A systematic review of the reproductive and oncologic outcomes of fertility-sparing surgery for early-stage cervical cancer

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Abstract

In this review, we aim to evaluate the current literature on reproductive and oncologic outcomes after fertility-sparing surgery for early-stage cervical cancer (stage IA1-IB1). This is a systematic review of the existing literature using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist to report on fertility-sparing surgery and its outcomes in early-stage cervical cancer. Outcomes of interest were subsequent clinical pregnancy rate, reproductive outcomes, and cancer recurrence outcomes. Included in this systematic review were 68 studies encompassing 3,592 patients who underwent fertility-sparing surgery. Of these, reproductive outcomes were reported in 1096 pregnancies. The mean clinical pregnancy rate was 53.2%. Those who underwent vaginal radical trachelectomy had the highest clinical pregnancy rate (67.5%). The mean live birth rate was 67.8% in our study. Twenty-one percent of pregnancies after fertility-sparing surgery required assisted reproductive technology. The mean cancer recurrence rate was 3.2%, and the cancer death rate was 0.6% after a median follow-up period of 40.1 months with no statistically significant difference across surgical approaches. Offering fertility-sparing surgery in early-stage cervical cancer is reasonable. Highest clinical pregnancy rate is associated with vaginal radical trachelectomy. Moreover oncologic outcomes of minimally invasive approaches were comparable with abdominal approaches. We encourage detailed preoperative counseling and multidisciplinary approach to achieve best outcomes. (J Turk Ger Gynecol Assoc 2022; 23: 287-313)

Keywords: Cervical cancer, fertility-sparing surgery, pregnancy outcomes

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Introduction

Cervical cancer is the fourth most common malignancy in women worldwide (1). The incidence of cervical cancer is reported to be highest between 35 and 49 years of age and decreases after that. In women between 20 to 45 years of age, this incidence has been reported as as 47.3 per 100,000 (2). Based on the International Federation of Gynecology and Obstetrics 2019 classification system, imaging data and pathology information are used to supplement clinical findings to stage cervical cancer. Details of this staging system is included in Table 1 (3,4). Global Papanicolaou screening and human papillomavirus vaccination have resulted a significant decline in the rate of cervical cancer. Currently the National Cancer Institute reports 90% 5-year survival rate in patients with localized cervical cancer (2). Traditionally total hysterectomy, radical hysterectomy with or without lymphadenectomy, or chemoradiation have been considered the only treatment

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options for cervical cancer. Given the fact that approximately 40% of patients diagnosed with cervical cancer are in the reproductive age, attention to alternative treatment methods for surgical and/or functional preservation of the reproductive system and lead to uterine, tubal, or ovarian factor infertility is of importance (5). Fertility-sparing surgery for early-stage cervical cancer (stage IA1-IB1) is now a viable option that can be offered per the National Comprehensive Cancer Network guidelines. Current fertility sparing options are cervical conization, simple and radical trachelectomy. Trachelectomy can be done abdominally, vaginally, and laparoscopic with or without robot assistance.

The invention and development of video-assisted laparoscopy by Dr. Camran Nezhat has impacted and improved the minimally invasive options as the standard of care in many surgical disciplines including gynecologic oncology (6-10). Reports of the first video-assisted laparoscopic radical hysterectomy, paraaortic and pelvic lymphadenectomy which was performed the Nezhats in 1989 have been previously published (11,12). The early work of surgeons Dargent, Salvat, Querleu, Nezhat, and Childers later on proved the feasibility and safety of retroperitoneal lymphadenectomy (13-16). Roboticassisted radical trachelectomy and pelvic lymphadenectomy have also been reported for the first time by Chuang and Nezhat in 2008, after which other's experiences have been published (17-19).

It is recommended that fertility-sparing surgery be offered to patients after extensive and detailed disclosure of risks, benefits and alternatives. Multidisciplinary meetings by gynecologic oncologists, infertility specialists and other appropriate services are strongly encouraged. Existing evidence offers fertility-sparing surgery in the setting of early-stage cervical cancer (IA1-IB1). In a prospective cohort study, 88 patients underwent laparoscopic radical trachelectomy for early-stage cervical cancer. Based on this study a tumor size of >2 cm was found to be associated with increased risk of cancer recurrence in the setting of fertility sparing surgery (as high as 20%) (20,21).

In patients with more advanced stage disease, those with more aggressive tumor histology like adenoma malignum, gastric adenocarcinoma, clear cell adenocarcinoma, embryonal rhabdomyosarcoma or small cell cancer, and those with no future fertility planning, fertility sparing options are contraindicated and definitive management should be offered. Even in those who undergo fertility sparing treatments radical hysterectomy should be offered when the fertility is no longer desired or when there is persistent HPV abnormality (3).

Based on retrospective and non-randomized research minimally invasive approach to radical hysterectomy for early-stage cancer is being considered safe and is associated with less short-term and long-term morbidity including shorter hospital stay, decreased blood loss (22-30). In a research that was done by Wang et al. (31) it was concluded that both 5-year recurrence free survival and overall survival rates are similar in laparoscopic versus abdominal radical hysterectomies. Another study in 2008 also concluded that the 3-year recurrence free survival and overall survival rates are similar in laparoscopic versus robotic radical hysterectomies for early-stage cervical cancer (32). After the the Laparoscopic Approach to Cervical Cancer (LACC) trial by Ramirez et al. (33), definitive management of early-stage cervical cancer in being considered via laparotomy route in many institutions. This study concluded that radical hysterectomy via minimally invasive routes are associated with lower rates of disease-free and overall survival rates as compared to open surgery. This is the only randomized trial to date that reports the comparison of outcomes of open approach versus minimally invasive options. This study was statistically powered as a noninferiority study with primary endpoint of disease-free survival at 4.5 years. Subjects were randomized to radical hysterectomy by either an abdominal or minimally invasive (laparoscopic or robotic-assisted) approach. The data and safety monitoring committee ended the study in June 2017 due to a safety issue with one of the blinded surgical treatment arms in one of

Table 1. Cervical cancer stages and fertility-sparing surgical treatment

Cervical cancer stage	Staging criteria	Treatment
IA1	Invasive carcinoma diagnosed on microscopy with stromal invasion <3 mm	No LVSI: Cone biopsy with negative margins. LVSI: Cone biopsy with negative margins and pelvic lymphadenectomy OR radical trachelectomy with pelvic lymphadenectomy. Consider sentinel lymph node mapping.
IA2	Invasive carcinoma diagnosed on microscopy with stromal invasion ≥3 mm and <5 mm in depth.	Cone biopsy with negative margins and pelvic lymphadenectomy OR radical trachelectomy with pelvic lymphadenectomy. Consider sentinel lymph node mapping.
IB1	Invasive carcinoma ≥5 mm depth of stromal invasion and lesion <2 cm in greatest dimension, limited to the cervix.	Radical trachelectomy with pelvic lymphadenectomy and possible para-aortic lymph node dissection. Consider sentinel lymph node mapping.

Adapted from 2019 FIGO staging for cervical cancer and National Comprehensive Cancer Network treatment guidelines (3,4). LVSI: Lymphovascular space invasion

the interim analyses. The authors reported the outcomes on 312 subjects in the abdominal hysterectomy arm versus 319 subjects under the minimally invasive arm (83% laparoscopy, 16% robotic surgery). The disease-free survival rate was 96.5% in the abdominal hysterectomy arm as compared to 86% in the minimally invasive surgery arm based on the intention to treat analysis; this corresponds to 13% difference decrease in hazard of death in open surgery arm. Moreover, the number of total disease recurrences in the minimally invasive arm was about four times higher than the number of recurrences after open surgery (27 vs. 7). In this research a significantly lower overall survival was reported in the minimally invasive arm (3 of 312 vs. 19 of 319; HR: 6.00; 95% confidence interval: 1.48-20.3; p=0.004). Based on this finding, the open approach was presented as the preferred route of radical hysterectomy for early-stage cervical cancer. There are some significant limitations associated with the LACC trial. 1) The minimally invasive arm was significantly skewed towards laparoscopic approach over robotic approach, which might not be an appropriate reflection of current practices. 2) In this study the majority of subjects were stage IB1. 3) There was a significant lack of detailed histopathologic data in the final study report. 4) The specific preoperative imaging strategy, and adequate follow up was lacking. 5) Additionally, as a multinational multicenter study in 33 surgical cneters around the world different surgical skills are not unexpected. All the recurrences had happened in 14 out of 33 recruiting centers however no additional informal is provided in the publication regarding details of surgical methodology and perioperative management in any of the other recurrence free institutes. Therefore, the surgical practices and techniques may have contributed significantly as confounding variables. The authors of this paper believe that the conclusion of of the LACC trial should be inetpreted with caution (34). We are in agreement with Donnez (35) who hypothesized that survival differences between minimally invasive and open surgeries will diminish with more surgical experience in minimally invasive approaches. In 2020, an international European cohort observational study compared minimally invasive surgery versus open abdominal radical hysterectomy in a patient with stage IB1 cervical cancer (36). They concluded that minimally invasive surgery in cervical cancer is associated with an increased risk of relapse and death as compared to open surgery. However, it is worth mentioning that in that study, by avoiding uterine manipulators and by using maneuvers to avoid tumor spread at the time of colpotomy in minimally invasive surgeries, outcomes were similar to open surgery.

At a time when open approach is recommended for management of early cervical cancer there is lack of evidence on the route of radical trachelectomy specifically. It is also unclear if the surgical approach (open versus minimally invasive) will affect the final cancer related outcomes.

In this study, we aim to report the result of systematic evaluation of current literature on fertility sparing interventions for early-stage cervical cancer and their associated cancer related, reproductive and obstetric outcomes.

Material and Methods

This paper is a systematic review of the current literature on fertility-sparing surgery for early-stage cervical cancer and the associated reproductive, obstetrics and oncologic outcomes. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was utilized. Medline database used to review the literature. The screening query was “uterine cervical neoplasms” AND “gynecoogic surgical procedures” AND “infertility.” We then performed a Medline search for the query “fertility-sparing surgery” and “cervical cancer.” Two independent authors reviewed the results. This study was exempt from institutional review board approval since there is no human subject research involved.

Included fertility sparing procedures were conization, vaginal radical trachelectomy, open radical trachelectomy, simple trachelectomy with and without lymphadenectomy, or minimally invasive radical trachelectomy (laparoscopic with or without robotic assistance). Literature were included if they specified pregnancy and/or reproductive outcomes per surgical approach. Only papers written in English language between May 1980 and August 2021 were included. Figure 1 depicts the details of the identification process. We excluded the studies that addressed subjects with greater than stage IB1, or those

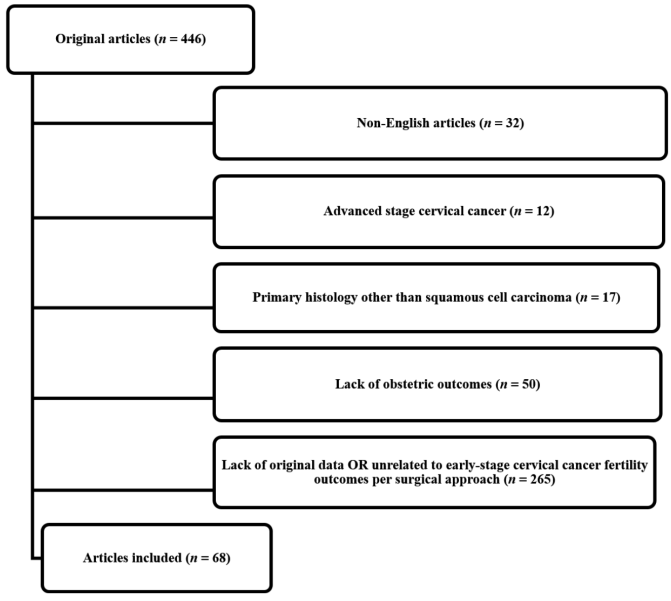

Figure 1. Identification process for studies included in the systematic review

with tumor size >2 cm or those who underwent experimental procedures. Unusual pathologies other than squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma were excluded too. Table 1 shows cervical cancer stages and associated fertility-sparing surgical treatments. D Any review article without any new patient data or any case reports or case series that addressed fewer than 2 subjects were also excluded. PubMed was last screened on 5 August 2021.

Our outcome variables were: live birth rate, clinical pregnancy rate, as well as rates for preterm delivery, cancer related death and cancer recurrence. We divided the number of subjects with minimum of one pregnancy to the number of those who were trying to conceive and defined the clinical pregnancy rate. When the number of patients who were conceiving was not reported; the absolute number of patients with at least one pregnancy was included instead. Preterm delivery was defined as delivery between 24- and 36-weeks' gestation. Per different surgical protocols some of the subjects had intact superior branches of the uterine artery versus in some the arteries were ligated at the origin; this rate was reported as percentage. Recommendation on delay in conception postoperatively was also addressed and reported.

Statistical Analysis

Analysis of variance (one tailed) with post-hoc Tukey tests were used for comparison. The p-value was calculated by the software as a function of F statistic and degrees of freedom for study numerator and denominators. Statistical analysis was performed using SPSS version 23.0. $P<0.05$ was considered statistically significant.

Results

A total of 68 studies were included in this study. Tables 2-6 show the data on 3592 patients based on surgical treatment (37-99, 110-112).

Of the total of 3,592 subjects who underwent fertility-sparing surgery, 1,391 (39%) attempted to conceive, resulting in 1,097 pregnancies. The subjects were followed up for a median of 41 months after their fertility sparing procedure. In 20 studies trying for conception was delayed between 3 to 48 months to monitor for cancer related symptoms prior to conception. The rate for cervical stenosis was 4.7% (169 patients). Analysis of mode of conceptions revealed the rates of 79%, and 29% for spontaneous conception versus assisted reproductive technology (ART) [including in-vitro fertilization, intrauterine insemination (IUI) with or without ovulation induction or cervical dilation with IUI], respectively.

Number of patients who were trying to conceive was reported in 49 studies; the mean clinical pregnancy rate after cancer treatment was 53.2% in this population. Further statistical evaluation of association of surgical approach and clinical pregnancy rate revealed higher rate in vaginal as compared with abdominal radical trachelectomy (67.5±20.0% versus 39.8±15.1%; $p<0.01$). No statistically significant association was found for other surgical routes.

The rate of live birth was reported in 62 studies revealing the mean rate of 67.8%. Further statistical evaluation of association of surgical approach and live birth rate revealed a higher live birth rate in subjects who underwent simple trachelectomy or conization (86.4±16.8%) as compared to vaginal radical trachelectomy (63.4±23.3%; $p=0.04$) and laparoscopic radical trachelectomy with or without robotic assistance (57.3±17.1%; $p=0.03$). No difference in this rate was found among other surgical approaches.

The rate of preterm delivery was reported in 51 studies revealing the mean rate of 29% after all fertility sparing surgical approaches. There was no association between this rate and the various surgical approaches ($F=0.22$; $p=0.8$). No association between various surgical approaches and the second trimester loss rate (8.2%) was found either ($F=0.385$; $p=0.764$).

Table 2. Reproductive and cancer outcomes in different fertility-preserving procedures

Procedure	Patients		Pregnancies		Obstetric Outcomes				Cancer Rates	
	Total (n)	TTC (n)	Total (n)	ART (n)	CPR (%)	LBR (%)	PDR (%)	Median follow-up (mo.)	Recurrence (%)	Death (%)
CKC/ST	283	83	131	8	65.0±20.0	86.4±16.8	25.1±33.4	47.5	1.4±2.1	0.2±0.8
VRT	1387	608	606	78	67.5±17.6	63.4±23.3	34.6±26.4	51.5	3.7±3.7	1.1±1.8
AbRT	1427	608	264	122	42.1±19.2	66.4±23.0	30.5±28.9	33	3.5±7.2	0.7±1.8
LART	335 (88 with RA)	81	96	21	53.2±29.1	57.3±17.1	31.5±22.9	27	3.4±7.0	0.1±0.4
Overall	3592	1391	1097	229	56.1±23.5	67.8±22.9	31.6±27.2	40.1	3.2±5.0	0.6±1.9

CKC: Cold knife conization, VRT: Vaginal radical trachelectomy, AbRT: Abdominal radical trachelectomy, LART: Laparoscopic-assisted radical trachelectomy, TTC: Trying to conceive, ART: Assisted reproductive technology, CPR: Clinical pregnancy rate, LBR: Live birth rate, PDR: Preterm delivery rate

The superior branches of the uterine artery remained intact in 100% of patient who underwent simple trachelectomy or conization, 88.9% of those who underwent vaginal radical trachelectomy, 44.6% of those who underwent abdominal radical trachelectomy, and 58.8% of those who underwent laparoscopic radical trachelectomy. The postoperative infections reported as follows: pelvic lymphocyst in 9 patients, pelvic inflammatory disease in 6 patients, pelvic abscess in 6 patients, pelvic peritonitis in 2 patients, and "pelvic infection" in one patient.

The cancer recurrence rate and cancer death rate after fertility-sparing procedure was reported in 65 studies. The overall mean cancer recurrence rate was 3.2%; no statistically significant association was found between this rate and the surgical approach ($F=0.536$; $p=0.659$). The overall mean cancer death rate was 0.7% with no significant association with surgical approach either ($F=1.759$, $p=0.163$).

Discussion

Our study shows that among all fertility-sparing treatments, vaginal radical trachelectomy has the highest clinical pregnancy rate (67%). Vaginal radical trachelectomy is a minimally invasive technique that can be associated with decreased rate of intraabdominal and pelvic adhesions. This approach is also associated with spared superior branches of uterine artery by the end of procedure. On the other hand, there is a higher potential to develop tuboovarian adhesion (as a known tubal factor for infertility) in the setting of abdominal procedure. Moreover, uterine arteries are ligated most of the times in the setting of abdominal radical trachelectomy; which may theoretically be associated with fertility rate (100). In a study by Tang et al. (101) patients with open procedure underwent computed tomography (CT) angiograms. Assessment of those with spared versus ligated uterine artery and the association with infertility was done. Interestingly, their study revealed that 87.5% of anatomically preserved uterine arteries occluded after surgery and overall 65.4% of subjects developed appropriate collateral circulation to perfuse their uteri (101). In another study by Muraji et al. (102), 18 subjects who underwent open radical trachelectomy with only inferior uterine artery branch ligation were studied and AMH level compared with control group; this study found no statistically significant difference in AMH as an index of ovarian reserve between cases and controls (102). This implies that ovarian reserve is likely unaffected by the ligation of inferior branches of uterine artery.

Obstetric outcomes

Per our systematic review revealed that the live birth rate was highest to lowest in simple trachelectomy/conization, followed by abdominal and then vaginal and then laparoscopic radical trachelectomy. Although those who underwent simple trachelectomy/cervical conization had the highest live birth rate as compared to all the other approaches, this can be attributed to selection bias with more advanced cancers are more likely to be treated via other routes. None of the reviewed studies mentioned cervical insufficiency as a potential complication of the fertility sparing procedures. We used second trimester pregnancy loss as a proxy for this variable and found to statistically significant difference across various surgical approaches.

We reported a 31% risk of preterm delivery after fertility sparing procedures. This rate seems to be significantly more than the 10.6% baseline risk in the general population (103). As a result of surgeon preference, some patients undergo a cervical cerclage placement at the time of trachelectomy routinely. To the best of our knowledge, there are no high-level evidence is available to date to support this intervention and its efficacy in preventing preterm delivery in the setting of fertility sparing surgery (17,40,54,73,104,105). We believe that all patients after fertility sparing procedures should be referred to maternal fetal medicine specialists for antepartum management.

Sufficient data and protocols to decrease the rate of preterm delivery in this population is lacking. One study found that magnetic resonance imaging (MRI) measurement of residual cervical length after radical trachelectomy might be a reliable predictor of preterm delivery or PPROM with significantly increased risk for cervical lengths <10 mm (105). Another study reported that a cervical length of less than 13 mm after abdominal radical trachelectomy was associated with increased risk of preterm delivery; they concluded that a routine second-trimester ultrasound screening can be used as a reliable screening measure (105).

Cervical stenosis

Our study revealed that about 5% of patients were diagnosed with cervical stenosis during their postoperative course. Based on the available data from the existing literature, it is unclear which exact types of fertility treatments were required in the setting of post procedure cervical stenosis. Only 40% of patients were trying to conceive during the study period after their fertility sparing surgery; although the reasons are unclear but potential associated factors can be planned delayed childbearing, postoperative dyspareunia or decreased libido. This topic deserves a further studies in future.

Cancer related outcomes

Based on our review, there was no association between in the different surgical approaches and the cancer recurrence or cancer death rate. Moreover, the authors believe that similar benefits to laparoscopic radical hysterectomy can be achieve

Table 3. Reproductive outcomes of conization or simple trachelectomy in the literature (21,36-47)

Study	Design	Patient		FIGO stage	UAP (%)	Cerclage (%)	Follow-up Interval (median, range mo.)	Conception	
		n	Age (median, range)					Delay (mo.)	TTC (n)
Bogani et al. (37)	**Prospective**	**26 (with LPL)**	**32 (26-40)**	**IA2-IB2**	**100**	12 (during pregnancy)	75 (12-184)	-	16
Okugawa et al. (38)	Retrospective	14 (with LPL)	33 (21-43)	AIS-IA1	100	100	61 (8-31)	3-6	4
Plante et al. (39)	Retrospective	35 (with LPL)	29 (22-44)	IA1-IB1	100	- 68.6 (prophylactic) - 2.9 (during pregnancy)	42 (1-100)	-	24
Andikyan et al. (40)	Prospective	9 (with LPL)	28 (18-36)	IA1-IB1	100	0	17 (1-83)	-	-
Fanfani et al. (41)	Retrospective	23 (with LPL)	30 (24-43)	IA2-IB1	100	16.7 (during pregnancy)	40 (32-125)	3-48	10
Lindsay et al. (42)	Retrospective	40 (with LPL)	29 (22-38)	IA2-IB1	100	15 (during pregnancy)	44 (0-91)	-	-
Biliatis et al. (43)	Prospective	35 (88.6% with LPL)	32 (26-43)	IB1	100	0	56 (16-132)	-	-
Palaia et al. (44)	Prospective	14 (with LPL)	32 (28-37)	IA2-IB1	100	0	38 (18-96)	-	-
Raju et al. (45)	Prospective	15 (with LPL)	28 (20-40)	IA2-IB1	100	100 (prophylactic)	96 (12-120)	12	5
Maneo et al. (46)	Prospective	36 (with LPL)	31 (24-40)	IB1	100	-	66 (6-168)	-	-
Rob et al. (21,47)	Prospective	- 32 - 10 cone (with LPL) 22 simple trachelectomy	28.3 (24-35)	IA2 (CKC)-1B1 (simple trachelectomy)	100	-	47 (12-102)	-	24
McHale et al. (48)	Retrospective	4 (without LPL)	30.75	IA1	100	-	48 (25-108)	-	-

FIGO: International federation of gynecology and obstetrics, UAP: Uterine artery preservation, TTC: Traying to conceive, ART: Assisted reproductive technology, CPR: Clinical pregnancy rate, PTD: Preterm delivery, LBR: Live birth rate, SAB: Spontaneous abortion, TAB: Therapeutic abortion, POI: Primary ovarian insufficiency

Obstetric Outcomes				Fertility complications	Cancer rates	
Total pregnancies (n)	**ART pregnancies**	**CPR**	**Details**		**Recurrence (%)**	**Death (%)**
11	-	69%	PTD (9.1%) Term delivery (72.7%) LBR (82%)2nd-trimester SAB (9.1%) Ongoing pregnancy (9.1%)	POI (3.8%)	0	0
1	100% (1 IVF)	25%	PTD (100%) LBR (100%) 2nd-trimester SAB (0) Hemorrhage during pregnancy (100%)	-	0	0
25	8% (1 IVF, 1 IUI)	75%	PTD (8%) Term delivery (72%) LBR (80%)1st-trimester SAB (20%) 2nd-trimester SAB (0)	Cervical stenosis (11.4%)	2.9	0
3	0	3 patients conceived	-	-	0	0
7	14% (1 IVF)	70%	PTD (14.2%) LBR (100%) Placenta previa (14.2%) 2nd-trimester SAB (0)	Cervical stenosis (4.4%)	0	0
18	-	18 patients conceived	PTD (22.2%) LBR (83.3%)1st-trimester SAB (5.6%) TAB (5.6%)	Infected pelvic lymphocyst (2.5%)	5	0
7	-	7 patients conceived	LBR (100%) 2nd-trimester SAB (0)	-	0	0
8	-	8 patients conceived	Term delivery (37.5%)	Cervical stenosis (14.3%)	0	0
4	0	80%	LBR (100%) 2nd-trimester SAB (0)	-	0	0
21	-	17 patients conceived	PTD (9.5%) LBR (66.7%)1st-trimester SAB (14.3%) 2nd-trimester SAB (4.8%) Tubal ectopic pregnancy (4.8%) TAB (4.8%) Ongoing pregnancy (4.8%)	-	5.5	2.8
23	17.4% (2 IUI, 2 IVF)	#######	PTD (13%) LBR (52.2%)1st-trimester SAB (8.7%) 2nd-trimester SAB (13%) Tubal ectopic pregnancy (4.3%) TAB (4.3%) Ongoing pregnancy (13%)	-	3.1	0
3	-	3 patients conceived	LBR (100%) 2nd-trimester SAB (0)	-	0	0

Table 4. Reproductive outcomes of vaginal radical trachelectomy in the literature (44,48-70)

Study	Design	Patients		FIGO Stage	UAP (%)	Cerclage (%)	Follow-up Interval (Median, Range mo.)	Conception	
		n	Age (Median, Range)					Delay (mo.)	TTC (n)
Malmsten et al. (49)	Retrospective	28	(24-37)	IA1-IB1	-	- 96.4 (prophylactic) - 3.6 (subsequently had cerclage outside of pregnancy)	(26.5-182.4)	-	-
Wang et al. (50)	Prospective	83	-	IA1-IB1	100	100 (prophylactic)	36.2 (24-96)	-	69
Wu et al. (51)	Retrospective	7	33 (29-39)	IB1	-	100 (prophylactic)	5 (3-13)	-	-
Zusterzeel et al. (52)	Retrospective	132	31 (24-43)	IA1-IB1	-	100 (prophylactic)	51 (2-153.2)	6	70
Hauerberg et al. (53)	Prospective	120	30 (22-42)	CIS-IB1	-	100 (prophylactic)	55.7 (5.5-147)	-	72
Kim et al. (54)	Prospective	35	33 (24-39)	IA2-IB1	100	- 88.9 (prophylactic) - 11.1 (during pregnancy)	-	6	-
Cao et al. (55)	Prospective	77	29 (18-38)	IA1-IB1	-	-	-	6	43
Speiser et al. (56,57)	Prospective	212	31.9 (21-48)	IA1-IB1	-	100 (prophylactic)	-	-	76
Kim et al. (58)	Retrospective	42	25-38	IA1-IB1	-	100 (prophylactic)	-	6	23

Obstetric outcomes				Fertility Complications	Cancer Rates	
Total Pregnancies (n)	**ART Pregnancies**	**CPR**	**Details**		**Recurrence (%)**	**Death (%)**
22	#######	14 patients	LBR (72.7%) PPROM (22.7%) 1st-trimester SAB (9.1%) 2nd-trimester SAB (4.5%)	- Cervical stenosis (14.3%) - Cerclage erosion (10.7%)	7.1	0
58	0	#######	PTD (13.8%) LBR (86.2%) PPROM (8%) 1st-trimester SAB (6.9%) 2nd-trimester SAB (0) TAB (6.9%)	Amenorrhea (2.4%)	1.2	0
3	-	3 patients conceived	PTD (0) LBR (0) 1st-trimester SAB (100%) 2nd-trimester SAB (0)	Cervical stenosis (14.3%)	14.3	0
47	#######	#######	PTD (25.5%) LBR (78.7%) 1st-trimester SAB (19.1%) 2nd-trimester SAB (0) TAB (2.1%)	- Cerclage erosion (6.1%)	6.8	3
77	#######	#######	PTD (42.9%) LBR (68.8%) PPROM (18.2%) 1st-trimester SAB (20.8%) 2nd-trimester SAB (2.6%) TAB (3.9%)	- Cervical stenosis (23.3%) - Postoperative sepsis (0.8%)	5.1	1.7
9	-	8 patients	PTD (66.7%) LBR (66.7%) PPROM (66.7%) Chorioamnionitis (66.7%) 2nd-trimester SAB (33.3%)	- Cerclage erosion (12.5%)	0	0
21	-	#######	PTD (19%) LBR (40.7%) TAB (23.8%) 1st-trimester SAB (9.5%) 2nd-trimester SAB (9.5%) Tubal ectopic pregnancy (4.8%)	-	9.1	2.6
60	-	#######	PTD (30%) LBR (75%) 1st-trimester SAB (8.4%) 2nd-trimester SAB (5%) Tubal ectopic pregnancy (1.7%) TAB (3.3%)	- Cervical stenosis (12.7%)	3.8	1.9
19	-	#######	PTD (26%) LBR (78.9%) Tubal ectopic pregnancy (18.8%) 1st-trimester SAB (4.3%) 2nd-trimester SAB (0) TAB (13%)	-	0	0

Table 4. Continued

Study	Design	Patients		FIGO Stage	UAP (%)	Cerclage (%)	Follow-up Interval (Median, Range mo.)	Conception	
		n	Age (Median, Range)					Delay (mo.)	TTC (n)
Persson et al. (59)	Retrospective	10	30 (24-38)	IA1-IB1	100	100 (prophylactic)	(48-115)	-	8
Raju et al. (45)	Prospective	49	28 (20-40)	IA2-IB1	100	100 (prophylactic)	96 (12-120)	12	19
Uzan et al. (60)	Retrospective	28	32 (28-40)	IA2-IB1	-	-	59 (3-132)	-	15
Plante et al. (61)	Prospective	125	31 (20-42)	IA1-IIA	-	-	93 (4-225)	6-12 months	61
Knight et al. (62)	Retrospective	3	30.5 (29-45)	IB1	-	100 (prophylactic)	-	-	3
Chen et al. (63)	Prospective	16	24-31	IA1-IB1	100	100 (prophylactic)	(8-50)	-	-
Pahisa et al. (64)	Retrospective	13	-	IB1	-	-	(2-95)	-	4
Sonoda et al. (65)	Retrospective	36	31 (20-40)	IA1-IB1	-	-	21 (3-60)	-	14
Hertel et al. (66)	Prospective	108	32 (21-41)	IA1-IB1	100	100 (prophylactic)	29 (1-128)	-	-
Shepherd et al. (67)	Retrospective	112	(21-45)	IA2-IB1	-	100 (prophylactic)	(1-120)	6	63

Obstetric outcomes				Fertility Complications	Cancer Rates	
Total Pregnancies (n)	**ART Pregnancies**	**CPR**	**Details**		**Recurrence (%)**	**Death (%)**
10	-	#######	PTD (100%) LBR (100%) 2nd-trimester SAB (0)	- Cervical stenosis (30%) - Cerclage erosion (30%) - Pelvic infection (10%)	0	0
17	17.6% (3 IVF)	#######	LBR (82.4%) 1st-trimester SAB (5.9%) 2nd-trimester SAB (5.9%) Tubal ectopic pregnancy (5.9%)	- Amenorrhea (4.1%) - Cervical stenosis (4.1%)	4.1	2
10	10%	60%	PTD (20%) LBR (80%) 1st-trimester SAB (20%) 2nd-trimester SAB (0)	-	7.1	0
106	7.50%	#######	PTD (18%) LBR (73%) 1st-trimester SAB (20%) 2nd-trimester SAB (3%) TAB (4.7%)	- Cervical stenosis (10%) - Pelvic abscess (2%)	4.8	1.6
4	25% (1 IVF)	100%	PTD (75%) LBR (75%) PPROM (25%) 1st-trimester SAB (25%) 2nd-trimester SAB (0)	Cervical stenosis (33.3%)	0	0
5	20% (1 IVF)	5 patients	LBR (40%) 2nd-trimester SAB (40%) Ongoing pregnancy (10%)	Cervical stenosis, hematometra (6.3%)	0	0
3	-	75%	LBR (33%) Ongoing pregnancies (66%) 2nd-trimester SAB (40%)	-	7.6	7.6
14	36%	#######	PTD (21.4%) LBR (28.6%) PTD (21.4%) TAB (11.8%) 1st-trimester SAB (7.1%) Ongoing pregnancy (28.6%)	Infected pelvic lymphocyst (5%)	2.3	0
18	-	-	LBR (66%) 1st-trimester SAB (5.5%) 2nd-trimester SAB (0) TAB (11.1%) Ongoing pregnancies (16.7%)	Cervical stenosis (7.4%)	4	2
55	#######	#######	LBR (50.9%) 2nd-trimester SAB (3.6%) 1st-trimester SAB (25.5%) TAB (3.6%) Tubal ectopic pregnancy (1.8%) Ongoing pregnancy (5.5%)	Uterine perforation (0.89%) Cervical stenosis (3.6%) Cerclage erosion (2.7%) Amenorrhea (2.7%)	3.3	1.8

Table 4. Continued

Study	Design	Patients		FIGO Stage	UAP (%)	Cerclage (%)	Follow-up Interval (Median, Range mo.)	Conception	
		n	Age (Median, Range)					Delay (mo.)	TTC (n)
Bernardini et al. (68)	Prospective	80	30 (25-36)	-	100	100 (prophylactic)	-	-	39
Burnett et al. (69)	Prospective	18	30 (23-41)	IA2-IB1	0	100 (prophylactic)	(8-81)	-	4
Schlaerth et al. (70)	Prospective	6	34 (25-44)	IA2-IB	100	100 (prophylactic)	(28-84)	-	-
Dargent et al. (71)	Prospective	47	(20-40)	IA1-IIB	-	-	52 (7-123)	-	25

FIGO: International federation of gynecology and obstetrics, UAP: Uterine artery preservation, TTC: Traying to conceive, ART: Assisted reproductive technology, CPR: Clinical pregnancy rate, PTD: Preterm delivery, LBR: Live birth rate, SAB: Spontaneous abortion, TAB: Therapeutic abortion, PPROM: Preterm prelabor rupture of membranes

Obstetric outcomes				Fertility Complications	Cancer Rates	
Total Pregnancies (n)	**ART Pregnancies**	**CPR**	**Details**		**Recurrence (%)**	**Death (%)**
22	27% (3 IVF, 3 IUI)	#######	PTD (27.3%) LBR (81.8%) PPROM (22.7%) Placenta previa (4.5%)	-	1.3	0
3	#######	75%	PTD (33.3%) LBR (66.7%) 2nd-trimester SAB (33.3%)	-	0	0
3	-	50%	-	Pelvic hematoma (16.7%)	0	0
20	15%	52%	LBR (50%)	POI (2.1%) Cervical stenosis (4.3%)	4.3	2.1

Table 5. Reproductive outcomes of abdominal radical trachelectomy in the literature (37,50,54,71-91,110)

Study	Design	Patients		FIGO stage	UAP (%)	Cerclage (%)	Follow-up interval (median, range mo.)	Conception	
		n	Age (median, range)					Delay (mo.)	TTC (n)
Li et al. (111)	Retrospective	360	31 (11-42)	IA1-IB1	-	64 (prophylactic)	65 (7-183)	-	149
Ayhan et al. (72)	Retrospective	22	33 (28-39)	IA1-IB1	100	0	47 (22-175)	-	9
Okugawa et al. (38)	Retrospective	- 137 - 89 radical trachelectomy- 48 modified radical trachelectomy	33 (21-43)	IA2-IIA1	0	100 (prophylactic)	61 (8-131)	3-6	57
Wu et al. (51)	Retrospective	3	31 (29-37)	IB1	-	100 (prophylactic)	3 (1-4)	-	-
Kasuga et al. (73)	Prospective	172	-	IA1–IB1	-	100 (prophylactic)	-	6	109
Tamauchi et al. (74)	Retrospective	28	31 (27-37)	IA2-IB1	100	100 (prophylactic)	43 (13-63)	-	12
Tokunaga et al. (75)	Prospective	42	32 (22-39)	IA1-IB1	-	-	29.9 (1-122)	-	18
Vieira et al. (76)	Retrospective	58	29.3 (21-40.3)	IA1-IB1	34.4	-	66 (11-147)	-	27

Obstetric outcomes					Cancer rates	
Total pregnancies (n)	**ART pregnancies**	**CPR**	**Details**	**Fertility complications**	**Recurrence (%)**	**Death (%)**
30	16	17.4	PTD (16.7%) Term delivery (46.6%) elective termination (6.7%) 1st trimester SAB (10%) 2nd trimester SAB (20%)	Cervical stenosis (27%), fallopian tube obstruction (23%), Infertility before surgery (12.6)	-	-
5	60%	-	PTD (40%) LBR (20%) Term delivery (20%) PPROM (20%) 1st-trimester SAB (20%) 2nd-trimester SAB (20%)	Cervical stenosis (4.5%)	4.5	0
20	71.4% (3 IUI, 13 IVF)	-	- PTD (40%) LBR (70%) 1st-trimester SAB (30%) PPROM (30%) Term delivery (30%) 2nd-trimester SAB (0) Hemorrhage during pregnancy (14.3%)	-	0.7	0
0	-	0 patients conceived	-	-	33.3	0
61	69% (3 IUI, 39 IVF)	44%	LBR (70.5%) PPROM (23%) Chorioamnionitis (14.8%) 1st-trimester SAB (16.4%) 2nd-trimester SAB (4.9%) Ongoing pregnancy (8.2%) Placenta previa (3.3%) Massive bleeding during pregnancy (9.8%)	-	0	0
8	87.5% (2 IUI, 5 IVF)	-	PTD (50%) LBR (62.5%) PPROM (37.5%) 1st-trimester SAB (37.5%) 2nd-trimester SAB (0) Term delivery (12.5%)	Cervical stenosis (28%) Amenorrhea (10.7%)	0	0
5	100%	-	LBR (60%) 1st-trimester SAB (20%) TAB (20%) PTD (40%) Term delivery (20%) 2nd-trimester SAB (40%)	-	7.1	4.8
16	-	-	PTD (50%) LBR (56.3%) Term delivery (6.3%) 1st-trimester SAB (18.8%) 2nd-trimester SAB (6.3%) Ongoing pregnancies (18.8%)	Cervical stenosis (8.6%) Cervical erosion (10.3%) Uterine avulsion (1.7%) Pelvic abscess (1.7%)	1.7	1.7

Table 5. Continued

Study	Design	Patients		FIGO stage	UAP (%)	Cerclage (%)	Follow-up interval (median, range mo.)	Conception	
		n	Age (median, range)					Delay (mo.)	TTC (n)
Capilna et al. (77)	Retrospective	26	32 (24-40)	IA2-IB2	0	0	20 (4-43)	-	7
Kucukmetin et al. (78)	Prospective	16	26 (24-36)	IB1	6.3	100 (prophylactic)	43 (8-110)	-	-
Van Gent et al. (79)	Retrospective	28	31 (21-37)	IA2-IB2	100	100	47 (6-122)	-	17
Cao et al. (55)	Prospective	73	31 (22-39)	IA1-IB1	-	-	20.6 (6-42)	6	34
Nishio et al. (80)	Retrospective	114	33 (25-40)	IA1-IB1	100	- 98.2 (prophylactic) - 1.8 (during pregnancy)	33 (25-40)	-	69
Testa et al. (81)	Retrospective	25	31 (22-40)	IA2-IB1	24	- 24 (prophylactic) - 8 (during pregnancy)	29.6 (6-68)	6	6
Muraji et al. (82)	Retrospective	20	25-42	IA1-IB1	60	-	(2-45)	12	10
Nick et al. (83); Pareja et al. (84)	Retrospective	24	29 (21-37)	IA1-IB1	0	100 (prophylactic)	26 (0-65)	6	-
Saso et al. (85)	Retrospective	30 (3 laparoscopic-assisted)	32.5 (23-41)	IA2-IIA	0	80 (prophylactic)	24 (7-113)	-	10
Wethington et al. (86)	Retrospective	70	31 (19-43)	IA1-IIA	0	47 (prophylactic)	(1-124)	-	38
Du et al. (87)	Prospective	60	33 (18-41)	IA2-IB1	-	- 48.3 (prophylactic) - 5 (during pregnancy)	38 (3-84)	6	15

Obstetric outcomes					Cancer rates	
Total pregnancies (n)	**ART pregnancies**	**CPR**	**Details**	**Fertility complications**	**Recurrence (%)**	**Death (%)**
3	-	-	PTD (0) LBR (33%) Term delivery (33%) 1st-trimester SAB (66%) 2nd-trimester SAB (0)	Amenorrhea (11.54%) Pelvic peritonitis (3.85%) Cervical stenosis (3.85%) POI (3.8%)	3.85	0
1	-	1 patient	PTD (0) LBR (100%) Term delivery (100%) 2nd-trimester SAB (0)	Vaginal erosion (6.3%) Cervical stenosis/ hematometra (6.3%)	6.25	0
14	14.3% (2 IVF)	-	PTD (0) LBR (100%) Term delivery (100%) 2nd-trimester SAB (0)	-	7.1	3.6
3	-	8.80%	PTD (0%) LBR (100%) Term delivery (100%) 2nd-trimester SAB (0)	-	0	0
31	71% (2 IUI, 20 IVF)	-	PTD (54.8%) LBR (67.7%) 1st-trimester SAB (12.9%) 2nd-trimester SAB (3.2%) Term pregnancy (12.9%) Ongoing pregnancy (16.1%) Placenta previa with accreta (3.2%)	Cervical stenosis (3.5%) PID (5.2%)	0	0
3	0	50%	PTD (66.7%) LBR (100%) Term delivery (33.3%) 2nd-trimester SAB (0)	Cervical stenosis (8%) Asherman syndrome (4%)	0	0
1	0	10%	PTD (100%) LBR (100%) 2nd-trimester SAB (0)	Cervical stenosis (10%) Amenorrhea (10%) Infected pelvic lymphocyst (5%)	0	0
4	25% (1 IVF)	3 patients conceived	PTD (25%) LBR (25%) 1st-trimester SAB (50%) 2nd-trimester SAB (25%)	Cerclage erosion (16.7%) Cervical stenosis (12.5%) Amenorrhea (29.2%) Pelvic abscess (4.2%)	0	0
3	33% (1 IVF)	30%	PTD (0) LBR (66.7%) PPROM (33%) 2nd-trimester SAB (33%) Term delivery (66.7%)	Uterine avulsion (3%) Cervical stenosis/ hematocolpos (3%)	10	6.7
31	-	74%	LBR (51.6%) 1st-trimester SAB (9.7%) 2nd-trimester SAB (19.5%)	Cervical stenosis (12%) Cerclage erosion (2%)	4	0
8	-	33%	PTD (25%) LBR (62.5%) PPROM (25%) 1st-trimester SAB (12.5%) 2nd-trimester SAB (0) Ongoing pregnancy (25%)	Cervical stenosis (28.3%) Infected pelvic lymphocyst (8.3%) Amenorrhea (5%)	3.3	0

Table 5. Continued

Study	Design	Patients		FIGO stage	UAP (%)	Cerclage (%)	Follow-up interval (median, range mo.)	Conception	
		n	Age (median, range)					Delay (mo.)	TTC (n)
Li et al. (88)	Retrospective	59	29.5 (11-41)	IA1-IB1	100	100 (prophylactic)	23 (1-78)	6	10
Yao et al. (89)	Retrospective	10	29 (28-30)	IA2-IB1	100	100 prophylactic (using mesh)	(4-68)	-	-
Olawaiye et al. (90)	Retrospective	10	32 (24-38)	IA1-2A	-	100 prophylactic	(1-74)	-	3
Ungar et al. (91)	Prospective	30	30.5 (23-37)	IA2-IB2	0	0	47 (14-75)	24	5
Rodriguez et al. (92)	Retrospective	3	26 (24-30)	IA2	33	100 (prophylactic)	(9-31)	-	-

FIGO: International federation of gynecology and obstetrics, UAP: Uterine artery preservation, TTC: Traying to conceive, ART: Assisted reproductive technology, CPR: Clinical pregnancy rate, PTD: Preterm delivery, LBR: Live birth rate, SAB: Spontaneous abortion, TAB: Therapeutic abortion, PPROM: Preterm prelabor rupture of membranes

Obstetric outcomes					**Cancer rates**	
Total pregnancies (n)	**ART pregnancies**	**CPR**	**Details**	**Fertility complications**	**Recurrence (%)**	**Death (%)**
2	50% (1 IVF)	20%	PTD (0%) LBR (50%) Term delivery (50%) Ongoing pregnancy (50%) 2nd-trimester SAB (0)	Cervical stenosis (8.5%) Infected pelvic lymphocyst (3.4%) - 5.1% POI	0	0
2	50% (1 IVF)	2 patients conceived	PTD (50%) LBR (100%) Term delivery (50%) 2nd-trimester SAB (0)	-	0	0
3	66.7% (1 IUI, 1 IVF)	-	PTD (33%) LBR (66.7%) Term pregnancy (33%) Ongoing pregnancy (33%) 2nd-trimester SAB (0)	Cervical stenosis (20%) Cerclage expulsion (20%)	0	0
3	33% (1 IVF)	60%	PTD (0) LBR (66.7%) 1st-trimester SAB (33.3%) Term delivery (66.7%) 2nd-trimester SAB (0)	Asherman syndrome (6.7%) Cervical stenosis (3.3%)	0	0
2	0	1 patient conceived	PTD (0) LBR (50%) Term delivery (50%) Ongoing pregnancy (50%) 2nd-trimester SAB (0)	Cervical stenosis (33%) Pelvic abscess (33%)	0	0

Table 6. Reproductive outcomes of laparoscopic radical trachelectomy with or without robotic assistance in the literature (20,57,62,69,75,77,82,92-98)

Study	Design	Patients		FIGO stage	UAP (%)	Cerclage (%)	Follow-up interval (median, range mo.)	Conception	
		n	Age (median, range)					Delay (mo.)	TTC (n)
Johansen et al. (93)	Prospective	48 (with RA)	29 (23-41)	IA1-IB1	95.8	100 (prophylactic)	24 (1-89)	-	21
Vieira et al. (76)	Retrospective	42 (22 with RA)	30.1 (25.4-40.6)	IA1-IB1	4.8	-	25 (10-69)	-	7
Kucukmetin et al. (78)	Prospective	11	28 (25-40)	IB1	9.1	100 (prophylactic)	9 (1-20)	-	-
Park et al. (20)	Prospective	79	31 (20-40)	IA2-IB1	-	-	29 (5-90)	-	-
Ebisawa et al. (94)	Retrospective	56	(22-42)	IA2-IB1	100	100 (prophylactic)	60 (4-138)	6	25
Lu et al. (95)	Retrospective	25	29 (22-34)	IA2-IB1	100	100 (prophylactic)	66 (1-82)	6	12
Kim et al. (58)	Retrospective	4 (with RA)	(25-38)	IA1-IB1	-	100 (prophylactic)	-	6	0
Nick et al. (83)	Retrospective	8 (with RA)	29 (21-37)	IA1-IB1	0	100 (prophylactic)	11 (0-65)	6	-
Martin et al. (96)	Retrospective	9	-	IA2-IB1	77.8	100 (prophylactic)	(6-32)	6	4
Burnett et al. (97)	Retrospective	6 (with RA)	27 (25-30)	IB1	100	100 (prophylactic)	(9-13)	-	-
Park et al. (98)	Retrospective	4	29.5 (25-33)	IA2-IB1	0	100 (prophylactic)	(27-37)	-	-

Obstetric outcomes				Fertility complications	Cancer rates	
Total pregnancies (n)	**ART pregnancies (%)**	**CPR**	**Details**		**Recurrence (%)**	**Death (%)**
20	5	81%	- LBR (80%) - 2nd-trimester SAB (5%) - 1st-trimester SAB (5%) - 2nd-trimester SAB (0) - Ongoing pregnancy (10%)	- Cerclage erosion (8.3%) - Cervical stenosis (2%)	4.2	0
3	-	-	- LBR (33%) - PTD (33%) - 1st-trimester SAB (33%) - 2nd-trimester SAB (0) - Ongoing pregnancy (33%)	- Cerclage erosion (11.9%) - Cervical stenosis (7.1%) - Uterine necrosis requiring hysterectomy (2.4%) - Peritonitis (2.4%)	0	0
0	-	0 patients conceived	-	-	0	0
17	-	13 patients conceived	- LBR (76.5%) - PTD (41.2%) - Term delivery (35.3%) - 1st-trimester SAB (23.5%) - 2nd-trimester SAB (0)	-	3.8	0
21	47.6	52%	- LBR (61.9%) - PTD (47.6%) - PPROM (38.1%) - 2nd-trimester SAB (9.5%) - 1st-trimester SAB (23.8%) - Ongoing pregnancy (4.8%)	Cervical stenosis (8.9%)	1.8	1.8
9	33.3	75%	- LBR (44%) - PTD (11.1%) - PPROM (11.1%) - Chorioamnionitis (11.1%) - 1st-trimester SAB (33.3%) - 2nd-trimester SAB (0) - Term delivery (33.3%) - Ongoing pregnancy (22.2%)	-	0	0
0	-	0	-	-	0	0
0	-	0 patients conceived	-	-	0	0
2	50	50%	- LBR (50%) - Term delivery (50%) - Ongoing pregnancy (50%) - PTD (0) - 2nd-trimester SAB (0)	-	11.1	0
0	0	0 patients conceived	-	Extrusion of cerclage (28%)	0	0
0	-	0 patients conceived	-	-	25	0

Table 6. Continued

Study	Design	Patients		FIGO stage	UAP (%)	Cerclage (%)	Follow-up interval (median, range mo.)	Conception	
		n	Age (median, range)					Delay (mo.)	TTC (n)
Chen et al. (63)	Prospective	16	27.6 (24-31)	IA1-IB1	100	100 (prophylactic)	28.2 (8-50)	-	-
Jolley et al. (99)	Retrospective	2	30.5 (29-32)	IB1	-	•50 (prophylactic)•50 (during pregnancy)	-	-	2
Schlaerth et al. (70)	Retrospective	4	28.5 (24-34)	IA2-IB	0	100 (prophylactic)	(28-84)	-	-

ART: Assisted reproduction technology, CPR: Clinical pregnancy rate, FIGO: International Federation of Gynecology and Obstetrics, LBR: Live birth rate, POI: Primary ovarian insufficiency, PPROM: Preterm prelabor rupture of membranes, PTD: Preterm delivery, RA: Robotic assistance, SAB: Spontaneous abortion, TTC: Trying to conceive, UAP: Uterine artery preservation

by performing laparoscopic radical trachelectomy with or without robotic assistance. These benefits include and are not limited to lower short- and long term moribidity, decreased blood loss and shorter hospital stay.

Since this is a relatively new procedure, we recommend that patients should be referred to centers of excellence in gynecologic oncology with extensive experience in the evaluation and surgical management of early-stage cervical cancer. In brief, our recommendation is to perform a thorough histopathologic and preoperative evaluation. Performing a pelvic MRI, contrast axial CT, and positron emission tomography for proper assessment of the parametrium and possible lymphadenopathy is encouraged.

The LACC trial recently provided the notion that use of uterine manipulator might be associated with cancer recurrence and decreased survival rate. For that reason, our recommendation is to avoid uterine manipulators especially in the setting of a visible cervical lesion. At times and if no visible cervical lesion is present, after the cervix and parametrium are completely mobilized and resected the uterine manipulator to assist with making colpotomy can be used. We recommend removing the specimen immediately after transected from the vagina and maybe in a specimen retrieval bag. Appropriate radicality of the procedure should be assessed by confirming cancer free margins. Anastomosis of the vagina to uterine corpus and possible cerclage placement can be done either laparoscopically or vaginally per surgeon's preference. In the setting that there is visible disease on cervix, laparoscopic approach can be used to mobilize the cervix and dissect the parametrium and then the procedure can be converted to vaginal route. Colpotomy can be done vaginally with adequate margins. We recommend to bring the vaginal mucosa over the cervix at this point and clamp with appropriate instruments to cover the diseased cervix. The cervix should be amputated with negative margins and then the reanastomosis procedure can be continued vaginally. We believe that the role of surgeon's learning curve in the outcomes of these minimally invasive procedures is significant; this will make designing a randomized controlled trials comparing laparoscopic radical trachelectomy, with and without robotic assistance, and other surgical approaches hard.

Conclusion

Our study has several strengths. To the best of our knowledge, this is the largest and most comprehensive review of obstetrics, reproductive and fertility outcomes of fertility sparing methods in the setting of early-stage cervical cancer. To calculate the clinical pregnancy rate, we included only those who were trying to conceive as opposed to all the patients who undergone fertility sparing procedure.

Potential limitations of our study were limitations of data presented in the literature, with a lack of control over confounders that may affect oncologic or reproductive outcomes. This includes previous infertility or potential comorbid diagnosis. Also there were limited information

Obstetric outcomes				Fertility complications	Cancer rates	
Total pregnancies (n)	ART pregnancies (%)	CPR	Details		Recurrence (%)	Death (%)
5	20	5 patients	- LBR (40%) - PTD (20%) - Term delivery (20%) - 2nd-trimester SAB (40%) - PPROM (20%) - Ongoing pregnancy (20%)	Cervical stenosis, hematometra (6.25%)	0	0
3	0	100%	- LBR (66.6%) - PTD (66.6%) -1st-trimester SAB (33.3%) - 2nd-trimester SAB (0)	Cerclage erosion (50%)	0	0
1	-	25%	-	Cervical stenosis (50%)	0	0

regarding the details of the ART methods and protocols in primary literature.

Although no statistically significant difference was found in the preterm delivery rate across different fertility sparing approaches, the data for iatrogenic preterm deliveries was not available in the primary literature. Initially obstetricians tend to iatrogenically deliver their patient at 34 weeks, after fertility sparing procedures (62,104). Since the use of cerclage to prevent preterm delivery is not supported by high level evidence-based literature patients recently have been scheduled for delivery closer to term (108). For this reason there is an iatrogenic component in higher rate of preterm delivery in older and compared to more recent literature.

Attention to multiple factors is required to determine the optimal approach to fer-tility sparing procedure in early-stage cervical cancer. Patient's preference, disease's stage, surgeon's experience and available surgical instrumentation are some of these important factors. In this review, we provided the most updated relevant data that can be used in preoperative counseling. Further research in high volume surgical centers are encouraged to address the outcomes of minimally invasive radical trachelectomy in more details. We encourage multidisciplinary patient counseling, with gynecologic oncologists, reproductive endocrinologists, and maternal fetal medicine specialists present to set reasonable expectations regarding treatment and outcomes.

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