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RESEARCH

Clinical features and management of thoracic endometriosis: a 20-year monocentric retrospective study

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Abstract

Purpose Although thoracic endometriosis (TE) represents the most common manifestation of extra-pelvic endometriosis, it is a rare condition and currently there is no established clinical guideline for the management of this condition. The study's primary objective was to assess patient satisfaction with the treatment provided. A secondary objective was to investigate the efficacy of different treatment modalities in terms of symptom and lesion recurrence.

Methods A retrospective review of the clinical records of all women with TE who had been referred to our institution, a tertiary referral center, was conducted between January 2000 and September 2021. A frequency analysis was performed for all the variables examined in the study. The Kaplan–Meier method was adopted to analyse the time from thoracic surgery to PNX recurrence. Lastly, an intention-to-treat analysis was performed.

Results Regarding clinical presentation, 50% of women (30/60; 95% CI 36.8–63.2) experienced at least one episode of pneumothorax (PNX). A total of 61.7% of the women in the study underwent surgical intervention, while 36.6% received pharmacological treatment. The cumulative recurrence rate of the first PNX following surgery was 0.26 (0.13–0.41) and 0.82 (0.44–0.95) at six months and 240 months, respectively. At the follow-up assessment, regardless of the administered treatment modality, over half of the women included in the study reported being satisfied with their treatment (PGIC). Additionally, most of them described their overall condition as having improved since the onset of the treatment (PGIS).

Conclusion Both surgical and pharmacological treatments are valuable options for TE. Rather than being considered mutually exclusive, these approaches should be viewed as complementary.

Keywords Menstruation · Catamenial pneumothorax · Hormonal therapy · Surgery · Endometriosis · Thoracic endometriosis

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What does this study add to the clinical work

While thoracic endometriosis is a rare condition, it is of significant clinical importance to be able to identify and treat these patients at the earliest possible stage. The use of pharmacological therapy in association with or in the alternative to surgery represents the gold standard of treatment.

Introduction

Thoracic endometriosis is among the most common forms of extrapelvic endometriosis, affecting diaphragm, pleura, or lungs, with the diaphragm being the predominant site of involvement [1, 2].

Among 9178 patients undergoing abdominal surgery for endometriosis, diaphragmatic involvement was found in only 2.3%, with earlier estimates even lower, suggesting TE is a rare diagnosis [3–5]. Even if thoracic and parietal (umbilical, groin, and abdominal wall) endometriosis are rare entities [3], they are considered the most common forms of extrapelvic endometriosis, occurring in 9–15% of patients [6]. The literature reports that the prevalence of diaphragmatic endometriosis ranges between 0.67% and 4.7% [7, 8].

The etiology of TE is not well understood. Possible factors include the migration of refluxed endometrial cells, coelomic metaplasia, and lymphatic or hematogenous spread of endometrial tissue [9, 10]. Retrograde menstruation is often cited as a primary explanation, as endometrial cells can reflux through the fallopian tubes and be transported via peritoneal circulation in a clockwise direction to the right hemidiaphragm and channeled onto the falciform and round ligaments of the liver [11, 12]. This migration is facilitated by the pressure gradient between the abdominal and thoracic cavities, explaining the prevalence of right-sided TE in 80–90% of cases [1, 13]. The coexistence of multiple thoracic localizations is extremely rare (1.1%) [13, 14].

Thoracic endometriosis lesions are most frequently found in the diaphragm (44.5%), with pleural (12.7%) and lung (4.5%) involvement being less common [1]. Symptoms typically arise within three days of menstruation and are linked to lesion location [13, 15, 16] although they may not manifest during every menstrual cycle [17]. Diaphragmatic pain is often felt in the scapula and less frequently in the chest (10%), while pleural lesions can cause catamenial chest pain in 23% of cases. Catamenial hemoptysis occurs in 82% of lung lesions [1, 18]. Symptoms associated with TE may be subtle and elude routine clinical evaluation [3].

Management of TE remains debated. Some advocate for pharmacological therapy as first-line treatment, reserving surgery for refractory cases [19], while others recommend video-assisted thoracic surgery with focal resection of pleural or diaphragmatic defects and laparoscopy as gold standard treatment [1]. Given the recurrence rate of up to one-third post-surgery, adjuvant pharmacological therapy and close ongoing surveillance are recommended [1, 20].

In this context, we conducted a retrospective study to analyse symptoms, recurrence PNX rates, psychological well-being, and quality of life in women with TE, focusing on their long-term satisfaction with different treatment modalities (surgical, pharmacological, or combined treatments).

Materials and methods

We retrospectively reviewed all cases of women with a clinical or surgical diagnosis of TE who were referred to our tertiary center, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy, between January 2000 and September 2021. The study was approved by the local Institutional Review Board (Ethics Committee Milan Area 2, reference 993_2021), and all participants provided informed consent for clinical data for research.

Two researchers (FL.O. and D.A.) examined clinical records and recorded patients' data into a digital dataset, collecting variables such as age at diagnosis of endometriosis, body mass index (BMI), medical, surgical, and obstetric history, concomitant endometriotic lesions, imaging results, treatment received for TE, follow-up duration, post-operative TE recurrence and time to recurrence (months).

The same investigators contacted participants to invite them for clinical examination and to complete standardized health questionnaires. Quality of life (QoL) was assessed with the Short Form-12 (SF-12) questionnaire [21], which measures women's perception of their overall health status, with higher scores indicating a better QoL. Psychological well-being was evaluated using the Italian version of the Hospital Anxiety and Depression Scale (HADS) [22], consisting of two seven-item scales for anxiety and depression (each scale scores ranging from 0 to 21), where higher scores indicate worse psychological conditions. Patients' general health status was analysed with the seven-item Patients' Global Impression of Change (PGIC) scale (ranging from "1" meaning "very much improved", to "7" meaning "very much worsened"). Pain symptoms were assessed using the Patients' Global Impression of Severity (PGIS) scale, consisting of five levels (none, little, a bit, much, very much) [23]. All questionnaires used in the study are available as supplemental materials (Online Resource 1, 2 and 3).

Participants were specifically queried about TE-related symptoms, recurrent catamenial PNX episodes, and

satisfaction with their treatment, according to a five-category scale (very satisfied, satisfied, neither satisfied nor dissatisfied, dissatisfied, very dissatisfied). Postoperative recurrence of catamenial PNX and thoracic symptoms, such as shortness of breath, pleuritic chest pain, shoulder pain, and cough were considered TE recurrences, regardless of radiological findings.

A frequency analysis was performed for all variables, with continuous variables reported as means and standard deviations. Categorical variables were analysed using the chi-square test or Fisher's exact test, presented as absolute values and percentages. The Kaplan–Meier method was adopted to assess the time from thoracic surgery to PNX recurrence, the primary symptom related to TE recurrence. An intention-to-treat analysis was performed, with patients lost to follow-up categorized as "not-satisfied".

Results

A total of 60 women with TE were referred to our endometriosis center during the study period. Eight (13.3%) did not reply to re-evaluation invitations and were considered lost to follow-up. Although these patients were included in the intention-to-treat analysis to evaluate the study's primary outcome, they were excluded from demographic and clinical data.

Table 1 reports the demographic and clinical characteristics of the enrolled women. Patients' mean age was 41.4 ± 7.1 years, with a mean TE diagnosis age of 34.5 ± 7.3 years. Regarding tobacco use, 67.3% (95% CI 52.9–79.7) were non-smokers, 11.5% (95% CI 4.4–23.4) were smokers, and 21.2% (95% CI 11.1–34.7) were former smokers. The mean BMI was 21.9 ± 3.3 kg/m^2. Nulliparity was reported in 56.7% (95% CI 43.2–69.4) of women, while 23.3% (95% CI 13.4–36.0) had previously had a vaginal delivery, and 20% (95% CI 10.8–32.3) had undergone a caesarean section.

The analysis of women's clinical manifestations revealed that 25% (95% CI 14.7–37.9) of women reported no thoracic symptoms, while 75% (95% CI 62.1–85.3) were symptomatic. The most common manifestation was right catamenial PNX (41.6%, 95% CI 29.1–55.1). Only 3.3% (95% CI 0.4–11.5) reported non-catamenial right PNX and 5% (95% CI 1.0–13.9) had both catamenial and non-catamenial right PNX. Left PNX was observed in only two patients with a history of recurrent right PNX. A total of 119 episodes of PNX were recorded during follow-up, with a mean of 4.0 ± 2.4 episodes per patient (*data not shown*).

The second most common clinical manifestation was catamenial right shoulder pain (38.3%, 95% CI 26.1–51.8). Catamenial pleuritic pain occurred in 28.3% of patients (95% CI 17.4–41.4) and catamenial dyspnoea in 11.6% (95% CI 4.8–22.6). Haemoptysis and cough were reported by one patient, diagnosed with an endometriotic pulmonary nodule.

A total of 51.9% of women underwent a chest X-ray (95% CI 37.6–66.0), 53.8% (95% CI 39.5–67.8) performed computed tomography, and 9.6% (95% CI 3.2–21.0) magnetic resonance imaging (Table 1). Despite this, only 6% received a confirmed diagnosis of TE (95% CI 1.2–16.0).

Extra-thoracic endometriosis was detected in 83.3% of women, with multiple sites possible within the same patient (Table 1).

Regarding treatment modality, 61.7% of women underwent surgery (95% CI 48.2–73.9), 36.6% (95% CI 24.6–50.1) received hormonal therapy, and one patient was untreated. Exploratory laparoscopy was performed in 55% (95% CI 41.6–67.9). Among the 37 women who had surgery, 8.1% (95% CI 1.7–22) were treated with pharmacological therapy before surgery and 32.4% (95% CI 18.0–49.8) received pharmacological treatment both before and after surgery. Only 25% (95% CI 12.1–42.2) of biopsies confirmed TE histologically (9/36) (Table 2), while the remaining 75% of cases presented with histological results that were negative for endometriosis, frequently demonstrating nonspecific findings. Overall, considering together women who underwent surgery and those with hormonal treatment only, 33.3% (95% CI 21.7–46.7) were treated with combined oral contraceptives (COCs) and progestogens, 26.7% (95% CI 16.1–40.0) with COCs only, 20% (95% CI 10.8–32.3) with progestogens only, and 15% (95% CI 7.1–26.6) with GnRH agonists for over six months. Only 5% of patients receive no pharmacological treatment (95% CI 1.04 –13.9).

Thoracoscopy was conducted in 73% of patients (27/37), and 27% (10/37) had laparoscopic resection of diaphragmatic lesions (Table 3). Diathermocoagulation of endometriotic lesions and lung resection with pleurodesis were our case series' most commonly performed surgical procedures (Table 3). During the study period, 40.7% (95% CI 22.4–61.2) of women underwent one thoracic surgery, while 59.3% (95% CI 38.8–77.6) underwent multiple surgeries.

The mean follow-up period was 109.8 ± 67.1 months (3 months to 22 years). During this time, the cumulative incidence of the first PNX recurrence after surgery, according to the Kaplan–Meier analysis, was 0.26 (0.13–0.41), 0.44 (0.26–0.61), 0.60 (0.39–0.76), 0.82 (0.44–0.95) at six months, 24 months, 36 months and 240 months, respectively. As regards the analysis of the second post-surgical recurrence of PNX, the cumulative incidence was 0.26 (0.09–0.47) at 12 months and 0.50 (0.21–0.74) at 240 months (Fig. 1).

The satisfaction of women undergoing surgical or hormonal treatment at the time of revaluation is shown in Fig. 2. A total of 80% (95% CI 56.3–94.3) of patients undergoing surgical treatment with a follow-up of 9 to 22 years said

Table 1 Clinical and demographic characteristics of recruited patients

Characteristics	Patients % (*n*/total)[a]
Age (years)	41.4 ± 7.1*
Smoke	
Never smoker	67.3 (35/52)
Current smoker	11.5 (6/52)
Ex-smoker	21.2 (11/52)
BMI (Kg/m^2)	21.9 ± 3.3*
Age at diagnosis (years)	34.5 ± 7.3*
Obstetric history	
Nulliparous	56.7 (34/60)
Multiparous	43.3 (26/60)
Vaginal delivery	23.3 (14/60)
Caesarean section	20 (12/60)
Chest diagnostic imaging[b]	
None	32.7 (17/52)
X-ray	51.9 (27/52)
CT	53.8 (28/52)
MRI	9.6 (5/52)
Thoracic symptoms	
Present	75 (45/60)
Absent	25 (15/60)
Pneumothorax[c]	
Absent	50 (30/60)
Right-sided non-catamenial	3.3 (2/60)
Right-sided catamenial	41.6 (25/60)
Right-sided catamenial and non-catamenial	5 (3/60)
Left-sided non-catamenial	1.7 (1/60)
Left-sided catamenial	1.7 (1/60)
Haemoptysis	
Absent	98.3 (59/60)
Non-catamenial	0 (0/60)
Catamenial	1.7 (1/60)
Lung nodules	
Absent	98.3 (59/60)
Present	1.7 (1/60)
Cough	
Absent	91.6 (55/60)
Non-catamenial	6.7 (4/60)
Catamenial	1.7 (1/60)
Dyspnoea	
Absent	81.7 (49/60)
Non-catamenial	6.7 (4/60)
Catamenial	11.6 (7/60)
Pleuritic pain	
Absent	66.7 (40/60)
Non-catamenial	5 (3/60)
Catamenial	28.3 (17/60)
Shoulder pain	
Absent	56.7 (34/60)
Right-sided non-catamenial	3.3 (2/60)
Right-sided catamenial	38.3 (23/60)
Left-sided non-catamenial	0 (0/60)
Left-sided catamenial	1.7 (1/60)
Presence of other endometriosis localizations	
Yes	83.3 (50/60)
Rectovaginal endometriosis	60 (30/50)
Ovarian endometriosis	48 (24/50)
Peritoneal endometriosis	26 (13/50)
Adenomyosis	24 (12/50)
Bladder/ureteral endometriosis	18 (9/50)
Umbilical endometriosis	12 (6/50)
Intestinal endometriosis	10 (5/50)
Hepatic endometriosis	4 (2/50)
Inguinal endometriosis	2 (1/50)
No	1.7 (1/60)
No, but not performed laparoscopy	15 (9/60)

BMI Body Mass Index, *CT* Computed Tomography, *MRI* Magnetic Resonance Imaging, *TES* Thoracic endometriosis syndrome

*Data are reported as mean ± standard deviation

[a]The total number of women is not always 60, due to the presence of missing data (patients lost to follow-up)

[b]The sum of percentages does not correspond to 100% because some women underwent multiple instrumental examinations

[c]The sum of percentages does not correspond to 100% because 2 women reported both right-sided and left-sided pneumothorax

they were "very satisfied" or "satisfied" with the surgery compared with 56.2% (95% CI 29.9 −80.2) of women in the same group but with a shorter follow-up, with no statistically significant differences ($p = 0.12$). Regarding satisfaction with the medical treatment received, the results were similarly positive, with 63.6% of women expressing high satisfaction levels. When stratifying women according to treatment and follow-up times, differences in satisfaction were not statistically significant ($p = 0.45$) (Fig. 2).

In the analysis of the 24 women with a post-surgical recurrence of PNX and/or of thoracic symptoms, pre-recurrence treatment modalities were the following: lung resection and subsequent pleurodesis in seven cases, lung resection and pleurectomy in four, pleurodesis alone in two, lung resection in one, bullectomy in another case, combined lung and diaphragmatic resection and pleurectomy with or without subsequent pleurodesis in six patients and diaphragm plication in three cases. Among patients with a postoperative PNX recurrence, 71% required further surgery (15/21; 95% CI 47.8–88.7, *data not shown*).

Of the 119 pneumothorax (PNX) episodes observed during follow-up, 18% (22 cases; 95% CI 12.0–26.6) occurred despite the use of COCs, 6% (7 cases; 95% CI 2.4–11.7) during progestogen therapy, and 3% (4 cases; 95% CI 1.0–8.4) while on GnRH agonists.

Table 2 Treatment modality and clinical characteristics of TE

	Patients % (*n*/total)
Surgical treatment	61.7 (37/60)
Pharmacological therapy only before surgery	8.1 (3/37)
Pharmacological therapy only after surgery	51.4 (19/37)
Pharmacological both before and after surgery	32.4 (12/37)
No hormone therapy	8.1 (3/37)
Histological confirmation of endometriosis[a]	
No	75 (27/36)
Yes	25 (9/36)
Recurrence after surgery	
No	35.1 (13/37)
Yes	64.9 (24/37)
Explorative laparoscopy	
No	45 (27/60)
Yes	55 (33/60)
Medical treatment hormonal therapy only	36.6 (22/60)
None	1.7 (1/60)
Type of Pharmacological Treatment[b]	
None	5 (3/60)
Oestrogen-progestogen	26.7 (16/60)
Progestogens	20 (12/60)
Oestrogen-progestogen and progestogens	33.3 (20/60)
GnRH agonist	15 (9/60)

GnRH Gonadotropin releasing hormone

[a]Out of a total of 37 women undergoing surgery, one woman had bipolar coagulation of diaphragmatic endometriotic foci without biopsy

[b]One women may have more types of pharmacological therapy

At follow-up, the PGIC questionnaire showed that 83.4% of women on hormone therapy had "very much improved" or "much improved" health conditions (15/18; 95% CI 58.6–96.4) and 75.8% of women who had surgery (25/33; 95% CI 57.7–88.9) (Table 4). According to the PGIS questionnaire assessing symptoms in the last four weeks, 50% of those on hormonal treatment (9/18; 95% CI 26.0–74.0) reported no symptoms, and 33.4% (6/18; 95% CI 13.3–59.0) reported mild symptoms. Among the surgical group, 39.4% (13/33; 95% CI 22.9–57.9) reported no symptoms and 39.4% (13/33; 95% CI 22.9–57.9) reported mild symptoms.

The results from the SF-12 and HADS questionnaires administered at clinical re-evaluation are shown in Table 5.

Discussion

Considering that, in addition to thoracic and parietal endometriosis, there are several other, even rarer, extrapelvic localizations—such as visceral (kidney, liver, and pancreas), central and peripheral nervous system, muscular, and nasal—there are currently no randomized controlled trials or guidelines defining the appropriate diagnostic and treatment approaches for any of these forms [1, 24, 25]. A systematic review from 2020, which included 34 trials and 628 patients, concluded that insufficient comparative studies exist to recommend the best diagnostic and treatment options for extra-pelvic endometriosis [1].

In our study, patient satisfaction with treatment was high, and both PGIC and PGIS scores indicated significant improvement in overall health status, regardless of the treatment type. Notably, 78% of women who underwent surgery and 84% who received pharmacological treatment reported either no or very mild TE-related symptoms. However, due to the small sample size, a statistical comparison between these groups was not possible.

These results suggest that both surgery and pharmacological treatment are valuable and should be seen as complementary options rather than mutually exclusive. The choice between them should be tailored to the individual woman's symptoms, preferences, and reproductive desires. Burghaus et al. (2021) recommend pharmacological therapy as the first-line treatment for TE, with surgery considered only when medical therapy fails or is contraindicated [19]. Surgical techniques may vary depending on the lesion type: thermal ablation for superficial lesions under 10 mm, "peritonectomy" for those larger, and partial or full-thickness diaphragm resection for deeper lesions. It is essential to explore the pleura if the thoracic cavity is accessed [3].

A multidisciplinary approach is pivotal. A 2022 joint statement by the *British Society for Gynaecological Endoscopy and the Royal College of Obstetricians and Gynaecologists* [26] emphasized that centralizing care for women with TE can enhance clinical outcomes and facilitate research.

During the follow-up period of our study, up to 20 years, a high recurrence rate of clinical symptoms and pneumothorax (PNX) post-surgery was observed. A total of 71% of women with recurrent symptoms required further surgery, and 73% underwent pleurodesis. Limitations in retrieving all surgical reports hindered a complete assessment of the excision extent, which is a key factor influencing recurrence [13]. Moreover, many surgeries were performed in non-referral centers immediately after PNX, potentially affecting the thoroughness of the procedures. Our high PNX recurrence rate, compared to recent reviews [1], might also stem from the limited number of diaphragm repairs performed (5/37 women).

Recurrent PNX is frequently linked to diaphragm defects, highlighting the critical need to address and repair all such defects during the initial surgical procedure [27] while pleurodesis has been shown to reduce recurrence rates [2, 10, 28]. In one study by Bagan et al. (2003), no recurrences occurred after diaphragm reinforcement [29]. Although a combined laparoscopic and thoracoscopic approach is

Table 3 Procedures performed in surgically treated patients ($n=37$)

	Patients % (*n*/total)
Thorascopic surgery[a]	
Pleurodesis	5.4 (2/37)
Pleurectomy and pleurodesis	2.7 (1/37)
Lung resection	
Lung resection and pleurodesis	16.2 (6/37)
Lung resection and pleurectomy	10.8 (4/37)
Lung resection	2.7 (1/37)
Bullectomy	2.7 (1/37)
Diaphragm surgeries	
Diaphragmatic duplicature and pleurodesis	8.1 (3/37)
Diaphragmatic resection and pleurodesis	2.7 (1/37)
Diaphragmatic resection and duplicature	2.7 (1/37)
Combined procedures	
Lung resection, diaphragmatic resection and pleurodesis	5.4 (2/37)
Lung resection, pleurodesis and diaphragmatic duplicature	8.1 (3/37)
Lung resection, pleurodesis and pleurectomy	2.7 (1/37)
Lung resection, diaphragmatic duplicature and pleurectomy	2.7 (1/37)
Laparoscopic surgery	
Bipolar coagulation of diaphragmatic endometriotic foci	21.6 (8/37)
Excision of diaphragmatic endometriosis	5.4 (2/37)

[a]The first thorascopy procedure performed by patients was considered

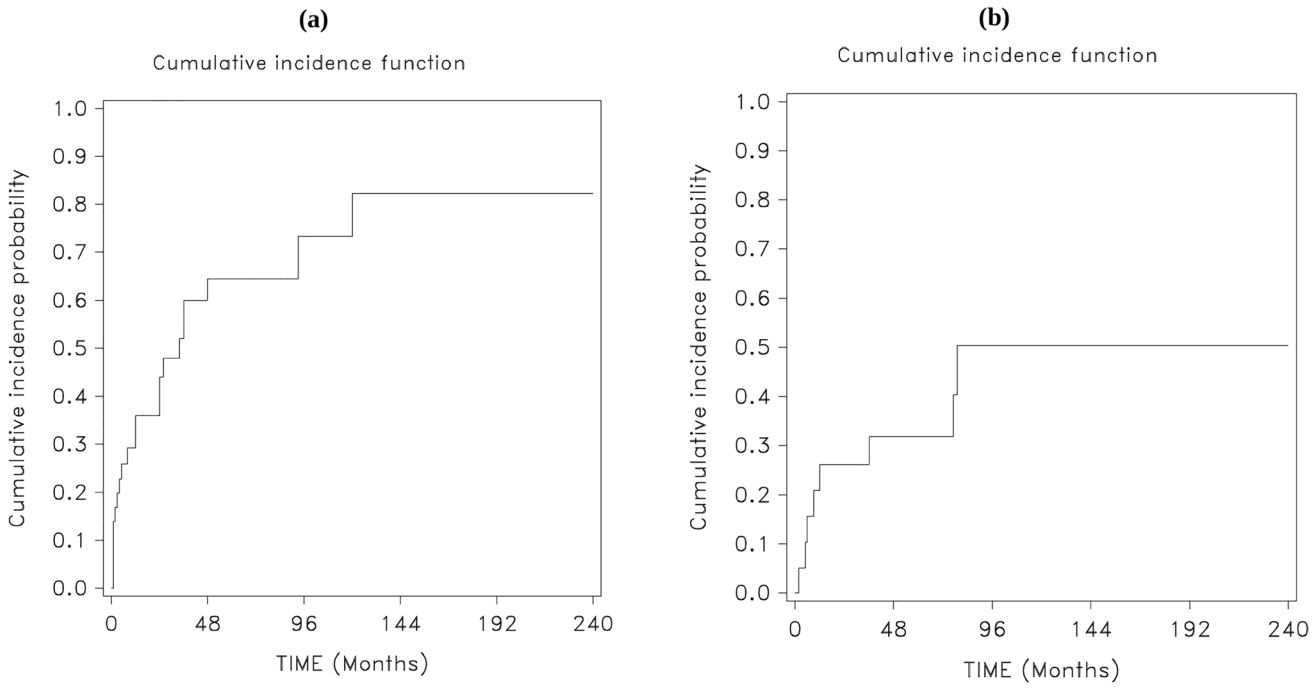
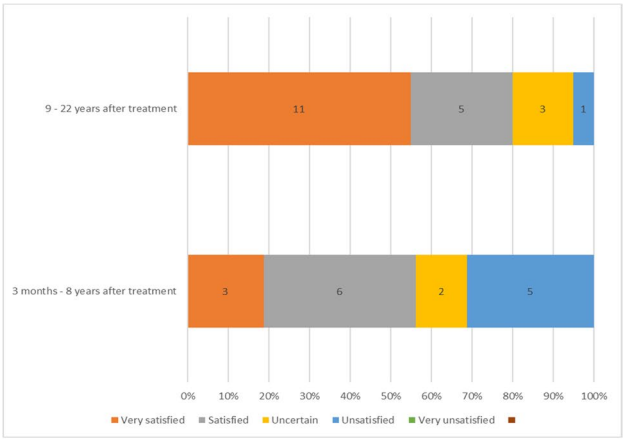


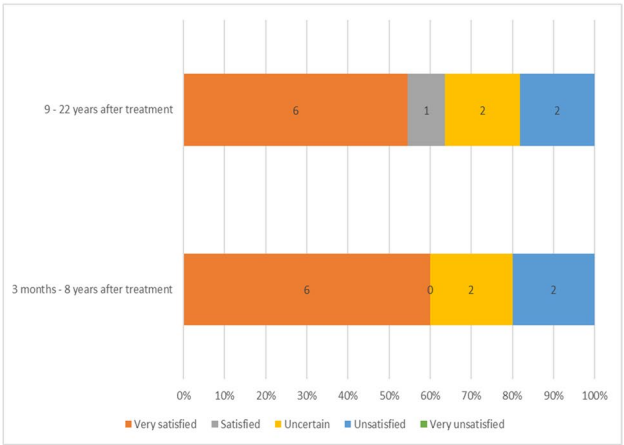
Fig. 1 Cumulative incidence of first recurrence of PNX represented with Kaplan–Meier curves (**a**) Cumulative incidence of second recurrence of PNX represented with Kaplan–Meier curves (**b**)

recommended, only 26% of women in our sample received it, mainly due to emergency treatment being provided in non-referral centers.

Radical surgery combined with diaphragmatic repair and pleurodesis, followed by hormonal treatment, appears to be the best strategy to reduce PNX recurrence [20, 30]. Several



(a)



(b)

Fig. 2 Degree of satisfaction in surgically treated patients (**a**) and in medically treated patients (**b**)

studies recommend post-operative dienogest to reduce the recurrence of both thoracic and pelvic symptoms [31, 32]. Interestingly in our series, 18% of PNX episodes occurred while women were taking combined oral contraceptives (COCs), 6% while they were on progestogens, and 3% while under GnRH agonists, suggesting that hormonal stimulation alone does not fully explain the pathogenesis of catamenial PNX. In deep abdominal endometriosis, a similar trajectory of the disease was observed during medical treatment, with 12% of lesions progressing [33]. TE recurrence may be interpreted as the persistence of the disease following surgery rather than as the ineffectiveness of suppressive therapy [13].

Diagnosis of TE is often challenging; chest CT and X-ray revealed TE in only 6% of our cases. While CT can identify pulmonary and pleural nodules [11, 34], the accuracy of imaging for TE lesions has not been well-studied [1].

Table 4 Degree of satisfaction with treatment in patients who completed follow-up

	Medical treatment[a] % (*n*/total)	Surgical treatment[b] % (*n*/total)
Global condition since beginning of therapy (PGIC)		
Very much improved	50 (9/18)	21.2 (7/33)
Much improved	33.4 (6/18)	54.6 (18/33)
Minimally improved	5.5 (1/18)	12.1 (4/33)
No change	11.1 (2/18)	6.1 (2/33)
Minimally worse	0 (0/18)	3 (1/33)
Much worse	0 (0/18)	3 (1/33)
Very much worse	0 (0/18)	0 (0/33)
Symptoms in the last 4 weeks (PGIS)		
None	50 (9/18)	39.4 (13/33)
Little	33.4 (6/18)	39.4 (13/33)
A bit	5.5 (1/18)	15.1 (5/33)
Much	11.1 (2/18)	6.1 (2/33)
Very much	0 (0/18)	0 (0/33)

PGIC Patients' Global Impression of Change, *PGIS* Patients' Global Impression of Severity

[a]The number of patients treated with medical therapy was 18, due to the presence of missing data

[b]The number of patients treated surgically is 33, due to the presence of missing data

Table 5 Results of standardized questionnaires on the health status of women who completed follow-up

	Mean ± SD[a]
HADS	
Anxiety score	6.3 ± 4.3
Depression score	4.3 ± 3.7
SF-12	
PCS	45.7 ± 10.7
MCS	50.9 ± 8.2

SD Standard Deviation

HADS Hospital Anxiety and Depression Scale. The total score for each subscale can range from 0 to 21, with higher scores indicating poorer psychological function

SF-12 Short form-12. Interpretation: the mean score of 50 represents the average health status of the general population. Scores above 50 indicate better-than-average health or functioning, while scores below 50 suggest worse-than-average health

PCS Physical Component Summary Score

MCS Mental Component Summary Score

[a]The number of patients considered is 52, due to the presence of missing data

Surgical diagnosis is crucial, and a thorough exploration of the diaphragm is recommended for the eradication of all visible lesions [3].

Clinical suspicion is vital for prompt diagnosis and optimal treatment, especially in women over 31 who are non-smokers and have right-sided PNX along with pelvic endometriosis [35]. In our cohort, thoracic biopsies confirmed endometriosis in only 25% of cases, similar to estimates reported by Andres et at. [1]. A recent survey of the British Society for Gynaecological Endoscopy revealed low screening rates for TE and fewer clinicians routinely looking for TE at the time of surgery [36], indicating a need for improved diagnostic skills among gynaecologists, pulmonologists, and thoracic surgeons in recognizing extra-pelvic endometriosis.

In a recent systematic review of pulmonary endometriosis by Nikolettos et al. (2024), it was reported that the majority of lesions (79.9%) were found unilaterally on the right side. Lesions localized exclusively on the left side were observed in only 7.9% of cases, while bilateral lesions accounted for 4.9% and only four patients had tracheal involvement [37]. Our study revealed a clear right predominance of thoracic lesions, with only two patients experiencing left pneumothorax (PNX) and one reporting left shoulder catamenial pain. This supports the hypothesis of a metastatic origin of thoracic endometriosis (TE) via retrograde menstruation [2, 38]. The clockwise circulation of peritoneal fluid moves endometrial cells from the pelvis toward the right paracolic fossa and hypochondrium at a retro-hepatic and subdiaphragmatic level, while the left side is less frequently affected due to the falciform ligament [9, 11]. Respiratory movements, gravity, and bowel peristalsis influence this flow, and increased intra-abdominal pressure may hinder the upward movement of fluid, impacting endometriotic cell implantation [39]. Additionally, in our series, six women with TE had umbilical endometriosis, and two had hepatic endometriosis, suggesting a common pathogenic mechanism for rare forms of extra-genital endometriosis.

Our sample showed a low mean BMI, aligning with a modest inverse relationship between endometriosis and adult BMI [40]. This observation is consistent with literature suggesting that women with endometriosis tend to have a lower BMI and lower obesity rates compared to controls [41]. A prospective study by Farland et al. (2017) found that women with medium and large body sizes at ages 20–25 years were at decreased odds of endometriosis compared to those with a lean body size [42]. While these findings suggest a potential link between low BMI and thoracic endometriosis, the evidence remains inconclusive. Body weight may be linked to endometriosis, but this could also result from biases like loss of appetite due to the disease, the connection between BMI and socioeconomic status, or the difficulty of diagnosing endometriosis in overweight women. Additionally, women with endometriosis often experience more irregular anovulatory menstrual cycles. We hypothesize that low weight may specifically increase the risk for TE.

The main limitation of this study is related to its retrospective nature. Clinical data collection may be biased by errors in consulting medical records and in reporting information that can no longer be verified directly. Moreover, recall bias in reconstructing women's clinical history increases proportionally to the length of follow-up, due to the greater risk of inaccuracy and forgetfulness. The long follow-up time (up to 20 years) was also associated with increased difficulty in contacting women for a re-evaluation, which led to some patients not being included in all statistical analyses due to a lack of response. To address potential biases arising from missing data and loss of follow-up, we performed an intention-to-treat (ITT) analysis, including all initially enrolled patients. Missing data were excluded from the analyses, as they could not be reliably imputed given the retrospective nature of the study. For patients lost to follow-up, we considered them as "unsatisfied" in our primary outcome analysis (patient satisfaction), as their lack of response could reflect dissatisfaction or disengagement from the study. However, this approach may have introduced a conservative bias, potentially overestimating the proportion of unsatisfied patients. Lastly, the observational study design does not allow a direct comparison between hormonal and surgical treatment. However, the rarity of this condition makes leading randomized controlled trials extremely challenging.

The long-term follow-up and a relatively large sample size, which is particularly relevant when studying a rare condition, should be considered as the major strengths of our study.

Conclusion

Thoracic endometriosis is a rare condition with variable clinical presentations that significantly affect women's quality of life. Diagnosing and treating TE requires collaboration among gynaecologists, thoracic surgeons, radiologists, pneumologists, and pathologists, emphasizing the need for a multidisciplinary approach. Care should be centralized in specialized centers.

Data suggests pharmacological therapy as a first-line treatment, particularly for paucisymptomatic women. Surgical intervention, involving radical excision of lesions and repair of diaphragmatic fenestrations, followed by postoperative hormonal continuous therapy, should be considered the gold standard for women with recurrent PNX. In our series, surgical and pharmacological treatments for TE were associated with patient satisfaction, although the PNX recurrence rate was quite high.

Although up to 10% of women with endometriosis may present with extrapelvic forms, there are currently no established guidelines for their diagnosis and management. Thoracic

endometriosis, while being the most common extrapelvic manifestation, remains a rare condition with severe and variable clinical presentations. Due to these challenges, high-quality clinical studies are lacking, preventing the development of standardized diagnostic and management protocols. Urgent action is needed to establish structured care pathways for women with extrapelvic endometriosis, particularly for thoracic endometriosis.

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Data availability All data generated or analysed during this study are included in this article.

Declarations

Conflicts of interest The authors declare no competing interests.

Institutional review board The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the local Institutional Review Board (Comitato Etico Milano Area 2); approval number 993_2021; date of approval 05/10/2021).

Informed consent Informed consent was obtained from all subjects involved in the study.

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