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Optimal treatment of pneumothorax in adolescents with Marfan syndrome

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ABSTRACT

Purpose: Pneumothorax often develops in patients with Marfan syndrome (MFS). Here, we examined the effects of conservative and surgical pneumothorax treatments in children with MFS.
Methods: In this study, 23 patients, less than 20 years old, diagnosed with both MFS and pneumothorax between 1999 and 2019 were included. All data were collected retrospectively from patients' medical records.
Results: In total, 18 of 23 patients (78%) had relapsed pneumothorax either on the ipsilateral or contralateral side. Among these 18 patients, 6 (26%) patients had multiple relapses. Conservative and surgical treatments of pneumothorax were attempted in 33 and 29 lungs, respectively. The conservative treatment was attempted as a definitive therapy in 21 lungs. Twelve conservative treatments (57%) failed, which required surgical intervention. In 9 lungs (43%) with successful conservative treatment, 6 (67%) had ipsilateral relapses. In contrast to the above findings, only 4 (13%) ipsilateral relapses were observed in 29 surgical treatments.
Conclusions: Our study revealed a low response and high relapse rate when MFS adolescents who diagnosed pneumothorax were subjected to the conservative treatment modality. Thus, we recommend surgical intervention as the first line of therapy to treat pneumothorax in adolescents diagnosed with MFS.
Level of Evidence: III (Treatment Study)

1. Introduction

Marfan syndrome (MFS) is a genetic disorder of connective tissue that primarily affects the skeletal, cardiovascular and ocular systems. The development of pneumothorax is common in MFS patients [1], and is often characterized by early onset at a young age and a high frequency of bullae [2-3]. However, the low prevalence of this disorder makes it challenging to determine an optimal treatment strategy to treat MFS associated pneumothorax [1-3]. In addition, there is no guideline for pediatric pneumothorax [4-5], and some study groups are now trying to build the new evidence of the management for pediatric pneumothorax [6-9]. In this study, we examined the effects of conservative and surgical treatments of pneumothorax in children and adolescents diagnosed with MFS.

2. Material and methods

In this study, patients, less than 20 years old, diagnosed with both MFS and pneumothorax at our hospital between 1999 and 2019 were included. All data were collected retrospectively from patients' medical records. Data on patients' characteristics, the clinical course of treatments, and relapse of pneumothorax were obtained. We divided all patients into two groups, conservative and surgical treatments groups. The conservative treatment groups included patients who were admitted to the hospital and treated by ways other than operative intervention. The surgical treatment groups included patients who had operation as first-line or second-line therapy followed by conservative treatment. All numerical data are expressed as median (interquartile range), unless otherwise mentioned. Statistical analyses were performed using JMP®Pro 15 (SAS Institute Inc., Cary, NC, USA). The cumulative treatment-failure and relapse free rate are illustrated by the Kaplan-Meier survival curves. The ethics committee at our institution approved this study. (2996- (6))

3. Results

A total of 1016 patients were diagnosed with MFS at our hospital between 1999 and 2019. Thirty-one of these 1016 patients were diagnosed with both MFS and pneumothorax. Twenty-three (14 male and 9 female) of these 31 patients were less than 20

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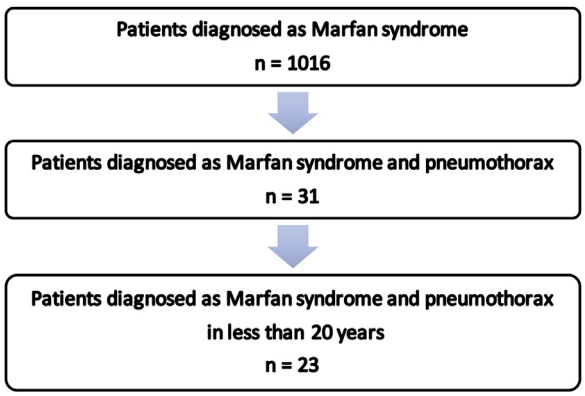

Fig. 1. A flow diagram of study.

Table 1
Baseline characteristics of 23 patients with pediatric pneumothorax in Marfan syndrome.

	n (%)
Sex	
male	14 (61%)
female	9 (39%)
Age* (years)	15 (13–16)**
Bulla	
exsist	21 (91%)
uni lung	14 (67%)
both lungs	7 (33%)
not exist	2 (9%)
Size of bulla (mm)	11 (8–21.5)**
Treatment (lung)	
conservative	33
surgery	29

*The age of the first episode of pneumothorax.
**Median (interquartile range).

years old (Fig. 1). The observation period was 1690 days (899.5–2364.5 days) and the median age was 15 years old (13–16 years old). Bullae were identified in 21 patients (91%) using computed tomography at the time of onset. Fourteen had bullae in one lung, while 7 patients had bullae in both lungs. The median size of the bullae was 11 mm (8–21.5 mm). Five patients (22%) did not experience relapse after the treatment, while 18 patients (78%) had relapsed pneumothorax either on the ipsilateral or contralateral side. Among these 18 patients, 6 patients (26%) had multiple relapses. The maximum number of relapse observed in this case series was 4.

Conservative and surgical treatments of pneumothorax were attempted in 33 lungs and 29 lungs, respectively (Table 1). The conservative treatment was attempted as a definitive therapy in 21 lungs. In this group, most patients had chest tube drainage and supplemental oxygen within the first 48 h after diagnosis and no one received simple aspiration in this study. Among these 21 conservative treatments, 12 (57%) conservative treatments failed, which required surgical intervention.

The chest drain placement duration in patients successfully treated with the conservative approach was 4 days (3.75–5.75 days). Length of hospitalization of these patients was 5 days (4–6 days). However, the chest drain placement duration in patients unsuccessfully treated with the conservative approach, requiring surgical intervention, was 6 days (4.25–8 days). Length of hospitalization of these patients was 12 days (10–13 days). In 9 lungs (43%) with successful conservative treatment, 6 (67%) had relapsed pneumothorax in the ipsilateral lung. These relapses occurred between 2 and 180 days after the conservative treatment. Therefore, only 3 out of 21 lungs (14%) with an attempted conservative treatment were cured without any relapse (Fig. 2).

In contrast to the above findings, only 4 (13%) ipsilateral relapses were observed in 29 surgical treatments (Fig. 3). Video-assisted thoracic surgery (VATS) was used for surgical interventions. Conversion to open thoracotomy was not required. Additionally, no perioperative surgical complications such as intraoperative organ injury, wound infection, or empyema were detected. The duration of the postoperative chest drain placement was 2.5 days (2–3 days), and the length of the postoperative hospitalization was 5 days (4–6 days).

4. Discussion

The incidence of primary spontaneous pneumothorax is estimated to be 5–10 per 100,000 individuals (0.005–0.001%). However, the incidence of pneumothorax in MFS patients is estimated to be 4–11% [3]. In our study, 31 of 1016 patients (3%) with MFS were diagnosed with pneumothorax and this result is in line with a previously published study [3]. Pneumothorax in MFS patients is often characterized by early onset at a young age and a high frequency of bullae [2-3]. Moreover, the first episode of pneumothorax was observed in 23 (74%) patients who were less than 20 years old. In this cohort, the median age was 15 years old. Bullae at the time of onset were detected in 21 cases (91%) and these results are consistent with previously published reports [2-3].

Both conservative treatments such as supplemental oxygen therapy and chest tube drainage and surgical treatments such as blebectomy are used for pneumothorax. The general guidelines on the management of primary spontaneous pneumothorax were published by the British Thoracic Society (BTS) and the American College of Chest Physicians (ACCP) [4-5]. However, the management of pneumothorax is not fully standardized and the treatment modality varies depending on the radiological findings (X-ray or computed tomography) and clinical symptoms [6]. Moreover, these guidelines are particularly applicable to adults. Thus, to date the management of pneumothorax in children has been largely dependent on data obtained from studies in adults. Although recently some evidence has been collected gradually in children, there is a controversy in particular about the timing of surgery (primary or secondary), and the ways of conservative treatment (chest tube drainage, simple aspiration, or observation with supplemental oxygen). In our study, the conservative treatment was attempted in most cases as the first line of therapy to treat pneumothorax, and operation was chosen after the failure of conservative treatment. In cases of relapse, patients were treated with chest tube drainage as first aid. Subsequently, these patients underwent surgical intervention without evaluating the effects of the chest tube drainage as a definitive therapy. In some cases, surgical treatment was selected as the first line of therapy because of the presence of bullae or coexisting MFS. In one particular relapse case, the selection of the conservative treatment to treat the relapse failed to produce positive results, ultimately necessitating surgical intervention. These observations highlight the need for developing an optimal treatment modality to treat pneumothorax in MFS patients.

Currently, there is little consensus on the optimal treatment modality to treat pneumothorax in MFS patients, particularly children [1-3]. The response rate in children undergoing the conservative treatment for spontaneous pneumothorax is estimated to be around 50% [7]. In our study, the response rate of the conservative treatment was extremely low (14%). In contrast to the above findings, the relapse rate of the surgical treatment in our study was similar to the relapse rate in pediatric spontaneous pneumothorax [8].

Our results demonstrate that the conservative treatment of pneumothorax in children with MFS produced limited results. Even when the conservative treatment was successful, many patients showed early relapse. These results suggest that the conservative

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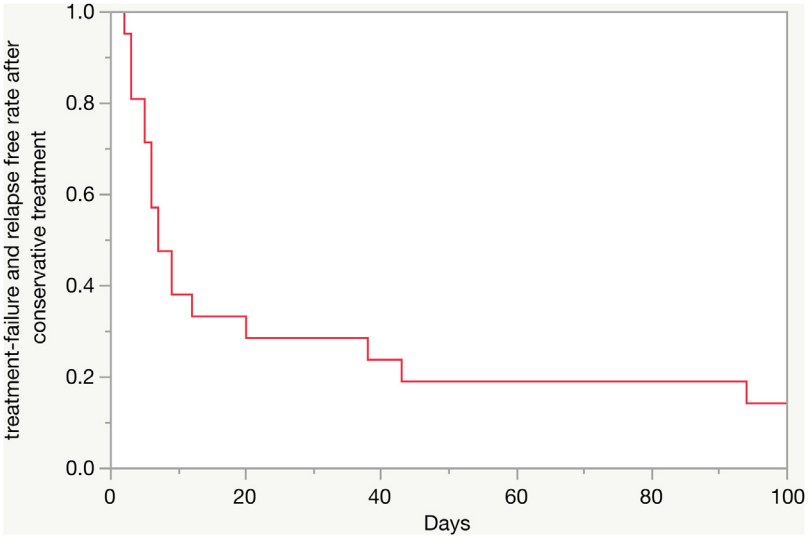

Fig. 2. The Kaplan-Meier cumulative treatment-failure and relapse free rate after conservative treatment.

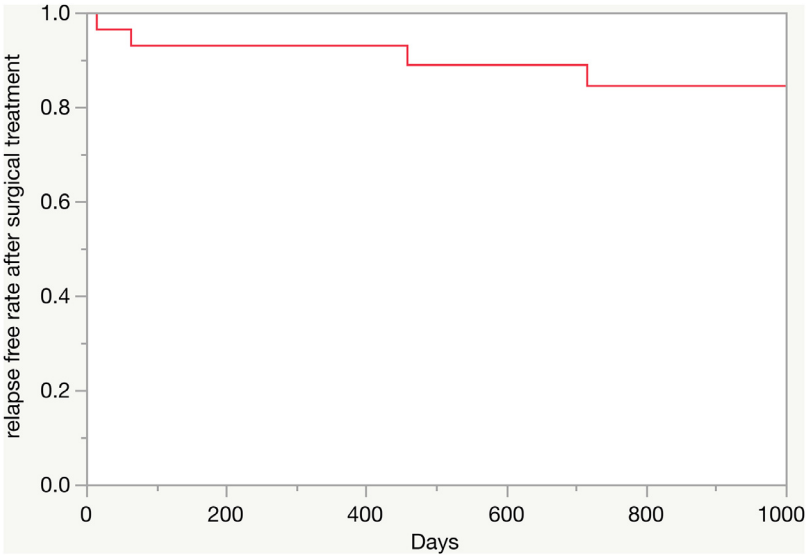

Fig. 3. The Kaplan-Meier cumulative relapse free rate after surgical treatment.

treatment could not be a definitive treatment modality for pneumothorax in patients with MFS. In contrast to the above findings, the VATS blebectomy, which is a standard procedure for treating pneumothorax in adults and children [10-11], was effective in treating pediatric patients diagnosed with both MFS and pneumothorax. We did not experience any difficulties in the perioperative management resulting from circulatory disorders associated with MFS or the VATS procedure resulting from skeletal abnormalities associated with MFS. In our study, the relapse rate of the surgical treatment was low and similar to that observed in the general pediatric population. Therefore, VATS blebectomy is a safe and reliable strategy for pneumothorax in children with MFS.

According to our results, conservative therapy such as chest tube drainage is not suitable as definitive treatment even for the first episode of pneumothorax in children with MFS due to the low response and high recurrence rate. In the view of preventing relapse and shortening the length of hospitalization, surgical treatment is recommended as soon as possible even for the first episode of pneumothorax in MFS

There are a few limitations in our study. All data were collected retrospectively from medical records and the selection of the treatment modality was dependent on the physician and patients' choice. Some of pneumothorax occurred in our MFS patients might not have been captured in this study, especially when the diagnosis and treatment of a patient were performed in another hospital. Our hospital is equipped with a multi-disciplinary clinic team designated to treat MFS patients. This could lead to a selection bias, and as such, the patient population in this study may not be an adequate representation of MFS patients.

Conclusion

Our study revealed a low response and high relapse rate of when pneumothorax in adolescents with Marfan syndrome were subjected to the conservative treatment modality. Thus, we recommend surgical intervention as the first line of therapy to treat pneumothorax in adolescents with MFS. Prospective clinical trials are needed to validate this strategy.

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References

[1] Hall JR, Pyeritz RE, Dudgeon DL. Pneumothorax in the Marfan syndrome: prevalence and therapy. Ann Thorac Surg 1984;37:500–4.
[2] Karpman C, Aughenbaugh GL, Ryu JH. Pneumothorax and bullae in Marfan syndrome. Respiration 2011;82:219–24.
[3] Wood JR, Bellamy D, Child AH, et al. Pulmonary disease in patients with Marfan syndrome. Thorax 1984;39:780–4.
[4] MacDuff A, Arnold A, Harvey J. Management of spontaneous pneumothorax: british Thoracic Society pleural disease guideline 2010. Thorax 2010;65 Suppl 2:ii18-31.
[5] Tschopp JM, Bintcliffe O, Astoul P, et al. ERS task force statement: diagnosis and treatment of primary spontaneous pneumothorax. Eur Respir J 2015;46:321–35.
[6] Robinson PD, Cooper P, Ranganathan SC. Evidence-based management of paediatric primary spontaneous pneumothorax. Paediatr Respir Rev 2009;10:110–17.
[7] Williams K, Oyetunji TA, Hsuing G, Hendrickson RJ, Lautz TB. Spontaneous pneumothorax in children: national management strategies and outcomes. J Laparoendosc Adv Surg Tech A 2018;28:218–22.
[8] Miscia ME, Lauriti G, Lisi G, Riccio A, Lelli Chiesa P. Management of spontaneous pneumothorax in children: a systematic review and meta-analysis. Eur J Pediatr Surg 2020.
[9] Lopez Monica E, et al. Management of the pediatric spontaneous pneumothorax: is primary surgery the treatment of choice? Am J Surg 2014;208(4):571–6.
[10] Ozcan C, McGahren ED, Rodgers BM. Thoracoscopic treatment of spontaneous pneumothorax in children. J Pediatr Surg 2003;38:1459–64.
[11] Stringel G, Amin NS, Dozor AJ. Video-assisted thoracoscopy in the management of recurrent spontaneous pneumothorax in the pediatric population. JSLS 1999;3:113–16.

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