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Original Research

Impact of surgical staging on prognosis in patients with borderline ovarian tumours: A meta-analysis

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Abstract ***Background:*** To quantify the effect of complete surgical staging (CSS) on prognosis in borderline ovarian tumour (BOT) patients through a meta-analysis.
Methods: We systematically reviewed published studies comparing CSS with incomplete surgical staging (ISS) in BOT patients through April 2015. End-points were recurrence and mortality rates. Study design features that possibly affected participant selection, recurrence/death detection, and manuscript publication were assessed. For pooled estimates of the effect of CSS on recurrence/death, random- or fixed-effects meta-analytical models were used after assessing cross-study heterogeneity.
Results: Eighteen observational studies (CSS, 1297 patients; ISS, 1473 patients) met our search criteria. Fixed-effects model-based meta-analysis indicated a reduced recurrence risk among CSS patients (odds ratio [OR]=0.64; 95% confidence interval [CI]: 0.47–0.87, $P < 0.05$, $I^2 = 25.6$). However, no significant between-group difference in mortality was observed (OR = 0.98; 95% CI: 0.42–2.29, $P = 0.97$, $I^2 = 0$). In subgroup analysis by histology, CSS was associated with a reduced recurrence risk in 16 studies of all histologic types (OR = 0.66; 95% CI: 0.48–0.91, $P < 0.05$, $I^2 = 31.9$) but not in two studies of only mucinous disease (OR = 0.41; 95% CI: 0.13–1.30, $P = 0.13$, $I^2 = 0$). In subgroup analyses with four studies with recurrence data according to fertility-sparing surgery, no significant association was found (OR = 0.51; 95% CI: 0.18–1.43, $P = 0.20$, $I^2 = 0$). There was no evidence of publication bias.

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Conclusions: In this meta-analysis based on observational studies, CSS appeared to significantly reduce recurrence among BOT patients. No survival impact was observed. Longer-term randomised controlled trials could verify this relationship but appear infeasible for this rare tumour.

1. Introduction

Borderline ovarian tumours (BOTs) are defined histologically by atypical epithelial proliferation without destructive stromal invasion and account for 10–15% of all epithelial ovarian tumours [1]. Although less invasive than epithelial ovarian cancer, BOTs occur frequently in premenopausal women and are usually confined to the ovary [2]. Most cases of BOT are surgically cured, with a 5-year overall survival rate of 95%; however, tumour-related deaths can occur due to invasive recurrence [3].

Surgical resection is the mainstay of BOT treatment. The International Federation of Gynecology and Obstetrics staging system for BOTs is the same for invasive ovarian cancers. However, given the absence of preoperative diagnostic tools [4] and limited value of intraoperative frozen section analysis [5], initial surgery for patients with BOT often leads to incomplete surgical staging (ISS) [6–10]. Although upstaging does occur (15–47%) with presumed stage I BOTs [11,12], reports regarding the impact of surgical staging on prognosis remain conflicted without reliable evidence from randomised trial. This information is, however, essential when obtaining preoperative informed consent for further operative procedures or counselling patients after ISS. Thus, there is a need for a meta-analysis to summarise the existing evidence.

The present study quantified and compared the effects of CSS and ISS on survival outcomes in patients with BOT through a meta-analysis. With the estimated effect of complete surgical staging (CSS) on prognosis, it would help clinicians and patients with BOT to balance the risks and benefits of CSS.

2. Materials and methods

2.1. Literature search

A systematic review was performed using the designed reporting guidelines [13,14]. The EMBASE and MEDLINE databases and Cochrane Central Register for Controlled Trials were searched up to 24th March, 2015, irrespective of language. Pre-publication papers were also included. The search strategy included the following keywords: borderline*[All] AND (Ovarian Neoplasms [Mesh] OR ((Ovary[Mesh] OR Ovary[TW] OR Ovarian [TW) AND (Neoplasm*[TW] OR cancer*[TW] OR tumor*[TW] OR tumour*[TW] OR malignant*[TW] OR low malignant potential))) AND (staging OR restaging OR stage). Titles and abstracts were screened to identify relevant articles, and full texts were retrieved for detailed reviews. References in retrieved papers and published reviews were manually checked to identify additional relevant studies. Two authors (SS and SL) independently conducted all searches.

2.2. Eligibility criteria

Inclusion criteria for this meta-analysis were as follows: (1) randomised controlled trial or prospective or retrospective cohort, nested case-control, or population-based case-control study; (2) participants receiving surgical treatment for BOT; (3) CSS as the intervention of interest; (4) outcome measure of recurrence or mortality rate measured via relative risks, odds ratios (ORs), or hazard ratios with 95% confidence intervals (CI) (or sufficient data for calculation); and (5) precise reporting of surgical staging procedures. For studies using duplicated or shared data, the most informative or recent study was included. Single-arm cohort studies were excluded.

2.3. Data extraction

The following data were extracted from each study: last name of the first author; publication year; study design, location, and period; age; sample size (cases/controls or cohort size), CSS exposure and details; tumour stage; histology; postoperative residual disease, follow-up duration; recurrence; death from disease; and variables controlled for the analysis. Surgical staging was considered complete if the following procedures were performed: bilateral salpingo-oophorectomy for menopausal patients or for premenopausal patients without intention of fertility preservation, peritoneal cytology, omentectomy, multiple peritoneal biopsies, and appendectomy in patients with mucinous BOT [15]. For patients undergoing fertility-sparing surgery (FSS; defined as preservation of the uterus and at least part of one ovary), surgical staging was considered complete if all aforementioned surgical procedures besides bilateral salpingo-oophorectomy had been performed. Each study was systematically reviewed for features that might introduce bias, similarity of risk factors for