

REVIEW ARTICLE

Surgical approaches towards fertility preservation in young patients with early invasive cervical carcinoma

A. Mandic, P. Novakovic, D. Nincic

Department of Gynecologic Oncology, Oncology Institute of Vojvodina, Sremska Kamenica, Serbia

Summary

Cervical cancer still remains one of the major problems in developing countries. The last decade of 20th century has seen a trend towards more conservative surgical approaches in the treatment of early-stage disease in young patients.

The trend of delaying childbearing, nowadays, increases preservation of fertility, and reproductive function is a major concern when counseling these young women with regard to the effects of treatment for cervical cancer.

Radical trachelectomy, either with abdominal or vagi-

nal surgical approach, showed promise as treatment option in young patients with early cervical cancer. The basic principle of such a surgical approach is an operation aiming at preserving the uterine body and removing the cervix, parametrium, with bilateral pelvic lymphadenectomy, and creating a utero-vaginal anastomosis, either laparoscopically or by laparotomy.

Both surgical approaches are evaluated after a search of the relevant literature in Pub Med or Medline.

Key words: cervical cancer, fertility preservation, trachelectomy

Introduction

Cervical carcinoma still represents one of the major problems in developing countries where cervical screening programmes have not been developed yet [1]. However, in developed countries, this approach enables the detection of cervical cancer in its early phase, making surgical treatment of early invasive cervical carcinoma possible. Usage of different therapeutic modalities in the group of patients with early-stage disease has produced different results. In most cases, the primary therapy consists of radical operation that includes radical hysterectomy with bilateral pelvic lymphadenectomy [2-6]. Standard surgical therapy has given excellent results in terms of 5-year overall survival (OS), which is 85-91% [7-9]. However, a great number of young women lose their fertility permanently.

Diagnosing cervical carcinoma at its early stages in younger patients makes it possible to manipulate them with surgical approaches that could possibly preserve fertility. Approximately 45% of surgically treat-

ed stage IB cancers occur in women under the age of 40 years [10].

Radical trachelectomy is a surgical method which, together with pelvic lymphadenectomy, represents a method of treating invasive forms of early-stage cervical carcinoma in women who are in their fertile age and who want to keep their reproductive function [11].

There are two approaches to radical trachelectomy: radical vaginal trachelectomy (RVT) and radical abdominal trachelectomy (RAT).

Radical trachelectomy

The concept of cervical tumor removal in order to treat bleeding from the cervix in a simplified manner was first presented by Hippocrates in 400 B.C. Although the foundations of contemporary radical technical procedures in the surgical treatment of cervical carcinoma were laid in the end of the 19th century, the idea of preserving the body of the uterus in case of early-stage in-

vasive cancer was simultaneously maturing [12-15]. An idea about preserving the uterine body in early cervical cancer in young patients continued to live throughout the 20th century too. Burghardt and Holzer also suggested in 1977 the unimportant removal of the uterus in cases of early-stage invasive cervical carcinoma [12].

Abdominal radical trachelectomy with uterus conservation

This is one of the two approaches to trachelectomy. The basic principle of such surgical approach is a radical operation aiming at retaining the body of the uterus and removing of the cervix, the parametria with bilateral pelvic lymphadenectomy, similarly to the technique applied for modified Wertheim-Meigs radical hysterectomy, by preserving the body of the uterus and creating an utero-vaginal anastomosis. The operative technique and later the principles of this approach were described by several authors [14,16-19]. This approach enables a wider resection of the parametria, an adequate upper vaginal resection and fewer possibilities of complications. The only limiting factor can be infiltration into the lower segment of the uterus beyond the isthmus (Figures 1-4).

The approach and the technique of this type of radical operation demands the surgeon's previous training regarding classical radical hysterectomy because the basic principles in this type of radical operations do not change.

Laparoscopic radical vaginal trachelectomy

The development of technology and operative procedures, as well as the proved significance of laparoscopy in gynecologic oncology have produced new



Figure 1. Cut vaginal end (original picture).



Figure 2. Cutting of the cervix below the isthmus uteri (original picture).

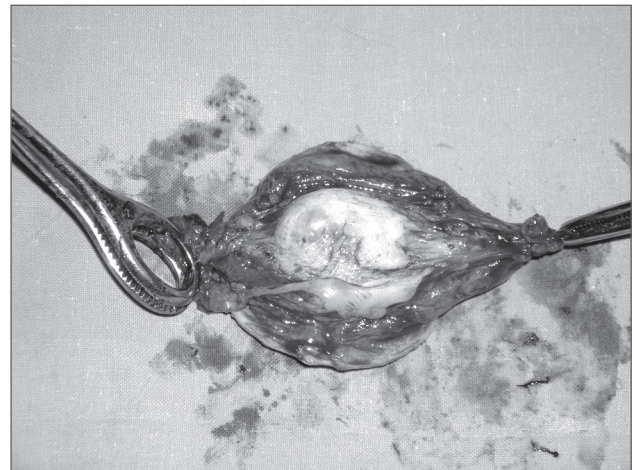


Figure 3. Cervix with parametria (original picture).

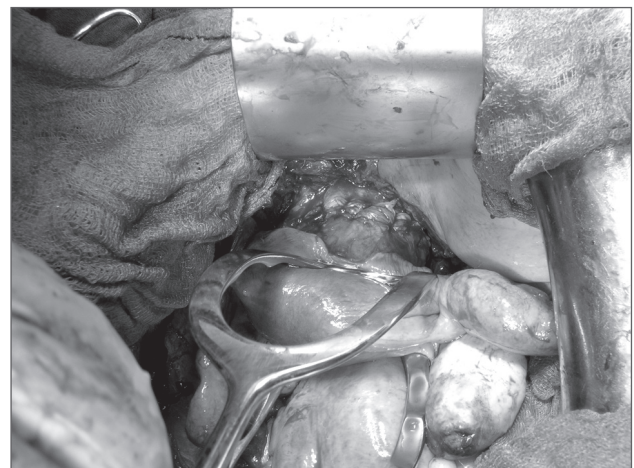


Figure 4. Utero-vaginal anastomosis (original picture).

guidelines in the application of this technique in such cases. Dargent [13,19-23] is considered as pioneer of this technique. In 1987, he performed laparoscopic lymphadenectomy with radical vaginal trachelectomy. With laparoscopy, the intra-abdominal area, the uter-

ine artery, cardinal ligaments and the paracolpium can be visualised, while the vaginal approach requires colpotomy, amputation of the cervix, separating the caudal paracolpium and anastomosing the uterus and the vagina. The cervix is cut below the isthmus in order to keep the competence of the internal ostium of the uterus during pregnancy [21-24].

In the study of Roy et al. (1991-1999), 37 patients had undergone radical vaginal trachelectomy. The follow up lasted 42 months. Two patients relapsed, one of them with a neuroendocrine tumor. Thirteen pregnancies were registered, 7 of which completed with delivery of healthy children. Two patients had spontaneous abortions while in the remaining this happened in the 2nd trimester [25].

Radical vaginal trachelectomy requires much longer training, with good skills in laparoscopic lymphadenectomy and a radical vaginal approach as a second part of the operation. The papers by Coven et al. [11], and Roy [26] have pointed out a somewhat larger number of complications with this procedure, which can be connected to the development of a new technique and the surgeons' training, which could lead to the suggestion that this procedure should be performed in highly specialized institutions with adequate experience and number of such patients.

Additionally, the approach to the parametria and the width of the cut may represent a problem with novices in this technique. Even Dargent stressed the difficulty of removing lateral tissue from the urethra through this vaginal approach [27].

The complications caused by this technique are usually connected to inexperience.

The most frequent complications with the first operations are the following [15]: perforation of the bladder, laceration of the external iliac artery, perirectal hematoma, lymphedema and lymph-cysts.

Indications for radical trachelectomy

The complexity of these procedures stems more from the strict indications for their application because the inadequate selection of patients for this operation discredits the operation itself, the technique, and what's more, the application of an inadequate therapeutic modality for the patients.

There is still no standard consensus for radical trachelectomy because the application of this method in the 1990s was limited by the rather low number of patients and the short follow up period, so that no firm conclusions about independent risk factors of relapse could be determined [10,11,17,28].

What currently appears to be true is that the indications for radical trachelectomy are as follows [17, 21,22]:

1. FIGO stage IA2-IB up to 2 cm with superficial invasion and without lymph and/or vascular invasion.
2. Negative pelvic lymph nodes.
3. Upper and lower as well as parametrial surgical margins must be clear on frozen section.
4. Desire to preserve fertility.

Adenocarcinoma of the cervix and histological grade III disease represent a relative contraindication because they are considered as adverse prognostic factors.

Pregnancies after radical trachelectomy

Koliopoulos et al., in their review, presented 210 female patients that had undergone radical trachelectomy with 55 verified pregnancies. In total, 35 pregnancies were successfully completed with childbirth along with 30-50% abortions before the 20th week of gestation. Apparently, despite this small number of births, the authors are emphasising the importance of this technique, all the more because infertility is 100% with standard procedures [29]. Hertel et al. reported that the percentage of pregnancies in women after radical trachelectomy was 70% [30]. In the Shepherd's review 406 patients had undergone radical vaginal trachelectomy in 7 centers [15]. Of them there were 171 verified pregnancies in 118 women. Only 17 pregnancies ended with births before the 32nd gestation week.

Plante analysed the outcomes of 603 patients with radical vaginal trachelectomy and found 4.5% recurrences (Table 1) [31].

In the Plante's review pregnancy was verified in 44% of patients after radical vaginal trachelectomy. Among them 35% had a term birth, 18% preterm delivery and 27% had abortion in the 1st and 2nd trimester [31]. There was no data in the Hertel's study with 100 vaginal radical trachelectomies [30]. Five percent of the patients had therapeutic abortion and extrauterine pregnancies (Table 2) [31].

In more recent studies, 50% had a term birth, 20% preterm delivery, and the remaining 30% aborted in the 1st or 2nd trimester of pregnancy [32,33].

The end of pregnancy is with caesarean section and it is necessary to explore the abdomen.

Follow up

Proper selection of patients for radical trachelec-

Table 1. Radical vaginal trachelectomy and disease outcomes (modified from [31])

<i>First author [Reference]</i>	<i>Number of treated patients</i>	<i>Median follow-up (months)</i>	<i>Recurrence rate n (%)</i>	<i>Deaths n (%)</i>
Hertel [30]	100	29	3 (3)	2 (2)
Marchiole [34]	118	95	7 (6)	5 (4)
Plante [35]	115	74	4 (3)	2 (2)
Shepherd [36]	112	45	3 (3)	2 (2)
Covens [37]	93	30	7 (7.5)	4 (4)
Sonoda [38]	36	21	1 (3)	0
Burnett [39]	19	21	2 (10.5)	—
Schlearth [40]	10	48	0	0
Total	603		27 (4.5)	15 (2.5)

Table 2. Pregnancy after radical vaginal trachelectomy (modified from [31])

<i>First author [Reference]</i>	<i>Number of patients</i>	<i>Number of pregnancies</i>	<i>Spontaneous abortions 1st/2nd trimester</i>	<i>Therapeutic abortion/extrauterine pregnancy</i>	<i>Number of term pregnancies</i>	<i>Births before 32nd gestation week</i>	<i>Deliveries 33-36 weeks</i>
Hertel [30]	100	18	1	2	No data	No data	No data
Plante [35]	115	82	20	4	47	3	8
Shepherd [36]	112	55	21	3	11	8	12
Sonoda [38]	36	11	3	0	4	0	0
Burnett [39]	19	3	1	0	1	1	0
Schlearth [40]	10	4	2	0	1	1	0
Total	392	173	48	9	64	13	20

tomy in the centres that apply this technique reduces the possibility of relapse, leaving at the same time the possibility to the woman to become pregnant 6-12 months after the operation.

Koliopoulos et al. point out that relapses after radical trachelectomy range between 0 and 8%, which is much the same with relapses after radical hysterectomies [29].

Hysterectomy is not necessary, except in situations with histological confirmation of local disease relapse [5].

Adjuvant therapy after radical trachelectomy is not recommended, provided the aforementioned criteria for the realization of this operation are met.

Special recommendations for the monitoring of these patients include the following [15]:

1. Sexual intercourse is recommended 6 weeks after the operation with adequate contraceptive protection.

2. Control check-ups every 3 months during the first year and every 4 months during the second year with clinical examination and isthmus and vaginal vault smear sampling.

3. After 6-12 months from the operation, a colposcopy may be done.

4. MRI may be done 6 and 12 months after the operation and then after 2 years.

5. If there is no relapse 6 months after the operation, the patient may become pregnant.

6. After 2 years, clinical examination with PAP and vaginal smear are done every 6 months for the next 3 years, and then once a year during the following 5 years if there is no relapse.

Conclusion

Radical trachelectomy seems to be a valid alternative surgical treatment for early-stage cervical carcinoma in patients of reproductive age who want to preserve their fertility.

The recurrence rate is not increased by performing this less aggressive procedure compared with standard radical approach.

Combined with an expected term delivery rate of more than 50% it seems to be the procedure of choice

for women with small early-stage cervical cancers wishing to preserve their fertility.

According to published papers vaginal radical trachelectomy seems to be the most acceptable procedure compared with abdominal radical trachelectomy but requires much longer training.

Due to a lack of long-term follow-up data, patients should be preoperatively informed about the risks of infertility, early-pregnancy spontaneous abortions, preterm delivery, and neonatal complications.

References

- Greenlee RT, Hill-Harmon MB, Murray T, Thun M. Cancer Statistics, 2001. *CA Cancer J Clin* 2001; 50: 7-33.
- Mandic A, Novakovic P, Erak M, Vitorovic S, Zikic D, Nincic D. Stage IB2 cervical carcinoma: brachytherapy followed by radical hysterectomy. *J BUON* 2005; 10: 371-375.
- Kesic V. Management of cervical cancer. *EJSO* 2006; 32: 832-837.
- Medical Practice and Ethics Committee; Management of Gynecologic Cancers. In: Society of Gynecologic Oncologists Clinical Practice Guidelines. Chicago: Society of Gynecologic Oncologists, 1996, pp 34-43.
- Averette HE, Nguyen HN, Donato DM et al. Radical hysterectomy for invasive cervical cancer. A 25-year prospective experience with the Miami technique. *Cancer* 1993; 71: 1422-1437.
- Landoni F, Bocciolone I, Perego P, Maneo A, Bratina G, Mangioni C. Cancer of the cervix, FIGO stages IB and IIA: patterns of local growth and paracervical extension. *Int J Gynecol Cancer* 1995; 5: 329-334.
- Levenback C. Cervical cancer. In: Barakar R, Bevers M, Gershenson D, Hoskins W (Eds): *Handbook of Gynecologic Oncology* (2nd Edn). Martin Dunitz Ltd, The Livery House, 2002, pp 231-249.
- Benedet JL, Hacker NF, Ngan HYS. Staging classifications and clinical practice guidelines of gynaecologic cancers. *Intern J Gynecol Obstet* 2000; 70: 36-54.
- Perez CA, Kurman RJ, Stehman FB, Thigpen JT. Uterine cervix. In: Hoskins WJ, Perez CA, Young RC (Eds): *Principles and Practice of Gynecologic Oncology*. Philadelphia: JB Lippincott, 1992, pp 591-662.
- Covens A, Rosen B, Murphy J et al. Changes in the demographics and perioperative care of stage IA(2)/IB(1) cervical cancer over the past 16 years. *Gynecol Oncol* 2001; 81: 133-137.
- Covens A, Shaw P, Murphy J et al. Is radical trachelectomy a safe alternative to radical hysterectomy for patients with stage IA-B carcinoma of the cervix? *Cancer* 1999; 86: 2273-2279.
- Burghardt E, Holzer E. Diagnosis and treatment of microinvasive carcinoma of the cervix uteri. *Obstet Gynecol* 1977; 49: 641-653.
- Dargent D, Brun JL, Roy M, Mathevet P, Remy I. La trachelectomie elargie (T.E.), une alternative l'hysterectomie radicale dans le traitement des cancers infiltrantes developpes sur la face externe du col uterin. *J Obstet Gynaecol* 1994; 2: 285-292.
- Shepherd JH, Crawford RAF, Oram D. Radical trachelectomy: a way to preserve fertility in the treatment of early cervical cancer. *Br J Obstet Gynaecol* 1998; 105: 912-916.
- Shepherd JH. Uterus-conserving surgery for invasive cervical cancer. *Best Pract Res Clin Obstet Gynaecol* 2005; 19: 577-590.
- Aburel E. Colpohysterectomy largita subfundica. In: Sirbu P (Ed): *Chirurgica Gynecologica*. Bucharest, Romania: Editura Medicala Publ, 1981, pp 714-721 (in Romanian).
- Rodriguez M, Guimares O, Rose PG. Radical abdominal trachelectomy and pelvic lymphadenectomy with uterine conservation and subsequent pregnancy in the treatment of early invasive cervical cancer. *Am J Obstet Gynecol* 2001; 185: 370-374.
- Cibula D, Slama J, Fischerova D. Update on abdominal radical trachelectomy. *Gynecol Oncol* 2008; 111 (Suppl 1): 111-115.
- Ungar L, Palfalvi L, Hogg R et al. Abdominal radical trachelectomy: a fertility-preserving option for women with early cervical cancer. *BJOG* 2005; 112: 366-369.
- Dargent D, Franzosi F, Ansquer Y, Martin X, Mathevet P, Adeline P. Extended trachelectomy relapse: plea for patient involvement in the medical decision. *Bull Cancer* 2002; 89: 1027-1030.
- Burnett AF, Roman LD, O'Meara AT, Morrow CP. Radical vaginal trachelectomy and pelvic lymphadenectomy for preservation of fertility in early cervical carcinoma. *Gynecol Oncol* 2003; 88: 419-423.
- Beiner ME, Covens A. Surgery insight: radical vaginal trachelectomy as a method of fertility preservation for cervical cancer. *Nat Clin Pract Oncol* 2007; 4: 353-361.
- Dargent D, Martin X, Sacchetoni A, Mathevet P. Laparoscopic vaginal radical trachelectomy: a treatment to preserve the fertility of cervical carcinoma patients. *Cancer* 2000; 88: 1877-1882.
- Dargent D. Radical trachelectomy: an operation that preserves the fertility of young women with invasive cervical cancer. *Bull Acad Natl Med* 2001; 185: 1295-1304; (Discussion 1305-6).
- Roy M, Plante M. Radical vaginal trachelectomy for invasive cervical cancer. *J Gynecol Obstet Biol Reprod (Paris)* 2000; 29: 279-281.
- Roy M, Plante M. Pregnancies following vaginal radical trachelectomy for early stage cervical cancer. *Am J Obstet Gynecol* 1998; 179: 1491-1496.
- Dargent D. Using radical trachelectomy to preserve fertility in early invasive cervical cancer. *Contemp Obstet Gynecol* 2000; 23-49.
- Dursun P, LeBlanc E, Nogueira MC. Radical vaginal trachelectomy (Dargent's operation): a critical review of the literature. *Eur J Surg Oncol* 2007; 33: 933-941.
- Koliopoulos G, Sotiriadis A, Kyrgiou M, Martin-Hirsch P, Makruidimas G, Paraskevaidis BE. Conservative surgical methods for FIGO stage IA2 squamous cervical carcinoma and their role in preserving women's fertility. *Gynecol Oncol* 2004; 93: 469-473.
- Hertel H, Köhler C, Grund D et al. Radical vaginal trachelectomy combined with laparoscopic pelvic lymphadenectomy: Prospective multicenter study of 100 patients with early cervical cancer. *Gynecol Oncol* 2006; 103: 506-511.
- Plante M. Vaginal radical trachelectomy: An update. *Gynecol Oncol* 2008; 111: S105-S110.
- Plante M, Renaud MC, Hoskins IA, Roy M. Vaginal radical trachelectomy: A valuable fertility-preserving in the manage-

- ment of early-stage cervical cancer. A series of 50 pregnancies and review of the literature. *Gynecol Oncol* 2005; 98: 3-10.
33. Boss EA, Golde T, Beerendonk M, Massuger G. Pregnancy after radical trachelectomy: a real option? *Gynecol Oncol* 2005; 99: S152-S156.
 34. Marchiole P, Benchaib M, Buenerd A, Lazlo E, Dargent D, Mathevet P. Oncological safety of laparoscopic-assisted vaginal radical trachelectomy (LARVT or Dargent's operation): a comparative study with laparoscopic assisted vaginal radical hysterectomy (LARVH). *Gynecol Oncol* 2007; 106: 132-141.
 35. Plante M, Renaud MC, Gregoire J, Roy M. Outcome of 87 pregnancies following radical trachelectomy for the treatment of early-stage cervical cancer. *Gynecol Oncol* 2008 (abstr #208).
 36. Shepherd JH, Spencer C, Herod J, Ind TE. Radical vaginal trachelectomy as a fertility-sparing procedure in women with early-stage cervical cancer; cumulative pregnancy rate in a series of 123 women. *BJOG* 2006; 113: 719-724.
 37. Covens A. Preserving fertility in early cervical cancer with radical trachelectomy. *Contemp Obstet Gynecol* 2003; 2: 48.
 38. Sonoda Y, Chi DS, Carter J, Barakat RR, Abu-Rustum NR. Initial experience with Dargent's operation: the radical vaginal trachelectomy. *Gynecol Oncol* 2008; 108: 214-219.
 39. Burnett AF. Radical trachelectomy with laparoscopic lymphadenectomy: review of oncologic and obstetrical outcomes. *Curr Opin Obstet Gynecol* 2006; 18: 8-13.
 40. Schlearth JB, Spirtos NM, Schlearth AC. Radical trachelectomy and pelvic lymphadenectomy with uterine preservation in the treatment of cervical cancer. *Am J Obstet Gynecol* 2003; 188: 29-34.