ORIGINAL ARTICLE

The importance of diaphragmatic surgery, chemical pleurodesis and postoperative hormonal therapy in preventing recurrence in catamenial pneumothorax: a retrospective cohort study

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Abstract

Background Catamenial pneumothorax (CP) is defined as a recurrent, spontaneous pneumothorax occurring within a day before or 72 h after the onset of menstruation. Most first episodes go undiagnosed and treated as primary spontaneous pneumothorax, and only after recurrence is the clinical suspicion of CP raised. No gold-standard management approach exists, especially in terms of managing diaphragmatic involvement.

Methods This study is a single-centre cohort retrospective study of 24 female patients who underwent surgery for pneumothorax due to diaphragmatic endometriosis between January 2008 and December 2016. Two groups were compared: a group that underwent pleurodesis alone (8 patients) and a group that underwent diaphragmatic surgery and pleurodesis (16 patients).

Results There were differences in BMI and smoking habits between the two groups. The right diaphragm was involved more often (6vs15, $p = 0.190$). VATS was the preferred surgical approach and only one conversion occurred in the diaphragmatic surgery group ($p = 0.470$). Diaphragmatic abnormalities were present in all the patients, brown/violet spots (100%) in the pleurodesis group and perforations (100%) in the diaphragmatic surgery group ($p < 0.001$). There were no differences in days of chest tube removal and length of stay. The recurrence rate was 100% in the pleurodesis alone group while it was only 12.5% in the diaphragmatic surgery group (< 0.001).

Conclusions In our experience, diaphragmatic surgery and pleurodesis followed by hormonal therapy was an effective approach in preventing recurrence in patients with catamenial pneumothorax and diaphragmatic involvement.

Keywords Catamenial pneumothorax · Endometriosis · Hormone therapy · Diaphragmatic surgery · Video-assisted thoracoscopic surgery (VATS)

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Introduction

Thoracic endometriosis syndrome (TES) is divided into five clinical entities, namely catamenial pneumothorax (CP) the most common presentation, non catamenial endometriosis related pneumothorax, catamenial haemothorax, catamenial haemoptysis and lung nodules [1]. CP is defined as a recurrent (more than 2 episodes) spontaneous pneumothorax occurring within a day before or 72 h after the onset of menstruation. The aetiology is not well understood and no gold-standard management approach exists [2]. A correlation between menstruation and haemoptysis was first noted by Schwarz in 1938 [3]. In 1953, Barnes described concurrent endometriosis and pleural haematomas [4], while the first case of recurrent pneumothorax during menstruation was reported by Maurere et al. in 1958 [5]. Lillington et al.

officially termed the phenomenon catamenial pneumothorax in 1972 [6]. Our study aimed to retrospectively compare the rate of recurrence, postoperative complications and length of hospital stay in two groups, one that underwent diaphragmatic surgery, pleurodesis and post-operative hormonal therapy and one that underwent pleurodesis alone for catamenial pneumothorax.

Patients and methods

This study is a single-centre cohort retrospective study of consecutive female patients who underwent surgery for pneumothorax due to diaphragmatic endometriosis between January 2008 and December 2016. The institutional review board of the hospital waived the requirement for ethics approval and informed consent for the collection, analysis, and publication of the retrospectively obtained anonymized data for this non interventional study.

Two groups were created. In the pleurodesis alone group, diaphragm involvement was considered dubious during surgery and left untouched and only pleurodesis and pulmonary resection was performed. In the diaphragmatic surgery group, diaphragmatic surgery was deemed necessary and performed along with pleurodesis.

The primary endpoint of this retrospective study was:

- Recurrence

The secondary end points were as follows:

- Complications
- Length of hospital stay (LOH)

All patients who underwent video-assisted thoracoscopic surgery (VATS) or open surgery for catamenial pneumothorax were included in the study. The exclusion criteria was no endometrial cells in the pathological specimen.

Patient demographics, surgical and hormonal therapy, post-operative complications, morbidity, mortality, and endometriosis related data were analysed. Indications for surgery were as follows: recurrent pneumothorax; prolonged (i.e., 5 days) air leak and/or pneumothorax despite adequate chest drainage; and failure of previous surgery.

In the pleurodesis alone group, the surgical procedure was carried out as a standard primary spontaneous pneumothorax, performing apical resection of the lung using a mechanical stapler and mechanical or chemical pleurodesis, according to the surgeon's preference.

In the diaphragmatic surgery group, after confirmation of diaphragmatic involvement (Fig. 1), one of the following procedures was performed: resection with a mechanical stapler in case of multiple perforations or spots; direct suture
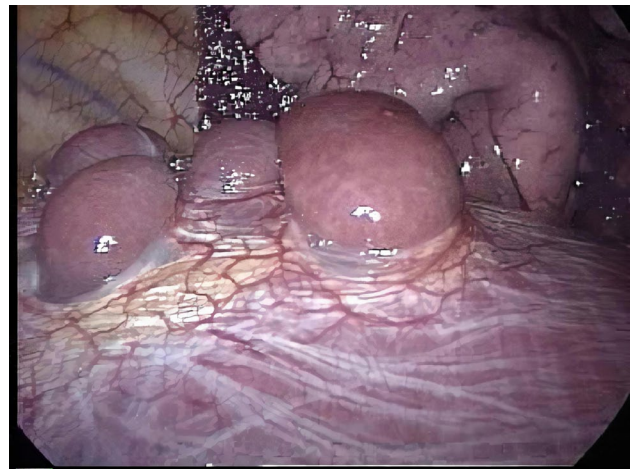

Fig. 1 Intraoperative view of holes of the right diaphragm with liver herniation

in case of small perforations; plication in case of relaxation; and suture and plication when relaxation and perforations were discovered. VATS constituted the operative technique of choice, except in one patient who underwent multiple surgeries for a recurrent pneumothorax in another centre. In both groups mechanical abrasion pleurodesis was carried out on all of the pleura, except the diaphragm, using a cautery tip cleaner, while chemical pleurodesis was performed using 4 g of sterile talc powder sprayed uniformly directly onto the parietal pleura using a single-use pressurised spray canister.

The chest tube was removed after confirming the absence of air leakage. Chest X-rays were performed one month after the operation or if necessary. Patients were surveyed for recurrence by phone interview 6 months and every year for 3 years after surgery (2–2.5 years of follow up after completing hormonal therapy). A recurrence was defined as an ipsilateral pneumothorax demonstrated by radiological examinations.

All the patients in the diaphragmatic surgery group were referred to the gynaecological department after surgery for hormonal therapy. The patients underwent routine hormonal treatment with gonadotropin-releasing hormone analogues for 6–12 months. The pleurodesis alone group did not receive any hormonal therapy after the first surgery but they were referred to the gynaecological department after the second surgery once the diagnosis was confirmed histopathologically.

Statistical analysis

Analyses were conducted with IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Continuous variables are expressed as a mean ± standard deviation (SD) or median and range when

appropriate, categorical variables are expressed as numbers and percentages.

The significance level was set to 5% ($p = 0.05$). The two groups were compared by the unpaired t test or Mann–Whitney U test applied to discrete or continuous data, and by the chi-square test, applied to dichotomous or categorical data.

Results

Demographics of the 24 patients are shown in Table 1. There were differences in BMI (higher in the diaphragmatic surgery group) and smoking habits (more frequent in the pleurodesis alone group). Only 2 patients in the diaphragmatic surgery group had a previous history of endometriosis. Surgical results are shown in Table 2. The most frequent indication for surgery was recurrence in both groups (87.5 vs. 93.8%, $p = 0.602$). The right side was prevalent (6 vs. 15, $p = 0.190$). VATS was the preferred surgical approach and only one conversion occurred in the diaphragmatic surgery group ($p = 0.470$). A lung resection was performed in all patients in the pleurodesis alone group and 11 in the diaphragmatic surgery group ($p = 0.076$). Diaphragmatic abnormalities were discovered in all the patients. In the pleurodesis alone group brown/violet spots (100%) in the diaphragmatic surgery group (100%) perforations were observed in the diaphragm, $p < 0.001$. In the diaphragmatic surgery group,

diaphragmatic surgery was performed as follows: resection with a mechanical stapler in 9 patients (56.3%), suture in 3 (18.8%), plication in 2 (12.5%) and suture and plication in 2 (12.5%). In the pleurodesis alone group mechanical pleurodesis was performed in 8 patients (100%) while in the diaphragmatic surgery group chemical pleurodesis was performed in 16 patients (100%), $p < 0.001$. Two patients in the diaphragmatic surgery group experienced complications: one had air leak and one a reaction to talc (fever and desaturation treated successfully with low-flow oxygen and corticosteroids). Nine patients in the diaphragmatic surgery group had a residual space, defined as a gap between the visceral pleura and the chest wall on a chest radiograph, but no patient had the same condition in the pleurodesis alone group ($p = 0.026$). There were no differences in days of chest tube removal, LOH and 90-day mortality.

Table 3 shows recurrence results of the two Groups. All patients in the pleurodesis alone group experienced a recurrence requiring surgery and diaphragmatic intervention, while just 2 patients experienced a recurrence in the diaphragmatic surgery group. Both of them underwent further surgery ($p < 0.001$). No recurrence occurred in the diaphragmatic surgery group after discontinuing hormonal therapy (2–2.5 years of follow up). Differences were observed in terms of postoperative smoking (5 vs. 2, $p = 0.011$) and hormonal therapy (0 vs. 16, $p < 0.001$). The second surgery was effective in every patient.

Table 1 Clinical characteristics of the patients

Variable	Group pleurodesis ($n = 8$)	Group diaphragmatic surgery ($n = 16$)	p-value
Age, years	27.75 ± 6.341	30.69 ± 6.343	0.296
BMI	19.64 ± 0.99	21.50 ± 2.28	0.040*
Smoking status			
Never	3 (37.5%)	13 (81.3%)	0.032*
Former or current	5 (62.5%)	3 (18.8%)	
Comorbidities			
None	8 (100%)	15 (93.8%)	0.470
Asthma	0 (0%)	1 (6.2%)	
Diagnosis of endometriosis before surgery	0 (0%)	2 (12.5%)	0.296
Surgical indication			
Recurrence	7 (87.5%)	15 (93.8%)	0.602
Persistent air leak (> 5 days)	1 (12.5%)	1 (6.2%)	
Side involved			
Right	6 (75.0%)	15 (93.8%)	0.190
Left	2 (25.0%)	1 (6.2%)	

Data are presented as mean (SD), median (P_{25}–P_{75}) or n (%)

BMI body mass index

*$p < 0.05$

Table 2 Surgical results of the patients

Variable	Group pleurodesis ($n=8$)	Group diaphragmatic surgery ($n=16$)	p-value
Surgical approach			
VATS	8 (100%)	15 (93.8%)	0.470
Open	0 (0%)	1 (6.2%)	
Conversion to standard VATS/thoracotomy	0 (0%)	1 (6.2%)	0.470
Pulmonary resection (yes/no)	8 (100%)	11 (68.8%)	0.076
Number of pulmonary resections			
None	0 (0%)	5 (31.3%)	0.127
One	6 (75.0%)	10 (62.5%)	
Two	2 (25.0%)	1 (6.2%)	
Pulmonary resection (lobe)			
Upper	6 (75.0%)	8 (50.0%)	0.234
Middle	0 (0%)	1 (6.2%)	
Lower	0 (0%)	1 (6.2%)	
Upper and lower	2 (25.0%)	1 (6.2%)	
Pleurodesis type			
Brushing	8 (100%)	4 (25.0%)	0.001*
Chemical	0 (0%)	12 (75.0%)	
Diaphragmatic endometriosis			
Yes	0 (0%)	15 (93.8%)	<0.001*
No	0 (0%)	0 (0%)	
Doubts	8 (100%)	1 (6.2%)	
Type of diaphragmatic endometriosis			
Perforations	0 (0%)	16 (100%)	<0.001*
Brown/violet spots	8 (100%)	0 (0%)	
Nodules	0 (0%)	0 (0%)	
Type of diaphragmatic surgery			
Resection with mechanical stapler	0 (0%)	9 (56.3%)	<0.001*
Suture	0 (0%)	3 (18.8%)	
Plication	0 (0%)	2 (12.5%)	
Suture and plication	0 (0%)	2 (12.5%)	
Complications	0 (0%)	2 (12.5%)	0.296
Type of complication			
Air leak	0 (0%)	1 (6.2%)	0.580
Talc reaction	0 (0%)	1 (6.2%)	
Residual space (yes/no)	0 (0%)	9 (56.3%)	0.026*
Residual space (mm)	0 (0)	4.75 ± 5.939	0.036*
Chest tube removal after surgery (days)	4.38 ± 0.916	4.56 ± 2.920	0.862
LOS (days)	5.38 ± 0.916	5.19 ± 1.682	0.773
90-day mortality	0 (0%)	0 (0%)	–

Data are presented as mean (SD), median (P_{25}–P_{75}) or n (%)

VATS video-assisted thoracoscopic surgery, *LOS* length of hospital stay

*$p<0.05$

Comment

Catamenial pneumothorax is defined as a recurrent pneumothorax that occurs between 24 h before and 72 h after the onset of menstruation, usually presenting with dyspnea and chest and/or shoulder pain [2]. It most often occurs on the right side in the absence of other lung diseases. In the past CP was treated conservatively with chest tube insertion and this is still performed in first-line emergency treatment, however the high rate of recurrence led to the adoption of an early surgical approach [7]. Initially it was believed that as many as 6% of spontaneous pneumothorax were due to

Table 3 Treatment and outcomes after recurrence

Variable	Group pleurodesis ($n=8$)	Group diaphragmatic surgery ($n=16$)	p-value
Recurrence	8 (100%)	2 (12.5%)	<0.001*
Timing of recurrence (months)	8.0 (6.0–12.0)	23.0 (1.0–45.0)	0.629
Hormonal therapy (yes/no)	0 (0%)	16 (100%)	<0.001*
Smoking after surgery	5 (62.5%)	2 (12.5%)	0.011*
Redu	8 (100%)	2 (12.5%)	<0.001*
Redu approach			
VATS	1 (12.5%)	1 (6.2%)	<0.001*
Open	7 (87.5%)	1 (6.2%)	
Type of diaphragmatic surgery			
Resection with mechanical stapler	3 (37.5%)	0 (0%)	<0.001*
Suture	5 (62.5%)	0 (0%)	
Plication	0 (0%)	1 (6.2%)	
Complications of redu	0 (0%)	0 (0%)	–
Recurrence after redu	0 (0%)	0 (0%)	–

Data are presented as mean (SD), median (minimum–maximum) or n (%)

VATS video-assisted thoracoscopic surgery

*$p < 0.05$

CP, but recent reports suggest that these cases could make up as many as 35% of primary spontaneous pneumothorax (PSP) in women [8–11]. The most likely explanation for this increase is the use of VATS to accurately examine the diaphragmatic surface, with one series reporting diaphragmatic changes in 89% of CP cases when undergoing diaphragmatic exploration in VATS [12]. Diagnosis is often difficult as one has to have a high clinical suspicion of CP, and therefore most first episodes are diagnosed as PSP. The most likely mechanism of CP development is the transdiaphragmatic passage of air via perforations or nodules on the diaphragmatic surface [5, 13, 14]. The most commonly discovered abnormalities during VATS for CP are found on the tendinous portion of the diaphragm [15–17]. These abnormalities consist of perforations usually a few millimetres wide or endometrial deposits less than 1 cm in size that vary in colour from brown to violet [15, 18].

The most important findings of our retrospective study comparing a group that underwent diaphragmatic resection and pleurodesis and a group that underwent pleurodesis alone was the recurrence of pneumothorax. In the diaphragmatic surgery group all 16 patients had TES presenting as perforations of the diaphragm while in the pleurodesis alone group all 8 patients presented with brown/violet spots that were considered to be non-conclusive by the operator and therefore were not removed. Only 12.5% of the diaphragmatic surgery group experienced recurrence while 100% of the pleurodesis group experienced recurrence ($p < 0.001$). The importance of diaphragmatic surgery is emphasized by the fact that all 8 cases in the pleurodesis group underwent diaphragmatic surgery after the initial failed operation and

no recurrence occurred after diaphragmatic resection. Our study is the first of its kind comparing two groups, one that underwent surgery of the diaphragm and one that did not in patients with suspected CP and diaphragmatic changes seen in VATS. Our findings confirm those of previous studies which suggest that the optimal treatment for CP with ectopic endometrium is diaphragmatic surgery, pleurodesis and postoperative hormonal therapy as this combination proved effective in 100% of patients in the diaphragmatic surgery group. Joseph et al. found that the recurrence rate after diaphragmatic surgery alone was 30% while after hormonal therapy alone it was 50% [7]. Other reports have concluded similar results of a 30–32% recurrence rate of CP [19, 20], while one study had a recurrence rate of 39.1% in which the conclusion was that the rate was higher due to their limited use of pleurodesis, further demonstrating the importance of performing diaphragmatic surgery and an effective pleurodesis to limit the recurrence rate [21]. Alifano et al. conclude in their extensive publication on the current knowledge of thoracic endometriosis that diaphragmatic resection is most likely the best approach to any evidence of endometrial tissue and perforations of the diaphragm [2]. Suturing of perforations without resection has been associated with recurrence and it does not provide tissue samples to obtain histological diagnosis of thoracic endometriosis [22]. Furthermore, it has been hypothesised that endometrial tissue left in place can cause further perforations of the diaphragm and can spread within the thoracic cavity [2]. Although definitive evidence has not been published from randomized controlled trials, recent studies have identified the best approach for this disease, which is a multimodal

approach with diaphragmatic resection followed by hormonal therapy that is not prolonged due to potential side effects [15, 18, 23–27]. Our data may confirm this hypothesis as we did not observe any recurrences after discontinuation of hormonal therapy. Subotic et al. published a series in which 9 of their patients who underwent diaphragmatic resection could not undergo postoperative hormonal therapy and none of them had disease recurrence [28]. Maramatsu et al. stress the mandatory nature of localising and removing diaphragmatic abnormalities as hormonal therapy cannot be maintained for a long period of time, due to the side effects [29]. The type of pleurodesis performed in our study was also significant as 100% of pleurodesis in the group that experienced recurrence was mechanical pleurodesis and 75% of pleurodesis in the diaphragmatic group was chemical. The superiority of chemical pleurodesis in reducing PSP recurrence rate has already been demonstrated [30], therefore we recommend, when possible, performing diaphragmatic resection in conjunction with a chemical pleurodesis, as suggested by Fournel et al. in order to obtain a more efficient and permanent pleurodesis preventing recurrence which frequently occurs at the lower chest [31].

The present study has several limitations to be acknowledged. First of all, this is a retrospective study, comparing two groups that differed for BMI and smoking status, we cannot rule out that the inclusion of patients with different clinical characteristics may have affected our results. Secondly, the pleurodesis alone group did not undergo postoperative hormonal therapy limiting the possible role of diaphragmatic surgery alone in preventing the pneumothorax recurrence. Furthermore, due to the limited sample size, future studies are warranted to generalise our conclusions.

Conclusion

Despite a large proportion of CP cases going undiagnosed, VATS has significantly improved the diagnosis and management of these cases. In our experience, performing a combined approach of diaphragmatic resection of perforations and/or endometrial spots, chemical pleurodesis and hormonal therapy proved effective when compared to pleurodesis alone. Hormonal therapy emerged as an independent predictive factor for recurrence of pneumothorax and therefore we suggest this treatment in the postoperative period.

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