



Original Research

Is lymphadenectomy necessary in mucinous ovarian cancer? A single institution experience



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HIGHLIGHTS

- No evidence of metastatic disease was found in the dissected pelvic nodes in patients with mucinous ovarian cancer.
- Overall survival (OS) in patients who did not undergo lymphadenectomy was 44 months (CI95% 23–64); in the lymphadenectomy group, mean survival was 83 months (CI95% 67–100).
- No significant differences were found that were independently associated with lower or greater overall survival.
- Our results suggest that routine lymphadenectomy may be excluded in women with clinically apparent primary mucinous ovarian cancer.

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ABSTRACT

Background: According to the International Federation of Gynecology and Obstetrics (FIGO) guidelines, every patient diagnosed with ovarian cancer (OC) should undergo a complete staging procedure to adequately assess tumor spread. The role of lymphadenectomy in the initial management of primary early mucinous ovarian cancer (MOC) remains unclear.

Objective: To describe the prevalence of pelvic and para-aortic node metastases in MOC.

Materials and Methods: The records of patients with MOC treated at our Institute during January 2005 to December 2011 were assessed. A descriptive and comparative analysis was conducted. Overall survival (OS) and diseases-free period (DFP) were calculated with the Kaplan-Meier method and were compared with the log-rank test.

Results: Of 31 patients with MOC, 14 (45.16%) underwent lymphadenectomy, obtaining 190 pelvic nodes, with a median of 9 pelvic lymph nodes removed per patient (interquartile range = 15). There was no evidence of metastatic disease in the dissected pelvic nodes.

Conclusion: These results suggest that complete surgical staging with lymph node dissection has no effect on recurrence, disease-free period, and overall survival of patients with early stage MOC.

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1. Introduction

Ovarian cancer is the most lethal gynecologic malignancy. Because of the lack of early symptoms and screening protocols, it is detected late in the clinical course of the disease. With a worldwide incidence of 6.3/100,000 women, it is the seventh most common cancer diagnosed [1].

Historically, all epithelial ovarian cancers have been treated

similarly, and clinical decision-making and prognostic information have been determined by pooling aggregated data from all epithelial cancer subtypes, including serous, mucinous, endometroid, clear cell, Brenner, mixed, and undifferentiated histologies [2].

Primary mucinous carcinomas of the ovary are not common and account for less than 5% of all invasive epithelial ovarian cancers [3,4]. When compared with serous carcinomas of the ovary, mucinous carcinomas have a distinct presentation, clinical course, and response to therapy [5,6].

According to the International Federation of Gynecology and Obstetrics (FIGO) guidelines, every patient diagnosed with ovarian cancer should undergo a complete staging procedure to adequately assess tumor spread and guide adjuvant chemotherapy recommendations. A complete staging procedure should include omentectomy, biopsy of all suspicious lesions, peritoneal washings, and lymph node sampling/dissection [7].

The majority of mucinous ovarian carcinomas (MOCs) are well or moderately differentiated and are usually borderline ovarian tumors or stage I without metastatic disease at the time of diagnosis that do not require additional therapy beyond surgical removal [4]. In these patients, prognosis is good, with a 5-year disease-free survival of 90.8% [8–10].

In contrast, outcomes in women with metastases beyond the ovaries or with recurrent disease are extremely poor. Response rates of MOC to conventional ovarian cancer chemotherapy agents (platinum agent + taxanes) are low, and the agents commonly used against primary gastrointestinal cancers (oxaliplatin, capecitabine, and 5-fluorouracil) show a better response [11,12].

The importance of systematic lymphadenectomy in the initial management of primary early ovarian cancer and its prognostic relevance remain unclear. Recent data suggest that in patients with mucinous tumors, lymph node involvement is exceedingly low or non-existent when surgical removal is performed [11].

Because of the low number of cases (31 cases) of MOC, there are no precise statistical data on lymph node involvement. Our objective was to delineate the relevance of pelvic and para-aortic node metastases in MOC.

2. Methods

Thirty-one patients with a confirmed pathological diagnosis of primary MOC and treated at this Cancer Institute in Mexico during January 2005 to December 2011 were retrospectively analyzed.

Prior to the collection of information, a specific instrument was designed to store all the information that, according to the literature, is important to have, including the risk factors and the symptomatology of ovarian cancer. The information was obtained directly from the electronic hospital record of each case.

Review of medical records was performed, and data including lymphadenectomy; preoperative and postoperative cancer antigen (CA) 125, CA 19-9, and carcinoembryonic antigen (CEA) levels; intraoperative findings (bilateral tumor, presence of ascites); tumor histology; number of resected and metastatic lymph nodes; adjuvant treatment; and follow-up were retrieved. Patterns of lymph node positivity including laterality and potential risk factors associated with occult advanced disease were assessed (ipsilateral vs. bilateral ovarian disease).

Descriptive statistics analysis was performed for demographic variables, reporting central tendency medians. Univariate analysis was performed by the Mann–Whitney *U* test for continuous variables, and the chi-square test or Fisher's exact test according to the case for ordinal variables. When feasible, the variables were included in the multivariate Cox analysis. Overall survival (OS) and disease-free interval (DFI) were analyzed by the Kaplan–Meier method, and the curves were compared using the log-rank test.

Statistical significance was defined with a value of $p < 0.05$. The IBM SPSS statistical package 2013 was used.

3. Results

Of the 31 patients, lymphadenectomy was performed in 14 patients (45.16%), obtaining 190 pelvic nodes, of which none had disease (median dissection of 9 pelvic lymph nodes per patient; interquartile range = 15). No evidence of metastatic disease was found in the dissected pelvic nodes. Para-aortic lymphadenectomy was performed in 10 patients, obtaining 66 para-aortic lymph nodes (median dissection of 5 para-aortic nodes per patient; interquartile range = 3.75). No evidence of metastatic disease was found.

The median age of patients in the lymphadenectomy group was 47.5 years (range, 30–63 years), and in the group without lymph node dissection was 54 years (range, 30–74 years) ($P = 0.57$).

The characteristics of the patients and tumors are shown in Table 1.

The mean tumor size was 23 cm (range, 7–30 cm): 18.7 cm in the non-lymphadenectomy group and 26.9 cm in the lymphadenectomy group ($P = 0.078$).

Tumor markers CA 125, CA 19-9, and CEA were measured. The mean initial CA 125 tumor marker in patients with lymphadenectomy was 45.9 U/mL, and it was 308 U/mL in the group without lymphadenectomy ($P = 0.016$). The tumor marker CA 19-9 was measured in eight patients, five of whom did not undergo lymphadenectomy, with a mean marker of 316 U/mL; the lymphadenectomy group had a mean CA 19-9 level of 22 U/mL ($P = 0.347$). CEA was measured in only seven patients, with no significant difference between groups ($P = 0.622$).

There was no statistical difference in the survival of the patients at the time of the analysis, because the number of living patients who underwent lymphadenectomy was similar to that of those who did not undergo lymphadenectomy ($P = 0.66$). Only six deaths were reported from the total of the studied group: four (12.9%) deaths occurred in the group who did not undergo lymphadenectomy, and two (6.4%) deaths occurred in the lymphadenectomy group.

Five recurrences of the cancer were recorded, of which three were locoregional and two were documented at a distance, just a recurrence (locoregional) in the lymphadenectomy group. ($P = 0.357$; Table 2).

The mean disease-free period (DFP) in patients who underwent lymphadenectomy was 73.6 (CI95% 59–88) months, whereas in those who did not undergo lymphadenectomy, it was 38 (CI95% 17–58) months, with an overall DFP of 64.2 months (log rank $P = 0.092$); the median was not achieved (Fig. 1A).

Overall survival (OS) in patients who did not undergo lymphadenectomy was 44 months (CI95% 23–64); in the lymphadenectomy group, mean survival was 83 months (CI95% 67–100), with an OS for the whole population of 73.4 months (log rank $P = 0.104$); the median of follow-up was not achieved (Fig. 1B).

A Cox multivariate analysis was performed to identify variables that could be associated with OS; no significant differences were found that were independently associated with lower or greater OS (Table 3).

4. Discussion

Complete surgical staging has been considered very important in the treatment of ovarian cancers, as it helps determine the real stage of the disease. The clinical features of mucinous ovarian neoplasms are distinct from their other epithelial counterparts, and certain characteristics are typical for primary mucinous ovarian

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