



Robotic Radical Trachelectomy for Early Stage Cervical Cancer: Oncological and Obstetrical Outcomes

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Abstract

Objectives: The aim of this study is to assess the reproductive and oncologic outcome following Robotic Radical Trachelectomy (RRT) in patients with early-stage cervical cancer interested in future fertility.

Material and Methods: A retrospective review was performed of patients from three institutions who underwent radical trachelectomy for early-stage cervical cancer from May 2012 to January 2019. Perioperative, oncologic, and fertility outcomes were retrieved from SERGS (Society of European Robotic Gynaecological Surgery) database and an additional review of patient files was performed.

Results: Twenty-six patients were included (one IA1 FIGO stage, three IA2, sixteen IB1, six IB2, and one IB3). The median age was 34.4 years, and median follow-up was 34.7 months. The average surgical time was 271 minutes ± 69. No laparoconversion occurred; we reported a ureteral injury, and 30.7% post-operative dysuria (n=8). Four trachelectomies were aborted in favor of a radical hysterectomy and/or chemoradiation due to nodal metastases (n=1), or insufficient margins (n=3). One nodal recurrence occurred in these women (35.9 months after chemotherapy for insufficient margins); and one distant recurrence was observed. Twenty-one patients remained fertile after treatment; among them, three patients conceived naturally. Two patients delivered after 37 weeks, the third patient had two miscarriages.

Conclusion: RRT is feasible with acceptable recurrence rate; to better evaluate fertility rate, larger sample and longer follow-up are needed.

Keywords: Cervical cancer; Fertility-sparing; Robotic surgery; Radical trachelectomy

Abbreviations

RRT: Robotic Radical Trachelectomy; VRA: Vaginal Radical Trachelectomy; ART: Abdominal Radical Trachelectomy; LVSI: Lymphovascular Space Invasion; SERGS: Society of European Robotic Gynaecological Surgery

Introduction

Even though the incidence of invasive cervical cancers is decreasing in western countries, these cancers are often diagnosed at early stages and in young patients. It is estimated that 40% of these cervical cancers are diagnosed in women of childbearing age. At the same time, women are becoming

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pregnant at an increasingly older age. It therefore seems important to be able to propose that fertility be retained by integrating it into the cancer care of these patients.

To this end, Professor Dargent described the Vaginal Radical Trachelectomy (VRT) for the first time in 1994 [1]. This procedure, after a laparoscopic pelvic lymphadenectomy, consists in resecting the uterine cervix, a vaginal portion, and the proximal parametria, preserving the ascending branch of the uterine artery.

There are also two techniques described of Abdominal Radical Trachelectomy (ART) that can be performed. One preserves the uterine artery in order to improve the obstetric prognosis but entails significant bleeding; the other consists of binding the uterine arteries in order to restrict bleeding, thus the uterine vascularization will not only depend on the gonadal vessels. The first open trachelectomy was described in 1997, and multiple series have been reported since [2-7]. With this very popular approach, the results on fertility have been very encouraging.

The classic laparoscopic approach was reported by Lee et al. in 2003, and 18 series have been described since then [8]. The results are rather encouraging but the technique remains complex.

The first RRT was published in 2008 [9]. Several studies followed with interesting results, in oncological terms comparable to the techniques described previously which are promising in terms of obstetric outcomes [10,11]. However, the follow-up periods are short and the cohorts small; the results are still only preliminary.

The objective of this multicentric study was to assess feasibility, oncological and obstetric outcomes after RRT.

Materials and Methods

Study population

This is a descriptive multicentric retrospective study including those French centers which have performed robot-assisted laparoscopic radical trachelectomies. These centers are the Toulouse University Cancer Institute (IUCT Oncopole), the European Hospital Georges Pompidou (HEGP) in Paris and Paoli Calmettes Institute in Marseilles. All patients having undergone a robot-assisted laparoscopic radical trachelectomy were included. The data was collected from the European Robotic Database SERGS EUROD and the medical records of the patients. These were all consulted and updated in each one of the 3 cities, Paris, Marseilles and Toulouse. This data included the details of the patients and their illness, the data on the surgery and hospital stay, the anatomo-pathological results of the surgical specimens and follow-up data (oncological and obstetric results, complications).

Robotic surgery

The robot used was a Da Vinci[®] Si HD or Xi robot from the Intuitive Surgical laboratory. The radical trachelectomy was performed after research into sentinel nodes and/or a bilateral lymph node dissection. The aim of this procedure is to remove the uterine cervix with a vaginal segment and at least the proximal parts of the parametria (equivalent to a radical colpohysterectomy of type B1 to C1 of the Querleu and Morrow classification [12]). An isthmic suture is then made before the isthmic-vaginal anastomosis. The patient is placed in the lithotomy position. The surgical table is prepared to secure the lower right side (to the height of the thigh) at a 45° angle from the spine. The 12 mm optical trocar is at a sub-umbilical position,

as long as a longer trocar is used for securing over the other arms (obese trocar position). The assistant trocar is placed infracostally at 2 cm on the right midclavicular line. The robotic trocars are placed under visual control at 8 cm to 10 cm from the umbilical and assistant trocar in line with the usual scheme. The Trendelenburg degree is approximately 20° to 25° and the intraperitoneal pressure during the operation may be decreased to 6 mmHg to 8 mmHg.

Statistical analysis

The description of the patients was made by calculating the population and percentages for the categorical variables and by the indicators of central tendency (mean, median) and dispersion (minimum, maximum, standard deviation and interquartiles) for the continuous variables. Analyses were performed using stata version 14.2 software (StataCorp).

Results

In total, 26 patients were treated by RRT for early-stage cervical cancer.

Details of the patients and their illness

The mean age was 34.4 years-old. Most of the patients were nulliparous (18 patients, i.e. close to 70% of the patients). The indication for conservative surgery was extended to 6 stages IB2 <30 mm, and to one stage IB2 with a 36 mm lesion. The latter patient initially received neoadjuvant chemotherapy (3 cycles of carboplatin Paclitaxel), with a complete response on re-evaluation MRI. RRT was then performed (Table 1).

Operative data

The average duration of the operation was 4 h 31 ± 1 h 09. Seven (26.9%) already had pelvic lymphadenectomy as a first step before RRT, 14 (53.8%) had pelvic lymphadenectomy and 5 (19.2%) had a sentinel lymph node biopsy at the same time as RRT. A frozen section analysis was performed before beginning RRT.

There was no laparoconversion. There was a single perioperative complication, an ureteral lesion requiring the installation of a JJ probe during the procedure.

Immediate post-operative effects

The average length of hospitalization was 5.2 days. The most

Table 1: Radical trachelectomies: Details of the patients and their illness.

	N	26
Age (in years)	Mean (SD)	34.4 (7.4)
BMI (kg/m ²)		23.4 (7.1)
Childlessness	N (%)	18 (69.2)
FIGO stages 2018 (29)		26 (100)
IA1	N (%)	1 (3.8)
IA2		3 (11.5)
IB1		16 (61.5)
IB2		7 (26.9)
Average size at MRI (mm)	Mean (SD)	18 (9)
Histology		26 (100)
Epidermoid carcinoma	N (%)	14 (53.8)
Cervical adenocarcinoma		11 (42.3)
Adenosquamous carcinoma		1 (3.8)
Presence of Lymphovascular Space Invasion (LVSI) on conization specimen		2 (7.7)

Table 2: Radical trachelectomies: follow-up care after cancer treatment.

Total number of cases		26
Length of follow-up (months)	Mean (SD)	34.7 (22.4)
Relapse	N (%)	2 (7.7)
- Local		0
- Locoregional		1 (3.8)
- Metastatic		1 (3.8)
Time from the relapse (months)	Mean (SD)	27.4 (12,0)
Deaths	N (%)	0
Long-term complications	N (%)	9 (34.6)
- Lymphedema		3 (11.5)
- Dysuria		5 (19.2)
- Bowel incontinence		1 (3.8)
- Chronic bleeding		2 (7.7)

frequent complication was dysuria (n=8, i.e., 30.7%) which required a urinary catheter and treatment with alpha-blockers. A patient suffered bacteremia requiring antibiotics and another patient was kept in hospital for drainage of a hematoma (Clavien-Dindo 3).

Anatomopathological results and adjuvant treatments

Three patients (11.5%) had damaged margins: two were stage IB2, the 3rd patient was a stage IB1 with an adenocarcinoma which spread more into the endocervix. The patient with stage IB2 of 36 mm who had received neo-adjuvant chemotherapy had pelvic lymph node involvement that was not diagnosed on sentinel node frozen section analysis. She therefore received adjuvant treatment with concurrent chemoradiation followed by utero-vaginal brachytherapy.

In total, four patients required complementary treatment for damaged margins or lymph node involvement. Two patients were kept in hospital for hysterectomies, one of which with adjuvant chemotherapy. Two patients had complementary concurrent chemoradiation followed by utero-vaginal brachytherapy.

Long-term follow-up

Oncological outcomes: The average duration of follow-up was 34.7 months (SD=22.4). Two patients suffered from a relapse: A nodal evolution in a patient who had been readmitted due to damaged margins (surgery then chemotherapy) at 35.9 months from surgery, and a metastatic bone evolution (single L5 spinal metastasis) in a patient who had a very early-stage IA1 illness with numerous LVSI. The two recurrences were treated with chemoradiation.

These two relapses occurred at 35.9 months and at 18.8 months respectively and were treated in June 2015 and May 2017. The patients have not suffered from a second relapse.

Obstetrical outcomes: Among the 21 patients in whom fertility was preserved, 3 patients were pregnant (i.e. 14%) and 2 patients had completed pregnancy (10%). One patient completed pregnancy and then requested a hysterectomy. One patient (accidentally) became pregnant 3 months after her trachelectomy and completed it; she then became pregnant again for which she requested a voluntary interruption of pregnancy. A third patient had two early miscarriages.

Discussion

This is the largest French series of RRT of 26 patients operated at three different centers. Theoretically, this surgery is proposed

to the patients with a maximum of stage IB1, with no unfavorable histoprognostic criteria and no lymph node involvement. In our study, 7 patients were stage IB2.

The largest series of RRT was reported by Johansen et al. [11]. Among 56 patients, seven ended up by requiring a radical hysterectomy or concurrent chemoradiation for positive margins or lymph node involvement, i.e. 12.5%. This result is comparable with that of our study (n=4, i.e. 15.4%). The relapse rate reported by Johansen was of 4% (n=2), i.e. lower than in our population (7.7, n=2). However, the initial FIGO stages were of a maximum of IB1. Concerning the obstetric outcomes, the rate of pregnancies in our study is much lower; only three patients became pregnant, and only two had a live birth. Johansen describes a very high pregnancy rate (over 80%) but patients with a very great desire to become pregnant were selected (n=21). If the number of pregnancies of the 56 patients is reported, the pregnancy rate is of 30.4%. In our study, only five patients stated they envisaged pregnancy. Of these five patients, two had at least one pregnancy and the 3rd patient had two early miscarriages. The other two patients were followed up by way of MAP (Medically Assisted Procreation).

The vaginal radical trachelectomy approach is the most described [1,13-16]. In the literature, of the 1,523 patients reported, 41 had damaged margins, i.e. 3%. A relapse rate of 4% and 2% death rate were reported. The size of the tumor and the presence of LVSI were clearly associated with the relapse risk. A pregnancy rate of 36.9% (500 pregnancies in 1355 cases) was reported, 18% of these pregnancies being followed up by way of MAP [17].

In comparison, the ART is more radical in terms of parametrial excision; it is also associated with an added risk of perioperative and post-operative complications (profound abscess, ureteral pain) [2-6,18,19]. There were also reports of a rate of more significant cervix and isthmus stenosis (negligible in other approaches) of 6% (52 cases in 866 patients) [20].

This therefore results in a lower pregnancy rate: Of 735 cases, 175 patients became pregnant (23.8%), more than a half of whom were followed up by way of medically assisted procreation (n=93, 53.1%).

The traditional laparoscopic approach described in 2002 is used less [7]. 252 cases have been reported in the literature, with small cohorts and an average follow-up of less than 24 months [8]. Six percent of patients had a relapse (most of whom were at a stage >IB1).

RRT was described by Persson in 2008, with a total of 101 patients reported [9,11,21-23]. The rate of positive margins in all series together is higher than in Johansen's last series, 11 positive margins were reported in 54 patients at stage IB1, i.e. 20% (20). The average follow-up period was generally short.

Mini-invasive surgery has recently been questioned following the LACC trial conducted by Ramirez, Obermair et al. in a randomized prospective trial comparing mini-invasive surgery with the open approach in the treatment of early-stage cervical cancer by radical hysterectomy [24]. There was a significant difference in survival in favor of the open approach. A similar more retrospective trial was conducted based on the American registry also found results in terms of survival in favor of the open surgery group [25].

A major international retrospective study conducted by the same team compares mini-invasive radical trachelectomies with the open approach for early-stage cervical cancers for patients wishing to retain

their fertility (IRTA) [26]. This study includes patients FIGO stage IA2 and IB1, and the centers must be trained (minimum 15 radical trachelectomies per centre). The preliminary results shown similar progression-free and overall survival for patients with tumors up to 2 cm undergoing open vs. minimally invasive radical trachelectomy [27]. The recently published ConCerv prospective study shows encouraging results in favor of de-escalation for very early cervical cancer [28].

Conclusion

The results concerning RRT are encouraging but are still at a preliminary stage. It is however important to select the patients who could benefit from this treatment, by limiting it to stages IB1, without LVSI and lymph node involvement. There must be added care with cervical adenocarcinomas in terms of safety margins in order to avoid positive wounds, which seem to be a factor of poor prognosis even in the case of complementary treatment.

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