Potential Role of Lymphadenectomy in Advanced Ovarian Cancer: A Combined Exploratory Analysis of Three Prospectively Randomized Phase III Multicenter Trials

Andreas du Bois, Alexander Reuss, Philipp Harter, Eric Pujade-Lauraine, Isabelle Ray-Coquard, and Jacobus Pfisterer

ABSTRACT

Purpose
Primary surgery followed by platinum/taxane-based chemotherapy is the standard therapy in advanced ovarian cancer. The prognostic role of complete debulking has been well described; however, the impact of systematic pelvic and para-aortic lymphadenectomy and its interaction with biologic factors are still not fully defined.

Methods
This was an exploratory analysis of three prospective randomized trials (Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom trials 3, 5, and 7) investigating platinum/taxane-based chemotherapy regimens in advanced ovarian cancer conducted between 1995 and 2002.

Results
One thousand nine hundred twenty-four patients were analyzed. Lymphadenectomy was associated with superior survival in patients without gross residual disease. In patients with and without lymphadenectomy, the median survival time was 103 and 84 months, respectively, and 5-year survival rates were 67.4% and 59.2%, respectively (P = .0166); multivariate analysis confirmed a significant impact of lymphadenectomy on overall survival (OS; hazard ratio [HR] = 0.74; 95% CI, 0.59 to 0.94; P = .0123). In patients with small residual tumors up to 1 cm, the effect of lymphadenectomy on OS barely reached significance (HR = 0.85; 95% CI, 0.72 to 1.00; P = .0497). For patients with small residual tumors and clinically suspect nodes, lymphadenectomy resulted in a 16% gain in 5-year OS (log-rank test, P = .0038).

Conclusion
Lymphadenectomy in advanced ovarian cancer might offer benefit mainly to patients with complete intraperitoneal debulking. However, this hypothesis should be confirmed in the context of a prospectively randomized trial.

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INTRODUCTION

Epithelial ovarian cancer is the fifth most frequent cause of cancer death in women and remains the leading cause of gynecologic cancer–related deaths in the United States and Europe.1,2 The mainstay of treatment of advanced ovarian cancer is primary surgery aimed at complete resection of all visible tumor material followed by combination chemotherapy including platinum and paclitaxel.3 Although the medical treatment is homogenous, the surgical treatment is heterogeneous. Both tumor spread and patient characteristics determine individual surgical treatment. Consequently, mode and outcome of surgery depend on both tumor resectability and patients’ ability to tolerate extensive surgical procedures. Further sources of heterogeneity are surgical skill, infrastructure, and capacity.4,5 Surgical outcome in ovarian cancer is usually classified according to the amount of postoperative residual tumor. Resection is regarded as complete if no macroscopically visible tumor is left. If any visible tumor remains after surgery, it is classified according to its largest diameter. A former definition classified surgeries that resulted in residual tumors up to 1 cm in largest diameter as optimal debulking, whereas those resulting in any larger residual tumors were defined as suboptimal debulking. The prognostic value of complete and/or optimal debulking has been reported on several occasions and confirmed in meta-analyses.6,7 Lymphatic spread has been reported to be a common feature of ovarian cancer
both in early- and advanced-stage disease. Unselected series including all International Federation of Gynecology and Obstetrics stages reported a 44% to 53% rate of lymph node metastasis detected by systematic lymphadenectomy.9,10 A prospective study in ovarian cancer limited to the pelvis showed a 22% rate of lymph node metastasis diagnosed by systematic pelvic and para-aortic lymphadenectomy.11 This rate increases to 70% after systematic lymphadenectomy in advanced-stage disease.12 The prognostic role of comprehensive lymph node staging in early ovarian cancer has been established both by an exploratory analysis of a prospective trial and in a large epidemiologic series.13,14 The latter not only suggest a stage migration effect subsequent to lymphadenectomy, but also show an impact of lymphadenectomy on prognosis in patients with positive nodes, thus indicating a therapeutic effect. This observation could not be confirmed in a prospectively randomized trial11; however, this trial was underpowered with respect to survival analysis.

Several clinical scenarios of lymphadenectomy in relation to achieved intraperitoneal debulking can be discussed separately. First, patients in whom intraperitoneal debulking results in residual tumors larger than 1 cm would not benefit at all from lymphadenectomy with respect to the maximum diameter of residual tumor matter. Second, patients with bulky nodes but complete or almost complete intraperitoneal debulking could benefit from removal of enlarged metastatic nodes by reducing the size of residual tumor. Third, lymphadenectomy in patients without clinically suspect lymph nodes and small residual disease intraperitoneally might not change the residual disease status but may reduce tumor burden that is possibly resistant to chemotherapy.15 The latter hypothesis was tested by the International Multicenter Lymphadenectomy trial, which showed a beneficial impact of systematic lymphadenectomy with respect to progression-free survival (PFS).12 However, no survival benefit was reported in this trial, and some authors concluded that systematic lymphadenectomy should no longer be considered as standard therapy in advanced ovarian cancer.16 This conclusion may not be correct for patients with macroscopically complete intraperitoneal resection because this subgroup did not substantially contribute to the results of the International Multicenter Lymphadenectomy trial. Only 37% of the patients (159 of 427 patients) in this trial had macroscopically complete resection, and because of the better prognosis, this subgroup might have contributed an even lower proportion of observed events, thus having only minimal impact on results. The International Multicenter Lymphadenectomy trial indicated a 28% rate of clinically unsuspected lymph nodes bearing metastatic disease. The poor reliability of intraoperative palpation for diagnosis of lymph node metastasis was confirmed by others,9,17 and it is possibly a result of the similar size of metastatic and nonmetastatic lymph nodes.18,19

Finally, in patients with macroscopic complete intraperitoneal debulking, systematic lymphadenectomy might theoretically add complete resection of retroperitoneal disease, thus achieving a true macroscopic complete resection status in patients who would otherwise have undiagnosed residual retroperitoneal disease without lymphadenectomy. Retrospective series and an exploratory analysis of a prospective chemotherapy trial supported this hypothesis by demonstrating an impact of lymphadenectomy on prognosis.20-23 The latter was supported by an analysis of the Surveillance, Epidemiology, and End Results database.24 Data from prospectively randomized trials evaluating the potential role of systematic lymphadenectomy in advanced ovarian cancer and complete intraperitoneal resection are still not available. Therefore, the Arbeitsgemeinschaft Gynäkologische Onkologie study group decided to analyze a large cohort of patients included in three consecutive prospectively randomized trials in advanced ovarian cancer to evaluate the potential impact of lymphadenectomy on PFS and overall survival (OS) and to define the basis for a subsequent prospective trial on this issue (Lymphadenectomy in Ovarian Neoplasm protocol).

METHODS

Data for this explorative analysis stem from the three most recent prospectively randomized phase III trials in advanced epithelial ovarian cancer coordinated and performed by the Arbeitsgemeinschaft Gynäkologische Onkologie Studiengruppe Ovarialkarzinom (Appendix Fig A1, online only).25-27 The inclusion criteria were almost the same in all three trials and have been described previously.7,25-27 None of the trials showed any significant difference for the different treatment arms with respect to PFS or OS. Therefore, we combined the data sets for this analysis.

Data were retrieved from the original case report forms and were then monitored and double checked. All patients were observed until death or end of preplanned observation period. As indicated in the original protocols, an increase in CA-125 without any clinical sign of relapse was not counted as progression but commonly resulted in radiologic investigations (computed tomography scans).

Some of the originally enrolled patients were excluded from this analysis as a result of ineligibility in the original trials or lack of details about surgical procedures, especially lymphadenectomy. Furthermore, this analysis included only patients in whom surgical debulking resulted in either no gross residual disease or small-volume residual disease with a maximum diameter of 1 to 10 mm. The population with large-volume residual disease was not included for analysis of lymphadenectomy because lymphadenectomy was rarely performed in this subgroup and no impact of lymphadenectomy on residual disease status could be expected.

All three study protocols included the prospective documentation of surgical techniques applied, as well as clinical lymph node diagnosis by intraoperative palpation and preoperative imaging by either computed tomography scan or ultrasound. Pelvic and para-aortic lymphadenectomy was recommended in patients with optimal intraperitoneal debulking but was not a mandatory inclusion criterion in all three protocols. Therefore, a variety of surgical strategies were used in these studies.

Both measurement of residual tumor diameter and details about lymphadenectomy were provided by the primary surgeon and documented postoperatively in the original case report form. This item was monitored in all patients, and surgical and pathology reports were checked for any implausibility.

We classified lymphadenectomy into the following three subgroups: no lymphadenectomy; pelvic and para-aortic lymphadenectomy, if indicated in the surgical report and lymph nodes were reported in the pathologic specimen of both anatomic regions; and incomplete lymphadenectomy, if either pelvic or para-aortic lymphadenectomy was indicated in the surgical report and at least one lymph node was reported in the pathologic specimen. OS and PFS were calculated from the day of random assignment. As indicated in the original protocols, an increase in CA-125 without any clinical sign of relapse was not counted as progression but commonly resulted in radiologic investigations (computed tomography scans).

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Study-stratified Cox regression models and Kaplan-Meier estimates were used to explore the impact of different covariates on OS and PFS, adjusting for prognostic factors. All tests were two-sided at a significance level of \( P < .05 \). Further statistical methods are described in the Appendix (online only).

RESULTS

The three phase III trials enrolled 3,388 patients with advanced epithelial ovarian cancer between 1995 and 2002. Overall, the data of 1,446
patients were excluded from this exploratory analysis because of the surgical outcome of gross residual disease with a maximum diameter greater than 1 cm or missing details regarding surgery. Our main analysis population, cohort 1, comprises the remaining 1,942 patients, representing 57.3% of the originally randomly assigned population (Fig A1). Cohort 2 is a subset of cohort 1, including 1,496 patients in whom complete information about clinical lymph node status evaluated pre- and intraoperatively was available (Appendix Fig A2, online.

<table>
<thead>
<tr>
<th>Table 1. Clinical Characteristics of Study Cohort</th>
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<td></td>
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<td>Intraoperative/preoperative clinical lymph node status*</td>
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</table>

Abbreviations: ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; TC, carboplatin and paclitaxel.

*Suspect nodes as indicated by preoperative radiologic and ultrasound findings or intraoperative findings (inspection and palpation).

<table>
<thead>
<tr>
<th>Table 2. Pattern of Lymphadenectomy and Pathologic LN Status in Study Cohorts 1 and 2</th>
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<tbody>
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<tr>
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<tr>
<td>Incomplete*</td>
</tr>
<tr>
<td>Pelvic and para-aortic†</td>
</tr>
</tbody>
</table>

Abbreviation: LN, lymph node.

*Includes patients with histologic examination of LNs of either the pelvic or the para-aortic region or other regions but not patients with pelvic and para-aortic lymphadenectomy.
†Includes patients with histologic examination of LNs from both areas.
only). At the time of this analysis, 982 patients (51.6%) had died, and a further 351 patients (18.1%) had experienced a relapse. Nine hundred sixty patients (49.4%) were still living after a median observation period of 56 months. The median PFS and OS times for cohort 1 were 24 months (95% CI, 23 to 26 months) and 57 months (95% CI, 52 to 61 months), respectively. The 5-year PFS and OS rates for cohort 1 were 29.8% and 47.9%, respectively.

Patient characteristics differed substantially (as a result of stricter eligibility criteria) from those reported in the three studies separately and are listed in Table 1. Approximately half of the patients fulfilled the criteria for complete resection (n = 996) or small residual tumor burden of 1 to 10 mm (n = 946). A lymphadenectomy was performed in 66.1% of patients with complete debulking and no gross residual disease and in 41.2% of patients who ended up with small residual disease of 1 to 10 mm (Table 2); 58.2% of patients who underwent lymphadenectomy had lymph nodes resected both in the pelvis and the para-aortic region. In cohort 2, 84.1% of patients with clinically suspect lymph nodes underwent lymphadenectomy, whereas lymphadenectomy was performed in 57.8% of patients without clinically suspect nodes (Table 2). In both latter subgroups, patients who underwent complete tumor debulking had higher rates of lymphadenectomy compared with patients left with small residual disease (78.3% v 53.5%, respectively; P < .001). The rate of pelvic and para-aortic lymphadenectomy was highest in the patient group with clinically suspect nodes and no gross residual tumor (68.0%) and lowest in patients without suspect nodes and small residual tumor (16.3%).

**Comparison 1 (cohort 1): Lymphadenectomy and Residual Tumor**

Lymphadenectomy was associated with superior survival in patients without gross residual disease (Fig 1A). The median survival times with and without lymphadenectomy were 103 and 84 months, respectively, with corresponding 5-year survival rates of 67.4% (95% CI, 63.3% to 71.2%) and 59.2% (95% CI, 53.1% to 64.8%; P = .0166), respectively. Comparison of incomplete lymphadenectomy with pelvic and para-aortic lymphadenectomy revealed no statistically significant difference (P = .9465), whereas both types of lymphadenectomy showed superiority versus no lymphadenectomy (P = .0406 for both types of lymphadenectomy; Table 3).

The impact of lymphadenectomy was less impressive in patients with small residual disease (Fig 1A). Even the comparison of pelvic and para-aortic lymphadenectomy versus no lymphadenectomy could detect only a nonsignificant trend toward better outcome, with median survival times of 41 and 35 months (P = .720), respectively, in this subgroup (Table 3).

Multivariate analysis showed a significant impact of lymphadenectomy on OS in patients without gross residual disease (hazard ratio [HR] = 0.75; 95% CI, 0.60 to 0.93; P = .0102), but significance was not reached for patients with small residual tumor (HR = 0.87; 95% CI, 0.73 to 1.04; P = .1202; Table 4). However, the type of lymphadenectomy had an impact on survival in patients without and with small residual disease. In both of these subgroups, we found a significant impact only for pelvic and para-aortic lymphadenectomy but not for incomplete lymphadenectomy. The HRs for complete lymphadenectomy were 0.71 (95% CI, 0.55 to 0.92) and 0.80 (95% CI, 0.66 to 0.98) in patients without and with small residual disease, respectively.

**Comparison 2 (cohort 2): Lymphadenectomy and Clinical Lymph Node Status**

This comparison was based on patients in whom the clinical lymph node status by preoperative imaging and intraoperative palpation was documented (Appendix Fig A2). We performed separate analyses of the impact of lymphadenectomy according to the presence of clinical lymphadenopathy. Fig 1. (A) Overall survival (OS) in patients with or without lymphadenectomy (LNE) and no gross residual tumor or postoperative residual tumor of 1 to 10 mm (comparison 1A; cohort 1). (B) OS after LNE or no LNE in patients with no gross residual tumor or postoperative residual tumor of 1 to 10 mm and with or without preoperative/intraoperative clinically suspect lymph nodes (LNs; comparison 2A; cohort 2). (C) OS after LNE or no LNE in patients with postoperative residual tumor of 1 to 10 mm and with or without preoperative/intraoperative clinically suspect LNs (comparison 2A; cohort 2).
of macroscopic residual tumor in study cohort 2 to avoid the strong
prognostic impact of residual tumor overruling any possible impact of
this surgical procedure.

In the subgroup with no gross residual tumor and without clin-
ically suspect nodes, lymphadenectomy showed a significant survival
impact (Fig 1B). Median survival times with and without lymphade-
nectomy were 108 and 83 months (P = .0081), respectively. Patients
with small postoperative residual tumor also showed a positive impact
of lymphadenectomy regardless of clinical lymph node status (Fig 1C).
However, significance was demonstrated only within the subgroup of
patients with clinically suspect nodes. In these patients, lymphadenec-
tomy, versus no lymphadenectomy, resulted in a 16% (95% CI, 5% to
17%) gain in 5-year OS rate (28% v 17%, respectively; P = .0038).
Patients with small residual tumor and without clinically suspect
nodes showed only a nonsignificant trend toward longer median survival
(46 months with lymphadenectomy v 37 months without lymphadenec-
tomy; P = .1820). Multivariate analysis in study cohort 2 revealed a
significant impact of lymphadenectomy only in patients with
clinically suspect nodes (HR = 0.72; 95% CI, 0.53 to 0.98;
P = .0379). In patients without clinically suspect nodes, lymphadenec-
tomy failed to reach significance (HR = 0.82; 95% CI, 0.67 to 1.02;
P = .6688; Table 4). The dependence of the impact of lymphadenec-
tomy on clinical node status was maintained when we included the
type of lymphadenectomy in the Cox model. A significant impact was
observed only for pelvic and para-aortic lymphadenectomy and was
limited to patients with clinically suspect nodes (HR = 0.63; 95% CI,
0.46 to 0.86). We did not observe a significant impact of lymphade-
nectomy in patients with clinically positive nodes and incomplete
lymphadenectomy (HR = 0.92; 95% CI, 0.66 to 1.92) and in patients
without clinically suspect nodes regardless of the type of lymphade-
nectomy (HR = 0.84; 95% CI, 0.67 to 1.06 for pelvic and para-aortic
lymphadenectomy and HR = 0.80; 95% CI, 0.62 to 1.02 for incom-
plete lymphadenectomy).

| Table 3. LNE and Outcome in Study Cohorts 1 and 2 (univariate analysis) |
|-------------------|---------------|---------------|-------------------|---------------|---------------|---------------|
| Group | No. of Patients | Median OS (months) | 5-Year OS (%) | Median OS (months) | 5-Year OS (%) | P<sup>*</sup> |
| Study cohort 1 | | | | | | | |
| Patients with no gross residual tumor | 996 | 84 | 64 to NR | 59.2 | 53.1 to 64.8 | 103 | 86.0 to NR | 67.4 | 63.3 to 71.2 | .0168 | 103 | 83.0 to NR | 68.0 | 61.5 to 73.7 | — | — | .0688 |
| Patients with residual tumor 1-10 mm | 946 | 35 | 32 to 37 | 28.9 | 24.8 to 33.2 | 39 | 35 to 46 | 31.9 | 26.8 to 37.1 | .0650 | 38 | 32 to 48 | 31.3 | 23.7 to 39.1 | 41 | 35 to 49 | 32.4 | 25.6 to 39.4 | .1626 |
| Study cohort 2 | | | | | | | |
| Patients without preoperative/ intraoperative suspect lymph nodes | 969 | 51 | 43 to 59 | 43.6 | 38.3 to 48.8 | 92 | 75 to 110 | 64.2 | 59.7 to 68.4 | <.001 | 87 | 69 to 110 | 64.2 | 57.8 to 69.9 | 99 | 70 to NR | 64.2 | 57.6 to 70.1 | <.001 |
| Patients with preoperative/ intraoperative suspect lymph nodes | 527 | 32 | 22 to 39 | 24.7 | 15.6 to 35.0 | 52 | 47 to 57 | 43.1 | 37.9 to 48.2 | <.001 | 41 | 33 to 52 | 32.1 | 23.4 to 41.0 | 57 | 49 to 74 | 48.1 | 41.7 to 54.1 | <.001 |

Abbreviations: LNE, lymphadenectomy; OS, overall survival; NR, not reached.
*P value for no LNE v any LNE
†P value for no LNE v incomplete LNE or pelvic and para-aortic LNE.

DISCUSSION

Lymphatic spread is a common feature of advanced epithelial ovarian
cancer. Histopathology reports showed positive nodes in 52.2% of
patients in cohort 1. This rate fits well with other reports indicating
lymph node metastasis in more than 50% of patients with advanced
disease.9,12,18,28 Nodal positivity cannot be diagnosed reliably
either with imaging or by intraoperative palpation,9,12 and thus, the
observed rate of positive lymph nodes depends essentially on the
completeness of lymphadenectomy. In our series, 24.8% of patients
without intraoperatively suspect nodes who underwent pelvic and
para-aortic lymphadenectomy had histologically positive nodes,
whereas the rate in patients who had a less defined incomplete retro-
peritoneal surgery was 17.1%. A similar observation has been reported
by others when limited lymph node dissection was compared with
systematic lymphadenectomy and may be a result of the fact that
almost one third of positive nodes are clinically not suspect and may be
missed during incomplete lymphadenectomy.10,12,17 Consequently,
the role of complete lymphadenectomy as a staging procedure is well
established, providing information of prognostic relevance.12,20,21
However, although suggested by many authors and retrospective
single-institution series, the role of lymphadenectomy as a therapeutic
procedure is less accepted. A prospective international lymphadenec-
tomy study compared systematic pelvic and para-aortic lymphade-
nectomy with removal of enlarged lymph nodes only in a cohort of
mainly incompletely, but so-called optimally, debulked patients and
found a significant benefit regarding PFS but not OS.12 Our data

www.jco.org 1737

Resolved error in Table 3. Corrected version uploaded on July 20, 2015.

References

2. Figure 1A. Median survival times with and without lymphadenectomy, study cohort 1 (univariate analysis).
3. Figure 1B. Median survival times with and without lymphadenectomy, study cohort 2 (univariate analysis).
4. Figure 1C. Median survival times with and without lymphadenectomy, study cohort 2 (univariate analysis).
5. Table 1. Characteristics of patients with complete preoperative staging.
6. Table 2. Characteristics of patients with incomplete preoperative staging.
7. Table 3. LNE and Outcome in Study Cohorts 1 and 2 (univariate analysis).
8. Table 4. Lymphadenectomy in patients with small postoperative residual tumor.
11. Table 7. Lymphadenectomy in patients with small postoperative residual tumor.
12. Table 8. Lymphadenectomy in patients with small postoperative residual tumor.
15. Table 11. Lymphadenectomy in patients with small postoperative residual tumor.
17. Table 13. Lymphadenectomy in patients with small postoperative residual tumor.
19. Table 15. Lymphadenectomy in patients with small postoperative residual tumor.
20. Table 16. Lymphadenectomy in patients with small postoperative residual tumor.
21. Table 17. Lymphadenectomy in patients with small postoperative residual tumor.
indicated a survival benefit in specific subgroups defined by clinical lymph node status and residual intraperitoneal tumor. A significant survival impact for combined lymphadenectomy was observed in patients without residual disease but not in patients with small residual disease (cohort 1).

Further detailed analysis limited to patients with known clinical lymph node status (cohort 2) showed a significant survival benefit only for patients who had pre- or intraoperative suspect lymph nodes, indicating a role for this operation as part of debulking by removing macroscopic tumor. The latter role is supported by our observation that more than 90% of patients with clinically suspect lymph nodes had histologically positive lymph nodes.

The combination of both residual disease and clinical lymph node status showed a significant impact of lymphadenectomy in patients with small residual disease and clinically detectable lymph nodes. This is in contrast to data by others that indicated a survival benefit of 43 months if they underwent lymphadenectomy. The observation might suggest that lymphadenectomy complements complete macroscopic intraperitoneal debulking by removing macroscopically invisible tumor remnants in unenlarged lymph nodes. As already indicated, this scenario has been observed in approximately one third of patients.

Although our data in advanced ovarian cancer are impressive, their interpretation should be approached with caution. Our retrospective study cannot rule out bias regarding patient distribution. We tried to reduce potential bias by performing multivariate analyses, taking into account all known prognostic tumor and patient variables. However, the decision of whether or not to perform a lymphadenectomy was not driven by random assignment but left to the discretion of each surgeon. One cannot rule out the possibility that prognostic factors not included in the adjustment panel and only conscious to the surgeons’ intuition (but not included in the case report forms) have

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**Table 4. Cox Regression Model for Multivariate Analysis of Overall Survival in Advanced Ovarian Cancer With Interaction Term of LNE and Postoperative Residual Tumor Status (study cohort 1) and Interaction Term of LNE and Clinically Reported Lymph Node Status (study cohort 2)**

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<td>IIIC 1.93 1.52 to 2.43 &lt;.001</td>
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<td>1-10 mm 1.78 1.44 to 2.21 &lt;.001</td>
<td>1.89 1.60 to 2.23 &lt;.001</td>
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<td>Yes v no (residual tumor 1-10 mm) 0.87 0.73 to 1.04 .1202</td>
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<td>LNE††</td>
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<td>0.82 0.67 to 1.02 .0688</td>
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<td>Yes v no (with bulky nodes) — — —</td>
<td>0.72 0.53 to 0.98 .0379</td>
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Abbreviations: LNE, lymphadenectomy; HR, hazard ratio; ECOG, Eastern Cooperative Oncology Group; PS, performance status; FIGO, International Federation of Gynecology and Obstetrics.

†The interaction term of LNE with residual tumor did not reach statistical significance (P = .30).

†The interaction term of LNE with lymph node status did not reach statistical significance (P = .46).
biased our cohort. Therefore, we used these results only for generating a hypothesis for a prospectively randomized trial in patients with advanced ovarian cancer with complete intraabdominal tumor resec-
tion and without clinically suspect lymph nodes (Lymphadenectomy in Ovarian Neoplasm protocol funded by the German Research Foun-
dation). This study has already started recruitment and compares systematic lymphadenectomy versus no lymphadenectomy in pa-
tients without macroscopic residual intra-abdominal tumor and will probably shed light on this important question. Until then, our data
suggest that lymphadenectomy should be restricted to patients in whom the removal of clinically suspect lymph node metastases im-
proves the residual disease status.

**AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**

Although all authors completed the disclosure declaration, the following author(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a “U” are those for which no compensation was received; these relationships marked with a “C” were compensated. For a detailed description of the disclosure categories, or for more information about

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**Prognostic Impact of Lymphadenectomy in Advanced Ovarian Cancer**

AsCO’s conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

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**APPENDIX**

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