

# Fertility Sparing Surgery and Borderline Ovarian Tumours

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Fertility sparing surgery (FSS) is now a widely acceptable treatment for the management of Borderline Ovarian Tumours (BOTs) in women of reproductive age. However, many clinicians face the dilemma of balancing the risks of disease recurrence with progression to lethal malignancy whilst preserving fertility, in the absence of clear standardized guidelines.

fertility-sparing surgery

borderline ovarian tumour

ultrasound guided laparoscopic ovarian wedge resection

ovarian cancer

## 1. Introduction

Globally, epithelial ovarian cancers account for the second-most-common cause of death from a gynaecological cancer <sup>[1][2]</sup>. Borderline Ovarian Tumours (BOTs) comprise of a separate entity of non-invasive epithelial neoplasms, with a recognised, albeit uncertain potential for malignancy, as acknowledged by the International Federation of Gynaecology and Obstetrics (FIGO) <sup>[3]</sup>. As such, BOTs account for 15% of all epithelial ovarian malignancies (EOMs) <sup>[4]</sup>. The incidence is low, with European series reporting 4.8:100,000 new cases per year <sup>[5]</sup>. Histologically, they show more complex architecture, cellular crowding, proliferative activity, and variable nuclear atypia when compared to benign ovarian tumours of the same histological subtype <sup>[6]</sup>. The absence of stromal invasion differentiates BOTs from ovarian carcinomas <sup>[7]</sup>.

BOTs can be of several histological subtypes, of which 53–65% are of the serous (sBOT) and 32% of the mucinous (mBOT) type. Less than 5% include the sub-types: clear cell, endometrioid and Brenner tumours <sup>[3][4][8]</sup>. BOTs are staged according to the FIGO staging; however, unlike ovarian carcinoma, at least 70–80% of cases are diagnosed at an earlier stage I <sup>[8]</sup>. Presentation of disease at stage II and III occurs in nearly 21% <sup>[9]</sup>, with <1% of women diagnosed at stage IV <sup>[3]</sup>. Approximately 16–30% are asymptomatic at diagnosis <sup>[10]</sup>. The prognosis of BOTs is excellent <sup>[11]</sup>, with the five-year survival rate for women with FIGO stages I–III described as 95–99.7% and stage IV disease as 77.1% <sup>[12]</sup>.

A third of patients diagnosed with BOTs are <40 years of age and comparatively present 10 years younger than women with ovarian carcinoma (45 versus 55 years old respectively) <sup>[13][14][15]</sup>. Given that the majority of women are of reproductive age at diagnosis, the demand for fertility preservation in the form of conservative surgery is

crucial. For women who no longer wish to preserve fertility, radical surgery, also referred to as complete debulking, aims to provide optimal management of the disease. This includes abdominopelvic exploration, peritoneal washings, and excision of the macroscopic tumour, followed by bilateral salpingo-oophorectomy (BSO), omentectomy, and peritoneal biopsy [16]. In women who wish to preserve their reproductive potential however, fertility sparing surgery (FSS) is the treatment option of choice where feasible. This includes resection of the BOT through conservative surgical procedures including ovarian cystectomy, unilateral salpingo-oophorectomy (USO), and more recently a novel technique of ultrasound-guided ovarian wedge resection (UGOWR) [16][17]. In women with bilateral ovarian involvement, a USO and ovarian cystectomy, or bilateral ovarian cystectomy, may also be indicated [6]. In such instances where peritoneal washing, omentectomy, and peritoneal biopsy is performed, women would be considered having undergone a complete staging of disease.

The predominant risk associated with FSS however, includes the recurrence of disease, which is reported to be between 5–34% [2][18]. Evidence also suggests recurrence is 2–4 fold higher when compared to radical surgery [19]. This is exemplified in various studies whereby 18–36% of women developed a recurrence following ovarian cystectomy, compared to 0–5.7% following radical surgery [20][21]. For this reason, individualised and carefully planned surgical management is imperative, to ensure the risks of disease recurrence are balanced with fertility preservation and restoration of the ovarian reserve. Post-operative surveillance with ultrasound monitoring for sonographic appearances is therefore essential in early detection of disease recurrence.

## 2. Ultrasound-Guided Ovarian Wedge Resection

Within the tertiary Gynaecological Oncology Centre, a specialist expert ovarian ultrasound clinic was dedicated to the diagnosis and management of BOTs. With improved technology in ultrasound quality and clinician expertise, researchers advocate that intra-ovarian deposits of ovarian borderline disease of increasingly smaller size can be detected earlier. Such deposits, too small for the naked eye, may be missed during therapeutic laparoscopic staging or resection of disease, resulting in patients being upstaged, thus undergoing oophorectomy to ensure complete resection. Alternatively, the plan may be to continue surveillance monitoring until the disease can be visualised laparoscopically, and only then surgically resected. As such, in the absence of expert scanning resources, the clinician may be inclined to over- or under-treat pathology.

Intra-operative ultrasound has been described as a novel adjunct to FSS, assisting the resection of small ovarian lesions and optimising the chances of complete resection of disease, whilst preserving maximum ovarian tissue [16]. When performing FSS on smaller borderline ovarian deposits, disruption to healthy ovarian follicles has been observed, as demonstrated by lower relative follicle densities during cystectomy for endometriomas [22]. Furthermore, this method has the potential to enhance intra-operative diagnostic accuracy when delineating pathology within the ovary [23]. In the context of sBOTs, one third of deposits present bilaterally [16]. Although previous practice suggested obtaining an ovarian biopsy of the contralateral ovary, this is no longer advised in the absence of visible disease [8]. Therefore, the use of detailed intra-operative ultrasound assessment of the contralateral ovary may assist the surgical staging of disease and the earlier diagnosis of recurrence.

Simultaneously, it may prevent injury to healthy follicles sustained from the disruption to the ovarian tissue when a biopsy is taken and thus, the consequential adhesions caused.

In a preliminary publication reporting outcomes in women undergoing laparoscopic UGOWR for recurrence of BOT taken from the data, six patients underwent the procedure for management of a first recurrence of sBOT [16].

The researchers have previously recommended the use of this novel technique for the management of second or third recurrences of disease, but only in women considered at high risk of declining ovarian reserve following surgery, whereby reproductive potential is limited and of high priority for the patient [16]. However, when used as the primary treatment for the initial management of BOT, the procedure has been successfully implemented, in which no recurrences have yet been reported. When UGOWR was performed in addition to other procedures considered FSS for the initial management of disease, there was one recurrence of sBOT. Furthermore, in six women who were treated for a first recurrence of BOT by UGOWR, 50% developed a second recurrence, which has either been managed conservatively, or with further UGOWR. It can be argued that the benefits of enabling the selected women to achieve pregnancy may considerably outweigh the risks of disease recurrence, in particular given the findings that recurrences of BOT in FSS are not malignant and can be detected early with surveillance ultrasound monitoring. When considering this treatment option for multiple recurrences of disease, it is at the clinicians' discretion and responsibility to ensure the woman is fully informed regarding her choices, in particular, considering the number of surgical procedures performed is negatively associated with pregnancy outcome ( $p < 0.001$ ) [2]. Although researchers appreciate the numbers presented in the study are too small to deduce significant conclusions, positive outcomes have been established from the data. However, further prospective studies are required to determine whether this adjunct to FSS impacts overall ovarian reserve and subsequent fertility outcomes in women with BOTs.

### 3. Reproductive Outcomes

Approximately 19.2% ( $n = 33$ ) of women attempted pregnancy in the cohort. However, the numbers are too small to deduce whether pregnancy outcome is determined by the type of FSS. Previous studies have also provided inconclusive findings. For example, the cumulative pregnancy rate was similar when comparing USO and ovarian cystectomy (45.4% vs. 40.3%, respectively) [24], whereas multivariate analysis has shown no association between the conception and the type of surgery amongst 252 women in a separate study [2].

The majority of pregnancies achieved were spontaneous (78.9%), slightly lower than 93.4% reported from a study of 212 attempts [2]. Nonetheless, the findings suggest that FSS may preserve a significant quantity of healthy ovarian tissue, enabling women to achieve pregnancies without the need for assisted conception. This is exemplified by the fact that 50% of women who achieved pregnancy ( $n = 14$ ), were able to conceive more than once postoperatively, thus fulfilling the purpose of FSS.

The pregnancy rate amongst the three histological subgroups ranged between 26–43%, consistent with previous reports [25][26]. However, not all studies within the literature that report a pregnancy rate were considered for the

bias of their population sample. For example, a number of studies may not consider the proportion of women who wish to conceive or the previous history of infertility or account for the influence of histological or staging of disease or the age of women with fertility outcomes [27]. Furthermore, there are various predictors of pregnancy success, such as history of previous successful pregnancy ( $p = 0.005$ ) and reduced number of surgeries performed that should be taken into consideration [2].

## 4. Conclusion

It is suggested that non-FSS is associated with negative oncological outcomes when compared to FSS, as evidenced by the higher rate of recurrences of LGSC. This may be attributed to the stringent long term follow-up and regular ultrasound surveillance that all FSS patients have in the centralised specialist clinic. This, in addition to the introduction of laparoscopic UGOWR, as a novel method of fertility preserving surgery, enables earlier detection and treatment of disease recurrence whilst preserving fertility. Furthermore, FSS has successfully enabled women attempting pregnancy to achieve spontaneous conceptions following management of disease.

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