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Use and Outcomes of Minimally Invasive Hysterectomy for Women with Non-Endometrioid Endometrial Cancers

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Abstract

Background—Minimally invasive hysterectomy is now routinely used for women with uterine cancer. Most studies of minimally invasive surgery (MIS) for endometrial cancer have focused on low-risk, endometrioid tumors with few reports of the safety of the procedure for women with higher risk histologic subtypes.

Objective—To examine the utilization and survival associated with minimally invasive hysterectomy for women with uterine cancer and high-risk histologic subtypes.

Study Design—We used the National Cancer Database was used to identify women with stages I-III uterine cancer who underwent hysterectomy from 2010-2014. Women with serous, clear cell carcinomas and sarcomas were examined. Women who had laparoscopic or robotic-assisted hysterectomy were compared to those who underwent open abdominal hysterectomy. After a propensity score inverse probability of treatment weighted analysis, the effect of MIS hysterectomy on overall, 30-day, and 90-day mortality was examined for each histologic subtype of uterine cancer.

Results—Of 94,507 patients identified, 64,417 (68.2%) underwent minimally invasive hysterectomy. Among women with endometrioid tumors (n=81,115), 70.8% underwent MIS hysterectomy. The rates of MIS in those with non-endometrioid tumors (n=13,392) was 57.6% for serous carcinomas, 57.0% for clear cell tumors, 47.3% for sarcomas, 32.2% for leiomyosarcomas, 47.9% for stromal sarcomas and 48.5% for carcinosarcomas. Performance of MIS increased across

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all histologic subtypes between 2010 and 2014. For non-endometrioid subtypes, robotic-assisted procedures accounted for 47.9%-75.7% of MIS hysterectomies by 2014. In a multivariable model, women with non-endometrioid tumors were less likely to undergo MIS than those with endometrioid tumors ($P<0.05$). There was no association between route of surgery and 30-day, 90-day, or overall mortality for any of the non-endometrioid histologic subtypes.

Conclusions—The use of minimally invasive surgery is increasing rapidly for women with stage I-III non-endometrioid uterine tumors. Performance of minimally invasive surgery does not appear to adversely impact survival.

Condensation—The use of minimally invasive surgery for women with stage I-III non-endometrioid uterine tumors does not appear to adversely impact survival.

Keywords

Endometrial cancer; uterine cancer; hysterectomy; laparoscopic hysterectomy; robotic hysterectomy

Introduction

Minimally invasive hysterectomy has become the preferred surgical approach for the treatment of women with early-stage uterine cancer.¹⁻⁸ Compared to laparotomy, minimally invasive hysterectomy is associated with fewer complications, less postoperative pain and bleeding, and a shorter length of stay.^{4,9,10} From an oncologic standpoint, several randomized controlled trials and large observational studies have shown that long term outcomes and survival after minimally invasive hysterectomy are not inferior to abdominal hysterectomy.¹⁻³

Given the benefits of minimally invasive hysterectomy, the procedure has become the standard of care for endometrial cancer.¹⁻³ Use of minimally invasive hysterectomy for early-stage endometrial cancer has been proposed as a quality metric and population-based data have suggested that uptake of the procedure has been increasing rapidly.¹¹ However, despite these benefits, most studies of minimally invasive hysterectomy have focused on women with low-risk endometrial tumors. Patients with high-risk histologic subtypes have been excluded from many trials or represent only a small number of subjects in other studies.^{2,10}

Theoretically, performance of minimally invasive surgery in women with high-risk histologic subtypes has a number of concerns. These patients often have larger tumors and uteri and are at higher risk for dissemination beyond the uterus. As such, women with high-risk histologic subtypes may be at higher risk for port-site metastases and tumor spillage and dissemination due to uterine manipulation and vaginal removal of the uterus during the procedure. Given the limited data describing the safety of minimally invasive hysterectomy for women with uterine cancer and high-risk histologic subtypes, we performed a population-based analysis to examine the outcomes of the procedure in these women. Specifically, we examined trends the use of minimally invasive hysterectomy and compared survival between abdominal and minimally invasive hysterectomy in women with stage I-III non-endometrioid uterine cancers.

Methods

Data Source and Cohort Selection

The National Cancer Data Base (NCDB) was used for analysis. NCDB is a nationwide registry developed by the American College of Surgeons and American Cancer Society.^{12,13} The database records all patients with newly diagnosed invasive cancers from over 1500 Commission on Cancer (CoC) affiliated hospitals located throughout the United States. The NCDB catalogues data on patient demographic factors, tumor characteristics and treatment data, staging, and survival. Data are abstracted by trained registrars and is audited regularly to ensure accuracy. It is estimated that approximately 67% of women with invasive cancer in the U.S. are captured in the NCDB.¹⁴ The study was deemed exempt by the Institutional Review Board of Columbia University.

Women with stage I-III uterine cancer diagnosed from 2004-2014 were included. Only patients who underwent total hysterectomy and had a known route of hysterectomy were included in the analysis (Figure 1). The route of hysterectomy was classified as abdominal, laparoscopic, and robotic-assisted. Patients who underwent either a laparoscopic or robotic-assisted procedure were classified as having undergone minimally invasive surgery. The cohort was limited to those women with positive histologic confirmation of endometrioid, serous, clear cell, sarcoma, and leiomyosarcoma, stromal sarcoma, and carcinosarcoma. Women with sarcomas without further classification as leiomyosarcoma, carcinosarcoma or stromal sarcoma were categorized as a separate subgroup. Women who received radiation prior to surgery were excluded from the cohort.

Clinical Characteristics and Outcomes

Demographic data analyzed included age (<50, 50-59, 60-69, 70-79, 80 years), race (white, black, Hispanic, other or unknown), insurance status (private, Medicare, Medicaid, other government, other or unknown), education (percentage of adults in a patient's zip code that did not graduate high school: 29%, 20-28.9%, 14-19.9%, <14%, unavailable), and median household income within a patient's zip code (<\$30,000, \$30,000 - \$35,999, \$36,000 - \$45,999, \$46,000, not available). Comorbidity was measured using the Deyo classification of the Charlson comorbidity score (0, 1, 2).^{15,16}

Tumor stage (stages IA-IIIC), tumor grade (well, moderate, poorly differentiated, or unknown), and tumor size (0-20, 21-40, 41-60, 61-80, 81-100, >100 mm, or unknown) was also noted for each patient. Treatment characteristics including lymph node assessment (yes, no, unknown), use of chemotherapy (yes, no, unknown), and use of radiation (external beam with or without brachytherapy, brachytherapy, none) were recorded for each individual. Hospital characteristics were analyzed and categorized by regional location (Eastern, South, Midwest, West, unknown) and urban/rural location (metropolitan, urban, rural, unknown). Based on the ACS CoC criteria, hospitals were classified as academic/research cancer centers or community cancer centers.

The primary endpoint of the analysis was survival. Short term survival was estimated as 30 and 90-day survival. Overall survival was estimated as the time from diagnosis until death from any cause or the date of last follow-up.

Statistical Analysis

We stratified demographic and clinical characteristics of women with endometrial cancer by route of hysterectomy (abdominal vs. minimally invasive). Frequency distributions between categorical variables were compared using χ^2 tests. Multivariable log-linear regression models with Poisson distribution and log link based on a generalized estimating equation (GEE) were developed to estimate the association between each covariate and the use of minimally invasive surgery after accounting for hospital clustering. The results are reported as adjusted rate ratios (aRR) with 95% confidence intervals (CI).

A propensity score analysis was used to limit the influence of measured confounders on survival.^{17,18} The propensity score was estimated as the predicted probability that a patient underwent a minimally invasive hysterectomy. The inverse probability of treatment weighting (IPTW) approach based on propensity score was used to balance the observed confounders between treatments (abdominal vs. minimally invasive hysterectomy). To calculate the propensity score, we fit a logistic regression model that included all of the clinical, oncologic, and hospital characteristics and two-way interaction terms. The predicted probability (the propensity score) ranging from 0 to 1 was estimated for each patient. The weighting assumptions of the IPTW approach assigns patients who underwent the treatment of interest a weight of $1/\text{propensity score}$ and those who did not undergo the treatment of interest a weight of $1/(1-\text{propensity score})$. To standardize the variability of IPTW and reduce the influence of extreme weights, we applied a stabilization that multiplies the weights from treatment and comparison groups by a constant, and employed a trimming technique that trims the stabilized weights within a specified range (0.10).¹⁹

After IPTW, the balance of measured confounders between treatments was assessed via a weighted regression approach, in which each covariate was regressed on the treatment variable. The coefficients and corresponding P-values in the weighted regression models were used to determine the clinically unimportant differences between treatment groups using a threshold value of the coefficients of less than 0.2.²⁰ Separate propensity score models were developed for each histologic subtype using backward selection. Individual models for endometrioid cancer, serous carcinoma and carcinosarcoma included all the main effects and two-way interaction terms with a significance level of 0.2-0.1 to allow for model convergence. Given the smaller sample size of some of the histologic subtypes, models for clear cell carcinoma, sarcoma, leiomyosarcoma, and stromal sarcoma included all covariates without interaction terms. All propensity score models had acceptable model discrimination of C-statistics between 0.7 and 0.8 and provided good fit to the data based on Hosmer-Lemeshow goodness-of-fit tests.²¹

After propensity score weighting, we compared 30-day and 90-day mortality based on surgical approach by marginal log-linear regression models accounting for inverse probability weight and lymph nodes dissection as well as hospital clustering. Marginal multivariable Cox proportional-hazard models were developed to evaluate the effect of surgical approach on overall survival after. Along with performance of lymph nodes dissection, the use of chemotherapy and radiation were adjusted in the overall mortality model. Results from Cox proportional-hazard models were reported as adjusted hazards ratios with 95% confidence intervals. Kaplan-Meier curves were developed to assess

survival based on use of minimally invasive hysterectomy compared to laparotomy. Separate curves were developed for each histologic subtype in the IPTW cohorts. Results were compared using log rank tests. Sensitivity analyses were performed to examine survival separately for each stage (stages I, II, III). All analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina). All statistical tests were two-sided. A P-value of <0.05 was considered statistically significant.

Results

A total of 94,507 women including 64,417 (68.2%) who underwent minimally invasive hysterectomy and 30,090 (31.8%) who underwent abdominal hysterectomy were identified (Table 1). Among women with endometrioid tumors, 70.8% underwent minimally invasive hysterectomy. The rates of minimally invasive hysterectomy in those with non-endometrioid tumors was 57.6% for serous carcinomas, 57.0% for clear cell tumors, 47.3% for sarcomas, 32.2% for leiomyosarcomas, 47.9% for stromal sarcomas and 48.5% for carcinosarcomas (Table 1).

Performance of minimally invasive hysterectomy increased across all histologic subtypes between 2010 and 2014 (Figure 2). For endometrioid tumors, minimally invasive hysterectomy rose from 54.8% in 2010 to 78.4% in 2014. Comparatively, by 2014 minimally invasive hysterectomy increased to 64.9% of serous carcinoma, 64.5% of clear cell tumors, 51.3% of sarcomas, 32.4% of leiomyosarcomas, 51.1% of stromal sarcomas and 56.2% of carcinosarcomas.

Among women with endometrioid tumors who underwent a minimally invasive hysterectomy, robotic-assisted procedures accounted for 68.3% of the cases in 2010 and rose over time to 77.1% by 2014 (Figure 3). Except for leiomyosarcomas, similar trends were noted for the other non-endometrioid histologic subtypes with robotic-assisted procedures accounting for 61.7%-75.7% of the minimally invasive hysterectomies by 2014. For women with leiomyosarcomas, robotic-assistance was used in less than 50% of the minimally invasive cases during most of the years of the study.

In a multivariable model, compared to endometrioid histologies, patients with the other histologic subtypes were less likely to undergo minimally invasive hysterectomy ($P<0.0001$ for all) (Table 2). Patients with sarcoma and leiomyosarcoma histologies were least likely to undergo MIS, with rate ratios of 0.77 (95% CI, 0.71-0.84) and 0.64 (95% CI, 0.58-0.70), respectively. More recent year of diagnosis, older age, white race, and higher zip code income were associated with greater likelihood of minimally invasive hysterectomy ($P<0.05$ for all). In contrast, non-commercial insurance, greater comorbidity, treatment at a community cancer program, higher grade, more advanced size and larger tumor size were all associated with a lower likelihood of a minimally invasive procedure ($P<0.05$ for all). Increasing stage significantly decreased the likelihood for undergoing MIS; compared to stage IA patients, rate ratios for use of MIS decreased with increasing stage from 0.97 (95% CI, 0.95-0.98) for stage IB patients, to 0.88 (95% CI, 0.85-0.90) for stage II patients, to 0.85 (95% CI, 0.61-0.87) for stage III patients.

After propensity score weighting the cohort was well balanced (Table 2). The median follow-up time for patients with non-endometrioid tumors was 27.9 months (IQR, 17.4-41.5). For each of the non-endometrioid histologic subtypes, there was no statistically significant association between route of surgery and either 30 or 90-day mortality (Table 3). Similarly, there was no association between route of surgery and overall mortality for any of the non-endometrioid histologic subtypes. Similar findings were noted in a series of Kaplan-Meier analyses stratified by histology ($P>0.05$ for all). The results were unchanged in a series of sensitivity analyses stratified by stage.

Comment

These findings demonstrate that the use of minimally invasive hysterectomy has increased rapidly for non-endometrioid uterine cancers. In addition to oncologic characteristics, a number of non-clinical factors are associated with the performance of minimally invasive hysterectomy. Importantly, for all of the non-endometrioid histologic subtypes examined there was no association between the route of hysterectomy and survival.

Despite the fact that data supporting the efficacy of minimally invasive hysterectomy for women with non-endometrioid tumors is limited, our findings suggest that the procedure has already gained widespread acceptance among clinicians. By 2014, over 50% of the hysterectomies performed for all of the histologic subtypes we examined except leiomyosarcoma were performed via a minimally invasive surgical approach. While diffusion of laparoscopic hysterectomy which was first described in the 1990's was initially slow, use of the procedure has substantially since 2005.^{4,22} The widespread acceptance of minimally invasive hysterectomy for women with endometrioid tumors likely promoted the rise of the procedure for other histologic subtypes despite the relative lack of data.

Minimally invasive surgery for high-risk non-endometrioid histologic subtypes present the technical challenge of manipulating larger tumors with greater potential for metastatic spread. During the operation, increased intra-abdominal pressure from carbon dioxide is required to maintain the pneumoperitoneum, often for a prolonged period, and this pressure may increase the risk of abdominal wall metastases (so-called port-site metastases), which are estimated to occur in just over 1% of women who undergo gynecologic surgery.²³ Also during the procedure, uterine manipulation may disrupt the uterine cavity and subsequently disseminate tumor cells into the vagina or through the fallopian tube. Large uteri, often associated with high-risk histologies or more advanced disease, are particularly apt to result in tumor spillage during manipulation or removal through the vagina. This could affect both short and long-term oncologic outcomes

Prior studies examining the safety of minimally invasive hysterectomy for non-endometrioid tumors have included relatively small numbers of women.² The LAP2 trial included 492 women with non-endometrioid (clear cell, serous, sarcoma, and mixed) tumors. In sub-group analyses among women with non-endometrioid tumors, minimally invasive hysterectomy was found to be non-inferior to laparotomy in all of the subtypes analyzed.² In contrast, the LACE trial excluded women with non-endometrioid histologic variants.^{1,10} Our findings are reassuring in that we found no difference in survival between laparotomy and minimally

invasive hysterectomy in 30 or 90 day mortality or overall survival for women with serous and clear cell carcinoma, carcinosarcoma, and other uterine sarcomas.

Robotic-assisted hysterectomy is now the most common minimally invasive surgical modality used in women with non-endometrioid tumors. For serous tumors and carcinosarcomas, robotically assisted procedures made up three quarters of the minimally invasive operations in our cohort. Studies of women with endometrioid tumors have also demonstrated rapid uptake of robotic-assisted surgery.²⁴ Prior work has shown that outcomes are comparable between laparoscopic and robotic-assisted hysterectomy but that robotic-assisted surgery is substantially more costly.²⁴

Although our study benefits from the inclusion of a large sample of patients, we recognize a number of important limitations. First, while the findings of no difference in survival was encouraging, our cohort was diagnosed from 2010 to 2014 and we cannot exclude the small possibility of a survival differential with longer follow-up. Second, we lack data on some important clinical characteristics including uterine size, tumor spillage at the time of surgery and patterns of recurrence. Third, our data are based on tumor registry data and we lack centralized pathology review. As such, there may be misclassification of a small number of women, particularly for those with uncommon histologic variants. Although perioperative complication rates have been compared for minimally invasive and open hysterectomy in a number of studies, there are few large studies limited to non-endometrioid uterine cancer. While analyzing complication rates is of interest, NCDB lacks detailed data on perioperative complications. Lastly, NCDB lacks data on toxicity, quality of life, and patient reported outcomes. As with any study of administrative data, we cannot capture individual patient and physician preferences that undoubtedly influenced treatment decision-making. However, from a patient standpoint, these outcomes have an important impact on medical decision-making and preferences and warrant future study.

As minimally invasive hysterectomy continues to diffuse into wider practice, monitoring outcomes of less-selected patients in real-world settings remains a priority. While minimally invasive oncologic surgery has proven safe for a number of procedures, recent data for cervical cancer in which mortality was higher for minimally invasive surgery highlights the importance of determining the comparative effectiveness of new procedures prior to widespread dissemination.²⁵ Our data suggest that minimally invasive hysterectomy for women with stage I-III non-endometrioid uterine tumors does not adversely affect survival. Given the benefits of minimally invasive hysterectomy compared to laparotomy the procedure appears to be a reasonable approach to the surgical management of women with non-endometrioid uterine cancers.

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AJOG at a Glance

Why was this study conducted?

While minimally invasive surgery (MIS) is routinely used for women with uterine cancer, most studies have focused on low-risk, endometrioid tumors with few studies of women with higher risk histologic subtypes.

What are the key findings?

The rates of MIS in those with non-endometrioid tumors was 57.6% for serous carcinomas, 57.0% for clear cell tumors, 47.3% for sarcomas, 32.2% for leiomyosarcomas, 47.9% for stromal sarcomas and 48.5% for carcinosarcomas. There was no association between route of surgery and 30-day, 90-day, or overall mortality for any of the non-endometrioid histologic subtypes.

What does this study add to what is already known?

The use of minimally invasive surgery for women with stage I-III non-endometrioid uterine tumors does not appear to adversely impact survival.

Figure 1.
Study flow chart.

Figure 2A. Trends in use of minimally invasive surgery stratified by histologic subtype. 2B. Trends in use of robotic-assisted hysterectomy among women who underwent minimally invasive surgery.

Figure 3. Survival stratified by use of minimally invasive hysterectomy for each histologic subtype. A.

Table 1.

Demographic and clinical characteristics of women with uterine cancer stratified by route of surgery.

	Minimally Invasive Surgery	
	N (%)	Adjusted RR (95%CI)
	64,417 (68.2)	
<i>Histology</i>		
Endometrioid	57,436 (70.8)	Referent
Serous	3418 (57.6)	0.90 (0.87 - 0.93) **
Clear cell	692 (57.0)	0.89 (0.85 - 0.94) **
Sarcoma	260 (47.3)	0.77 (0.71 - 0.84) **
Leiomyosarcoma	287 (32.2)	0.64 (0.58 - 0.70) **
Stromal Sarcoma	388 (47.9)	0.81 (0.76 - 0.87) **
Carcinosarcoma	1936 (48.5)	0.83 (0.79 - 0.86) **
<i>Age (years)</i>		
<50	7254 (65.3)	Referent
50-59	19,125 (68.9)	1.02 (1.01 - 1.04) *
60-69	23,711 (69.2)	1.04 (1.02 - 1.05) **
70-79	10,701 (67.8)	1.04 (1.02 - 1.06) *
80	13,626 (65.1)	1.04 (1.01 - 1.07) *
<i>Race</i>		
White	51,409 (70.6)	Referent
Black	4794 (54.3)	0.86 (0.83 - 0.90) **
Hispanic	3607 (62.2)	0.95 (0.90 - 1.00)
Other	2625 (67.0)	0.96 (0.93 - 1.00) *
Unknown	1982 (62.2)	0.95 (0.87 - 1.03)
<i>Insurance Status</i>		
Private	34,536 (71.0)	Referent
Medicaid	2896 (57.8)	0.88 (0.85 - 0.91) **
Medicare	23,540 (67.5)	0.96 (0.95 - 0.98) **
Other Government	742 (73.2)	0.85 (0.80 - 0.91) **
Not Insured	2097 (55.7)	1.02 (0.98 - 1.06)
Unknown	606 (49.1)	0.73 (0.56 - 0.97) *
<i>Education of not receiving high school</i>		
29%	8889 (61.1)	Referent
20-28.9%	13,783 (67.1)	1.03 (1.01 - 1.07) *
14-19.9%	14,717 (67.5)	1.03 (0.99 - 1.07)
<14%	24,884 (71.9)	1.08 (1.04 - 1.12) *
Not Available	2144 (71.6)	0.99 (0.69 - 1.42)
<i>Median household Income</i>		

Minimally Invasive Surgery		
	N (%)	Adjusted RR (95%CI)
< \$30,000	6657 (60.3)	Referent
\$30,000 - \$35,999	10,020 (66.1)	1.04 (1.01 - 1.08) *
\$36,000 - \$45,999	17,275 (68.4)	1.06 (1.02 - 1.11) *
\$46,000	28,330 (70.6)	1.05 (1.00 - 1.11) *
Not Available	2135 (71.6)	1.15 (0.79 - 1.66)
<i>Urban/Rural</i>		
Metropolitan	51,625 (68.0)	Referent
Urban	9778 (68.2)	1.03 (1.00 - 1.07)
Rural	1227 (69.0)	1.06 (0.99 - 1.13)
Unknown	1787 (71.1)	1.01 (0.97 - 1.06)
<i>Comorbidity</i>		
0	47,721 (68.8)	Referent
1	13,726 (67.3)	0.99 (0.98 - 1.01)
2	2970 (63.0)	0.95 (0.92 - 0.98) *
<i>Year of diagnosis</i>		
2010	8768 (52.4)	Referent
2011	11,397 (63.7)	1.21 (1.18 - 1.25) **
2012	13,290 (70.4)	1.34 (1.29 - 1.39) **
2013	15,351 (75.6)	1.44 (1.38 - 1.50) **
2014	15,611 (75.5)	1.44 (1.38 - 1.50) **
<i>Stage</i>		
INOS	4042 (62.8)	0.93 (0.89 - 0.97) *
IA	41,293 (73.2)	Referent
IB	10,453 (66.4)	0.96 (0.94 - 0.97) **
II	2647 (56.2)	0.87 (0.85 - 0.89) **
III NOS	87 (43.5)	0.73 (0.61 - 0.88) *
IIIA	1609 (54.0)	0.84 (0.81 - 0.87) **
IIIB	468 (51.8)	0.86 (0.81 - 0.92) **
IIIC	3818 (53.7)	0.83 (0.81 - 0.86) **
<i>Grade</i>		
Well	27,223 (72.8)	Referent
Moderate	16,069 (68.3)	0.97 (0.95 - 0.99) *
Poorly	9556 (56.9)	0.92 (0.89 - 0.94) **
Unknown	11,569 (68.8)	0.98 (0.95 - 1.01)
<i>Tumor size</i>		
0-20mm	14,509 (73.5)	Referent
21-40mm	20,422 (72.7)	1.00 (0.99 - 1.01)
41-60mm	11,297 (66.8)	0.96 (0.94 - 0.98) **

	Minimally Invasive Surgery	
	N (%)	Adjusted RR (95%CI)
61-80mm	3976 (59.1)	0.89 (0.87 - 0.92) **
81-100mm	1354 (47.8)	0.76 (0.73 - 0.80) **
>100mm	872 (33.9)	0.59 (0.56 - 0.63) **
Unknown	11,987 (68.0)	0.97 (0.94 - 1.01)
<i>Facility location</i>		
Eastern	13,706 (68.4)	Referent
South	17,545 (71.0)	1.06 (0.98 - 1.15)
Midwest	20,154 (64.7)	0.96 (0.88 - 1.03)
West	11,159 (70.6)	1.03 (0.95 - 1.11)
Unknown	1853 (66.5)	1.06 (1.00 - 1.13)
<i>Facility type</i>		
Community	1591 (50.5)	0.76 (0.67 - 0.85) **
Comprehensive Community	25,371 (70.8)	1.03 (0.97 - 1.09)
Academic/Research Program	27,239 (66.4)	Referent
Integrated Network Cancer Program	8363 (71.1)	1.05 (0.96 - 1.15)
Unknown	1853 (66.5)	1.00 (0.99 - 1.03)

*
P<0.05;

**
P<0.0001.

INOS: stage I not otherwise specified.

Table 2.

Demographic and clinical characteristics of women with endometrial cancer stratified by MIS in unadjusted and IPTW adjusted cohort

	Unadjusted Cohort		<i>P-value</i>	IPTW Cohort		<i>P-value</i>
	Minimally invasive surgery			Minimally invasive surgery		
	Yes	No		Yes	No	
	(n=64,417)	(n=30,090)		(n=68,399)	(n=38,638)	
	N (%)	N (%)		N (%)	N (%)	
<i>Histology</i>			<0.0001			0.989
Endometrioid	57,436 (89.2)	23679 (78.7)		58687 (85.8)	33141 (85.8)	
Serous	3418 (5.3)	2519 (8.4)		4310 (6.3)	2425 (6.3)	
Clear cell	692 (1.1)	522 (1.7)		875 (1.3)	492 (1.3)	
Sarcoma	260 (0.4)	290 (1.0)		398 (0.6)	231 (0.6)	
Leiomyosarcoma	287 (0.4)	603 (2.0)		649 (0.9)	369 (1.0)	
Stromal Sarcoma	388 (0.6)	422 (1.4)		587 (0.9)	352 (0.9)	
Carcinosarcoma	1936 (3.0)	2055 (6.8)		2891 (4.2)	1628 (4.2)	
<i>Age (years)</i>			<0.0001			0.9874
<50	5401 (8.4)	2922 (9.7)		8061 (11.8)	4580 (11.9)	
50-59	19,125 (29.7)	8627 (28.7)		20055 (29.3)	11286 (29.2)	
60-69	23,711 (36.8)	10575 (35.1)		24793 (36.2)	13993 (36.2)	
70-79	10,701 (16.6)	5089 (16.9)		11432 (16.7)	6492 (16.8)	
80	3626 (5.6)	1943 (6.5)		4057 (5.9)	2287 (5.9)	
<i>Race</i>			<0.0001			0.8736
White	51,409 (79.8)	21371 (71)		52680 (77)	29681 (76.8)	
Black	4794 (7.4)	4029 (13.4)		6415 (9.4)	3645 (9.4)	
Hispanic	3607 (5.6)	2196 (7.3)		4176 (6.1)	2420 (6.3)	
Other	2625 (4.1)	1291 (4.3)		2833 (4.1)	1593 (4.1)	
Unknown	1982 (3.1)	1203 (4)		2295 (3.4)	1299 (3.4)	
<i>Insurance Status</i>			<0.0001			0.8148
Private	34,536 (53.6)	14085 (46.8)		2718 (4.0)	1530 (4.0)	
Medicaid	2896 (4.5)	2116 (7.0)		35204 (51.5)	19842 (51.4)	
Medicare	23,540 (36.5)	11323 (37.6)		3638 (5.3)	2064 (5.3)	
Other Government	742 (1.2)	271 (0.9)		25265 (36.9)	14275 (36.9)	
Not Insured	2097 (3.3)	1668 (5.5)		734 (1.1)	414 (1.1)	
Unknown	606 (0.9)	627 (2.1)		839 (1.2)	515 (1.3)	
<i>Education of not receiving high school</i>			<0.0001			0.9833
29%	8889 (13.8)	5653 (18.8)		10582 (15.5)	5975 (15.5)	
20-28.9%	13,783 (21.4)	6770 (22.5)		14851 (21.7)	8383 (21.7)	
14-19.9%	14,717 (22.8)	7072 (23.5)		15783 (23.1)	8960 (23.2)	
<14%	24,884 (38.6)	9745 (32.4)		25041 (36.6)	14094 (36.5)	
Not Available	2144 (3.3)	850 (2.8)		2142 (3.1)	1225 (3.2)	
<i>Median household Income</i>			<0.0001			

	Unadjusted Cohort			IPTW Cohort		
	Minimally invasive surgery		<i>P-value</i>	Minimally invasive surgery		<i>P-value</i>
	Yes	No		Yes	No	
	(n=64,417)	(n=30,090)		(n=68,399)	(n=38,638)	
	N (%)	N (%)		N (%)	N (%)	
< \$30,000	6657 (10.3)	4377 (14.5)		7983 (11.7)	4519 (11.7)	
\$30,000 - \$35,999	10,020 (15.6)	5131 (17.1)		10984 (16.1)	6152 (15.9)	
\$36,000 - \$45,999	17,275 (26.8)	7965 (26.5)		18313 (26.8)	10359 (26.8)	
\$46,000	28,330 (44)	11772 (39.1)		28983 (42.4)	16385 (42.4)	
Not Available	2135 (3.3)	845 (2.8)		2136 (3.1)	1223 (3.2)	
<i>Urban/Rural</i>			0.0101			0.9231
Metropolitan	51,625 (80.1)	24262 (80.6)		54919 (80.3)	31086 (80.5)	
Urban	9778 (15.2)	4551 (15.1)		10378 (15.2)	5802 (15)	
Rural	1227 (1.9)	551 (1.8)		1285 (1.9)	724 (1.9)	
Unknown	1787 (2.8)	726 (2.4)		1817 (2.7)	1026 (2.7)	
<i>Comorbidity</i>			<0.0001			0.9972
0	47,721 (74.1)	21671 (72)		50197 (73.4)	28363 (73.4)	
1	13,726 (21.3)	6678 (22.2)		14779 (21.6)	8346 (21.6)	
2	2970 (4.6)	1741 (5.8)		3423 (5.0)	1930 (5.0)	
<i>Year of diagnosis</i>			<0.0001			0.9592
2010	7254 (11.3)	3856 (12.8)		12147 (17.8)	6855 (17.7)	
2011	11,397 (17.7)	6501 (21.6)		12931 (18.9)	7299 (18.9)	
2012	13,290 (20.6)	5598 (18.6)		13643 (19.9)	7780 (20.1)	
2013	15,351 (23.8)	4957 (16.5)		14720 (21.5)	8270 (21.4)	
2014	15,611 (24.2)	5074 (16.9)		14957 (21.9)	8434 (21.8)	
<i>Stage</i>			<0.0001			0.8183
INOS	4042 (6.3)	2399 (8)		4633 (6.8)	2643 (6.8)	
IA	41,293 (64.1)	15127 (50.3)		40830 (59.7)	23040 (59.6)	
IB	10,453 (16.2)	5294 (17.6)		11410 (16.7)	6428 (16.6)	
II	2647 (4.1)	2059 (6.8)		3424 (5)	1916 (5)	
III NOS	87 (0.1)	113 (0.4)		121 (0.2)	88 (0.2)	
IIIA	1609 (2.5)	1372 (4.6)		2147 (3.1)	1217 (3.2)	
IIIB	468 (0.7)	436 (1.4)		647 (0.9)	374 (1)	
IIIC	3818 (5.9)	3290 (10.9)		5186 (7.6)	2931 (7.6)	
<i>Grade</i>			<0.0001			0.9433
Well	27,223 (42.3)	10166 (33.8)		27078 (39.6)	15263 (39.5)	
Moderate	16,069 (24.9)	7450 (24.8)		16958 (24.8)	9601 (24.8)	
Poorly	9556 (14.8)	7232 (24.0)		12215 (17.9)	6866 (17.8)	
Unknown	11,569 (18)	5242 (17.4)		12148 (17.8)	6909 (17.9)	
<i>Tumor size</i>			<0.0001			0.9985
0-20mm	14,509 (22.5)	5228 (17.4)		14283 (20.9)	8021 (20.8)	
21-40mm	20,422 (31.7)	7688 (25.6)		20332 (29.7)	11464 (29.7)	
41-60mm	11297 (17.5)	5606 (18.6)		12242 (17.9)	6955 (18.0)	

	Unadjusted Cohort			IPTW Cohort		
	Minimally invasive surgery		<i>P-value</i>	Minimally invasive surgery		<i>P-value</i>
	Yes	No		Yes	No	
	(n=64,417)	(n=30,090)		(n=68,399)	(n=38,638)	
	N (%)	N (%)		N (%)	N (%)	
61-80mm	3976 (6.2)	2754 (9.2)		4879 (7.1)	2773 (7.2)	
81-100mm	1354 (2.1)	1481 (4.9)		2072 (3)	1173 (3)	
>100mm	872 (1.4)	1701 (5.7)		1858 (2.7)	1055 (2.7)	
Unknown	11,987 (18.6)	5632 (18.7)		12732 (18.6)	7198 (18.6)	
<i>Facility location</i>			<0.0001			0.9504
Eastern	13,706 (21.3)	6328 (21)		14557 (21.3)	8149 (21.1)	
South	17,545 (27.2)	7182 (23.9)		17917 (26.2)	10134 (26.2)	
Midwest	20,154 (31.3)	10995 (36.5)		22447 (32.8)	12709 (32.9)	
West	11,159 (17.3)	4651 (15.5)		11471 (16.8)	6492 (16.8)	
Unknown	1853 (2.9)	934 (3.1)		2007 (2.9)	1154 (3)	
<i>Facility type</i>			<0.0001			0.9886
Community	1591 (2.5)	1557 (5.2)		2289 (3.3)	1284 (3.3)	
Comprehensive Community	25,371 (39.4)	10443 (34.7)		25950 (37.9)	14642 (37.9)	
Academic/Research Program	27,239 (42.3)	13760 (45.7)		29632 (43.3)	16727 (43.3)	
Integrated Network Cancer Program	8363 (13)	3396 (11.3)		8520 (12.5)	4831 (12.5)	
Unknown	1853 (2.9)	934 (3.1)		2007 (2.9)	1154 (3)	

IPTW: inverse probability of treatment weighed. NOS: stage not otherwise specified.

Table 3.

Comparison of overall mortality and mortality within 30 or 90 days of surgery between treatment.

	Serous	Carcinosarcoma	Clear Cell	Leiomyosarcoma	Stromal Sarcoma	Sarcoma
30-day mortality						
Abdominal (%)	0.8	1.8	1.4	0.4	0.9	2.2
Minimally invasive (%)	0.3	0.6	0.0	0.5	0.0	0.0
aRR (95% CI) ^Δ	0.63 (0.24 - 1.63)	0.51 (0.22 - 1.17)	NA	0.96 (0.09 - 10.57)	NA	NA
90-day mortality						
Abdominal (%)	1.7	4.4	2.6	2.5	4.3	5.8
Minimally invasive (%)	1.0	2.8	0.0	0.9	1.7	0.0
aRR (95% CI) ^Δ	0.83 (0.47 - 1.45)	1.00 (0.63 - 1.59)	NA	0.33 (0.07 - 1.50)	0.98 (0.31 - 3.12)	NA
Overall mortality						
Abdominal (%)	27.8	42.6	27.8	40.4	25.2	29.6
Minimally invasive (%)	21.6	34.4	21.3	25.5	14.2	17.0
aHR (95% CI) ^{ΔΔ}	1.09 (0.95 - 1.24)	1.07 (0.93 - 1.23)	1.11 (0.82 - 1.51)	0.77 (0.54 - 1.08)	1.00 (0.67 - 1.50)	0.80 (0.48 - 1.33)

* P<0.05;

** P<0.0001.

^Δ Adjusted for lymphadenectomy in IPTW log linear model.

^{ΔΔ} Adjusted lymphadenectomy, radiation and chemotherapy in IPTW marginal multivariable Cox proportional hazard model.