

## Prothrombin Time Test in Patient with Spontaneous Pneumothorax

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### Abstract:

**Objectives:** We saw a patient with spontaneous pneumothorax who had a coagulopathy, but did not have clinical manifestations of a bleeding tendency. We re-examined the prothrombin time (PT) test in patients with PT coagulopathy.

**Patients and methods:** The clinical records of patients treated for a spontaneous pneumothorax from April 2012 to December 2020 were retrospectively reviewed. A total of 67 patients underwent repeat PT testing. Patients were divided into 2 groups as follows: Patients whose contentious repeat PT results deviated from normal (DN) and patients whose repeat PTs were normal (N). The first PTs were compared between the 2 groups of patients.

**Results:** The DN group consisted of 35 patients and the N group consisted of 32 patients. PT-international normalized ratio (PT-INR) were statistically significant difference between two groups ( $1.22\pm 0.09$  vs  $1.15\pm 0.04$ ). Regarding the timing of re-examination, there was a significant difference between the two groups on a monthly or yearly basis (PT-INR; monthly  $1.21\pm 0.07$  vs  $1.12\pm 0.02$ ,  $p<0.001$ , yearly  $1.25\pm 0.10$  vs  $1.16\pm 0.03$ ,  $p=0.025$ ).

**Conclusion:** The initial PT-INR value was significantly higher in the patients with abnormal PT values. There are patients with persistently abnormal PT values even years after surgery.

**Key Words:** Prothrombin time test Spontaneous pneumothorax Young patients Prothrombin time international normalized ratio

**Abbreviations:** PT: prothrombin time, PT-INR: prothrombin time- international normalized ratio

### 1. INTRODUCTION

We have found that the results of the prothrombin time (PT) test have deviated from normal levels only in patients with spontaneous pneumothorax

[1]. The deviation has tended to be associated with young patients with a primary spontaneous pneumothorax. In this study, we re-examined PT tests for patients showing a PT test result that deviated from the normal ranges the first time

they underwent PT testing. We considered whether there was difference in a first PT test between the patient with normal level and with deviation from normal level after reexamination.

### 2. PATIENTS AND METHODS

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the institutional review board of Sapporo City General Hospital (approval IRB No. R02-059-689). Considering the retrospective nature of this study, informed consent was obtained in the form of an opt-out clause on our website, and patients who rejected this option were excluded. The clinical records of patients treated for a spontaneous pneumothorax from April 2012 to December 2020 at Sapporo City General Hospital Pneumothorax Center were retrospectively reviewed. Patients taking anticoagulant medications were excluded. The first PT test were performed when pneumothorax was diagnosed. Sixty seven cases (62 males and 5 females) who were reexamined a PT test were enrolled. The results of the PT tests were assessed from a patient's first episode of pneumothorax or second episode of pneumothorax or more than 6 months after surgery.

The mean age of the study patients was 22.0 years (range, 14–73 years). There were 61 patients with primary spontaneous pneumothorax and 6 with secondary spontaneous pneumothorax (Table 1). Patients were divided 2 groups, those with continuous deviation from the normal range (DN) and those with normal levels after a repeat PT test (N). The value of PT at first test were compared with two groups.

Each blood sample (1.8 mL) was mixed with 0.2 mL of 3.2% sodium citrate in a glass test tube. The specimen was centrifuged at 1500 g for 15 min and the plasma was removed for testing. To

measure the PT, the plasma (0.1 mL) was heated at 37°C for 3 min, PT reagent (Coagpia-N; Sekisui Medical Co., Ltd., Tokyo, Japan) was added to the sample, and the amount of time to clotting was measured. An autoanalyzer (Sysmex CS-5100) was used to measure the PT by measuring the formation of fibrin. The analyzer displays PT-international normalized ratio (PT-INR) of 0.90–1.10 is considered normal [2]. An abnormal result is defined as a deviation from normal for PT-INR results.

Statistical analysis assessed the data for normal distribution and the dispersion of the target groups. The Welch t test, and Mann-Whitney U test were used for comparisons between 2 groups. SPSS version 22 (IBM Corporation) was used for statistical analysis. A P value of  $\geq 0.05$  was considered significant.

### 3. RESULTS

There were 35 patients in DN group and 32 patients in N group. The mean age of the patients in N group was 22.9 years (range, 14–73 years). There were 28 male and 4 female; 28 had a primary and 4 had a secondary spontaneous pneumothorax. The mean PT-INR was  $1.15 \pm 0.04$ . The mean age of the patients in DN group was 21.4 years (range, 14–62 years). There were 34 male patients and 1 female patient; 33 had a primary spontaneous and 2 had a secondary pneumothorax. The mean PT-INR was  $1.22 \pm 0.09$ . There were significant differences between the 2 groups (Table. 2).

Repeat testing after the first episode of pneumothorax was performed 1 to 20 days after the first test (mean 6.8 days). Table 3 shows the results. The PT-INR values for the DN group and N group were  $1.17 \pm 0.05$  and  $1.22 \pm 0.09$ , respectively. The differences were not significant. Repeat testing after the second episode of

pneumothorax was performed 1 to 38 months after the first test (mean 6.8 months). Table 4 shows the results. The PT-INR values for the N group and DN group were  $1.12 \pm 0.02$  and  $1.21 \pm 0.07$ , respectively. The differences between the 2 groups were significant.

The results of re-examination in more than 6 months after surgery (reexamination day; 1-80 months [mean, 26.8 months]) is shown in Table 5. The PT-INR values for the N group and DN group were  $1.16 \pm 0.03$  and  $1.25 \pm 0.01$ , respectively. The differences between the 2 groups were significant.

**Table1.** Characteristics of reexamination of PT test

		n=67
Age	Year old (average)	14-73(22)
Gender	Male : Female	62:5
Classification of pneumothorax	Primary : Secondary	61:6
After reexamination	Abnormal ; Normal	35:32

**Table2.** Characteristics of abnormal and normal patients after reexamination

		DN group	N group	p value	
		n=35	n=32		
Age	Year old (average)	14-62 (21.4)	14-73 (22.9)		
Gender	Male : Female	34 : 1	28 : 4		
Classification of pneumothorax	Primary : Secondary	33 : 2	28 : 4		
Initial PT test	PT-INR (average, deviation)	1.22±0.09	1.15±0.04	<0.001	*

\*: Mann-Whitney’s U test

**Table3.** Characteristics of reexamination in the first episode of pneumothorax

		DN group	N group	P value	
		n=25	n=9		
Age	Year old (average)	15-41 (21)	16-63 (27)		
Gender	Male : Female	24 : 1	6 : 3		
Classification of pneumothorax	Primary : Secondary	24 : 1	7 : 2		
Initial PT test	PT-INR (average, deviation)	1.22±0.09	1.17±0.05	0.12	*

\*: Mann-Whitney’s U test

**Table4.** Characteristics of reexamination in the second episode of pneumothorax

		DN group	N group	P value	
		n=19	n=14		

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Age	Year old (average)	14-36(19)	14-39(19)		
Gender	Male : Female	19:0	14:0		
Classification of pneumothorax	Primary : Secondary	19:0	13:1		
Initial PT test	PT-INR (average, deviation)	1.21±0.07	1.12±0.02	<0.001	*

\*: Mann-Whitney's U test

**Table5.** Characteristics of reexamination in more than 6 months after surgery.

		DN group	N group	P value	95% confidence interval	
		n=10	n=13			
Age	Year old (average)	16-62(25.3)	14-73(22.6)			
Gender	Male : Female	10:0	12:1			
Classification of pneumothorax	Primary : Secondary	9:1	12:1			
Initial PT test	PT-INR (average, deviation)	1.25±0.10	1.16±0.03	0.025	0.01339-0.16632	* *

\*\* : Welch's t test

### 4. DISCUSSION

We previously reported that the patients with spontaneous pneumothorax and mild disorders of blood coagulation without bleeding tendency clinically [1]. The major was young patient with primary spontaneous pneumothorax, and was abnormality of PT test. We repeated the PT test to determine if the abnormal PT result was due to pneumothorax or an error in the measurement.

In the whole reexamination, the difference of value of PT -INR in first test between two groups were significant. In the patients with continuous deviation from normal level of PT, the mean PT-INR was 1.22. Among the 32 patients in N group, 3 had PT-INR values greater than 1.20. On the other hand, among the 35 patients in DN group 20 of 35 patients had PT-INR values ranging from 1.11 to 1.19 after reexamination. As for this, the slight abnormalities of the PT test results were recognized, and the abnormalities were shown to be persistent.

Differences between the 2 patient groups based on the period of the reexamination were examined. Unfortunately, the differences between the 2 patient groups upon repeat testing after the first episode of pneumothorax were not significant. The result might be accounted for by the small number of patients who were normalized by reexamination. At all of a reexamination period except the period of first pneumothorax, PT-INR in patients in DN group indicated more than 1.21 on average in first PT test.

We have two theories that might account for the findings of this study. First, something causes an abnormal PT test result when pneumothorax occurs in a patient. And with improvement in the pneumothorax, the result of the PT test is normalized. It may be that there is a temporary release of an inhibitor into the circulatory system that is associated with the presence of a pneumothorax. We think the second explanation

is supported by the results of the patient in CG group who underwent PT testing more than 6 months after surgery. We think that that patient had an inherent abnormality in his or her coagulation system.

This study has several limitations. First, this was a retrospective single-center study. Second, the study patients were from Japan only. It is possible that there may be local differences in Japan. It is also not known if the results could have been affected by race or ethnicity. Indeed, the findings may be unique to Asians. We hope to investigate our findings in other areas. Third, the coagulation test is difficult to perform accurately. A blood specimen must be obtained carefully and the specimen must be handled carefully [3,4]. The method for obtaining blood specimens and the protocols for inspection have been standardized in our hospital. Moreover, the cardiology division at our hospital uses therapeutic anticoagulant agents in division of cardiovascular disease. Therefore, we thinking that the inspection processes at our institution are very precise.

At present we cannot definitively prove that there is an association between pneumothorax and abnormal PT test results. However, it is clear that abnormal PT test results occur in patients with spontaneous pneumothorax. Additional investigations on the relationship between pneumothorax and abnormal PT test results are needed.

## 5. CONCLUSION

The initial PT-INR value was significantly higher in DN group patients. There are patients with abnormal PT values that persist even years after surgery. In the future, it is necessary to analyze further investigations are needed on the relationship between pneumothorax and the mechanisms of abnormal coagulation.

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## ETHICS APPROVAL

This retrospective study was approved by the Ethics Committee of our institution (IRB No. R02-059-689).

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