GYNECOLOGY

Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy

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BACKGROUND: A recent trial demonstrated decreased survival in women with early-stage cervical cancer who underwent radical hysterectomy via minimally invasive surgery compared with laparotomy; however, outcomes following trachelectomy have yet to be studied.

OBJECTIVE: To examine trends, characteristics, and survival of reproductive-aged women with early-stage cervical cancer who underwent minimally invasive trachelectomy.

STUDY DESIGN: This is a retrospective study examining the National Cancer Database between 2010 and 2015. Women aged <50 years who underwent trachelectomy for stage IA2-IB cervical cancer were grouped by mode of surgery. Clinicopathologic characteristics and outcomes were compared between minimally invasive surgery and laparotomy groups.

RESULTS: A total of 246 women were included, 144 (58.5%, 95% confidence interval, 52.4%–64.7%) of whom had trachelectomy with a minimally invasive surgery approach. Median age was similar between the minimally invasive surgery and laparotomy groups (median, 31 vs 29 years, $P = .20$). There was a significant increase in the use of minimally invasive surgery from 29.3% in 2010 to 75.0% in 2015 ($P < .001$). Specifically, minimally invasive surgery became the dominant approach for trachelectomy by year 2011 (54.8%). Hospitals registered in the West (75.0% vs 25.0%) were more likely, whereas those registered in the Midwest (46.9% vs 53.1%) were less likely, to perform minimally invasive surgery ($P = .02$). Median follow-up was 37 months (interquartile range, 23–51) for the minimally invasive surgery group and 40 months (interquartile range, 26–67) for the laparotomy group. During follow-up, there were 11 (5.3%) deaths, 4 (3.5%) in the minimally invasive surgery group and 7 (7.6%) in the laparotomy group ($P = .25$).

CONCLUSION: Minimally invasive surgery has become the dominant modality for trachelectomy in reproductive-aged women with stage IA2-IB cervical cancer after year 2011. Survival of women with stage IA2-IB cervical cancer who underwent trachelectomy is generally good regardless of surgical modality. Although our study showed no difference in survival between the minimally invasive surgery and laparotomy approaches, effects of MIS on survival remain unknown and further study is warranted.

Key words: cervical cancer, minimally invasive, survival, trachelectomy

The incidence of cervical cancer has decreased over the past several decades, and it is now the 13th most common female malignancy in the United States.[1] However, young women continue to be disproportionately affected. Between 2012 and 2014, it was estimated that 1 in 368 women younger than the age of 50 years was diagnosed with cervical cancer in the United States.[1] Cervical cancer continues to be the second-leading cause of female cancer-related death among women 20–39 years of age.[1]

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EDITORS' CHOICE

Unique treatment considerations exist in this population of young women with cervical cancer, as many face the dilemma of deciding between definitive cancer treatment with hysterectomy vs uterine preservation for reproductive function. In conjunction with national trends toward delayed childbearing, fertility-preserving treatment options in this population are becoming increasingly important.[2,3]

One treatment option for such women is fertility-sparing trachelectomy.[4] Mounting evidence has demonstrated the oncologic safety and subsequent favorable pregnancy outcomes in reproductive-aged women with early-stage cervical cancer who desire fertility preservation.[5-10] A previous study in the United States has shown that ~40% of women aged <40 years who underwent definitive surgical treatment with radical hysterectomy actually expressed interest for fertility preservation and nearly one half were indeed candidates for fertility-sparing trachelectomy based on their surgical–pathologic factors.[11] In the past several years, there has been a significant recent increase in the use of trachelectomy in this population in the United States.[5,8,12]

One clinical entity that has not been addressed in the literature regarding trachelectomy for cervical cancer is the oncologic safety of minimally invasive surgery (MIS) as compared with laparotomy and radical vaginal trachelectomy, which remains unknown. Given the results of a recent randomized trial and an observational study that demonstrated decreased survival with MIS radical hysterectomy in women with early-stage cervical cancer, this clinical question is of great importance.[13,14] We examined trends, characteristics, and survival of reproductive-aged women with early-stage cervical cancer who underwent trachelectomy with a MIS approach.

AJOG at a Glance

Why was the study conducted?

Recent studies have shown that women with early-stage cervical cancer who underwent minimally invasive surgery for radical hysterectomy had poorer survival compared with those with laparotomy; however, outcomes following minimally invasive trachelectomy have yet to be studied.

Key findings

An analysis of National Cancer Database examining women aged <50 years with stage IA2-IB cervical cancer who underwent trachelectomy found that the minimally invasive surgery approach has significantly increased from 29.3% to 75.0% between 2010 and 2015.

What does this add to what is known?

Survival of women who underwent trachelectomy in this population is generally good regardless of surgical modality, exhibiting 4-year rates of 92%–95%. Although there was no difference in survival between the minimally invasive surgery and laparotomy approaches, effects of minimally invasive surgery on survival remains unknown, and further study is warranted.

Materials and Methods

Data source

This is a retrospective study examining the National Cancer Database (NCDB). This database is a nationwide tumor registry that collects >1 million invasive cancer cases, representing approximately 70% of all new invasive cancers in the United States.[15] Nearly 1500 Commission on Cancer–affiliated institutions participate in the database through a partnership between the Commission on Cancer of the American College of Surgeons and the American Cancer Society Society.[15] Information extracted from the NCDB included patient demographics, tumor characteristics, treatment type, cancer staging, follow-up, and survival outcome. The study used publicly available deidentified data thus was deemed exempt by the Columbia University institutional review board (ethical committee exemption: AAAN2900).

Study population

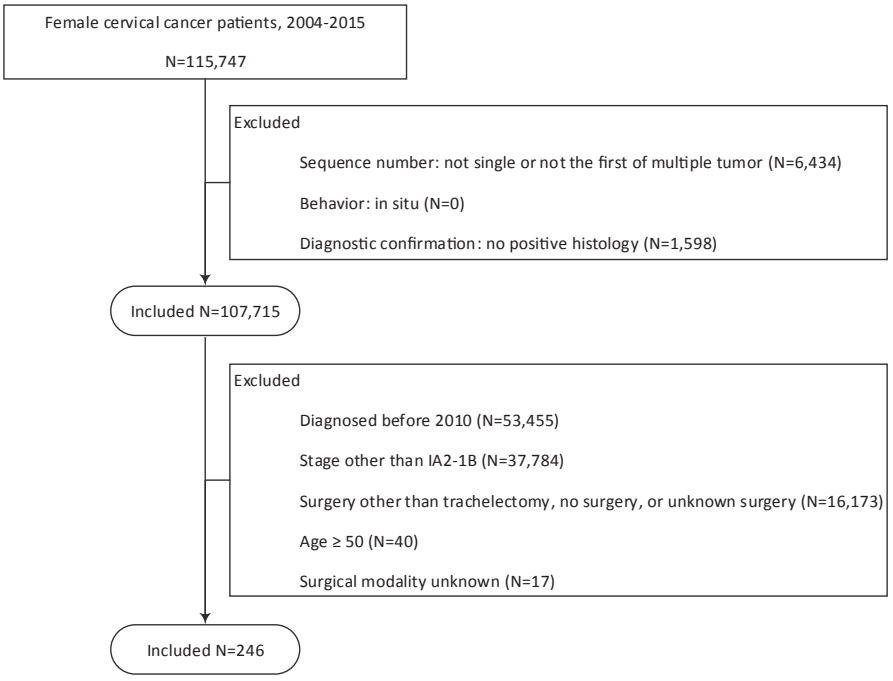
Women <50 years of age who were diagnosed with stage IA2-IB cervical cancer between 2010 and 2015 who underwent trachelectomy either with MIS or laparotomy were eligible for the study. Stage was grouped according to International Federation of Gynecology and Obstetrics system and defined using the American Joint Committee on Cancer (AJCC) clinical stage if available, Collaborative Staging Site-Specific Factor 1 if AJCC clinical stage was unknown, and AJCC pathologic stage when the former 2 were unknown. The age cutoff was of 50 years was chosen based on the World Health Organization for reproductive age.[16] The inclusion of cancer stage IA2 and IB disease was chosen per the guideline recommendation for fertility-sparing trachelectomy only in early-stage cervical cancer.[4]

Women ≥50 years as well as those with cancer in situ, absence of diagnostic confirmation, or cervical cancer stage other than IA2-IB were excluded. Patients who had multiple tumors and cervical cancer not as the first were excluded. Women who did not undergo surgery or who had surgery other than trachelectomy, unknown surgery type, or trachelectomy with unknown surgical modality were also excluded from the study.

Study definition

MIS trachelectomy in this study refers to conventional laparoscopic trachelectomy or robotic-assisted trachelectomy, and the codes in the database were unable to distinguish vaginal radical trachelectomy. The starting time point of 2010 was chosen based on the

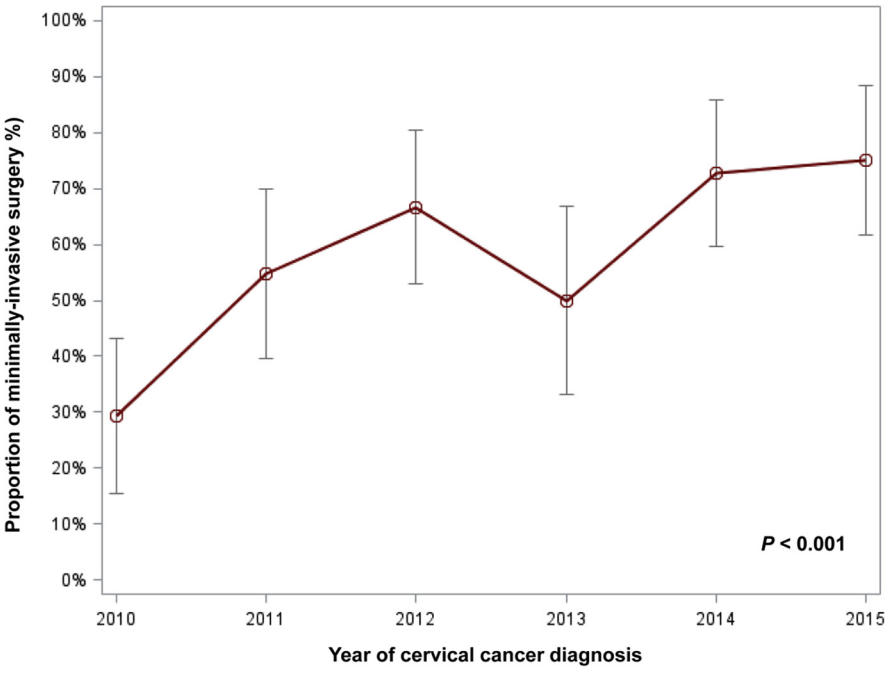
FIGURE 1
Study schema



Cohort selection criteria from the National Cancer Database.

Matsuo et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. Am J Obstet Gynecol 2019.

FIGURE 2
Trend of trachelectomy use between 2010 and 2015



Cochran–Armitage trend test for *P*-value. *Dots* represent observed value and *bars* represent 95% confidence interval for minimally invasive trachelectomy.

Matsuo et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. Am J Obstet Gynecol 2019.

rationale that the first case entry of MIS trachelectomy was recorded in the database in 2010. MIS trachelectomy cases resulted in laparotomy conversion was grouped as the MIS group (intention-to-treat). Of note, the extent of trachelectomy (simple vs radical) was not distinguishable via the procedure codes in the database.

Clinical information

The following abstracted data variables were categorized based on a previous study.[5] Demographic information of interest included age (in years), race/ethnicity (white, black, Hispanic, other, or unknown), year of diagnosis, insurance type (private, Medicare, Medicaid, uninsured, other government or unknown), median household income (<$38,000, $38,000–47,999, $48,000–62,999, ≥$63,000), education (measured as percentage of adults in the patient's zip code who did not graduate from high school and grouped as ≥21%, 13%–20%, 7.0%–12.9%, <7%), and urban–rural location (metropolitan, urban, rural, or unknown).

Charlson Comorbidity Index for medical comorbidities was based on the Deyo classification (0, 1, or ≥2). Hospital information included facility type per the Commission on Cancer criteria (academic/research, community cancer programs, comprehensive community cancer programs, or integrated network cancer program), and geographic location (Northeast, Midwest, South, West).

Tumor characteristics included stage (IA2, IB1, IB2, or IB not otherwise specified), histology (squamous, adenocarcinoma, or others), grade (well-, moderately, poorly differentiated, or unknown), lymphovascular space invasion (absent, present, or unknown), and tumor size (<1, 1–2, >2 cm, or unknown). Information for regional lymph node status included performance of lymph node dissection for assessment (not examined, examined, or unknown) and presence of lymph node metastasis (no vs yes).

For survival outcome, overall survival, defined as the time interval between the cervical cancer diagnosis and death from any reason (all-cause), was collected. Cases deemed alive at the last follow-up were censored.

Statistical consideration

The primary objective of analysis was to examine performance and characteristics related to MIS trachelectomy. The secondary objective was to examine survival after MIS trachelectomy. Continuous variables were reported with the median and interquartile range, and statistical difference was assessed with Wilcoxon rank-sum test. Categorical variables were reported as frequencies per group, and statistical difference was assessed with χ^2 test. A trend curve depicting MIS use per calendar year was constructed, and statistical difference was assessed with the Cochran–Armitage trend test. The Kaplan–Meier method was used to plot survival curves, and statistical difference was assessed with the log-rank test.

Multivariable analyses to assess the independent prognostic factors for as well as factors contributing to MIS use were not preplanned in this study, as we estimated that trachelectomy with a MIS approach is a relatively new treatment modality and study size as well as survival events would not be adequate to perform adjusted models. All hypothesis testing was 2-sided, and a $P < .05$ was considered statistically significant. SAS 9.4 (SAS Institute, Cary, NC) was used for all analyses.

Results

The study selection schema is shown in Figure 1. There are 246 women aged <50 years with stage IA2-IB cervical cancer who underwent trachelectomy via a MIS or laparotomy approach represented the study population. Among the 246 women, 144 (58.5%, 95% confidence interval [CI], 52.4%–64.7%) underwent MIS trachelectomy and 102 (41.5%) women underwent laparotomy. Of the 144 MIS patients, there are 96 (66.7%) robotic assisted, 46 (31.9%) laparoscopic, and 2 (1.4%) laparoscopic converted to open.

TABLE 1
Patient demographics (N = 246)

Characteristic	Laparotomy n	Laparotomy (%)	MIS[a] n	MIS[a] (%)	*P* value
Number	102	(41.5)	144	(58.5)	
Age					
Median (IQR)	29	(27-35)	31	(28-36)	.20
Race/ethnicity					.34
White	69	(40.6%)	101	(59.4%)	
Black	12	(63.2%)	[b]	[b]	
Hispanic	11	(40.7%)	16	(59.3%)	
Other	[b]	[b]	18	(66.7%)	
Unknown	[b]	[b]	[b]	[b]	
Year of diagnosis					<.001
2010	29	(70.7%)	12	(29.3%)	
2011	19	(45.2%)	23	(54.8%)	
2012	15	(33.3%)	30	(66.7%)	
2013	17	(50.0%)	17	(50.0%)	
2014	12	(27.3%)	32	(72.7%)	
2015	10	(25.0%)	30	(75.0%)	
Insurance					.46
Uninsured	[b]	[b]	[b]	[b]	
Private	79	(40.3%)	117	(59.7%)	
Medicaid	14	(53.8%)	12	(46.2%)	
Medicare	[b]	[b]	[b]	[b]	
Other[c]	[b]	[b]	[b]	[b]	
Income					.82
<$38,000	14	(42.4%)	19	(57.6%)	
$38,000–$47,999	21	(45.7%)	25	(54.3%)	
$48,000–$62,999	26	(37.1%)	44	(62.9%)	
≥$63,000	41	(42.3%)	56	(57.7%)	
Education					.47
≥21%	15	(41.7%)	21	(58.3%)	
13%–20%	30	(46.9%)	34	(53.1%)	
7.0%–12.9%	25	(34.2%)	48	(65.8%)	
<7%	32	(43.8%)	41	(56.2%)	
Urban rural					.61
Metropolitan	92	(42.2%)	126	(57.8%)	
Urban	[b]	[b]	14	(63.6%)	
Rural	[b]	[b]	[b]	[b]	
Unknown	[b]	[b]	[b]	[b]	

Matsuo et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. Am J Obstet Gynecol 2019. (continued)

TABLE 1
Patient demographics (N = 246) *(continued)*

Characteristic	Laparotomy n	Laparotomy (%)	MIS[a] n	MIS[a] (%)	*P* value
Comorbidity					.56
0	97	(42.2%)	133	(57.8%)	
1	[b]	[b]	10	(66.7%)	
≥2	[b]	[b]	[b]	[b]	
Facility type					.23
Community cancer	[b]	[b]	[b]	[b]	
Comprehensive community cancer	25	(39.1%)	39	(60.9%)	
Academic/research	66	46.2%)	77	(53.8%)	
Integrated network cancer	10	(28.6%)	25	(71.4%)	
Facility location					.02
Northeast	29	(45.3%)	35	(54.7%)	
Midwest	26	(53.1%)	23	(46.9%)	
South	33	(42.9%)	44	(57.1%)	
West	14	(25.0%)	42	(75.0%)	
Regional nodes					.47
Not examined	[b]	[b]	[b]	[b]	
Examined	96	(41.0%)	138	(59.9%)	
Unknown	[b]	[b]	[b]	[b]	

Age was compared using Wilcoxon rank-sum test; the other categorical variables were compared using χ^2 tests.

IQR, interquartile range; *MIS*, minimally invasive surgery.

[a] Intention-to-treat analysis, including 2 cases converted to laparotomy; [b] Suppress reporting because some cell sizes were <10; [c] Including government or unknown.

Matsuo et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. Am J Obstet Gynecol 2019.

The trend in use of MIS for trachelectomy was examined between 2010 and 2015 (Figure 2). There was a significant increase in the use of MIS during the study period from 29.3% in 2010 to 75.0% in 2015 ($P < .001$). Specifically, although MIS accounted for less than one third of trachelectomies performed in 2010 (29.3%; 95% CI, 15.3%−43.2%), by 2011, MIS became the dominant approach for trachelectomy (54.8%; 95% CI, 39.7%−69.8%). By 2015, nearly three quarters of all the trachelectomies at the NCDB sites were performed with MIS (75.0%; 95% CI, 61.6%−88.4%). MIS with robotic approach increased from 38.1% to 60.0% between 2011 and 2015.

Patient demographics based on treatment modality are shown in Table 1. Age at cervical cancer diagnosis was similar between the 2 groups (median, MIS vs laparotomy, 31 vs 29, $P = .20$). Percentages between the 2 groups for race/ethnicity, insurance type, household income, education, hospital, and type differed but did not show statistical difference (all, $P > .05$). Hospital location was significantly associated with MIS use, and the hospitals in the West (MIS vs laparotomy, 75.0% vs 25.0%) were more likely, whereas those registered in Midwest (46.9% vs 53.1%) were less likely, to perform MIS trachelectomy ($P = .02$). The vast majority of women in the study also underwent regional lymphadenectomy (94.1% in laparotomy vs 95.8% in patients undergoing MIS).

Tumor characteristics were compared between the 2 groups (Table 2). In both groups, the majority of tumors were stage 1B1 (MIS vs laparotomy, 74.3% vs 76.1%) and ≤2 cm in size (51.4% vs 48.1%). Notably, tumors >2 cm accounted for nearly one third of cases in this study population (29.9% vs 31.4%) but tumors assigned as stage IB2 disease were rare in this study population (<3%). Nearly 1 in 6 tumors had no information for tumor size (16.3%). Overall, cancer stage, histologic subtype, tumor size, presence of lymphovascular space invasion, and presence of regional lymph node metastasis were all similar between the MIS and laparotomy groups (all, $P > .05$).

The median follow-up for the cohort was 37 months (interquartile range, 23−51) for the MIS group and 40 months (interquartile range, 26−67) for the laparotomy group, corresponding to 4301 and 3857 person-months at risk, respectively. During the follow-up period, among 206 patients with survival data, there were 11 (5.3%) deaths recorded; 4 (3.5%) deaths occurred in

TABLE 2
Tumor characteristics (N = 246)

Characteristic	Laparotomy n	Laparotomy (%)	MIS[a] n	MIS[a] (%)	*P* value
Number	102	(41.5)	144	(58.5)	
Stage					.21
1A2	12	(48.0%)	13	(52.0%)	
1B1	73	(40.6%)	107	(59.4%)	
1B2	[b]	[b]	[b]	[b]	
1B NOS	17	(47.2%)	19	(52.8%)	
Histology					.41
Squamous cell	51	(45.9%)	60	(54.1%)	
Adenocarcinoma	40	(37.0%)	68	(63.0%)	
Other	11	(40.7%)	16	(59.3%)	
Grade					.16
Well differentiated	23	(54.8%)	19	(45.2%)	
Moderately differentiated	43	(36.4%)	75	(63.6%)	
Poorly differentiated	29	(44.6%)	36	(55.4%)	
Unknown	[b]	[b]	14	(66.7%)	
Tumor size, cm					.80
<1	21	(44.7%)	26	(55.3%)	
1–2	28	(36.8%)	48	(63.2%)	
>2	32	(42.7%)	43	(57.3%)	
Unknown	21	(43.8%)	27	(56.3%)	
LVSI					.68
Absent	55	(39.6%)	84	(60.4%)	
Present	33	(42.3%)	45	(57.7%)	
Unknown	14	(48.3%)	15	(51.7%)	
Regional nodal metastasis[c]					.28
No	86	(40.0%)	129	(60.0%)	
Yes	10	(52.6%)	[b]	[b]	

Categorical variables were compared using χ^2 tests.

LVSI, lymphovascular space invasion; *MIS*, minimally invasive surgery; *NOS*, not otherwise specified.

[a] Intention-to-treat analysis, including 2 cases converted to laparotomy; [b] Suppress reporting because some cell sizes were <10; [c] Regional nodal metastasis no/yes were compared restricting to patients with nodes examined.

Matsuo et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. Am J Obstet Gynecol 2019.

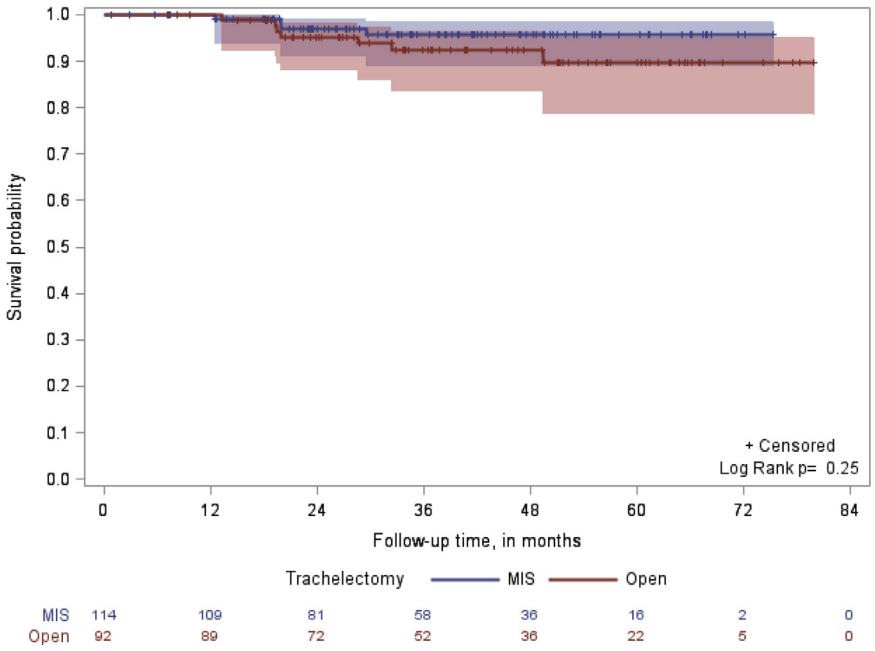
the MIS group and ranged from 12-30 months after diagnosis, and 7 (7.6%) deaths occurred in the laparotomy group with a range of 13-49 months after the cervical cancer diagnosis (unadjusted hazard ratio, 0.50; 95% CI, 0.15–1.70, $P = .25$; Figure 3). The 4-year overall survival rates were estimated as 95.7% (95% CI, 88.7–98.4) for the MIS group and 92.3% (95% CI, 83.5–96.5) for the laparotomy group, respectively. Survival estimates of other clinicopathologic factors are shown in Supplemental Table 1.

Comments

Our findings suggest that in the United States, MIS has been rapidly adopted for women who undergo trachelectomy for cervical cancer. Although our power is limited, there was no difference in survival between MIS and open trachelectomy in contrast to recent studies demonstrating inferior survival for minimally invasive compared with open radical hysterectomy.

Our analysis demonstrated that the performance of MIS trachelectomy in young women with early-stage cervical cancer has significantly increased over a

FIGURE 3
Overall survival based on treatment modality



Colored areas represent 95% confidence intervals.

MIS, minimally invasive surgery.

Matsuo et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. Am J Obstet Gynecol 2019.

short period of 6 years. By 2015, the vast majority of trachelectomies were performed using a minimally invasive approach. This increase clearly reflects the recent practice patterns among US gynecologic oncologists in that MIS is considered the preferred approach over laparotomy for radical trachelectomy.[17]

The use of fertility-sparing trachelectomy, regardless of surgical approach, for women aged <45 years with stage IA2-IB1 (≤2 cm) cervical cancer has increased from 2.0% to 6.8% between 1998 and 2014 in the United States.[8] This increase was most pronounced in women <30 years of age.[5] Our study demonstrates that the majority of these procedures are now performed with a minimally invasive approach, particularly with use of the robotic platform. This increased use of MIS for trachelectomy parallels the trends observed for radical hysterectomy for early-stage cervical cancer in the United States. Specifically, use of MIS for radical hysterectomy has significantly increased from 2% to 58% between 2006 and 2013.[13,18]

It is speculated that the increasing use of MIS in the surgical treatment of early-stage cervical cancer, including trachelectomy, is influenced by the results of studies on the use of MIS in the surgical treatment of endometrial cancer and other solid tumors.[19-24] Previously, multiple phase III randomized trials reported comparable oncologic outcomes and decreased perioperative complication rates with MIS hysterectomy compared to laparotomy for endometrial cancer.[19,20] Although prospective data specifically examining MIS use for cervical cancer have been lacking, a sizable body of evidence has previously demonstrated noninferiority of survival with MIS approach until recent.[25-29]

In 2018, Ramirez et al reported the results of a phase III trial examining oncologic outcomes following MIS radical hysterectomy vs laparotomy for women with early-stage cervical cancer (LACC trial).[14] Of note, the study is known to be the first randomized controlled trial examined the efficacy of MIS radical hysterectomy for early-stage cervical cancer. This trial was designed with a noninferiority hypothesis based on previous nonrandomized studies[26-29]; however, the results showed that MIS radical hysterectomy was associated with a nearly 4-fold increased risk of recurrence and 6-fold increase in all-cause mortality compared with laparotomy.[14]

Although there is an expert opinion that disease-free survival rate of 97% among the laparotomy group in their trial is greater and the survival in the MIS group (86%) is what seems expected compared with the historical controls (80%−88%),[30] another population-based observational study that examined multiple US tumor registries also showed the similar results to the LACC trial in that MIS radical hysterectomy was associated with ∼50% increased risk of all-cause mortality compared with the laparotomy approach.[13] Their analysis even found that there is a trend of decreasing a 4-year survival rate for ∼1% per year annually in women undergoing radical hysterectomy for cervical cancer, which began concurrently with the rapid increasing use of MIS radical hysterectomy that started in 2006.[13] These 2 studies call into question the use of MIS for radial hysterectomy but did not examine outcomes of women who underwent MIS trachelectomy.

Given the concerning results of these 2 studies and the rapid adoption of MIS approaches for trachelectomy in addition to radical hysterectomy, there is clearly a need to document the safety of MIS for trachelectomy. To date, available evidence related to MIS trachelectomy is limited in that these are small sample sizes, lack in a comparator with laparotomy, are retrospective, and have short follow-up periods.[31-35] In the current analysis there was no statistical difference in survival for women who underwent open and minimally invasive trachelectomy. But, as expected, our results are underpowered due to small sample size and few survival events to

TABLE 3
Sample size estimation

Hypothesis	Increase in mortality			Decrease in mortality		
Difference (%)	10%	25%	50%	10%	25%	50%
Distribution	Asymptotic normal	Asymptotic normal	Asymptotic normal	Asymptotic normal	Asymptotic normal	Asymptotic normal
Method	Normal approximation	Normal approximation	Normal approximation	Normal approximation	Normal approximation	Normal approximation
Laparotomy 4-year mortality risk	0.0770	0.0770	0.0770	0.0770	0.0770	0.0770
MIS 4-year mortality risk	0.0847	0.0963	0.1155	0.0693	0.05775	0.0385
Laparotomy weight (1:1 allocation)	1	1	1	1	1	1
MIS weight (1:1 allocation)	1	1	1	1	1	1
Nominal power	0.8	0.8	0.8	0.8	0.8	0.8
Number of sides	2	2	2	2	2	2
Null proportion difference	0	0	0	0	0	0
Alpha (2-sided)	0.05	0.05	0.05	0.05	0.05	0.05
Actual power	0.80	0.80	0.80	0.80	0.80	0.80
Total sample size	39,350	6670	1842	35,900	5322	1152

Pearson χ^2 test for proportion difference. Observed 4-year survival rates were used for sample size estimation. Laparotomy group served as the control.

MIS, minimally invasive surgery.

Matsuo et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. Am J Obstet Gynecol 2019.

draw any clinically meaningful conclusions.

Our study demonstrated that the majority of MIS trachelectomies were performed with the robotic-assisted approach. We did not examine trends or outcomes of robotic-assisted MIS trachelectomy specifically as the number was few. Because the recent trial evaluating outcomes following MIS radical hysterectomy predominately consisted of hysterectomies performed via conventional laparoscopy (>80%) but not robotic approach,[14] it is of interest to see whether outcomes differ between conventional laparoscopic vs robotic-assisted approaches. A recent review reported comparable outcomes between the 2 modalities, but sample size remains limited, and further study is warranted.[31]

A strength of this study is that our sample size is likely among the largest in the literature examining MIS trachelectomy for cervical cancer. However, we also acknowledge a number of weaknesses in this study. First, this is a retrospective study likely with several unobserved confounding factors that influenced the decision to perform trachelectomy as well as the surgical approach for the procedure. Surgeon's level of experience with MIS trachelectomy is likely one of the most important factors affecting outcomes. In addition, the database does not include information regarding the use of intrauterine manipulators as well as vaginal colpotomy type, both of which are potential factors affecting tumor spread following MIS.[36,37]

Some surgeons also advocate for the use of neoadjuvant chemotherapy before trachelectomy or a vaginal trachelectomy approach, both of which were not assessed in this study either due to small cases (n = 2 for neoadjuvant therapy) or nonspecific coding (vaginal trachelectomy).[38-41] Although radical vaginal trachelectomy is performed infrequently in the United States, we recognize the inability to subclassify these patients as an important limitation of the study. As an intrauterine manipulator is not used and intraperitoneal tumor exposure does not occur, the potential risk of tumor dissemination may be mitigated in women who undergo radical vaginal trachelectomy.[42] If lymphadenectomy was assessed with laparoscopic/robotic approach, then, cases with radical vaginal trachelectomy would have been classified in the MIS group.

Second, we could not examine perioperative complications or reproductive outcomes following MIS trachelectomy, which in addition to survival, are important outcomes related to trachelectomy. Third, we did not specify the type of trachelectomy as radical vs simple as the coding in the database does not specify the 2 modalities; however, we believe our study population most likely consists of women who underwent radical trachelectomy, as this is the standard trachelectomy approach for

stage IA2-IB cervical cancer.[4] Recurrence information is not available in this database, and the detailed association for oncologic outcome was not assessable.

Lastly, given the favorable prognosis for this population of women, our study lacks the power to determine modest differences in survival. As an example, assuming a 1-to-1 case mix for open and minimally invasive trachelectomy (α-level of 0.05 and a power of 80%) and an increased mortality for laparotomy as described in recent studies,[13,14] we estimated that a total sample size of 39,350, 6670, and 1842 of cases would be needed to detect a 10%, 25%, and 50% difference in 4-year mortality, respectively (Table 3). Conversely, assuming that MIS trachelectomy is associated with decreased mortality, we estimated total sample sizes are 35,900, 5322, and 1152 cases to detect 10%, 25%, and 50% difference in mortality, respectively.

If the association of surgical approach for radical trachelectomy and survival is to be examined in women with early-stage cervical cancer, an ideal approach would be a randomized controlled trial. In such case, (1) surgical approaches (laparoscopy, robotic-assisted, vaginal, and laparotomy), (2) surgical technique (intra-uterine manipulator and colpotomy), and (3) tumor factors (size and tumor location) would be all controlled. However, given the limited number of subjects, prospective trials comparing minimally invasive and abdominal trachelectomy will likely not be feasible.

In conclusion, these data demonstrate that the use of MIS for trachelectomy for early-stage cervical cancer has increased significantly in recent years. Given the concerns surrounding the influence of MIS for women who undergo radical hysterectomy, further study to monitor outcomes in these women who undergo minimally invasive trachelectomy is a necessity. ■

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SUPPLEMENTAL TABLE 1
Prognostic factors for overall survival (n = 206)

Characteristic	HR (95% CI)	*P* value
Age (continuous)	0.95 (0.85–1.05)	.28
Race/ethnicity		
White	1	
Black	2.89 (0.60–13.91)	.19
Hispanic	1.17 (0.14–9.53)	.88
Other	1.04 (0.13–8.50)	.97
Unknown	—	—
Year of diagnosis		
2010	1	
2011	0.37 (0.07–1.90)	.23
2012	0.38 (0.07–1.96)	.25
2013	0.28 (0.03–2.43)	.25
2014	0.37 (0.04–3.37)	.38
2015	—	—
Insurance		
Private	1	
Medicaid	1.66 (0.35–7.82)	.52
Medicare	—[a]	.99
Uninsured	1.80 (0.23–14.41)	.58
Other government/unknown	—[a]	.99
Income		
<$38,000	1	
$38,000–$47,999	0.47 (0.09–2.58)	.39
$48,000–$62,999	0.23 (0.04–1.23)	.09
≥$63,000	0.29 (0.06–1.28)	.10
Education		
≥21%	1	
13-20%	3.03 (0.34–27.16)	.32
7.0-12.9%	2.27 (0.25–20.30)	.46
<7%	1.17 (0.11–12.96)	.90
Urban rural		
Metropolitan	1	
Rural	—[a]	.99
Unknown	—[a]	.99
Urban	1.27 (0.16–9.89)	.82
Comorbidity		
0	1	
1	—[a]	.99
≥2	—[a]	.99

Matsuo et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. Am J Obstet Gynecol 2019. *(continued)*

SUPPLEMENTAL TABLE 1
Prognostic factors for overall survival (n = 206) *(continued)*

Characteristic	HR (95% CI)	*P* value
Facility type		
Academic/research	1	
Community cancer	—[a]	.99
Comprehensive community cancer	2.66 (0.77–9.21)	.12
Integrated network cancer	1.22 (0.14–10.41)	.86
Facility location		
Northeast	1	
Midwest	1.35 (0.27–6.70)	.71
South	1.59 (0.36–7.11)	.54
West	0.44 (0.05–4.19)	.47
Stage		
1A2	—[a]	.99
1B1	1	
1B2	—[a]	.99
1B NOS	1.02 (0.22–4.74)	.98
Histology		
Squamous cell	1	
Adenocarcinoma	0.27 (0.06–1.35)	.11
Adenosquamous	1.98 (0.49–7.91)	.34
Grade		
Well differentiated	1	
Moderately differentiated	—[a]	.99
Poorly differentiated	—[a]	.99
Unknown	—[a]	.99
Tumor size, cm		
<1	1	
1-2	1.07 (0.10–11.81)	.96
>2	3.67 (0.45–29.85)	.22
Unknown	0.79 (0.05–12.71)	.87
Tumor size, cm		
<2	1	
2-4	3.18 (0.82–12.29)	.09
>4	—[a]	.99
Unknown	0.69 (0.07–6.61)	.75
LVSI		
Absent	1	
Present	2.44 (0.69–8.66)	.17
Unknown	0.89 (0.10–7.94)	.91

Matsuo et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. Am J Obstet Gynecol 2019. *(continued)*

SUPPLEMENTAL TABLE 1
Prognostic factors for overall survival (n = 206) *(continued)*

Characteristic	HR (95% CI)	*P* value
Regional nodes		
Not examined	1	
Examined	0.63 (0.08–4.96)	.66
Unknown	–[a]	.99
Regional nodal metastasis[b]		
Negative	1	
Positive	1.04 (0.13–8.25)	.97
Unknown	–	–
Surgical approach		
Open	1	
MIS	0.50 (0.15–1.70)	.27

Univariable analysis with Cox proportional hazard regression model for analysis. In total, 2015 patients were excluded because of missing survival data.

CI, confidence interval; *HR*, hazard ratio; *LVSI*, lymphovascular space invasion; *MIS*, minimally invasive surgery; *NOS*, not otherwise specified.

[a] Nonestimable; [b] Nodes positive/negative were compared restricting to patients with nodes examined.

Matsuo et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. Am J Obstet Gynecol 2019.