

Original Research Article

Pelvic lymphadenectomy as a component of interval cytoreduction for ovarian cancer: is there a benefit? A pilot study

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ABSTRACT

Background: Management strategy in ovarian cancer includes a combination of cytoreductive surgery and chemotherapy. Interval cytoreductive surgery has been shown to be oncologically non-inferior to primary cytoreduction with the additional benefit of reduced morbidity. Lymphadenectomy as a component of cytoreductive surgery has been controversial with an unproven therapeutic benefit.

Methods: Records of patients with a histological diagnosis of ovarian cancer and treated with interval cytoreduction were evaluated. Disease related, pathological and treatment data collected for analysis.

Results: The study included 32 patients with a mean age of 56 years (41-76). Serous papillary tumors (42%) were the predominate histology and the majority were in stage III disease (84%). Optimal cytoreduction was achieved in 93%. The mean nodal harvest was 9.8 nodes with left pelvic dissection yielding slightly more nodes than the right (4.5 vs 5.2). Nodal positivity was observed in just one patient (3%). A total of 314 were nodes examined with only 2 (0.6%) yielding persistent disease. The nodal positivity yield tested as a categorical variable by the binomial test returned $P=0.0001$.

Conclusions: It is possible to omit pelvic nodal dissection during interval cytoreduction in otherwise optimally cytoreduced patients particularly when imaging and intraoperative assessment are not suggestive of pelvic nodal metastasis.

Keywords: Interval cytoreduction, Ovarian cancer, Pelvic lymphadenectomy

INTRODUCTION

Ovarian cancers account for only 23% of all gynaecological malignancies but are responsible for 47% of all deaths due to female genital tract cancers.¹ The five-year survival for all stages is 45.6% and at least two thirds of the patients present with locoregionally advanced disease. Management strategy revolves around a combination of cytoreductive surgery and chemotherapy, but up to 80% relapse and are incurable.² Cytoreductive surgery involves extensive surgical procedures with morbidity paralleling the extent of surgery. Interval cytoreductive surgery in selected stage III and IV ovarian cancer has been shown to be non-

inferior to primary cytoreduction with the advantage of reduced morbidity.³

The role of lymphadenectomy in ovarian cancers has been controversial with clear evidences supporting its staging and prognostic role, however a therapeutic benefit particularly in advanced in disease continues to be debatable.⁴ In contrast to results of retrospective studies the only prospective study till date has reported no overall survival benefit to systematic pelvic and para aortic lymphadenectomy.⁵ In the absence of a survival benefit removal of bulky nodes only or random sampling as opposed to a full lymphadenectomy has the benefit of reduction in surgical morbidity.

We performed a retrospective analysis of our records to assess if a systematic pelvic lymphadenectomy is required as a component of interval cytoreductive surgery for ovarian cancer.

METHODS

Medical records of patients with a diagnosis of ovarian cancer and treated at our institution in 2016 were evaluated for study inclusion. Patients with a histological or cytological diagnosis of ovarian cancer and in presumed clinical stages III or IV were selected for the study. All the patients prior to interval cytoreduction were treated with at least 3 cycles of a platin/taxane combination chemotherapy. A thorough physical examination, comparison of pre-and post-chemotherapy tumor marker levels (CA-125 and CEA) and CT abdomen was done to determine the suitability for interval cytoreduction. Persistence of gross ascites or unequivocal imaging evidence predictive of suboptimal cytoreduction were excluded from the study. None of the study patients met imaging criteria of nodal involvement at presentation. Patients with incomplete records, metastatic cancers to ovary or presenting with synchronous ovarian and other malignancy were also excluded from the study. Treatment with a combination chemotherapy other than platin /taxane was also used as an exclusion criteria.

Debulking surgery involved total abdominal hysterectomy, bilateral pelvic lymphadenectomy, supra colic omentectomy and other additional procedures as required for an optimal cytoreduction. Routine para aortic nodal dissection was not practiced however suspicious nodes were sampled for pathological assessment. The pathological specimen was evaluated by a single pathologist as per college of American pathologist guidelines.⁶ The presence of residual disease, histological type, nodal yield and nodal positivity determined. Over all nodal positivity of the study cohort determined and statistical significance tested with a binomial test. An estimated probability of 0.66 for nodal positivity was used for the binomial test based on results from published literature. A P value of less than 0.05 was considered as a significant result.

RESULTS

The study included 32 patients with a mean age of 56 years (41-76). Serous papillary tumors (42%) were the predominate histology and the majority were in stage III disease (84%). Six patients achieved a pathological complete response with no demonstrable tumor on histological examination. Optimal cytoreduction was achieved in 93%. The mean nodal harvest was 9.8 nodes with left pelvic dissection yielding slightly more nodes than the right (4.5 vs 5.2). Nodal positivity was observed in just one patient (3%). A total of 314 were nodes examined with only 2 (0.6%) yielding persistent disease. The nodal positivity yield tested as a categorical variable

by the binomial test returned $P=0.0001$. The baseline study characteristics and results are shown in Table 1.

Table 1: Baseline study data.

| Sample size | N=32 (%) |
|---|------------------------|
| Age (mean) | 56 years (41-76 years) |
| Histology | |
| Serous | 15 (46%) |
| Endometrioid | 08 (25%) |
| Mucinous | 03 (09%) |
| Un typeable | 06 (18%) |
| Grade | |
| High | 26 (81%) |
| Low | 02 (06%) |
| Stage | |
| III | 27 (84%) |
| IV | 05 (16%) |
| Nodal yield Right vs left (4.5 vs 5.2) | Mean 9.8 nodes |
| Nodal positivity $P=0.0001$ (Binomial test) | 01 (3%) |
| Optimal cytoreduction | |
| Yes | 30 (93%) |
| No | 02 (07%) |

DISCUSSION

Lymphadenectomy as a component of cytoreductive surgery has been strongly contested over a few years with retrospective studies claiming a survival benefit. The extent of lymphadenectomy is another debatable issue with some arguing for full paraortic and pelvic nodal dissection in the optimally cytoreduced patients while others recommend practicing only excision of bulky nodes. It is important to realize these studies have been done on primarily cytoreduced patients with no preoperative chemotherapy and consequently a nodal positivity rate of 65% (macro and microscopic) has been reported.⁷⁻¹⁰ However in contemporary practice most patients are subjected to interval cytoreduction after neoadjuvant chemotherapy. It is possible the nodal positivity rate may be much lesser obviating the need for nodal dissection as a part of interval cyto reduction. Present study has demonstrated a positive nodal rate of only 3% suggesting a comprehensive pelvic nodal dissection may be reserved for only nodes with bulky disease after neoadjuvant chemotherapy.

Fagotti et al in a retrospective study observed a 2-year progression-free survival rate of 36 versus 25% ($p=0.834$), and 2-year overall survival rate of 69 versus 88% ($p=0.777$), between systematic lymphadenectomy compared with no lymphadenectomy during interval cytoreduction. They also noted significant higher operating times and more blood transfusion in the lymphadenectomy group A non-significant trend of lesser nodal recurrences (4 vs 7%) was observed in the lymphadenectomy group.¹¹ Iwase et al in a recent

retrospective review noted that after interval debulking, despite positive pelvic and para aortic nodes identified in 39% of patients, no progression free or overall survival difference was observed between systematic lymphadenectomy and no nodal dissection. This study also confirmed higher morbidity associated with systematic nodal dissection.¹² A similar result was also reported by Schwartz et al.¹³

Present study has a few limitations including a small sample size and a lesser nodal yield. Pacini et al defined an adequate pelvic lymphadenectomy as yielding at least 25 nodes but rouzier et al in a SEER data base review of 49,783 patients found a significant difference in survival among nodal groups 0, 1-9 and more than 10 nodes hence our mean nodal yield of 9.8 nodes is unlikely to confound results.¹⁴ It is also possible that preoperative chemotherapy has modified the nodal positivity and perhaps these study patients had low nodal involvement as evidenced by no patient unequivocally satisfying imaging criteria suggestive of nodal metastasis. The other major limitation is the absence of survival data to prove the absence of a clinical benefit in omitting a comprehensive nodal dissection during interval cytoreductive surgery.

CONCLUSION

A systematic pelvic lymphadenectomy for stage III and IV ovarian cancer during interval cytoreductive surgery appears to have low positive nodal yield. It is possible to omit pelvic nodal dissection during interval cytoreduction in otherwise optimally cytoreduced patients particularly when imaging and intraoperative assessment are not suggestive of pelvic nodal metastasis. These results warrant a larger, well designed prospective study with incorporation of survival endpoints to prove the lack of a clinical benefit to routine full pelvic lymphadenectomy at interval cyto reductive surgery.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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