# Influence of Department Volume on Survival for Ovarian Cancer: Results From a Prospective Quality Assurance Program of the Austrian Association for Gynecologic Oncology

*Christian Marth,* Sonja Hiebl,† Willi Oberaigner,‡ Raimund Winter,§ Sepp Leodolter,¶ and Paul Sevelda||*

**Objective:** The Austrian Association for Gynecologic Oncology initiated in 1998 a prospective quality assurance program for patients with ovarian cancer. The aim of this study was to evaluate factors predicting overall survival especially under consideration of department volume.

**Methods:** All Austrian gynecological departments were invited to participate in the quality assurance program. A questionnaire was sent out that included birth date, histology, date of diagnosis, stage, and basic information on primary treatment. Description of comorbidity was not requested. Patient life status was assessed in a passive way. We did record linkage between each patient's name and birth date and the official mortality data set collected by Statistics Austria. No data were available on progression-free survival. Patients treated between January 1, 1999 and December 31, 2004 were included in the analysis. Mortality dates were available to December 31, 2006. Data were analyzed by means of classical statistical methods. Cut-off point for departments was 24 patients per year.

**Results:** A total of 1948 patients were evaluable. Approximately 75% of them were treated at institutions with fewer than 24 new patients per year. Patient characteristics were grossly similar for both department types. Multivariate analysis confirmed established prognostic factors such as International Federation of Gynecologists and Obstetricians (FIGO) stage, lymphadenectomy, age, grading, and residual disease. In addition, we found small departments (<24 patients per year) to have a negative effect on overall survival (hazards ratio, 1.38: 95% confidence interval, 1.2–1.7; and $P < 0.001$).

**Conclusions:** The results indicate that in Austria, rules prescribing minimum department case load can further improve survival for patients with ovarian cancer.

**Key Words:** Ovarian cancer, Survival rate, Department volume, Minimum case load

(*Int J Gynecol Cancer* 2009;19: 94–102)

Optimal treatment of patients with ovarian cancer consists of aggressive upfront surgery and chemotherapy. To achieve this goal, it has been advocated that patients be centralized in comprehensive cancer centers providing interdisciplinary collaboration. Several studies have shown that the survival of patients with advanced ovarian cancer improved when they were treated by a specialist in gynecologic oncology or at a specialized institution. Olaitan et al[1] demonstrated that gynecological oncologists were 2.06 times more likely to achieve optimal cytoreduction. This was also confirmed by Bailey et al[2]; however, they were unable to observe a difference in overall survival despite a significant discrepancy in surgical outcome. Kehoe et al,[3] in a retrospective analysis, found the general surgeon to be an independent adverse prognostic factor and concluded that a gynecologist should be involved in the treatment of patients with ovarian pathologic conditions. Even better results, however, can be achieved when gynecologists have special training in gynecological oncology because they were reported to debulk tumors more efficiently and prolong patient survival.[4] For patients with International Federation of Gynecologists and Obstetricians (FIGO) stage IIIc ovarian cancer, centralization to a cancer center contributed to better survival.[5] Paulsen et al[6] analyzed data from the Norwegian Cancer Registry and demonstrated that survival of patients with ovarian cancer who were operated on at a teaching hospital was significantly better than when operated on at non-teaching hospitals (hazards ratio, 1.83). Moreover, patients operated on by a specialist rather than a general gynecologist had 20% increased short-term survival. Several other authors confirm an

*Department of Obstetrics and Gynecology, Innsbruck Medical University, Innsbruck; †Department of Gynecology, Hospital of Barmherzige Schwestern Linz, Linz; ‡Cancer Registry of Tyrol, Department of Clinical Epidemiology of the Tyrolean State Hospitals Ltd, Innsbruck; §Department of Obstetrics Gynecology, Medical University of Graz, Graz; ¶Department of Obstetrics Gynecology, Medical University of Vienna, Vienna; and ||Department of Obstetrics and Gynecology, Hospital Hietzing, Vienna, Austria.

Address correspondence and reprint requests to Christian Marth, MD, Department of Obstetrics and Gynecology, Innsbruck Medical University, Anichstrasse 35, A-6020-Innsbruck, Austria.
E-mail: christian.marth@i-med.ac.at.



ISSN: 1048-891X
DOI: 10.1111/IGC.0b013e31819915cb

**TABLE 1.** Characteristics of 1948 patients with ovarian cancer who were treated in Austria between 1999 and 2004

| Characteristics | Patients per year ≤23 | Patients per year ≥24 | P |
|---|---|---|---|
| n (%) | 1456 (74.7) | 492 (25.3) | |
| Median age (Quartiles 1–3) | 63 (53–73) | 61 (50–72) | 0.022* |
| FIGO stage, n (%) | | | |
| I | 364 (25) | 117 (24) | 0.075† |
| II | 118 (8) | 34 (7) | |
| III | 692 (48) | 279 (57) | |
| III Not otherwise specified | 51 (7.4) | 1 (0.4) | |
| IIIA | 40 (5.8) | 16 (5.7) | |
| IIIB | 83 (12.0) | 46 (16.5) | |
| IIIc | 518 (74.9) | 216 (77.4) | |
| IV | 177 (12) | 55 (11) | |
| Not staged | 105 (7) | 7 (1) | 0.001‡ |
| CA 125, n (%) | | | |
| <35 U/mL | 195 (13.4) | 58 (11.8) | 0.427 |
| >35–150 U/mL | 267 (18.3) | 101 (20.5) | |
| >150 U/mL | 819 (56.3) | 273 (55.5) | |
| Not known | 175 (12.0) | 60 (12.2) | |
| Histology, n (%) | | | |
| Serous | 806 (55) | 340 (69) | <0.001§ |
| Endometrioid | 187 (13) | 49 (10) | |
| Mucinous | 102 (7) | 47 (10) | |
| Clear cell | 50 (3) | 18 (4) | |
| Poorly differentiated | 158 (11) | 22 (5) | |
| Other | 117 (8) | 14 (3) | |
| No histology | 36 (2) | 2 (0.4) | 0.002¶ |
| Grading, n (%) | | | |
| 1 | 156 (11) | 77 (16) | 0.022‖ |
| 2 | 390 (27) | 124 (25) | |
| 3–4 | 739 (51) | 244 (50) | |
| No grading | 171 (12) | 47 (10) | 0.214** |
| Surgery performed, n (%) | | | |
| Hysterectomy†† | 796 (64) | 274 (69) | 0.131 |
| BSO†† | 1021 (82) | 320 (80) | 0.297 |
| Omentectomy†† | 961 (78) | 313 (78) | 0.836 |
| Bowel resection††, ‡‡ | 206 (17) | 73 (21) | 0.045 |
| Peritoneal cytology | 1061 (73) | 420 (85) | <0.001 |
| Lymphadenectomy | 661 (45.4) | 212 (43) | 0.402 |
| No. nodes, median (q1–q3) | 17 (10–26) | 26 (12–44) | <0.001 |
| Residual disease, n (%) | | | |
| None | 628 (43) | 225 (46) | <0.001§§ |
| Macroscopic but <1 cm | 276 (19) | 45 (10) | |
| 1–2 cm | 92 (6) | 56 (11) | |
| >2 cm | 340 (23) | 138 (28) | |
| No information | 120 (8) | 28 (6) | 0.076¶¶ |

Age versus patients per year (Kruskal-Wallis equality-of-populations rank test).
†Staged I-II/III-IV versus patients per year.
‡Not staged versus patients per year.
§Histology groups versus patients per year.
¶No histology versus patients per year.
‖Grading 1–4 versus patients per year.
**No grading versus patients per year.
††Data for years 2000–2004 only.
‡‡Data missing for 1 department for years 2003–2004.
§§Residual disease <1 cm versus patients per year.
¶¶No information versus patients per year.

association between experience and specialization of the treating physician or of patient volume of the hospitals and survival of patients with ovarian cancer.[7–10] Oberaigner and Stühlinger showed for Tyrol, an Austrian state that is home to approximately 10% of the Austrian population, an association between department volume and survival in patients with ovarian cancer.[11] Fifty percent of patients were treated in small institutions, that is, performing fewer than 24 ovarian cancer surgeries per year, and the hazards ratio for overall survival was 1.27 compared with those of large institutions (doing more than 24 procedures per year). These findings are not restricted to ovarian cancer only. An overview published in 2000[12] concludes that there is an association between center size and survival for all solid cancer types requiring complex therapy. However, most of these studies have been retrospective and worked with cancer registries. The quality of these data is difficult to assess, and various sources of confounding biases cannot be excluded.

Comprehensive cancer centers and specialization in gynecologic oncology are recommended to improve outcome quality. Unfortunately, neither has been introduced to Austria. The Austrian Association for Gynecologic Oncology thus initiated a quality assurance program.[13] Cancer-treating gynecology departments were invited to complete a questionnaire for all consecutive patients with cancer including information on prognostic factors and primary treatment. This allowed prospective collection of data by the primary treating physician. The aim of this study was to evaluate factors predicting overall survival in this quality assurance program, especially under consideration of department volume. Our hypothesis, derived from the recent manuscript by Oberaigner and Stühlinger,[11] was that patients in institutions with more than 23 newly diagnosed ovarian cancers have a better prognosis.

## PATIENTS AND METHODS

All Austrian gynecology departments were invited to participate in a quality assurance program. A patient record form including important diagnosis and treatment variables such as date of birth, histology, date of diagnosis, FIGO stage, type and extent of surgery, and other basic information on primary treatment was sent out to study participants. Participating centers agreed to submit information on all patients with ovarian cancer. Data on chemotherapy were not collected before 2002 and were therefore excluded from the analysis. Only primary surgery was evaluated. Patients with interventional surgery were included, but results of the second surgery were not taken into consideration or included in the analysis. Therefore, these patients were regarded as having residual disease of more than 2 cm. Description of comorbidity

**TABLE 2.** Residual disease at FIGO IIIc

| Characteristics | No. patients per year, (%) ≤23 | No. patients per year, (%) ≥24 | P |
|---|---|---|---|
| Residual disease | | | |
| None | 110 (21) | 53 (25) | 0.001* |
| Macroscopic but <1 cm | 139 (27) | 24 (11) | |
| 1–2 cm | 58 (11) | 21 (10) | |
| >2 cm | 178 (34) | 109 (50) | |
| No information | 33 (6) | 9 (4) | 0.297† |

*Residual disease versus patients/year.
†No information versus patients per year.

was not collected, nor was the progression-free survival. Department volumes were divided into 2 groups; those with ≥24 patients per year were termed large departments and those with ≤23 patients per year were termed small departments. Classification was performed by calculating the mean number of patients registered annually for each year in which the departments contributed. This cut-off point was

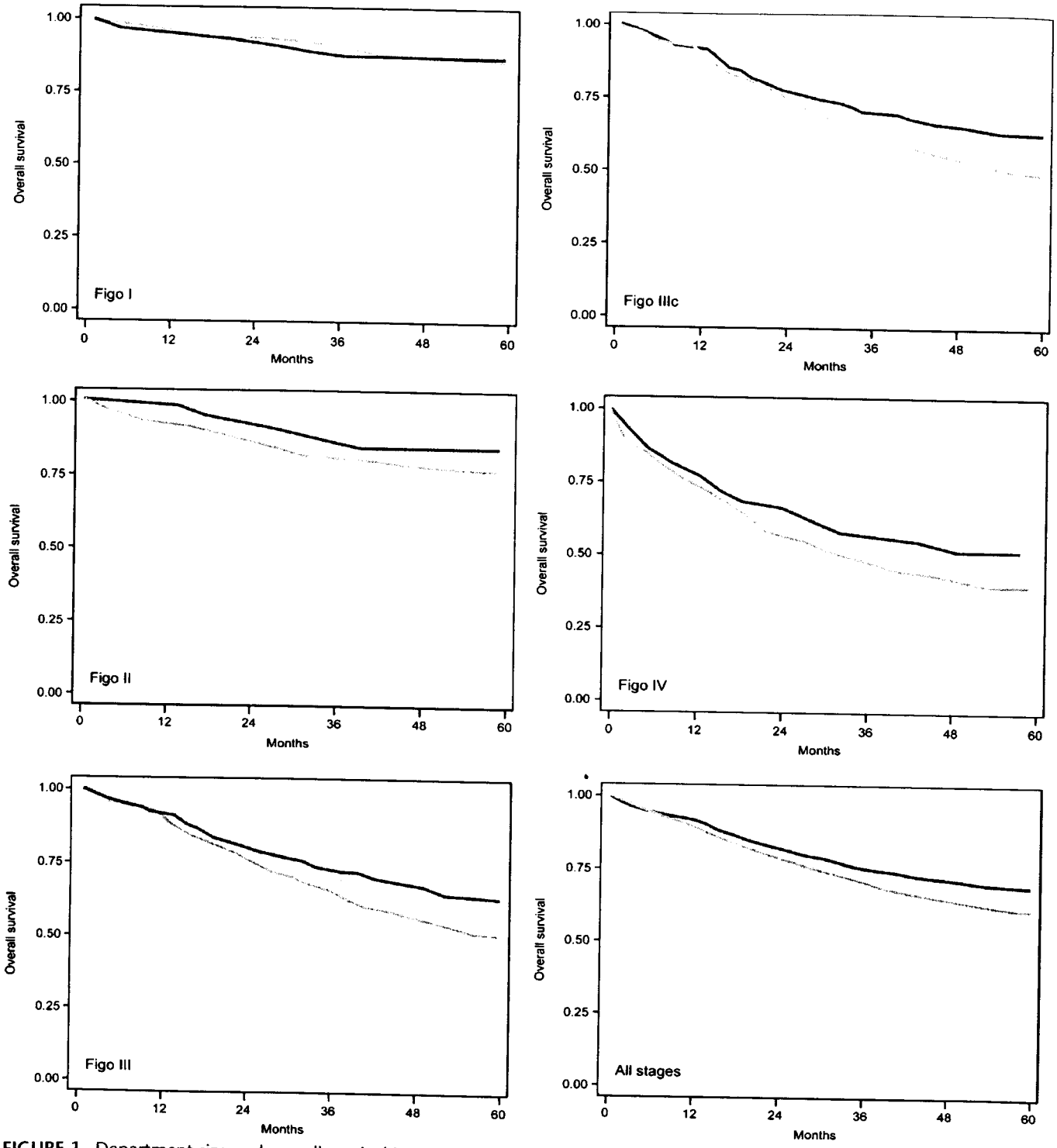


**FIGURE 1.** Department size and overall survival in patients with ovarian cancer. Kaplan-Meier curves for overall survival of patients with ovarian cancer in various FIGO stages are shown as indicated. Patients were stratified according to the treating institution (black line: patients from large departments; gray line: patients from small institutions). $P = 0.941$, $P = 0.406$, $P = 0.002$, $P = 0.007$, $P = 0.150$, and $P = 0.001$ for FIGO stages I, II, III, IIIc, IV, and all stages, respectively. Patients at risk were 364 and 117, 118 and 34, 692 and 279, 518 and 216, 177 and 55, and 1456 and 492 for small and large departments and FIGO stages I, II, III, IIIc, IV, and all stages, respectively.

chosen in keeping with our previous publication,[11] distinguishing departments with more or less than 2 surgeries per month. Data collected between January 1, 1999 and December 31, 2004 were included in the analysis. Patient record forms were collected annually and checked for major errors, but centers were not audited. Mortality data were available up to December 31, 2006. Patient life status was assessed in a passive way. Patients' name and birth date were submitted to Statistics Austria, which did a record linkage with the official Austrian mortality data set. No patient was lost to follow-up. All patients alive as of December 31, 2006 were analyzed as censored patients. The time between diagnosis and death or December 31, 2006 for survivors was used as survival time.

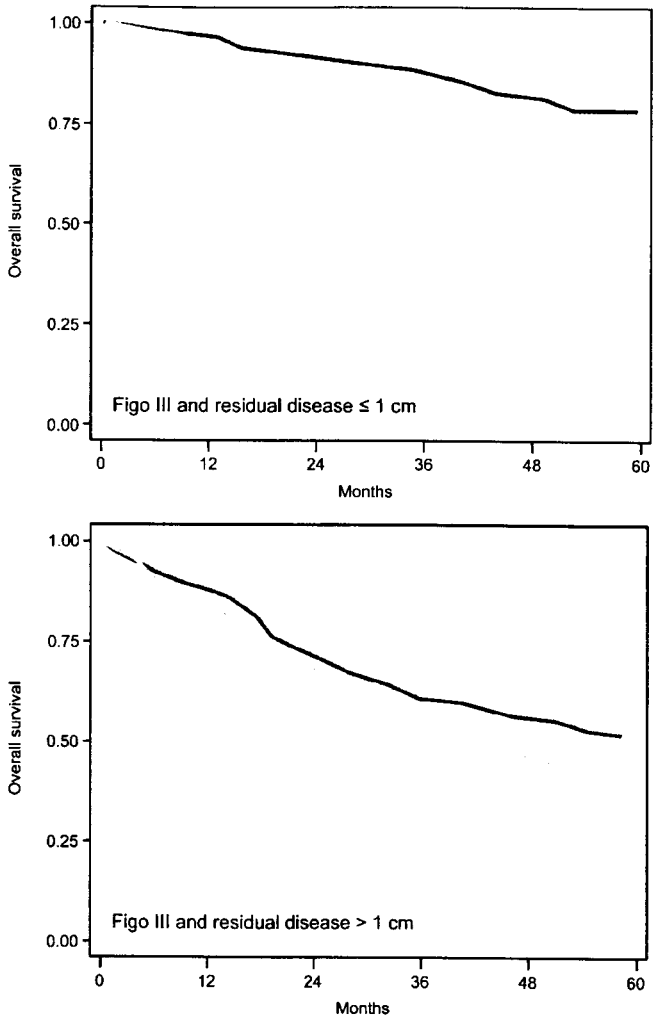


**FIGURE 2.** Department size and overall survival in FIGO stage III patients with ovarian cancer. Kaplan-Meier curves for overall survival of patients with ovarian cancer in FIGO stage III only and dependent on the amount of residual disease are shown as indicated. Patients were stratified according to the treating institution (black line: patients from large departments; gray line: patients from small institutions). $P < 0.001$ for residual disease of 1 cm or less and $P = 0.136$ for residual disease of more than 1 cm. Patients at risk in small departments were 109 and 363, with residual disease of 1 cm or less, and in large departments, 154 and 280, with residual disease of more than 1 cm.

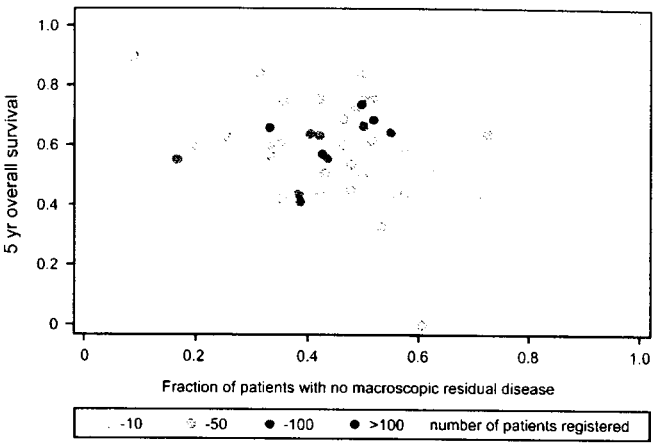


**FIGURE 3.** Scatter plot for debulking surgery and survival according to department size. For all participating institutions, the fraction of patients optimally debulked was calculated and indicated on the *x*-axis. In addition, for each institution, the 5-year survival rate was estimated and given on the *y*-axis. Each dot represents 1 department, and the color shows the total number of patients registered in the 6-year period. Correlation analysis failed to demonstrate significant association (Spearman rank correlation coefficient, −0.17; $P = 0.2$).

## Statistical analysis

The Kruskal-Wallis test, Mann-Whitney *U* test, and Pearson $\chi^2$ test were used when applicable to determine the differences in patient characteristics, FIGO staging, histology, tumor grading, and surgery performed by large- and small-volume departments. Survival analysis for the 5-year period between the 2 department volumes was performed using Kaplan-Meier curves and the log-rank test. After univariate analysis, a multivariate Cox model was fitted with all variables entered (large department group classified as reference group), and the most parsimonious model was achieved via backward elimination. The influence of variables was checked with the likelihood ratio test and the proportional hazards ratio assumption using the stphtest in Stata. Correlation analysis was performed by means of the Spearman rank correlation coefficient. All statistical analyses were performed using Stata for Windows (Version 9, Stata Inc, College Station, Tex) with 2-sided significance accepted at $\alpha = 0.05$.

## RESULTS

The current study included 1948 patients, or roughly 40% of all patients with cancer who were treated in Austria from 1999 to 2004. A total of 51 of the 93 Austrian gynecological departments agreed in 1999 to participate in the quality assurance program. Over time, this figure increased to 70 departments in 2004. The median number of reported patients was 4 per department in 1999 and did not significantly change in subsequent years (5.5 in 2004). For the 18 departments participating every year, the median number of patients was 8 in 1999 and 6 in 2004 (n.s.). In 49 departments (70%), the median number of patients was up to 5 per year, 17 departments (24%) treated between 6 and 24 patients per year, and only 4 departments (6%) had more than 24 patients per year. The median follow-up time of surviving patients was 43 and 46 months for large and small departments, respectively (not significant).

Patient characteristics are shown in Table 1. A total of 1456 patients were treated at 66 small departments and 492 patients at 4

large departments. Patient characteristics were unequally distributed between the 2 types of department. Stage information was not adequately collected or was missing more frequently in the small departments (7% and 1%, respectively; $P < 0.001$). In the adequately staged patients, FIGO III or IV was reported more frequently by larger departments than by small departments (69% and 61%, respectively; $P < 0.01$). Interestingly, in FIGO stage III, a significant percentage of patients did not undergo any further classification at small departments.

The histological diagnosis of serous tumors was more common at large departments than at small departments (69% and 55%, respectively; $P < 0.001$). No difference was seen in frequencies of clear cell carcinoma between the departments. However, the rate of poorly differentiated carcinomas was more than double that in small departments. In contrast to the histological findings, no major differences in grading were reported.

Surgical procedures according to general consensus such as hysterectomy, bilateral salpingo-oophorectomy (BSO), omentectomy, and lymph node dissection were equally reported by both types of department. However, bowel resection was performed more frequently at large departments. The median number of lymph nodes removed was also greater for large departments (26 and 17, respectively; $P < 0.001$). The result of debulking surgery was analyzed as submitted by the centers. Surgical reports were not checked and photo documentation was not mandatory. Complete debulking with no macroscopic residual disease was achieved more frequently at large departments ($P < 0.01$). However, tumor reduction to less than 1 cm was documented more often at small departments (62% and 56%, respectively; $P < 0.001$).

To analyze the effect of surgery, FIGO stage IIIc was examined in detail (Table 2). No residual disease was documented to a similar degree by both types of department, but macroscopic residual disease of up to 1 cm was registered in 11% and 27% of cases at large and small departments, respectively. Interestingly, suboptimal or no debulking was more frequent at large departments.

For all stages, survival was significantly longer at large than at small departments, with 5-year survival rates of 69% and 61%, respectively ($P = 0.01$; Fig. 1 and Table 1). Survival data were

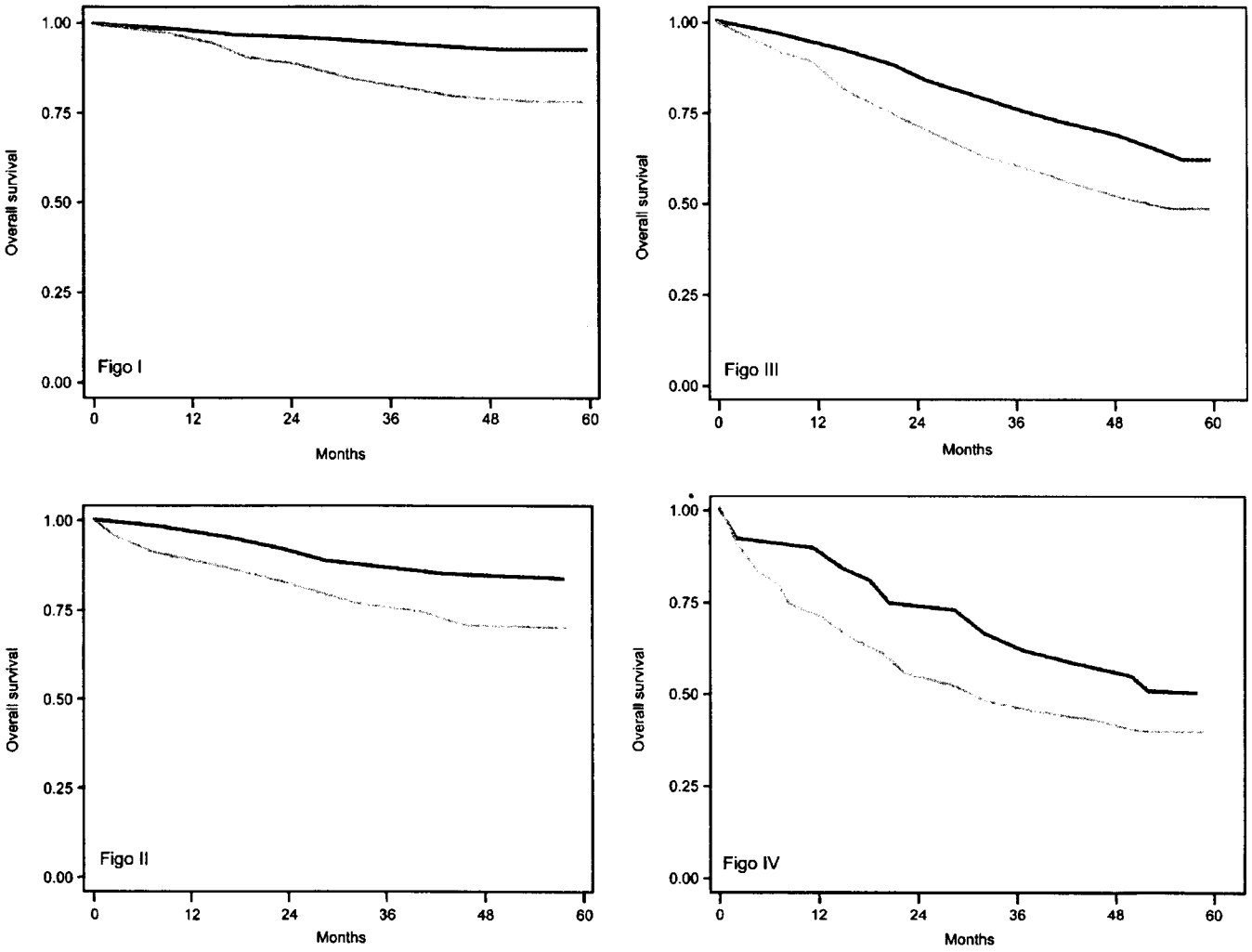


**FIGURE 4.** Lymphadenectomy and survival in patients with ovarian cancer. Kaplan-Meier curves for overall survival of patients with ovarian cancer in various FIGO stages are shown as indicated. Patients were stratified according to lymphadenectomy (black line: patients with removed nodes; gray line: patients without lymphadenectomy). $P < 0.001$, $P = 0.228$, $P < 0.001$, and $P = 0.087$ for FIGO stages I, II, III, and IV, respectively. Patients at risk were 291 and 190, 94 and 58, 413 and 558, and 44 and 188, with or without lymphadenectomy, for FIGO stages I, II, III, and IV, respectively.

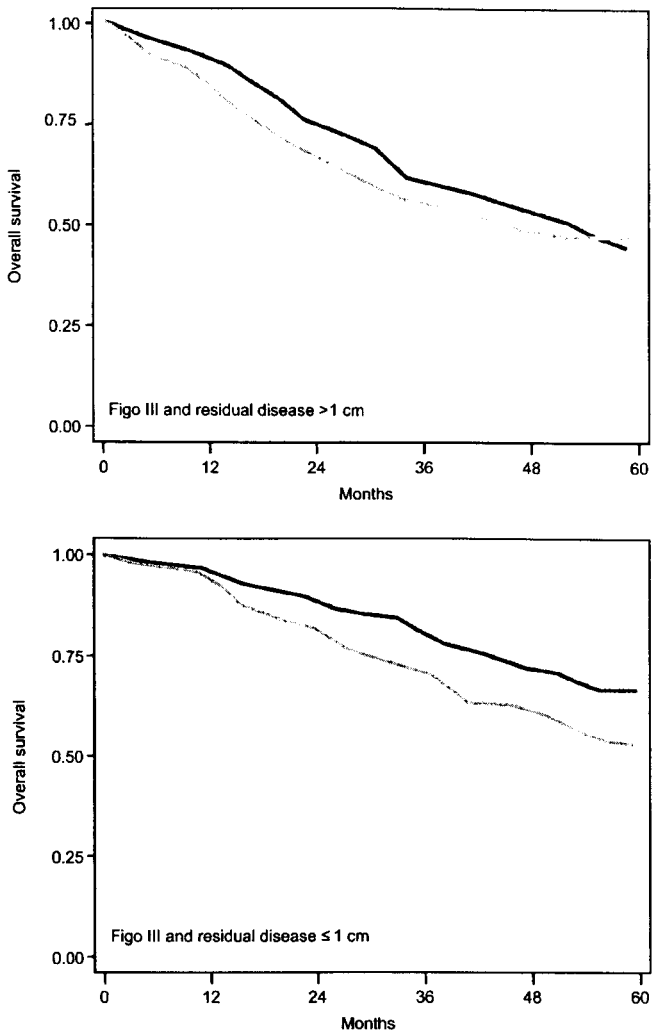


**FIGURE 5.** Lymphadenectomy and survival in FIGO stage III patients with ovarian cancer. Kaplan-Meier curves for overall survival of patients with ovarian cancer in FIGO stage III only and according to the amount of residual disease are shown as indicated. Patients were stratified according to lymphadenectomy (black line: patients with removed nodes; gray line: patients without lymphadenectomy). $P = 0.692$ and $P < 0.001$ for residual disease of more than 1 cm and 1 cm or less, respectively. Patients at risk were 84 and 350, and 305 and 167, with or without lymphadenectomy, for residual disease of more than 1 cm and 1 cm or less, respectively.

stratified according to FIGO stage. At FIGO stage I, overall survival was similar in both groups. Overall survival for FIGO stage III was significantly better at large departments, whereas at FIGO stages II and IV, the difference in survival did not achieve statistical significance.

Patients in FIGO stage III were further stratified according to residual disease. Those patients who were optimally debulked to less than 1 cm showed better outcome at large than at small departments (Fig. 2). No statistically significant difference was noted in FIGO stage III suboptimally debulked patients, regardless of the size of the department where surgery was performed (Fig. 2). It is well known that residual disease is one of the most important prognostic factors. It is therefore interesting to evaluate how participating institutions were able to debulk tumors and correlate this fraction with patient survival. To visualize this relationship, a scatter plot was calculated between an institution's surgical skills and survival (Fig. 3). A correlation analysis of the fraction of patients in each department in whom cytoreduction was achieved and 5-year overall survival rate revealed no significant association (Spearman rank correlation coefficient, −0.17; $P = 0.2$).

Lymphadendectomy was associated with better survival (Fig. 4). FIGO stages I and III patients who underwent lymphadenectomy showed significantly better survival. In FIGO stages II and IV, the observed difference was not significant. Because lymphadenectomy might be a surrogate marker for more extensive surgery, we stratified patients in FIGO stages III (Fig. 5) and IIIc (data not shown) according to residual disease after primary surgery. Only those patients with successful cytoreductive surgery benefited from the additional removal of lymph nodes. Similar results were obtained for FIGO stage IIIc (data not shown).

A multivariate Cox model was calculated to determine variables independently predicting overall survival (Table 3). In addition to the listed variables, histology was also evaluated in the model but was excluded because of lack of significance. Department size was an independent predictor of survival, with a hazards ratio of 1.39 for patients treated in small institutions. FIGO stage was themost important variable, whereas residual disease did not contribute to survival estimation to the same extent. The well-established prognostic factors age and grading were also confirmed by our multivariate analysis. Because residual disease is also dependent on department size, a Cox model was calculated without inclusion of this covariate. Department size proved again to

**TABLE 3.** Multivariate Cox model (overall survival) of prognostic covariates in patients with ovarian cancer (n = 1948)

| Variables | Hazards Ratio | *P* | 95% CI |
|---|---|---|---|
| No. patients per year | | | |
| >24 (large) | 1 | | |
| ≤ 23 (Small) | 1.38 | 0.001 | 1.15–1.65 |
| FIGO | | | |
| I | 1 | | |
| II | 1.62 | 0.024 | 1.06–2.46 |
| III | 2.91 | <0.001 | 2.18–3.89 |
| IV | 3.61 | <0.001 | 2.59–5.05 |
| Not staged | 2.15 | <0.001 | 1.42–3.26 |
| Lymphadenectomy | | | |
| No | 1 | | |
| Yes | 0.74 | 0.001 | 0.62–0.89 |
| Age, y | | | |
| <49 | 1 | | |
| 50–69 | 1.16 | 0.236 | 0.91–1.48 |
| 70+ | 1.78 | <0.001 | 1.39–2.28 |
| Grading | | | |
| 1 | 1 | | |
| 2 | 1.56 | 0.019 | 1.08–2.25 |
| 3–4 | 1.66 | 0.005 | 1.17–2.37 |
| No grading | 2.08 | <0.001 | 1.40–3.11 |
| Residual disease[6] | | | |
| <1 cm | 1 | | |
| ≥ 1 cm | 1.50 | <0.001 | 1.25–1.81 |
| No information | 1.38 | 0.027 | 1.04–1.83 |

be an independent variable, with a hazards ratio of 1.34 and a 95% confidence interval of 1.1–1.6.

## DISCUSSION

This study clearly demonstrates that patients with ovarian cancer who were treated at large departments can achieve better survival than those treated at small departments. This study used prospectively collected data from a quality assurance program, and therefore databases were not subject to retrospective analysis, which may improve data quality and prevent erroneous allocation of patients to departments. Limitations of the study are mainly derived from the lack of possibility to scrutinize data correctness. We were able to check for plausibility of information but not veracity. Moreover, 55% to 75% of departments treating ovarian cancer only participated in this quality assurance program. For this reason, we cannot exclude a participation bias because all university departments and hospitals in the Austrian state capitals contributed. The impact of hospital volume might therefore be underestimated, because most of the nonparticipating centers are those with small patient numbers. Characteristics of patients at small and large departments were roughly similar. Those treated at large institutions were somewhat younger (median 2 years) but more frequently in advanced FIGO stage III or IV. The observed difference in the occurrence of serous tumors between the 2 department types is difficult to explain, but no central pathological review was performed. Several investigators have shown that age and performance status as well as tumor-related factors (such as stage, histologic type, and tumor grading) are independent factors of survival for patients with ovarian cancer. These variables can hardly be influenced by department size.[14] However, department size can indeed influence the group of patients treated. It is clear from clinical practice that large departments have more patients in advanced tumor stages, obviously preoperative bulky disease, and more complex cases. The current study supports this observation because advanced stages of ovarian cancer are more frequent at large departments than at small departments (68% vs 60%). Furthermore, interpretation of tumor stage may vary from institute to institute depending on use and availability of preoperative diagnostic methods and adherence to guidelines for correct staging (such as performance of peritoneal cytology and assessment of residual disease). Especially at small institutions, this could result in understaging and consequently inappropriate treatment. In 73% of patients operated on at small departments, information on peritoneal cytology was recorded, whereas this information was available for 85% of patients at large institutions. In addition, FIGO stage III was not further classified in 7.4% of patients at small departments but only in 1 patient (0.4%) at a large institution. Therefore, tumor staging at small departments was significantly more often inappropriate than at large departments. This could, however, prompt a stage shift, which would favor those hospitals with better staging quality. A comparison by FIGO stage would then compare different patient populations (eg, FIGO stage IIIc at larger hospitals performing more lymphadenectomies would include patients with presumed FIGO stage I tumors, which were only up-staged by lymphadenectomy, although this favorable FIGO stage IIIc subgroup is missing at hospitals not performing lymphadenectomy in presumed FIGO stage I). One possible way to overcome this bias is to analyze the entire group irrespective of FIGO stage. These analyses are therefore very important, and subgroup evaluation should be read with caution. The literature suggests that patients with ovarian cancer benefit most when operated on by a specialist in gynecologic oncology,[5] and that gynecologists are better than general surgeons.[1–3] Paulsen et al[6] demonstrated a relationship between short-term survival when treating advanced ovarian/tubal/peritoneal cancer and the type of operating physician and the level of hospital. Overall, 198 patients were evaluated; women operated on by a specialist in gynecologic oncology had a 20% increased short-term survival rate, and women operated on at teaching hospitals had a significantly better survival rate than those operated on at nonteaching hospitals (79% vs 62%). Similar benefits of centralized surgery of primary ovarian cancer were reported by other authors.[8,11,15]

The postoperative residual tumor was reported to be one of the most important independent prognostic factors for survival of patients with ovarian cancer.[15–20] The extent of residual disease depends on the preoperative tumor load and its biologic characteristics, which cannot be influenced. The most important human factor is, however, the skill and experience of the physician to provide optimal surgical management.[21] Recommended surgical therapy for ovarian cancer comprises total abdominal hysterectomy, bilateral salpingoophorectomy, omentectomy, peritoneal debulking, and, if necessary, comprehensive tumor debulking. Lymphadenectomy is recommended if complete tumor debulking in the peritoneal cavity was possible. Aggressive primary surgery and optimal debulking of ovarian cancer were suggested to bring a survival advantage.[16] Between the 2 department types, we observed no major differences in type of surgery, except for bowel resection and the number of lymph nodes removed. In our study, we observed a disappointingly small number of patients undergoing radical surgery. Possibly because neoadjuvant chemotherapy recently became very popular, a remarkable fraction of advanced patients with ovarian cancer underwent interventional debulking. Interestingly, our study showed no correlation between operative radicality and survival (Fig. 3). This is in contrast to the results reported by Bristow et al,[18] which showed that maximal cytoreduction is one of the most powerful determinants of survival among patients with ovarian cancer. Their meta-analysis demonstrated that at some institutions, percent maximal cytoreductive surgery is the strongest predictor of median survival of patients treated at that department, and each 10% increase in percent maximal cytoreductive surgery was associated with a 5.5% increase in median survival time. According to Tingulstad et al,[15] one reason for the discrepancy could be better overall management at large institutions, which is also a significant predictor of overall survival at teaching hospitals. Unfortunately, we started to collect information on chemotherapy only in 2002. Preliminary data on 760 patients revealed platinum- and taxane-based chemotherapy to a similar extent in both groups of departments. However, a more detailed look at the data shows this reason to be not very probable as the sole explanation. At FIGO stage III with residual disease of up to 1 cm, overall survival was statistically significantly better at large departments, which suggests same surgical result: better outcome at large departments. However, FIGO stage III patients with residual disease of more than 1 cm no longer showed this benefit derived at large departments. If better chemotherapy and general management cause the difference, why does it not also hold true for suboptimally debulked patients? It therefore seems more likely that documentation of residual disease was less accurate at smaller departments than at larger institutions; this produces an erroneously higher fraction of patients who are supposedly optimally debulked. This hypothesis is also supported by the finding that peritoneal cytology was frequently not performed at small institutions. Moreover, at small departments, there was a marked frequency for patients to be documented with residual disease between 0 and 1 cm. For future quality assurance programs, we therefore recommend photographic documentation at the end of surgery to visualize residual tumor and unaffected peritoneum.

Another interesting observation of this study is the potential therapeutic role of lymph node dissection in ovarian cancer. It is a

matter of major controversy whether lymphadenectomy allows only correct staging or also improves survival. Previous retrospective reports support lymphadenectomy in ovarian cancer.[22,23] More recent analysis of a Surveillance, Epidemiology, and End Result database containing almost 14,000 patients confirmed by multivariate Cox regression the extent of lymph node dissection as an independent prognosticator.[24] However, others did not find systematic lymphadenectomy to be associated with a benefit.[25] Panici et al[26] reported the results of the only prospective trial in 427 patients with optimally debulked FIGO stages IIIB to IV ovarian cancer randomized to systematic lymphadenectomy and resection of bulky nodes only. Those who underwent lymphadenectomy showed improved progression-free survival but no benefit in overall survival. Because in FIGO stage I lymphadenectomy is clearly necessary for correct staging, our finding of improved survival can be explained by the stage shift. The group of patients without lymphadenectomy probably included patients with unremoved positive nodes, who were not correctly staged as FIGO III. This argument is, however, not valid for advanced stages. It is interesting that only those patients who were optimally debulked demonstrated significantly improved survival following lymphadenectomy, whereas those with residual disease of more than 1 cm showed unchanged prognosis after the removal of lymph nodes. Because the extent of residual disease is crucial in benefiting from additional retroperitoneal lymph node dissection, it is recommended that a new randomized trial be conducted exclusively in patients who are optimally debulked, that is, patients with no macroscopic tumor.

In summary, we found significantly better survival at large institutions, especially in patients with advanced stages. Patient load might be a surrogate for higher specialization, better physician training, or stricter adherence to clinical trials. Although a large number of patients were collected in a nationwide program, it is difficult to clarify which of these dependent variables is the best predictor of survival. Nevertheless, because a specially trained physician enrolling patients in clinical trials is more probable to find in a large-volume institution, our data advocate centralization of patients with ovarian cancer in comprehensive cancer centers and a formal specialization in gynecological oncology.

## ACKNOWLEDGMENTS

*The authors thank the following departments and physicians for contributing to this study: Krankenhaus der Barmherzigen Brüder Vienna, Dr Gerhard Wagner; Rudolfsstiftung Vienna, Dr Werner Grünberger; Kaiser-Franz-Josef-Spital Vienna, Dr Walther Gruber; St. Josef-Krankenhaus Vienna, Dr Franz Brandstetter; Hanusch-Krankenhaus Vienna, Dr Michael Medl; Wilhelminenspital Vienna, Dr Heinrich Salzer; Krankenhaus Göttlicher Heiland Vienna, Dr Albert Mayer; SMZ-Ost Vienna, Dr Karl Philipp; Landesklinikum Mostviertel Amstetten, Dr Karl Weghaupt; Landesklinikum Thermenregion Baden, Dr Frank Girardi; Landesklinikum Weinviertel Hollabrunn, Dr Karl Anzböck; Landesklinikum Waldviertel Horn, Dr Johann Klobasa; Krankenhaus Klosterneuburg, Dr Hans Stopfer; Landesklinikum Krems, Dr Karl Christian Schieder; Landesklinikum Voralpen Lilienfeld, Dr Sepp Bosak; Landesklinikum Mostviertel Melk, Dr Aburumieh Abdul Rahman; Landesklinikum Weinviertel Mistelbach Gänserndorf, Dr Roland Schmid; Landesklinikum Thermenregion Mödling, Dr Paul Riss; Krankenhaus Neunkirchen, Dr Beda Hartmann; Landesklinikum Mostviertel Scheibbs, Dr Peter Diridl; Landesklinikum St. Pölten, Dr Matthias Klein; Landesklinikum Donauregion Tulln, Dr Alfred Kerak; Krankenhaus Wiener Neustadt, Dr Christian Gamper; Landesklinikum Waldviertel Zwettl, Dr Rüdiger Deix; Landeskrankenhaus Freistadt, Dr Josef Sabbagh; Landeskrankenhaus Bad Ischl, Dr Alfred Bichler; Landeskrankenhaus Gmunden, Dr Wolfgang Fellner; Krankenhaus St. Franziskus Grieskirchen, Dr Gottfried Trabitzsch; Landeskrankenhaus Kirchdorf, Dr Florian Marberger; Krankenaus der Elisabethinen Linz, Dr Rudolf Leikermoser; Krankenhaus der Stadt Linz, Dr Helmut Stöger; Konventspital der Barmherzigen Brüder Linz, Dr Harald Gründling; Landesfrauenklinik Linz, Dr Gernot Tews; Krankenhaus der Barmherzigen Schwestern Ried, Dr Walter Dirschlmayer; Landeskrankenhaus Rohrbach, Dr Peter Stumpner; Landeskrankenhaus Schärding, Dr Thomas Puchner; Landeskrankenhaus Steyr, DDr Hermann Enzelsberger; Landeskrankenhaus Vöcklabruck, Dr Wolfgang Fellner; Klinikum Kreuzschwestern Wels, Dr Klaus Reisenberger; Krankenhaus Hallein, Dr Alexander Albrecht; Krankenhaus Oberndorf, Dr Wilfried Rösslhuber; Landeskrankenhaus Salzburg, Dr Alfons Staudach; Krankenhaus der Barmherzigen Brüder Salzburg, Dr Michael Batka; Kardinal Schwarzenberg'sches Krankenhaus Schwarzach i.P., Dr Wieland Zeilmann; Krankenhaus Tamsweg, Dr Peter Csaicsich; Bezirkskrankenhaus Hall, Dr Burghard Abendstein; Bezirkskrankenhaus Lienz, Dr Peter Anderl; Bezirkskrankenhaus Schwaz, Dr Dieter Kölle; Krankenhaus Dornbirn, Dr Walter Neunteufel; Landeskrankenhaus Feldkirch, Dr Peter Schwärzler; Krankenhaus der Barmherzigen Brüder Eisenstadt, Dr Lothar Fuith; Landeskrankenhaus Oberpullendorf, Dr Martin Fabsits; Landeskrankenhaus Oberwart, Dr Roland Pavelka; Landeskrankenhaus Bruck an der Mur, Dr Ralph George; Landeskrankenhaus Deutschlandsberg, Dr Peter Hofmann; Landeskrankenhaus Feldbach, Dr Hannes Hofmann; Krankenhaus der Barmherzigen Brüder Graz, Dr Peter Lang; Landeskrankenhaus Hartberg, Dr Kurt Resetarits; Landeskrankenhaus Judenburg-Knittelfeld, Dr Peter Klug; Landeskrankenhaus Rottenmann, Dr Peter Klug; Krankenhaus Spittal an der Drau, Dr Heinz Hetzel; Krankenhaus der Barmherzigen Brüder St. Veit an der Glan, Dr Andreas Roth; Landeskrankenhaus Villach, Dr Jörg Keckstein; and Landeskrankenhaus Wolfsberg, Dr Maurus Demmel.*

## REFERENCES

1. Olaitan A, Weeks J, Mocroft A, et al. The surgical management of women with ovarian cancer in the south west of England. *Br J Cancer.* 2001;85(12):1824–1830.
2. Bailey J, Murdoch J, Anderson R, et al. Stage III and IV ovarian cancer in the South West of England: five-year outcome analysis for cases treated in 1998. *Int J Gynecol Cancer.* 2006;16(1):25–29.
3. Kehoe S, Powell J, Wilson S, et al. The influence of the operating surgeon's specialisation on patient survival in ovarian carcinoma. *Br J Cancer.* 1994;70(5):1014–1017.
4. Junor EJ, Hole DJ, McNulty L, et al. Specialist gynaecologists and survival outcome in ovarian cancer: a Scottish national study of 1866 patients. *Br J Obstet Gynaecol.* 1999;106(11):1130–1136.
5. Oksefjell H, Sandstad B, Trope C. Improved survival for stage IIIC ovarian cancer patients treated at the Norwegian Radium Hospital between 1984 and 2001. *Eur J Gynaecol Oncol.* 2007;28(4):256–262.
6. Paulsen T, Kjaerheim K, Kaern J, et al. Improved short-term survival for advanced ovarian, tubal, and peritoneal cancer patients operated at teaching hospitals. *Int J Gynecol Cancer.* 2006;16(suppl 1):11–17.
7. Elit L, Bondy SJ, Paszat L, et al. Outcomes in surgery for ovarian cancer. *Gynecol Oncol.* 2002;87(3):260–267.
8. Ioka A, Tsukuma H, Ajiki W, et al. Influence of hospital procedure volume on ovarian cancer survival in Japan, a country with low incidence of ovarian cancer. *Cancer Sci.* 2004;95(3):233–237.
9. Kumpulainen S, Grenman S, Kyyronen P, et al. Evidence of benefit from centralised treatment of ovarian cancer: a nationwide population-based survival analysis in Finland. *Int J Cancer.* 2002; 102(5):541–544.
10. Chan JK, Kapp DS, Shin JY, et al. Influence of the gynecologic oncologist on the survival of ovarian cancer patients. *Obstet Gynecol.* 2007;109(6):1342–1350.
11. Oberaigner W, Stuhlinger W. Influence of department volume on cancer survival for gynaecological cancers—a population-based study in Tyrol, Austria. *Gynecol Oncol.* 2006;103(2):527–534.

12. Hillner BE, Smith TJ, Desch CE. Hospital and physician volume or specialization and outcomes in cancer treatment: importance in quality of cancer care. *J Clin Oncol.* 2000;18(11):2327–2340.
13. Obermair A, Oberaigner W, Marth C. Wie gut ist die Behandlung des Ovarialkarzinoms in Österreich? *Frauenarzt.* 2003;7:732–736.
14. Winter WE, 3rd, Maxwell GL, Tian C, et al. Prognostic factors for stage III epithelial ovarian cancer: a Gynecologic Oncology Group study. *J Clin Oncol.* 2007;25(24):3621–3627.
15. Tingulstad S, Skjeldestad FE, Hagen B. The effect of centralization of primary surgery on survival in ovarian cancer patients. *Obstet Gynecol.* 2003;102(3):499–505.
16. Wimberger P, Lehmann N, Kimmig R, et al. Prognostic factors for complete debulking in advanced ovarian cancer and its impact on survival. An exploratory analysis of a prospectively randomized phase III study of the Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian Cancer Study Group (AGO-OVAR). *Gynecol Oncol.* 2007; 106:69–74.
17. Eisenkop SM, Spirtos NM, Friedman RL, et al. Relative influences of tumor volume before surgery and the cytoreductive outcome on survival for patients with advanced ovarian cancer: a prospective study. *Gynecol Oncol.* 2003;90(2):390–396.
18. Bristow RE, Tomacruz RS, Armstrong DK, et al. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol.* 2002;20(5): 1248–1259.
19. Chi DS, Eisenhauer EL, Lang J, et al. What is the optimal goal of primary cytoreductive surgery for bulky stage IIIC epithelial ovarian carcinoma (EOC)? *Gynecol Oncol.* 2006;103(2):559–564.
20. von Georgi R, Franke FE, Munstedt K. Influence of surgery and postoperative therapy and tumor characteristics on patient prognosis in advanced ovarian carcinomas. *Eur J Obstet Gynecol Reprod Biol.* 2003;111(2):189–196.
21. Aletti GD, Gostout BS, Podratz KC, et al. Ovarian cancer surgical resectability: relative impact of disease, patient status, and surgeon. *Gynecol Oncol.* 2006;100(1):33–37.
22. Burghardt E, Pickel H, Lahousen M, et al. Pelvic lymphadenectomy in operative treatment of ovarian cancer. *Am J Obstet Gynecol.* 1986; 155(2):315–319.
23. Scarabelli C, Gallo A, Zarrelli A, et al. Systematic pelvic and para-aortic lymphadenectomy during cytoreductive surgery in advanced ovarian cancer: potential benefit on survival. *Gynecol Oncol.* 1995;56(3): 328–337.
24. Chan JK, Urban R, Hu JM, et al. The potential therapeutic role of lymph node resection in epithelial ovarian cancer: a study of 13,918 patients. *Br J Cancer.* 2007;96(12):1817–1822.
25. Spirtos NM, Gross GM, Freddo JL, et al. Cytoreductive surgery in advanced epithelial cancer of the ovary: the impact of aortic and pelvic lymphadenectomy. *Gynecol Oncol.* 1995;56(3):345–352.
26. Panici PB, Maggioni A, Hacker N, et al. Systematic aortic and pelvic lymphadenectomy versus resection of bulky nodes only in optimally debulked advanced ovarian cancer: a randomized clinical trial. *J Natl Cancer Inst.* 2005;97(8):560–566.