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## Article

# Robotic Radical Trachelectomy in Early-Stage Cervical Cancer

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**Abstract: Background/Aim:** Radical trachelectomy represents an alternative for early-stage cervical cancer in patients who want to preserve fertility. This procedure can be performed by vaginal, open or minimal invasive approach. The robotic approach may offer some advantages, especially for the surgeon's ergonomics. Since the evidence is still scarce, larger studies are needed. Our objective is to present a retrospective review of our experience with robotic radical trachelectomy. **Methods:** Descriptive study carried out in Clinico San Carlos University Hospital, Madrid, Spain. We included all our patients with early- stage cervical cancer that wished to preserve fertility, from 2023 to 2022. The surgery included bilateral pelvic lymphadenectomy followed by radical trachelectomy and cervical cerclage after confirmation of absence of nodal metastasis. Demographic data of the study population, perioperative and oncological outcomes were analyzed. **Results:** 7 patients who underwent radical robotic trachelectomy were studied. Median patient age was 30 (range 23-35) years old. Median body mass index was 24 (range 19-28). Tumor histology was squamous cell carcinoma in 57% (4) and adenocarcinoma in 43% (3) of the patients. Median surgical time was 285 (range 247-315) minutes. The median of pelvic nodes obtained was 15 (range 12-40). Two postoperative complications were observed. One patient tried to conceive and had preterm labor. One patient died of the disease. **Conclusions:** In selected cases robotic radical trachelectomy is a safe option for patients that wish to preserve their fertility with similar rates of oncological safety and complications than open procedures and a shorter recovery time.

**Keywords:** robotic; early-stage; cervical; fertility

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## 1. Introduction

Cervical cancer is one of the most frequent tumors affecting women worldwide; with over half a million new cases diagnosed annually. It is the fourth most common cancer in women, and the second most frequent in ages from 15 to 44 years old [1]. Its development is mainly influenced by HPV infection, so its prevalence is highly variable, with important differences according to the grade of development of the countries [2]. Access to HPV vaccination, an adequate screening program and treatment of pre-malignant disease are the main factors that cause important differences regarding incidence among countries [3]. These factors cause that, in some countries, its incidence becomes higher than endometrial or ovarian cancer.

Cervical cancer may affect patients of a broad age range, so it is not rare its diagnosis in young patients. This fact, added to the current increase of the maternity age, makes necessary the development of new treatments that may enable, in selected cases, the preservation of fertility on the patients that wish to.

Surgery is the standard treatment for early-stage cervical cancer, although radiotherapy can be considered in some cases, with equal results [4]. Nonetheless, surgery is usually chosen as the standard treatment because its morbidity is lower and it provides a histological examination that

allows the obtainment of prognostic factors; radiotherapy as treatment for early-stage tumors is not frequently used. Radiotherapy is more often used as adjuvant treatment in selected high- risk patients after surgery or as primary treatment with concomitant chemotherapy in advanced- stage tumors.

When the tumor is amenable for surgery, its extension and, therefore, radicality, is based on FIGO stage. Stage IA1 with no invasion of lymph vascular space may be treated by a cervical conization or single hysterectomy [5]; in the remaining surgical stages, the standard treatment consists on radical hysterectomy. Surgery for cervical cancer includes dissection and removal of both parametrium, since cervical cancer tends to spread through the parametrial tissue. The degree of radicality needed is also based on FIGO stage.

Despite the higher or lower grade of parametrial radicality needed, standard radical surgery for cervical cancer includes the removal of the uterine body along with the cervix, entailing the loss of fertility, so other treatments have been considered in order to allow the accomplishment of childbearing wishes.

Radical trachelectomy consists on the removal of the cervix and the parametrium with the preservation of the uterine body and its suture to the vaginal cuff. This surgical procedure was first described by Eugen Aburel in the 1950s, not being used anymore until a French group headed by Dargent started to perform it again in 1994 [6]. This surgery can either have vaginal or abdominal approach; the abdominal approach includes laparotomy, laparoscopy and robotics. Radical trachelectomy is indicated when an early-stage cervical tumor is diagnosed in a young patient with desire of fertility sparing. In addition to those requirements, some other criteria need to be taken into account, as histological type, tumor size and absence of lymph node and metastatic disease.

Robotic surgery is known, among others, to ease an improved dexterity and higher rates for instrument movement and a three-dimensional view, in addition to ergonomic and tremor less, which may help to preserve important adjacent structures without compromising the mandatory oncological radicality [7].

Many studies have been published about fertility sparing surgery for cervical cancer, but few of them describe robotic radical trachelectomy; furthermore, they include a small number of patients and a yet short follow- up time. The experience of robotic surgery in non-fertility- sparing procedures for cervical cancer is bigger; studies comparing vaginal and abdominal approach, including laparotomic, laparoscopic and robotic, showed no important differences between vaginal or abdominal minimally invasive surgery (MIS) regarding oncological safety, mean operating time, perioperative or postoperative complications [8]. On the other hand, laparotomic surgery has a similar rate of recurrences but with a higher number of complications. Nonetheless, LACC study postulates an opposite theory, showing lower rates of disease- free survival and overall survival when a laparoscopic or robotic radical hysterectomy is performed, compared to laparotomic approach [9]. Since these results were unexpected, shortly after their release, some other studies were carried out in order to clarify if MIS actually increased risk for recurrence. IRTA study was published in 2022, and aimed to compare open vs. MIS radical trachelectomy; no differences in prognosis were found in these study [10].

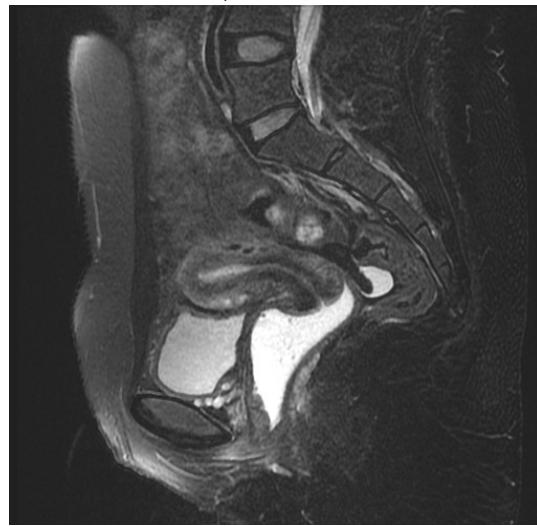
Our objective is not only to add to literature new cases of robotic radical trachelectomy, with a longer follow- up time, but to compare the so far published data with our own data, in order to prove feasibility and safety of robotic radical trachelectomy as fertility sparing surgery.

## 2. Material and Methods

Seven patients that underwent robotic radical trachelectomy from 2013 to 2022 at Hospital Clinico San Carlos were analyzed. They were all young patients with early-stage cervical cancer and wished fertility preservation. They were explained that it was not the standard procedure; moreover, they all fulfilled inclusion criteria and signed a consent form. The study was approved by the local ethic committee.

After diagnosis, patients that demanded fertility preservation and were candidates underwent a preoperative study including a magnetic resonance image to assure tumoral size (Figure 1), absence of distant metastasis and no lymph node involvement.

The surgery was a standard procedure in all cases, and was performed with Da Vinci surgical system. Until March 2015 da Vinci standard was used; beyond that date, the hospital changed the robotic platform and achieved the Xi da Vinci, which was the one used from that date onwards.



**Figure 1.** Cervical tumor seen on MRI.

Surgery was performed as follows: the patient was placed in lithotomy position. Umbilical incision for Hasson's technique was used. Pneumoperitoneum with pressures maximum to 12 mmHg was established and three 8 mm robotic trocars were placed; through those trocars the monopolar scissor (arm 1), bipolar fenestrated forceps (arm 3) and prograsp grasper (arm 4) were placed. An auxiliary trocar of 5 mm or 10 mm was placed on the left side of the umbilicus, and was used by the assistant for conventional laparoscopy. Detail of the trocar placement is shown on Figure 2.



**Figure 2.** Placement of trocars during robotic surgery.

First, a bilateral pelvic lymphadenectomy was performed and the lymph nodes were sent to frozen section for intraoperative histological analysis. In case of positive nodes, the tumor was upstaged due to lymph node involvement, so the patient was not amenable for radical surgery. In that case, a transperitoneal infrarenal paraaortic lymphadenectomy was done and the patient was derived to chemo- radiotherapy as definitive treatment. If pelvic lymph nodes were negative, a nerve-sparing radical trachelectomy was performed with the preservation of both uterine arteries. The

cervix was sectioned below the isthmus and removed vaginally leaving the uterus attached to the ovaries, the round ligaments and the uterine arteries. A frozen section of the upper margin was then performed to confirm clear margins. A permanent cervical cerclage with a non-absorbable suture was placed just below the isthmus. Finally, anastomosis between the remaining uterine body and the vaginal cuff was performed robotically with an absorbable suture. The radical removal of the parametrium made it advisable to leave an urinary catheter for urinary monitoring.

### 3. Results

A total of seven patients who underwent radical robotic trachelectomy were studied. The range of ages were from 23 to 35 years old, with a median patient age of 30 years old. Their body mass index was from 19 to 28, with a mean of 24. Staging was based on FIGO stage system. Since there was an update in 2018 but the majority of patients were diagnosed prior to that new staging, we decided to use the FIGO stage 2009 in the article for standardization. Final clinical stage was IA2 in 1 patient, IB1 in 5 patients and IB2 in 1 patient. Histology of the tumor was squamous cell carcinoma in 4 patients (57%) and HPV adenocarcinoma in the remaining 3 patients (43%). Surgery was performed with Da Vinci standard in 3 (43%) of the patients and Da Vinci Xi in 4 (57) %. Time of surgery was divided on skin-to-skin time, which was defined as the time of the radical trachelectomy procedure only, and total operating time, which also included docking time of the robot. The mean total surgical time was 285 minutes, ranging from 247 to 315. The mean skin-to-skin time was 215 minutes, ranging from 183 to 247.

There were not intraoperative complications, but 2 patients (28.5%) experienced postoperative complications such as hematomata and femoral neuropathy. At a median follow- up of 53.3 months (range from 18 to 115 months), one patient experienced tumor recurrence and finally died of disease. Two patients tried to get pregnant. The first underwent an in vitro fertilization and delivered by cesarean section at 37 weeks of pregnancy a healthy newborn. The second also underwent an in vitro fertilization and had a premature delivery by cesarean section at 28 weeks of pregnancy. All robotic radical trachelectomy results are summarized in Table 1.

**Table 1.** Patient's data, perioperative outcomes and complications.

PATIENT	1	2	3	4	5	6	7
Age	31	33	25	27	35	30	29
Previous parity	No	Yes	No	Yes	No	No	No
Body mass index	28.1	26.6	19.1	19.5	22.7	26	24.3
(kg/ m <sup>2</sup> )							
FIGO stage and size	IB1, 2 cm	IA2	IB3*, 3 cm	IB1, 2 cm	IA2	IB1, 10 mm	IA2, 6 mm
Number of lymph nodes	26	15	12	40	14	N/c	N/c
Free margins	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Histology	Squamous	Squamous	Squamous	Squamous	Squamous	Squamous	Adenocarcinoma
Robot model	standard	standard	standard	Xi	Xi	Xi	Xi
Skin-to-skin time (minutes)	199	212	183	209	247	245	N/c
Total surgery time (minutes)	270	285	247	263	315	315	N/c
Estimated blood loss (ml)	275	175	250	210	200	200	N/c
Intraoperative complications	No	No	No	No	No	No	No
Postoperative complications	Cleisis and hematometra	No	No	No	Femoral neuropathy	No	No
Hospital stay (days)	2	4	4	3	5	4	3
Recurrences	0	0	1	0	0	0	0

Pregnancies	1	0	0	0	0	1	0
Decease	0	0	1	0	0	0	0
Follow-up time (months)	63	115	17 until relapse 31 until decease	60	30	56	18

\* At the moment of diagnosis there was a different FIGO staging system, so the tumor was stage IB2 and no restriction of size was firm at that time.

The patient that had relapse of the disease underwent a preoperative pelvic magnetic resonance that described a 15 millimeters tumor, so she was referred to conservative surgery. The final histological analysis reported a 3 centimeters tumor with lymph vascular space invasion and deep cervical stromal invasion. According to those risk factors, she was proposed adjuvant treatment, but she had strong childbearing desire, so she refused to undergo any type of adjuvant treatment or completion of surgery, despite medical advice. After 12 months of follow-up, the image techniques, pelvic examination, pap-smear and HPV test were all negative so she was allowed to try to get pregnant. Shortly after, she consulted for an episode of metrorrhagia, with normal clinical examination. She underwent a hysteroscopy, that observed a tumoral mass, which was confirmed by biopsy. A pelvic magnetic resonance image observed a pelvic tumor of 27x15 millimeters involving the muscular of the bladder. A treatment with chemo-radiotherapy was initiated, but was not effective, with local disease progression and vagino-vesical fistula. The positron emission tomography scan did not evidence signs of distant metastasis, so anterior pelvic exenteration was proposed and performed afterwards, with tumor-free margins. The patient recovery was adequate, with a hospital discharge after 33 days of the surgery. Five months later, pulmonary metastatic disease was found followed by peritoneal carcinomatosis; that lead to her decease four months later.

#### 4. Discussion

Radical trachelectomy is a thrilling option for fertility sparing surgery after diagnosis of cervical cancer in young patients [11]. As for all treatments, it is important to offer similar rates of complications and oncological prognosis than standard procedures, in order to establish it as a safe treatment for our patients.

Surgery for cervical cancer has to be radical in order to assure the removal of the parametrium, as it is mandatory for an adequate treatment in the majority of cases. Robotic surgery has the advantages of minimally invasive surgery in terms of shorter hospital stay and less postoperative pain comparing to laparotomic approach. Robotics has also some advantages inherent to the robot itself, as the addition of extreme accuracy for dissection, but also reduction in surgeon-dependent factors such as tremor [12]. The use of robotic surgery does not imply less surgical radicality, as there are no differences in length of parametrial tissue removed comparing to different surgical options [13]. As vaginal approach is also a widespread surgical option, it has been compared with robot-assisted surgery. No differences were found on remaining cervical length among them; furthermore, robotic surgery enables a more accurate placement of the cerclage, closer to the inner cervical os [14].

Considering complications, MIS has shown similar rates of intraoperative and postoperative complications than open surgery, with a significantly lower blood loss [15]. Some groups have even found lower rates of blood loss with the use of robotic surgery, compared to conventional laparoscopy [16]. Robotics also provide an improvement in postoperative recovery, with shorter hospital stay [17]. No significant differences were found regarding mean operative time when compared to open surgery. In our series, only two minor postoperative complications were reported (28.6%). All our patients had a quick recovery and a short hospital stay.

Once advantages of MIS and especially robotic surgery are shown, it is time to discuss risk factors that may condition the indication of conservative procedures. There are many factors that have influence on prognosis for cervical cancer. For conservative procedures, the main factors are tumor size, FIGO stage and margins condition [18]. Lymph node status does not play a role, since the presence of tumoral cells in lymph nodes is a contraindication for any type of surgical treatment in

cervical cancer. FIGO stage and, therefore, tumoral size, has a huge impact in prognosis. In the beginning, fertility sparing surgery was a possible option in tumors up to 4 cm, as long as tumor-free margins were assured [19]; nonetheless, some groups were already more restrictive, using 2 cm limit [20]. Currently, there is a consensus to limit the size in all cases to 2 cm, so trachelectomy is an option only for stages IB1 (FIGO stage 2018) or less [21]. Some studies discuss the possibility of neoadjuvant chemotherapy followed by conservative procedures, to enable conservative procedures in bigger tumors, although it is not a widespread management [22]. The state of surgical margins is a key point for fertility sparing surgery, since the presence of disease in the upper margin would lead to extended cervical resection if free margins were feasible; if free margins were not obtained, a hysterectomy would be mandatory. Prior to consider surgery for cervical cancer, it is mandatory to histologically assure absence of lymph node involvement, even for standard radical hysterectomy.

Taking into account the expected prognosis of conservative procedures for cervical cancer, many studies have been published. Initially, MIS procedures were scarce, so some groups compared it to open surgery and even to different procedures such as conization [23]. In this study, recurrences were reported in all groups; deaths were present in all the groups except for the robotic trachelectomy. The rate of recurrences was higher in tumors bigger than 2 centimeters. Data are summarized in Table 2.

**Table 2.** Recurrences and deaths in fertility- sparing procedures. Modified from Bentivegna et al.

	Dargent's procedure	Single trachelectomy or conization	Neoadjuvant chemotherapy plus conservative surgery*	Laparotomic radical trachelectomy	Laparoscopic radical trachelectomy	Robotic radical Median trachelectomy
Cases	1364	230	99	660	238	89
Recurrences	58 (4.0%)	6 (2.4%)	6 (6%)	31 (5%)	15 (6.3%)	2 (2.2%) 4.3%(2.2-6.3)
Recurrences in tumors > 2 cm	14 (17%)	**	5 (9.6%)	8 (4.8%)	7 (16.6%)	Unknown
Deaths	24 (2%)	1 (0.4%)	2 (2%)	9 (1.3%)	3 (1.2%)	0 1.1% (0- 2)
Deaths in tumors > 2 cm	Unknown	**	Unknown	Unknown	Unknown	Unknown

\* Conservative surgery: radical trachelectomy, simple trachelectomy or conization. \*\* Tumor size in this group was smaller than 2 centimeters.

Some other studies consider exclusively robot-assisted radical trachelectomy, for early-stage cervical cancer. When FIGO stages are IA1- IA2, no recurrences were reported during follow-up [24]. Over time, restrictions on tumoral size were less strict, so conservative procedures were applicable to bigger tumors, proving also low rates of recurrences; this study reports only 4% of local recurrence after radical trachelectomy for stages IA1- IB1 [25]. It is important to highlight that the majority of these studies do not specify tumoral size; when they do, it is less than 2.5 centimeters [26].

Undoubtedly, special mention deserves LACC study, as it unexpected results led to a turning point in the surgical management of cervical cancer. LACC study conferred worse prognosis for minimally invasive surgery compared to open surgery, causing a change in surgical practice worldwide. Many studies were conducted afterwards in order to rebate those results and add evidence to bring MIS back as a safe option for cervical cancer. Factors such as tumor size above 2 centimeters, impact of pneumoperitoneum and use of a uterine manipulator were identified as potential causes for recurrences increase [27]. Those results have resulted in a change of paradigm with the appearance of protective maneuvers to avoid tumor spread, such as vaginal cuff closure while tumor manipulation [28]. Also, prior conization has been proposed as a strategy to minimize risk of spread [29]. Limitation on tumor size < 2 centimeters has also become mandatory, and it is considered probably the main factor having influence in prognosis [30]. All data are shown on Table 3.

**Table 3.** Comparison of robotic radical trachelectomy studies. Includes only studies with robotic radical trachelectomy as primary treatment.

Study	N	FIGO stage 2009	Tumor size (cm)	Follow- up time	Complications and percentage	Type of complications	Recurrences	Deaths
Burnett et al	6	IB1	-	11 (9-13)	Yes (33%)	Small bowel herniation. Inferior epigastric vessels hemorrhage	0	0
Vieira et al	42	MIS 69% IB1	-	25 (10- 69)	Yes (4.7%)	Bladder injury Fallopian tube injury	0	0
Nick et al	12	IA1 + LSVI* - IB1	Median 2,15 (0,43-24,6)	10,8	Yes (25%)	Hematometra Irregular menstrual bleeding Amenorrhea	0	0
Hong et al	3	IB1	< 2	8 (6- 9)	No	-	0	0
Johansen et al	48	IA1**- IB1	-	24 (1- 89)	Yes (6.25%)	Vesicovaginal fistula Compartment syndrome Cervical stenosis	0	0
Ramirez et al	4	IA1+ LSVI - IA2	-	3,5 (2,7- 7,2)	Yes (25%)	Femoral neuropathy	0	0
Andou et al	10	IA2- IB1	< 2,5	-	-	-	-	-
Persson et al	13	IA1 + LSVI - IB1	Median 1,2 (0,8- 3,3)	24 (6- 54)	No	-	0	0
Our study	7	IA2- IB2	≤3	53.3 (18- 115)	Yes (28.5%)	Femoral neuropathy Cleisis and hematometra	1 (14.3%)	1 (14.3%)

\* LSVI: lymphovascular space involvement.\*\* In this group, stage IA1 included one of the following: positive cone margins, linfovascular space involvement or multifocal tumor.

In our study, one (14.3%) case of recurrence was reported, that led to the patient's death. It is important to identify risk factors that may have played a role in this adverse outcome, in order to prevent it from happening again. The six patients that remain free of disease at the time of the data collection had a tumor smaller than 3 centimeters. The patient that had the recurrence had a three-centimeter tumor with extensive lymph vascular space invasion and deep cervical stromal invasion. At the time of her diagnosis, there was no strict size criteria that prohibited the conservative procedure. Nonetheless, the patient was advised to undergo standard procedure due to the tumoral size, but she refused due to her strong childbearing wishes. After conservative surgery, since tumor had an extensive ILV she was recommended for adjuvant therapy, that she also refused. Considering published studies that only describe robotic radical trachelectomy, none of them had recurrences nor deaths; analyzing tumor characteristics, all of them had a size of less than two centimeters. That fact would have had a great impact on the good prognosis

Therefore, we believe the limitation of size to offer fertility-sparing surgery for cervical cancer is mandatory, since recurrences are strongly related to tumor size, with the subsequent impact on prognosis.

Our study has some limitations: it is a retrospective study so data collection may have some missing data. Moreover, some of our patients were referred to our hospital for surgery, and returned to their own hospitals which were located at a different city for follow- up, so the results need to be carefully considered due to the possibility of some missing data. Second, it is a still short series of patients and, the presence of one death due to disease has great impact on the final results; nonetheless, we think our results are useful for the literature, since we have learned the importance of tumor size limitation.

In conclusion, with the results published so far, we strongly believe that robot-assisted radical trachelectomy is a safe option for patients that wish to preserve their fertility, as long as strict inclusion criteria are fulfilled. In the absence of those criteria, patients should be referred to standard

surgery, with the subsequent loss of the uterine body. Robotic surgery has similar rates of oncological safety and complications than open procedures, with a shorter recovery time.

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**Conflicts of Interest:** The authors declare no conflicts of interest.

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