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Fertility preservation in Borderline Ovarian Tumors

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Background of the Topic

Borderline ovarian tumors (BOT) constitute a significant proportion, ranging from 10% to 20% of all ovarian epithelial tumors. Typically diagnosed at a median age of 45 years, with a notable 34% of patients falling under the age of 40, BOTs present a unique clinical challenge(1). These tumors exhibit features reminiscent of malignant cancer but lack stromal invasion, making their management complex. While malignant transformation is infrequent, patients diagnosed with BOTs face a considerable risk of recurrence.

Surgical intervention stands as the primary treatment modality for BOTs. The conventional approach is typically bilateral salpingo-oophorectomy with or without hysterectomy, which is recommended due to its low recurrence rate, ranging from 0-5%. However, in cases where fertility preservation is desired, conservative surgery becomes an option, aiming to retain the uterus and at least a portion of one ovary. In conservative surgery, studies have indicated a higher risk of recurrence, reaching up to 25%. Additionally, recurrent cases often necessitate a second surgery, further increasing the risk of diminished ovarian reserve.

Fertility preservation holds particular significance for BOT patients, especially considering the prevalence (ranging from 10% to 35%) of previous history of infertility particularly in patients diagnosed with serous BOT, bilateral tumors, or those displaying a micropapillary pattern(2). The use of controlled ovarian stimulation (COS) in BOT patients has stirred debate due to concerns regarding its potential impact on tumor growth and recurrence. Expression of estrogen receptors and progesterone receptors in epithelial cells of borderline tumors has raised questions about the hormonal sensitivity of BOT (3). While some studies have suggested an increased risk of BOT recurrence in women undergoing ovarian stimulation, in vitro studies have not shown any evidence of gonadotropins inducing cell proliferation in primary cultures of BOT cells(4).

Several questions persist in this area and require clarification: concerning the safety regarding recurrence with hormonal stimulation, is there a risk of disease spreading post-oocyte pick-up, and what challenges arise in oocyte retrieval when an ovarian mass is present?

Summary of the paper's contents

The impact of ovarian stimulation on the progression of BOT has been a subject of concern.

However, several studies have provided insights into the safety and efficacy of COS in BOT patients.

A study on BOT cell cultures reported no stimulatory effect of FSH or estradiol (E2), indicating that gonadotropins could be safely used(5). In addition, previous retrospective clinical studies have also yielded promising results regarding the use of in vitro fertilization (IVF) in BOT patients reporting a pregnancy rate up to of 40% following IVF. Importantly, in a literature review the recurrent rate of BOT after COS was 19.4% (12 out of 62 cases), with none of the relapses resulting in death(6).

Critical evaluation

The majority of studies to date are retrospective and involve small patient populations. While the evidence generally supports IVF as a feasible option for fertility preservation in early-stage BOT patients, further research is needed to evaluate the safety and efficacy in advanced-stages.

We present our recent retrospective multicenter study that included 165 patients, to evaluate the oncological safety of COS in BOT patients, including those with advanced and bilateral disease. This research represented the largest series of BOT patients undergoing COS, even in advanced stages. The study found no significant impact of COS on recurrence rates in BOT patients with advanced-stage and bilateral disease, attributing recurrence primarily to disease stage rather than COS. The median recurrence time was 28 months. Moreover, fertility preservation through COS and subsequent IVF significantly increased the chances of live birth in BOT patients treated conservatively (Table 1). No deaths from the disease or intraperitoneal or vaginal dissemination were observed after oocyte retrieval. No adverse outcomes related to IVF were reported.

Conclusion

Existing evidence suggests that COS does not significantly contribute to recurrence risk in BOT patients, even in advanced stages. FP through COS enhances the likelihood of live births in these patients. Although Larger prospective studies are warranted to further investigate the relationship between COS and BOT recurrence, particularly in patients with advanced-stage disease, our results clearly demonstrate that fertility preservation through COS and IVF offers promising outcomes for young women with BOT diagnosis.

Table 1. Pregnancy outcomes

	Patients with COS (n=41)	Patients without COS (n=124)
N of women pregnant after BOT diagnosis	13 (39.4%)	27 (26%)
Number of pregnancies	0.77 (1.02)	0.38 (0.74)
Number of spontaneous pregnancies	0.2 (0.48)	0.29 (0.59)
Live birth	12 (38.7%)	24 (23.1%)

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*Please note: The newsletter reflects the opinion of the author and not of the ISFP.