

Review

Surgical, oncological, and obstetrical outcomes after abdominal radical trachelectomy – A systematic literature review

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HIGHLIGHTS

- Abdominal radical trachelectomy is associated with excellent oncologic outcomes.
- Pregnancy rates are similar to those of vaginal radical trachelectomy.
- Most frequent complication after abdominal radical trachelectomy is cervical stenosis.

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ABSTRACT

Objective. Radical trachelectomy is a standard treatment for selected patients with early-stage cervical cancer. Outcomes are well established for vaginal radical trachelectomy (VRT), but not for abdominal radical trachelectomy (ART).

Methods. We searched MEDLINE, EMBASE, and CINAHL (October 1997 through October 2012) using the terms: *uterine cervix neoplasms, cervical cancer, abdominal radical trachelectomy, vaginal radical trachelectomy, fertility sparing, and fertility preservation.* We included original articles, case series, and case reports. Excluded were review articles, articles with duplicate patient information, and articles not in English.

Results. We identified 485 patients. Ages ranged from 6 to 44 years. The most common stage was IB1 (331/464; 71%), and the most common histologic subtype was squamous cell carcinoma (330/470; 70%). Operative times ranged from 110 to 586 min. Blood loss ranged from 50 to 5568 mL. Three intraoperative complications were reported. Forty-seven patients (10%) had conversion to radical hysterectomy. One hundred fifty-five patients (35%) had a postoperative complication. The most frequent postoperative complication was cervical stenosis (n = 42; 9.5%). The median follow-up time was 31.6 months (range, 1–124). Sixteen patients (3.8%) had disease recurrence. Two patients (0.4%) died of disease. A total of 413 patients (85%) were able to maintain their fertility. A total of 113 patients (38%) attempted to get pregnant, and 67 of them (59.3%) were able to conceive.

Conclusion. ART is a safe treatment option in patients with early-stage cervical cancer interested in preserving fertility.

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Introduction

The standard recommendation for the treatment of patients with early-stage cervical cancer (stages IA2–IB1) is radical hysterectomy or, for those interested in preserving fertility, radical trachelectomy [1].

In 1994, Dargent et al. [2] were the first to report on the utility of vaginal radical trachelectomy (VRT) with laparoscopic lymph node dissection for the treatment of early-stage cervical cancer. Since that time, more than 900 cases of VRT have been reported, establishing the obstetrical and oncological outcomes of this procedure [3–11]. Radical trachelectomy can also be done entirely laparoscopically [12,13] or by robotic approach [14–16], but for these approaches, the number of reported cases is low and the follow-up times are too short to permit conclusions regarding the procedures' safety.

In 1997, Smith et al. published the first report of abdominal radical trachelectomy (ART) [17]. Since then, several authors have reported on the safety and feasibility of this procedure [16,18–45]. The advantages of ART include the reproducibility of the technique, the fact that the procedure can be performed without training in radical vaginal surgery and requires no laparoscopic equipment, and the wider parametrial resection than can be achieved with abdominal radical trachelectomy. However, the oncological and obstetrical outcomes of ART are not well established. The aim of this review was to evaluate the surgical, oncological, and obstetrical outcomes of all reported cases of ART.

Methods

We performed a systematic review of the English-language literature on fertility-sparing surgery in patients with cancer of the

uterine cervix. The MEDLINE, EMBASE, and CINAHL databases were searched for articles published during the period from 1997 through 2012. The terms used in the search were *uterine cervix neoplasms*, *early cervical cancer*, *abdominal radical trachelectomy*, *vaginal radical trachelectomy*, *fertility sparing*, and *fertility preservation*. Reference lists of all articles identified by our searches were reviewed. The inclusion criteria were as follows: articles published in English and articles including information about patient age, histologic subtype, stage, operative time, estimated blood loss, transfusion rates, intra-operative and postoperative complications, number of lymph nodes retrieved, residual disease, adjuvant therapy, follow-up period, obstetrical outcomes, and oncological outcomes. These criteria were used as reference for inclusion; however, noting that in a review article some publications analyzed would either lack specific information or such information would be provided in a limited fashion. We excluded review articles, articles with duplicate patient information, and studies updating series.

Our initial searches identified a total of 46 articles. Two case series were excluded because they contained very limited information. Of the remaining 44 articles, 29 met the inclusion criteria and were included in this review.

The rate of fertility preservation was determined based on the number of patients who were offered a radical trachelectomy and ultimately had the intended procedure. We also analyzed the rate of fertility preservation in patients who underwent a radical trachelectomy by excluding those who required adjuvant therapy. The pregnancy rates were calculated based on a total number of women who were able to conceive out of all patients who retained their fertility. The information was summarized using measures of central

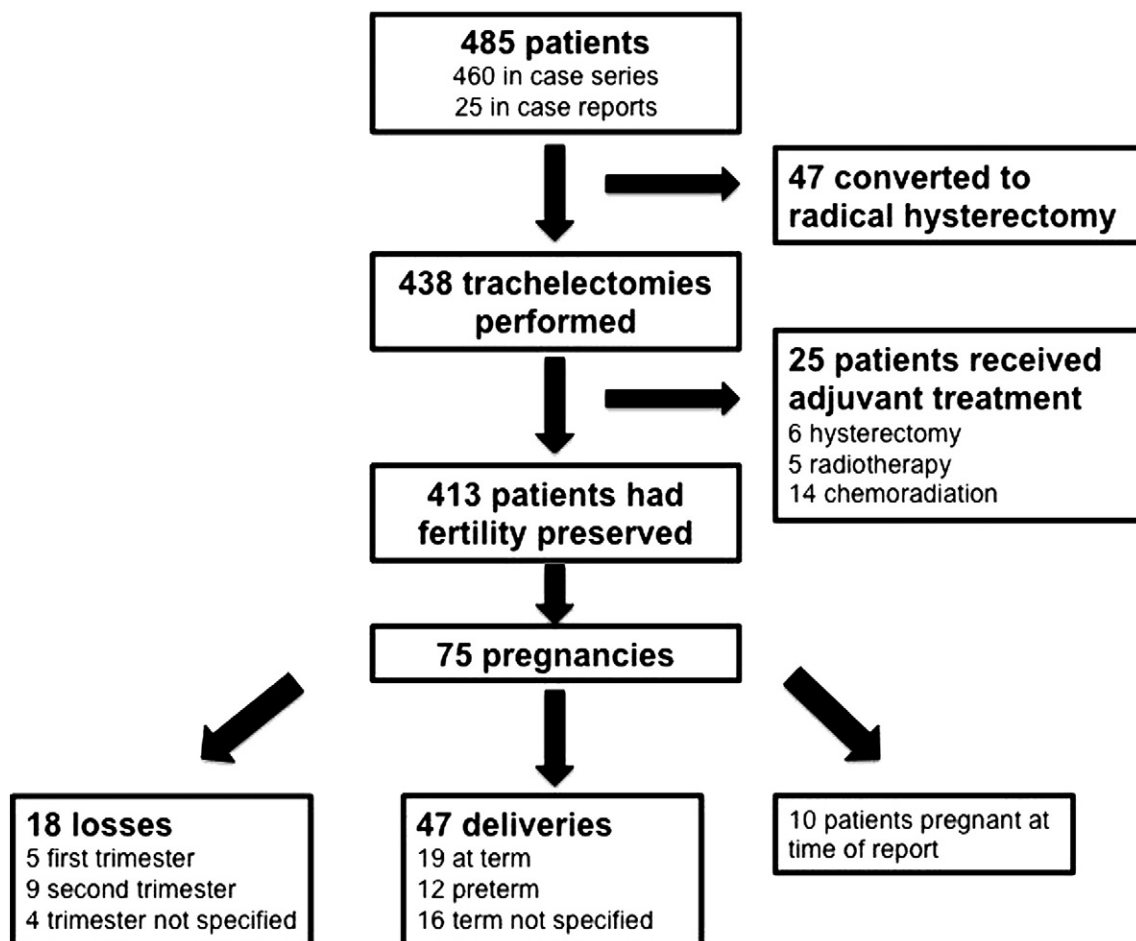


Fig. 1. Abdominal radical trachelectomy outcomes.

tendency and dispersion for continuous variables and proportions for categorical or ordinal variables. The results of the frequencies of the different variables were assessed using descriptive statistics. These results are presented in tables and graphs of frequency distribution. The data were processed using STATA 12.1 version.

Results

The 29 articles included in this review were 12 reports of case series, which included a total of 460 patients, and 17 case reports that included 25 patients. Thus, this review includes information on 485 patients who underwent ART (Fig. 1). Demographic and tumor information is summarized in Table 1. The patients ranged in age from 6 to 44 years. The most common histologic subtype was squamous cell carcinoma (331/470; 70%), and the second most common was adenocarcinoma (110/470; 23%). The remaining 29 patients for whom histologic subtype was known had adenosquamous carcinoma ($n = 18$), sarcoma botryoides ($n = 4$), glassy cell carcinoma ($n = 3$), clear cell carcinoma ($n = 3$), and lymphoepithelioma-like carcinoma ($n = 1$). The majority of patients (330/464; 71%) had stage IB1 disease. Tumor size was reported for 202 patients. Of these, 166 (82.1%) had a tumor size smaller than 2 cm. The percentage of patients with lymph-vascular space invasion ranged from 8% to 80.3%.

Intraoperative and postoperative outcomes are summarized in Table 2. The operative time ranged from 110 to 586 min. The estimated blood loss ranged from 50 to 5568 mL, and the transfusion rates ranged from 9% to 98.4%. Data on cerclage placement were available for 328 patients. Of these, 251 (76.5%) had a cerclage placed at the time of surgery. The number of pelvic lymph nodes removed ranged from 2 to 69. A total of 438 patients had lymph node status reported and of these fifty-seven (13%) had positive nodes. The percentage of patients with no residual disease in the final pathology specimen was 49.5% (104/210). The length of hospitalization ranged from 2 to 63 days.

Intraoperative and postoperative complications are summarized in Table 3. Intraoperative complications were reported for 422 patients and postoperative complications were reported for 438 patients. There were 3 intraoperative complications. One patient suffered severe hemorrhage from the right vesicouterine ligament that necessitated a reoperation. Another patient had a ureteral injury, and the third patient had an injury to the external iliac artery. There were no intraoperative deaths. One hundred fifty-five of 438 patients

(35.4%) had a postoperative complication. The most frequent postoperative complication was cervical stenosis (42 patients; 9.5%). Infection, abscess, or antibiotic use occurred in 38 patients (8.6%), and lymphocyst occurred in 26 patients (5.9%).

Follow-up time was reported for 471 patients. The median follow-up time was 31.6 months (range, 1 to 124). Sixteen patients after ART (3.8%) had a recurrence. The locations of recurrence were as follows: pelvic sidewall (4 patients), residual cervix (4), pelvic nodes (2), abdominal wall (1), paraaortic nodes (1), sacral bone (1), and not reported (3). Only two patients (0.4%) died from cervical cancer after ART.

Information on fertility preservation, pregnancy, and obstetrical outcomes is summarized in Table 4. Seventy-two patients (14.8%) were not able to maintain their fertility after ART. The reasons were as follows: immediate conversion to radical hysterectomy (47 patients), post-trachelectomy radical hysterectomy (6), and postoperative adjuvant radiotherapy and/or chemotherapy (19). The remaining 413 patients (85%) were able to maintain their fertility.

Information on pregnancy and obstetrical outcomes was available for 298 patients. A total of 113 patients (38%) attempted to get pregnant, and 67 of them (59.3%) were able to conceive. Of all patients who retained their fertility, 67 (16.2%) were able to get pregnant. There were 18 pregnancy losses (5 occurred in the first trimester, 9 occurred in the second trimester, and the timing was not reported for the other 4). Forty-seven deliveries were reported, 19 at term, 12 before 36 weeks, and 16 not specified. Of note, there were 10 pregnancies ongoing at the time of the published reports. Ten patients underwent ART during pregnancy [36, 39, 42, 43, 45].

Discussion

The findings of this review indicate that ART is a reproducible and safe procedure for treating early cervical cancer in women who wish to preserve their fertility. The surgical and oncological outcomes were very favorable. ART was associated with similar pregnancy rates to those reported for VRT (16% vs. 24%).

We found that the intraoperative complication rate for ART (0.7%) was lower than the rate previously reported for VRT (5.6%) in other large series [8]. The rate of postoperative complications for ART was 35%, this complication rate was higher than the postoperative complication rate of 8% previously reported by Milliken et al. for VRT [46].

Table 1
Demographic and tumor information for patients who underwent abdominal radical trachelectomy.

Author (year)	N	Median age (range), y	Histology			Stage					Tumor size	LVSI + preop N° (%)
			SCC	AC	Other	IA1 + LVSI	IA2	IB1	Other			
Ungar (2005)	33 ^a	30.5 (23–37) ^e	26	1	3 (1 adsq, 2 glassy)	0	10	15	5 (IB2)		NR	8 (26.6)
Pareja (2008)	15	30 (25–38)	11	4	0	0	3	12	0		<2 cm	5 (33)
Nishio (2009)	71 ^b	33 (26–44)	58	2	1 (adsq)	4	8	49	0		NR	49 (80.3)
Jeremic (2009)	12	30.5 (22–40) ^e	12	0	0	2	7	3	0		<2 cm	NR
Yao (2010)	10	29 (28–30) ^e	8	2	0	0	5	5	0		<2 cm	NR
Du (2011)	68	28 (18–41) ^e	68	0	0	3	28	37	0		56 < 2 cm, 12 > 2 cm	NR
Li (2011)	64 ^c	29.5 (11–41)	50	8	4 (3 bot, 1 adsq)	16	7	36	0		45 < 2 cm, 14 > 2 cm	NR
Nick (2011)	25	28.8 (21.4–37.2)	7	15	3 (adsq)	2	7	16	0		NR	2 (8)
Saso (2012)	30	32.5 (23–41) ^e	15	10	5 (4 adsq, 1 glassy)	0	2	25	3 (2 IB2, 1 IIA)		25 < 2 cm, 5 > 2 cm	NR
Muraji (2012)	23	33 (25–42)	16	6	1 (adsq)	2	2	19	0		NR	5 (21.7)
Karateke (2012)	8	27 (18–35)	4	3	1 (clear)	0	0	7	1 (IIA)		3 < 2 cm, 5 > 2 cm	3 (37.5)
Wethington (2012)	101	31 (19–43) ^e	40	54	7 (6 adsq, 1 clear)	3	8	88	2 (IB2, IIA)		NR	47 (47)
Case reports ^d	25	(6–37)	16	5	4 (3 clear, 1 bot)	1	3	18	–		NR	–
Total	485		331	110	29	33	90	330	11			

AC, adenocarcinoma; adsq, adenosquamous carcinoma; bot, sarcoma botryoides; clear, clear cell carcinoma; glassy, glassy cell carcinoma; LVSI, lymph-vascular space invasion; NR, not reported; preop, preoperative; SCC, squamous cell carcinoma.

^a Histology and stage not reported for 3 patients.

^b Histology and stage not reported for 10 patients.

^c Histology not reported for 2 patients; stage and tumor size not reported for 5 patients.

^d Stage not reported for 3 patients.

^e Mean.

Table 2
Intraoperative and postoperative outcomes for patients who underwent abdominal radical trachelectomy.

Author (year)	No. of planned trachelectomies	Trachelectomy done, n (%)	Immediate hysterectomy, n (%)	Outcomes of trachelectomy						
				Median surgical time (range), min	Median blood loss (range), mL	Transfusions, n (%)	Median no. of pelvic nodes removed (range)	No. of patients with positive pelvic nodes	No residual disease, n (%)	Hospital stay, days (range)
Ungar (2005)	33	30 (90.9)	3 (9)	226 (170–300) ^c	NR	20 (66.6)	32.2 (17–44) ^c	2	NR	14 (12–22) ^c
Pareja (2008)	15	15 (100)	0	265 (210–330)	400 (200–1000)	4 (27)	26 (11–48)	0	7 (47)	3 (2–7)
Nishio (2009)	71	61 (85.9)	10 (14)	436 (317–586)	1169 (352–5568)	60 (98.4)	38 (17–69)	15	33 (54)	23 (11–63)
Jeremic (2009)	12	11 (91.6)	1 (8.3)	NR	NR	NR	NR	1	NR	NR
Yao (2010)	10	10 (100)	0	261 (204–345) ^c	370 (150–500) ^c	NR	NR	0	NR	21.5 (19–29) ^c
Du (2011)	68	60 (88.2) ^a	8 (11.8)	NR	NR	NR	NR	8	NR	NR
Li (2011)	64	62 (96.8)	2 (3.12)	148 (110–230)	362 (100–700)	4 (6.45)	25 (12–53)	5	NR	10.14 (7–21)
Nick (2011)	25	24 (96)	1 (4)	328 (203–392)	300 (50–1100)	2 (8)	18 (7–33)	3	16 (64)	4 (3–9)
Saso (2012)	30	30 (100)	0	170 (110–300) ^c	813 (50–4300) ^c	6 (20)	24 (7–52)	3	NR	NR
Muraji (2012)	23	21 (91.3)	2 (8.7)	NR (175–352)	NR (200–988)	NR	NR	1	17 (68)	NR
Karateke (2012)	8	8 (100)	0	163 (120–210)	NR	NR	32 (19–48)	0	2 (25)	8 (5–12)
Wethington (2012)	101	81 (80)	20 (20)	NR	NR	NR	24 (2–60)	19	29 (44)	NR
Case reports ^b	25	25 (100)	0	–	–	–	–	–	–	–

Most case reports, did not provide enough complete information. NR, not reported.

^a Twenty-one patients received adjuvant chemotherapy.

^b No available data to calculate outcomes.

^c Mean.

The most frequent complication was cervical stenosis and this was most likely associated with cerclage placement or failure to use tools or techniques that would prevent stenosis such as an intrauterine cannula. In a comparative series of robotic radical trachelectomy vs. abdominal radical trachelectomy, Nick et al. [16] showed that the rate of cervical stenosis prior to use of an intrauterine cannula (Smitt sleeve) was 14% and after implementation of this new technique the rate was zero percent.

We found that the great majority of patients undergoing ART were able to preserve fertility immediately after the procedure: 85%, which was similar to the 91.1% rate of fertility preservation in previously reported series of VRT [47] (Table 5). In our review of the literature we found that the proportion of women trying to become pregnant

ranged from 17.8% [27] to 54% [31]. The rate of pregnancy loss after ART (24%) appeared lower than those previously reported for VRT (30%) [47] but higher to those in the general population (12%) [48]. We found that the pregnancy rates in patients undergoing ART was 16.2%. The pregnancy rate in those who underwent VRT, according to the article by Ribeiro [47], was 24%. However, we must recognize that these figures are calculated based on the total number of women who conceive of all women who retained their fertility. This does not include the total number of women who attempted to get pregnant and were unable to conceive.

Whether cerclage influences perinatal outcomes is a subject of controversy. In our review, we found that 76% of patients had a cerclage. In a study by Cibula et al. [22], the investigators reported

Table 3
Intraoperative and postoperative complications for patients who underwent abdominal radical trachelectomy.

Reference	No. of patients undergoing trachelectomy	Intraoperative complications	Postoperative complications
Ungar (2005)	30	Ureteral injury (n = 1)	Antibiotic use (n = 14), endometrial cavity obliteration (n = 2)
Pareja (2008)	15	Injury to external iliac artery (n = 1)	Tuboovarian abscess (n = 1), cerclage expulsion (n = 2), voiding dysfunction (n = 1), pelviperitonitis (n = 1)
Nishio (2009)	61	Secondary hemorrhage necessitating laparotomy (n = 1)	Cervical stenosis (n = 1), amenorrhea (n = 5), postsurgical infection (n = 15), lymphocyst requiring drainage (n = 9)
Jeremic (2009)	11	Not reported	Hematometra (n = 1)
Yao (2010)	10	None	Lymphocyst (n = 1)
Du (2011)	60	None	Cervical stenosis (n = 17), leg lymphedema (n = 7), infected pelvic lymphocyst (n = 5), amenorrhea (n = 3)
Li (2011)	62	None	Cervical stenosis (n = 5), infected lymphocyst (n = 2), vesical dysfunction (n = 1)
Nick (2011)	24	None	Urinary tract infection or urinary retention (n = 7), fever (n = 5) abnormal uterine bleeding or amenorrhea (n = 8) cerclage erosion (n = 4), cervical stenosis (n = 3)
Saso (2012)	30	None	Hematocolpos (n = 1), uterovaginal suture detachment (n = 1), omental prolapse through vaginal sutures (n = 1)
Muraji (2012)	21	None	Amenorrhea (n = 2), lymphocyst (n = 4), cervical stenosis (n = 2)
Karateke (2012)	8	None	Pelvic abscess (n = 1), leg edema (n = 1), lymphocyst (n = 1)
Wethington (2012)	81	None	Cervical stenosis (n = 12), lymphocyst (n = 4), ileus (n = 4), cerclage erosion (n = 2), pulmonary embolism (n = 1)
Case reports	25	Not reported (n = 5) None (n = 20)	Cervical stenosis (n = 2), pelvic abscess (n = 1), acute vulvar edema (n = 1)

Table 4
Pregnancy rates and obstetrical outcomes for patients who underwent abdominal radical trachelectomy.

Author	No. of planned trachelectomies	Trachelectomy done, n (%)	Fertility preserved, n (%)	Attempting to conceive, n (%)	Pregnancies	Miscarriages		Deliveries		Patients pregnant at time of report
						1st term	2nd term	At term	Preterm	
Ungar (2005)	33	30 (90.9)	NR	NC	3	1	0	2	0	0
Pareja (2008)	15	15 (100)	14 (93.3)	6/14 (42.8)	3	0	0	2	1	0
Nishio (2009)	71	61 (85.9)	57 (80.2)	29/57 (50.8)	4	0	0	2	2	0
Jeremic (2009)	12	11 (91.6)	10 (83.3)	NR	NR	NR	NR	NR	NR	NR
Yao (2010)	10	10 (100)	10 (100)	NR	2	0	0	1	1	0
Du (2011)	68	60 (88.2)	60 (88.2)	15/60 (25)	8	1 ^a		3	2	2
Li (2011)	64	62 (96.8)	59 (92.1)	10/59 (16.9)	2	0	0	1	0	1
Nick (2011)	25	24 (96)	21 (84.0)	11/21 (52.3)	3	1	1	0	1	0
Saso (2012)	30	30 (100)	NR	NC	3	0	1	2	0	0
Muraji (2012)	23	21 (91.3)	20 (86.9)	NR	1	0	0	0	1	0
Karateke (2012)	8	8 (100)	8 (100)	NR	3	0	1	1	1	0
Wethington (2012)	101	81 (80)	70 (69.3)	38/70 (54.2)	31	3	6	16 ^b		6
Case reports	25	25 (100)	22 (88%)	4/17 (23.5) ^c	12	3 ^a		5	3	1
Total	485	438 (90.3)		113/298 (37.9)	75	9	9	35	12	10

NC, not calculable. NR, not reported.

^a Trimester in which miscarriage occurred not indicated.

^b Delivery time not indicated.

^c Attempting to conceive not reported in 8 patients.

on 24 patients who underwent ART. None of these patients had cerclage placement. In this study there was 1 miscarriage and 5 deliveries, 3 preterm and 2 at term. The most frequent postoperative complication in our review was cervical stenosis and this was noted in 42 patients (9.5%).

The relapse rate after ART (3.8%) was similar to that previously reported after VRT (4.2%) [47]. The death rate after ART (0.4%) was smaller than that previously reported after VRT (2.9%) [47]. However, one must take into account that VRT was performed in earlier years than ART, when the selection criteria were not as strict, and that VRT series included patients at very high risk of recurrence, such as patients with larger tumors and high-risk histologic subtypes. The oncological safety of VRT was addressed in a recently reported meta-analysis that compared VRT vs. radical hysterectomy and included 587 women. The analysis showed that there was no significant difference between the two groups in recurrence rate [hazard ratio (HR) for radical trachelectomy vs. radical hysterectomy, 1.38; 95% CI, 0.58–3.28; $p = 0.47$], 5-year recurrence-free survival rate (HR, 1.17; 95% CI, 0.54–2.53; $p = 0.69$), or 5-year overall survival rate (HR, 0.86; 95% CI, 0.30–2.43; $p = 0.78$) [49].

This study is, to our knowledge, the largest analysis of ART thus far in the literature. Our study is, however, limited by several factors. As it was a review of retrospective studies, not all variables were reported consistently, nor were the selection criteria for ART the same. In addition, in the majority of the series, the follow-up time

was short, which could have led to an underestimation of pregnancy rates. Similarly, because of the short follow-up time, the oncological outcomes may seem more optimistic than those seen in patients who underwent VRT. We also recognize that the strategies of follow-up of patients may vary between institutions, leading to differences in rates of detection of recurrence. Also, given the retrospective nature of these studies, there is a potential for selection and publication bias. In addition, surgical techniques may vary between institutions, leading to differences in operative bleeding and rates of transfusion.

In summary, the findings from our review indicate that ART is safe and feasible. The oncological safety of ART is evidenced by the low number of deaths from cervical cancer after ART and the relapse rate of less than 4%. The overall pregnancy rate among women who maintained their fertility after ART was similar to those seen with VRT.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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Table 5
Obstetric outcome of abdominal vs. vaginal radical trachelectomy.^a

Parameter	Abdominal	Vaginal
No. of patients planned trachelectomy	485	1088 ^b
Pregnancies, n	75	436
Pregnancy rate overall	16.2%	24.0%
Fertility preserved, n (%)	413 ^c (85.1)	992 (91.1)
Pregnancy rate among women with preserved fertility	18.1%	43.9%
Deliveries, n	47	279
Delivery rate among women with preserved fertility	11.3%	28.1%
Rate of pregnancy loss	24%	30%

^a Data on abdominal radical trachelectomy are from the current report; data on vaginal radical trachelectomy are from Ribeiro et al. [47].

^b This number was obtained from Ribeiro's Table 2 (Characteristics and oncological outcome of RVT) adding Lanowska [9] and Danska-Biazinska [50].

^c This figure was obtained as the sum of all patients who had documented radical trachelectomy; however, several articles (Ungar [18] and Saso [28]) as well as 1 case report (Dharan [42]); do not specify the number of patients who underwent adjuvant therapy. Therefore, the number of patients who had fertility preservation may be overestimated. There was no information on 61 patients.

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