Staging for low malignant potential ovarian tumors: a global perspective

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OBJECTIVE: We describe current evidence for staging low malignant potential ovarian tumors and their conformity to current consensus guidelines and practice from an international perspective.

DATA SOURCES: A search of MEDLINE, EMBASE, and SCOPUS databases was conducted for articles published between January 1990 and April 2015.

STUDY ELIGIBILITY CRITERIA: Studies on low malignant potential ovarian tumors that evaluated the prognostic value of disease stage, staging vs no staging, complete vs incomplete staging, or discrete components of staging were eligible. Studies that described only crude survival rates were excluded.

STUDY APPRAISAL AND SYNTHESIS METHODS: Eligible studies were categorized according to their outcome (disease stage, staging procedure, or discrete staging elements). Data were abstracted using a standard form. Inconsistencies on data abstraction were resolved by consensus among the authors. Risk of bias was assessed using the Newcastle-Ottawa Scale.

RESULTS: Of 1116 studies, 702 were excluded for irrelevance and 364 for not meeting inclusion criteria. Nine studies were excluded for describing crude survival rates without a comparative conclusion. We found that studies supporting the value of defining disease stage or staging procedures (mostly conducted in northern Europe) included more patients than studies that did not find disease stage or staging useful (predominantly from North America, 4072 vs 3951). Disease stage correlated with survival in 13 of 25 studies, whereas none of the studies that evaluated the value of staging found it beneficial (9 studies, 1979 patients). Studies that evaluated isolated components of staging found no benefit to these procedures. Regional guidelines and consensus reviews drew conclusions based on a limited number of studies that generally originated from the same region.

CONCLUSIONS: Although the correlation of stage with survival was mixed, performing staging procedures for low malignant potential ovarian tumors is not supported by the best available evidence. Guidelines in support of staging based their recommendations on a few regional studies and conflict with better-quality data that do not support staging procedures. An international consensus statement is needed to standardize the surgical management of low malignant potential ovarian tumors.

Key words: borderline ovarian tumors, surgical staging, systematic review

Low malignant potential ovarian tumors were first described by Taylor in 1929.[1] At that time, this category of ovarian tumors was addressed as semimalignant, a description that may explain the persistence of controversy in their management for the last century. Low malignant potential accounts for 14-15% of all primary ovarian tumors and has been variably placed in a gray zone between benign and malignant.[2] Although the prognosis of low malignant potential ovarian tumors remains more favorable than invasive tumors,[3] the histological types and microscopic and macroscopic architecture resemble invasive malignant tumors.[4,5]

Preoperative ultrasonographic diagnosis is reliant on finding typical features of multiloculated or septated cyst with papillary projection; however, up to one third may present as uniocular cysts.[6,7] Therefore, 78% of low malignant potential ovarian tumors are encountered and managed by general obstetrician-gynecologists, whereas only 10% are managed by gynecological oncologists.[8]

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Management among surgeons, particularly general obstetrician-gynecologists, is inconsistent; 35% do not perform staging biopsies, whereas 9% tend to perform complete staging.[8] Full surgical staging has been justified by some because of the difference in prognosis between early and advanced disease stage.[9-11] However, the prognostic value of disease stage has not been evident in other studies.[12] Furthermore, there is no evidence that adjuvant therapy improves outcomes for higher staged tumors.[13]

Accordingly, it is unclear whether defining stage or performing surgical staging is of value. This lack of strong evidence regarding surgical staging weakens practice guidelines and makes them less likely to be followed.[8,14] Because disease recurrence or persistence is reported in up to 14% of cases,[15] it is important to define an appropriate treatment strategy to

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reduce unnecessary procedures or the need for reintervention.

Materials and Methods

Objective

The aim of this systematic review is to assess current evidence on surgical staging from a global perspective and to appraise congruence of current consensus statements or guidelines with the best available evidence. This review also summarizes surgeons' attitude toward staging and to what extent it has been influenced by evidence and clinical guidance.

Literature search

A search was conducted for studies that addressed the value of staging compared with no staging, complete vs incomplete staging, the value of discrete components of staging, and the prognosis of early vs advanced International Federation of Gynecology and Obstetrics stages of low malignant potential ovarian tumors based on the final pathology report.

Based on this review protocol and in collaboration with an expert librarian, a search on MEDLINE, EMBASE, and SCOPUS databases was done for articles published between January 1990 and April 2015. Search key words included borderline ovarian tumors or ovarian low malignant potential tumors and surgical staging or staged or unstaged or lymphadenectomy or omentectomy or peritoneal biopsy or cytology and recurrence or prognosis or outcome or survival. References from related studies and reviews were searched. No language restriction was applied. The detailed search strategy is provided in the Appendix.

Eligibility criteria and study selection

All abstracts were screened for selection of relevant studies, and full texts were reviewed for eligibility prior to inclusion. Studies were categorized according to whether they described the prognostic impact of early vs late stages, surgical staging vs no staging, complete vs incomplete staging, or discrete staging components (lymphadenectomy, omentectomy, peritoneal biopsy, or cytology). Studies that described only crude survival rates without comparative conclusions were excluded. Sample size alone was not a criterion for exclusion. The outcomes of interest include whether the staging procedure or a knowledge of stage was correlated to the patient outcomes and whether the study origins or the statistical methods applied in these studies influenced their conclusion.

To identify consensus statements or guidelines from different regions and congruence with current evidence, we searched MEDLINE, EMBASE, and SCOPUS databases for the articles that contain the following terms: borderline ovarian tumors or low malignant potential ovarian tumors and guidelines or consensus or recommendations. We recorded the publication date, the country of origin, recommendations, and the evidence cited to support these recommendations. For the evaluation of gynecological surgeons' attitudes toward staging, we searched for the terms the following terms: borderline ovarian tumors or low malignant potential ovarian tumors and survey. We reported the publication date, the country of origin, the surveyed population, and a summary of survey results.

Study selection

Of 1116 abstracts initially available based on search terms, 702 were excluded for not being relevant to the primary objectives. Additional 364 articles were screened out during review of full texts for not meeting the inclusion criteria. During data extraction, 9 studies were excluded because they provided only crude survival rates without comparative conclusion. Overall, 41 studies with data on 8023 women were eligible (Figure 1). One investigation was considered in the study count but excluded from population size analysis because of the duplication of patients with another study.[16]

Data abstraction

Extraction of the data from the full articles was performed using a standardized form that included authors, year of the study, country of origin, type of study, time frame of data collection, sample size, primary method of statistical analysis, duration of follow-up, outcomes, and conclusions. Data were extracted from the main text, tables, and figures. Inconsistencies between reviewers on study selection and data extraction were resolved by consensus among the authors; discrepancies found were minor. For simplicity, studies were categorized based on their conclusion to either prognostically valuable or prognostically not valuable according to whether a study found disease stage and/or staging procedure(s), useful or not. Observational studies were assessed using the Newcastle-Ottawa Scale.[17]

Pooled analysis was not feasible because of the heterogeneity of the cohort criteria (spectrum of disease stage, histopathology of the tumor), statistical analysis, duration of follow-up, and primary outcomes. Furthermore, some studies presented their results as descriptive statements of conclusion rather than quantitative conclusions. An analysis was performed using Microsoft Office Excel 2010 (Microsoft, Redmond, WA).

Results

All studies were retrospective and originated from 16 countries (Table 1). [T1] Twelve studies were conducted in middle and northern Europe.[9,16,18-22,26,27] Another 12 studies originated in southern Europe and the Middle East.[28-39] There were 8 studies from North America, 7 studies from Asia,[40-46] and 2 from Australia.[47,48]

Prognostic variables and outcomes were analyzed using a Cox proportional hazards model in 12 studies,[16,18,19,29,30,42-44,46,47,49,50] Kaplan-Maier survival curves in 12 [F1] studies,[9,20,26,31,33,36,38,40,41,48,51,52] multivariate logistic regression in 3 studies,[22,25,53] univariate analyses in 12 studies,[21,23,24,27,28,32,34,37,39,45,54,55] and descriptive data in 2 studies.[35,56] In these descriptive studies, the authors provided conclusions based on the subjective comparison of outcomes between study groups without statistical analysis. In terms of methodological quality, most studies had Newcastle-Ottawa Scale scores of 5−7, indicating good quality.

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