Published in final edited form as:

Obstet Gynecol. 2018 June ; 131(6): 1085–1094. doi:10.1097/AOG.0000000000002613.

Trends in Use and Survival Associated With Fertility-Sparing Trachelectomy for Young Women With Early-Stage Cervical Cancer

Rosa R. Cui, MD¹, Ling Chen, MD, MPH¹, Ana I. Tergas, MD^{1,3,4,5}, June Y. Hou, MD^{1,4,5}, Caryn M. St Clair, MD^{1,4,5}, Alfred I. Neugut, MD, PhD^{2,3,4,5}, Cande V. Ananth, PhD, MPH^{1,3}, Dawn L. Hershman, MD^{2,3,4,5}, and Jason D. Wright, MD^{1,4,5}

¹Department of Obstetrics and Gynecology, Columbia University College of Physicians and Surgeons, New York, NY

²Department of Medicine, Columbia University College of Physicians and Surgeons, New York, NY

³Department of Epidemiology, Joseph L. Mailman School of Public Health, Columbia University, New York, NY

⁴Herbert Irving Comprehensive Cancer Center, Columbia University College of Physicians and Surgeons, New York, NY

⁵New York Presbyterian Hospital, New York, NY

Abstract

Objective—To assess the trends in use of trachelectomy in the United States and to examine the outcomes of the procedure compared to hysterectomy in young women with cervical cancer.

Methods—Data were analyzed from women < 50 years of age with stage IA2-IB2 cervical cancer treated with hysterectomy or trachelectomy from 2004 to 2014 who were registered in the National Cancer Database. After propensity score matching, we used Cox proportional hazards models to examine the association between treatment and survival.

Results—We identified 15,150 cervical cancer patients, including 14,714 (97.1%) who underwent hysterectomy and 436 (2.9%) who underwent trachelectomy. Trachelectomy rates increased from 1.5% in 2004 to 3.8% by 2014 ($P<0.001$). The greatest increase in the rate of trachelectomy was seen in women <30 years of age (4.6% in 2004 to 17.0% in 2014, $P<0.001$). Among women who underwent trachelectomy, 29.6% had tumors >2 cm in diameter. In a multivariable model, younger women and those more recently diagnosed were more likely to

Corresponding Author: Jason D. Wright, M.D., Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Columbia University College of Physicians and Surgeons, 161 Fort Washington Ave, 8th Floor, New York, NY 10032, Telephone: (212) 305-3410, Fax: (212) 305-3412, jw2459@columbia.edu.

Financial Disclosure Dr. Wright has served as a consultant to Tesaro and Clovis Oncology. Dr. Neugut has served as a consultant to Pfizer, Teva, Eisai, Hospira, Otsuka, and United Biosource Corporation. He is on the medical advisory board of EHE, Intl. The other authors did not report any potential conflicts of interest.

Each author has indicated that he or she has met the journal's requirements for authorship.

Presented as poster at the 49th SGO Annual Meeting on Women's Cancer, March 24–27, 2018. New Orleans, LA.

undergo trachelectomy while Medicaid recipients (RR=0.39; 95% CI, 0.28–0.54) and the uninsured (RR=0.67, 95% CI, 0.45–1.00) were less likely to undergo trachelectomy. After propensity-score matching, there was no association between trachelectomy and the risk of mortality (HR=1.24; 95% CI, 0.70–2.22) (mortality rates was 6.0% for hysterectomy vs. 5.2% for trachelectomy). Similarly, 5-year survival rates were similar between trachelectomy and hysterectomy for all of the stages examined.

Conclusions—Use of trachelectomy for early-stage cervical cancer has increased in the U.S., particularly among women younger than 30 years of age. Within this population, survival is similar for trachelectomy and hysterectomy.

Introduction

Early-cervical cancer is traditionally managed surgically with radical hysterectomy (RH) and pelvic lymphadenectomy. For a subset of women who desire future fertility, radical trachelectomy (RTr) with removal of the cervix and preservation of the uterus is an option. Radical trachelectomy was first performed vaginally and has been described using abdominal and minimally invasive approaches as well.^{1,2}

Data comparing RTr versus RH in early-stage cervical cancer patients who desire fertility is currently largely limited to a few single institution studies^{3–7} and one meta-analysis.⁸ These studies demonstrated similar oncologic outcomes between the two techniques. However, these studies were also significant for selection bias based on age^{3–7} and tumor size.^{4,5,7} Currently, the National Comprehensive Cancer Network (NCCN) guidelines suggest that radical trachelectomy is a treatment option for women with early-stage cervical cancers 2cm in diameter with negative lymph nodes. Further, trachelectomy can be considered in select stage IB1 cancers up to 4cm.⁹

Despite the fact that radical trachelectomy has been performed since 1994, little is known about the current patterns of use of the procedure and little population-based data is available to describe the safety of the operation. Using the National Cancer Database (NCDB), we examined the patterns of trachelectomy use in the United States as well as to compare outcomes for women with early-stage cervical cancer undergoing trachelectomy versus hysterectomy.

Materials and Methods

Data from the NCDB were used for analysis. The NCDB is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society Society.¹⁰ NCDB is a nationwide registry that represents approximately 70% of newly diagnosed cases of invasive cancer from over 1500 CoC-affiliated hospitals in the United States. Recorded data include patient demographics, tumor characteristics, treatment, staging, follow-up and survival. The study utilized de-identified data and was deemed exempt by the Columbia University Institutional Review Board.

We included women diagnosed with cervical cancer who were less than 50 years of age between 2004 and 2014 with FIGO stage IA2 to IB2 treated with hysterectomy or

trachelectomy, given the rationale that fertility-sparing trachelectomy is offered only to patients with early-stage cervical cancer. Demographic information of interest included age (<30, 30–39, 40–49 years), race and ethnicity (white, black, Hispanic, other, unknown), year of diagnosis, insurance status (private, Medicare, Medicaid, other, uninsured, unknown), and income (<\$38,000, \$38,000–47,999, \$48,000–62,999, ≥\$63,000, unknown). Medical comorbidities were estimated using the Deyo classification of the Charlson comorbidity score (0, 1, 2). Hospital characteristics included location (metropolitan, urban, rural, unknown), facility type based on the CoC criteria (academic/research, community cancer programs, comprehensive community cancer programs), and geographic location (Northeast, Midwest, South, West, unknown). Tumor data included stage, histology, grade, and tumor size (<20mm, 20–40mm, 41–60mm, >60mm, unknown).

Categorical variables were reported as frequencies and compared using χ^2 tests. Trends of trachelectomy were reported graphically and compared using Cochran-Armitage tests. To examine factors associated with trachelectomy, generalized estimating equations were fitted including all patient and hospital characteristics and accounting for hospital-level clustering. Associations were reported as adjusted risk ratios and 95% confidence intervals. Kaplan-Meier curves were plotted and compared using log-rank tests. To examine the association between treatments and survival, we fit marginal Cox proportional hazard models adjusted for treatment, patient and hospital characteristics, and accounting for hospital-level clustering. We also fit separate models stratified by stage or tumor size. The associations were reported as adjusted hazard ratios and 95% confidence intervals with the hysterectomy group as the referent group.

To reduce the influence of observed confounding on treatment selection, we developed a matched propensity score (PS) analysis. The propensity score was estimated as the probability that a patient had trachelectomy. A series of multivariable logistic regression models were constructed and assessed based on the goodness of fit. The final model included all patient and hospital characteristics and two-way interaction terms with a *P*-value of <0.15.

Each patient's propensity score was calculated from the model, and then a Greedy 5-to-1 match was performed with a case to control ratio of 1:2. Mortality was compared between the PS-matched groups using Kaplan-Meier curves and five-year survival rates with log-rank tests. Marginal Cox proportional hazard models in the PS-matched groups were fitted to examine the association and reported as hazard ratios and 95% confidence intervals. A sensitivity analysis using marginal Cox proportional hazard models in the unmatched cohort was also performed. All analyses were conducted using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina). All hypothesis testing was two-sided and a *P*-value of <0.05 was considered statistically significant.

Results

We identified a total of 15,150 patients from 981 hospitals with stage IA2 to IB2 cervical cancer including 14,714 (97.1%) who underwent hysterectomy and 436 (2.9%) who underwent trachelectomy (Table 1). The median follow-up time was 54 months (IQR, 29–83

months) for those who underwent hysterectomy and 47 months (IQR, 26–72 months) for women who had trachelectomy. Performance of trachelectomy increased from 1.5% (95% CI, 0.8–2.2%) in 2004 to 3.8% (95% CI, 2.7–4.8%) by 2014 ($P<0.001$) (Figure 1A). The increased use of trachelectomy was most pronounced in women <30 years of age. In this age group, trachelectomy increased from 4.6% (95% CI, 1.0–8.2%) in 2004 to 17.0% (95% CI, 10.2–23.7%) in 2014 ($P<0.001$) (Figure 1B). The rates of trachelectomy in women age 30–39 ($P=0.13$) and 40–49 ($P=0.07$) remained relatively stable over the course of the study period.

The majority of trachelectomies were performed in women with IB1 tumors (Table 1). Among women with tumors <20 mm in diameter, 3.8% of women underwent trachelectomy. Trachelectomy was performed in 2.1% of patients with tumors that were 20–40 mm and in 1.0% of those with tumors 41–60 mm in greatest dimension.

In the multivariable model, younger women and those diagnosed more recently were more likely to undergo trachelectomy (Table 2). Non-black, non-Hispanic women (RR 1.59; 95% CI, 1.07–2.35) were more likely than white women to undergo trachelectomy, while Medicaid recipients (RR=0.39; 95% CI, 0.28–0.54) and uninsured women (RR=0.67, 95% CI, 0.45–0.9994) were less likely than those with commercial insurance to undergo trachelectomy. Women with larger, more advanced stage tumors were less likely to undergo trachelectomy, whereas women with higher grade tumors were less likely ($P<0.05$ for all). Women with adenocarcinomas were 48% more likely to undergo trachelectomy (RR 1.48; 95% CI, 1.19–1.85) than those with squamous cell tumors.

After propensity score matching, the clinical and demographic characteristics were relatively well balanced between the groups (Table 1). Among all patients, there was no association between trachelectomy and increased risk of mortality (HR 1.24; 95% CI, 0.70–2.22). Similar findings were noted for women with stage IB1 (HR 1.59; 95% CI, 0.63–3.99) and IB NOS (HR 1.09; 95% CI, 0.43–2.77) tumors (Table 3). Five-year survival rates for the overall cohort for hysterectomy and trachelectomy were 92.4% (95% CI, 89.7–94.4) and 92.3% (95% CI 88.5–94.9, $P=0.70$), respectively (Table 4). Subgroup analyses also showed similar 5-year survival rates for women who underwent hysterectomy and trachelectomy for those with stage IA2 tumors (95.4%, 95% CI 82.6–98.9%, vs. 96.6%, 95% CI 77.9–99.5%, respectively, $P=0.95$), IB1 tumors (92.1%, 95% CI 88.2–94.8%, versus 93.6%, 95% CI 88.0–96.6%, respectively, $P=0.44$), and IBNOS neoplasms (92.8%, 95% CI 87.8–95.8%, vs. 92.7%, 95% CI 85.2–96.4%, respectively, $P=0.81$). Figure 2 shows the Kaplan-Meier survival curves of the propensity-matched patients. Data for stage IB2 were excluded due to its small sample size.

In a sensitivity analysis examining the unmatched cohort, we noted similar trends (Table 5). There was no association between the performance of trachelectomy and survival (HR 0.94; 95% CI, 0.58–1.53). The findings were largely unchanged for sub-group analyses limited to each particular stage.

Discussion

These data suggest that the use of trachelectomy in the United States has increased between 2004 and 2014, particularly among women under the age of 30 in whom the rate more than tripled during this time period. A possible explanation for this rise in trachelectomy is the trend in delayed childbearing in women in the United States¹¹. In the main propensity score matched analysis and a sensitivity analysis utilizing covariate adjusted survival models, we observed similar mortality hazards among women who underwent trachelectomy and hysterectomy.

The majority of previous studies examining outcomes of radical trachelectomy versus radical hysterectomy for early-stage cervical cancer patients were limited to single-institution series^{3–7}. Although these studies were heterogeneous in surgical approach and inclusion criteria of cancer stage, all found similar oncologic outcomes for RTr and RH in early-stage cervical cancer patients. A systematic review of three single-institution, prospectively controlled clinical trials by Xu and coworkers that included 587 patients with early-stage cervical cancer found similar survival outcomes comparing radical hysterectomy to radical trachelectomy (recurrence rate: OR 1.38, 95% CI, 0.58–3.28; 5-year recurrence free survival: OR 1.17, 95% CI, 0.54–2.53, 5-year overall survival: OR 0.83, 95% CI, 0.30–2.43).⁸ No differences were found in the intra-operative and post-operative complication rates; however, radical trachelectomy was associated with less blood loss and decreased length of stay compared to radical hysterectomy.⁸

In line with current NCCN guidelines, increasing tumor size was associated with decreased likelihood of undergoing trachelectomy (size 2–4cm: RR 0.61, size 4.1–6cm: RR 0.46). Nevertheless, our study shows that 30% of all trachelectomies were performed for women with tumors greater than 2 cm in diameter, including 4% for women with tumors greater than 4cm in diameter. While 2 cm is often considered as a cutoff for the upper limit of tumor size for vaginal trachelectomy, several studies have suggested the oncologic safety of abdominal radical trachelectomy in women with tumors between 2–4 cm given the wider parametrial resection through an abdominal approach compared to a vaginal approach.^{12–15} The largest series with a total of 62 cases from China, found that fertility potential was preserved in 89% of patients, and 5-year recurrence free survival and overall survival were similar between abdominal RTr and abdominal RH patients.¹² However, over one-third of patients in each group received adjuvant chemotherapy for high-risk features.¹² While we noted no statistically significant decrease in survival for trachelectomy in women with tumors >2 cm, our sample size was relatively small. More data is clearly needed in these women and at present, use of trachelectomy should be approached with caution.

Somewhat surprisingly, we found that women with adenocarcinomas were more likely than those with squamous cell tumors to undergo radical trachelectomy. Those women with visible lesions on the ectocervix are generally thought to be the most appropriate candidates for trachelectomy. The more frequent performance of trachelectomy in women with adenocarcinomas may reflect the younger age of diagnosis in these patients. While these data are encouraging that trachelectomy did not adversely effect survival in those with

adenocarcinomas, our study included a relatively small subset of these women who underwent trachelectomy and thus should be interpreted with caution.

Our study has several important limitations. First, the sample size is limited by the small number of patients who undergo radical trachelectomy, and this study may be underpowered to detect small differences in survival. Although the NCDB database captures significant breadth of information on cervical cancer care in the United States, it does not provide data on recurrence or type of chemotherapy used in patients. As a result, overall survival was the only available endpoint, and other outcomes data on disease-specific survival, local and distal failure rates, and treatment-related toxicity were unable to be assessed. Furthermore, approximately 30% of the patient cohort was classified as stage IB NOS, which makes it difficult to draw conclusions generalizable to the IB1 population. In addition, it is not known how many women received neoadjuvant chemotherapy, which may have implications on survival in patients with larger tumors. Likewise, further data is needed on the role of neoadjuvant chemotherapy in young women with cervical cancer and we did not include this variable in the analysis. Propensity score matching was utilized to reduce the influence of selection bias; however, we cannot control for unmeasured confounders, and the large imbalances of patient and disease characteristics resulted in a propensity score model that only matched a subset of patients. We acknowledge that the findings may be confounded by the selection of patients undergoing trachelectomy who had unmeasured prognostic factors contributing to improved outcomes. Lastly, the NCDB lacks data on fertility outcomes after trachelectomy, which would be of great interest in future studies.

There has been increased interest in less radical surgical approaches for women with early-stage cervical cancer. The trachelectomy procedure has evolved significantly since it was initially described and now encompasses several approaches. In patients with early-stage cervical cancer with larger tumors or other high-risk factors such as the positive LVSI, or deep stromal invasion, options of neoadjuvant and adjuvant therapy may allow the performance of a fertility-sparing procedure. Conversely, patients with low-risk, low-volume early-stage cervical cancers may be carefully selected to undergo even more conservative fertility-sparing surgery, such as simple trachelectomy with or without pelvic lymphadenectomy or cervical conization in order to minimize the morbidity of parametrial dissection without compromising outcomes.¹⁶ Our data suggest that trachelectomy does not adversely affect survival for appropriately selected women with stage I cervical cancer and supports consideration of the procedure in women who desire fertility preservation.

Acknowledgments

Dr. Wright (NCI R01CA169121-01A1) and Dr. Hershman (NCI R01 CA166084) are recipients of grants and Dr. Tergas is the recipient of a fellowship (NCI R25 CA094061-11) from the National Cancer Institute.

References

1. Bentivegna E, Gouy S, Maulard A, Chargari C, Leary A, Morice P. Oncological outcomes after fertility-sparing surgery for cervical cancer: a systematic review. *Lancet Oncol.* 2016; 17:e240–e53. [PubMed: 27299280]

2. Dargent D, Martin X, Sacchetoni A, Mathevet P. Laparoscopic vaginal radical trachelectomy: a treatment to preserve the fertility of cervical carcinoma patients. *Cancer*. 2000; 88:1877–82. [PubMed: 10760765]
3. Beiner ME, Hauspy J, Rosen B, et al. Radical vaginal trachelectomy vs. radical hysterectomy for small early stage cervical cancer: a matched case-control study. *Gynecol Oncol*. 2008; 110:168–71. [PubMed: 18539313]
4. Diaz JP, Sonoda Y, Leitaio MM, et al. Oncologic outcome of fertility-sparing radical trachelectomy versus radical hysterectomy for stage IB1 cervical carcinoma. *Gynecol Oncol*. 2008; 111:255–60. [PubMed: 18755500]
5. Marchiole P, Benchaib M, Buenerd A, Lazlo E, Dargent D, Mathevet P. Oncological safety of laparoscopic-assisted vaginal radical trachelectomy (LARVT or Dargent's operation): a comparative study with laparoscopic-assisted vaginal radical hysterectomy (LARVH). *Gynecol Oncol*. 2007; 106:132–41. [PubMed: 17493666]
6. van Gent MD, van den Haak LW, Gaarenstroom KN, et al. Nerve-sparing radical abdominal trachelectomy versus nerve-sparing radical hysterectomy in early-stage (FIGO IA2-IB) cervical cancer: a comparative study on feasibility and outcome. *Int J Gynecol Cancer*. 2014; 24:735–43. [PubMed: 24651626]
7. Zhang D, Li J, Ge H, et al. Surgical and pathological outcomes of abdominal radical trachelectomy versus hysterectomy for early-stage cervical cancer. *Int J Gynecol Cancer*. 2014; 24:1312–8. [PubMed: 24987922]
8. Xu L, Sun FQ, Wang ZH. Radical trachelectomy versus radical hysterectomy for the treatment of early cervical cancer: a systematic review. *Acta Obstet Gynecol Scand*. 2011; 90:1200–9. [PubMed: 21718255]
9. The National Cancer Database. Accessed at <https://www.facs.org/quality-programs/cancer/ncdb>
10. Bilimoria KY, Stewart AK, Winchester DP, Ko CY. The National Cancer Data Base: a powerful initiative to improve cancer care in the United States. *Ann Surg Oncol*. 2008; 15:683–90. [PubMed: 18183467]
11. Hamilton BE, Martin JA, Osterman MJ, Curtin SC, Matthews TJ. Births: Final Data for 2014. *Natl Vital Stat Rep*. 2015; 64:1–64.
12. Li J, Wu X, Li X, Ju X. Abdominal radical trachelectomy: Is it safe for IB1 cervical cancer with tumors ≥ 2 cm? *Gynecol Oncol*. 2013; 131:87–92. [PubMed: 23872192]
13. Li X, Li J, Wen H, et al. The Survival Rate and Surgical Morbidity of Abdominal Radical Trachelectomy Versus Abdominal Radical Hysterectomy for Stage IB1 Cervical Cancer. *Ann Surg Oncol*. 2016; 23:2953–8. [PubMed: 27044448]
14. Lintner B, Saso S, Tarnai L, et al. Use of abdominal radical trachelectomy to treat cervical cancer greater than 2 cm in diameter. *Int J Gynecol Cancer*. 2013; 23:1065–70. [PubMed: 23722476]
15. Wethington SL, Sonoda Y, Park KJ, et al. Expanding the indications for radical trachelectomy: a report on 29 patients with stage IB1 tumors measuring 2 to 4 centimeters. *Int J Gynecol Cancer*. 2013; 23:1092–8. [PubMed: 23714706]
16. Baiocchi G, de Brot L, Faloppa CC, et al. Is parametrectomy always necessary in early-stage cervical cancer? *Gynecol Oncol*. 2017; 146:16–9. [PubMed: 28392128]

Figure 1.

Percentage of trachelectomy overall (**A**) ($P < .001$) and stratified by age group (**B**). Error bars represent 95% confidence interval ($P < .001$ for <30 years of age; $P = .13$ for 30–39 years of age, 0.13; $P = .07$ for 40–49 years of age). P values calculated using Cochrane-Armitage trend tests.

Figure 2.

Kaplan-Meier curves of the 2:1 propensity score matched cohort overall (**A**) (N=1,139, trachelectomy: n=379, hysterectomy: n=76, $P=.70$); stage 1A2 (**B**) (n=109, trachelectomy: n=37, hysterectomy: n=72; $P=.95$); stage 1B1 (**C**) (n=677, trachelectomy: n=226, hysterectomy: n=451; $P=.44$); stage 1B not otherwise specified (**D**) (n=332, trachelectomy: n=108, hysterectomy: n=224; $P=.81$). P values derived from log-rank tests.

Table 1

Demographics and clinical characteristics of the cohort and the propensity-score-matched cohort.

	All				Propensity score matched cohort				
	Hysterectomy		Trachelectomy		P-value	Hysterectomy		Trachelectomy	
	N	(%)	N	(%)		N	(%)	N	(%)
All	14,714	(97.1)	436	(2.9)		854	(66.7)	427	(33.3)
Propensity score (mean, SD)	-	-	-	-	-	0.096	(0.090)	0.096	(0.091)
Age					<0.001				0.01
<30	1,295	(8.8)	154	(35.3)		287	(33.6)	145	(34.0)
30-39	6,259	(42.5)	222	(50.9)		448	(52.5)	222	(52.0)
40-49	7,160	(48.7)	60	(13.8)		119	(13.9)	60	(14.1)
Race					<0.001				0.04
White	10,119	(68.8)	321	(73.6)		620	(72.6)	313	(73.3)
Black	1,469	(10.0)	*	*		43	(5.0)	*	*
Hispanic	2,193	(14.9)	52	(11.9)		102	(11.9)	52	(12.2)
Other	719	(4.9)	34	(7.8)		78	(9.1)	34	(8.0)
Unknown	214	(1.5)	*	*		11	(1.3)	*	*
Year of diagnosis					0.001				0.17
2004	1,229	(8.4)	19	(4.4)		43	(5.0)	19	(4.4)
2005	1,341	(9.1)	24	(5.5)		58	(6.8)	24	(5.6)
2006	1,408	(9.6)	35	(8.0)		76	(8.9)	35	(8.2)
2007	1,332	(9.1)	33	(7.6)		70	(8.2)	32	(7.5)
2008	1,339	(9.1)	42	(9.6)		67	(7.8)	42	(9.8)
2009	1,348	(9.2)	56	(12.8)		82	(9.6)	55	(12.9)
2010	1,393	(9.5)	46	(10.6)		92	(10.8)	46	(10.8)
2011	1,365	(9.3)	48	(11.0)		88	(10.3)	47	(11.0)
2012	1,388	(9.4)	45	(10.3)		86	(10.1)	43	(10.1)
2013	1,293	(8.8)	38	(8.7)		98	(11.5)	36	(8.4)
2014	1,278	(8.7)	50	(11.5)		94	(11.0)	48	(11.2)
Insurance status					<0.001				0.08
Private	9,802	(66.6)	359	(82.3)		693	(81.1)	350	(82.0)

	All						Propensity score matched cohort					
	Hysterectomy			Trachelectomy			Hysterectomy			Trachelectomy		
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Medicare	354	(2.4)	*	*	19	(2.2)	*	*	40	(9.4)	*	*
Medicaid	2,890	(19.6)	40	(9.2)	80	(9.4)	*	*	*	*	*	*
Other	227	(1.5)	*	*	48	(5.6)	23	(5.4)	*	*	*	*
Uninsured	1,128	(7.7)	23	(5.3)	*	*	*	*	*	*	*	*
Unknown	313	(2.1)	*	*	<0.001		*	*	*	*	*	*
Income												0.06
<\$38,000	2,907	(19.8)	*	*	155	(18.1)	73	(17.1)				
\$38,000–\$47,999	3,656	(24.8)	73	(16.7)	252	(29.5)	133	(31.1)				
\$48,000–\$62,999	3,822	(26.0)	136	(31.2)	339	(39.7)	166	(38.9)				
\$63,000+	4,185	(28.4)	170	(39.0)	*	*	*	*				
Unknown	144	(1.0)	*	*	814	(95.3)	405	(94.8)				
Comorbidity					0.08							0.07
0	13,486	(91.7)	411	(94.3)	*	*	*	*				
1	1,071	(7.3)	*	*	*	*	*	*				
2	157	(1.1)	*	*	<0.001		*	*				
Urban/Rural												0.05
Metropolitan	11,891	(80.8)	390	(89.4)	766	(89.7)	383	(89.7)				
Urban	2,137	(14.5)	33	(7.6)	61	(7.1)	33	(7.7)				
Rural	227	(1.5)	*	*	*	*	*	*				
Unknown	459	(3.1)	*	*	*	*	*	*				
Facility type					<0.001							0.03
Academic/research	3,388	(23.0)	31	(7.1)	57	(6.7)	31	(7.3)				
Community cancer	380	(2.6)	*	*	*	*	*	*				
Comprehensive community cancer	2,548	(17.3)	*	*	*	*	*	*				
Integrated network cancer	844	(5.7)	*	*	*	*	*	*				
Other/unknown	7,554	(51.3)	376	(86.2)	735	(86.1)	367	(85.9)				
Facility location					<0.001							0.08
Northeast	1,209	(8.2)	15	(3.4)	22	(2.6)	15	(3.5)				
Midwest	1,690	(11.5)	10	(2.3)	26	(3.0)	10	(2.3)				

	All						Propensity score matched cohort					
	Hysterectomy			Trachelectomy			Hysterectomy			Trachelectomy		
	N	(%)	N	(%)	P-value		N	(%)	N	(%)	Standardized difference	
South	2,854	(19.4)	20	(4.6)			45	(5.3)	20	(4.7)		
West	1,407	(9.6)	15	(3.4)			26	(3.0)	15	(3.5)		
Unknown	7,554	(51.3)	376	(86.2)			735	(86.1)	367	(85.9)		
<i>Stage</i>					<0.001						0.05	
1A2	1,301	(8.8)	45	(10.3)			85	(10.0)	45	(10.5)		
1B1	7,385	(50.2)	268	(61.5)			524	(61.4)	260	(60.9)		
1B2	1,284	(8.7)	10	(2.3)			15	(1.8)	10	(2.3)		
1B NOS	4,744	(32.2)	113	(25.9)			230	(26.9)	112	(26.2)		
<i>Histology</i>					<0.001						0.03	
Squamous cell	7,890	(53.6)	188	(43.1)			375	(43.9)	186	(43.6)		
Adenosquamous	805	(5.5)	26	(6.0)			47	(5.5)	26	(6.1)		
Adenocarcinoma	4,759	(32.3)	190	(43.6)			363	(42.5)	183	(42.9)		
Other	1,260	(8.6)	32	(7.3)			69	(8.1)	32	(7.5)		
<i>Grade</i>					0.03						0.04	
1	2,444	(16.6)	71	(16.3)			140	(16.4)	70	(16.4)		
2	6,144	(41.8)	193	(44.3)			374	(43.8)	188	(44.0)		
3	4,354	(29.6)	105	(24.1)			197	(23.1)	103	(24.1)		
Unknown	1,772	(12.0)	67	(15.4)			143	(16.7)	66	(15.5)		
<i>Tumor size</i>					<0.001						0.07	
<20 mm	5,446	(37.0)	214	(49.1)			409	(47.9)	206	(48.2)		
20–40 mm	5,056	(34.4)	110	(25.2)			236	(27.6)	110	(25.8)		
41–60 mm	1,515	(10.3)	*	*			*	*	*	*		
>60 mm	439	(3.0)	*	*			*	*	*	*		
Unknown	2,258	(15.3)	93	(21.3)			178	(20.8)	92	(21.5)		
<i>Regional nodes examined[#]</i>					0.51						–	
None	1,266	(8.6)	32	(7.3)			62	(7.3)	32	(7.5)		
Yes	13,407	(91.1)	402	(92.2)			789	(92.4)	393	(92.0)		
Unknown	41	(0.3)	*	*			*	*	*	*		
<i>Radiation[#]</i>					<0.001						–	

	All				Propensity score matched cohort				
	Hysterectomy		Trachelectomy		P-value	Hysterectomy		Trachelectomy	
	N	(%)	N	(%)		N	(%)	N	(%)
None/unknown	10,809	(73.5)	386	(88.5)	<0.001	675	(79.0)	377	(88.3)
Yes	3,905	(26.5)	50	(11.5)		179	(21.0)	50	(11.7)
Chemotherapy [#]									—
No/unknown	11,831	(80.4)	389	(89.2)		714	(83.6)	380	(89.0)
Yes	2,883	(19.6)	47	(10.8)		140	(16.4)	47	(11.0)

* Suppress reporting because some cell sizes <10.

Logistic regression model was fitted to calculate the propensity score, including age, race, year of diagnosis, insurance status, income, comorbidity, urban/rural, facility type, facility location, stage, histology, grade, tumor size and all possible two-way interactions. The Greedy 5-to-1 match algorithm was used to match hysterectomy patients to trachelectomy patients at 2:1 ratio.

[#] Variables not included in the propensity score model.

Table 2

Multivariable model of predictors of trachelectomy.

	RR
<i>Age</i>	
<30	Referent
30–39	0.27 (0.22–0.32) *
40–49	0.08 (0.04–0.16) *
<i>Race</i>	
White	Referent
Black	0.69 (0.46–1.02)
Hispanic	0.91 (0.68–1.21)
Other	1.59 (1.07–2.35) *
Unknown	1.05 (0.44–2.49)
<i>Year of Diagnosis</i>	
1 year increase	1.06 (1.01–1.12) *
<i>Insurance</i>	
Private	Referent
Medicare	0.61 (0.29–1.31)
Medicaid	0.39 (0.28–0.54) *
Other	0.45 (0.18–1.14)
Uninsured	0.67 (0.45–0.9994) *
Unknown	0.39 (0.13–1.14)
<i>Income</i>	
<\$38,000	Referent
\$38,000–\$47,999	0.88 (0.64–1.21)
\$48,000–\$62,999	1.40 (1.002–1.97) *
\$63,000+	1.44 (0.997–2.07)
Unknown	1.94 (0.69–5.47)
<i>Comorbidity</i>	
0	Referent
1	0.91 (0.64–1.30)
2	0.40 (0.06–2.87)
<i>Urban/Rural</i>	
Metropolitan	Referent
Urban	0.58 (0.40–0.83) *
Rural	0.58 (0.19–1.78)
Unknown	0.56 (0.26–1.23)
<i>Facility location</i>	
Northeast	Referent
Midwest	0.55 (0.20–1.52)
South	0.70 (0.28–1.74)

RR	
West	0.89 (0.34–2.32)
Unknown	–‡
<i>Stage</i>	
1B1	Referent
1A2	0.87 (0.64–1.18)
1B2	0.41 (0.22–0.76) *
1B NOS	0.80 (0.54–1.17)
<i>Histology</i>	
Squamous cell	Referent
Adenosquamous	1.41 (0.97–2.05)
Adenocarcinoma	1.48 (1.19–1.85) *
Other cell	1.00 (0.68–1.48)
<i>Grade</i>	
1	Referent
2	1.40 (1.04–1.88) *
3	1.14 (0.85–1.53)
Unknown	1.40 (0.99–1.99)
<i>Tumor size</i>	
<20 mm	Referent
20–40 mm	0.61 (0.49–0.76) *
41–60 mm	0.46 (0.28–0.78) *
>60 mm	0.31 (0.09–1.02)
Unknown	1.15 (0.91–1.46)

Generalized estimating equation (GEE) was fitted in the overall cohort including age, race, year of diagnosis, insurance status, income, comorbidity, urban/rural, facility location, stage, histology, grade, tumor size accounting for facility-level clustering. Facility type was not included as a covariate in the GEE because of convergence issue.

* *P*-value <0.05

Table 3

The association between trachelectomy and mortality in the propensity score matched cohort.

	All HR	Stage 1A2 HR	Stage 1B1 HR	Stage 1B NOS HR
<i>Treatment</i>				
Hysterectomy	Referent	Referent	Referent	Referent
Trachelectomy	1.24 (0.70–2.22)	$\neq$	1.59 (0.63–3.99)	1.09 (0.43–2.77)

HR: hazard ratio. The overall mortality rate was 6.0% in women who underwent hysterectomy vs. 5.2% in those who underwent trachelectomy.

142 patients in the matched cohort with missing follow-up time and vital status were excluded (N=1139).

$\neq$ Non-estimable

Table 4

Five-year survival rates of the propensity score matched cohort

	Propensity score 2:1 matched cohort		
	Hysterectomy	Trachelectomy	<i>p</i> -value
	5-year survival rate (95% CI)	5-year survival rate (95% CI)	
<i>All</i>	92.4 (89.7–94.4)	92.3 (88.5–94.9)	0.70
<i>Stage 1A2</i>	95.4 (82.6–98.9)	96.6 (77.9–99.5)	0.95
<i>Stage 1B1</i>	92.1 (88.2–94.8)	93.6 (88.0–96.6)	0.44
<i>Stage 1B NOS</i>	92.8 (87.8–95.8)	92.7 (85.2–96.4)	0.81

The overall mortality rate was 6.0% in women who underwent hysterectomy vs. 5.2% in those who underwent trachelectomy.

142 patients in the matched cohort with missing follow-up time and vital status were not included.

Table 5

Multivariable models of predictors of mortality.

	All aHR	Stage 1A2 aHR	Stage 1B1 aHR	Stage 1B2 aHR	Stage 1B NOS aHR
<i>Age</i>					
<30	Referent	Referent	Referent	Referent	Referent
30–39	0.72 (0.59–0.87)*	0.20 (0.05–0.75)*	0.74 (0.55–1.01)	0.62 (0.41–0.95)*	0.75 (0.53–1.06)
40–49	0.63 (0.46–0.86)*	0.56 (0.06–4.99)	0.84 (0.55–1.31)	0.40 (0.21–0.76)*	0.53 (0.30–0.92)*
<i>Race</i>					
White	Referent	Referent	Referent	Referent	Referent
Black	1.25 (1.04–1.51)*	1.85 (0.46–7.46)	1.30 (0.94–1.79)	1.33 (0.87–2.02)	1.14 (0.86–1.51)
Hispanic	0.64 (0.52–0.79)*	0.45 (0.07–2.97)	0.55 (0.38–0.80)*	1.01 (0.68–1.51)	0.59 (0.43–0.80)*
Other	1.29 (0.98–1.70)	0.37 (0.04–3.84)	1.39 (0.92–2.10)	1.67 (0.84–3.32)	1.19 (0.78–1.82)
Unknown	0.77 (0.43–1.36)	—	0.74 (0.30–1.86)	0.98 (0.26–3.69)	0.69 (0.28–1.73)
<i>Year of Diagnosis</i>					
1 year increase	1.04 (1.01–1.06)*	1.16 (0.94–1.44)	1.07 (1.02–1.11)*	1.01 (0.95–1.07)	1.03 (0.98–1.08)
<i>Insurance</i>					
Private	Referent	Referent	Referent	Referent	Referent
Medicare	2.06 (1.58–2.70)*	—	2.18 (1.34–3.55)*	1.13 (0.47–2.67)	2.51 (1.69–3.73)*
Medicaid	1.13 (0.98–1.31)	3.24 (1.13–9.32)*	1.18 (0.94–1.50)	0.89 (0.61–1.29)	1.13 (0.88–1.44)
Other	0.89 (0.51–1.56)	—	0.67 (0.26–1.71)	1.45 (0.45–4.61)	1.00 (0.46–2.22)
Uninsured	0.91 (0.71–1.17)	2.74 (0.68–11.04)	0.96 (0.63–1.47)	0.65 (0.37–1.16)	0.93 (0.65–1.34)
Unknown	0.53 (0.31–0.92)*	—	0.96 (0.35–2.60)	1.01 (0.22–4.65)	0.38 (0.22–0.68)*
<i>Income</i>					
<\$38,000	Referent	Referent	Referent	Referent	Referent
\$38,000–\$47,999	0.88 (0.75–1.03)	0.42 (0.13–1.35)	0.87 (0.66–1.16)	0.78 (0.50–1.22)	0.97 (0.75–1.24)
\$48,000–\$62,999	0.83 (0.69–0.99)*	0.43 (0.12–1.57)	0.79 (0.59–1.06)	1.09 (0.73–1.64)	0.79 (0.59–1.06)
\$63,000+	0.74 (0.61–0.89)*	0.25 (0.03–2.05)	0.75 (0.55–1.01)	0.78 (0.52–1.17)	0.74 (0.54–1.004)
Unknown	2.23 (1.43–3.47)*	4.61 (0.62–34.43)	2.52 (1.26–5.01)*	0.45 (0.08–2.63)	2.65 (1.37–5.14)*

	All	Stage 1A2	Stage 1B1	Stage 1B2	Stage 1B NOS
	aHR	aHR	aHR	aHR	aHR
<i>Comorbidity</i>					
0	Referent	Referent	Referent	Referent	Referent
1	1.18 (0.96–1.46)	0.99 (0.23–4.31)	1.22 (0.89–1.67)	0.90 (0.51–1.58)	1.27 (0.90–1.80)
2	1.76 (1.16–2.66)*	1.34 (0.09–20.05)	1.57 (0.73–3.40)	1.73 (0.56–5.36)	2.05 (1.03–4.09)*
<i>Urban/Rural</i>					
Metropolitan	Referent	Referent	Referent	Referent	Referent
Urban	1.16 (0.97–1.39)	0.92 (0.24–3.51)	1.15 (0.88–1.51)	0.98 (0.65–1.47)	1.25 (0.95–1.63)
Rural	1.29 (0.83–2.01)	1.82 (0.34–9.86)	0.97 (0.42–2.25)	1.50 (0.60–3.77)	1.63 (0.89–2.99)
Unknown	1.32 (0.97–1.79)	1.90 (0.30–11.85)	1.44 (0.82–2.54)	1.85 (1.01–3.40)*	1.12 (0.69–1.80)
<i>Facility</i>					
Academic/research	Referent	Referent	Referent	Referent	Referent
Community cancer	1.07 (0.75–1.52)	0.83 (0.05–12.96)	1.58 (0.83–2.99)	0.80 (0.34–1.86)	0.90 (0.51–1.59)
Comprehensive community cancer	0.96 (0.77–1.20)	1.11 (0.25–4.91)	1.06 (0.75–1.50)	0.79 (0.48–1.30)	0.96 (0.70–1.31)
Integrated network cancer	1.13 (0.84–1.53)	0.99 (0.24–4.00)	1.17 (0.76–1.80)	1.35 (0.68–2.67)	1.01 (0.63–1.62)
Other/unknown	≠	≠	≠	≠	≠
<i>Location</i>					
Northeast	Referent	Referent	Referent	Referent	Referent
Midwest	0.99 (0.70–1.39)	0.95 (0.13–6.95)	0.80 (0.50–1.28)	1.47 (0.73–2.96)	1.03 (0.59–1.78)
South	1.22 (0.90–1.66)	1.53 (0.22–10.50)	0.89 (0.57–1.39)	1.38 (0.73–2.60)	1.64 (1.01–2.65)*
West	1.21 (0.86–1.70)	≠	0.78 (0.45–1.36)	1.51 (0.74–3.06)	1.66 (0.98–2.83)
Unknown	≠	≠	≠	≠	≠
<i>Stage</i>					
1B1	Referent	–	–	–	–
1A2	0.46 (0.31–0.67)*	–	–	–	–
1B2	1.40 (1.14–1.71)*	–	–	–	–
1B NOS	1.29 (1.11–1.49)*	–	–	–	–
<i>Histology</i>					
Squamous cell	Referent	Referent	Referent	Referent	Referent
Adenosquamous	1.39 (1.11–1.74)*	6.42 (1.27–32.41)*	1.60 (1.12–2.29)*	1.28 (0.76–2.17)	1.24 (0.88–1.75)

	All	Stage 1A2	Stage 1B1	Stage 1B2	Stage 1B NOS
	aHR	aHR	aHR	aHR	aHR
Adenocarcinoma	0.89 (0.76–1.04)	0.46 (0.12–1.70)	0.83 (0.66–1.06)	1.16 (0.77–1.74)	0.88 (0.69–1.13)
Other	1.40 (1.16–1.69)*	0.94 (0.18–4.83)	1.71 (1.27–2.29)*	1.29 (0.84–1.97)	1.14 (0.85–1.53)
Grade					
1	Referent	Referent	Referent	Referent	Referent
2	1.84 (1.43–2.38)*	1.07 (0.21–5.40)	1.71 (1.13–2.60)*	3.85 (1.53–9.70)*	1.69 (1.17–2.44)*
3	2.59 (1.96–3.43)*	3.08 (0.45–20.94)	2.42 (1.54–3.79)*	6.09 (2.45–15.15)*	2.13 (1.43–3.17)*
Unknown	1.34 (0.97–1.87)	1.84 (0.30–11.10)	1.14 (0.62–2.08)	4.26 (1.54–11.73)*	1.14 (0.73–1.80)
Tumor size					
<20 mm	Referent	Referent	Referent	Referent	Referent
20–40 mm	2.10 (1.78–2.48)*	3.27 (0.61–17.39)	1.95 (1.54–2.47)*	2.68 (0.82–8.69)	2.24 (1.75–2.86)*
41–60 mm	3.27 (2.62–4.09)*	≠	3.17 (2.13–4.71)*	2.93 (0.95–8.99)	4.32 (3.20–5.83)*
>60 mm	4.13 (3.14–5.45)*	5.27 (0.47–59.35)	4.33 (2.41–7.80)*	4.15 (1.32–13.09)*	4.71 (3.05–7.27)*
Unknown	1.72 (1.38–2.14)*	1.36 (0.48–3.86)	1.39 (0.96–2.01)	4.83 (1.41–16.59)*	1.80 (1.35–2.42)*
Treatment					
Hysterectomy	Referent	Referent	Referent	Referent	Referent
Trachelectomy	0.94 (0.58–1.53)	2.57 (0.26–25.76)	0.93 (0.51–1.69)	2.35 (0.80–6.92)	0.82 (0.35–1.93)

1330 patients with missing follow-up time and vital status were excluded.

Marginal Cox proportional hazard models were fitted for the overall cohort, and for each stage separately. The models included age, race, year of diagnosis, insurance status, income, comorbidity, urban/rural, facility type, facility location, stage, histology, grade, tumor size and accounted for facility-level clustering.

aHR: adjusted hazard ratio

≠ Non-estimable

* *P*-value <0.05