

**Title:**

**Coexistence of endometriosis and inflammatory bowel disease: a case series and practical diagnostic review**

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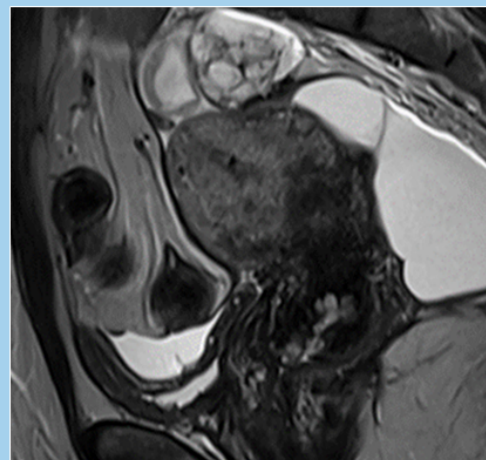
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## Endometriosis and inflammatory bowel disease: clinical experience and review of literature

**Objectives:** Inflammatory bowel disease and endometriosis represent chronic inflammatory conditions presenting overlapping clinical manifestations that frequently lead to misdiagnosis and inappropriate management. Our objective is to evaluate the correlation between these disorders through case report analysis and review of contemporary literature, emphasising diagnostic and therapeutic challenges. **Case presentation:** We report four cases managed at Hospital Universitari Germans Trias i Pujol during 2019-2024. Case one involved a 35-year-old pregnant woman with Crohn's disease presenting acute abdominal pain initially considered as appendiceal plastron; endometriosis was subsequently confirmed postpartum following laparoscopic appendectomy. Case two concerned a 68-year-old woman with Crohn's disease and rectovesical fistula complications, where histopathological analysis of resected sigmoid tissue revealed concurrent deep infiltrating endometriosis. Case three presented a 36-year-old woman with ileal Crohn's disease experiencing persistent pelvic pain initially misattributed to inflammatory bowel pathology before definitive endometriosis diagnosis. Case four involved a 43-year-old woman with Crohn's disease and axial spondylitis, whose chronic pelvic symptoms were ultimately attributed to deep infiltrating endometriosis. **Conclusions:** The coexistence of endometriosis and IBD presents significant diagnostic and therapeutic challenges requiring multidisciplinary evaluation. Early recognition and targeted imaging strategies are fundamental for preventing delayed diagnoses and optimising patient outcomes.



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## Coexistence of endometriosis and inflammatory bowel disease: a case series and practical diagnostic review

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### Abstract

**Objectives:** The objective of this review is to identify key clinical lessons and highlight diagnostic and therapeutic strategies derived from case reports and recent literature. Particular attention is given to recognising overlapping presentations, optimising multimodal imaging and endoscopic evaluation, and promoting multidisciplinary collaboration between gastroenterologists, gynaecologists, radiologists, and pathologists to enhance diagnostic accuracy and guide patient-centred management.

**Methods:** A case series was conducted at Hospital Universitari Germans Trias i Pujol (2019-2024), including patients with confirmed inflammatory bowel disease and histologically or radiologically verified endometriosis. A literature review was performed using PubMed and Scopus databases (1990-2024) with search terms: "endometriosis," "inflammatory bowel disease," "Crohn's disease," "ulcerative colitis," "diagnosis," and "multidisciplinary management."

Case presentation: Case one involved a 35-year-old pregnant woman with Crohn's disease presenting acute abdominal pain initially considered as appendiceal plastron; endometriosis was subsequently confirmed postpartum following laparoscopic appendectomy. Case two concerned a 68-year-old woman with Crohn's disease and rectovesical fistula complications, where histopathological analysis of resected sigmoid tissue revealed concurrent deep infiltrating endometriosis. Case three presented a 36-year-old woman with ileal Crohn's disease experiencing persistent pelvic pain initially misattributed to inflammatory bowel pathology before definitive endometriosis diagnosis. Case four involved a 43-year-old woman with Crohn's disease and axial spondylitis, whose chronic pelvic symptoms were ultimately attributed to deep infiltrating endometriosis.

Conclusions: The coexistence of endometriosis and IBD presents significant diagnostic and therapeutic challenges requiring multidisciplinary evaluation. Early recognition and targeted imaging strategies are fundamental for preventing delayed diagnoses and optimising patient outcomes.

**Keywords:** Endometriosis. Inflammatory bowel disease. Crohn's disease. Chronic pelvic pain. Diagnostic challenges. Multidisciplinary approach.

#### **Statement of Interests**

Research ethics: Not applicable.

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#### **Statement of Generative AI and AI-assisted technologies in the writing process**

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#### **Inclusion and Diversity Declaration**

We support inclusive, diverse, and equitable research.

## Data availability statement

Data supporting the study findings are not available as this is a literature review article based on published data.

## Introduction

Endometriosis is an inflammatory disorder affecting 10% of fertile women (1,2), characterized by the growth of extrauterine endometrial tissue and inflammatory responses in ectopic areas. It has three forms: superficial peritoneal, ovarian, and deep endometriosis, with the latter potentially infiltrating intraperitoneal organs like the bowel (3).

Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is a group of chronic gastrointestinal disorders with increasing global prevalence (4). Its pathogenesis remains unclear, involving genetic and environmental factors, alterations of the intestinal microbiota and the immune response. While UC affects the mucosa of the colon, CD can involve any layer of the intestinal wall along all the gastrointestinal tract (5,6).

Over time, evidence has progressed from isolated surgical case reports in the 1990s to larger observational and molecular studies in recent years. Early reports focused on histopathological confirmation of endometriosis in patients with presumed IBD, while later cohorts and systematic reviews explored diagnostic overlap, imaging strategies, and management outcomes. Recent population-based and genomic analyses have further examined shared inflammatory mechanisms. Full study details are available in the Supplementary Table (7).

## Material and methods:

Four cases were retrospectively identified from the clinical database of the Department of General and Digestive Surgery at Hospital Universitari Germans Trias i

Pujol between 2019 and 2024. Selection criteria included confirmed diagnosis of inflammatory bowel disease and histologically or radiologically verified endometriosis, with sufficient clinical and imaging documentation to illustrate relevant diagnostic or management dilemmas. A complementary literature search was conducted using PubMed and Scopus databases, restricted to English-language publications from 1990 to 2024. The search combined terms related to “endometriosis,” “inflammatory bowel disease,” “Crohn’s disease,” “ulcerative colitis,” “diagnosis,” and “multidisciplinary management.” Relevant case reports, case series, and reviews were examined to contextualise the clinical observations.

## Case reports

### Case 1: Diagnostic Complexity in Pregnancy

A 35-year-old pregnant woman with ileal Crohn’s disease, treated with Adalimumab, presented with acute abdominal pain at 17 weeks. MRI revealed a perforated appendiceal plastron (Fig.1A), managed conservatively. At postpartum, she returned with right iliac fossa pain, and imaging showed an inflammatory mass in the cecum and ileum (Fig.1B). After conservative treatment, a laparoscopic appendectomy revealed unexpected endometriosis. This case highlights the diagnostic challenges during pregnancy, where abdominal pain is often misattributed to IBD, delaying endometriosis diagnosis until after delivery.

### Case 2: Deep Infiltrating Endometriosis Mimicking Fistulising Crohn’s Disease

A 68-year-old woman with a 4 months history of fistulising Crohn’s disease presented with pneumaturia and faecaluria. Imaging revealed a rectosigmoid fistula and another fistulous tract between a pelvic collection and the bladder dome, leading to open sigmoidectomy with an end-to-end stapler anastomosis. Pathological examination of the resected sigmoid segment identified deep infiltrating endometriosis. This case demonstrates how deep endometriosis can mimic or exacerbate Crohn’s disease, particularly when it manifests in a fistulising form, leading to complex surgical challenges and prolonged patient morbidity.

### Case 3: Chronic Pelvic Pain and the Diagnostic Dilemma



A 36-year-old woman with ileal Crohn's disease since 2016 experienced persistent pelvic pain despite treatment. Initially suspected to have pelvic congestion syndrome, she underwent vein embolization without relief. In 2018, an endometrioma was found, confirming endometriosis. She began hormone therapy and underwent hysterectomy with bilateral salpingectomy in 2019. This case highlights the need to consider endometriosis in patients with persistent pelvic pain and Crohn's disease to avoid treatment delays.

#### Case 4: Deep Endometriosis Overlooked in a Complex Medical History

A 43-year-old woman with Crohn's disease, axial spondylitis, and a history of multiple surgeries experienced chronic pelvic pain, initially attributed to her conditions. In 2023, advanced imaging (Fig. 4) revealed deep endometriosis. Treatment with decapeptyl resolved her pain, highlighting the importance of considering endometriosis in patients with complex medical histories and chronic IBD.

### **Discussion**

IBD and endometriosis are chronic inflammatory conditions that often present in young women and share overlapping gastrointestinal and pelvic symptoms, which may delay accurate diagnosis. A nationwide cohort of 37,661 patients confirmed a strong association between both conditions, particularly in surgically verified endometriosis, persisting over 20 years of follow-up (7). A case-control study also found an increased risk of stricturing disease among these patients, though treatment patterns did not differ significantly by IBD type (8). Further studies, including Mendelian randomization analyses, have reinforced this association (9). Shared inflammatory and immune pathways—such as altered cytokine signalling, macrophage activation, and reduced natural killer cell function—may explain their coexistence (10–14).

Clinically, the main challenge lies in differentiating bowel endometriosis from Crohn's disease. Up to 92% of cases may initially be misdiagnosed (15,16). While endometriosis generally involves the serosa or muscularis, it can extend to the mucosa and mimic Crohn's lesions endoscopically (17). Immunohistochemistry helps confirm the diagnosis: ectopic endometrial glands express CK7 and ER, and the stroma expresses

CD10 and ER, whereas intestinal glands show CK20 and CDX2 positivity (18).

A multimodal imaging strategy is central to diagnosis. MRI, ideally combined with transvaginal ultrasound performed by an experienced endometriosis specialist, offers the highest diagnostic yield. In women with IBD and persistent pelvic pain, MRI enterography with tailored multiplanar sequences can identify deep infiltrating lesions and clarify indeterminate bowel inflammation (1,19,20).

Management should be multidisciplinary, involving gastroenterologists, gynaecologists, radiologists, and colorectal surgeons. Hormonal therapy and NSAIDs remain first-line for endometriosis (21–23), while IBD treatment follows conventional stepwise protocols including aminosalicylates, corticosteroids, immunomodulators, and biologics (24). Surgical intervention is indicated when medical therapy fails or complications arise, emphasising bowel-sparing and minimally invasive approaches (5,6,25–27). Early interdisciplinary coordination is essential to avoid unnecessary procedures and optimise long-term outcomes.

## Conclusion

In patients with IBD, clinicians should maintain a high index of suspicion for gynaecological disorders when women present with pelvic pain, dysmenorrhoea, infertility, or abnormal uterine bleeding. Likewise, in women with endometriosis who report gastrointestinal symptoms, colonoscopy and meticulous histopathological assessment are warranted, as distinguishing between the two conditions can be challenging. A multimodal imaging strategy plays a pivotal role in enhancing diagnostic accuracy and guiding management.

Management of patients with concurrent IBD and endometriosis benefits from close collaboration between gastroenterologists, gynaecologists, surgeons, radiologists, and pathologists to ensure coordinated care. Therapeutic plans may require individual adaptation to address the overlapping symptomatology and potential treatment interactions.



While current guidelines provide limited direction for these complex cases, a multidisciplinary, patient-centred approach remains fundamental to optimising outcomes and ensuring comprehensive evaluation of all relevant systems.

### **List of abbreviations**

Inflammatory bowel disease (IBD), ulcerative colitis (UC), Crohn's disease (CD), magnetic resonance imaging (MRI), diffusion weighted imaging (DWI), hematoxylin and eosin staining (H&E), cluster of differentiation 10 (CD10), estrogen receptor (ER), non-steroidal anti-inflammatory drugs (NSAIDs), cytokeratin 7 (CK7), cytokeratin 20 (CK20), caudal-related homeobox 2 (CDX2), computed tomography (CT).

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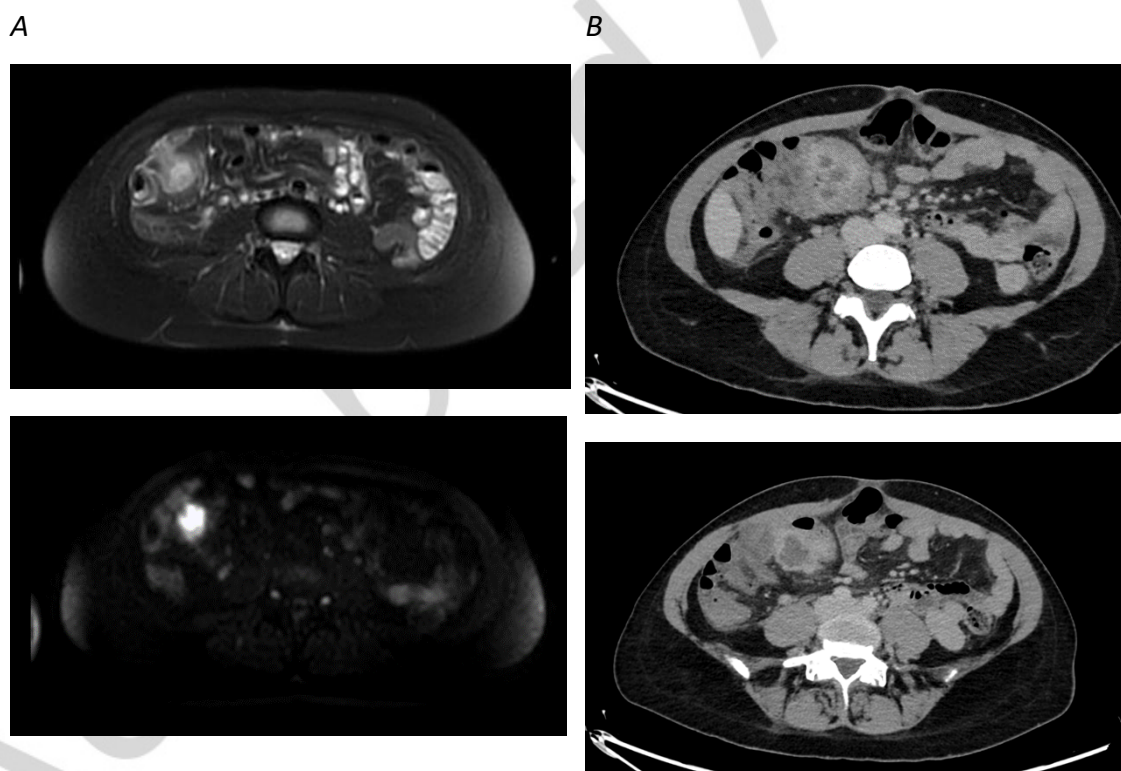
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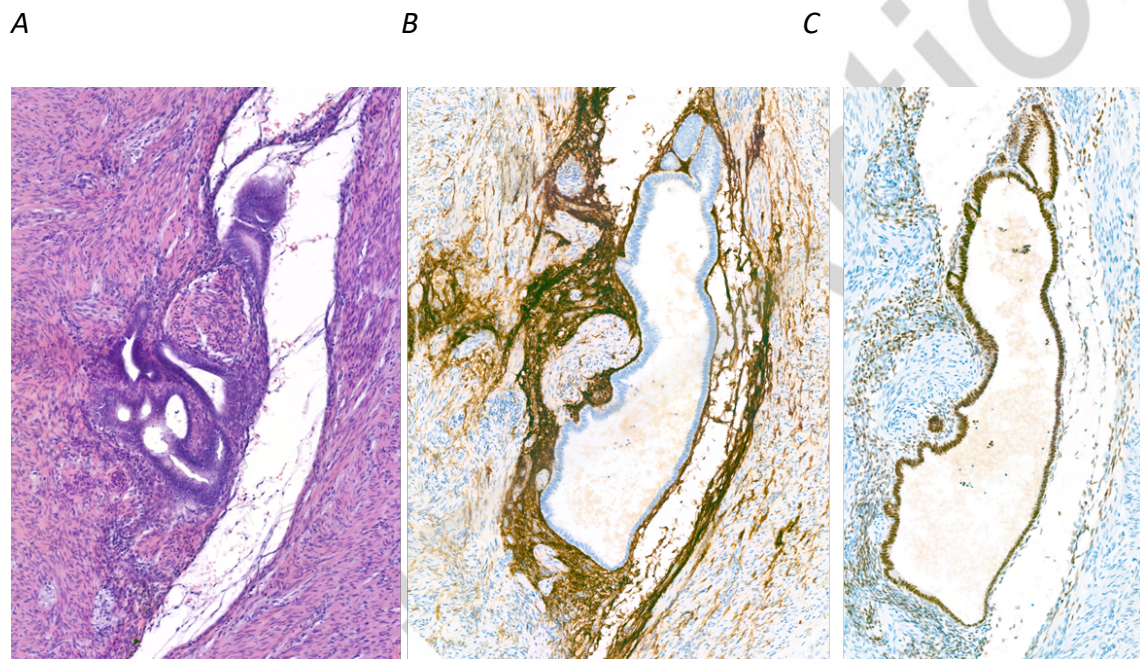
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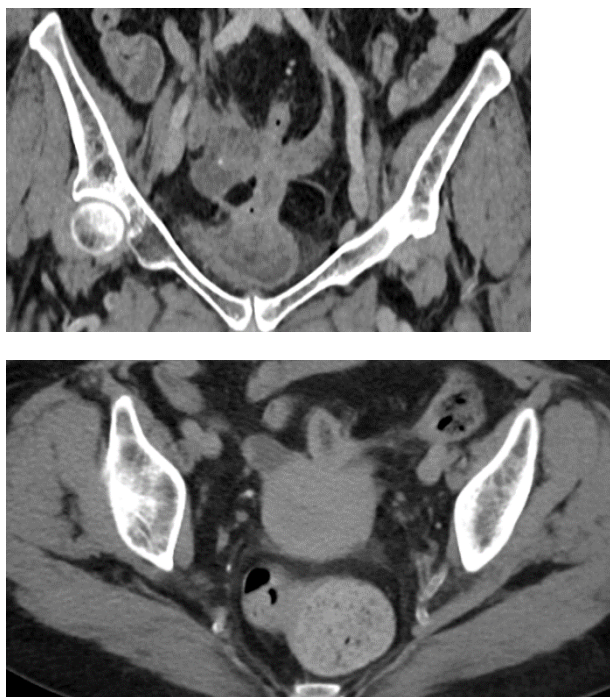
**Figure 1.** *Multimodal imaging of Case 1.* A: MRI reveals an oval-elongated heterogeneous structure contacting the cecal wall with T2 hyperintensity, T1



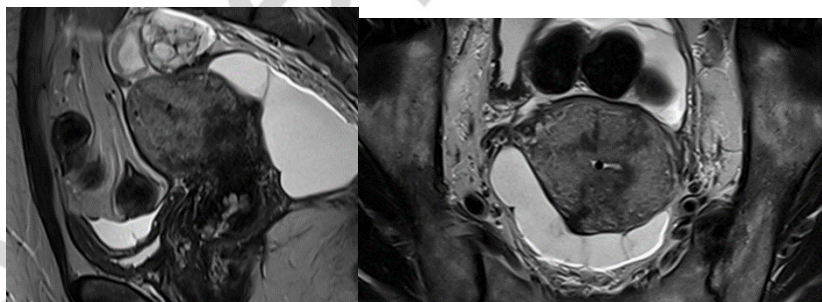
isointensity, and restricted DWI diffusion. Encapsulated fluid with perilesional inflammation suggests acute suppurative appendicitis. B: CT shows significant enlargement of the inflammatory mass contacting the cecum, terminal ileum, and ileocecal valve with fat stranding. The appendix is not identified, likely incorporated within the mass.



**Figure 2:** *Histopathological confirmation of endometriosis in Case 2.* A: H&E staining shows endometrial glands and stroma (100 $\times$ ; 200  $\mu$ m). B: CD10 immunohistochemistry demonstrates positive stromal staining with unstained glands (100 $\times$ ; 200  $\mu$ m). C: Estrogen receptor immunohistochemistry shows positive expression in glands and stroma (100 $\times$ ; 200  $\mu$ m). Findings confirm deep infiltrating endometriosis.



**Figure 3.** CT multiplanar reconstructions of Case 2: Deep infiltrating endometriosis. Axial and sagittal reformatted CT images demonstrate medialized ovaries located in the retrouterine space, appearing adherent ("kissing ovaries"), with fibrotic tracts exerting traction on the mid sigmoid colon toward the supravescical space. These radiological findings are highly suspicious for deep infiltrating endometriosis with bowel involvement.



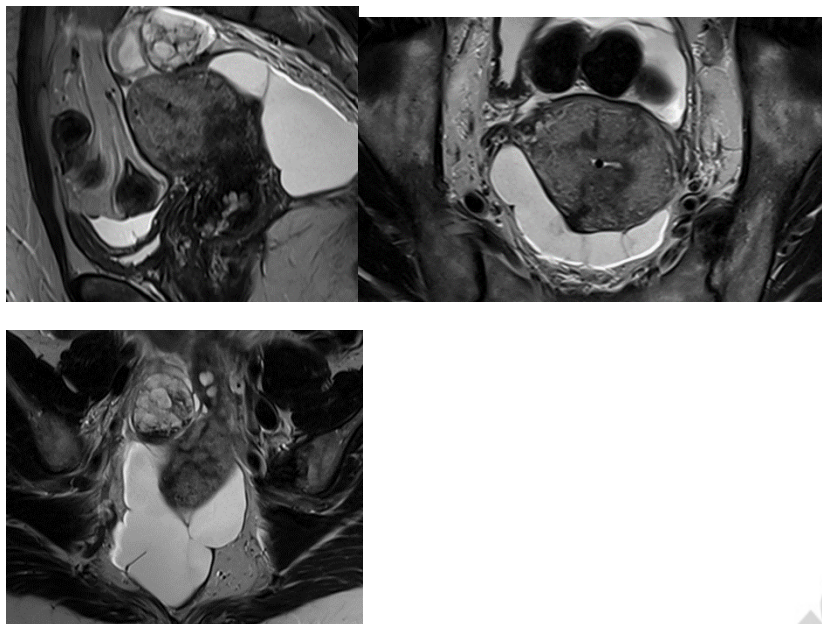




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**Figure 4.** *MRI findings in Case 4.* A tubular cystic structure is present in the retrouterine space, suggestive of pelvic adhesive disease. The ovaries are elevated above their expected position and medialized, adherent to the uterine fundus. There is also retrouterine thickening with a fibrotic appearance. These findings should raise suspicion of endometriosis if supported by clinical correlation.

**Table 1.** *Published studies related to IBD and endometriosis:* Research on endometriosis–IBD coexistence has progressed from isolated case reports (2011–2016) utilizing surgical histopathology to contemporary prospective studies and large-scale investigations employing diverse methodologies including ultrasound imaging and genetic analysis (2017–2024). This evolution reflects the field's transition from descriptive documentation to rigorous and consolidated investigation.

Year	Authors	Type article	n	Diagnostic tool	Treatment
2011	Jess et al.	Retrospective cohort study	376 61	Surgical (histopathology)	Medical / Surgery
2012	Ong et al.	Case report	1	Surgical (histopathology)	Surgery
2015	Lee et al. (ECCO)	Case control	98	Surgical (histopathology)	-
2016	Lee et al. (IBD)	Retrospective case control	153	Surgical (histopathology)	Medical / Surgery
2016	Fortuna et al.	Retrospective case-control	298	Biopsy / Surgical (histopathology)	Medical
2019	Andres et al.	Systematic review	920	Images / Surgical (histopathology)	Medical/ Surgery
2020	Chiaffarino et al.	Systematic review	-	-	-
2020	Miller-Ocuin et al.	Poster case-control	2	Surgical (histopathology)	Surgery
2020	Klein et al.	Case report	1	Biopsy (histopathology)	Medical
2020	Porpora et al.	Case-control study	298	Surgical (histopathology)	-
2021	Foulon et al.	Letter to editor	1	Surgical (histopathology)	Surgery
2023	Keever et al.	Review of the literature	-	-	-

Year	Authors	Type article	n	Diagnostic tool	Treatment
2023	Dang & Zhang	Mendelian randomization analyses	106.450	-	-
2023	Neri et al.	Prospective nested case-control	35	Ultrasound scan	-
2024	Zhang et al.	Original research	178	Genomic analysis	-