An update of oncologic and obstetric outcomes after abdominal trachelectomy using the FIGO 2018 staging system for cervical cancer: a single-institution retrospective analysis

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Original Article

An update of oncologic and obstetric outcomes after abdominal trachelectomy using the FIGO 2018 staging system for cervical cancer: a single-institution retrospective analysis

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ABSTRACT

Objective: To apply the International Federation of Gynecology and Obstetrics (FIGO) 2018 staging system to all patients who underwent trachelectomy in our previous study and to update the oncologic and obstetric results.
Methods: We retrospectively reviewed the medical records of patients in whom abdominal trachelectomy was attempted between June 2005 and September 2021. The FIGO 2018 staging system for cervical cancer was applied to all patients.
Results: Abdominal trachelectomy was attempted for 265 patients. Trachelectomy was converted to hysterectomy in 35 patients, and trachelectomy was completed successfully in 230 (conversion rate: 13%). Applying the FIGO 2018 staging system, 40% of the patients who underwent radical trachelectomy had stage IA tumors. Among 71 patients who had tumors measuring ≥2 cm, 8 patients were classified as stage IA1 and 14 as stage IA2. Overall recurrence and mortality rates were 2.2% and 1.3%, respectively. One hundred twelve patients attempted to conceive after trachelectomy; 69 pregnancies were achieved in 46 patients (pregnancy rate: 41%). Twenty-three pregnancies ended in first-trimester miscarriage, and 41 infants were delivered between gestational weeks 23 and 37; 16 were deliveries at term (39%) and 25 were premature deliveries (61%).
Conclusion: This study suggested that patients judged to be ineligible for trachelectomy and patients receiving overtreatment will continue to appear using the current standard eligibility criteria. With the revisions to the FIGO 2018 staging system, the preoperative eligibility criteria for trachelectomy, which were based on the FIGO 2009 staging system and tumor size, should be changed.

Keywords: Uterine Cervical Neoplasms; Trachelectomy; FIGO 2018 Staging System; Treatment Outcome

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Synopsis
We updated the oncologic and obstetric results, applied the International Federation of Gynecology and Obstetrics (FIGO) 2018 staging system to all patients who underwent trachelectomy. Applying the FIGO 2018 staging system, 40% of the patients had stage IA tumors. Overall recurrence and mortality rates were 2.2% and 1.3%, respectively. Sixty-nine pregnancies were achieved in 46 patients and 41 infants were delivered.

INTRODUCTION

The International Federation of Gynecology and Obstetrics (FIGO) staging system for cervical cancer was revised in 2018 [1,2]. In the new staging system, the lateral extension measurement was removed from stage IA tumor; stage IB tumor with measured deepest invasion >5 mm was divided into three subgroups; and tumor with retroperitoneal lymph node metastasis was assigned stage IIIC. Furthermore, "clinically visible lesions limited to the cervix uteri" which was the definition of stage IB tumor in the former staging system [3], was removed from the new staging system. In Japan, FIGO 2018 staging began to be applied to patients with cervical cancer treated after 2021.

Cervical cancer is the fourth most common cancer and the fourth leading cause of cancer death among females, and 604,000 new cases and 342,000 cancer deaths were estimated globally in 2020 [4]. Because of the recent increase in human papillomavirus vaccination and cancer screening with a Papanicolaou test and a human papillomavirus test, cervical cancer incidence and mortality have been declining. However, cervical cancer is still the second most common cancer and the second most common cause of cancer death among women of childbearing age (20–39 years) [5,6]. Therefore, it is expected that the demand for fertility-preserving treatment for young patients with early-stage cervical cancer will continue.

Currently, radical trachelectomy is performed by vaginal and open approaches as well as by minimally invasive approaches, as a fertility-preserving surgery, worldwide [7-10]. The preoperative indication for radical trachelectomy has focused on stage and tumor size to date. As stated in the National Comprehensive Cancer Network guideline (version 1.2022, Cervical Cancer), the current standard preoperative indication for radical trachelectomy is considered stage I tumors measuring ≤2 cm [11]. We began a clinical trial of abdominal trachelectomy in 2005 and previously reported the oncologic and obstetric outcomes of our first 151 patients [12]. We also reported that abdominal trachelectomy was safe, even in patients with tumors measuring ≥2 cm, using intraoperative frozen sections of sentinel lymph nodes (SLN) and cervical margins [13]. However, following the revision of the FIGO staging system for cervical cancer, it is expected that future preoperative indications for trachelectomy will change. To investigate the future preoperative indications for trachelectomy, we updated the oncologic and obstetric results, applied the FIGO 2018 staging system to all patients who underwent trachelectomy and compared the present results with our previous results, in this article.

MATERIALS AND METHODS

In June 2005, we began a clinical trial of abdominal radical trachelectomy (ART), abdominal modified radical trachelectomy (AmRT), and abdominal simple trachelectomy (AST) after

obtaining institutional review board approval (authorization number: 247). All patients provided written informed consent before surgery.

Patients eligible for trachelectomy were between 20 and 45 years of age and wished to preserve their fertility. The preoperative eligibility criteria were as follows: 1) squamous cell carcinoma measuring ≤3 cm in diameter (including stage IIA1 tumors with slight vaginal involvement) or adeno/adenosquamous carcinoma measuring ≤2 cm in diameter; 2) >1 cm cancer-free space between the tumor's edge and the internal os confirmed by preoperative magnetic resonance imaging (MRI); and 3) absence of extrauterine spread based on imaging findings. Patients whose tumors had highly malignant potential (e.g., small cell carcinoma) were excluded from undergoing trachelectomy. Neoadjuvant chemotherapy (NAC) with paclitaxel and carboplatin was administrated to some patients whose tumor diameters were near the upper limits of the eligibility criteria, after sufficient explanation. If a positive SLN or cervical margin was confirmed by intraoperative frozen section, trachelectomy was converted to hysterectomy. The cervical margin was evaluated using a section located 5 mm from the margin of the extirpated cervix. Patients whose tumors were diagnosed as intermediate- or high-risk postoperatively received adjuvant treatment comprising chemotherapy, such as with taxanes and carboplatin, radiotherapy, or hysterectomy. Stromal invasion deeper than two-thirds with lymphovascular space invasion (LVSI), diffuse cervical invasion (diffuse and extensive invasion within the cervical stroma, forming small aggregates), skip lesions in the vagina, and LVSI in the cardinal ligament and vagina were classified as intermediate-risk factors, and parametrial invasion and pelvic lymph node (including SLN) metastasis were classified as high-risk factors, as described in our previous report [14].

The following are the surgical techniques and indications for each trachelectomy procedure. Briefly, the surgical procedures for resecting the parametrium and vagina in ART, AmRT, and AST were performed as in radical hysterectomy, modified radical hysterectomy, and simple hysterectomy, respectively. Generally, the criteria for AmRT were stage IB1 tumors without deep stromal invasion and IA2 cancer, and the criteria for AST were stage IA1 tumors or precancerous lesions that could not be completely resected by conization alone.

We retrospectively reviewed the medical records of patients in whom abdominal trachelectomy was attempted at our institution between June 2005 and September 2021, and we extracted clinical information and oncologic and obstetric outcomes. This study and an opt-out consent method were reviewed and approved by the Institutional Review Board of Kyushu University, authorization number: 21051-00. In this analysis, we applied the FIGO 2018 staging system for cervical cancer for patients who were treated both before and after 2018. Because tumors shrank with the administration of NAC, we assigned the cancer stage before surgery in patients who received NAC (except for one patient with pelvic lymph node metastasis). Tumor size was comprehensively determined by preoperative visual inspection, preoperative MRI, or pathological examination of surgical specimens. Even if a tumor was a clinically visible cancer by visual inspection or MRI, when the measured stromal invasion in the surgical specimen was ≤5 mm in depth, we classified these tumors as stage IA in accordance with the description in the FIGO 2018 staging system and the Japanese classification of cervical cancer. Biochemical pregnancy that was confirmed only by elevated human chorionic gonadotropin concentration was included in spontaneous abortion in this study.

Recurrence-free survival (RFS) and overall survival (OS) were defined as the time from trachelectomy to recurrence and the time from trachelectomy to death, respectively.

Regarding the survival analysis, follow-up data until December 2021 was used; no data after this date was used. RFS and OS were analyzed using the Kaplan-Meier method.

RESULTS

Oncologic results

From June 2005 to September 2021, abdominal trachelectomy was attempted for 265 patients at our institution. All patients underwent open surgery, and none underwent minimally invasive surgery. As shown in **Table 1**, ART, AmRT, and AST were planned for 166, 84, and 15 patients, respectively. Intraoperatively, positive SLNs were found in 17 patients in whom ART was attempted and in one patient in whom AmRT was attempted. Positive margins were found in 15 patients in whom ART was attempted and two patients in whom AmRT was attempted. Consequently, trachelectomy was converted to hysterectomy in 35 patients, and trachelectomy was successfully completed in the remaining 230 (conversion rate: 13%). Among patients in whom AST was attempted, trachelectomy was not converted to hysterectomy in any patient; all planned AST procedures were completed. The conversion rates for ART, AmRT, and AST were 19.3%, 3.6%, and 0%, respectively.

The oncologic characteristics, marital status, and parity of the 230 patients who underwent trachelectomy are summarized in **Table 2**. The median age for the entire cohort at trachelectomy was 33 years (range, 21–44 years). Approximately two-thirds of the patients who underwent trachelectomy were unmarried, and 87% of these were nulliparous at the time of trachelectomy. Overall, approximately 55% of the patients underwent conization before trachelectomy. In comparison, all patients who underwent AST underwent conization before trachelectomy. Applying the FIGO 2018 staging system, 3 patients had high-grade squamous intraepithelial lesions or adenocarcinoma in situ, 60 had stage IA1 tumors, 77 had stage IA2 tumors, 56 had stage IB1 tumors, 18 had IB2 tumors, 7 had stage IIA1 tumors, and 9 had IIIC1p tumors. In all nine patients who had stage IIIC1p tumors, lymph node metastasis was confirmed by postoperative histological examination. Among the patients who underwent ART, 64 patients had tumors measuring <2 cm, and 70 patients had tumors measuring ≥2 cm. Among the patients who underwent AmRT, 1 patient had a tumor measuring ≥2 cm. All of the patients who underwent AST had tumors measuring <2 cm. Overall, 159 patients (69.1%) had tumors measuring <2 cm, and 71 (30.9%) had tumors measuring ≥2 cm. Among the 71 patients who had tumors measuring ≥2 cm, 8 patients had tumors with stromal invasion measuring ≤3 mm in depth, and 14 patients had tumors with stromal invasion measuring >3 mm to ≤5 mm in depth. Of patients who underwent ART, nine patients received two to three courses of combination chemotherapy with paclitaxel and carboplatin (TC) as NAC, one of whom also received 2 courses of bevacizumab. Postoperatively, 27 patients (11.7%) received adjuvant therapy. Fifty patients developed cervical stenosis after trachelectomy and underwent cervical dilatation (data not shown). With a median follow-up of 81 months (range,

Table 1. Surgical procedure results for the 265 patients for whom trachelectomy was planned

	Total (n=265)	ART (n=166)	AmRT (n=84)	AST (n=15)
Trachelectomy completed	230	134	81	15
Conversion to hysterectomy				
Positive SLN	18	17	1	0
Positive margin	17	15	2	0

AmRT, abdominal modified radical trachelectomy; ART, abdominal radical trachelectomy; AST, abdominal simple trachelectomy; SLN, sentinel lymph node.

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Table 2. Characteristics of the 230 patients who underwent trachelectomy

Characteristics	Total (n=230)	ART (n=134)	AmRT (n=81)	AST (n=15)
Age (yr)	33 (21–44)	33 (21–42)	34 (24–44)	34 (26–41)
Marital status (%)				
Married	77 (33.5)	41	32	4
Unmarried	153 (66.5)	93	49	11
Parity (%)				
Nullipara	200 (87.0)	123	63	14
Multipara	30 (13.0)	11	18	1
Preoperative conization (%)				
No	103 (44.8)	86	17	0
Yes	127 (55.2)	48	64	15
Stage (FIGO 2018)				
HSIL/AIS	3 (1.3)	0	0	3
IA1	60 (26.1)	17	31	12
IA2	77 (33.5)	37	40	0
IB1	56 (24.3)	46	10	0
IB2	18 (7.8)	18	0	0
IIA1	7 (3.0)	7	0	0
IIIC1p	9 (3.9)	9	0	0
Tumor size (%)				
<2 cm	159 (69.1)	64	80	15
≥2 cm	71 (30.9)	70	1	0
Histology (%)				
SCC	152 (66.1)	89	58	5
Adeno	64 (27.8)	32	23	9
AS	14 (6.1)	13	0	1
LVSI (%)				
Positive	72 (32.4)	54	17	1
Negative	150 (67.6)	77	59	14
Unknown	8	3	5	0
NAC (%)				
No	221 (96.1)	125	81	15
Yes	9 (3.9)	9	0	0
Adjuvant therapy				
No	203	110	78	15
Chemotherapy	25	23	2	0
Radiation	1	1	0	0
Hysterectomy	1	0	1	0
Recurrence (%)	5 (2.2)	3	2	0

Values are presented as median (range) or number of patients (%).
Adeno, adenocarcinoma; AIS, adenocarcinoma in situ; AmRT, abdominal modified radical trachelectomy; ART, abdominal radical trachelectomy; AS, adenosquamous carcinoma; AST, abdominal simple trachelectomy; FIGO, The International Federation of Gynecology and Obstetrics; HSIL, high-grade squamous intraepithelial lesion; LVSI, lymphovascular space invasion; NAC, neoadjuvant chemotherapy; SCC, squamous cell carcinoma.

1–187 months), three and 2 patients developed recurrence after ART and AmRT, respectively, and the overall relapse rate was 2.2%. Kaplan-Meier curves for RFS according to the type of trachelectomy are shown in **Fig. 1A**. The 5-year RFS rate in patients who underwent ART, AmRT, and AST was 98.2%, 98.7%, and 100.0%, respectively. Detailed oncologic information for the 5 patients who developed recurrence are listed in chronological order of trachelectomy in **Table 3**. Patient No. 5 with a stage IA1 tumor underwent conization before trachelectomy; the tumor was not visible before conization. The conization specimen revealed that the depth of invasion was 3 mm and the horizontal extension was 13 mm. In Patient No. 3, preoperative MRI indicated a tumor diameter of 2.8 cm; however, the diameter of the excised specimen was 4 cm. Because postoperative pathology showed that the depth of invasion was only 5 mm, the patient was diagnosed as stage IA2. In addition to 2 patients (Patients No. 3 and 4) who died of cervical cancer, one patient who underwent ART died suddenly of an unknown

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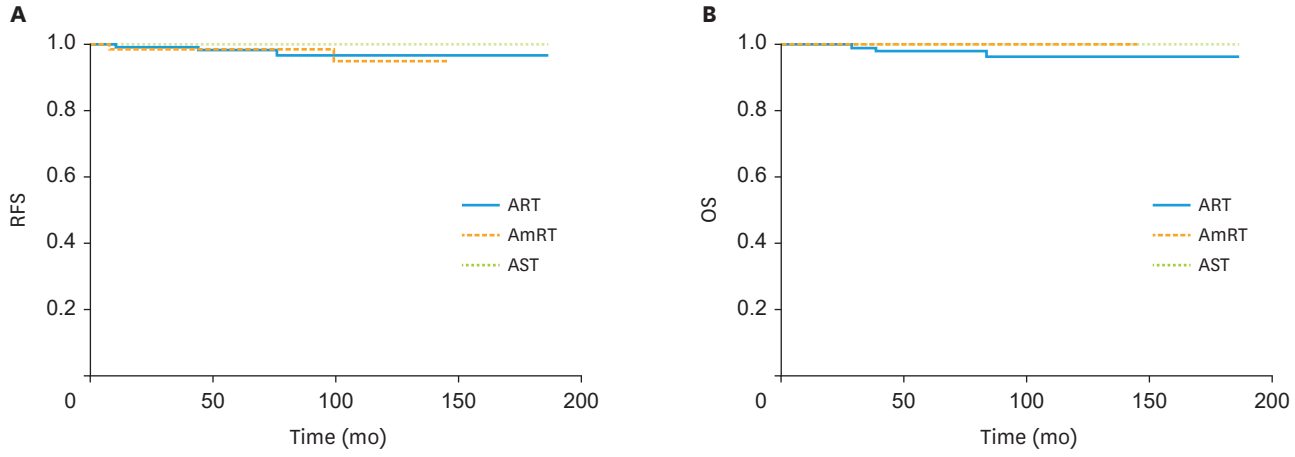

No. at risk								
ART	134	116	96	75	49	30	14	4
AmRT	81	69	59	40	24	9	0	0
AST	15	14	13	13	11	8	5	3

No. at risk								
ART	134	117	97	76	50	30	14	4
AmRT	81	70	59	40	25	10	0	0
AST	15	14	13	13	11	8	5	3

Fig. 1. Kaplan-Meier curves according to the surgical procedure. RFS (A) and OS (B).
AmRT, abdominal modified radical trachelectomy; ART, abdominal radical trachelectomy; AST, abdominal simple trachelectomy; OS, overall survival; RFS, recurrence-free survival.

Table 3. Characteristics of the patients who developed recurrence after trachelectomy

No.	Age at surgery (yr)	Stage (FIGO 2018)	Histology	Procedure	Adjuvant therapy	Time to recurrence after surgery (mo)	Recurrence site	Therapy after recurrence	Present status
1	29	IB1	SCC	AmRT	-	99	Left internal iliac lymph node	Lymphadenectomy, CCRT	No evidence of disease
2	29	IB1	AS	ART	-	44	Lung	Lobectomy, TC + bevacizumab	No evidence of disease
3	40	IA2	SCC	ART	6 cycles of TC	76	Bone, Brain, Lung	Radiotherapy, TC + bevacizumab	Died of disease
4	28	IIIC1p	SCC	ART	6 cycles of TC	10	Uterine cervix	Hysterectomy, radiotherapy, CCRT, tumor resection	Died of disease
5	29	IA1	Adeno	AmRT	-	8	Uterine cervix	Hysterectomy	No evidence of disease

Patients are listed in chronological order of trachelectomy.
Adeno, adenocarcinoma; AmRT, abdominal modified radical trachelectomy; ART, abdominal radical trachelectomy; AS, adenosquamous carcinoma; CCRT, concurrent chemoradiotherapy; FIGO, The International Federation of Gynecology and Obstetrics; LVSI, lymphovascular space invasion; SCC, squamous cell carcinoma; TC, paclitaxel + carboplatin.

cause 29 months after trachelectomy. Consequently, 3 patients in the entire cohort died after trachelectomy, and the overall mortality rate was 1.3%. Among patients who underwent AmRT or AST, no patients died after trachelectomy. Kaplan-Meier curves for OS according to the type of trachelectomy are shown in **Fig. 1B**. The 5-year OS rate in patients who underwent ART, AmRT, and AST was 98.2%, 100.0%, and 100.0%, respectively.

Obstetric results

One hundred twelve patients (64 ART, 44 AmRT, and 4 AST) attempted to conceive after trachelectomy, and 46 patients achieved pregnancy. The overall pregnancy rate among patients who attempted to conceive was 41%. The oncologic characteristics and parity of the 46 patients who became pregnant after trachelectomy are summarized in **Table 4**. The median age at trachelectomy was 32 years (range, 24–43 years). At the time of trachelectomy, 40 patients (87.0%) were nulliparous, 5 had 1 child, and 1 had 2 children. ART, AmRT, and AST were performed in 22, 22, and 2 patients, respectively, and the pregnancy rate after ART,

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Table 4. Oncologic characteristics of the 46 patients who became pregnant after trachelectomy

Characteristics	Values
Median age at operation (yr)	32 (24–43)
Parity	
Nullipara	40 (87.0)
Multipara	6 (13.0)
Stage (FIGO 2018)	
AIS	1 (2.2)
IA1	16 (34.8)
IA2	17 (37.0)
IB1	6 (13.0)
IB2	5 (10.9)
IIA1	1 (2.2)
Histology	
SCC	26 (56.5)
Adeno	20 (43.5)
AS	0 (0.0)
NAC	
No	43 (93.5)
Yes	3 (6.5)
Type of trachelectomy	
ART	22 (47.8)
AmRT	22 (47.8)
AST	2 (4.3)
Adjuvant therapy	
No	45 (97.8)
Chemotherapy	1 (2.2)
Recurrence	0 (0.0)

Values are presented as median (range) or number of patients (%).
Adeno, adenocarcinoma; AIS, adenocarcinoma in situ; AmRT, abdominal modified radical trachelectomy; ART, abdominal radical trachelectomy; AS, adenosquamous carcinoma; AST, abdominal simple trachelectomy; FIGO, The International Federation of Gynecology and Obstetrics; NAC, neoadjuvant chemotherapy; SCC, squamous cell carcinoma.

AmRT, and AST was 34%, 50%, and 50%, respectively. NAC was administrated to 3 patients; one patient also received postoperative adjuvant chemotherapy. Among the patients who became pregnant, no patient experienced recurrence.

The obstetric outcomes of the pregnancies after trachelectomy are summarized in **Table 5**. After trachelectomy, 28 patients had 1 pregnancy, 14 had 2 pregnancies, 3 had 3 pregnancies, and 1 had 4 pregnancies. In total, 69 pregnancies were achieved in 46 patients. The median time from trachelectomy to first post-trachelectomy pregnancy was 38 months (range, 9–118 months). Fourteen pregnancies were achieved naturally, and the remaining 55 pregnancies were achieved after infertility treatment. Regarding complications during pregnancy, threatened abortion and/or threatened premature labor, preterm premature rupture of membranes (pPROM), varices around the uterovaginal anastomotic site, and placenta previa occurred in 20, 15, 10, and 4 cases, respectively. Among all 69 pregnancies, 23 pregnancies ended in first-trimester miscarriage, and two cases of ectopic pregnancy occurred. Forty-one infants were delivered by cesarean section between gestational weeks 23 and 37. Because of placenta accreta, one patient underwent cesarean hysterectomy. Among the 41 deliveries, 16 were deliveries at term (39.0%) and 25 were premature deliveries (61.0%). Among the 25 premature deliveries, 14 cases (56.0%) of pPROM occurred. At the time of writing this article, two women were still pregnant.

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Table 5. Obstetric outcomes of the pregnancies after trachelectomy

Outcomes	Values
Total number of pregnancy cases	69
Number of post-trachelectomy pregnancies	
1	28
2	14
3	3
4	1
Time from trachelectomy to first pregnancy (mo)	38 (9–118)
Method of conception	
NC	14
AIH	7
IVF-ET	28
ICSI	20
Obstetric complications*	
TA/TPL	20
PROM	1
pPROM	15
Chorioamnionitis	2
Varices	10
Placenta previa	4
Outcome	
Spontaneous abortion	23
Ectopic pregnancy	2
Stillbirth	1
Premature delivery	25
Delivery at term	16
Ongoing pregnancy	2

Values are presented as median (range) or number of patients.
AIH, artificial insemination with husband's sperm; ICSI, intracytoplasmic sperm injection; IVF-ET, in vitro fertilization and embryo transfer; NC, natural conception; pPROM: preterm premature rupture of membranes; PROM, premature rupture of membranes; TA, threatened abortion; TPL, threatened premature labor.
*There was some overlap.

DISCUSSION

We began performing abdominal trachelectomy in 2005, and we reported 10 years of results for this procedure (2005–2015) in 2017 [12]. In the previous report, we described the oncologic outcomes of 151 patients who underwent abdominal trachelectomy and the obstetric outcomes, with 21 post-trachelectomy pregnancies in 15 patients, based on the FIGO 2009 staging system [12]. In 2018, the FIGO staging system for cervical cancer was revised [1, 2]. The major changes to the FIGO 2018 staging are as follows: 1) the lateral extent of the lesion is no longer considered in stage I; 2) stage IB was divided into stages IB1–IB3; 3) "clinically visible lesions limited to the cervix uteri" was removed from the definition of stage IB; and 4) stage IIIC was newly added to stage III. In this article, we applied the FIGO 2018 staging system to all patients who underwent trachelectomy and updated the oncologic and obstetric results from our previous study. To our knowledge, this article is the first report to apply the FIGO 2018 staging system to all patients who underwent trachelectomy.

Among 265 patients for whom trachelectomy was planned, positive SLNs and positive margins were found intraoperatively in 18 patients and 17 patients, respectively. The number of patients with positive SLNs and the number of patients with positive margins were similar. In total, the rate of conversion from trachelectomy to hysterectomy was 13%. By the type of surgical procedure, the conversion rates for ART, AmRT, and AST were 19.3%, 3.6%, and 0%, respectively. Trachelectomy was converted to hysterectomy more often in patients for

whom ART was planned than for patients for whom AmRT and AST was planned. Smith et al. [15] reported a conversion rate with ART of 12.6% in their systematic review. The conversion rate with ART in our study was higher than that of Smith et al.'s review [15], which may be because we also targeted tumors that were larger than 2 cm. In our previous report based on the FIGO 2009 staging system, the numbers of patients who underwent ART with stage IA1, IA2, and IB1 tumors were 0 (0%), 7 (7.9%), and 79 (88.8%), respectively [12]. In contrast, in the current report, which is based on the FIGO 2018 staging system, the numbers of patients who underwent ART with stage IA1, IA2, and IB1 tumors were 17 (12.7%), 37 (27.6%), and 46 (34.3%), respectively. As described above, the distribution of stage changed drastically after applying the FIGO 2018 staging system. Consequently, 54 patients with stage IA tumors underwent ART, which may have been overtreatment for stage IA tumors. The reasons why the distribution of stage changed greatly after applying the FIGO 2018 staging system in this study were as follows: 1) cervical cancers were diagnosed as stage IB1 (FIGO 2009) preoperatively because they were clinically visible tumors; however, postoperative pathology revealed only microinvasive cancers with stromal invasion of ≤5 mm in depth. As a result, these tumors were diagnosed as stage IA1 or IA2 based on the FIGO 2018 staging system. 2) The stage of cervical cancers diagnosed as stage IB1 (FIGO 2009) based on conization specimens showing the deepest invasion of ≤5 mm but the largest extension of >7 mm changed to stage IA1 or IA2 after applying the FIGO 2018 staging system.

As stated in the National Comprehensive Cancer Network guideline, the current standard preoperative indication for radical trachelectomy is stage I tumors measuring ≤2 cm [11]. However, when the FIGO 2018 staging system was applied to 71 patients who had tumors measuring ≥2 cm in this study, 8 patients were reclassified as stage IA1 and 14 patients as stage IA2. Under the current standard preoperative indication, these patients, who had tumors measuring ≥2 cm, would not be eligible for trachelectomy. However, these tumors are actually stage IA1 or IA2 tumors based on the FIGO 2018 staging system. As we mentioned, if the FIGO 2018 preoperative indication will be used hereafter, patients who have tumors measuring ≥2 cm in diameter and stromal invasion ≤5 mm will lose the chance to undergo trachelectomy. Therefore, exophytic growth tumors measuring ≥2 cm should not readily be judged ineligible for trachelectomy. Even if the tumor is larger than 2 cm, when the tumor is exophytic and presumed to have shallowly invaded the stroma by MRI, we should consider that diagnostic conization is necessary to judge the patient's eligibility for trachelectomy. Takahashi et al. [16] reported that 36.0% of patients classified as FIGO 2009 stage IB1 with tumors measuring <2 cm were reclassified as FIGO 2018 stage IA. The authors suggested that cervical cancer patients with tumors measuring <2 cm should be carefully diagnosed by performing cervical conization before hysterectomy [16]. New technology for accurately measuring stromal invasion using MRI is also required.

In this series, five patients developed recurrence, two patients died of cervical cancer, and one patient died of an unknown cause after trachelectomy. Although only one patient developed recurrence and none died of cervical cancer in our previous report [12], the number of patients who developed recurrence and died of cancer increased over time. Based on the overall relapse rate and overall mortality rate in this study of 2.2% and 1.3%, respectively, oncologic outcomes were excellent. Reported relapse and mortality rates after ART are 3.3%–4.0% and 0.7%–1.5%, respectively, and these rates are lower than those after vaginal radical trachelectomy in recent systematic reviews [15,17-19]. When limiting the findings to ART in this study, the relapse and cancer-specific mortality rates were 2.2% and 1.5%, respectively, and these results were consistent with the results of the above systematic reviews. Because no patients developed

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recurrence after AST and no patients died of cancer after AmRT and AST, the log-rank test and statistical survival analysis between AST, AmRT, and ART could not be performed. However, analyzing the Kaplan-Meier curves, it was clear that there were no differences in RFS and OS between the three surgical procedures. Thus, we evaluated RFS and OS using the 5-year RFS and OS, in this report. As the 5-year RFS and the 5-year OS show, there were only slight differences in RFS and OS between ART, AmRT, and AST.

We previously reported the effectiveness of adjuvant chemotherapy after abdominal trachelectomy [14]. In the current study, 25 patients with intermediate- or high-risk cervical cancer received postoperative adjuvant chemotherapy with taxanes and carboplatin, and two patients developed recurrence after this therapy. This study also suggests that post-trachelectomy adjuvant chemotherapy could be effective, as shown in our previous report [14]. Moreover, one patient had three pregnancies and delivered two children after adjuvant chemotherapy. It is considered that fertility preservation is a benefit of choosing chemotherapy as an adjuvant treatment.

After trachelectomy, 49% (112/230) of the patients attempted to conceive, and 46 patients achieved pregnancy, with a pregnancy rate of 41%. There were minimal differences in the pregnancy rates after ART, AmRT, and AST in our previous report [12]; however, patients tended to be less likely to become pregnant after ART in this study. We reported that 61 patients attempted to conceive, and 15 patients achieved pregnancy, with a pregnancy rate of 25% and a median follow-up of 61 months (range, 8–131 months) in our previous report [12]. Because the median follow-up was 81 months (range, 1–187) in this study, both the number of patients who attempted to conceive and the number of patients who achieved pregnancy increased, and the pregnancy rate also increased to 41%. The reported pregnancy rates after ART ranged from 36% to 42% in recent systematic reviews, and these rates were nearly the same as those in our study [17,19].

Nezhat et al. [17] reported in their systematic review that, among 229 pregnancies after ART, 104 cases (45.4%) required infertility treatments. In this study, among 69 pregnancies, 55 cases (79.7%) required infertility treatments. Furthermore, a high miscarriage rate (34% of all pregnancies without ongoing pregnancies), a high premature delivery rate (61% of all deliveries), and a high pPROM rate (37% of all deliveries) were also observed in this study. As described in our previous paper [12], more radical resection of the uterine cervix with ART than that with vaginal radical trachelectomy may have caused high rates of infertility treatment, miscarriage, premature delivery, and pPROM. Among all pregnancies except ongoing pregnancies, 4 cases (6.0%) of placenta previa were identified. The reported prevalence of placenta previa is approximately 5 per 1,000 pregnancies (0.5%) [20]; however, the incidence rate of placenta previa in our study was much higher than that in the previous report. It is possible that anatomical changes owing to removal of a large section of the uterine cervix affected the implantation site and increased the placenta previa rate, in our study.

In conclusion, in this study, we updated the oncologic and obstetric results in our previous study by adding new patients who underwent trachelectomy to September 2021. We applied the FIGO 2018 staging system to all patients, and compared the present results with those in our previous report. With the revisions to the FIGO 2018 staging system, the preoperative eligibility criteria for trachelectomy, which have been based on the FIGO 2009 staging system and tumor size, should be changed going forward. To formulate more accurate preoperative

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eligibility criteria for trachelectomy, data accumulation and analysis of patients who undergo trachelectomy and who are staged based on the FIGO 2018 staging system are necessary.

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