

Original Article



Reproductive counseling and pregnancy outcomes after radical trachelectomy for early stage cervical cancer

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Received: Sep 3, 2018

Revised: Oct 30, 2018

Accepted: Dec 17, 2018

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ABSTRACT

Objective: To evaluate patient perceptions of preoperative reproductive counseling and to evaluate complications and pregnancy outcomes in women who had radical trachelectomy (RT) for early stage cervical cancer.

Methods: Patients who underwent RT from January 1, 2004, through July 31, 2017, and had been cancer free for more than 1 year after RT were eligible; consented patients were sent a 16-item online survey.

Results: Of the 58 eligible patients, 39 patients (67%) completed the questionnaire. Eighteen patients (46%) reported receiving reproductive counseling and 26 (68%) reported receiving counseling about pregnancy risks and complications prior to RT, mainly delivered by gynecologic oncologists. Twenty-nine patients (74%) reported having a complication after RT, and cervical stenosis was the most common complication, occurring in 13 patients (33%). Twenty-four patients actively attempted to conceive after RT, and 20 pregnancies were achieved in 13 patients for a pregnancy rate of 54%. Eight pregnancies were spontaneous and 12 required a fertility treatment. There were 5 spontaneous first-trimester miscarriages; 14 of the 20 pregnancies (70%) resulted in live births. The median time to conception was 13.5 months (range, 1-120).

Conclusion: A significant proportion of women with early stage cervical cancer do not receive adequate reproductive counseling before RT, and many women undergoing RT experience complications that can negatively impact their fertility. We recommend a preoperative consultation with a reproductive endocrinologist for all patients considering RT.

Keywords: Cervical Cancer; Fertility Preservation; Pregnancy; Radical Trachelectomy; Reproductive Counseling

INTRODUCTION

Approximately 46% of cervical cancer patients are of reproductive age. It is important to discuss fertility-sparing surgery in candidates with newly diagnosed early stage (stage IB1 or less) cervical cancer [1]. Per the National Comprehensive Cancer Network guidelines, radical

Presentation

This research was presented in part at the 66th Annual Meeting of the Pacific Coast Reproductive Society; March 2018; Indian Wells, California.

Funding

This research was funded by: The Cancer Center Support Grant (P30CA016672).

Conflict of Interest

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

Author Contributions

Conceptualization: S.J.S., W.T.L., F.M.; Data curation: S.J.S., F.M.; Formal analysis: S.J.S.; Funding acquisition: F.M.; Investigation: S.J.S., W.T.L., R.P.T., F.N.D., F.M.; Methodology: S.J.S., W.T.L., R.P.T., F.M.; Project administration: S.J.S., W.T.L., R.P.T., F.N.D., F.M.; Resources: S.J.S., W.T.L., R.P.T., F.M.; Software: S.J.S., F.M.; Supervision: S.J.S., W.T.L., R.P.T., F.N.D., F.M.; Visualization: S.J.S., J.N.D., W.T.L., R.P.T., F.N.D.; Writing - original draft: S.J.S., J.N.D., R.P.T., F.N.D., F.M.; Writing - review & editing: S.J.S., J.N.D., W.T.L., R.P.T., F.N.D., F.M.

trachelectomy (RT) is a safe oncologic treatment in patients with early stage cervical cancer [1,2]. Many studies have concluded that pregnancy after RT is feasible and can be successful [3-5]. However, this surgery comes with potential postoperative complications that may make pregnancies high risk [6]. Common complications include cervical stenosis and cervical insufficiency, which can lead to difficulty conceiving, infertility, preterm delivery, first- or second-trimester miscarriage, and preterm premature rupture of membranes [3,4,6-9].

A systematic review analyzing fertility and pregnancy outcomes among women who underwent RT performed by all surgical approaches (i.e., vaginal RT, abdominal RT, minimally invasive RT) concluded that the rates of pregnancy (patients with at least 1 pregnancy/total number of patients attempting pregnancy), live birth, and prematurity (<36 weeks) were 55%, 71%, and 49%, respectively [8]. Carter et al. [10] reported that postoperative complications can affect patients physically and emotionally and highlighted the importance of informing patients of what to expect from RT and of future implications for their health. Carter et al. [11] also demonstrated no significant differences in mood, quality of life, distress, or sexual function between patients with early stage cervical cancer who underwent RT and those who underwent radical hysterectomy. This information can help reproductive endocrinologists give patients reasonable expectations about fertility and pregnancy outcomes and can assist gynecologic oncologists when counseling patients on the recovery process.

After RT, possible outcomes that may increase the rate of infertility include cervical stenosis, lack of cervical mucus to facilitate sperm migration, subclinical endometritis, and vascular compromise [6,8,12]. Prior studies have investigated sexual function [13], quality of life [1,11], emotional and physical well-being [11], and pregnancy outcomes [3,8] after RT, but there is a paucity of data describing the role and extent of reproductive counseling in this patient population [14]. The purpose of this study was to determine how patients perceive preoperative reproductive counseling (i.e., effects on future fertility, pregnancy risks/complications) and to evaluate postoperative complications and pregnancy outcomes in patients who underwent RT for early stage cervical cancer.

MATERIALS AND METHODS

This survey-based cross-sectional study was approved by the Institutional Review Board at The University of Texas MD Anderson Cancer Center (PA17-0641). All patients who underwent RT at MD Anderson Cancer Center from January 1, 2004, through July 31, 2017, and had been cancer free for more than 1 year after RT were eligible. These patients were initially contacted via a mailed letter that introduced and described the research study and were then contacted by a telephone call or by an email message sent through MD Anderson Cancer Center's secure web-based system to determine if they were willing to participate. Once a patient was consented, demographic information, pregnancy outcomes, surgical details, and postsurgical complications were obtained by retrospective chart review. A 16-item online questionnaire was developed by our multidisciplinary research team containing a combination of quantitative and qualitative items (**Supplementary Data 1**). Survey questions were presented as multiple choice, Likert scale, or open-ended questions. All collected patient information was confidential, and no identifiers were used in the analysis. Surveys were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at MD Anderson Cancer Center [15]. Patients who had agreed to participate but not

started the survey were sent an email reminder via REDCap up to 3 times. We followed the Strengthening the Reporting of Observational Studies in Epidemiology [16] guidelines in reporting the results of our study. Descriptive statistics were used to report all variables of interest; categorical variables were analyzed using the sign test and Fisher's exact test. A p-value less than 0.05 was considered statistically significant.

RESULTS

1. Demographics

Fifty-eight eligible patients were identified, and 39 patients (67%) completed the questionnaire and were included in our analysis. The median age was 30 years (range, 25–37), and the median body mass index was 24 kg/m² (range, 16–46). The majority of the patients were Caucasian (92%) (**Table 1**). Twelve women (31%) had prior pregnancies resulting in live births, and 27 patients were nulliparous. Twenty patients had robotic-assisted total laparoscopic RT, 16 had

Table 1. Demographic and clinicopathologic characteristics of patients with early stage cervical cancer who underwent radical trachelectomy (n=39)

Characteristics	No. (%)
Race	
African American	2 (5)
Asian or Pacific Islander	1 (3)
Caucasian	36 (92)
Ethnicity	
Hispanic	7 (18)
Non-Hispanic	32 (82)
History of smoking	8 (21)
Nulliparous	27 (69)
Surgical approach	
Pure laparoscopic	3 (8)
Abdominal	16 (41)
Robotic-assisted laparoscopic	20 (51)
Stage	
IA1	5 (13)
IA2	14 (36)
IB1	20 (51)
Grade	
1	13 (33)
2	15 (39)
3	11 (28)
Histology	
Adenocarcinoma	23 (59)
Adenosquamous carcinoma	1 (3)
Squamous cell carcinoma	15 (38)
Cerclage type	
0 Ethibond	30 (77)
1-0 Ethibond	6 (15)
Mersilene	3 (8)
Stenosis prevention device	
Pediatric foley catheter	11 (28)
Smit sleeve	28 (72)
Closure method	
Barbed running	15 (38)
Vicryl interrupted	21 (54)
Vicryl running	3 (8)
Lymphovascular space invasion	10 (26)*

*On final pathology, there were no positive nodes or margins for these patients.

abdominal RT, and 3 had a pure laparoscopic RT. To help prevent cervical stenosis, 28 patients had a Smit sleeve placed, and 11 had a pediatric foley catheter placed. Approximately half of the patients had stage IB1 cervical cancer, and adenocarcinoma was the most common histological type. No recurrences were noted during the surveillance period.

2. Reproductive counseling

Eighteen patients (46%) reported receiving reproductive counseling prior to RT; 14 patients received counseling from a gynecologic oncologist, and 7 received counseling from a reproductive endocrinologist (**Table 2**). Four patients received counseling from at least 2 different providers. Of the 18 patients who received reproductive counseling, 16 patients believed it was adequate and helped them make an informed decision about choosing RT.

Twenty-six patients (68%) reported receiving counseling about pregnancy risks and complications; one patient did not complete this question. Twenty-five patients received pregnancy and complication counseling solely from a gynecologic oncologist. Of the 26 patients who received pregnancy and complication counseling, 23 believed it was adequate and helped them make an informed decision about choosing RT.

Using the Likert scale, the median patient anxiety level about fertility was similar before and after RT ($p=0.31$). Desire for pregnancy was significantly lower 6 months after RT than it was at the time of RT ($p=0.02$). Representative patient comments on information they wished they had known prior to RT are presented in **Table 3**.

Table 2. Reproductive counseling, counseling regarding pregnancy risks and complications, desire for pregnancy, and anxiety about fertility in patients with early stage cervical cancer who underwent RT (n=39)

Characteristics	Value
Reproductive counseling prior to RT*	
Counseling received	18/39 (46)
Counseling delivered by	
Gynecologic oncologist	14/18 (78)
Reproductive endocrinologist	7/18 (39)
Maternal-fetal specialist	1/18 (6)
Women's health nurse	1/18 (6)
Counseling was adequate	16/18 (89)
Counseling helped patient make an informed decision	16/18 (89)
Counseling on pregnancy risks/complications prior to RT*	
Counseling received	26/38 (68)
Counseling delivered by	
Gynecologic oncologist	25/26 (96)
Reproductive endocrinologist	2/26 (8)
Maternal-fetal specialist	1/26 (4)
Counseling was adequate	23/26 (88)
Counseling helped patient make an informed decision	22/26 (85)
Desire for pregnancy†	
Prior to surgery	6
6 months after surgery	5
At time of survey	6
Anxiety level‡	
Prior to surgery	5
After surgery	7

RT, radical trachelectomy.

*Data are presented as number of patients/total number of patients who responded to that question (%); patients may have received counseling from more than one provider; †Median value on a Likert scale of 1–10 with 1 indicating no desire and 10 indicating strong desire; ‡Median value on a Likert scale of 1–10 with 1 indicating no anxiety and 10 indicating extremely anxious.

Table 3. Patient feedback on importance of preoperative reproductive counseling and positive impact of radical trachelectomy

Importance of reproductive counseling prior to surgery	
<ul style="list-style-type: none"> • “The information given had to be requested initially. I think this is something that should be offered to all patients without having to ask. Cancer can be traumatic and sometimes you don't think to ask about certain things.” • “We talked about potential issues that may arise due to not having a cervix, but I didn't realize how much smaller my uterus would be following the surgery and how that may affect if I am able to successfully carry a child.” • “A consult with a fertility specialist to learn more about the different fertility methods (e.g., intrauterine insemination, in-vitro fertilization, etc.) and other options (e.g., egg freezing, donor egg, gestational carrier, etc.) would have been helpful as most of this information was either discovered pre-surgery on my own through research or post-surgery. We realized this once we were having trouble getting pregnant and consulted a fertility specialist 3.5 years after surgery.” • “I was only told that my surgery may make pregnancy more high-risk. Being young and facing cancer, I didn't fully understand what that meant. I should have had a consultation with a fertility specialist and a high-risk obstetrician before surgery.” • “I wish I would have been made more aware of the likelihood of cervical stenosis and the impact on my fertility.” 	
Positive impact of radical trachelectomy on patients' lives	
<ul style="list-style-type: none"> • “Even if I never get pregnant, at least the radical trachelectomy gives me the option. I was not ready for a hysterectomy and I still wanted the option of becoming pregnant.” • “It was so traumatic knowing that my ability to have children would be taken away at such a young age and it was comforting to know that I could still carry a child with radical trachelectomy.” • “Because there is still a chance to conceive.” • “I had my surgery at 25 years old. A complete hysterectomy would have been absolutely devastating for my husband and me. We only have been married for 2 years and have future plans to start a family.” • “Radical trachelectomy gave me hope and made me feel empowered.” • “I was able to give life.” 	

3. Pregnancy outcomes

Pregnancy outcomes are summarized in **Table 4**. Twenty-four patients (62%) reported actively attempting to conceive postoperatively. The reasons of the 15 patients who did not attempt to conceive included: not ready for pregnancy (50%), no partner (25%), anxiety (19%), cost (19%), worry of miscarriage (19%), age (13%), other medical conditions (13%), and sexual dysfunction (6%). Patients were given the option to report more than one reason.

Of the 24 patients who attempted to conceive after RT, 20 pregnancies were achieved in 13 patients for a pregnancy rate of 54% (**Table 4**). Five patients conceived more than one time; 8 patients conceived once, 3 patients conceived twice, 2 patients conceived 3 times, 9 patients failed to conceive, and 2 patients had unsuccessful embryo transfers after successful autologous in vitro fertilization (IVF). The median time to conception was 13.5 months (range, 1–120). Eleven patients attempted to conceive spontaneously with 8 pregnancies resulting from 5 patients. Thirteen patients attempted to conceive with a fertility treatment; 11 patients pursued IVF and ovulation induction/intrauterine insemination in 2 patients with

Table 4. Outcomes of 20 pregnancies in 13 patients and distribution of pregnancies by surgical approach

Variables	Pregnancy outcome ^{a,†}	Distribution of pregnancies by surgical approach		
		Abdominal	Robotic	Pure laparoscopic
Spontaneous miscarriage <12 wk deliveries	5/20 (25)	0	5	0
20–24 wk	1/20 [‡] (5)	1	0	0
24.1–32 wk	4/20 (20)	2	2	0
32.1–36.6 wk	7/20 (35)	2	4	1
>37 wk	3/20 (15)	0	3	0
Live birth	14/20 (70)	4	9	1

Data are presented as number (%).

^aTwenty pregnancies were among 13 patients: 8 patients conceived once, 3 patients conceived twice, and 2 patients conceived 3 times; [†]24 patients attempted to conceive; pregnancy rate—13/24 (54%); [‡]Intrauterine fetal demise occurred at 21 weeks.

12 pregnancies resulting from 8 patients. One patient underwent IVF and used a gestational carrier due to cervical stenosis and while another patient had a failed IVF cycle and ended up using frozen donor oocytes with a gestational carrier. The pregnancy rate was similar when a fertility treatment was utilized compared to spontaneous conception ($p=0.21$). The pregnancy rate also did not differ by surgical approach ($p=0.62$).

Five spontaneous first-trimester miscarriages (25%) occurred in 5 patients, 2 who conceived spontaneously and 3 who conceived by IVF, and all of these miscarriages occurred in patients who had robotic-assisted total laparoscopic RT. Of the 20 pregnancies, 14 resulted in a live birth (70%). All patients underwent cesarean deliveries. The preterm (20–36.6 weeks) delivery rate was 80% (12/15), and 7 of the deliveries (47%) occurred between 32 and 36.6 weeks' gestation.

4. Complications affecting fertility

Twenty-nine patients (74%) reported they had one or more complications after RT that might have affected their fertility. The most commonly reported of these complications were cervical stenosis, which occurred in 13 patients (33%); lymphedema, which occurred in 4 patients (10%); and cerclage issues, which occurred in 3 patients (8%). We found that cervical stenosis did not differ by surgical approach ($p=0.55$) occurring in 7 patients who underwent abdominal RT (44%), 5 who underwent robotic-assisted laparoscopic RT (25%), and one patient who underwent pure laparoscopic RT (33%) ($p=0.55$). Eleven of the 29 patients with complications (38%) underwent fertility treatments, which resulted in 6 live births from 5 patients; 1 patient with complications after RT had 2 live births without any fertility treatment. Three patients with complications eventually opted for a hysterectomy because of cervical stenosis, chronic pelvic pain, or abnormal uterine bleeding.

Four patients (10%) reported that given their experiences and what they now knew, they would have chosen radical hysterectomy over RT if they had the chance to make the decision again. The reasons they cited were chronic pain (3 patients) and emotional distress due to multiple failed pregnancy attempts (1 patient). Nine patients (23%) reported a decrease in their quality of life after RT due to cervical stenosis, dyspareunia, or chronic pelvic pain; 2 of these patients were among the patients who ultimately opted for a hysterectomy. However, the majority of patients (90%) reported they would still choose RT over radical hysterectomy. Patients expressed gratitude for the opportunity to undergo RT and stated that RT had positively impacted their lives; representative supporting comments from patients are presented in **Table 3**.

DISCUSSION

This study explored how patients with early stage cervical cancer who underwent RT perceived preoperative reproductive counseling; the study also evaluated the patients' postoperative complications and pregnancy outcomes. Our survey response rate of 67% exceeds the goal of 60% that has been established by researchers as an adequate recruitment goal in survey studies [17]. Our study demonstrated that a significant proportion of patients who underwent RT at our institution reported not receiving reproductive or pregnancy risks and complications counseling in the preoperative period. Patients in our study reported that they would have preferred more detailed reproductive counseling with a reproductive endocrinologist prior to surgery. Given the significant rate of infertility or subfertility and higher obstetrical risks associated with RT, we recommend a preoperative consultation with

a reproductive endocrinologist for all patients who are considering RT for treatment of early stage cervical cancer.

With our results, our institutional policy has changed to offer preoperative consultation with a reproductive endocrinologist to all eligible RT patients. Having provider-initiated conversations regarding future fertility are important as patients with a recent diagnosis of cervical cancer may be focusing more on the cancer and its treatment than on future fertility. Early preoperative counseling by a reproductive endocrinologist can complement oncologic care by helping patients understand how RT may affect future fertility, discuss reproductive outcomes and complications, and help standardize reproductive counseling [6,12,18]. If counseling is done preoperatively, the reproductive endocrinologist can evaluate a patient's reproductive potential by evaluating a patient ovarian reserve, ruling out ovulatory dysfunction or tubal factor, and discuss any pertinent reproductive history (i.e., recurrent miscarriages, uterine cavity abnormalities) to ensure the patient is an appropriate candidate for RT from a future fertility standpoint. In addition, the reproductive endocrinologist can discuss different fertility treatments and future management strategies if necessary [6,18]. Having reproductive and oncologic counseling in 2 separate sessions may allow patients to give the attention needed for the important information delivered by the physician.

Before RT, reproductive counseling can also help set realistic expectations regarding pregnancy after RT and return to postsurgical changes (i.e., change in the level of sexual desire, dyspareunia, menstrual changes, emotional stress) [1,10]. If patients have realistic expectations, they may be more proactive in trying to conceive by seeing a reproductive endocrinologist prior to surgery instead of waiting for 1 to 2 years before pursuing a fertility treatment (e.g., IVF, intrauterine insemination, ovulation induction) if needed. Other studies have demonstrated that patients who have undergone RT often need some sort of fertility treatment in order to conceive and have a successful live birth [2,3,9,19]. This is consistent with our data and supports the need for a consultation with a reproductive endocrinologist preoperatively before RT allowing patients to seek a fertility treatment sooner if needed and decrease the time to conception.

Similar to other studies, our study demonstrated that live births were possible after RT [2,8]. Our pregnancy rate of 54% (13/24 patients) is similar to the pregnancy rate in a systematic review (55%, 515/938) that included all surgical approaches for RT [8]. Compared to the findings of another systematic review, on pregnancy outcomes after abdominal and vaginal RT, our pregnancy rate (54% vs. 66%), live birth rate (70% vs. 63%), and rate of spontaneous miscarriage were all similar (25% vs. 24%) [7].

Our finding that cervical stenosis effected 33% of patients is higher than the average rate of 10.5% calculated in a published meta-analysis reviewing this complication [20]. There is, however, a wide range of cervical stenosis rates reported in the literature. For example, in that study 20% of the publications reviewed reported a stenosis rate >20% with one large series describing the complication in 73% of patients while 4 studies described 0% of patients experiencing cervical stenosis [20]. The rate of cervical stenosis reported in this study may be higher than the average in that meta-analysis as we relied upon self-reporting by patients and not physician assessed cervical stenosis.

Patients with infertility for other reasons may have inaccurately attributed their difficulties getting pregnant to cervical stenosis as opposed to other etiologies. Our study has some

limitations. This survey was not validated; however, the survey questions were developed by a team consisting of gynecologic oncology and reproductive endocrinology with the intent of soliciting the data to best capture patient responses. With a survey format and use of medical terminology, patients may not have interpreted the questions as we intended. In future studies, defining reproductive and pregnancy risk/complication counseling while minimizing medical terminology in survey questions may limit variations in patient interpretation. Despite having an adequate response rate, the overall low number of patients needs to be considered when interpreting our conclusions. Documentation of reproductive counseling by providers was inconsistent and not able to be used as a comparison with our survey responses. Recall bias or variation in patient perception may have influenced our data. Future studies should correlate patient perceptions to documentation of reproductive counseling by providers. Additionally, since the study included patients treated over an 11-year period, fertility treatment options markedly changed from 2004 to 2017 which may have influenced how reproductive counseling was performed and patients desire for pregnancy. Given our study was conducted at one institution, our conclusions may not be generalizable to all centers who offer RT; reproductive counseling assessment needs to be studied at other institutions. Further research is needed to accurately assess patient perceptions of preoperative reproductive counseling and how they may be impacted by including consultation with a reproductive endocrinologist in the preoperative counseling process.

To our knowledge, this is one of the first studies to provide data on the frequency and patient perceptions of preoperative reproductive counseling in patients undergoing RT for early stage cervical cancer. In addition, we report on obstetrical outcomes after abdominal or pure laparoscopic RT and one of the few studies to provide obstetrical outcomes after robotic-assisted laparoscopic RT. Our data demonstrated that many patients who undergo RT do not receive preoperative reproductive counseling. Having a preoperative consultation with a reproductive endocrinologist can increase patient education by helping patients understand how RT may affect future fertility, ensure patients are adequately informed before making surgical treatment decisions, and facilitate a proactive approach towards achieving a successful pregnancy.

ACKNOWLEDGMENTS

The authors thank Gary B. Chisholm, Senior Programmer Analyst, Department of Gynecologic Oncology and Reproductive Medicine, MD Anderson Cancer Center, for performing the statistical analysis.

SUPPLEMENTARY MATERIAL

Supplementary Data 1

[Click here to view](#)

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