Hospital case-volume and mortality after ovarian cancer surgery: a population-based retrospective cohort study

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Research

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Abstract

Background

The goal of ovarian cancer surgery has recently shifted from optimal cytoreduction to more complete resection. This study attempted to reassess and update the association between surgical case-volume and both in-hospital and long-term mortality after ovarian cancer surgery using recent data.

Methods

Data from all adult patients who underwent ovarian cancer surgery in Korea between 2004 and 2017 were obtained from the database of Korean National Health Insurance Service. Hospitals were categorized by average annual number of surgeries considering overall distribution of case-volume. Postoperative in-hospital and 1, 3, 5-year mortality were analyzed using logistic regression.

Results

During the study period, 23,487 ovarian cancer surgeries were performed in 354 hospitals. High-, medium-, and low-volume centers were defined as > 100 cases/year, 30–100 cases/year, and < 30 cases/year, respectively. In-hospital mortality was significantly higher in medium-volume (1.63%; adjusted odds ratio, 2.28; confidence interval, 1.64–3.17; $P < 0.001$) and low-volume (1.62%; adjusted odds ratio; 2.12; confidence interval, 1.55–2.90; $P < 0.001$) centers compared to high-volume centers (1.13%). In addition, 1-year mortality after ovarian cancer surgery was 6.26%, 7.07%, and 8.06% for high-volume, medium-volume, and low-volume centers, respectively, and the differences among the groups were significant. However, case-volume effect was not apparent in 3- and 5-year mortality after ovarian cancer surgery.

Conclusions

Case-volume effect was observed for in-hospital and 1-year mortality after ovarian cancer surgery while no clear association was found between the case-volume and 3- or 5-year mortality.

Introduction

Ovarian cancer is projected to be the fifth leading cause of cancer death in 2020 for women in the US [1], and accounts for nearly 4% of female cancer deaths in Korea [2]. Despite the recent decrease in the incidence and advances in treatment, the overall survival rate is still relatively low with a reported 5-year survival rate around 50% [3].

The standard treatment for ovarian cancer has been surgical resection aiming for complete tumor removal followed by adjuvant chemotherapy. The goal of surgical resection has evolved from cytoreduction to complete resection in recent years [4, 5]. Extensive and sophisticated surgery is often required for complete tumor resection as more than 70% of the patients are diagnosed in the advanced stage [6].

The impact of surgical volume on patient outcome has been widely studied for complex surgical procedures with significant postoperative morbidity such as major cancer resections, cardiovascular procedures, and solid organ transplantation [7–10]. The 0 has also been suggested for ovarian cancer surgery [11–14]. The change in the surgical paradigm towards a more complete resection of ovarian cancer calls for a reassessment of the case volume effect on both short- and long-term outcome after ovarian cancer surgery.

The purpose of this study was to analyze the association between the hospital case-volume of ovarian cancer surgery and in-hospital mortality along with 1, 3, 5-year mortality using the database from the Korean National Health Insurance Service (NHIS). It was hypothesized that higher surgical case-volume may be associated with lower in-hospital and long-term mortality after ovarian cancer surgery.

Patients And Methods

Data source and study population

The Korean NHIS governs the single payer universal health coverage system of Korea, the National Health Insurance (NHI) program and the Medical Aid program. Data obtained from the Korean NHIS database contains nearly all data of cancer surgeries that were performed for the Korean residents.[17]

Adult patients (≥ 19 years) who underwent ovarian cancer surgery between 2004 and 2017 were identified by using the NHI procedure codes. Procedural code of extirpation of adnexal tumor for malignancy, staging, pelvic exenteration, and pelvic and para-aortic lymphadenectomy. Operations were categorized according to the extent of the surgery. Radical resection was defined as extirpation of the adnexal tumor with removal of parametrium or lymph nodes. Data from patients with malignant neoplasm of ovary, defined by the International Classification of Diseases, 10th revision (ICD-10) diagnosis code of C56, were extracted.

Variables and study endpoints

Baseline characteristics including age, sex, and comorbidities such as hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, chronic liver disease, chronic kidney disease, and cerebrovascular disease were extracted from the database using ICD-10 diagnosis codes. Hypertension was defined as ICD codes for hypertension with anti-hypertensive drugs prescribed for more

than 1 month. Diabetes mellitus was defined both ICD code for diabetes and insulin or oral hypoglycemic agents prescribed for more than 1 month. Adjuvant and neoadjuvant therapy data were collected using procedural codes. Data on in-hospital and 1, 3, 5-year mortality were extracted as primary and secondary outcomes.

Definition of case-volume

The institutional case-volume was defined as the average annual number of ovarian cancer surgeries between 2004 and 2017. The cutoff values for categorizing centers according to case volume were not predetermined before data analysis. Predesignated factors to determine the cutoff values included overall distribution of case volume, comparable patient number in each group, and sufficient number of centers in each group for statistical comparison.

Statistical analyses

Continuous variables were presented as mean [standard deviation (SD)] or median [interquartile range (IQR)] and were analyzed using the *t*-test or Mann–Whitney U-test. Categorical variables were expressed as number (%) and were analyzed using Pearson's chi-square test. In-hospital and 1, 3, 5 year-mortality after ovarian cancer surgery was evaluated according to the case-volume groups. Using multivariable logistic regression, potential risk factors were evaluated with adjustment for age, sex, adjuvant therapy, transfusion, and comorbidities. The results of the logistic regression were expressed as odds ratio (OR), 95% confidence interval (CI), and p-value.

All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC), and $P < 0.05$ was considered statistically significant.

Ethical approval

This population-based retrospective cohort study was determined to be exempt from review by the institutional review board of Seoul National University Hospital (E-1905-098-1034). Informed consent was also waived due to the retrospective nature of the study design and study feasibility.

Results

A total of 23,487 ovarian cancer patients underwent surgery in 354 hospitals in Korea between 2004 and 2017. Medical centers were categorized as low-volume centers (<30 cases/year), medium-volume centers (30-100 cases/year), or high-volume centers (>100 cases/year) according to the institutional case-volume. Patient and center characteristics are summarized in Table 1. More than one third of the ovarian

cancer patients were operated in 5 high-volume centers of which median annual case volume was 118.21 (Table 1). Most of the patients were under 50 years old at the time of the operation and adjuvant chemotherapy was performed in almost all ovarian cancer patients (Table 1). More than half of the patients underwent radical extirpation of adnexal tumor with hysterectomy which includes bilateral salpingo-oophorectomy and removal of parametrium or lymph nodes (Table 1).

The overall in-hospital mortality after ovarian cancer surgery was 1.33% (312/23487). After adjusting for age, operation type, comorbidities, neoadjuvant chemotherapy, and transfusion, low-volume (adjusted OR, 2.12; CI, 1.55-2.90) and medium-volume (adjusted OR, 2.28; CI, 1.64-3.17) centers showed significantly higher in-hospital mortality compared to high-volume centers (Table 2). Older age, hypertension, diabetes mellitus, coronary artery disease, and perioperative transfusion were also identified as risk factors for in-hospital mortality (Table 2).

Table 3 showed the result of logistic regression for long-term mortality after ovarian cancer surgery. The overall all-cause 1, 3, and 5-year mortality after ovarian cancer surgery were 7.18% (1665/23175), 23.04% (4330/18790), and 33.91% (5094/15023), respectively. Patients who received the operation in high-volume centers showed significantly lower 1-year mortality compared to patients who received care in medium and low volume centers. The case volume effect was not identifiable at 3 and 5 years after surgery (Table 3). Older age and perioperative transfusion were consistent risk factor for mortality at all time points. Patients who received neoadjuvant chemotherapy in addition to adjuvant chemotherapy showed significantly higher long-term mortality (Table 3).

Discussion

In this study, the institutional case-volume of ovarian cancer surgery was identified as an independent risk factor for in-hospital or 1-year mortality. No definite correlation was found between case volume and 3-year or 5-year mortality.

The standard treatment for ovarian cancer has been surgery with an aim for complete tumor removal followed by adjuvant chemotherapy. The use of neoadjuvant chemotherapy or radiotherapy is limited to specific circumstances and require more evidence [15-16]. Ovarian cancer can be considered as a high-risk surgery as more than 70% of the patients are diagnosed in the advanced stage with cancer involvement of the peritoneal cavity and adjacent organs [6, 17]. Extensive resections including salpingo-oophorectomy, hysterectomy, omentectomy, and occasionally resection of the bowel, bladder, liver, spleen, diaphragm or other organs are required to achieve maximal cytoreduction which is associated with long-term prognosis [18, 19]. A relatively small prospective observational study of 275 patients in Finland demonstrated that higher hospital operative volume (>20 cases/year) was associated with more optimal cytoreduction and a significant prognostic factor for 5-year survival [13]. Recently, complete resection of all macroscopic tumor was emphasized as the cornerstone for ovarian cancer treatment as residual tumor of even less than 1 cm in diameter was associated with worse prognosis compared to complete resection [5, 20].

Previous studies have reported conflicting results regarding the association between the surgical case volume of ovarian cancer and postoperative outcomes [11-14]. An analysis of 100,725 patients using the National Cancer Database of the US, both 2- and 5-year survival were lower in low-volume centers (1-2 cases/year) compared to high-volume centers (≥20 cases/year) after categorizing the hospitals into quintiles according to annual case volume (64.4% *vs*. 77.4% for 2-year survival, $P<0.001$; 39.3% *vs*. 51.0% for 5-year survival, $P<0.001$) [21]. Another report that investigated advanced-stage epithelial ovarian cancer showed that hospital volume ≥21 cases/year was a strong predictor of 5-year overall survival after analyzing 45,929 patients from the National Cancer Database of the US [12]. To the contrary, another study that evaluated 2,952 patients aged 65 years or older did not show any association between hospital surgical volume and 60-day mortality or overall survival when hospitals were grouped into tertiles based on hospital surgical volume (cutoff value of 13 and 29 cases/year) between 1992 to 1999 [14]. While prior studies defined high-volume center as an annual volume 20 or more cases per year, the determined cutoff value in our study was 30 and 100 cases per year for medium- and high-volume center respectively after visual inspection of the distribution of the annual case volume and number of patients. It seems likely that there may be another cutoff past 20-29 cases per year, beyond which patient outcome may improve, yet again.

Ovarian cancer surgery is often accompanied by significant postoperative morbidity. According to a previous analysis of 28,651 women who underwent ovarian cancer surgery, the complication rate ranged from 17.1% in patients under 50 years to 31.5% of in patients over 80 years of age [22]. Another study reported that severe postoperative complications within 90 days after primary debulking surgery for advanced epithelial ovarian cancer showed that events requiring invasive interventions or re-operation, organ systems failure, or postoperative death occurred in 22.3% (138/620) of patients [23]. In another study that classified hospitals into tertiles based on case volume, failure to rescue rates (defined as the mortality following a major complication), were higher in patients treated at low-volume hospitals compared to patients treated in high-volume hospitals (8.0% vs. 4.9%, $P<0.001$) [24]. In this regard, accumulated experience in coping with postoperative complications may play an important role in case-volume effect.

Unlike previous reports, the surgical case-volume effect was not demonstrated at 3 or 5 years after surgery in the present study [12, 21]. Potential mechanisms behind the dilution of case volume effect over time may include the relatively high level of access to care. As a small country with complex transportation infrastructure, large hospitals which are high volume centers can be accessed from anywhere in the country within 3-4 hours. It is also relatively easy to seek care in high volume centers as the requirements are easy to meet. Considering that the stage of the ovarian cancer at the time of surgery was not available in the data, and therefore not adjusted for, concentration of patients in advanced stages in high volume centers may have contributed to the dilution of the case volume effect.

Case-volume effect on patient outcome has been demonstrated mainly in high-risk procedures such as major cancer resections, cardiovascular procedures, and heart transplantation [7-10] while relatively simple surgical procedures such as laparoscopic cholecystectomy showed no significant case-volume

effect [25, 26]. Experienced surgical teams, nurses, and anesthesiologists are more likely to be prepared to optimally manage anticipated and unanticipated complications that may occur during high-risk surgical procedures. With regards to ovarian cancer surgery, collaboration with other specialists such as general surgeons, urologic surgeons, or thoracic surgeons are often required for optimal treatment. In this respect, comprehensive perioperative care by multidisciplinary team consisting of sufficient and skilled medical personnel as well as accumulated experience of individual surgeons may explain, to some extent, the case-volume effect in high-volume centers. The suggested amount of experience that may lead to the best patient outcome in this study was 100 cases of ovarian cancer surgery per year.

Several limitations should be considered when interpreting the result of this study. First, this study was a retrospective analysis of an administrative database. Therefore, the results may be subject to biases and limitations of retrospective studies and database not designed/collected for research. However, the database used in our study contains data from all 23,487 patients who received surgery for ovarian cancer in Korea during the study period, which may compensate for the shortcomings stated above and provide a relatively strong explanatory power. Second, clinical information such as staging, histologic diagnosis, or laboratory findings were not available. Although these clinical variables are likely to influence patient treatment and subsequent outcomes, individual clinical data could not be obtained due to the nature of the administrative database. Potential confounders that could be identified such as operation type, adjuvant therapy, and comorbidities were adjusted for. Third, the determined cutoff values of volume criteria were not previously validated. However, cutoff criteria for case volume may be bound to differ depending on the healthcare system, geographical circumstances, and the type of surgical procedure. Therefore, cutoff values for determining case volume effect may not need external validation as it would not be feasible to apply cutoff values determined from studies performed in different settings and time.

Conclusion

In conclusion, low-volume hospitals showed significantly higher in-hospital and 1-year mortality after ovarian cancer surgery. No clear association was found between the case-volume and 3- or 5-year mortality.

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Declarations

Ethics approval and consent to participate: Ethics approval was waived by the Seoul National University Hospital IRB due to anonymity of the data.
Consent for publication: Not applicable
Availability of data and materials: The data that support the findings of this study are available from the Korean National Health Insurance Service database, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Korean National Health Insurance Service.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions

Conception and design: all authors.

Data acquisition: H.K., E.J.J., J.J.

Data analysis: E.J.J., J.J.

Manuscript drafting: B.R.K., H.K., H.L., H.G.R

Manuscript revision: B.R.K., S.J., H.L. H.G.R.

Final approval: all authors.

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Tables

Table 1. Patient and center characteristics

	Total	Low-volume (<30 cases/year)	Medium-volume (30-100 cases/year)	High-volume (>100 cases/year)	*P*
Number of centers	354	336	13	5	
Number of patients	23487	9278	6253	7956	
Annual case volume	0.33 [0.14, 3.43]	0.29 [0.14, 1.50]	42.43 [37.79, 57.07]	118.21 [116.36, 178.93]	<0.001
Age	52.14 (13.56)	52.51 (14.12)	51.33 (13.83)	52.33 (12.64)	<0.001
19 – 60	16685 (71.04%)	6458 (69.61%)	4489 (71.79%)	5738 (72.12%)	<0.001
61 - 70	4244 (18.07%)	1629 (17.56%)	1141 (18.25%)	1474 (18.53%)	
71 - 80	2177 (9.27%)	986 (10.63%)	535 (8.56%)	656 (8.25%)	
≥81	381 (1.62%)	205 (2.21%)	88 (1.41%)	88 (1.11%)	
Operation type					<0.001
Radical resection without hysterectomy	3059 (13.02%)	1258 (13.56%)	879 (14.06%)	922 (11.59%)	
Radical resection with hysterectomy	13475 (57.37%)	4432 (47.77%)	3547 (56.72%)	5496 (69.08%)	
Simple resection without hysterectomy	3307 (14.08%)	1691 (18.23%)	825 (13.19%)	791 (9.94%)	
Simple resection with hysterectomy	2266 (9.65%)	1354 (14.59%)	512 (8.19%)	400 (5.03%)	
Others	1380 (5.88%)	543 (5.85%)	490 (7.84%)	347 (4.36%)	
Comorbidities					
Hypertension	5830 (24.82%)	2467 (26.59%)	1510 (24.15%)	1853 (23.29%)	<0.001
Diabetes mellitus	3627 (15.44%)	1388 (14.96%)	936 (14.97%)	1303 (16.38%)	0.018
Coronary artery disease	1421 (6.05%)	545 (5.87%)	397 (6.35%)	479 (6.02%)	0.472
Chronic obstructive pulmonary disease	560 (2.38%)	151 (1.63%)	105 (1.68%)	304 (3.82%)	<0.001
Chronic liver disease	6080 (25.89%)	2223 (23.96%)	1824 (29.17%)	2033 (25.55%)	<0.001
Chronic kidney disease	162 (0.69%)	78 (0.84%)	39 (0.62%)	45 (0.57%)	0.072
Cerebrovascular disease	929 (3.96%)	399 (4.30%)	224 (3.58%)	306 (3.85%)	0.066
Adjuvant therapy					
Neoadjuvant chemotherapy	11116 (47.33%)	3758 (40.50%)	2593 (41.47%)	4765 (59.89%)	<0.001
Adjuvant chemotherapy	23441 (99.80%)	9252 (99.72%)	6237 (99.74%)	7952 (99.95%)	0.001
Neoadjuvant radiotherapy	51 (0.22%)	15 (0.16%)	16 (0.26%)	20 (0.25%)	0.336
Adjuvant radiotherapy	372 (1.58%)	156 (1.68%)	109 (1.74%)	107 (1.34%)	0.106
Chemoradiotherapy	417 (1.78%)	170 (1.83%)	124 (1.98%)	123 (1.55%)	0.128
Transfusion required	12614	4619 (49.78%)	3336 (53.35%)	4659 (58.56%)	<0.001

	(53.71%)

Values are expressed as mean (standard deviation), median [interquartile range] or n (%).

Table 2. Logistic regression analysis for in-hospital mortality after ovarian cancer surgery

	In-hospital mortality [n/N (%)]	Unadjusted		Adjusted	
		OR (95% CI)	*P*	OR (95% CI)	*P*
50	134/16685 (0.80%)	1		1	
70	77/4244 (1.81%)	2.28 (1.72-3.03)	<0.001	1.53 (1.13-2.07)	0.006
80	89/2177 (4.09%)	5.26 (4.01-6.91)	<0.001	2.71 (1.98-3.71)	<0.001
	12/381 (3.15%)	4.02 (2.21-7.32)	<0.001	1.99 (1.05-3.75)	0.034
bidities					
ertension	149/5830 (2.56%)	2.81 (2.25-3.52)	<0.001	1.40 (1.07-1.85)	0.016
etes mellitus	96/3627 (2.65%)	2.47 (1.94-3.15)	<0.001	1.35 (1.03-1.78)	0.031
nary artery disease	48/1421 (3.38%)	2.89 (2.11-3.95)	<0.001	1.41 (1.00-1.99)	0.050
nic obstructive pulmonary disease	12/560 (2.14%)	1.65 (0.92-2.96)	0.092	1.07 (0.59-1.97)	0.819
nic liver disease	109/6080 (1.79%)	1.55 (1.22-1.96)	<0.001	1.10 (0.86-1.41)	0.439
nic kidney disease	9/162 (5.56%)	4.47 (2.26-8.84)	<0.001	1.71 (0.84-3.48)	0.139
brovascular disease	25/929 (2.69%)	2.15 (1.42-3.25)	<0.001	0.92 (0.59-1.43)	0.703
on type					
cal resection without hysterectomy	32/3059 (1.05%)	1		1	
cal resection with hysterectomy	150/13475 (1.11%)	1.06 (0.73-1.56)	0.748	0.81 (0.55-1.20)	0.300
ole resection without hysterectomy	55/3307 (1.66%)	1.60 (1.03-2.48)	0.036	2.23 (1.42-3.49)	0.001
ole resection with hysterectomy	43/2266 (1.90%)	1.83 (1.15-2.90)	0.010	1.57 (0.98-2.52)	0.060
rs	32/1380 (2.32%)	2.25 (1.37-3.68)	0.001	1.94 (1.17-3.21)	0.011
uvant chemotherapy					
	140/12371 (1.13%)	1		1	
	172/11116 (1.55%)	1.37 (1.1-1.72)	0.006	1.12 (0.88-1.42)	0.363
usion					
	18/10873 (0.17%)	1		1	
	294/12614 (2.33%)	14.39 (8.94-23.18)	<0.001	15.64 (9.64-25.39)	<0.001
olume					
-volume centers	60/7956 (0.75%)	1		1	
0 cases/year)					
ium-volume centers	102/6253 (1.63%)	2.18 (1.58-3.01)	<0.001	2.28 (1.64-3.17)	<0.001
100 cases/year)					
-volume centers	150/9278 (1.62%)	2.16 (1.60-2.92)	<0.001	2.12 (1.55-2.90)	<0.001
cases/year)					

OR, odds ratio; CI, confidence interval

Table 3. Multivariable logistic regression analysis for 1, 3, 5-year mortality after ovarian cancer surgery

	1-year mortality			3-year mortality			5-year mortality		
	n/N (%)	OR (95% CI)	*P*	n/N (%)	OR (95% CI)	*P*	n/N (%)	OR (95% CI)	*P*
Age									
19 - 60	862/16551 (5.21%)	1		2562/13584 (18.86%)	1		3132/10978 (28.53%)	1	
61 - 70	357/4167 (8.57%)	1.39 (1.21, 1.59)	<0.001	950/3307 (28.73%)	1.44 (1.31, 1.58)	<0.001	1134/2583 (43.90%)	1.60 (1.45, 1.76)	<0.001
71 - 80	357/2088 (17.10%)	2.69 (2.31, 3.13)	<0.001	697/1627 (42.84%)	2.60 (2.30, 2.93)	<0.001	713/1254 (56.86%)	2.70 (2.36, 3.09)	<0.001
≥81	89/369 (24.12%)	4.11 (3.15, 5.37)	<0.001	121/272 (44.49%)	3.07 (2.37, 3.98)	<0.001	115/208 (55.29%)	2.88 (2.14, 3.87)	<0.001
Comorbidities									
Hypertension	633/5681 (11.14%)	1.17 (1.03, 1.33)	0.018	1367/4509 (30.32%)	1.07 (0.98, 1.17)	0.154	1533/3545 (43.24%)	1.05 (0.95, 1.16)	0.323
Diabetes mellitus	390/3531 (11.05%)	1.15 (1.00, 1.31)	0.055	845/2764 (30.57%)	1.09 (0.98, 1.21)	0.099	948/2139 (44.32%)	1.13 (1.02, 1.26)	0.025
Coronary artery disease	163/1373 (11.87%)	1.02 (0.85, 1.24)	0.822	351/1119 (31.37%)	1.01 (0.87, 1.17)	0.879	419/926 (45.25%)	1.04 (0.90, 1.22)	0.576
Chronic obstructive pulmonary disease	57/548 (10.40%)	1.05 (0.78, 1.40)	0.766	137/507 (27.02%)	0.86 (0.70, 1.07)	0.167	185/463 (39.96%)	0.87 (0.70, 1.06)	0.169
Chronic liver disease	532/5971 (8.91%)	1.11 (0.99, 1.25)	0.066	1369/4699 (29.13%)	1.30 (1.20, 1.41)	<0.001	1544/3655 (42.24%)	1.34 (1.24, 1.46)	<0.001
Chronic kidney disease	28/153 (18.30%)	1.48 (0.96, 2.27)	0.079	37/104 (35.58%)	1.00 (0.66, 1.53)	0.998	45/76 (59.21%)	1.60 (0.98, 2.61)	0.061
Cerebrovascular disease	125/904 (13.83%)	1.20 (0.97, 1.48)	0.096	217/695 (31.22%)	0.94 (0.78, 1.12)	0.493	259/551 (47.01%)	1.06 (0.88, 1.28)	0.552
Operation type									
Radical resection without hysterectomy	182/3027 (6.01%)	1		491/2528 (19.42%)	1		606/2030 (29.85%)	1	
Radical resection with hysterectomy	831/13325 (6.24%)	0.82 (0.69, 0.97)	0.023	2426/10498 (23.11%)	0.96 (0.86, 1.08)	0.502	2896/8182 (35.39%)	1.00 (0.89, 1.12)	0.961
Simple resection without hysterectomy	275/3252 (8.46%)	1.68 (1.37, 2.05)	<0.001	590/2727 (21.64%)	1.39 (1.20, 1.60)	<0.001	614/2252 (27.26%)	1.11 (0.97, 1.29)	0.139
Simple resection with	223/2223	1.47	<0.001	461/1867	1.22	0.012	529/1575	1.08	0.341

hysterectomy	(10.03%)	(1.19, 1.82)		(24.69%)	(1.04, 1.42)		(33.59%)	(0.93, 1.25)	
Others	154/1348 (11.42%)	1.84 (1.46, 2.32)	<0.001	362/1170 (30.94%)	1.64 (1.38, 1.93)	<0.001	449/984 (45.63%)	1.75 (1.48, 2.08)	<0.001
Neoadjuvant chemotherapy									
No	725/12231 (5.93%)	1		1966/10361 (1.90%)	1		2437/8632 (28.23%)	1	
Yes	940/10944 (8.59%)	1.29 (1.16, 1.44)	<0.001	2364/8429 (28.05%)	1.43 (1.32, 1.53)	<0.001	2657/6391 (41.57%)	1.50 (1.39, 1.61)	<0.001
Transfusion									
No	416/10855 (3.83%)	1		1173/8812 (13.31%)	1		1461/7096 (20.59%)	1	
Yes	1249/12320 (10.14%)	2.97 (2.63, 3.35)	<0.001	3157/9978 (31.64%)	2.96 (2.73, 3.20)	<0.001	3633/7927 (45.83%)	3.07 (2.84, 3.32)	<0.001
Case volume									
High-volume (>100 cases/year)	494/7896 (6.26%)	1		1470/6154 (23.89%)	1		1706/4694 (36.34%)	1	
Medium-volume (30-100 cases/year)	435/6151 (7.07%)	1.18 (1.02, 1.35)	0.022	1087/5108 (21.28%)	0.92 (0.84, 1.01)	0.084	1317/4194 (31.40%)	0.87 (0.79, 0.96)	0.004
Low-volume (<30 cases/year)	736/9128 (8.06%)	1.28 (1.13, 1.45)	<0.001	1773/7528 (23.55%)	1.06 (0.97, 1.15)	0.214	2071/6135 (33.76%)	1.02 (0.94, 1.12)	0.621

OR, odds ratio; CI, confidence interval