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Minimally invasive interval debulking surgery for advanced ovarian cancer after neoadjuvant chemotherapy

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Abstract

Objective: Assess outcomes of interval debulking surgery (IDS) after neoadjuvant chemotherapy via minimally invasive surgery (MIS) compared with laparotomy in patients with advanced epithelial ovarian cancer.

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Kirsten Jorgensen: Conceptualization, Data curation, Methodology, Writing original draft & editing. **Alexander Melamed**: Methodology, Writing original draft & editing. **Chi-Fang Wu**: Data curation, Formal analysis, Methodology, Validation, Writing original draft & editing. **Roni Nitecki**: Writing original draft & editing. **Rene Pareja:** Writing original draft & editing. **Anna Fagotti**: Writing original draft & editing**. John O Schorge**: Writing original draft & editing. P**edro T Ramirez**: Writing original draft & editing. **Jose Alejandro Rauh**-Hain: Conceptualization, Methodology, Supervision, Writing original draft & editing.

Declaration of Competing Interest

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Alexander Melamed: served on AstraZeneca advisory board

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Methods: Patients diagnosed with stage IIIC or IV epithelial ovarian cancer between 2013–2018 who received neoadjuvant chemotherapy and IDS were identified in the National Cancer Database. Primary outcome was overall survival. Secondary outcomes were 5-year survival, 30- and 90-day postoperative mortality, extent of surgery, residual disease, hospitalization duration, surgical conversions, and unplanned readmissions. Propensity score matching was used to compare MIS and laparotomy for IDS. Association of treatment approach with overall survival was assessed using Kaplan-Meier method and Cox regression. Sensitivity analysis was conducted for effect of unmeasured confounders.

Results: A total of 7,897 patients met inclusion criteria; 2,021 (25.6%) underwent MIS. Percentage undergoing MIS increased from 20.3%–29.0% over the study period. After propensity score matching, mean overall survival was 35.9 months in the MIS group versus 34.5 months in the laparotomy group [hazard ratio (HR) 0.86 (95%CI 0.79–0.94)]. Five-year survival probability was higher in MIS versus laparotomy (38.3% vs 34.8%, p<0.01). There was lower 30- and 90-day mortality (0.3% vs 0.7% [p=0.04] and 1.4% vs 2.5% [p=0.01], respectively), shorter length of stay (mean 3.7 vs 5.7 days, p<0.01), lower residual disease (23.9% vs 26.7%, p<0.01), and lower additional cytoreductive procedures (59.3% vs 70.8%, p<0.01) in MIS compared to laparotomy, with similar rates of unplanned readmission (2.7% vs 3.1%, p=0.39).

Conclusions: Patients who undergo IDS by MIS have similar overall survival and decreased morbidity compared with laparotomy.

Keywords

Laparoscopic surgery; interval debulking; minimally invasive surgery; ovarian cancer

1. Introduction

Primary debulking surgery performed via laparotomy followed by adjuvant chemotherapy has traditionally been the standard of care for advanced epithelial ovarian cancer, with a presumed survival advantage mainly based on its ability to achieve maximal cytoreduction.[1] Over the past decade, four randomized controlled trials demonstrated equivalent overall and progression-free survival as well as decreased morbidity for neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) compared to primary debulking surgery (PDS).[2–5] Additionally, retrospective studies demonstrated higher rates of complete resection in patients who underwent NACT and IDS versus PDS followed by adjuvant chemotherapy.[6] Subsequently, there has been a shift toward increased use of NACT for advanced ovarian cancer,[7,8] raising the question of optimal surgical approach for IDS.

Typically, NACT for epithelial ovarian cancer is administered as three to four cycles of platinum-based chemotherapy, leaving diminished remaining abdominal tumor. This makes minimally invasive surgery (MIS) a more feasible option in order to achieve no gross residual disease on IDS.[9] Prior studies of MIS for interval debulking of advanced ovarian cancer consist mainly of case reports and small series in which this approach appeared to be safe and effective.[9,10] Additionally, MIS has been linked to earlier initiation of adjuvant chemotherapy, as well as decreased perioperative morbidity, postoperative pain and hernia rates when compared with laparotomy.[11] We previously analyzed the National

Cancer Database (NCDB) from 2010 to 2012 and identified 450 patients who underwent laparoscopic interval debulking. We observed equivalent 3-year survival with decreased morbidity compared to laparotomy.[12] This initial study population likely reflected very early adopters of MIS for IDS, given early feasibility studies were published around the same time and the patients were very highly selected. In the current study, we sought to assess the survival, surgical, and clinical outcomes of interval debulking surgery performed by minimally invasive approach compared with laparotomy in a more contemporary (2013–2018) and larger population of patients with advanced epithelial ovarian cancer who had previously received neoadjuvant chemotherapy.

2. Methods

2.1 Study population and data sources

This was a retrospective cohort study using data from the NCDB, a dataset sourced from hospital registry data. The data are collected from more than 1,500 Commission on Cancer accredited facilities and represents more than 70% of all newly diagnosed cancer cases in the United States. The NCDB is a joint project of the American Cancer Society and the American College of Surgeon's Commission on Cancer. The data used in this study were in an existing, deidentified database, therefore exemption was granted by the Institutional Review Board at MD Anderson Cancer Center.

All patients diagnosed with epithelial ovarian cancer from 2013 to 2018 in the 2019 NCDB participant user data file (the most recent file available with complete survival data) were included. Patients with American Joint Commission on Cancer (AJCC) stage IIIC and stage IV were selected. Pathologic stage was used when clinical stage was not available. The stage groups were TNM-based according to the seventh and eight editions of the *AJCC Cancer Staging Manual*.[13,14] Serous, mucinous, clear cell, endometrioid and other histologies were selected, using the International Classification of Diseases for Oncology, Third Edition (Table 1).[15] Cases were then excluded in the setting of no or unknown receipt of surgery (n=27,527) or chemotherapy (n=529), pre-existing cancer diagnosis (n=8,753), no microscopic confirmation (n=173), no treatment at reporting facility (n=3,242), surgery before chemotherapy (n=3,198), unknown sequence of treatment (n=27), and unknown surgical approach (n=1), such that the cases that remained after exclusion included only those patients with advanced epithelial ovarian cancer who underwent NACT followed by IDS with known surgical approach (Figure 1).

Cases were categorized based on patient and tumor characteristics. The NCDB does not provide data regarding clinical or pathologic response to chemotherapy. Age was defined as a continuous variable in years. Race and ethnicity were categorized as American Indian, Asian or Pacific Islander, Hispanic, Non-Hispanic Black, Non-Hispanic White, and none of the above. Race and ethnicity data were used because results of prior studies demonstrated different rates of minimally invasive gynecologic surgery by race and ethnicity.[16,17] Geographic locations were categorized by US Census division of the reporting facility: New England, Middle Atlantic, South Atlantic, East-North Central, East-South Central, West-North Central, West-South Central, Mountain, Pacific, and unknown. Year of diagnosis was defined as the initial date of diagnosis whether clinically, pathologically, or

retrospectively defined by physician. Charlson-Deyo comorbidity scores (0–3) were used to measure comorbidity. These scores are weighted and derived from the sum of scores for comorbid conditions. A value greater than or equal to 1 indicated the presence of comorbidities as defined by the International Classification of Diseases (ICD), Ninth or ICD Tenth Revision, Clinical Modification secondary diagnosis codes. Patients' annual median household incomes were categorized as <$40,227, $40,227–50,353, $50,354–63,332 and ≥$63,333. Median income data is obtained by the NCDB based on the ZIP code of patient residence, collected via the 2016 American Community Survey. Insurance status was categorized as private insurance, Medicaid and other government insurance, Medicare, uninsured, or unknown. Rural-Urban status was categorized as metropolitan, rural, urban, or unknown, based on census data and the Rural-Urban Continuum Codes as defined by the United States Department of Agriculture Economic Research Service. The treating facility type was evaluated by program structure, services provided, and number of cases per year, as determined by the Commission on Cancer, and categorized as academic and research program, community cancer program, comprehensive community cancer program or integrated network cancer program. Medicaid expansion was classified as a non-expansion, January 2014 expansion, early expansion, late expansion, or unknown, based on the status of the state Medicaid expansion in the patient's state at the time of diagnosis.

2.2 Statistical analysis

The primary outcome was overall survival, defined as months from cancer diagnosis to death or date of the last contact. Secondary outcomes included overall survival at 5 years after diagnosis, 30- and 90-day mortality, length of hospitalization, residual disease status, extent of surgery, percentage of surgical conversions, and unplanned readmissions. Extent of surgery was classified as "gynecologic" (hysterectomy and/or oophorectomy) with or without omentectomy, or "additional cytoreductive procedures" (including surgery to the bowel, urinary tract, other organs, or radical surgery). Analysis was performed as intention to treat based on surgical approach at initiation of surgery (laparotomy vs MIS). Patients who underwent MIS (laparoscopic or robot-assisted) that was then converted to laparotomy were included in the minimally invasive cohort.

We compared categorical variables using χ^2 or Fisher's exact tests and continuous variables using independent sample t-tests in univariate analysis of patient characteristics. We fit a multivariate logistic regression model to estimate the probability of receiving MIS; independent variables included age (categorized as <50, 50–59, 60–69, 70–79, and ≥80 years), year of diagnosis, race and ethnicity, treating facility type, Charlson-Deyo comorbidity score, state Medicaid expansion status, insurance status, annual median household income, United States region, rural-urban status, cancer stage, and histology.

Propensity score matching was performed to create a cohort in which patients who underwent MIS and patients who underwent laparotomy for IDS were balanced on the covariates used in the multivariate regression model, as those covariates may confound the effect of treatment approach on survival.[18] Each patient who received MIS was matched with a patient who underwent laparotomy who had the same propensity to undergo MIS using Greedy nearest neighbor matching.[19] Standardized differences of covariates in the

propensity-matched cohort were assessed for balance. We then compared overall and 5-year survival between patients who underwent MIS versus laparotomy in the propensity score matched cohort using the Kaplan-Meier method and Cox proportional hazards regression model was used to estimate the hazard ratio (HR) and 95% confidence interval (CI) for the association of MIS with survival. We calculated 30- and 90-day mortality, extent of surgery, unplanned readmission rate, and residual disease between the two groups in the propensity-matched cohort using χ^2 or Fisher's exact test.

2.3 Sensitivity Analyses

We repeated all analyses for the primary outcome after excluding patients who had a conversion from MIS to laparotomy and repeated all analyses again after excluding those with clear cell, mucinous, or "other" histologies.

Although we adjusted for a large number of observed confounders using propensity score analysis, we additionally conducted a sensitivity analysis using the "E-value" to evaluate the robustness of derived estimates to potential unmeasured confounding.[20] The E-value uses estimates from the study data to quantify the strength of association an unmeasured confounder must have with the exposure and outcome to fully explain an observed relationship. We used the E-value to calculate the magnitude of the association an unmeasured confounder would need to have with both the exposure (MIS versus laparotomy) and the outcome (overall survival) to fully explain the derived estimate (HR). We also calculated the E-value required to explain the confidence limit of the HR closest to the null and to explain an inverse relationship with survival.

All statistical tests were two-sided, and differences were considered statistically significant at $P < 0.05$. All statistical analysis was performed using SAS Enterprise Guide version 7.1.

3. Results

We identified 7,897 patients with stage IIIC and IV epithelial ovarian cancer who underwent NACT followed by IDS and met all inclusion criteria (Figure 1). A minimally invasive approach was initiated in 2,021 (25.6% overall, with increase from 20.3% of cases in 2013 to 29.0% of cases in 2018). Of the 2,021 cases, 1,157 (57.2%) underwent conventional laparoscopic approach and 864 (42.8%) underwent robotic-assisted laparoscopic approach. Conversion from MIS to laparotomy occurred in 208 cases (10.3%) and among the converted cases, residual disease was noted in 64.9%. Reasons for conversion are not provided in the NCDB dataset.

3.1 Patient demographic, clinical, and tumor characteristics

Univariate analysis of patient characteristics demonstrated several important differences among the laparotomy versus MIS groups (Table 2). Compared with patients undergoing laparotomy, those undergoing MIS were more likely to be older (65.2 years vs 63.8 years, p<0.001), have fewer comorbidities (Charlson-Deyo comorbidity score of 0; 79.6% vs 77.0%), to receive treatment at a Comprehensive Community Cancer Program (36.3% vs 26.3%), use Medicare insurance (50.8% vs 46.4%), and be diagnosed later in the cohort (p<0.001). Serous histology was the most common, comprising 6,981 cases (88.4%). There

was no difference in MIS versus laparotomy according to disease stage (IIIC vs IV), race and ethnicity, or histology.

In a multivariate analysis, factors associated with increased use of MIS included: age ≥80 years (vs 60–69 years), Hispanic race/ethnicity (vs non-Hispanic White race/ethnicity), Charlson-Deyo comorbidity score of 0 (vs 1), New England region (vs Middle Atlantic, and all Central regions), Mountain region (vs New England), metropolitan status (vs unknown rural-urban status), treatment at a comprehensive community cancer program (vs community cancer program), income of $50,354-$63,332 (vs <$40,227), private insurance (vs Medicaid or other government insurance), and diagnosis between 2015–2018 (vs 2013) (Table 3).

Propensity score matching between the MIS and laparotomy groups yielded 100% match rate for the 2,021 patients in the MIS group. After propensity score matching, there were no significant differences between the MIS and laparotomy groups with respect to clinical or demographic variables (Table 2), and an assessment between groups found all variables to be balanced (Appendix A).

3.2 Survival analysis

Figure 2 shows Kaplan-Meier survival curves for the groups in the propensity-matched cohort. The mean overall survival in this cohort was 35.9±18.3 months for the MIS group and 34.5±18.9 months in the laparotomy group (p=0.01). In addition, 5-year survival probabilities were 38.3% (95% CI, 35.5–41.2%) and 34.8% (95% CI, 32.1–37.5%) in the MIS and laparotomy groups, respectively (p<0.01). Overall, patients in the MIS group had a 14% decreased hazard of all-cause mortality compared with patients in the laparotomy group (HR=0.86; 95% CI, 0.79–0.94). Within the propensity-matched cohort, 30- and 90-day mortality probabilities were 0.3% and 1.4%, respectively, in the MIS group, and 0.7% and 2.5%, respectively, in the laparotomy group (p=0.04 for 30-day mortality, p=0.01 for 90-day mortality).

3.3 Secondary outcomes analyses

Secondary outcomes of the propensity-matched cohort are listed in Table 4. Minimally invasive surgery was associated with a significantly shorter mean hospitalization duration (3.7 days vs 5.7 days, p<0.01). There was overall a significant difference in residual disease status, with a higher percentage of no residual disease among patients undergoing IDS via MIS than laparotomy (43.2% versus 38.6%, p<0.01), although documentation of residual disease was not available for 33.8% of cases (32.9% the MIS group and 34.7% in the laparotomy group). There was a lower percentage of additional cytoreductive procedures performed as part of the surgery in the MIS group than laparotomy group (59.3% vs 70.8%, p<0.01). Readmission rates were overall low, with a non-significant difference between the groups (unplanned readmission rates of 2.7% in the MIS group and 3.1% in the laparotomy group, p=0.39).

3.4 Sensitivity analyses

We performed a sensitivity analysis using only the cases that were initiated and completed minimally invasively (n=1,813), after excluding cases that were converted to laparotomy

(n=208). Propensity score matching was repeated, demonstrating 100% match rate for all 1,813 cases and balance between groups for each variable. Cox regression analysis demonstrated decreased hazard of all-cause mortality in the MIS group compared to laparotomy, consistent with results of the intention-to-treat analysis (HR=0.88 [95% CI 0.80–0.96] see Appendix B for further details). A second sensitivity analysis was performed using only those with high grade serous or endometrioid histologies (n=1,210) and found no difference in overall survival between the MIS and laparotomy groups (HR=0.94 [95% CI 0.84–1.05], see Appendix C for further details).

We calculated E-values to assess the sensitivity of our primary outcome finding to unmeasured confounding. For overall survival, the observed HR of 0.86 in favor of MIS, conditional on measured covariates, could be explained by an unmeasured confounder that was associated with both the surgical approach (MIS or laparotomy) and overall survival by a risk ratio (RR) of 1.45. To move the 95% CI to include the null, an unmeasured confounder associated with both surgical approach and overall survival by a RR of at least 1.25 was required. An unmeasured confounder would have to be associated with both surgical approach and survival by an RR of 2.96 to shift the HR to 2.0. This would reverse the finding in this study and conclude a clinically meaningful increase in HR of death for MIS compared to laparotomy.

4. Discussion

Among patients who receive NACT for advanced ovarian cancer, it may be possible to reduce morbidity by performing IDS using minimally invasive surgical techniques.[9,12,21–25] As NACT has become a more common approach in the upfront management of advanced epithelial ovarian cancer,[26,27] the use of minimally invasive techniques for IDS has also risen, accounting for 29% of all interval debulking surgeries in 2018 (see Appendix D for supplemental figure 1). In the present large national database study examining surgical approach after NACT, MIS was not associated with worse overall survival compared with laparotomy. This finding was robust to potential unmeasured confounders and remained significant in sensitivity analyses after excluding those requiring surgical conversions from MIS to laparotomy, and those with clear cell, mucinous, or “other” histologies.

Despite the increasing popularity of MIS for IDS, evidence reporting its oncologic safety and efficacy is limited. Among patients with ovarian cancer, resection to no residual disease is the goal of any debulking surgery. Critics of MIS in this setting state that abdominal exploration without tactile feedback may lead to higher rates of occult residual disease and that MIS may be associated with cancer spread or inability to fully debulk large volume disease.[28] Furthermore, studies of minimally invasive cancer surgery for other gynecological malignancies have yielded contradictory results. Among patients with early-stage endometrial cancer, MIS improves perioperative outcomes without impairing survival.[29,30] In contrast, among patients diagnosed with early-stage cervical cancer, minimally invasive radical hysterectomy, until recently a standard approach, has been found to be inferior to open radical hysterectomy.[31–34]

Notwithstanding these concerns, current National Comprehensive Cancer Network guidelines suggest that minimally invasive techniques may be used for IDS in "select patients."[35] It is unclear exactly who these "select" patients may be. This study found differences in likelihood of undergoing MIS by race/ethnicity, geography, comorbidity scores, and income, however, the study was not powered to address these disparities given the high percentage of non-Hispanic White patients (77%), those with comorbidity scores of 0 (79%), and relatively lower numbers of patients with annual household incomes below $50,000 or living in non-Metropolitan areas. It is more likely patient-specific factors outside of those reported here may play an important role in selection for MIS. Prior observational studies demonstrated a high rate of complete cytoreduction, good perioperative outcomes, and excellent progression-free survival among patients who underwent minimally invasive interval cytoreductive surgery after responding to NACT.[9,12,21–25] In these studies, researchers may have selected the most favorable patients for MIS, such as those with better responses to chemotherapy based on pre-operative findings, those with better performance statuses, or those with fewer comorbidities, than patients who underwent laparotomy. These factors can result in differences in the distribution of prognostic factors between patients who are treated with these two surgical approaches. In the present investigation, we used propensity score matching to adjust for many variables traditionally associated with treatment approach.

Although the extent of surgery was noted to be more extensive in the laparotomy group than in the MIS group, which may explain why there was increased residual disease in the former, these differences did not result in survival gains for laparotomy. Furthermore, we tested the robustness of the overall survival HR to potential unmeasured confounders, and we found that moderate unmeasured confounding would be required to fully explain away the significance of our primary outcome, and that moderate unmeasured confounding would be required to reverse the overall survival finding in this study.

A notable aspect of the retrospective nature of this study that must be addressed is the possibility of inadvertent selection bias, as the intent of each surgeon when selecting the surgical approach was unknown, the NACT regimen(s) and the patient-specific response to NACT were not available. The sensitivity analysis performed on cases that initiated and completed debulking by a minimally invasive approach was an attempt to remove the possibility of bias due to cases that were perhaps initiated laparoscopically with intent to either pursue laparotomy or abort the debulking procedure entirely. After removal of cases that were initiated via a MIS approach and converted to laparotomy, there was no change in overall survival outcomes, suggesting that surgical conversion did not adversely affect the results of the MIS cohort.

A strength of this study was the use of information from a large national database that reflects actual practice patterns for all settings in the United States where patients with ovarian cancer receive care. Nevertheless, it is important to note several limitations. Although the NCDB does not account for surgeon intent or chemotherapy response, we used clinical factors used to assess surgical fitness (age and comorbidities). The MIS group did not appear to be definitively more healthy and thus better surgical candidates than the laparotomy group based on available information, as the surgical approach did not differ

based on disease stage, and older patients were more likely to undergo MIS than younger ones. A lack of data regarding functional status and disease burden limited the ability to determine pre-surgical survival estimates for patients, and missing data regarding residual disease status may limit interpretation of this result. Additionally, mortality outcomes in the NCDB are not cancer-specific, and progression-free survival is not assessed in the NCDB, thus limiting the ability to interpret our findings. Use of propensity score matching enabled us to compare people diagnosed in similar years, thus minimizing the effect between groups of changes in therapy within the last decade owing to use of therapeutics such as bevacizumab or poly(ADP)-ribose polymerase) inhibitors. However, data on the specific chemotherapy regimens for each patient were not included in the dataset.

In conclusion, we found that MIS is not associated with higher mortality than laparotomy after NACT. Our findings were robust to large differences in potential unmeasured confounders. Although the data presented here is promising, it is unknown if minimally invasive interval cytoreductive surgery for advanced ovarian cancer delivers long-term oncologic outcomes similar to those achieved with laparotomy, and the role of MIS in this population remains controversial. The data presented in this study suggest MIS is increasingly utilized for IDS and clinicians and patients thus far have reasons to be optimistic about its use. Forthcoming data from a prospective, multicentric randomized trial (the LANCE Trial) may mitigate many of the limitations of this and prior retrospective studies.[36]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Minimally invasive interval debulking in advanced ovarian cancer is associated with similar survival to laparotomy.
- Minimally invasive interval debulking surgery is associated with improved morbidity compared to laparotomy.
- Use of minimally invasive surgery for interval debulking is gaining popularity but prospective data is missing.

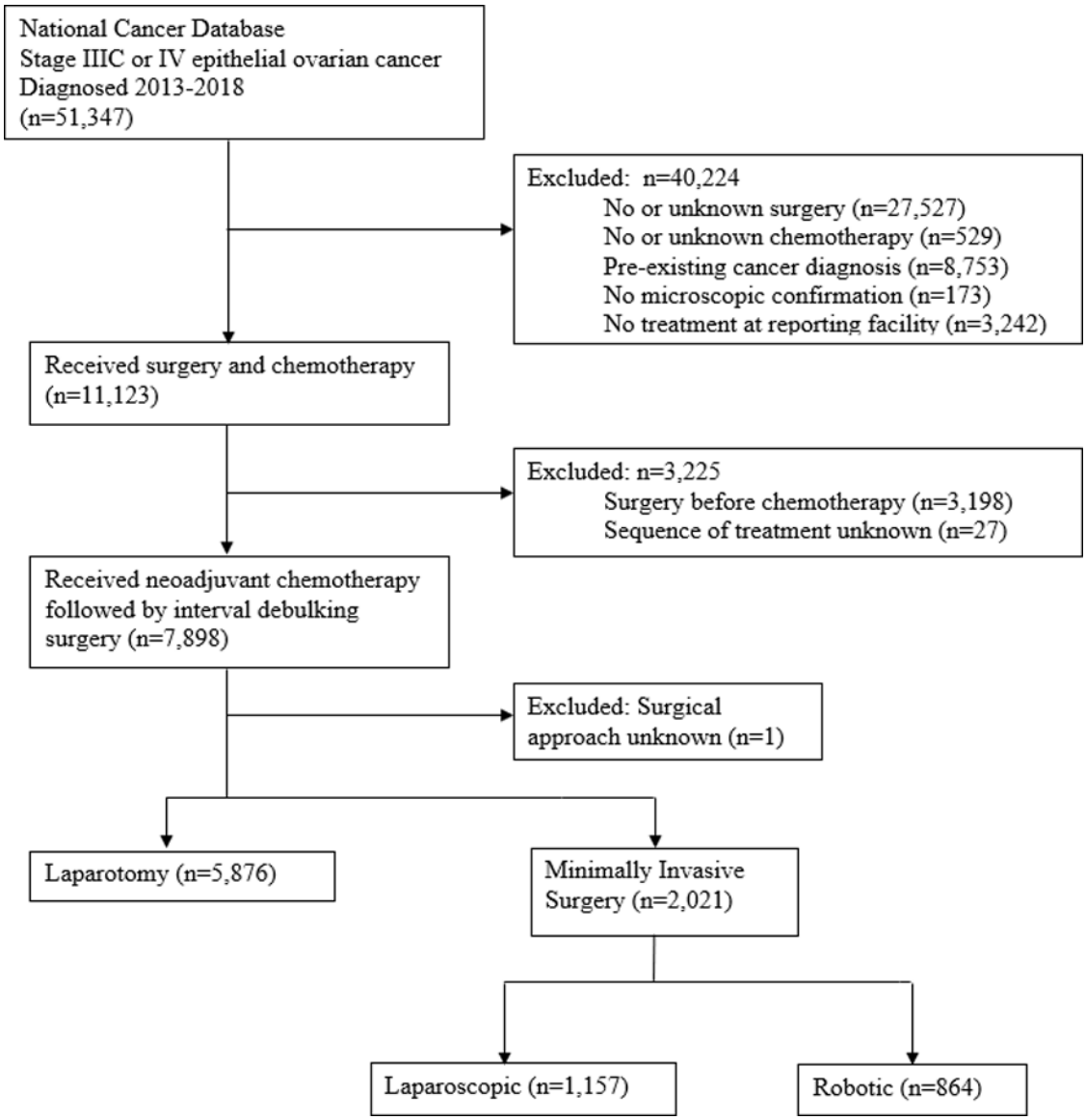

Figure 1:
Flow diagram for the selection of patients from the National Cancer Database.

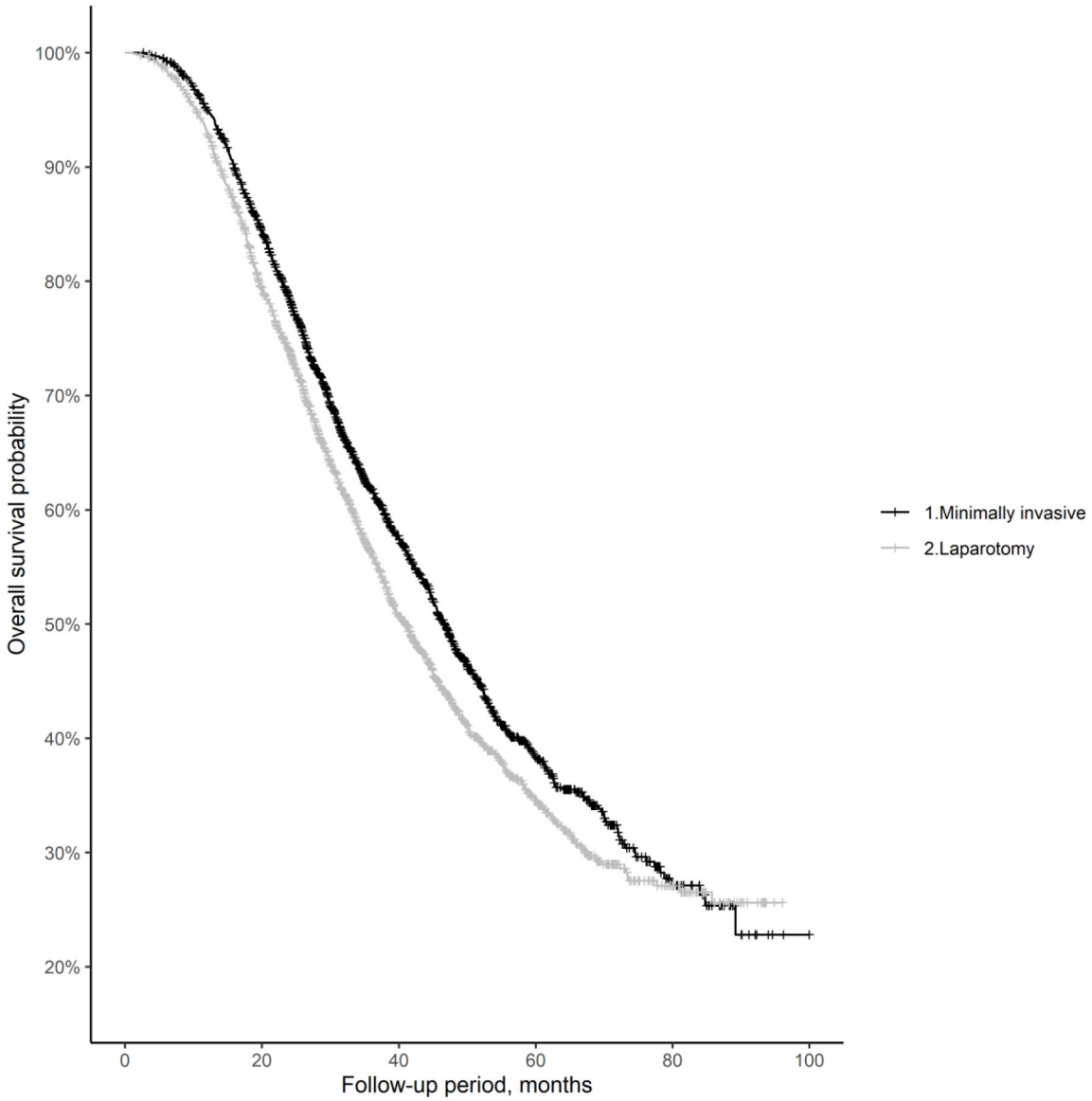

Figure 2:
Kaplan-Meier overall survival curves for the propensity-matched cohort.

Table 1

Epithelial ovarian cancer histology codes included in this analysis.

Histologic Type	ICD-O-3 Code
Serous carcinoma	8441, 8460–8463
Mucinous carcinoma	8470, 8471, 8480, 8481
Endometrioid Carcinoma	8380, 8381
Clear cell carcinoma	8310, 8313
Other adenocarcinoma	8050, 8140, 8144, 8255, 8260, 8263, 8290, 8320, 8323, 8340, 8440, 8450, 8490, 8560, 8574, 8940

Abbreviation: ICD-O-3, International Classification of Diseases for Oncology, Third Edition.

Table 2:

Patient demographic, clinical, and tumor characteristics before and after propensity score matching.

	Before propensity score matching			After propensity score matching		
	MIS	**Laparotomy**	**P value**	**MIS**	**Laparotomy**	**P value**
Variable	n=2021	n=5876		n=2021	n=2021	
Age at diagnosis, years (Mean, SD)	65.16 (10.60)	63.83 (10.53)	<.001	65.16 (10.60)	65.11 (10.25)	0.90
Race/Ethnicity (n, %)			0.22			0.94
American Indian	11 (0.5%)	19 (0.3%)		11 (0.5%)	10 (0.5%)	
Asian	92 (4.6%)	241 (4.1%)		92 (4.6%)	80 (4.0%)	
Hispanic	157 (7.8%)	390 (6.6%)		157 (7.8%)	153 (7.6%)	
Non-Hispanic Black	169 (8.4%)	510 (8.7%)		169 (8.4%)	178 (8.8%)	
Non-Hispanic White	1562 (77.3%)	4644 (79.0%)		1562 (77.3%)	1572 (77.8%)	
Unknown	30 (1.5%)	72 (1.2%)		30 (1.5%)	28 (1.4%)	
Charlson-Deyo comorbidity score (n, %)			0.03			0.98
0	1608 (79.6%)	4526 (77.0%)		1608 (79.6%)	1604 (79.4%)	
1	290 (14.3%)	1006 (17.1%)		290 (14.3%)	298 (14.7%)	
2	84 (4.2%)	243 (4.1%)		84 (4.2%)	82 (4.1%)	
3	39 (1.9%)	101 (1.7%)		39 (1.9%)	37 (1.8%)	
United States region (n, %)			<.001			1.0
New England	111 (5.5%)	286 (4.9%)		111 (5.5%)	108 (5.3%)	
Middle Atlantic	272 (13.5%)	1009 (17.2%)		272 (13.5%)	267 (13.2%)	
South Atlantic	482 (23.8%)	1053 (17.9%)		482 (23.8%)	500 (24.7%)	
East-North Central	276 (13.7%)	990 (16.8%)		276 (13.7%)	271 (13.4%)	
East-South Central	101 (5.0%)	440 (7.5%)		101 (5.0%)	98 (4.8%)	
West-North Central	142 (7.0%)	517 (8.8%)		142 (7.0%)	138 (6.8%)	
West-South Central	188 (9.3%)	617 (10.5%)		188 (9.3%)	190 (9.4%)	
Mountain	120 (5.9%)	194 (3.3%)		120 (5.9%)	116 (5.7%)	
Pacific	307 (15.2%)	682 (11.6%)		307 (15.2%)	307 (15.2%)	
Unknown	22 (1.1%)	88 (1.5%)		22 (1.1%)	26 (1.3%)	
Rural-Urban status (n, %)			<0.01			0.76
Metropolitan	1691 (83.7%)	4731 (80.5%)		1691 (83.7%)	1694 (83.8%)	
Urban	233 (11.5%)	738 (12.6%)		233 (11.5%)	224 (11.1%)	
Rural	29 (1.4%)	95 (1.6%)		29 (1.4%)	37 (1.8%)	
Unknown	68 (3.4%)	312 (5.3%)		68 (3.4%)	66 (3.3%)	
Annual median household income (n, %)			0.001			0.73
< $40,227	260 (12.9%)	855 (14.6%)		260 (12.9%)	243 (12.0%)	
$40,227-$50,353	353 (17.5%)	1005 (17.1%)		353 (17.5%)	345 (17.1%)	
$50,354-$63,332	440 (21.8%)	1145 (19.5%)		440 (21.8%)	457 (22.6%)	
≥$63333	704 (34.8%)	1927 (32.8%)		704 (34.8%)	690 (34.1%)	

	Before propensity score matching			After propensity score matching		
	MIS	**Laparotomy**	**P value**	**MIS**	**Laparotomy**	**P value**
Unknown	264 (13.1%)	944 (16.1%)		264 (13.1%)	286 (14.2%)	
Facility type (n, %)			<.001			0.93
Community cancer program	12 (0.6%)	53 (0.9%)		12 (0.6%)	13 (0.6%)	
Comprehensive community cancer program	733 (36.3%)	1547 (26.3%)		733 (36.3%)	751 (37.2%)	
Academic/research program	901 (44.6%)	2998 (51.0%)		901 (44.6%)	890 (44.0%)	
Integrated network	353 (17.5%)	1190 (20.3%)		353 (17.5%)	341 (16.9%)	
Unknown	22 (1.1%)	88 (1.5%)		22 (1.1%)	26 (1.3%)	
Insurance type (n, %)			<.001			0.92
Private	799 (39.5%)	2405 (40.9%)		799 (39.5%)	778 (38.5%)	
Medicaid and other government	130 (6.4%)	517 (8.8%)		130 (6.4%)	133 (6.6%)	
Medicare	1026 (50.8%)	2729 (46.4%)		1026 (50.8%)	1035 (51.2%)	
None	45 (2.2%)	173 (2.9%)		45 (2.2%)	50 (2.5%)	
Unknown	21 (1.0%)	52 (0.9%)		21 (1.0%)	25 (1.2%)	
State Medicaid expansion status (n, %)			<.001			0.85
Non-expansion	819 (40.5%)	2242 (38.2%)		819 (40.5%)	832 (41.2%)	
January 2014 expansion	534 (26.4%)	1732 (29.5%)		534 (26.4%)	544 (26.9%)	
Early expansion	425 (21.0%)	1042 (17.7%)		425 (21.0%)	416 (20.6%)	
Late expansion	221 (10.9%)	772 (13.1%)		221 (10.9%)	203 (10.0%)	
Not available	22 (1.1%)	88 (1.5%)		22 (1.1%)	26 (1.3%)	
Year of diagnosis (n, %)			<.001			0.82
2013	200 (9.9%)	785 (13.4%)		200 (9.9%)	202 (10.0%)	
2014	261 (12.9%)	827 (14.1%)		261 (12.9%)	285 (14.1%)	
2015	311 (15.4%)	982 (16.7%)		311 (15.4%)	324 (16.0%)	
2016	395 (19.5%)	1117 (19.0%)		395 (19.5%)	392 (19.4%)	
2017	418 (20.7%)	1097 (18.7%)		418 (20.7%)	394 (19.5%)	
2018	436 (21.6%)	1068 (18.2%)		436 (21.6%)	424 (21.0%)	
Histology (n, %)			0.10			0.90
Serous carcinoma	1786 (88.4%)	5195 (88.4%)		1786 (88.4%)	1779 (88.0%)	
Clear cell carcinoma	19 (0.9%)	96 (1.6%)		19 (0.9%)	24 (1.2%)	
Endometrioid carcinoma	16 (0.8%)	53 (0.9%)		16 (0.8%)	15 (0.7%)	
Mucinous carcinoma	6 (0.3%)	27 (0.5%)		6 (0.3%)	4 (0.2%)	
Other adenocarcinoma	194 (9.6%)	505 (8.6%)		194 (9.6%)	199 (9.8%)	
Cancer stage (n, %)			0.13			0.23
IIIC	993 (49.1%)	3001 (51.1%)		993 (49.1%)	955 (47.3%)	
IV	1028 (50.9%)	2875 (48.9%)		1028 (50.9%)	1066 (52.7%)	

Abbreviations: MIS, minimally invasive surgery; SD, standard deviation; n, number.

Table 3:

Multivariate analysis of independent predictors of the use of minimally invasive surgery for interval debulking surgery.

Demographic or clinical variable	OR (95%CI)*
Age, years (reference = 60–69)	
<50	0.92 (0.74–1.15)
50–59	1.00 (0.86–1.17)
70–79	1.14 (0.99–1.31)
≥80	1.59 (1.28–1.96)
Race and ethnicity (reference = non-Hispanic White)	
American Indian	1.80 (0.83–3.91)
Asian or Pacific Islander	1.20 (0.92–1.55)
Hispanic	1.26 (1.02–1.56)
Non-Hispanic Black	1.13 (0.93–1.38)
None of the above	1.28 (0.81–2.01)
Charlson-Deyo comorbidity score (reference = 0)	
1	0.80 (0.69–0.92)
2	0.92 (0.71–1.20)
3	0.96 (0.65–1.42)
United States region (reference = New England)	
Middle Atlantic	0.62 (0.48–0.82)
South Atlantic	1.01 (0.76–1.35)
East-North Central	0.73 (0.56–0.96)
East-South Central	0.55 (0.40–0.78)
West-North Central	0.64 (0.47–0.86)
West-South Central	0.66 (0.48–0.90)
Mountain	1.44 (1.03–2.01)
Pacific	0.88 (0.65–1.17)
Rural-urban status (reference = metropolitan)	
Urban	0.94 (0.79–1.12)
Rural	0.95 (0.62–1.47)
Unknown	0.69 (0.52–0.91)
Annual median household income (reference = <$40,227)	
$40,227-$50,353	1.15 (0.95–1.39)
$50,354-$63,332	1.22 (1.00–1.47)
≥$63,333	1.14 (0.95–1.38)
Unknown	0.90 (0.73–1.11)
Facility type (reference = community cancer program)	
Comprehensive community cancer program	2.40 (1.26–4.57)

Demographic or clinical variable	OR (95%CI)*
Academic or research program	1.62 (0.85–3.09)
Integrated network	1.48 (0.78–2.83)
Insurance type (reference = private)	
Medicaid or other government insurance	0.71 (0.57–0.89)
Medicare	1.01 (0.87–1.17)
Uninsured	0.80 (0.56–1.13)
Unknown	1.23 (0.72–2.09)
State Medicaid expansion status (reference = non-expansion)	
January 2014 expansion	0.92 (0.78–1.09)
Early expansion	1.08 (0.85–1.37)
Late expansion	0.93 (0.75–1.16)
Year of diagnosis (reference = 2013)	
2014	1.21 (0.98–1.50)
2015	1.25 (1.02–1.54)
2016	1.39 (1.14–1.69)
2017	1.49 (1.22–1.81)
2018	1.62 (1.33–1.97)
Histology (reference = serous carcinoma)	
Clear cell carcinoma	0.62 (0.37–1.02)
Endometrioid carcinoma	0.88 (0.48–1.63)
Mucinous carcinoma	0.63 (0.26–1.55)
Other adenocarcinoma	1.18 (0.98–1.41)
Stage (reference = stage IIIC)	
Stage IV	1.10 (0.99–1.22)

* An odds ratio (OR) >1 indicates an increased likelihood of IDS performed via MIS. OR<1 indicates an increased likelihood to have IDS performed via laparotomy.

Abbreviations: OR, odds ratio; CI, confidence interval.

Table 4:

Secondary surgical and clinical outcomes according to surgical approach in the propensity-matched cohort.*

Variable	Minimally Invasive	Laparotomy	p-value
Extent of surgery, n (%)			<0.01
Gynecologic ± omentectomy	817 (40.7)	588 (29.2)	
Additional cytoreductive procedures	1190 (59.3)	1428 (70.8)	
Residual disease, n (%)			0.01
No residual tumor	873 (43.2)	780 (38.6)	
Residual tumor	483 (23.9)	539 (26.7)	
Unknown	665 (32.9)	702 (34.7)	
30-Day mortality, n (%)	6 (0.3)	15 (0.7)	0.04
90-Day mortality, n (%)	28 (1.4)	50 (2.5)	0.01
Hospitalization duration, days (mean, SD)	3.7 (5.0)	5.7 (5.3)	<0.01
Readmission within 30 Days, n (%)			0.39
No readmission	1926 (95.3)	1927 (95.4)	
Unplanned readmission	55 (2.7)	63 (3.1)	
Planned readmission	33 (1.6)	22 (1.1)	
Unknown	7 (0.4)	9 (0.5)	
Overall survival, months (mean, SD)	35.9 (18.3)	34.5 (18.9)	0.01

* Percentages in the table may not equal 100% due to rounding.

Abbreviations: n, number; SD, standard deviation.