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Patterns of utilization and outcome of ovarian conservation for young women with minimal-risk endometrial cancer☆,☆☆

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HIGHLIGHTS

- Patterns and outcomes of ovarian conservation for young women with minimum-risk endometrial cancer were examined.
- There is substantial variability in the utilization of ovarian conservation, exhibiting ~50% of inter-group difference.
- Patient, surgical, and hospital factors attribute to utilization of ovarian conservation.
- Ovarian conservation may be associated with decreased length of stay after hysterectomy.

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ABSTRACT

Objective. To profile patient characteristics associated with and outcomes of ovarian conservation at the time of hysterectomy in young women with minimal-risk endometrial cancer.

Methods. A population-based retrospective analysis of the Nationwide Inpatient Sample between 2007 and 2015 was performed. Women aged <50 with minimal-risk endometrial cancer who had ovarian conservation ($n = 2314$) were compared to those who had oophorectomy ($n = 8191$). A classification-tree model with recursive partitioning analysis was constructed to examine patterns of ovarian conservation. Propensity score matching was performed and length of stay and perioperative complications were compared. Two validation cohorts were also analyzed in a similar fashion (benign gynecologic disease and cervical cancer).

Results. There were nine distinct patterns of patient characteristics identified, and ovarian conservation rates ranged from 11.7% (women aged 40–49 who underwent abdominal hysterectomy at an urban teaching hospital) to 60.5% (non-obese women aged <40 with median household income ≥$63,000) (absolute difference, 48.8%, 95% confidence interval 39.9–57.7; $P < 0.001$). After propensity score matching, ovarian conservation was significantly associated with a decreased likelihood of hospitalization >2 days (relative risk reduction, 16.7%, $P < 0.001$). Rates of surgical complications were not different between the two groups (8.2% *versus* 8.3%, $P = 0.91$). In the benign gynecologic disease and cervical cancer cohorts, ovarian conservation was also associated with decreased length of hospitalization (all, $P < 0.05$).

Conclusion. There is substantial variability in the utilization of ovarian conservation in young women with minimal-risk endometrial cancer based on patient, surgical, and hospital factors. Our study suggests that guidelines for ovarian conservation in this population would be helpful for improving patient selection and rates of ovarian conservation.

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1. Introduction

Endometrial cancer is the most common gynecologic cancer in the United States, and its incidence continues to rise [1]. About 15% of endometrial cancers are diagnosed in women before the age of 50 and 5% before the age of 40 [2,3]. These tumors generally present at early stage and have excellent oncologic outcomes with surgical treatment alone. Conventional, standard treatment for endometrial cancer includes oophorectomy at the time of hysterectomy to obviate the risk of potential metastatic disease to the ovary, detect synchronous occult ovarian malignancy, prevent possible metachronous ovarian malignancy, and decrease estrogenic stimulation of possible residual or recurrent disease [4–7]. However, treatment of endometrial cancer in young premenopausal women poses unique considerations due to the immediate and long-term sequelae of surgical menopause and estrogen deprivation.

Ovarian conservation has been shown to be safe in patients with early-stage, low-grade endometrial cancer, without impact on cancer-related mortality [6–12]. Recent studies have also reported improved long-term overall survival in young women who undergo ovarian conservation as opposed to oophorectomy at the time of surgery, posited to be secondary to cardiovascular protection from ovarian hormones; however, data evaluating the short-term or immediate postoperative outcomes of ovarian conservation in this setting are lacking [13–17].

Additionally, despite the recent data demonstrating the safety of ovarian conservation, it is estimated that ovarian conservation is rarely utilized even in young women with early-stage low-grade endometrial cancer, and there are currently no published guidelines for ovarian conservation or recommendations for surveillance in women who have had ovarian conservation [6–9]. The objective of this study was to profile patient characteristics and patterns associated with ovarian conservation in young women with minimal-risk endometrial cancer as well as to assess the short-term, perioperative outcomes following ovarian conservation.

2. Materials and methods

2.1. Data source

A population-based retrospective analysis of patients with a diagnosis of endometrial cancer was performed using hospital discharge data from the Nationwide Inpatient Sample. This database is a publically available and deidentified database that is distributed as part of the Healthcare Cost and Utilization Project by the Agency for Healthcare Research and Quality [18]. It provides demographic, clinical, and resource-use information for >36 million hospitalizations per year when weighted, representing >90% of the United States population [18].

2.2. Sample selection

Women aged <50 years with minimal-risk (presumed early-stage and low-grade) endometrial cancer who underwent primary hysterectomy between January 2007 and September 2015 were eligible for the study. Diagnosis and procedure codes as specified by the International Classification of Disease 9th revision were utilized to select the cohort for analysis [19].

As the Nationwide Inpatient Sample database does not have information regarding tumor characteristics such as cancer stage, tumor grade, or histologic type, identifying the subpopulation of patients with minimal-risk endometrial cancer was performed by rigorous exclusion of those with advanced-stage or high-grade disease *via* surrogate markers. Patients with any type of metastatic disease or nodal disease as well as those who received radical hysterectomy, lymphadenectomy, chemotherapy, or radiotherapy were excluded from all analyses. In addition, those with other types of malignancy were excluded. Details of the coding used are listed in Supplemental Table S1.

The study starting point of 2007 was chosen because it was a pivotal year in trends of lymphadenectomy performance [20]. A recent study reported that prior to 2007, routine lymph node dissection was performed in the vast majority of women with endometrial cancer, even in those with early-stage low-grade disease. However, performance of lymphadenectomy declined consistently after 2007 with the emergence of new data suggesting that it may be unnecessary in low-risk populations [20,21]. Limiting our study population to cases in which lymphadenectomy was not performed after 2007 more accurately delineated the study population to those with only minimal-risk disease. The study conclusion date of September 2015 was chosen based on the shift from International Classification of Disease 9th revision to 10th revision.

2.3. Clinical information

Among eligible cases, the following information was abstracted from the database: patient baseline demographics, hospital information, operative details, and outcomes of the index admission. Patient demographics included age, race/ethnicity, medical comorbidities, primary expected payer, and median household income. Charlson comorbidity index was calculated for each patient based on the codes for the specified medical conditions in each category and weighted appropriately to calculate a final score (Table S1) [22]. Hospital data included year of hospitalization, hospital region, hospital size, and teaching status. Operative details included route of hysterectomy (abdominal *versus* minimally-invasive) and oophorectomy status. The outcomes selected for analysis were length of hospital stay and perioperative complications during the index admission.

2.4. Study definition

Patients were grouped based on performance of oophorectomy; those who did not undergo oophorectomy at the time of surgery were classified as having received ovarian conservation. The codes for performance of oophorectomy, either for bilateral salpingo-oophorectomy or removal of a remaining ovary in a case where an ovary may have been previously removed, were used to define the oophorectomy group (Table S1).

Perioperative complications were defined as the presence of any of the following in the index admission for hysterectomy: urinary tract injury, intestinal injury, vascular injury, hemorrhage, postoperative shock, wound complications, thromboembolism, cerebrovascular disease or stroke, myocardial infarction, pneumonia, respiratory failure, systemic inflammatory response syndrome or sepsis, ileus or small bowel obstruction, and/or acute kidney injury (Table S1). The database captions complications including intraoperative complications and postoperative complications until hospital discharge.

2.5. Validation cohorts

As an internal validation of our study cohort among the same database, we analyzed two other cohorts of patients undergoing hysterectomy with or without ovarian conservation. The first cohort consisted of women <50 years of age who underwent hysterectomy for benign gynecologic disease, including leiomyoma uteri or adenomyosis, between January 2001 and September 2015 (Table S2). Patients with any malignancy or adnexal pathology were excluded. The second validation cohort consisted of women <50 years of age with cervical cancer who underwent hysterectomy. In both cohorts, exclusion criteria also included performance of radical hysterectomy and/or lymphadenectomy as well as history of radiotherapy and/or chemotherapy (Table S3).

2.6. Study aims

The primary objective of analysis was to examine patterns of ovarian conservation at the time of hysterectomy in young women with minimal-risk endometrial cancer. The secondary objectives were to examine length of hospital stay and perioperative complications during the index admission at the time of hysterectomy, stratified by ovarian conservation. These outcomes were also examined in the same manner in the two validation cohorts.

2.7. Statistical methods

Differences in continuous and categorical variables between the two groups were assessed with the Mann-Whitney *U* test and chi-square test, respectively. A binary logistic regression model was used for multivariable analysis to determine the independent contributing factors for ovarian conservation. All the collected variables for patient demographics, hospital information, and surgical performance were entered in the final model. Magnitude of statistical significance was expressed with odds ratios (OR) and 95% confidence intervals (CI). The ratio of events of interest per the entered variables were assessed for over-fitting (cutoff level < 10) [23]. The variance inflation factor was determined among covariates in multivariable analysis, and a value of ≥2.0 was interpreted as multicollinearity in this study [24].

In an attempt to examine patterns of utilization for ovarian conservation in young women with minimal-risk endometrial cancer, a recursive partitioning analysis was performed to construct a classification-tree model for ovarian conservation utilization [25]. All independent covariates for ovarian conservation on multivariable analysis were entered in the final analysis, and the chi-square automatic interaction detector method was used to create the classification-tree model. Frequencies of ovarian conservation were examined among the determined nodes in this analysis.

As patient demographics were substantially different between the oophorectomy and ovarian conservation groups, propensity score matching was performed to adjust for these background differences [26]. Unweighted cases were matched according to age, year of hysterectomy, race/ethnicity, income, primary payer, hospital type, Charlson comorbidity index, obesity, and hysterectomy approach. The propensity score for ovarian conservation was computed by multivariable logistic regression analysis, and all the aforementioned covariates were entered in the propensity score model.

An automated algorithm was used for 1-to-1 propensity score matching between the ovarian conservation and oophorectomy groups, with a greedy matching method using a propensity score radius difference of 0.01 [27]. In the post-matching assessment, standardized difference was examined to determine frequency distributions between the two groups, and a value ≤0.10 was considered to indicate good balance. All subsequent analyses were then performed using propensity score matched cases with appropriate weighting.

The Joinpoint Regression Program (version 4.4.0.0), which is provided by the National Cancer Institute, was utilized to evaluate temporal trends in ovarian conservation [28]. Time point data was examined biannually or every year of age to identify temporal changes as previously described [20]. Temporal trend was examined using the linear segmented regression test, and log-transformation was performed to determine the annual percent change with a 95% CI.

All statistical analyses were based on two-tailed hypotheses, and a $P < 0.05$ was considered statistical significant. Statistical Package for Social Sciences (IBM SPSS, version 24.0, Armonk, NY) was used for the analysis. The STROBE guidelines were consulted for the performance of this observational cohort study [29].

3. Results

The patient selection schema is shown in Fig. S1. There were 400,336 women with a diagnosis of endometrial cancer during the study period, 45,162 (11.3%) of whom were <50 years of age. After excluding patients with surrogate codes for advanced-stage or high-grade disease, there were 10,505 women who met the inclusion criteria with minimal-risk endometrial cancer and who underwent hysterectomy during their hospital admission. Of these women, 2314 (22.0%, 95% CI 21.2–22.8) women had ovarian conservation and 8191 (78.0%) women underwent oophorectomy.

The age-specific trend of ovarian conservation was examined (Fig. 1). Ovarian conservation rate decreased between age 25 and 49 years old from 74.1% to 9.5% (87.2% relative decrease, $P < 0.01$), and the decrease in the ovarian conservation rate accelerated after 44 years old (annual percent change −15.5 *versus* −4.6 between 25 and 44).

On univariable analysis (Table 1), age, race/ethnicity, obesity, extent of medical comorbidity, household income, primary expected payer, hospital size, hospital teaching status, hospital region, and hysterectomy mode were all statistically significantly different in the ovarian conservation and oophorectomy groups (all, $P < 0.001$). On multivariable analysis (Table 2), younger age, non-obese body habitus, private insurance including HMO, lower household income, medium size hospital, rural hospital setting, hospital location in the Northeast, and minimally-invasive hysterectomy approach were all independently associated with ovarian conservation (all, $P < 0.05$). In contrast, greater medical comorbidity was significantly associated with decreased utilization of ovarian conservation ($P = 0.001$). Annual rates of ovarian conservation did not change significantly over time in this study population ($P = 0.27$).

Patterns of ovarian conservation were examined (Fig. 2 and Table 3). A classification-tree model analysis identified nine distinct patterns of ovarian conservation utilization based on patient, surgical, and hospital factors. In this model, age was the strongest factor that predicted ovarian conservation, followed by body habitus, hospital teaching status, hysterectomy approach, and household income (Fig. 2; all, $P < 0.001$). The group with the highest rates of ovarian conservation (60.5%, 95% CI 51.7–69.3) was non-obese women <40 years of age with a household income of ≥$63,000, representing 1.1% of the study population. The group with the lowest rates of ovarian conservation, representing

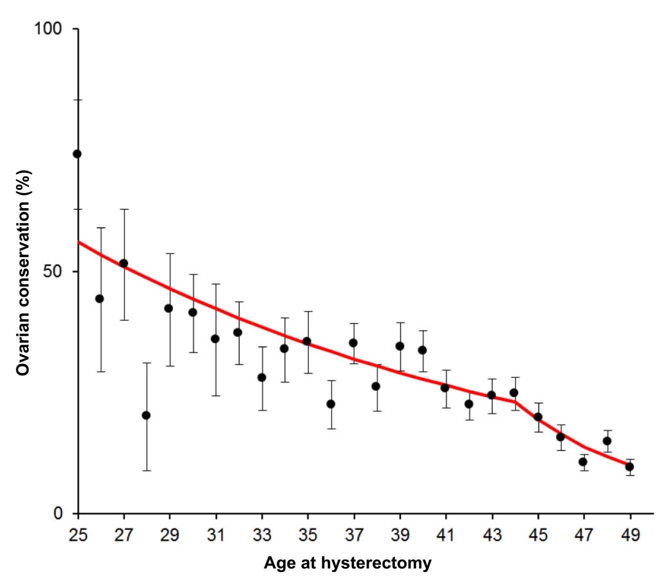

Fig. 1. Age-specific trend of ovarian conservation. Utilization of ovarian conservation at hyserotomy was examined. Annual percent change was −4.6 (95% confidence interval −6.2 to −2.9, $P < 0.001$) between 25 and 44 years old and −15.5 (95% confidence interval −24.8 to −5.0, $P = 0.007$) between age 44 and 49.

Table 1
Patient demographics before propensity score matching (endometrial cancer cohort).

Characteristics	Oophorectomy	Ovarian conservation	*P*-value
Number	*n* = 8191	*n* = 2314	
Age (years)	43.2 (±5.3)	40.2 (±6.2)	<**0.001**
<40	1816 (22.2%)	935 (40.4%)	
≥40	6375 (77.8%)	1379 (59.6%)	
Year			0.34[a]
2007	1207 (14.7%)	400 (17.3%)	
2008	1079 (13.2%)	324 (14.0%)	
2009	1128 (13.8%)	285 (12.3%)	
2010	979 (12.0%)	317 (13.7%)	
2011	918 (11.2%)	297 (12.8%)	
2012	1005 (12.3%)	195 (8.4%)	
2013	755 (9.2%)	240 (10.4%)	
2014	690 (8.4%)	170 (7.3%)	
2015	430 (5.2%)	85 (3.7%)	
Race/ethnicity			**0.001**
White	4347 (53.1%)	1199 (51.8%)	
Black	657 (8.0%)	165 (7.1%)	
Hispanic	1323 (16.2%)	432 (18.7%)	
Asian or Pacific Islander	399 (4.9%)	94 (4.1%)	
Native American	96 (1.2%)	43 (1.9%)	
Other	221 (2.7%)	44 (1.9%)	
Missing	1147 (14.0%)	336 (14.5%)	
Obesity			<**0.001**
No	4550 (55.5%)	1571 (67.9%)	
Yes	3641 (44.5%)	743 (32.1%)	
Charlson Index			<**0.001**
0	5171 (63.1%)	1611 (69.6%)	
1	2197 (26.8%)	585 (25.3%)	
2	517 (6.3%)	77 (3.3%)	
3	203 (2.5%)	35 (1.5%)	
≥4	103 (1.3%)	[b]	
Median household income			<**0.001**
$1–$38,999	1018 (12.4%)	320 (13.8%)	
$39,000–$47,999	929 (11.3%)	205 (8.9%)	
$48,000–$62,999	959 (11.7%)	191 (8.3%)	
≥$63,000	777 (9.5%)	236 (10.2%)	
Missing	4508 (55.0%)	1361 (58.8%)	
Primary expected payer			<**0.001**
Medicare	615 (7.5%)	113 (4.9%)	
Medicaid	1188 (14.5%)	333 (14.4%)	
Private including HMO	5367 (65.5%)	1579 (68.3%)	
Self-pay	554 (6.8%)	150 (6.5%)	
No charge	82 (1.0%)	57 (2.5%)	
Other	346 (4.2%)	81 (3.5%)	
Missing	39 (0.5%)	[b]	
Hospital bed size			<**0.001**
Small	722 (8.8%)	168 (7.3%)	
Medium	1735 (21.2%)	580 (25.1%)	
Large	5632 (68.8%)	1554 (67.2%)	
Missing	102 (1.2%)	11 (0.5%)	
Hospital teaching status			<**0.001**
Rural	466 (5.7%)	193 (8.3%)	
Urban non-teaching	1935 (23.6%)	709 (30.6%)	
Urban teaching	5689 (69.4)	1402 (60.6%)	
Missing	102 (1.2%)	11 (0.5%)	
Hospital region			<**0.001**
Northeast	1661 (20.3%)	532 (23.0%)	
Midwest	1816 (22.2%)	413 (17.8%)	
South	2644 (32.3%)	736 (31.8%)	
West	2070 (25.3%)	634 (27.4%)	
Hysterectomy approach			<**0.001**
Abdominal	5331 (65.1%)	1258 (54.4%)	
Minimally invasive	2827 (34.5%)	1056 (45.6%)	
Missing	34 (0.4%)	[b]	

Chi-square test or Student *t*-test for *P*-values. Significant *P*-values are emboldened.
[a] Joinpoint regression model for temporal trend analysis (examined every six month time period).
[b] Indicated number of ≤10, required to suppress per the Healthcare Cost and Utilization Project.

Table 2
Multivariable analysis for ovarian conservation (endometrial cancer cohort).

Characteristics	Adjusted-OR (95% CI)	*P*-value
Age (years)	0.91 (0.90–0.91)	<**0.001**
Race/ethnicity		**0.002**
White	1	
Black	1.07 (0.88–1.31)	0.50
Hispanic	0.99 (0.86–1.15)	0.93
Asian or Pacific Islander	0.82 (0.64–1.05)	0.11
Native American	1.97 (1.26–3.07)	**0.003**
Other	0.67 (0.47–0.96)	**0.028**
Missing	1.14 (0.98–1.33)	0.09
Obesity		
No	1	
Yes	0.53 (0.48–0.59)	<**0.001**
Charlson Index		**0.001**
0	1	
1	1.08 (0.96–1.21)	0.20
2	0.67 (0.52–0.88)	**0.004**
3	0.85 (0.58–1.26)	0.42
≥4	0.28 (0.11–0.71)	**0.007**
Median household income		<**0.001**
$1–$38,999	1	
$39,000–$47,999	0.74 (0.60–0.91)	**0.005**
$48,000–$62,999	0.65 (0.53–0.81)	<**0.001**
≥$63,000	0.86 (0.69–1.06)	0.16
Missing	0.93 (0.79–1.08)	0.35
Primary expected payer		<**0.001**
Medicare	1	
Medicaid	1.26 (0.98–1.62)	0.07
Private including HMO	1.26 (1.01–1.57)	**0.047**
Self-pay	1.23 (0.92–1.65)	0.16
No charge	3.51 (2.27–5.43)	<**0.001**
Other	1.14 (0.82–1.59)	0.44
Hospital bed size		<**0.001**
Small	1	
Medium	1.45 (1.19–1.78)	**0.001**
Large	1.12 (0.93–1.36)	0.23
Hospital teaching status		<**0.001**
Rural	1	
Urban non-teaching	0.88 (0.72–1.08)	0.23
Urban teaching	0.59 (0.48–0.71)	<**0.001**
Hospital region		**0.001**
Northeast	1	
Midwest	0.74 (0.63–0.87)	<**0.001**
South	0.77 (0.67–0.89)	<**0.001**
West	0.91 (0.78–1.06)	0.22
Hysterectomy approach		<**0.001**
Abdominal	1	
Minimally invasive	1.65 (1.49–1.83)	<**0.001**

A binary logistic regression model for *P*-values. Significant *P*-values are emboldened. All the covariates with $P < 0.05$ on univariable analysis shown in Table 1 were entered in the final model. Abbreviations: OR, odds ratio; CI, confidence interval; and na, not available.

30.1% of the study population, included women 40–49 years of age who underwent abdominal hysterectomy at an urban teaching hospital (11.7%, 95% CI 10.6–12.8). The absolute difference in ovarian conservation rates between the highest and lowest groups was 48.8% (95% CI 39.9–57.8; Table 3).

After propensity score matching (Table S4 and Fig. S2), all covariates were equally distributed between the oophorectomy and ovarian conservation groups (all, standardized difference ≤ 0.10). In both pre- and post-matching models, ovarian conservation was significantly associated with a shorter length of hospital stay (both, $P < 0.001$; Table 4). Post-matching, the proportion of patients requiring hospital stays >2 days was 36.2% in the ovarian conservation group and 43.5% for the oophorectomy group (relative risk reduction 16.7%, $P < 0.001$). While postoperative complication rates were significantly higher in the oophorectomy group compared to the ovarian conservation group before propensity score matching (10.2% *versus* 8.1%, $P = 0.002$), there was no difference in postoperative complication rates in the post-matching model (8.3% *versus* 8.2%, $P = 0.91$).

In a sensitivity analysis of the benign gynecologic disease cohort (n = 1,432,046), 1,084,703 (75.7%, 95% CI 75.7–75.8) women had ovarian conservation at the time of hysterectomy and 347,343 (24.3%) women underwent oophorectomy (Fig. S3 and Table S5). After

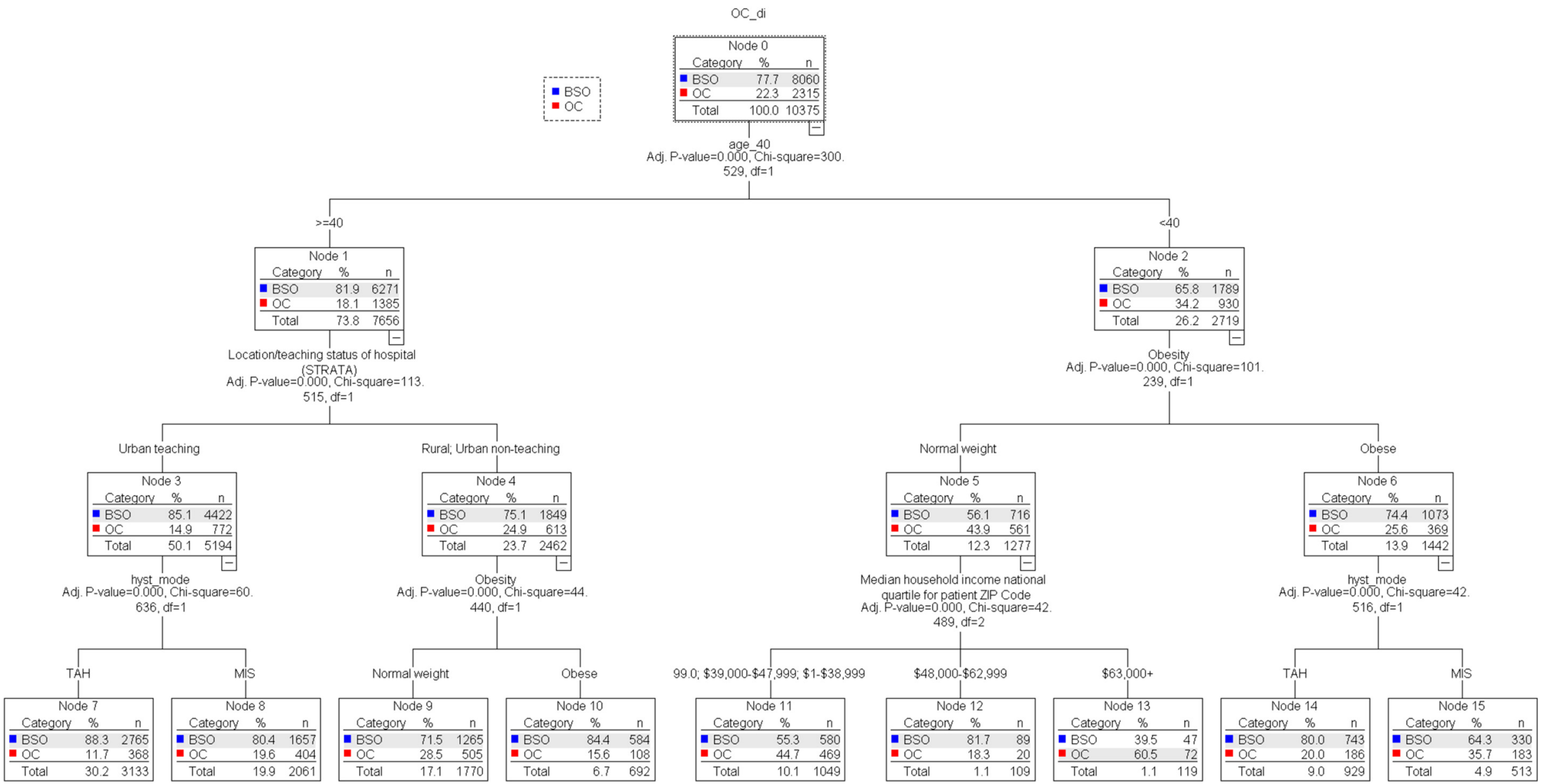

Fig. 2. Classification-tree model for ovarian conservation in the endometrial cancer cohort. Results of classification-tree model with and chi-square automatic interaction detector method are shown. All the significant covariates on multivariable analysis were entered in the final model. Abbreviation: OC, ovarian conservation; BSO, oophorectomy; TAH, hysterectomy with laparotomy; MIS, minimally invasive hysterectomy; and 99, no information.

Table 3
Frequency of ovarian conservation use based on contributing factors (endometrial cancer cohort).

Age	Hospital type	Hysterectomy	Body habitus	Household income	No.	Ovarian conservation (%)
<40			Non-obese	4th QT	119 (1.1%)	72 (60.5%)
<40			Non-obese	1st–2nd QT	1049 (10.1%)	469 (44.7%)
<40		MIS	Obese		513 (4.9%)	183 (35.7%)
≥40	Urban non-teaching, rural		Non-obese		1770 (17.1%)	505 (28.5%)
<40		Abdominal	Obese		929 (9.0%)	186 (20.0%)
≥40	Urban teaching	MIS			2061 (19.9%)	404 (19.6%)
<40			Non-obese	3rd QT	109 (1.1%)	20 (18.3%)
≥40	Urban non-teaching, Rural		Obese		692 (6.7%)	108 (15.6%)
≥40	Urban teaching	Abdominal			3133 (30.2%)	368 (11.7%)

Abbreviations: MIS, minimally invasive surgery; 1st QT, <$38,999; 2nd QT, $39,000–$47,999; 3rd QT, $48,000–$62,999; and 4th QT, ≥$63,000.

propensity score matching (Table S6 and Fig. S2), patient demographics were well matched (all, standardized difference ≤ 0.10). The proportion of hospital stays >2 days (27.8% *versus* 30.9%, relative risk reduction 10.1%, $P < 0.001$) was lower in the ovarian conservation group than in the oophorectomy group (Table 4). Perioperative complication rates were clinically similar between the two groups (9.0% *versus* 9.2%).

The study schema for the sensitivity analysis of the cervical cancer cohort is shown in Fig. S4 ($n = 7001$). Patient demographics are shown in Table S7 (ovarian conservation $n = 4941$ [70.6%], and oophorectomy $n = 2060$ [29.4%]). Patient characteristics were well balanced after propensity score matching (Table S8 and Fig. S2). Ovarian conservation once again was associated with a lower proportion of hospital stays >2 days (29.5% *versus* 34.9%, relative risk reduction 15.5%, $P = 0.006$) and similar perioperative complication rate (11.0% *versus* 12.3%, $P = 0.29$) compared to oophorectomy (Table 4).

4. Discussion

A key finding of our study is that patterns of ovarian conservation in young women with endometrial cancer vary widely even in the setting of minimal-risk disease. Significant variability in the utilization of ovarian conservation has been described in the non-oncologic setting, and our study confirms this in the oncologic setting as well. Specifically, a prior study reported 54% between-hospital variability in the decision to offer ovarian conservation during hysterectomy for benign gynecological diseases, which was unexplained by patient, surgical, or hospital

Table 4
Hospital stay and perioperative complication based on ovarian conservation.

	Characteristics	Before matching			After matching		
		Oophorectomy	Ovarian conservation	*P*-value	Oophorectomy	Ovarian conservation	*P*-value
Endometrial cancer	Hospital stay (days)			**<0.001**			**<0.001**
	≤1	2051 (22.0%)	737 (31.9%)		656 (30.8%)	675 (31.7%)	
	2	2169 (26.5%)	749 (32.4%)		549 (25.8%)	681 (32.0%)	
	3	1993 (24.3%)	442 (19.1%)		492 (23.1%)	423 (19.9%)	
	4	962 (11.7%)	217 (9.4%)		255 (12.0%)	197 (9.3%)	
	5	361 (4.4%)	58 (2.5%)		92 (4.3%)	49 (2.3%)	
	6	196 (2.4%)	14 (0.6%)		[a]	14 (0.7%)	
	7	82 (1.0%)	28 (1.2%)		15 (0.7%)	23 (1.1%)	
	>7	377 (4.6%)	68 (2.9%)		63 (3.0%)	64 (3.0%)	
	Periop complication			**0.002**			0.91
	No	7355 (89.8%)	2126 (91.9%)		1954 (91.7%)	1953 (91.8%)	
	Yes	836 (10.2%)	187 (8.1%)		177 (8.3%)	17 (8.2%)	
Benign gynecologic disease	Hospital stay (days)			**<0.001**			**<0.001**
	≤1	82,050 (23.6%)	347,545 (32.0%)		80,902 (24.3%)	86,720 (26.0%)	
	2	157,196 (45.3%)	466,802 (43.0%)		149,211 (44.8%)	153,771 (46.2%)	
	3	75,543 (21.7%)	196,645 (18.1%)		71,945 (21.6%)	67,873 (20.4%)	
	4	17,129 (4.9%)	41,049 (3.8%)		16,366 (4.9%)	13,605 (4.1%)	
	5	5544 (1.6%)	13,139 (1.2%)		5203 (1.6%)	4363 (1.3%)	
	6	2954 (0.9%)	6548 (0.6%)		2788 (0.8%)	2167 (0.7%)	
	7	1829 (0.5%)	3835 (0.4%)		1734 (0.5%)	1189 (0.4%)	
	>7	5098 (1.5%)	9128 (0.8%)		4833 (1.5%)	3274 (1.0%)	
	Periop complication			**<0.001**			**0.004**
	No	315,123 (90.7%)	992,948 (91.5%)		302,397 (90.8%)	303,056 (91.0%)	
	Yes	32,220 (9.3%)	91,755 (8.5%)		30,585 (9.2%)	29,912 (9.0%)	
Cervical cancer	Hospital stay (days)			**<0.001**			**0.006**
	≤1	547 (26.6%)	2294 (46.5%)		470 (33.0%)	472 (33.0%)	
	2	726 (35.3%)	1640 (33.2%)		457 (32.1%)	536 (37.5%)	
	3	401 (19.5%)	631 (12.8%)		269 (18.9%)	243 (17.0%)	
	4	174 (8.5%)	187 (3.8%)		109 (7.7%)	89 (6.2%)	
	5	62 (3.0%)	80 (1.6%)		32 (2.2%)	30 (2.1%)	
	6	37 (1.8%)	16 (0.3%)		22 (1.5%)	[a]	
	7	34 (1.7%)	28 (0.6%)		25 (1.8%)	19 (1.3%)	
	>7	78 (3.8%)	61 (1.2%)		39 (2.7%)	34 (2.4%)	
	Periop complication			**<0.001**			0.29
	No	1821 (88.4%)	4588 (92.9%)		1248 (87.7%)	1271 (89.0%)	
	Yes	239 (11.6%)	352 (7.1%)		175 (12.3%)	157 (11.0%)	

Number (percent per column) is shown. Chi-square test for *P*-values. Significant *P*-values are emboldened.
[a] Indicated number of ≤10, required to suppress per the Healthcare Cost and Utilization Project.

factors [30]. Our study validates their results, demonstrating nearly 50% inter-group variability. Taken together, this data reflects a lack of consensus or standardization for offering ovarian conservation in young women, both in women with malignancy and those without, despite the established benefits of ovarian conservation for cardiovascular and bone health as well as all-cause mortality.

Heterogeneous patterns in the utilization of ovarian conservation seen in our study suggest that the value to make a decision for ovarian conservation likely reflects not only patient preferences but also surgeon perspectives about this procedure. The level and extent of understanding of the risks and benefits of ovarian conservation in the setting of endometrial cancer on the part of both the patient and the surgeon could not be assessed in this study. Thus, further study to address how both patients and surgeons value ovarian conservation is warranted. A discrete-choice experiment design would be ideal to identify important factors related to ovarian conservation on both sides, and subsequently strategic approach can be constructed to guide the joint decision-making process [31].

Our study also found that those who had ovarian conservation at the time of hysterectomy stayed fewer days in the hospital than those who underwent oophorectomy in all three study cohorts. Another study that used this same database but an earlier study period found that patients undergoing elective oophorectomy at the time of hysterectomy had longer hospital stays compared to those who had ovarian conservation [32]. Our analysis, however, showed no difference in perioperative complication rates between oophorectomy and ovarian conservation after matching. Longer hospitalization in those who underwent oophorectomy may be due to the fact that surgeons may opt for oophorectomy in more difficult cases, either due to higher degree of patient comorbidity or surgical difficulty, and these complicating factors may prolong hospital stay.

Another possible cause of increased hospital stay in the oophorectomy group is that patients who undergo oophorectomy may have acute hormonal changes in the immediate postoperative period necessitating additional symptom workup or treatment prolonging hospital stay. Oophorectomy leads to abrupt hormonal changes, notably with a fall in estradiol, progesterone, and inhibin as well as a rise in FSH [33,34]. Serum FSH is reported to rise as early as 12 h after oophorectomy, and acute menopausal symptoms can present nearly immediately [33,35]. An early study reported that over half of women experienced vasomotor symptoms prior to discharge from the hospital following oophorectomy, and within the first postoperative month, women also frequently experienced somatic, psychological, and genitourinary symptoms [33,36]. Another study examining cardiovascular homeostasis following oophorectomy found acute elevations in blood pressure within the first 24 h postoperatively [37]. It is well-established that early surgical menopause has long-term deleterious effects on the cardiovascular system, however, this data suggests that these long-term consequences may actually begin in the immediate postoperative period [13,38].

We observed no significant change in rates of ovarian conservation over time, which is consistent with a prior analysis that also reported stable trends between 1998 and 2012 [9]. This may suggest that a relatively fixed subset of young patients with the most low-risk disease has historically been offered ovarian conservation, and there has not yet been expansion of indication criteria to include others that might also benefit from ovarian conservation based on recent data confirming its oncologic safety.

Strengths of this study include the use of a large population-based dataset and rigorous statistical analyses. Propensity score matching was utilized to ensure minimal effect of confounders, and analysis of validation cohorts was performed to demonstrate reproducibility of results even in cohorts where ovarian conservation is predominant (>70%). Limitations of all studies of this type include potential misclassification of cases. Additionally, an increase in the performance of minimally-invasive hysterectomies in ambulatory surgery centers, which are not captured by this database, may have led to decreased numbers of patients available for study in later years [39].

Perhaps the most critical limitation of this analysis, however, is the lack of data on parity and desire for future fertility, tumor information, including stage, grade, histology, nodal status, genetic information, and surgeon type (gynecologist *versus* gynecologic oncologist), which in practice all greatly impact treatment decision-making for oophorectomy and may have contributed to unmeasured confounders in this analysis. Misclassification of disease risk by surrogate markers may be responsible for our high ovarian conservation rate (22%) compared to what has been previously reported in the literature (7.2–12%) [7–9]. Exclusion of cases in which lymphadenectomy was performed for advanced or high-risk disease may have also erroneously excluded cases in which sentinel lymph node biopsy was performed for low-risk endometrial cancer.

Further, specific reasons for prolonged hospitalization could not be analyzed, and there is also no opportunity for follow-up with use of this dataset. Thus, survival or oncologic outcomes, treatment-related complications remote from hospitalization, patterns of adjuvant or hormonal replacement therapy, use of fertility treatment, or other indirect costs of treatment could not be evaluated and represent future directions of study [40]. Because diagnosis and treatment information was derived from an administrative database based on discharge diagnoses instead of preoperative, distinguishing incidental occult endometrial cancer was not feasible. Together with the lack of stage/grade information, these limitations could imply that the patterns of ovarian conservation noted in our study may differ from true treatment patterns.

In conclusion, there is great variability in the decision to offer ovarian conservation in young women with minimal-risk endometrial cancer based on patient, surgical, and hospital factors, implying that future guidelines should be established with recommendations regarding ovarian conservation. Moreover, ovarian conservation may provide the opportunity for future fertility *via in-vitro* fertilization and gestational surrogacy. Given the oncologic safety of ovarian conservation in young women with early-stage and low-grade endometrial cancer, our results support increasing utilization of ovarian conservation in this population.

Disclosure statement

Consultant, Clovis Oncology and Tesaro (J.D.W.); consultant, Merck (D.S.); consultant, Tempus Labs (L.D.R.); honorarium, Chugai, book editorial, Springer, and meeting expense, VBL therapeutics (K.M.); none for others.

Author contributions

Conceptualization: K.M.; Data curation: R.S.M.; Formal analysis: K. M.; Funding acquisition: K.M.; Investigation: all authors; Methodology: K.M., L.C., J.D.W.; Project administration: K.M.; Resources: K.M., R.S.M.; Software: K.M.; Supervision: L.D.R., J.D.W.; Validation: K.M..; Visualization: K.M.; Writing - original draft: K.M.; Writing - review & editing: all authors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2019.04.653.

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