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Review

Conservative surgery in ovarian borderline tumours: A meta-analysis with emphasis on recurrence risk

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Abstract Background: Recent reports have stirred the debate regarding the optimal conservative treatment for both serous and mucinous borderline ovarian tumour (BOT). The aim of this study is to examine the optimal oncological approach of conservative surgery in unilateral BOT (cystectomy (C) versus unilateral salpingo-oophorectomy (USO)) and in bilateral BOT (bilateral C (BC) versus USO + contralateral C (CC)), as well as fertility outcomes.

Materials and methods: The PubMed database and Cochrane Library were searched using the search terms (((Borderline) OR (low malignant potential)) AND (ovarian)) AND ((tumour OR (cancer)) AND (((fertility sparing) OR (conservative)) AND surgery).

Results: We analysed 39 studies that included 5105 women (2624 patients with serous-, 2120 patients with mucinous- and the remaining with other types of BOT), 2752 of which underwent conservative surgery (817 underwent C, 89 BC, 1686 USO and 118 USO + CC). Eight studies included only stage I patients, in 14 studies more than 90% of patients were stage I and five studies included only late-stage patients. Seven studies included only patients with serous borderline ovarian tumour (sBOT) and two only mucinous borderline ovarian tumour (mBOT). A total of 296 patients with non-invasive-, 76 patients with invasive- and 50 patients with unspecified implants were pooled. Of the patients undergoing C, BC, USO and USO + CC the pooled recurrence estimates were respectively 25.3%, 25.6%, 12.5% and 26.1%. In meta-analysis, USO was significantly favored over C with an OR for recurrence reduction = 2.200, 95% CI = 0.793–2.841 and $p < 0.0001$. The pooled recurrence estimate as invasive ovarian cancer was 15.4% and the pooled 95% CI was 0.120–0.196. The cumulative pregnancy rate was 55.7% with 45.4% for USO and 40.3.0% for C.

Conclusion: Cystectomy in unilateral serous BOT is significantly associated with a higher recurrence rate, albeit no impact on survival can be demonstrated. Whether this is related to the duration of follow-up, remains to be proven. Nonetheless, recent data seem to suggest that USO is advisable in the case of mucinous BOT. On the contrary, a more conservative

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approach (BC) should be definitively favored in bilateral BOT, which is almost always serous, because no significant difference is seen in terms of recurrence rate when compared to USO + CC.

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1. Introduction

Borderline ovarian tumours (BOTs) are a disease of younger, fertile women, with generally a benign course. However, a minority of patients progress and eventually succumb to the disease. Having an incidence of 1.8–4.8 out of 100,000 women per year, patients tend to be relatively youthful with a mean age of 38 years, but the highest frequency relative to invasive ovarian cancer of these tumours occurs in the 15–29 year-old age group [1]. Being mainly a disease of the young fertile patient, preserving fertility is often a concern. While fertility sparing surgery is widely accepted and performed, there is a lack of randomised controlled trials evaluating its outcome and consequently there is a lack of standardised treatment guidelines. Recent reports have stirred the debate regarding the optimal conservative treatment for women with BOT [2–5]. The aim of the present study is to examine the optimal oncological approach of fertility sparing surgery in women with unilateral BOT (cystectomy (C) versus unilateral salpingo-oophorectomy (USO)) and in women with bilateral BOT (C + contralateral C (CC) versus USO + CC), as well as fertility outcomes. A systematic review of literature and meta-analysis was performed. Given BOT general good prognosis, low mortality rates and general short-follow-up of most studies, the end-point of these studies was recurrence free survival, even though it is known that most BOT recurrences can be properly salvaged with surgical treatment. Nonetheless, a proportion of patients recur with invasive ovarian cancer (IOC), often carrying a dire prognosis so that avoiding disease recurrence should be an important goal.

2. Methods

2.1. Protocol registration

The protocol was not registered.

2.1.1. Study and participants characteristics

2.1.1.1. Types of studies.

2.1.1.1.1. *Inclusion criteria.* Peer-reviewed articles regardless of their retrospective or prospective nature, examining the role of different forms of fertility sparing surgery (namely C, BC, USO and USO + CC) in women with primary BOT.

2.1.1.1.2. *Exclusion criteria.* We excluded reports in which:

- The follow-up of patients who were treated with fertility sparing surgery was not reported separately from those treated with non-fertility sparing surgery.
- The histological diagnosis of BOT as currently defined by FIGO was not up-to-date.
- **The outcomes of the different treatment groups (conservative surgical approaches ie C, BC, USO, USO + CC) were provided together.**
- The follow-up was short (mean duration of follow-up <20 months).
- Individual case reports and small case series (<18 patients treated with fertility sparing surgery).

For the analysis of the outcomes of patients with advanced stage disease all series, regardless of sample size and duration of follow-up (apart from single case reports), were analysed.

2.1.2. Types of participants

2.1.2.1. *Inclusion criteria.* Women with a histological diagnosis of primary BOT of any variant.

2.1.2.2. *Exclusion criteria.* Women with concurrent ovarian cancer or other malignant tumours of the ovary, as well as women with recurrent BOT.

2.1.2.3. *Types of outcome measure.* Primary outcome measure: disease free survival; secondary outcome measure: overall survival.

2.1.2.4. *Search strategy, identification and selection of studies.* The PubMed database and Cochrane Library were searched using the search terms ((Borderline) OR (low malignant potential) AND (ovarian)) AND ((tumour) OR (cancer)) AND ((fertility sparing surgery) OR (conservative surgery)). All titles and abstracts retrieved by electronic searching were examined. Those that clearly did not meet the inclusion criteria were excluded, while the full text of potentially relevant references was obtained.

2.1.3. Types of intervention and comparison

We compared four types of fertility sparing interventions, namely C, BC, USO and USO + CC. Fertility sparing surgery was defined as uni- or bilateral C, USO with or without CC, and radical surgery was defined as BSO with or without TAH. We further compared the outcomes of fertility sparing surgery to radical surgery.

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