Published in final edited form as:

Gynecol Oncol. 2014 January ; 132(1): 254–259. doi:10.1016/j.ygyno.2013.09.004.

Management of low-risk early-stage cervical cancer: Should conization, simple trachelectomy, or simple hysterectomy replace radical surgery as the new standard of care?

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Abstract

The standard treatment for women with early-stage cervical cancer (IA2-IB1) remains radical hysterectomy with pelvic lymphadenectomy. In select patients interested in future fertility, the option of radical trachelectomy with pelvic lymphadenectomy is also considered a viable option. The possibility of less radical surgery may be appropriate not only for patients desiring to preserve fertility but also for all patients with low-risk early-stage cervical cancer. Recently, a number of studies have explored less radical surgical options for early-stage cervical cancer, including simple hysterectomy, simple trachelectomy, and cervical conization with or without sentinel lymph node biopsy and pelvic lymph node dissection. Such options may be available for patients with low-risk early-stage cervical cancer. Criteria that define this low-risk group include: squamous carcinoma, adenocarcinoma, or adenosquamous carcinoma, tumor size <2 cm, stromal invasion <10mm, and no lymph-vascular space invasion. In this report, we provide a review of the existing literature on the conservative management of cervical cancer and describe ongoing multi-institutional trials evaluating the role of conservative surgery in selected patients with early-stage cervical cancer.

Introduction

Cervical cancer is one of the leading causes of cancer and cancer-related deaths among women worldwide, with an estimated 500,000 new cases and 275,000 related deaths

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Conflict of Interest: The authors report no conflict of interest.

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annually [1]. The standard treatment for women diagnosed with early-stage (stage IA2-IB1) cervical cancer is radical hysterectomy and pelvic lymphadenectomy. However, for patients interested in future fertility, an alternative is radical trachelectomy and pelvic lymphadenectomy [2]. Multiple studies have demonstrated the safety and feasibility of radical trachelectomy [3–5]. In addition, data from retrospective studies have confirmed that oncologic outcomes of radical hysterectomy and radical trachelectomy are equivalent [6]. These data have also raised the possibility that less radical surgery may be appropriate not only for patients desiring to preserve fertility but for all patients with low-risk early-stage cervical cancer.

Similar to radical hysterectomy, radical trachelectomy requires removal of the parametria and may be associated with significant morbidity. Among the most common side effects are lower urinary tract dysfunction, sexual dysfunction, and colorectal motility disorders associated with autonomic nerve damage [3]. In addition, previous studies have shown that approximately 60% of patients who undergo a radical trachelectomy have no residual disease in their surgical specimen, indicating that perhaps those patients could have been treated with less radical surgery [7].

Several studies have explored less radical surgical options for early-stage cervical cancer, including simple hysterectomy, simple trachelectomy, and cervical conization with or without sentinel lymph node biopsy and pelvic lymph node dissection. In this report, we review the studies published to date on the conservative management of cervical cancer to determine whether conservative surgery may be appropriate for patients with low-risk early-stage disease. Studies only published in abstract form were not included. We also describe ongoing multi-institutional studies evaluating the role of conservative surgery in selected patients with early-stage cervical cancer.

Rationale for Conservative Management of Cervical Cancer

Multiple retrospective studies have shown very low rates of parametrial involvement in patients with early-stage cervical cancer with favorable pathologic characteristics who have undergone radical hysterectomy. These reports suggest that these patients could be managed in a more conservative approach.

An early report by Kinney et al. [8] in 1995, suggested that a subset of patients at low risk of parametrial spread or disease recurrence might be candidates for less radical surgery. The authors evaluated 387 patients treated for squamous cell carcinoma confined to the cervix. Of these 387 patients, 83 (21.4%) had favorable pathologic characteristics including depth of invasion greater than 3 mm but tumor diameter no greater than 2 cm and no lymphovascular space invasion (LVSI), and no patient in this subgroup had parametrial nodal metastases.

Subsequently, several other groups published studies on the risk of parametrial spread in patients with early-stage cervical cancer. Covens et al. [9] reported on 842 patients with stage IA1 through IB1 cervical cancer who underwent radical hysterectomy. The goal of the study was to determine the incidence and factors predictive of parametrial involvement and to identify a population at low risk for pathologic parametrial involvement. Thirty-three

patients (4%) had pathologic parametrial involvement, eight in the parametrial lymph nodes and 25 in the parametrial tissue (none had both). Compared with patients without parametrial involvement, those with parametrial involvement were older (42 vs. 40 years, $P<0.04$), had larger tumors (median, 2.2 vs. 1.8 cm, $P<0.04$), had a higher incidence of LVSI (85% vs. 45%, $P=0.0004$), were more likely to have grade 2 or 3 tumors (95% vs. 65%, $P=0.001$), had greater depth of invasion (median, 18 vs. 5 mm, $P<0.001$), and were more likely to have pelvic lymph node metastases (44% vs. 5%, $P<0.0001$). The incidence of parametrial involvement in patients ($n=536$) with negative lymph nodes, tumor size 2 cm or smaller, and stromal invasion 10 mm or less was 0.6%.

Wright and colleagues [10] aimed to determine factors predictive of parametrial tumor spread and to define a subset of patients at low risk for parametrial disease. A total of 594 patients with invasive cervical cancer who underwent radical hysterectomy were retrospectively reviewed. Parametrial metastases were documented in 64 patients (10.8%). Factors associated with parametrial disease were high-risk histology, advanced grade, deep cervical invasion, LVSI, large tumor size, advanced stage, uterine or vaginal involvement, and pelvic or para-aortic lymph node metastases ($P<0.0001$ for each). A subgroup analysis was performed to identify patients at low risk for parametrial spread. They noted that in women with negative lymph nodes, no LVSI, and tumors smaller than 2 cm, the incidence of parametrial disease was only 0.4%.

Frumovitz et al. [11] conducted a similar study in which the rate of parametrial involvement was determined in 350 patients who underwent a radical hysterectomy. In that study, the overall rate of parametrial involvement was 7.7%. However, when the authors stratified for low-risk characteristics, they found that the rate of parametrial involvement was zero in the 125 patients who met the following criteria: adenocarcinoma, squamous cell carcinoma, or adenosquamous carcinoma; tumor size smaller than 2 cm; and no LVSI.

The compiled data from these studies demonstrated that in patients with low-risk characteristics, the rate of parametrial involvement was less than 1%. These retrospective findings suggest that perhaps there is a subset of patients with early-stage cervical cancer who are unnecessarily exposed to radical procedures such as radical hysterectomy or radical trachelectomy.

Data from Studies on Conservative Management

Several small retrospective series have provided initial data suggesting the safety and feasibility of a conservative approach in patients with low-risk early-stage cervical cancer. Here, we review these series in chronological order from oldest to newest (Tables 1–3).

One of the earliest studies evaluating the role of conservative management of low-risk early-stage cervical cancer was published by Naik et al. [12] in 2007. This was a study of 17 patients with stage IB1 cervical cancer. Five women underwent a cone biopsy with or without laparoscopic pelvic node dissection, and 12 women underwent a laparoscopic-assisted vaginal hysterectomy or total abdominal hysterectomy with or without pelvic node dissection. There were no cases of residual disease in the final surgical specimen. There

were also no cases of metastatic disease in the pelvic nodes. With a median follow-up time of 29 months, there were no documented recurrences.

In 2008, Rob et al. [13] published the results of a pilot study to determine the feasibility and safety of using less radical, fertility-preserving surgery in patients with early-stage cervical cancer. In that study, 40 patients underwent laparoscopic sentinel lymph node identification, with frozen-section analysis, and if negative, a complete pelvic lymphadenectomy was performed as the first step of the treatment. The inclusion criteria for this study were tumor size <2cm in largest diameter or <50% infiltration of cervical stroma based on magnetic resonance imaging and ultrasound volumetry. Disease was stage IA1 in 3 patients (all with LVSI), IA2 in 10 patients (40% with LVSI), and IB1 in 27 patients (38.5% with LVSI). Thirty-two patients had squamous cell carcinoma, 7 had adenocarcinoma, and 1 had adenosquamous carcinoma. Six frozen sections (15%) were positive, and in these 6 patients, a radical hysterectomy was performed. The authors noted that 24 of 32 patients whose reproductive ability had been maintained tried to conceive. Of these 24 women, 17 (71%) became pregnant. Eleven women gave birth to 12 children; with three premature deliveries at 24, 34, and 35 weeks; respectively. Nine term deliveries were reported.

In 2009, Pluta et al. [14] published the results of a pilot study to evaluate the feasibility and safety of laparoscopic lymphadenectomy followed by a simple vaginal hysterectomy in 60 patients with early-stage cervical cancer and negative sentinel lymph nodes. Patients who did not desire future fertility and had the following favorable pathologic characteristics were included: stage IA1 disease with LVSI or stage IA2 or IB1 disease with tumor size less than 2 cm and less than 50% stromal invasion. Fifty patients had squamous cell carcinoma, and 10 patients had adenocarcinoma. Three patients had stage IA1 disease, 11 had stage IA2 disease, and 46 had stage IB1 disease. The median age was 44.6 years (range, 33–64 years). Five patients (8%) had positive sentinel nodes. The median follow-up time was 47 months (range, 12–92 months). No recurrences were noted in any of the 60 patients in the study.

A subsequent study on less radical surgery for cervical cancer was published by Maneo et al., in 2011 [15]. These authors evaluated the role of simple conization and pelvic lymphadenectomy in patients with stage IB1 disease. A total of 37 patients were scheduled for surgery but one patient was taken to surgery and the procedure abandoned secondary to grossly enlarged lymph nodes; therefore 36 patients were included in the final analysis. The median age was 31 years (range, 24–40 years), and the median tumor size was 11.7 mm (range, 8–25 mm). Twenty-four patients (67%) had squamous cell carcinoma, and 12 (33%) had adenocarcinoma. Five patients (14%) had LVSI. All patients had undergone a prior conization, and 8 patients also underwent a re-conization. All final conization and re-conization specimens were free of margin involvement. The median follow-up time was 66 months (range, 18–168 months). One patient had a recurrence in the pelvis 34 months after initial therapy. Twenty-one pregnancies occurred in 17 patients, and 14 live babies were born (3 were born preterm, at 27, 32, and 33 weeks; respectively). One patient was still pregnant at the time of the report. The remaining 6 pregnancies ended as follows: first-trimester miscarriage (n = 3), second-trimester fetal demise (n = 1), ectopic pregnancy (n = 1), and elective pregnancy termination due to genetic anomaly (n = 1). The authors concluded that cervical conization represents a feasible form of conservative management of

stage IB1 cervical cancer and that cervical conization is associated with a low risk of relapse.

Also in 2011, Fagotti et al. [16] reported on a series of 17 patients with early-stage cervical cancer (IA2-IB1) who were younger than 45 years and whose tumors measured 2cm or less. The goal of the study was to explore the role of excisional cone biopsy instead of radical trachelectomy as fertility-sparing surgery. All patients had negative pelvic lymph nodes on magnetic resonance imaging prior to surgery. All patients underwent laparoscopic pelvic lymphadenectomy and simple conization. In case of positive lymph nodes at frozen section or definitive pathologic analysis, patients were treated with radical hysterectomy and pelvic and para-aortic lymphadenectomy.

Interestingly, the authors noted that only 17 of 41 patients (41.5%) who met the inclusion criteria were willing to enter the trial. The median age was 33 years (range, 30–43 years). The stage was IA2 in 4 patients (24%) and IB1 in 13 patients (76%). The most common histologic subtype was squamous cell carcinoma, which was seen in 12 patients (71%). LVSI was present in 4 patients (23%). The median nodal count was 18 (range, 11–51). Four patients (23%) required radical hysterectomy, 3 for infiltration of the margins and 1 for a positive lymph node. Two patients were treated with adjuvant chemotherapy because of positive resection margins. After a median follow-up time of 16 months (range, 8–101 months), no recurrences were observed. Five patients tried to conceive. Two of them had spontaneous pregnancies, and the remaining 3 underwent in vitro fertilization without success. No miscarriages or preterm deliveries were noted. The authors concluded that conization and laparoscopic pelvic lymphadenectomy is safe and feasible in this low-risk group of patients.

In 2012, Palaia et al. [17] reported on the safety and feasibility of simple trachelectomy plus pelvic lymphadenectomy in 14 young patients affected by early-stage cervical cancer. Inclusion criteria for their study were age 38 years or younger, strong desire to maintain fertility, stage IB1 or earlier disease, tumor size less than 2 cm, no LVSI, and no evidence of nodal metastasis. All patients underwent a laparoscopic bilateral pelvic lymphadenectomy. The lymph nodes were then analyzed by frozen section. If the pelvic nodes were positive for disease, standard abdominal radical hysterectomy was performed. In the absence of nodal metastasis at frozen section analysis, a simple vaginal trachelectomy was performed.

The median age was 32 years (range, 28–37 years). Eleven patients had squamous carcinoma, and 9 patients had stage IB1 disease. The median tumor size was 17 mm (range, 14–19 mm). The median operative time was 120 minutes (range, 95–210 minutes), and the median estimated blood loss was 200 mL (range, 100–400 mL). The median follow-up time was 38 months (range, 18–96 months). At last follow-up, 13 patients were alive without evidence of disease. One patient died from other cause (vesical cancer). No recurrences were observed. Eight patients had become pregnant, and 3 of them had had a term delivery. The authors concluded that patients with low-risk early-stage cervical cancer could be safely treated with simple trachelectomy.

Also in 2012, Raju et al. [18] evaluated 66 patients who underwent either a simple vaginal trachelectomy (n = 15) with pelvic lymphadenectomy or radical vaginal trachelectomy (n = 51) with pelvic lymphadenectomy for stage IA2 or IB1 cervical cancer. The criteria for performing a simple vaginal trachelectomy were a loop electrosurgical excision procedure or cone biopsy specimen with tumor-free margins, tumor not larger than 1 cm in greatest diameter, no evidence of LVSI, and tumor grade 1 or 2. Of the 15 patients who underwent simple vaginal trachelectomy, 5 had stage IA2 disease, and 10 had stage IB1 disease. Nine had squamous cell carcinoma, and 6 had adenocarcinoma. No patient had LVSI. There was no residual disease in the surgical specimen in 8 of the 15 patients (53%) who underwent simple vaginal trachelectomy (compared with 29% of the patients who underwent radical vaginal trachelectomy). The median follow-up time for the patients who underwent simple vaginal trachelectomy was 96 months (range, 12–120 months). No recurrences were observed. Five patients (33%) attempt to conceive, 4 patients (80%) became pregnant, and all 4 of these patients had a term delivery. The authors concluded that it is possible to select patients for a less radical fertility-sparing procedure through identification of measurable low-risk factors.

Biliatis et al. [19] evaluated survival and obstetrical outcomes following conservative management of small-volume stage IB1 cervical cancer. In this series the authors offered an update on the previous publication by Naik et al. [12]. Small-volume disease was defined as a tumor less than 500 mm³ in a loop biopsy specimen. A total of 62 women were identified with a median age of 35 years (range, 27–67 years). Histologic subtype was squamous cell carcinoma in 49 patients (79%), adenocarcinoma in 11 patients (17.7%), and adenosquamous carcinoma in 2 patients (3.3%). Thirty-five women (56%) were treated with loop biopsy, while 27 (46%) had a simple hysterectomy. Fifty-seven (92%) had pelvic lymphadenectomy, and 1 positive node was detected. The median number of lymph nodes removed was 11 (range, 3–25). There were no cases of residual disease in the definitive treatment specimen. After a median follow-up of 56 months (range, 13–132 months), no recurrences were noted. In the group of women treated with loop excision, 7 pregnancies were recorded, and 7 live babies were born. No preterm deliveries or second-trimester miscarriages were noted.

A recent publication by Plante et al. in 2013 [20] evaluated the feasibility of simple vaginal trachelectomy and node assessment in 16 patients with low-risk early-stage cervical cancer (<2 cm). All patients underwent a simple vaginal trachelectomy preceded by laparoscopic sentinel node mapping plus or minus pelvic node dissection. Four patients had stage IA1 disease with LVSI, 6 patients had stage IA2 disease, and 6 patients had stage IB1 disease. Ten patients had squamous cell carcinoma, and 10 patients had grade 1 disease. Only 4 patients had LVSI. The median operative time was 150 minutes (range, 120–180 minutes), and median blood loss was 50 mL (range, 50–150 mL). On final pathology, lymph nodes were negative in all patients. Thirteen patients (81%) had either no residual disease (n = 6) or residual dysplasia only (n = 7) in the trachelectomy specimen. Margins were negative in all cases. With a median follow-up time of 27 months (range, 1–65 months), there were no recurrences. Eight patients had conceived: 4 had term deliveries, and 4 pregnancies were ongoing at the time of publication. The authors concluded that simple trachelectomy and

lymph node evaluation seems to be a safe alternative in well-selected patients with low-risk early-stage cervical cancer.

Summary of Data from Retrospective Studies of Conservative Management

To date, 260 women with early-stage cervical cancer managed conservatively have been described in the literature (Table 1). Of these women, 197 (75.8%) had a diagnosis of squamous cell carcinoma, and 59 (22.7%) had a diagnosis of adenocarcinoma. Most women (80.4%) had stage IB1 disease. The rate of LVSI in patients with a conservative approach ranged from 0 to 42%. The LVSI status is considered a surrogate for lymph node involvement. However, it is important to note that even with conservative management, all patients routinely undergo sentinel node identification or complete pelvic lymphadenectomy. Equally, the oncologic outcomes are very favorable as detailed below. Follow-up time in the series published to date ranged from 1 to 168 months. At the time the reports were published, 2 patients had relapsed, and 1 patient had died of recurrent disease (Table 2). A total of 73 pregnancies have been reported, with 46 deliveries documented and 8 pregnancies ongoing at the time of publication (Table 3).

Prospective Trials of Conservative Surgical Management of Low-Risk Cervical Cancer

Currently, 3 prospective trials are evaluating a conservative approach in patients with low-risk early-stage cervical cancer.

The first is a prospective trial lead by Schmeler and colleagues at The University of Texas MD Anderson Cancer Center [7]. The trial (*ConCerv*) is a multi-institutional international trial evaluating the safety and feasibility of performing conservative surgery in women with early-stage cervical cancer with favorable pathologic characteristics. The inclusion criteria are stage IA2 or IB1 disease; tumor size 2cm or smaller; and squamous cell carcinoma (any grade) or adenocarcinoma (grades 1 or 2). Patients with high-risk histology or LVSI are excluded. Patients desiring future fertility undergo only cervical conization and pelvic lymph node dissection with lymphatic mapping. Patients not desiring future fertility undergo a simple hysterectomy and pelvic lymph node dissection with lymphatic mapping. The primary objective is to evaluate the safety and feasibility of performing conservative surgery in this group of patients. Secondary objectives include assessing treatment-associated morbidity and quality of life compared with historical outcomes in matched patients treated with radical hysterectomy. In addition, the sensitivity of lymphatic mapping and sentinel lymph node biopsy is being estimated. The sample size for the study will be 100 patients across all participating institutions. At the time of this writing, the study had accrued 25 patients from 4 collaborating sites.

The second ongoing study is a Gynecologic Cancer Intergroup trial led by Plante and colleagues. The study is known as the SHAPE Trial [21]. This is a randomized trial comparing radical hysterectomy and pelvic node dissection to simple hysterectomy and pelvic node dissection. The inclusion criteria are stage IA2 or IB1 disease, tumor size smaller than 2cm, squamous cell carcinoma or adenocarcinoma, and less than 10mm stromal

invasion on LEEP/cone biopsy or less than 50% stromal invasion on pelvic magnetic resonance imaging. All tumor grades are allowed, and patients with LVSI are eligible. The exclusion criteria include high-risk histologic subtype (clear cell carcinoma or small cell carcinoma), stage IA1 disease, evidence of lymph node metastases or extrauterine disease, neoadjuvant chemotherapy, pregnancy, and desire to preserve fertility. Patients will be randomized 1:1 to the control treatment, which is a radical hysterectomy and pelvic lymphadenectomy with or without sentinel node mapping (as this is optional), or the experimental treatment, which is a simple hysterectomy with pelvic lymphadenectomy with or without sentinel node mapping. The primary objectives are to determine whether simple hysterectomy in patients with low-risk cervical cancer is safe and associated with less morbidity than radical hysterectomy and to determine whether overall survival is significantly different between the 2 arms of the study. The secondary end points include treatment-related side effects, extrapelvic relapse-free survival, overall survival, rate of sentinel node detection, rate of metastasis to the parametria, surgical margin status, pelvic node status, and quality of life. The total anticipated accrual is 700 patients.

The third ongoing trial is Gynecologic Oncology Group protocol 278. This multi-institutional trial, led by Alan Covens, is titled “Evaluation of physical function and quality of life before and after non-radical surgical therapy (extrafascial hysterectomy or cone biopsy with pelvic lymphadenectomy) for stage IA1 (LVSI+) and IA2-IB1 (≤ 2 cm) cervical cancer” [22]. The primary objectives are to determine the impact of nonradical surgery on bladder, bowel, and sexual function and to determine the incidence and severity of lymphedema after nonradical surgery. The secondary objectives are to investigate whether nonradical surgery is associated with better physical function and less toxicity compared to historical data on radical surgery; to evaluate the incidence and severity of treatment-related adverse events; to explore the relationships between functional outcomes, adverse events, cancer worry, surgical complications, and overall quality of life; and to determine participants’ intention for conception, determine the fertility rate, and assess the reproductive concerns for women following cone biopsy and pelvic lymphadenectomy. The eligibility criteria include histologic diagnosis of squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the cervix; stage IA1 (LVSI positive), IA2, or IB1 disease; tumor size 2 cm or smaller; and any grade. All patients must have had a cone biopsy or loop electrosurgical excision procedure with margins negative for carcinoma and high-grade dysplasia. Depth of invasion must be no greater than 10 mm. Similarly, patients must have no evidence of metastasis on magnetic resonance imaging or computed tomography scan of the pelvis and chest imaging. In this study, patients will be stratified according to their fertility wishes to either cone biopsy and pelvic lymphadenectomy or simple hysterectomy and pelvic lymphadenectomy. The minimum sample size for this study is anticipated to be 200 eligible patients. Depending on results from interim analyses and feasibility assessments, this study may accrue up to 600 patients.

Conclusion

The current literature demonstrates that patients with low-risk early-stage cervical cancer may be ideal candidates for conservative surgery. Depending on the patient’s interest in future fertility, either cervical conization or simple hysterectomy with bilateral pelvic

lymphadenectomy may be adequate. It is critical to highlight the fact that conservative surgery for patients with stage IA2-IB1 remains an approach that should only be considered in the setting of clinical trials. Equally, it is very important to assure that before embarking on a conservative approach all pathology should be carefully reviewed by an expert gynecologic pathologist who will provide accurate information on histologic subtype, grade, depth of invasion, margin status, and LVSI status. Lastly, very thorough patient counseling is recommended to assure the patient is aware of guidelines dictating current standard of care. Ongoing, prospective trials will provide more concrete evidence on the role of conservative surgery in these low-risk patients.

Acknowledgments

Financial support: The University of Texas MD Anderson Cancer Center is supported in part by the National Institutes of Health through Cancer Center Support Grant CA016672.

The authors wish to thank Ms. Stephanie Deming for her editorial contribution to the manuscript.

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Highlights

Conservative surgery is feasible in patients with low-risk early-stage cervix cancer

Conization, simple trachelectomy, or simple hysterectomy are safe options for low-risk patients

Prospective trials are ongoing evaluating role of conservative surgery: ConCerv, SHAPE, and GOG 278

Table 1
Patient and tumor characteristics from published studies of conservative surgical treatment for early-stage cervical cancer

Author (year)	N	Median age (range), y	Histology			Stage			LVSI N (%)
			SCC	AC	Other	IA1+LVSI	IA2	IB1	
Rob (2008)	40	28.3 ^a	32	7	1 adsq	3	10	27	17 (42)
Pluta (2009)	60	44.6 (33–64)	50	10	0	3	11	46	19 (32)
Maneo (2011)	36	31 (24–40)	24	12	0	0	0	36	5 (14)
Fagotti (2011)	17	33 (30–43)	12	4	1 glassy	0	4	13	4 (23)
Palaia (2012)	14	32 (28–37)	11	3	0	0	5	9	0
Raju (2012)	15	28 (20–40) ^a	9	6	0	0	5	10	0
Biliatis (2012)	62	35 (27–67)	49	11	2 adsq	0	0	62	14 (22)
Plante (2013)	16	30 (22–44)	10	6	0	4	6	6	4 (25)
Total	260		197 (75.8%)	59 (22.7%)	4 (1.7%)	10 (3.8%)	41 (15.8%)	209 (80.4%)	

AC, adenocarcinoma; adsq, adenosquamous carcinoma; glassy, glassy cell carcinoma; LVSI, lymphovascular space invasion; SCC, squamous cell carcinoma.
^aMean age.

Table 2
Surgical procedure in published studies of conservative surgical treatment for early-stage cervical cancer

Author (year)	No. of planned surgeries	Sentinel lymph node biopsy	Radical hysterectomy	Less radical procedures	Positive lymph nodes	Adjuvant radiotherapy	Adjuvant chemotherapy	Follow-up time, median (range), months	Relapses	Deaths
Rob (2008)	40	Yes	6	Cone biopsy + PLND = 10 Simple trach + PLND = 24	6	0	0	47 (12–102)	1	0
Pluta (2009)	60	Yes	3	TH + PLND = 57	5	5	0	47 (12–92)	0	0
Manco (2011)	37	No	N/A	Cone biopsy + PLND = 36	0	0	0	66 (18–168)	1	1
Fagotti (2011)	17	No	4	Cone biopsy + PLND = 13	1	0	2	16 (8–101)	0	0
Palaia (2012)	14	No	0	Simple trach + PLND = 14	0	0	0	38 (18–96)	0	0
Raju (2012)	15	No	0	Simple trach + PLND = 15	0	0	0	96 (12–120)	0	0
Biliatis (2012)	62	No	0	Cone biopsy + PLND = 35 ^a TH + PLND = 27 ^b	1	0	0	56 (13–132)	0	0
Plante (2013)	16	Yes	0	Simple trach + PLND = 16 ^c	0	0	0	27 (1–65)	0	0
Total	261		13	247	13	5	2		2	1

PLND, pelvic lymphadenectomy; TH, total hysterectomy; trach, trachelectomy.

^aNo PLND in 4 patients.

^bNo PLND in 1 patient.

^cSix patients had sentinel lymph node mapping alone.

Table 3
Obstetrical outcomes in published studies of conservative surgical treatment for early-stage cervical cancer

Author (year)	Planned surgeries	Less radical surgery	Attempting to conceive	Became pregnant	Number of Pregnancies	Miscarriages		Deliveries		Patients pregnant at time of report
						1st term	2nd term	Preterm	At term	
Rob (2008)	40	34	24/32 (75%)	17	23	5	3	3	9	3
Maneo (2011)	37	36	NR	17	21	5	1	3	11	1
Fagotti (2011)	17	13	5/13 (38%)	2	2	0	0	0	2	0
Palaia (2012)	14	14	NR	8	8	NR	NR	NR	3	NR
Raju (2012)	15	15	5	4	4	0	0	0	4	0
Biliatis (2012)	35	35	NR	NR	7	0	0	0	7	0
Plante (2013)	16	16	8	8	8	0	0	0	4	4
Total	174*	163*	---	56	73	10	4	6	40	8

NR, not reported.

*The total number of planned surgeries and total number of less radical surgery were recalculated to reflect the fact that all patients in the Pluta study (14) underwent a hysterectomy and that 27 patients in the Biliatis study (19) also underwent a hysterectomy.