Effect of the N Factor on the Prognosis of pT3C Ovarian Cancer With Optimal Debulking Surgery

Fumitoshi Terauchi, Takahisa Ishikawa, Ryoko Omura, Tetsuya Moritake, Rina Kato, Yasukazu Sagawa, Hirotaka Nishi, Hiroe Ito, Keiichi Isaka

Abstract

We analyzed the effect of the N factor on prognosis of T3C ovarian cancer patients who underwent optimal surgery (OpS). According to the analyses of N factor in OpS group, prognosis was poor in N1 group, however prognosis was significantly better in the complete group than in the other group with residual tumor of less than 1 cm.

Introduction: The primary debulking surgery that is performed to achieve complete debulking is one of the most important prognostic factors in patients with advanced ovarian cancer. However, the relationship between lymph node metastases and the surgical outcome is still unclear. This study analyzed the effect of the N factor on the prognosis of patients with pT3C ovarian cancer who underwent optimal surgery (OpS). Patients and Methods: The participants were 68 patients with pT3C serous adenocarcinoma. The overall survival (OS) and the median survival time (MST) were analyzed by the diameter of the residual tumor and by lymph node metastasis using the Kaplan-Meier method and the log-rank test. The patients received retroperitoneal lymph node dissection in the pelvic cavity up to the para-aortic lymph nodes. The patients in the OpS group were further divided into a complete-surgery group with no residual tumor and a group with residual tumor of less than 1 cm, and differences were analyzed. Results: The OS rates in the OpS group and Sub-OpS group were 77.5% and 11.1%, respectively. According to the analyses made by different levels of lymph node metastasis in all patients, the OS rates in patients with N0 and N1 disease were 77.1% and 47.5%, respectively; the prognosis was significantly poorer in the N1 group. According to the analyses of the N factor in the OpS group, the prognosis was significantly poorer in the N1 group even with OpS compared with that in the N0 group (53.7% and 86.6%, respectively). Furthermore, in the N1 group with OpS, the prognosis was significantly better in the complete-surgery group than in the other group with residual tumor of less than 1 cm (77.8% and 16.7%, respectively). Conclusion: The prognosis of pT3CpN1 ovarian cancer with OpS was as poor as with Sub-OpS. However, the results suggested that the prognosis could be improved if the tumor was completely resected in OpS.
investigated the relationship between the outcome of maximal debulking surgery and lymph node metastasis in patients with pT3C.

**Patients and Methods**

A total of 68 patients with pT3C serous adenocarcinoma (including serous papillary adenocarcinoma) who were treated in the authors’ facility were enrolled in this study. PDS was performed in all patients without neoadjuvant chemotherapy. Retroperitoneal lymphadenectomy meant lymph node dissection extending from the pelvic lymph nodes to the para-aortic lymph nodes at the height of the renal veins. After PDS, all patients were treated with postoperative combined chemotherapy with paclitaxel/carboplatin. Overall survival (OS) and median survival time (MST) were analyzed by using the Kaplan-Meier method and the log-rank test, dividing the OpS group into a CS group and a group with residual tumor of less than 1 cm.

**Results**

Of 68 patients, 59 (86.8%) received OpS; the other 9 (13.2%) received Sub-OpS. There were 47 patients in the OpS group who had no residual tumor (CS group), and 12 patients had residual tumor less than 1 cm. Of 68 patients, 20 (29.4%) had retroperitoneal lymph node metastasis (N-positive group).

The MST of patients in the OpS group was not detected, and the 5-year OS was 77.51%. In the Sub-OpS group, the MST was 589 days, and the 5-year OS was 11.11%. Thus, the prognosis was significantly better in the OpS group (\(P < .001\)) (Figure 1).

The MST of patients in the CS group was not detected, and the 5-year OS was 85.31%. The MST of patients with residual tumor less than 1 cm was 1390 days, and the 5-year OS was 47.62%. The prognosis was significantly better in the OpS group (\(P = .0014\)) (Figure 2).

In the N-negative group, the MST was not detected, and the 5-year OS was 77.15%. In the N-positive group, the MST was 1390 days, and the 5-year OS was 47.5%. The prognosis was significantly better in the N-negative group (\(P = .0194\)) (Figure 3).

In the 20 patients of the N-positive group, 16 (80.0%) received OpS and 4 (20.0%) received Sub-OpS. In the OpS/N-positive group, the MST was not detected, and the 5-year OS was 53.57%. In the Sub-OpS/N-positive group, the MST was 589 days, and the 5-year OS was 25.0%. There was no significant difference (\(P = .1388\)) (Figure 4).

In the 16 patients of the OpS/N-positive group, 10 (62.5%) were in the CS group and 6 (37.5%) had residual disease less than 1 cm. In the OpS/N-positive/CS group, the MST was not detected, and the 5-year OS was 77.78%. In the group with OpS/N-positive and with residual disease less than 1 cm, the MST was 910 days, and the 5-year OS was 16.6%. The prognosis was significantly better in the OpS/N-positive/CS group (\(P = .0074\)) (Figure 5).

The prognosis in the OpS/N-positive/CS group was significantly better compared with the group with OpS/N-positive and with residual tumor less than 1 cm and compared with the Sub-OpS/N-positive group (\(P = .0074\) and \(P = .0170\), respectively). However, there was no significant difference between the group with OpS/N-positive and with residual tumor less than 1 cm and the Sub-OpS/N-positive group (\(P = .9339\)) (Figure 6).

**Discussion**

The diagnostic role of retroperitoneal lymphadenectomy in surgery for ovarian cancer is established as the means to identify the precise stage, but its therapeutic role is not established. Regarding early-stage ovarian cancer, a retrospective study of the outcomes of 6686 patients with clinical stage I found that the prognosis was

---

**Figure 1** Kaplan-Meier Analysis of Overall Survival: Optimal Surgery Versus Suboptimal Surgery

Abbreviation: MST = median survival time.
significantly better in those with retroperitoneal lymphadenectomy than in those without retroperitoneal lymphadenectomy. In a randomized comparative study with or without retroperitoneal lymphadenectomy in patients with early-stage disease, a clear conclusion was not provided because of the small number of patients.

Regarding advanced ovarian cancer, in a randomized comparison study dividing patients with stage pTIIIb-pTIV disease into a “systematic retroperitoneal lymphadenectomy group” and a “bulky nodes resection alone group,” progression-free survival (PFS) was significantly better, but there was no significant difference in OS. Furthermore, another study found that retroperitoneal lymphadenectomy improved PFS in patients who underwent OpS.

The role of retroperitoneal lymphadenectomy in advanced cases is different from the role in early cases. Its diagnostic role regarding stage decision is not significant. In terms of a therapeutic role with a contribution to prognostic improvement, surgical removal of bulky lymph nodes as an organ, based on the concept of maximal debulking surgery, is meaningful considering achievement of CS. The point in controversy is whether retroperitoneal lymphadenectomy should be performed in advanced ovarian cancer cases without macroscopically apparent metastasis or palpable metastasis.
Advanced cases require initial postoperative chemotherapy as soon as possible, so one should consider omission or reduction of retroperitoneal lymphadenectomy, which can be highly invasive. On the other hand, because potential lymph node metastasis or future recurrence in lymph nodes (or both) are very likely in advanced cases, the idea to conduct retroperitoneal lymphadenectomy as a prophylactic measure is a persuasive strategy. To clarify this issue, the present authors retrospectively examined the relationship between the diameter of the residual tumor and the prognosis with retroperitoneal lymph node metastasis. To eliminate any bias from different histologic types in the effects of chemotherapy, the examination was restricted to only the serous type. Also, the International Federation of Gynecology and Obstetrics (FIGO) stage was standardized as pT3C for the analysis.

First, just as many reports have said, the prognosis of the OpS group was significantly better than that of the Sub-OpS group. Similarly, in the OpS group, the prognosis of the CS group was significantly better than the prognosis of the less-than-1-cm group. Moreover, despite the outcome of maximal debulking surgery, the prognosis was significantly poorer in the N-positive group than in...
the N-negative group. Similarly, when limiting the comparison to the OpS group only, the prognosis of the OpS/N-negative group was better than that of the OpS/N-positive group.

However, when limiting the comparison to the N-positive group only, despite the outcome of maximal debulking surgery, there was no significant difference between OpS and Sub-OpS. Upon division of the OpS/N-positive group into a CS group and a less-than-1-cm group, the prognosis was significantly better in the OpS/N-positive/CS group than in the OpS/N-positive/less-than-1-cm group. On the other hand, there was no significant difference between the OpS/N-positive/less-than-1-cm group and the Sub-OpS/N-positive group.

Contrary to previous reports, the analysis that divided the OpS group into a CS group and a less-than-1-cm group found improvement of the prognosis not only in PFS but also in OS. However, even if the outcome of maximal debulking surgery was OpS, when lymph node metastasis was considered, there was no difference in prognosis between the less-than-1-cm group and the Sub-OpS group.
Conclusion

Although the prognosis of advanced ovarian cancer with lymph node metastasis is poor, improvement of its prognosis can be expected by aiming for CS with maximal debulking surgery as conventional policy. On the other hand, when maximal debulking surgery has not been able to achieve CS, a change to the strategy of early postoperative chemotherapy with omission of retroperitoneal lymphadenectomy should be considered; but with regard to this point, further studies are necessary.

Clinical Practice Points

- The prognosis of pT3CpN1 ovarian cancer with OpS was as poor as with Sub-OpS. However, the results of this study suggested that the prognosis could be improved if the tumor was completely resected in OpS.

Disclosure

The authors have stated that they have no conflicts of interest.

References