

CASE REPORT

DOI: 10.5336/jcog.2024-103700

Recurrence and Malignant Transformation Risk After Fertility Sparing Surgery of Recurrent Ovarian Mucinous Cystadenoma on Young Women: Case Report and Systematic Review

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ABSTRACT Mucinous ovarian cystadenoma is a common epithelial benign tumor in young women. However, recurrence and malignant transformation of mucinous ovarian cystadenoma are rarely reported. We report a 32-years old nulliparous woman who was diagnosed with mucinous ovarian cystadenoma, initially presenting with distended stomach and pelvic pain. After initial left partial oophorectomy, the patient had recurrence of abdominal mass, of which left salpingo-oophorectomy was performed. Several months after previous surgery, the abdominal mass recurred, which from imaging and pathological examination was diagnosed as borderline mucinous ovarian cystadenoma FIGO class IIIB. A systematic review of 19 articles showed risk of total recurrence and malignant transformation on mucinous ovarian cystadenoma were 13.9% and 1.8%, respectively. Furthermore, choosing fertility sparing surgery could increase the risk of recurrence of borderline ovarian cystadenoma.

Keywords: Mucinous ovarian cystadenoma; fertility sparing surgery; recurrence; malignant transformation

Mucinous ovarian cystadenoma is an epithelial tumor which accounts for around 8-10% of ovarian tumors. Majority of mucinous cystadenoma is benign and could grow in large dimensions. However, 20% of mucinous cystadenoma could progress and transform to borderline and malignant mucinous ovarian tumor.¹ Borderline and benign ovarian tumor is common in reproductive young women. Borderline ovarian tumors are usually found in premenopausal age, with most of them in the range of 34-40 years old.²

Surgery is the main therapy for ovarian tumors. There are two methods of surgery: Complete surgical staging and conservative (fertility sparing surgery). To decide the surgery method, oncologists should

consider age, parity, desire for fertility preservation, and histology characteristic of the tumor. Complete surgical staging including total abdominal hysterectomy, omentectomy, bilateral salpingectomy, peritoneal washing, and biopsy of pelvic and paraaortic lymph node were performed to prevent malignant progression of ovarian tumor that is caused by remaining tumor cells or leakage and intraoperative rupture.³

Fertility sparing surgery can be considered for mucinous ovarian cystadenoma in young women of reproductive age. Research from Loizzi et al. stated that fertility sparing surgery in borderline ovarian tumors have the risk for recurrence and malignant

TO CITE THIS ARTICLE:

Hamurajib KC, Alma NA, Sofhia H, Tan GR, Fahmi MN. Recurrence and malignant transformation risk after fertility sparing surgery of recurrent ovarian mucinous cystadenoma on young women: Case report and systematic review. JCOG. 2024;34(3):106-10.

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Peer review under responsibility of Journal of Clinical Obstetrics & Gynecology.

Received: 07 May 2024

Received in revised form: 01 Sep 2024

Accepted: 15 Oct 2024

Available online: 16 Oct 2024

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transformation. However, research on the risk of recurrence and malignant progression on patients with mucinous ovarian tumors was limited.² This article aimed to study a case report on a young woman with recurrences and malignant progression after undergoing two fertility sparing surgeries. The data were strengthened with a systematic review and meta-analysis which evaluated the recurrence and malignant transformation on patients with mucinous ovarian tumor after conservative procedure.

CASE REPORT

A 32-years-old married nulliparous woman who has not had children after 3 years of marriage was treated for distended stomach and pelvic pain without urinary or defecation problems. In 2021, the patient had complained of abdominal mass, with Ca-125 found to be 12.01 U/mL. During surgery, a mass sized 15x15x5 cm was found. Thus, laparotomy and left partial oophorectomy were performed. Histology analysis showed mucinous cystadenoma (Figure 1a).

In April 2023, the patient had the same complaint and Ca-125 was 30.4 U/mL. Re-laparotomy and left salpingo-oophorectomy were decided to be performed. A mass sized 30x15x10 cm was discovered and the histology examination showed mucinous cystadenoma (Figure 1b).

Five months after surgery, the patient complained of a recurrent abdominal mass. Radiology examination showed a mucinous cystic multilocular mass sized 20.3x17.21x18.83 cm with IOTA adnex model 73.6% benign possibility. Moreover, magnetic resonance imaging showed insistence on sigmoid colon and ureter which caused bilateral hydronephrosis (left Grade III and right Grade II). Tumor marker was evaluated, Ca-125 was 15.9 U/mL and Ca-19-9 was 7.44 U/mL. The kidney function tests showed a significant increase in creatinine (6.09), thus hemodialysis was performed.

On September 26th 2023, a mass was found intraoperatively from the right adnexa, sized 30x28x25 cm implanted on the omentum, and a mass sized 3x3 cm implanted on the intestines. Frozen examination of mass showed mucinous cystadenoma borderline FIGO class IIIB (Figure 1c, 1d, 1e). Figure 1c shows the gross examination picture of the mass extracted

from the right adnexa. Figure 1d and 1e shows the histological examination of the mass. From the imaging, gross examination and the histological examination, we diagnosed the patient with mucinous ovarian cystadenoma borderline FIGO class IIIB. The patient was decided to undergo relaparotomy, total abdominal hysterectomy with right salpingo-oophorectomy. Written informed consent for publication of the patient's clinical details and/or clinical images was obtained from the patient, ensuring that the patient's identity is not disclosed.

DISCUSSION

Benign mucinous cystadenoma is commonly found in young women who want fertility preservation. Some studies and case reports showed conservative surgery is preferable for reproductive young women.⁴⁻⁶ For women in late reproductive period, the majority performed complete surgical staging. Conservative surgery, including complete tumor resection without disruption or spill, was the primary choice in mucinous cystadenoma. Cyst rupture and cystectomy procedure increased the risk of residue occurrence, which could cause recurrence. However, recurrence also took place due to the microscopic residue of the tumor.⁷ To explore the risk of recurrence and malignant transformation of mucinous cystadenoma in young women with fertility sparing surgery, we conducted a systematic review.

The methodology employed to conduct this systematic review was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Up to December 2023, we searched the PubMed and Cochrane databases using the key words “(((Mucinous) OR (low malignant potential)) AND (ovarian)) AND ((tumour)) AND (((fertility sparing) OR (conservative)) AND surgery)”. Original research, both retrospective and prospective, about fertility sparing surgery (cystectomy, bilateral cystectomy, unilateral salpingo-oophorectomy, or cystectomy and unilateral salpingo-oophorectomy) on women with mucinous ovarian tumor was included in this review.

A total of 670 articles were found from database searching on PubMed and Cochrane. After exclusion of duplication, 119 articles were screened for eligi-

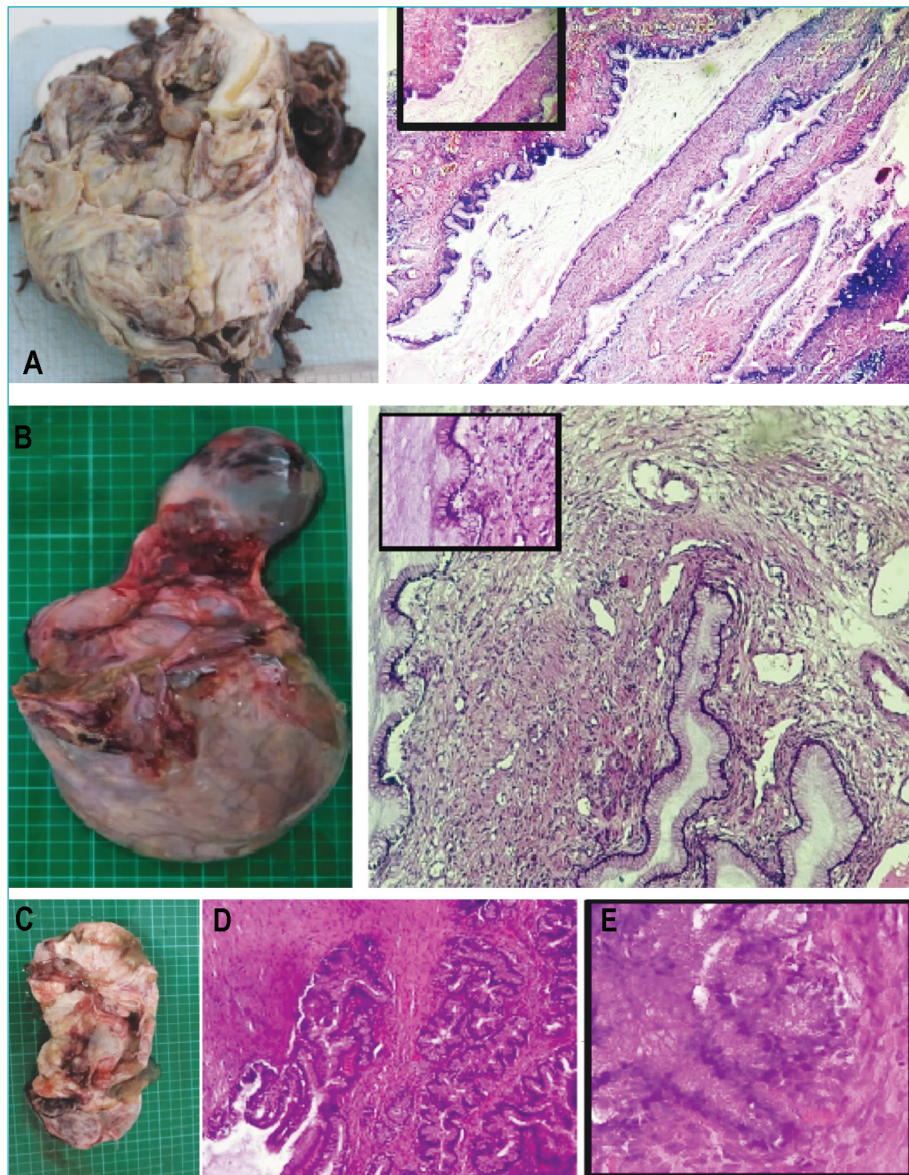


FIGURE 1: Gross examination and histological examination of the ovarian mass. **A)** Gross examination showed a white-brownish multilocular ovarian mass with a smooth surface and cystic component, filled with viscous mucoid material. Histological examination revealed multilocular cystic neoplasm composed of multiple cysts and glands with some papillary infoldings, lined by simple columnar epithelium. The epithelial cells are uniform, with large vacuolated mucin. The nuclei are round to oval, basally located, with a regular nuclear membrane and finely chromatin. There are no mitotic activity and microinvasion (H&E, x100 and x400). **B)** Gross examination showed a 11.5x6x4.8 cm white-brownish multilocular ovarian mass with a smooth surface and cystic component, filled with viscous mucoid material. Histological examination revealed cystic multilocular mass with some papillary infoldings, lined by simple columnar epithelium. The epithelial cells are uniform, with large vacuole contained mucin. The nuclei are round to oval, basally located, with a regular nuclear membrane and finely chromatin. There are no mitotic activity and microinvasion (H&E, x100 and x400). **C)** Gross examination showed a 13.2x11.1x7.1 cm yellowish-white ovarian mass with cystic components measuring 0.3-0.5 cm, containing cloudy whitish mucinous fluid. **D)** Histological examination revealed cystic multilocular mass with some papillary infoldings and tufting formation, lined by columnar epithelium. The epithelial cells are mild polymorphic, crowded, with an increased N/C ratio, abundant mucinous cytoplasm, and large vacuoles. The nuclei are round to oval, basally located, with a regular nuclear membrane and mild hyperchromasia. There is scant mitotic activity (H&E, x100). Histological examination revealed **E)** Focal glands with microinvasion (<5 mm in the greatest dimension) were identified within normal ovarian stroma without desmoplastic changes (H&E, x400).

bility. In the end, 19 eligible articles were analyzed (Figure 2). Seventeen articles were published between 2013 and 2023, and two articles published in 2006 and

2007. A total of 1,465 patients with mean age of 39 years (range 20-49 years) were included. From all patients, 709 patients had undergone fertility sparing

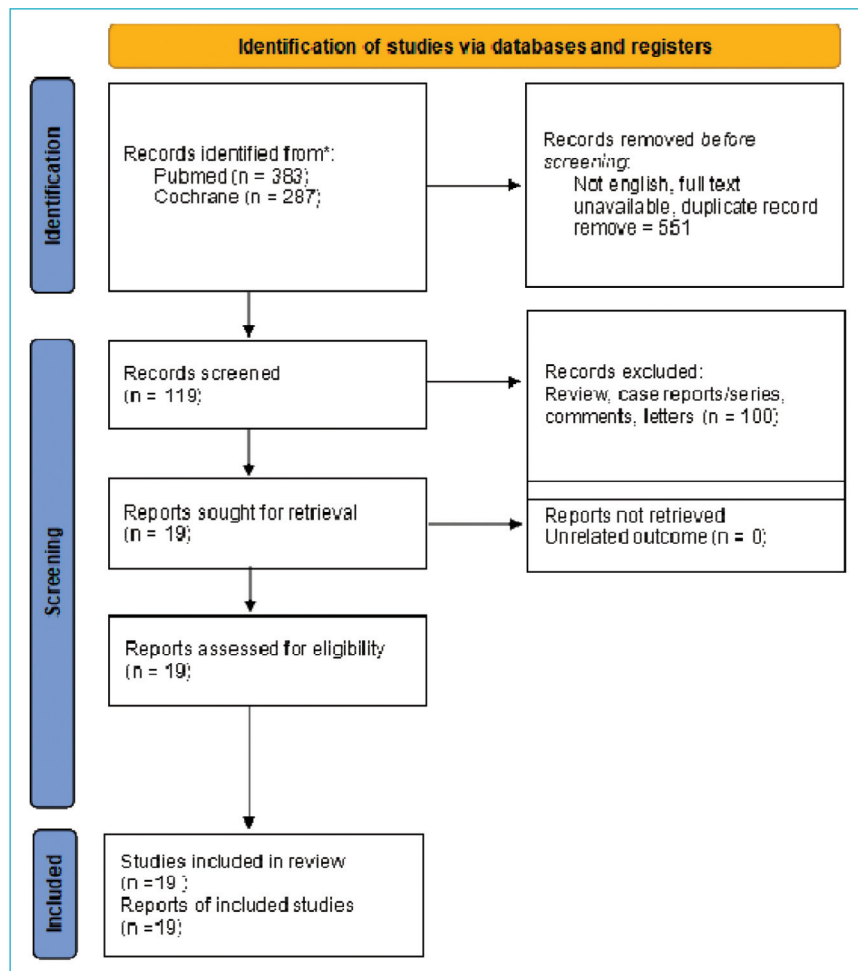


FIGURE 2: PRISMA flow diagram for systematic search.

surgery and 756 patients had undergone complete surgical staging. Most of the surgeries were performed using laparotomy (61%) and laparoscopy (39%).

This research showed overall recurrence and malignant progression from mucinous cystadenoma 13.9% and 1.8%, respectively. Majority of patients got recurrences 38 months after surgery. On patients with recurrence of mucinous cystadenoma, an article showed tumor marker Ca-125 to be in normal range, whereas, nine articles showed escalation of average Ca-125 which were not different significantly from non-recurrence mucinous cystadenoma. Patients who had undergone fertility sparing surgery had increased recurrence risk compared to patients who had undergone complete surgical staging (CI 1.53, 2.90, moderate heterogeneity). The laparotomy technique did not increase the recurrence risk on mucinous cystade-

noma compared to laparoscopic technique (11.5% vs 9.9%, CI 0.56, 1.21, moderate heterogeneity).

In our case, several conservative surgeries (partial oophorectomy and unilateral oophorectomy) were performed, considering the young age and nulliparity. During the procedure, there was no cyst rupture or spillage. Therefore, the recurrence was allegedly related to microscopic residue. Analysis from systematic review found that recurrence risk was increased two times on fertility sparing surgery. The surgery technique using laparoscopy and laparotomy was allegedly related to recurrence rate. However, the meta-analysis showed that the surgery technique using laparoscopy or laparotomy on conservative surgery was not related to recurrence of mucinous cystadenoma.

This case showed early onset recurrence (4 months from the previous surgery). Consequently,

malignant transformation was revealed through histology examination and radiology imaging, which showed borderline mucinous cystadenoma FIGO Stage IIIB with recurrence on the contralateral ovary and implantation of more than 2 cm on omentum and intestines. Up until this case report and systematic review was written, case reports that demonstrated progression on histology examination from benign to borderline was limited. Furthermore, some studies reported that the incidence of malignant transformation from benign or borderline ovarian mucinous cystadenoma were rare, which is in accordance with our findings. This review revealed 1.8% transformation of benign and borderline ovarian mucinous cystadenoma to malignant.

Majority of borderline ovarian tumors were found in early stage (Stage I) with good prognosis (recurrence 15%, 5 years survival rate 100%). However, in the late stage (Stage II-IV), the stage progression was related to worse prognosis. In the late stage, the prognosis was influenced by age and invasive implantation.⁸ Patients that had FIGO Stage III with invasive implantation had high recurrence rate, ranging from 31-45% with median recurrence onset at 24 months.⁹ Conservative surgery was considered for borderline ovarian tumor FIGO Stage I and II. On patients that had FIGO Stage III with invasive im-

plantation, complete surgical staging remained as standard therapy.¹⁰

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Kuky Cahya Hamurajib; **Design:** Kuky Cahya Hamurajib, Moh Nailul Fahmi; **Control/Supervision:** Moh Nailul Fahmi; **Data Collection and/or Processing:** Kuky Cahya Hamurajib, Nurulita Ainun Alma, Hafni Sofhia; **Analysis and/or Interpretation:** Kuky Cahya Hamurajib, Nurulita Ainun Alma, Hafni Sofhia, Moh Nailul Fahmi; **Literature Review:** Kuky Cahya Hamurajib, Nurulita Ainun Alma, Hafni Sofhia, Giovanna Renee Tan; **Writing the Article:** Kuky Cahya Hamurajib, Nurulita Ainun Alma, Moh Nailul Fahmi, Giovanna Renee Tan; **Critical Review:** Kuky Cahya Hamurajib, Moh Nailul Fahmi, Giovanna Renee Tan; **References and Fundings:** Kuky Cahya Hamurajib, Nurulita Ainun Alma, Giovanna Renee Tan.

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