosed by thoracic surgery specialists. If the pneumothorax space was minimal (less than 5% of the total hemi-thorax area), then close observation and oxygen therapy via nasal cannula were applied; alternatively, a chest tube was inserted. A 12-French chest tube was usually selected, but a larger tube (24- or 28-French) was chosen when chemical pleurodesis seemed to be required to stop the air leak. If chest CT was not performed around the pneumothorax event, CT was checked before discharge. The patients were usually discharged 1 day after removal of the chest tube because pneumothorax sometimes re-

develops soon after the removal of the chest tube. However, additional management strategies were considered in the following situations: (I) prolonged air leakage lasting more than 3 days; (II) a second pneumothorax occurrence during admission; and (III) large or multiple bullae discovered by radiological study. Subsequent management included wedge resection of the lung parenchyma or chemical pleurodesis. All procedures were chosen with the consideration of the patient's cardiopulmonary reservoir and medical problems.

Wedge resection or chemical pleurodesis

The indication of surgery or wedge resection were as follows; ECOG 0-2 and (I) continuous air leakage (>3 days) or recurrent pneumothorax, (II) total collapse of the lung, (III) frequently recurred pneumothorax despite of chemical pleurodesis. Although they showed ECOG 3, we tried surgery in the absence of other treatment options. Chemical pleurodesis or chest tube drainage were used in a patient who refused surgery. Not all bullous or emphysematous lesions were removed but we inspected the lung under the water to decide the air leakage site, which should be cut. Even when prominent bullae were not found on chest CT, exploration of the pleura was carried out, and apical regions of the parenchyma were resected. Video-assisted thoracic surgery (VATS) was preferred over thoracotomy. The 5th and 7th intercostal spaces were usually chosen for VATS, but only the 7th was selected in uniport VATS surgery. Then, the target lung parenchyma was resected with one or two mechanical staplers. All stapled regions were covered with polyglycolic acid (PGA) felt (Neoveil, Gunze Ltd, Kyoto, Japan). However, chemical pleurodesis was chosen in patients with a poor general condition or in cases with diffuse lung lesions, where it was difficult to locate the air leakage site. The chemical agent was an extract of *Viscum album* (Abnoba Viscum, Abnoba GmbH, Germany). Two ampules of Abnoba Viscum were injected into the chest tube, and the patients were placed in six positions (supine, prone, right and left decubitus, sitting, and Trendelenburg) for 2 hours. A repeated injection was attempted if the air leakage persisted 2 days after the procedure.

Statistical analysis

Basic clinical characteristics, including smoking history, radiological findings, methods of management, and clinical outcomes were described and analyzed. Continuous normally distributed variables were presented as mean

and standard deviation, and skewed continuous variables, as median and interquartile range. Categorical variables were presented as percentages. Differences between the two groups were assessed using an independent sample *t*-test (normally distributed continuous variables), a Mann-Whitney test (skewed distributed continuous variables), or a chi-squared test (categorical variables). The associations between risk factors and the recurrence of pneumothorax were assessed by logistic regression analyses. Univariate analysis was first performed, and variables yielding a P value below 0.1 were selected for multinomial logistic regression analysis to identify risk factors for recurrence. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). All statistical tests were two-tailed with a significance level set at 0.05 and were performed using Stata software version 10.0 (Stata, College Station, TX, USA).

Results

Characteristics of the study population

We encountered 438 patients with spontaneous pneumothorax during the study period. Of these, 317 patients were excluded as they did not meet the criteria, and one died suddenly a day after admission. Hence, 120 patients were included in the study. There were 61 in group A and 59 in group B. The number of men exceeded that of women in both groups. More patients in group B had quit smoking ($P<0.04$), had pulmonary diseases ($P<0.01$), or radiological findings of emphysema ($P<0.01$). Group A had more current smokers and individuals with a history of pneumothorax or the accompanying surgery, but these differences were not statistically significant. Other variables, included a history of pulmonary tuberculosis or radiological findings of bullae, bronchiectasis, or old tuberculosis, and were not significantly different between groups. Detailed information can be found in *Table 1*.

Management of current and recurrent pneumothorax

The management of the current pneumothorax was not different between groups, except for the use of chemical pleurodesis. Most of the patients required chest tube drainage (over 93% in both groups), but chemical pleurodesis was applied more frequently in the older group (27% vs. 11%, $P=0.03$). About 20% ($n=12$) of group A patients required surgery for pneumothorax; the causes of surgery were continuous air leakage, recurrence, and other reasons (e.g., totally collapsed lung or large bullae).

Table 1 Basic demographics of the pneumothorax patients

Variables	Group A (45–64 years) (n=61)	Group B (≥65 years) (n=59)	P
Basic demographics			
Gender			0.43
Male	46 [75]	48 [81]	
Female	15 [25]	11 [19]	
Smoking			
Quit	28 [46]	38 [64]	<0.04
Current	25 [41]	11 [19]	<0.01
Pack per year, mean [SD]	13 [16]	14 [30]	0.71
Previous illness history			
COPD/ILD	7 [11]	20 [34]	<0.01
Sequelae of tuberculosis	17 [28]	19 [32]	0.60
Pneumothorax	15 [25]	10 [17]	0.30
Chest tube drainage	14 [23]	10 [17]	0.41
Operation	6 [10]	1 [2]	0.06
Radiologic findings			
Bullae or blebs	27 [44]	24 [41]	0.89
Bronchiectasis	7 [11]	6 [10]	0.90
Emphysema	22 [36]	39 [66]	<0.01
ILD or IPF	1 [2]	6 [10]	0.04
Sequelae of tuberculosis	13 [21]	14 [24]	0.63

Continuous variables are presented as means and standard deviations and categorical variables are presented as numbers and proportions. COPD, chronic obstructive pulmonary disorder; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis.

However, only 8% (n=5) of patients in group B underwent surgery for prolonged air leakages.

The recurrence rate was not different between groups (P=0.93). In the younger group, recurrences were mostly on the same side. In the older group, recurrences were not dominated by ipsilateral recurrence. The length of hospital stay was longer in group B (P<0.01). There was a tendency for more complications in the older group, but it was not significantly different (P=0.09). Complications were respiratory distress and pneumonia in group B, but only lidocaine shock during pleurodesis in group A. Interestingly management of recurrence was significantly different

Table 2 Management and clinical outcomes of pneumothorax

Variables	Group A (45–64 years) (n=61)	Group B (≥65 years) (n=59)	P
Current management			
Observation	3 [5]	1 [2]	0.33
Chest tube drainage	58 [95]	58 [98]	0.18
Chemical pleurodesis	7 [11]	16 [27]	0.03
Operations	12 [20]	5 [8]	0.08
Cause of operations			
Recurrence	2 [17]	0 [0]	0.23
Continuous air leakage	7 [58]	5 [100]	
Others*	3 [25]	0 [0]	
Clinical outcomes			
Length of hospital stay	5.9 [4.7–7.2]	8.8 [7.0–70.7]	<0.01
Complications**	1 [2]	5 [8]	0.09
Recurrence			
Overall	17 [28]	16 [27]	0.93
Ipsilateral	17 [28]	13 [22]	
Post-pleurodesis	2 [29]	4 [25]	
Post-operative	0 [0]	1 [20]	
Management of recurrence			
Observation	1 [6]	0 [0]	0.02
Chest tube drainage, only	3 [18]	10 [63]	
Chemical pleurodesis	5 [29]	5 [31]	
Operations	8 [47]	1 [6]	

Continuous variables are presented as means and standard deviations and categorical variables are presented as numbers and proportions. *, others included total collapse, previous operation, and large bullae; **, complications included respiratory distress and pneumonia.

(P=0.02). A less invasive procedure (chest tube drainage; n=10, 63%) was applied more often in the older group, but invasive management (operations; n=8, 47%) was performed more often in younger patients. This information is described in *Table 2*.

Positive and negative factors for recurrence

The overall treatment and recurrence are summarized in

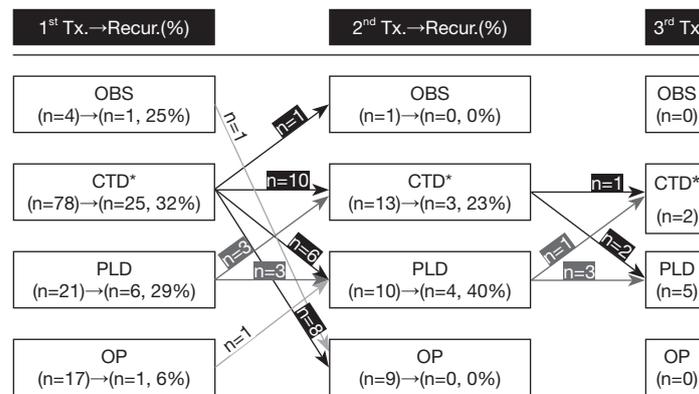


Figure 1 Flow chart of sequential treatment and recurrence for patients over 45 years old with pneumothorax. Patients who received pleurodesis suffered frequent recurrence, but those who received an operation did not. *CTD indicates a patient who underwent chest tube drainage without pleurodesis. If the patient was managed by chest tube drainage and pleurodesis simultaneously, then he/she was defined as PLD. OP was when the patient underwent an operation regardless of previous treatment. Tx., treatment; Recur., recurrence; OBS, observation; CTD, chest tube drainage; PLD, pleurodesis; OP, operation.

the flow chart (Figure 1). In the first event of pneumothorax, 41 (34%) patients were unable to resolve air leakage with chest tube alone, so chemical pleurodesis was performed in 21 patients and surgery in 17 patients. The recurrence rate was 29% in the patients with pleurodesis, but 6% in surgery. In second event of pneumothorax, 19 (58%) patients were required more than a chest tube drainage to stop the air leakage. Of them, 10 patients underwent pleurodesis but four (40%) recurred. On the contrary, no one recurred in nine patients who were performed surgery. In the third event of pneumothorax, five patients underwent pleurodesis, and two did chest tube drainage

To find out the positive and negative factors for recurrence, variables were analyzed by logistic regression (Table 3). Univariate analysis was performed for basic clinical characteristics, radiological findings, and various management options for current pneumothorax. Radiological findings of bullae/blebs ($P < 0.01$) or emphysema ($P < 0.01$) were significantly associated with recurrence. Variables of gender ($P = 0.05$) and surgery ($P = 0.06$) were also included in multivariate analysis, along with these two radiological features. For multivariate analysis, findings of bullae/blebs (OR = 5.57; 95% CI = 2.06–15.1) and emphysema (OR = 3.83; 95% CI = 1.34–10.9) were associated with recurrence. Moreover, surgery was negatively associated with recurrence (OR = 0.11; 95% CI = 0.01–0.93).

Discussion

Management of pneumothorax in elderly patients is not easy and sometimes frustrating because they often have several diseases other than pneumothorax. This can make patients more susceptible to pneumothorax, which can sometimes be fatal because their respiratory function may be deteriorated already (9,10). Moreover, the recurrence rate of SSP is higher than that of PSP (11) and the anxiety about recurrence was prominent in older patients (1). Therefore, prevention of recurrence can be more urgent in patients with SSP (10). In this study, radiological bullae/blebs or emphysema were high-risk factors for recurrence. Moreover, although surgery was the only procedure that could decrease the recurrence rate, it was less adopted in older patients (group B).

Emphysema and bullae/blebs on preoperative chest CT were prognostic factors for recurrence in this study. Various researches have shown that emphysema is one of the major risk factors for pneumothorax (12–14), as confirmed by the present study. Goddard classification score, which is a scoring system of emphysematous lung (0–24, worst as higher), could be a useful marker for deciding methods of treatment (15,16). Interestingly emphysema, not bullae/blebs, was more prevalent in older groups, but the rate of recurrence was not different between the groups. This may be due to the rate of

Table 3 Factors affecting recurrence

Variables	Univariate			Multivariate		
	OR	95% CI	P	OR	95% CI	P
Age	1.00	0.97–1.03	0.83			
Gender [†]	0.28	0.07–0.99	0.05	0.71	0.16–3.05	0.64
Previous history of						
COPD/ILD	1.79	0.72–4.46	0.21			
Pneumothorax	2.01	0.83–5.28	0.12			
Operation	0.42	0.05–3.64	0.43			
Smoking						
Current	0.66	0.26–1.66	0.38			
Quit	1.95	0.85–4.51	0.12			
Radiologic findings						
Bullae/blebs [†]	5.23	2.14–12.8	<0.01	5.57	2.06–15.1	<0.01
Bronchiectasis	2.32	0.71–7.51	0.16			
Emphysema [†]	4.78	1.86–12.3	<0.01	3.83	1.34–10.9	0.01
ILD/IPF	1.9	0.40–9.00	0.42			
Sequelae of tuberculosis	1.3	0.51–3.27	0.59			
Management						
Observation	0.88	0.09–8.72	0.91			
Chest tube drainage	0.55	0.09–3.47	0.53			
Chemical pleurodesis	0.91	0.33–2.57	0.87			
Operation [†]	0.14	0.02–1.09	0.06	0.11	0.01–0.93	0.04

[†], these factors were included in the multivariate analysis. OR, odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disorder; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis.

current smoking, which is known to be one of the most influential factors for pneumothorax (2), and was lower among older patients. This suggests that current smoking has more influence on the recurrence of pneumothorax than the length of the smoking period.

Regardless of the type of pneumothorax, surgical management remains the most effective treatment for preventing recurrence (17,18). Although surgery is still being performed via thoracotomy, and surgery with pleurectomy shows the lowest recurrence rate, less invasive surgery, such as VATS, is currently preferred (10,19,20). In this study, VATS was adopted for all patients, except for one who underwent “conversion to thoracotomy” because of severe adhesion. All of the bullae or blebs were resected using a mechanical stapler, and the stapling line was covered

with PGA felt. Not only surgery itself, but also newer instruments and materials, would be positive factors related to recurrence (21,22).

There are some limitations to this study. First, a selection bias may have been present. Patients who underwent surgery, especially among the elderly, were highly selected. As patients with severe systemic and pulmonary problems could not undergo single lung ventilation under general anesthesia, surgical patients were more likely to be relatively healthy. Second, this research was not a randomized prospective study, and thus some pneumothorax patients who had serious or fatal medical conditions other than pneumothorax would be excluded. Therefore, the patient population in this study should be regarded as a relatively healthy population. Despite these limitations, this study

is important in that it examined the factors predicting the recurrence of pneumothorax in middle-aged or older patients and suggested a method to decrease the recurrence rate. Moreover, this paper suggests that surgery for pneumothorax should be encouraged regardless of age if the indications are met.

In summary, radiological findings of emphysema or bullae/blebs are risk factors for recurrence of pneumothorax in middle-aged or older patients. Surgery in highly selected patients may be an effective method for decreasing the recurrence rate. Further studies are required to identify the surgical indications accurately.

Acknowledgments

Funding: This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (2017R1C1B5015969).

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was reviewed and approved by the Institutional Review Board (IRB) of Chungbuk National University Hospital (2018-04-005).

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Cite this article as: Nam SH, Kim KW, Kim SW, Kim SW, Hong JM, Kim D. Fate of spontaneous pneumothorax from middle to old age: how to overcome an irritating recurrence? *J Thorac Dis* 2019;11(11):4782-4789. doi: 10.21037/jtd.2019.10.30