

Usefulness of Computed Tomography in Determining Risk of Recurrence After a First Episode of Primary Spontaneous Pneumothorax: Therapeutic Implications

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OBJECTIVE: The main cause of primary spontaneous pneumothorax is the rupture of subpleural blebs or bullae. The presence of bullae may also lead to an increased risk of recurrence. The best way to detect them is by means of computed tomography (CT). Our objective in the present study was to determine whether bullae detected by CT represent an increased risk of recurrence after a first episode of primary spontaneous pneumothorax. We also evaluated therapeutic implications.

PATIENTS AND METHODS: We carried out a prospective study that included 55 patients (41 men and 14 women) with primary spontaneous pneumothorax. For all patients, the therapeutic recommendations of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) were followed. After resolution of the episode, a chest CT was performed and the presence, location, number, and size of bullae were evaluated. Subsequently, the number of recurrences in each group was evaluated.

RESULTS: The mean follow-up period was 30.7 months (95% confidence interval, 24-37 months). Twenty-six patients presented bullae, and 6 of these experienced recurrence. Of the 29 patients without bullae, 7 experienced recurrence. No association was found between the presence or absence of bullae and recurrence ($P=.92$). Bullae in the right lung led to more frequent recurrence of pneumothorax ($P=.03$). The number and size of the bullae had no significant influence on recurrence ($P=.51$).

CONCLUSIONS: The present study could not demonstrate that the presence, size, or number of bullae on CT scans has any influence on recurrence rate. We cannot recommend surgery after a first episode of primary spontaneous pneumothorax based on the presence of bullae on the CT scan.

Key words: *Pneumothorax. Recurrence. Bullae. Blebs. Computed tomography.*

Utilidad de la tomografía computarizada para determinar el riesgo de recidiva tras un primer episodio de neumotórax espontáneo primario. Implicaciones terapéuticas

OBJETIVO: La causa fundamental del neumotórax espontáneo primario es la rotura de bullas o *blebs* subpleurales. Estas bullas podrían también condicionar un mayor riesgo de recidiva. La mejor forma de detectarlas es mediante tomografía axial computarizada (TAC). Nos planteamos aquí si las bullas en la TAC suponen un riesgo mayor de recidivas tras un primer episodio de neumotórax espontáneo primario. Asimismo, se valoran las implicaciones terapéuticas.

PACIENTES Y MÉTODOS: Se trata de un estudio prospectivo en el que se incluyó a 55 pacientes (41 varones y 14 mujeres) con neumotórax espontáneo primario. En todos ellos se siguieron las recomendaciones terapéuticas de la Sociedad Española de Neumología y Cirugía Torácica (SEPAR). Tras la resolución del episodio se efectuó una TAC de tórax y se valoraron la presencia, la localización, el número y el tamaño de bullas. Posteriormente, se evaluó el número de recidivas en cada grupo.

RESULTADOS: El tiempo medio de seguimiento fue de 30,7 meses (intervalo de confianza del 95%, 24-37 meses). Presentaron bullas 26 pacientes, de los que en 6 hubo recidiva. De los 29 pacientes sin bullas, 7 presentaron recidiva. No se encontraron diferencias entre la presencia o ausencia de bullas y la recidiva ($p = 0,92$). Las bullas derechas recidivaron con mayor frecuencia ($p = 0,03$). El número y el tamaño de las bullas no tuvieron influencia significativa ($p = 0,51$).

CONCLUSIONES: El estudio no ha podido demostrar que la presencia de bullas en la TAC, su tamaño o su número influyan en el índice de recidivas. No se puede recomendar la cirugía tras un primer episodio de neumotórax espontáneo primario por presentar bullas en la TAC.

Palabras clave: *Neumotórax. Recidiva. Bullas. Blebs. Tomografía computarizada.*

Introduction

Spontaneous pneumothorax is a relatively common disease. In Spain, the annual incidence ranges from 7.4 to 28 cases per 100 000 inhabitants in men and from 1.2 to 10 cases per 100 000 inhabitants in women.¹ It is generally accepted that spontaneous pneumothorax in otherwise

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healthy patients is usually caused by rupture of subpleural bullae or blebs thereby forming a fistula between the bronchial tree and the pleural cavity, resulting in collapse of the lung.² If the presence of bullae is a risk factor for a first episode of spontaneous pneumothorax, it follows that such lesions might also be associated with the risk of recurrence.

Chest computed tomography (CT) has been shown to be considerably more sensitive than simple chest x-ray for the detection of such bullae,³ and their presence on the CT scan could represent a greater risk of recurrence after a first episode of spontaneous pneumothorax. This prompted us to formulate the following working hypothesis: the presence of bullae on the CT scan after a first episode of spontaneous pneumothorax is associated with an increased risk of recurrence of pneumothorax and can serve as a basis for the indication of elective surgery.

Patients and Methods

We designed a prospective study that included patients with a first episode of primary or idiopathic spontaneous pneumothorax confirmed by anteroposterior chest x-ray. Patients with recurrences of pneumothorax were excluded if the first episode had occurred before the beginning of the study. Patients diagnosed with concomitant lung disease either before or after the pneumothorax episode were also excluded.

Between May 1999 and December 2005, 55 patients (41 men and 14 women) attended the Hospital General of Castellón, Spain, with a first episode of primary spontaneous pneumothorax. All patients were admitted to the Chest Surgery Unit of the General and Digestive Surgery Department and the therapeutic recommendations of the Spanish Society of Pulmonary and Thoracic Surgery (SEPAR)² were followed in all cases. Thus, asymptomatic patients with a pneumothorax size less than 20% (calculated according to the formula of Collins et al⁴) in the chest x-ray were managed with a conservative approach of observation and a radiographic examination after 24 to 48 hours. Symptomatic patients (dyspnea, intense pain, decrease in oxygen saturation) with a pneumothorax size more than 20%, or those initially managed by observation only in whom the pneumothorax had increased in volume were treated by pleural drainage with a 20-, 24-, or 28-French chest tube. In all cases the tube was inserted in the fifth or sixth intercostal space on the anterior axillary line. If there was no air leak after 48 hours, the tube was clamped and then removed, provided re-expansion of the lung was confirmed by chest x-ray. Patients with air leaks persisting for more than 5 days were indicated for surgery and excluded from the study.

Once resolution of the pneumothorax had been confirmed by a chest x-ray showing complete and persistent re-expansion of the lung, a chest CT scan was performed between the first and the sixteenth week following the pneumothorax episode. The radiographic study was performed with an Asteion helical CT scanner (Toshiba, Tokyo, Japan) with 4 helices. The scanner was configured with 3-mm collimation and a pitch of 5.5 for apex-to-base scans of the lung parenchyma with a lung filter. The presence, number, size, and location of bullae were evaluated. All images were interpreted by the same radiologist, who was unaware of the symptoms, the location of the pneumothorax, and the treatment used in each case.

Patients were subsequently scheduled for annual follow-up visits. At study closure, all patients were contacted by telephone to determine whether the disease had recurred since the last visit. Recurrence was considered to have taken place when a pneumothorax was detected on chest x-rays taken for any reason.

Statistical Analysis

Data were collected for descriptive analysis, grouped according to presence or absence of recurrence; inferential statistics were then based on comparison of those same variables. For qualitative variables we initially used the χ^2 test. However, if any predicted value in any cell of the contingency tables was less than 5, the Fischer exact test was used. For quantitative variables, the nonparametric Mann-Whitney U test was used, as a normal distribution could not be assumed. The Kaplan-Meier method was used to analyze the recurrence-free survival. The Breslow test was used to test the significance of differences in survival according to the presence or absence of bullae. The log-rank test was not applied, as risk proportionality could not be assumed. The statistical analysis was carried out using the SPSS statistical package, version 12.0.1. *P* values less than the traditionally accepted .05 were considered statistically significant.

The variables analyzed were presence, location, number, and size of bullae.

Results

Follow-Up Duration

Mean follow-up time was 30.7 months, with a 95% confidence interval (CI) of 24.0 to 37.0 months. Median follow-up time was 22.0 months (range, 1.0-76.0 months). The 25th percentile was 9.7 months and the 75th was 51.0 months—an interquartile range of 41.3 months. These 41 months covered the follow-up period of the most representative cases of the sample (Table 1).

TABLE 1
Percentiles of Follow-Up Time (Weighted Average in Months)

	Percentiles						
	5	10	25	50	75	90	95
Without recurrence	2.95	8.67	16.63	39.08	55.94	69.22	71.83
With recurrence	1.00	1.00	1.50	5.00	20.00	39.60	—
Overall	1.00	2.02	9.70	22.00	51.00	67.25	71.40

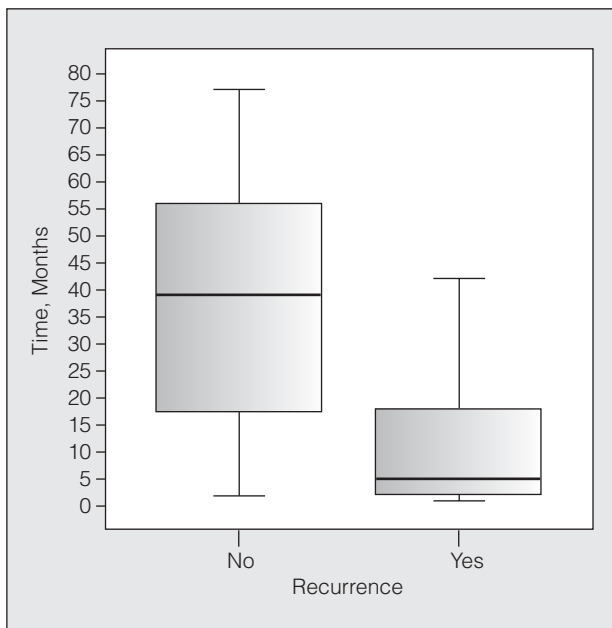


Figure 1. Box Plot of Follow-Up Time According to Appearance of Recurrence

Certain differences were observed on comparison of follow-up time of patients with recurrence with that of those without recurrence (Figure 1). Thus, in the group with no recurrence, median follow-up time was 39 months, with a minimum of 2 months and a maximum of 76 months. The 25th percentile of 16.6 months and the 75th percentile of 55.9 months corresponded to an interquartile range of 39.3 months. Thus, in the group of patients without recurrence, the most characteristic patients had a duration of follow-up between these 2 values. In the group with recurrence, as follow-up ended when the recurrence occurred, median follow-up time was 5 months, with a minimum of 1 month (earliest recurrence) and a maximum of 42 months (latest recurrence). The 25th percentile and 75th percentile were 1.5 months and 20.0 months, respectively—an interquartile range of 19.5 months. Given that follow-up times were equivalent to the times to

recurrence, we can conclude that the most representative recurrences occurred between 1.5 months and 20.0 months of the initial episode in this group. As the median (thick horizontal line inside the box plots of Figure 1) was lower than the arithmetic mean, recurrence generally occurred during the first year.

Presence of Bullae Detected by CT and Recurrence

Of the 55 patients, 26 (47.3%) presented bullae and 29 (52.7%) did not. Six of the patients in the group with bullae relapsed (46.2% of all relapsed patients) compared to 7 patients in the group without bullae (53.8% of all relapsed patients). We found no significant differences between patients with or without recurrence in the group with bullae on CT scans ($\chi^2=0.009$; 1-sided test, $P=.92$) (Table 2).

Location of Bullae and Recurrence

For the 26 patients with bullae found on the CT scans, the sites were as follows: 12 in the right lung, 2 in the left lung, and 12 bilateral. No patient with bilateral bullae relapsed, while 5 patients with bullae in the right lung and 1 patient with bullae in the left lung did. The statistical significance obtained with the Fisher exact test was sufficient ($P=.03$) to affirm an association between the location of bullae and subsequent recurrence. Recurrence of pneumothorax occurred in more patients with bullae in the right lung than in those with bullae in the left lung (Table 2).

Number of Bullae and Recurrence

Of the 55 patients included in the study, 29 (52.7%) had no bullae on the CT scans. There were 7 recurrences in this group. One bulla was detected in 11 (20%) patients. In this group, there were 5 recurrences. In 12 cases, 2 bullae were detected, but none of these patients relapsed. In 2 patients, 3 bullae were detected, and 1 of the patients relapsed. One patient presented 7 bullae but did not relapse. One might conclude that there is a greater tendency toward recurrence in patients with a single bulla on the CT scan than in those with more bullae, but this may be due to chance (Mann–Whitney U test, $P=.51$) (Table 2).

Size of Bullae and Recurrence

The mean size of the largest bulla detected by CT was 0.5 cm, with a minimum size of 0 cm and a maximum size of 2 cm. Mean (SD) size was 0.6 (0.7) cm in the group of patients who experienced recurrence and 0.5 (0.8) cm in the group that did not. Thus, there were no differences in recurrence rate according to size of bullae.

Recurrence-Free Survival According to Presence or Absence of Bullae

Analyzing survival curves using the Kaplan–Meier method (Figure 2), we observed the results given below. It must be borne in mind, however, that patients were

TABLE 2
Recurrences According to the Variables Analyzed*

Variable	No. of Patients With Recurrence	% of Patients With Recurrences	P
Bullae detected by CT	6	46.2	.92†
Location of bullae	0		.03‡
Right lung	5	38.3	
Left lung	1	7.7	
Bilateral	0	0	
No. of bullae			0.51§
0	7	53.8	
1	5	38.5	
2	0	0	
3	1	7.7	
7	0	0	

*CT indicates computed tomography. † χ^2 test. ‡Fischer exact test. §Mann–Whitney U test.

censored if they did not relapse and therefore completed follow-up until closure of the study.

1. In patients without bullae, mean recurrence-free survival was 53 months (SE, 5 months; 95% CI, 42-63 months). As can be seen in Figure 2, the cumulative probability of recurrence-free survival decreased from 0.9 in month 1 to 0.7 in month 42.

2. In patients with bullae, mean recurrence-free survival was 59 months (SE, 6 months; 95% CI, 46-71 months). Cumulative recurrence-free survival decreased from 1.0 in month 1 to 0.7 in month 36.

While no significant differences in recurrence-free survival were found between patients with or without bullae (Breslow test, $P=0.88$), some comments on the results obtained are appropriate. As reflected in the Kaplan-Meier survival curve, patients with bullae tended to relapse in the first 6 months following a first episode of pneumothorax and recurrence-free survival dropped sharply, but then leveled off. In patients without bullae, however, recurrence-free survival decreased, but more gradually. Recurrences were sporadic and apparently random, and showed no clear temporal pattern.

Discussion

Recurrence is the most common complication of primary spontaneous pneumothorax. The probability of recurrence increases from 20% following a first episode, to 60% following a second episode and 80% following a third episode.²

In 1991, Lippert et al⁵ identified 4 factors that significantly increased the risk of recurrence after a first episode of spontaneous pneumothorax: age over 60 years, presence of pulmonary fibrosis, being a nonsmoker, and being tall and thin. However, these authors did not study the presence of bullae. Senac et al,⁶ while not providing exact figures in their preliminary study, had already mentioned 4 CT scan findings that could be associated with a greater risk of recurrence: tension bullae, size greater than 3 cm, greater number of lesions (number unspecified), and apical bullae. Warner et al⁷ were the first to evaluate the importance of the number of bullae in the recurrence of pneumothoraces. In their interesting study, they claimed that the natural history of pneumothorax could be predicted by chest CT findings, although they admitted that the number of cases ($n=26$) was too small to determine the number of bullae that could influence recurrence. Subsequently, Sihoe et al⁸ published a study of 28 patients in which they concluded that the presence of bullae detected by CT was indeed a risk factor for recurrence in the contralateral lung after a first episode of spontaneous pneumothorax and that CT could therefore be used to determine whether bilateral surgery was indicated in patients with such lesions. Despite these encouraging results, the study of Sihoe et al⁸ was later criticized because of serious methodological errors.^{9,10} Torres-Lanzas and Rivas de Andrés¹¹ claimed, however, that the presence of bullae detected by thoracoscopy during a first episode of pneumothorax was

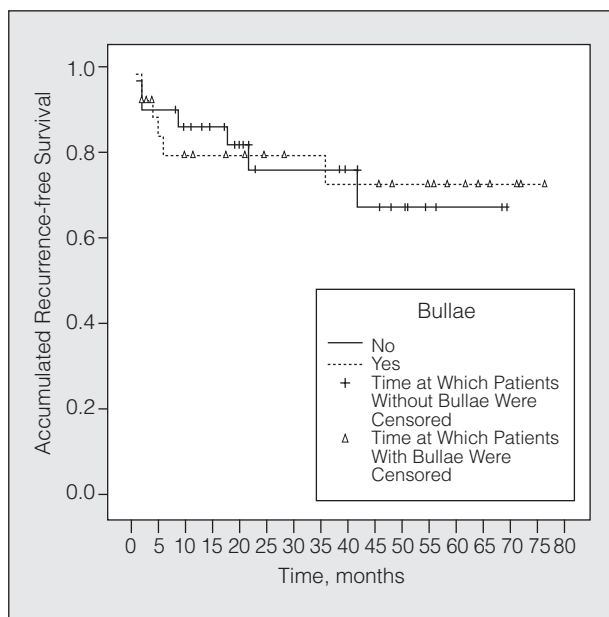


Figure 2. Kaplan-Meier Survival Curve

predictive of recurrence and recommended surgery in such cases.

The results of the present study, in line with those of other authors,^{3,12,13} were not conclusive enough to show that the presence of bullae detected by CT was predictive of recurrence after a first episode of spontaneous pneumothorax, or that their size or number was of any prognostic value. The only factor that reached statistical significance was the side on which the bullae were located. In patients presenting bullae on the CT scan, the probability of recurrence was greater if the bullae were located in the right lung rather than in the left or in both lungs.

Characteristically, the majority of recurrences occurred within a year of the initial episode. The greatest risk of recurrence can therefore be considered to lie in this period. These findings were consistent with those reported by other authors.^{1,14} On comparing recurrence-free survival of patients with and without bullae, we found that recurrence occurred mainly during the first 6 months when bullae were present but was unpredictable, with episodes of sporadic recurrence, especially during the first 2 years, when they were not present.

Treatment and follow-up of spontaneous pneumothorax have not yet been standardized and therapeutic recommendations are generally based on consensus statements, which differ considerably from one scientific society to another.^{2,15-17} However, since the beginning of the 1990s, video-assisted thoracoscopic surgery has become widely accepted and used in the treatment of many respiratory diseases.¹⁸ It is currently considered the procedure of choice for the treatment of pneumothorax requiring surgery, as it reduces postoperative pain, makes rapid functional recovery possible, and offers better aesthetic results. The safety of this procedure and the postintervention recurrence rate are similar to those of open surgery.^{2,19,20} In view of this clear reduction in morbidity and mortality, some authors have recommended

surgical resection after a first episode of spontaneous pneumothorax when bullae are detected with CT.^{6,21,22} In our opinion, there is not enough scientific evidence to justify such a recommendation, even if bullae are detected by CT. No surgical procedure is ever completely free of risk and given that the rate of recurrence after a first episode of pneumothorax is between 20% and 45%,^{1,21} the number of patients who would never experience recurrence and who nevertheless undergo surgical resection is, in our opinion, too high for surgery to be recommended as prophylaxis.

In our opinion, the usefulness of CT in cases of spontaneous pneumothorax lies not in its ability to predict recurrence, thereby allowing early surgical intervention, but rather in its ability to detect lesions and diseases that are potential causes of pneumothorax (secondary pneumothorax) and, of course, to detect other conditions for which surgery might be indicated.

Our results do not show that bullae increase the chance of recurrence after a first episode of primary spontaneous pneumothorax. Even though the presence of bullae has little influence on recurrence, there is a tendency toward earlier recurrence in patients with bullae, although this may be due to chance. On the basis of our findings, therefore, we cannot consider surgery to be clearly indicated for the prevention of recurrence in patients who present bullae on a CT scan after a first episode of spontaneous pneumothorax, especially if a year or more has passed since that first episode.

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