

# Analysis of clinicopathological features of primary diaphragm tumors: A single-center study

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## Abstract

**Background and Objectives:** Primary diaphragm tumors are rare. The aim of this study was to explore the clinicopathological features of primary diaphragm tumor patients who underwent surgical treatment in our center to improve the diagnosis and treatment of this disease.

**Methods:** Clinical data of patients with primary diaphragm tumor who underwent surgery in our hospital from 2004 to 2019 were reviewed and analyzed.

**Results:** A total of 18 patients were enrolled. The male:female ratio was 8:10, and the median age was 58 years old (35–74 years old). Most patients included in this study had no typical clinical symptoms. Nine tumor cases were distributed in the left and right diaphragms separately, whereas 11 cases were located at the diaphragm angle. The diaphragm of 12 patients was reconstructed by direct suture. All postoperative pathologies showed that the tumors were benign, and cysts were observed in most of the cases (5/18).

**Conclusions:** There are no difference in distribution of gender and distribution on both sides of the diaphragm. In addition, primary diaphragm tumor is common in middle-age patients. Most cases occur in the diaphragm angle and are characterized by cyst lesions. Surgical resection is an effective treatment option for primary diaphragm tumor.

## KEYWORDS

clinical manifestations, diaphragm reconstruction, pathology, primary diaphragm tumor, surgery

## INTRODUCTION

Primary tumor of the diaphragm is an extremely rare disease. The incidence of primary diaphragm tumor (PDT) is lower compared with that of secondary diaphragm tumor that metastasizes from lung cancer, mesothelial malignancies, thymic cancer, and liver cancer. Approximately 200 cases of PDT have been reported in literature.<sup>1</sup> Currently, there is no clear process or guideline for diagnosis and treatment of PDT because of the low incidence, the various types of the disease, and the complex anatomic structures. The aim of this study was to analyze retrospectively PDT cases diagnosed and treated at our center in the past 15 years. The clinicopathological characteristics of the cases

were explored to provide clinical information on diagnosis and treatment of PDT in the future.

## MATERIALS AND METHODS

A retrospective analysis was conducted on PDT patients that underwent surgical treatment in Peking Union Medical College Hospital from 2004 to 2019. Clinical information, surgical and postoperative follow-up data, pathology diagnoses, and other related information of the enrolled patients were collected. Gender and age distribution, clinical manifestations, surgical methods, and pathological types of the cases were analyzed.

**TABLE 1** Summary of basic clinical information of enrolled patients

No.	Gender	Age (yr)	Diameter (cm)	Symptoms	Side	Approach	Site	Reconstruction methods	Pathology
1	Male	35	4	Asymptomatic	Right	Open	DA	Direct suture	Hemangioma
2	Male	74	3	Asymptomatic	Left	Open	DA	Direct suture	Lipoma
3	Female	40	10	Asymptomatic	Right	Open	DA	Direct suture	Cyst
4	Female	62	1.9	Chest pain	Left	VATS	DA	Direct suture	Fibroma
5	Female	63	0.8	Chest pain	Left	VATS	DD	Simply dissection	Cyst
6	Female	48	8	Asymptomatic	Right	Open	DD	Direct suture	Cyst
7	Female	69	4.3	PH	Right	Open	DD	Direct suture	Paraganglioma
8	Female	54	1.2	Asymptomatic	Right	VATS	DA	Simply dissection	Vascular malformation
9	Female	43	5.4	Asymptomatic	Right	Open	DA	Direct suture	Cyst
10	Male	47	0.9	Asymptomatic	Left	VATS	DD	Simply dissection	Fiber collagen
11	Male	63	3.1	Asymptomatic	Right	VATS	DA	Simply dissection	Fibrous lipoma
12	Female	62	7	FBS	Right	Open	DD	Direct suture	Leiomyoma
13	Male	59	4.7	Asymptomatic	Left	VATS	DA	Direct suture	Cyst
14	Male	54	1	Asymptomatic	Right	Open	DD	Direct suture	Fibrous calcified nodule
15	Female	58	8.6	Asymptomatic	Left	VATS	DA	Simply dissection	Fibroblastoma
16	Male	57	6	Asymptomatic	Left	VATS	DA	Simply dissection	Fatty tissue
17	Male	54	2	Asymptomatic	Right	LAP	DA	Direct suture	Foreign body granuloma
18	Female	62	1	Asymptomatic	Left	VATS	DD	Direct suture	Glassy degeneration

Abbreviations: DA, diaphragm angle; DD, diaphragmatic dome; FBS, foreign body sensation; VATS, video-assisted thoracic surgery; LAP, laparoscope; PH, paroxysmal hypertension.

## RESULTS

A total of 18 PDT cases were included in this study. Detailed information of included patients is shown in Table 1. The ratio of male:female patients enrolled in this study was 8:10, and the median age was 58 years old (35–74 years old). Of the 18 patients, 14 patients showed no clinical symptoms before surgery, two patients presented with chest pain, one patient reported a foreign body sensation in the upper abdomen, and one patient diagnosed with primary paraganglioma of the diaphragm with neuroendocrine activity presented with paroxysmal hypertension. Of the 14 asymptomatic patients, PDT was accidentally discovered in three patients during lung or liver surgery. The two patients with chest pain showed tumors 1.9 and 0.8 cm in size, and the tumors were characterized by fibromas and cysts. The size of tumor for the patient who complained of foreign body sensation in the upper abdomen was 7 cm, which was consistent with the clinical symptom.

The median maximum diameter of the primary tumor of the diaphragm for patients included in this study was 3.55 cm (0.8–10 cm). In this study, nine tumor cases were reported on each side implying that there was no significant difference in distribution of tumors on both sides of the diaphragm. In addition, of the 18 patients included in this study, 11 cases were diagnosed with tumors located at the diaphragm angle, whereas tumors in seven cases were located at the diaphragmatic dome. Among the patients included in this study, 17 cases were diagnosed with a single diaphragmatic tumor, whereas one case was diagnosed with

multiple tumors (on the same side), in which pathological diagnosis was presence of cysts.

All 18 patients in this study underwent surgery for PDT resection. A total of 10 patients were treated through a minimally invasive approach, whereas eight patients underwent an open surgical approach. A total of 12 patients underwent direct suture as the diaphragm reconstruction approach after tumor resection, whereas six patients underwent only tumor resection. No artificial patch or other materials were used for diaphragm reconstruction in patients enrolled in this study. The average postoperative hospital stay of the patients included in this study was 5 days (2–9 days). All patients recovered and were discharged after the operation except for one patient who had a second surgery for repair of diaphragmatic hernia after operation. That patient developed a diaphragmatic hernia 9 months after the surgery, causing intestinal obstruction symptoms. The patient underwent emergency surgery, and the diaphragm was directly sutured again under laparoscope.

Postoperative pathological analysis of the 18 patients included in this study showed that all tumors were benign. Pathological details are shown in Table 1. Notably, all patients had no definite pathological diagnosis before surgery.

## DISCUSSION

Diaphragm tumor is characterized by low incidence tumor and is comprised of primary and secondary diaphragm

tumor. The incidence of PDT is lower compared with that of secondary diaphragm tumor. Studies that explored PDT previously are mainly case reports, and only a few systematic retrospective studies have been reported because of its low incidence. Therefore, data available on PDT is limited, and its diagnosis and effective treatment approaches have not been fully explored. This study retrospectively analyzed PDT patients diagnosed and treated in our center for a period of 15 years, to improve understanding of PDT diagnosis and treatment.

In this study, clinicopathological characteristics of 18 patients with PDT were retrospectively analyzed. Analysis showed no significant difference in incidence between men and women (8:10). The median age of the patients enrolled in this study was 58 years, and most of the patients (11 cases) were between 30–60 years of age. Previous studies report primary bronchogenic cysts of the diaphragm found the clinical symptoms of PDT patients are not specific to tumors or have no correlation with diaphragm tumors. Patients with clinical symptoms present with pain as the main symptom of discomfort or report respiratory symptoms, such as persistent or intermittent cough.<sup>2</sup> Among the 18 patients enrolled in this study, 14 patients did not report discomfort before operation, and three patients were accidentally diagnosed with PDT when undergoing lung or liver surgery. Of the four patients with clinical symptoms, two patients presented with chest pain and further examination showed that the symptom was not significantly correlated with the PDT. In this study, one patient showed clinical symptoms associated with the primary tumor as manifested by a large tumor diameter (7 cm). The diaphragm is located between the chest and abdominal cavity, and the tumor of diaphragm can protrude to the chest or abdominal cavity and has a large growth space; clinical symptoms rarely develop before the tumor volume reaches a certain degree or affect an important organ. In addition, one patient in this study showed systemic symptoms because of diaphragmatic paraganglioma, which is a pheochromocytoma with neuroendocrine activity. The patient presented with symptoms that included paroxysmal hypertension, headache, and dizziness.

In this study, there was no significant difference in the distribution of PDT between the left and right side of the diaphragm. A retrospective study of 13 cases of diaphragmatic interstitial cysts by Kandemerli et al. reported that all cysts were distributed on the right diaphragm.<sup>3</sup> This study comprised a small sample size; further studies should explore distribution of PDT case on the diaphragm using a larger sample size. The findings of this study showed that most PDT cases were located at the angle of the diaphragm. The central area of the diaphragm comprises mainly the central tendon, and the diaphragm is surrounded by muscle fibers that migrate to the center. These anatomic characteristics show that diaphragm tumors are more likely to originate from the diaphragm angle.

Currently, there is no consensus in treatment of PDT, especially cysts. Previous studies report that volume of

primary diaphragm cysts stay stable and even decreased spontaneously after conservative observation.<sup>3,4</sup> Some studies report that use of puncture injection sclerotherapy for primary diaphragmatic cysts can significantly reduce the volume of cysts and achieve complete remission.<sup>4,5</sup> Although there are some advantages of this treatment approach, they are also associated with a few shortcomings. Bronchogenic cysts may undergo malignant degeneration after treatment using these methods.<sup>2,6</sup> All the patients included in this study underwent surgical treatment. Although open and minimally invasive approaches, as well as thoracic and abdominal approaches, are available, all patients in this study received complete surgical resection. In this study, six patients underwent simple tumor resection, whereas 12 patients underwent diaphragm reconstruction during the surgery. All the cases were directly sutured and no artificial patch or other materials were used for diaphragm reconstruction. A previous study enrolled 21 patients diagnosed with diaphragmatic bronchogenic cysts and reported that 69.2% of the patients underwent direct suture to reconstruct the diaphragm.<sup>2</sup> Reconstruction of the diaphragm defect by artificial patch or autologous tissue is performed if the diaphragm defect is large or the diaphragm is completely removed. Most commonly used synthetic patch materials include polytetrafluoroethylene, polypropylene, and polyolefin. The most commonly used autologous tissues are the pedicled latissimus dorsi and anterior muscle flap and the fascia lata.<sup>1</sup> In the present study, one patient developed diaphragmatic hernia 9 months postoperatively and presented with intestinal obstruction symptoms. This finding implies that diaphragmatic hernia may develop long after diaphragm reconstruction. Therefore, intra-abdominal pressure should be controlled and monitor the patient for any complications.

Incidence of benign and malignant primary tumors of the diaphragm is similar.<sup>1</sup> Most common benign PDT includes cysts and lipomas that are divided into mesothelial cysts and bronchial cysts based on the overlying epithelium of the cystic wall.<sup>7</sup> Most common primary malignant tumors of the diaphragm include rhabdomyosarcoma and fibrosarcoma.<sup>1,7</sup> All the cases in this study were benign and consistent with previous studies, cysts (5/18) were the most common lesion type. Because this study is a retrospective study and the incidence of primary diaphragm tumors is extremely low, the number of patients enrolled is small, and these may be the reasons why all tumors are benign. Solid tumors such as lipomas, hemangiomas, and fibroma were also reported. The patients included in this study did not show definite pathological diagnosis before operation, and pathology was confirmed by surgical resection. This further explains the limitation of biopsy methods such as puncture used for diagnosis of PDT.

This study has a few limitations. First, incidence of primary diaphragmatic tumors is relatively low, and this study was a single-center study. Therefore, the number of cases included in this study was small. A higher number of enrolled cases can be obtained through multi-center studies.

In addition, pathological types in this study were complex; therefore, it was impossible to conduct an in-depth analysis of a specific pathological type of PDT.

## CONCLUSIONS

This study explored the clinicopathological characteristics of PDT patients who were diagnosed and treated at our center in the past 15 years. The findings showed that there are no difference in gender and distribution on both sides of the diaphragm. Most of the patients diagnosed with PDT were middle-age patients. In addition, most PDT cases originated from the diaphragmatic angle sources, and most patients were diagnosed with cyst lesions. Surgical resection achieved complete tumor resection and accurate pathological diagnosis. Studies should further explore diagnosis and treatment of PDT through multi-center collaborative research.

## CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

## DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article.

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