

Why Radical Trachelectomy and not Radical Hysterectomy for the treatment of early stage cervical cancer?

Nikolaos Thomakos¹, Sofia-Paraskevi Trachana¹, Michalis Liontos², Aristotelis Bamias², Alexandros Rodolakis¹

- ¹ First Department of Obstetrics and Gynecology, Division of Gynecological Oncology.

 National and Kapodistrian University of Athens, Alexandra General Hospital, Athens, Greece
- ² Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Alexandra General Hospital, Athens, Greece

Correspondence

Dr. Nikolaos Thomakos, MD, Ph.D, Consultant in Obstetrics and Gynecology. "Alexandra General Hospital", First Department of Obstetrics and Gynecology, 80 Vas. Sofias Av. 11528, Athens, Greece **E - mail:** thomakir@hotmail.com

Abstract

Cervical cancer is one of the most popular and lethal gynecological cancers worldwide. The standard treatment for early stage cervical cancer is radical hysterectomy combined with bilateral pelvic lymph node assessment. The infertility and the serious complications follow the radical hysterectomy, has lead gynecologic-oncologists to revise radical surgical approaches, in order to preserve fertility without increasing the risk of recurrence and mor-

tality. The safety and feasibility of less radical surgery, such as radical trachelectomy, has been clearly demonstrated while the oncologic outcomes support that radical trachelectomy is suitable for low risk early stage cervical cancer patients wishing to preserve fertility.

Key Words: trachelectomy; cervical; cancer; fertility; preservation

Introduction

Cervical cancer holds the second place among the most common gynecological cancers worldwide and the first place of death among gynecological malignancies¹. More than 500,000 new cases of invasive cervical cancer are estimated to be diagnosed worldwide every year². Although the average patient age of cervical cancer diagnosis, is 50 years³, it affects women of all ages, including those in their childbearing years. With the use of cervical carcinoma screening, a noticeable shift from more advanced to earlier stage disease diagnosis have been mentioned, with sub-

sequent many women to be diagnosed at a relatively young age and at an early stage⁴. The International Federation of Gynecology and Obstetrics (FIGO), defines early stage cervical cancer as FIGO stage IA to IB1. It is estimated that a percentage of 25-30% of all cases are diagnosed in women younger than 40 years. Because of the postponement of childbearing to older age, women <45 years old who are diagnosed with cervical carcinoma have a strong demand for fertility - preserving surgery.

In 1900, Wertheim was first reported the use of abdominal hysterectomy as treatment of early cer-

vical cancer⁵. Nowadays, radical hysterectomy combined with bilateral pelvic lympadenectomy or pelvic radiotherapy are the traditionally recommended treatments for patients with early-stage cervical cancer. However, this strategy does not preserve fertility. The innovative approach of radical trachelectomy was made popular by Dargent in 1994^{6,7}. Dargent's procedure involved resection of the cervix, the upper part of the vagina, and the proximal part of the parametria via a vaginal approach, combined with laparoscipic pelvic lyphadenectomy, whilst preserving the uterine corpus. Subsequently, abdominal radical trachelectomy (ART) was described, as many surgeons were more familiar to this procedure due to its similarities with radical abdominal hysterectomy8. Since this procedure was conceived by Dargent, conservative surgery has become a real breakthrough for patients who desire fertility preservation^{6, 9}. Furthermore, considering that cervical cancer rarely spreads superiorly to the uterus, ART is now described as the proposed surgical procedure for early-stage cervical cancer. In recent years, two other methods, the laparoscopic and robotic assisted radical trachelectomy were developed. Each procedure has advantages and disadvantages based on the different abilities of the surgeon performing the procedure and the available technical equipment. Up to now, several authors have reported on safety and efficacy of these two procedures, demonstrating both the obstetrical and the oncological outcomes 10-13.

When Radical Trachelectomy could be performed

Traditionally, the standard surgical management for early stage cervical carcinoma remains the radical abdominal hysterectomy and pelvic, with or without para-aortic lymph node dissection. The oncological safety of this procedure is well studied and generally accepted¹⁴. However, radical hysterectomy is obviously eliminating the possibility of future conception¹⁵. For this reason the management of early-stage cervical carcinoma in young women who desire future fertility remains a challenge to gynecological oncologists.

Radical trachelectomy, is a fertility-sparing procedure that has recently gained worldwide acceptance and is increasingly being offered as an alternative choice in young women. Nevertheless, it is almost universally accepted that radical trachelectomy should be offered only in well-selected patients due to its doubtful results in large tumors. The best oncological results are seemed in patients with excellent prognostic factors. The selection criteria include firstly and most importantly, the age of the woman and the strong desire for fertility preservation. Women in reproductive age who do not wish to preserve their fertility may be excluded. Tumor size and thus disease stage, is the second main criterion when fertility-sparing surgery is considered, due to the high risk of recurrence. Lesions larger than 2 cm in size, involves a higher risk of recurrence: 12.5% versus 1.2% for lesions <2 cm¹⁶. For this reason radical trachelectomy has been advised not to be performed in patients with tumors ≥ 2 cm in size.

The histological type of the cancer should also be taken into account. Squamous cell, adenocarcinoma, and adenosquamous carcinoma are acceptable for radical trachelectomy, while small-cell neuroendocrine carcinoma is not suitable, even if the tumor size is small, because it has the worst prognosis due to its association with lymph node metastasis, local/distant relapse and need for postoperative chemotherapy.

Depth of stromal invasion and lymphovascular space involvement (LVSI), are also important criteria for fertility-preservasion surgery. These factors are prognostic for recurrence in early-stage disease¹⁷ and thus radical hysterectomy should be offered to these patients. Finally the lymph-node status assessment is necessary for performing fertility-sparing surgery. Evidence of pelvic lymph node metastasis or other distant metastasis is contraindication for radical trachelectomy.

To assess the exact characteristics of the tumor, preoperative examinations are essential. Colposcopy is the first basic procedure before the surgery, because is very helpful in assessing the diameter of exocervical tumor and the degree of spreading in the

vagina¹⁸⁻²⁰. MRI (magnetic resonance imaging), is the best imaging technique in this context as it provide accurately the tumor size, the depth of stromal invasion (determination of tumor growth in anterioposterior, craniocaudal, and transverse directions), and the distance between the superior part of the tumor and the internal os ²¹ and can help to identify preoperatively high-risk patients who require radical hysterectomy²².

Why radical trachelectomy and not radical hysterectomy

Radical surgery deprives patients of potential future reproductive capacity. Many young patients with cervical carcinoma wish to preserve their fertility. In recent years, RT has been used with increasing frequency in the treatment of early stage cervical cancer to preserve patient reproductive function. For these patients radical hysterectomy is not the appropriate procedure due to the removal of the uterus and adnexa. Radical trachelectomy, should be offered in well-selected patients who wish to preserve their fertility and fulfill the above mentioned selection criteria. The informed consent of the patient must contain information about the relative risk of recurrence, which is not increased by fertility preserving surgery per se, but may influence the decision of the patient to choose standard surgery. According to some authors, it should be emphasized to the patient that the only well established treatment for early stage cervical cancer, remains radical-hysterectomy^{23, 24}. Also no guarantee for future pregnancy should be given to the patient after RT, and it must be clear that a possible pregnancy will be considered as a high-risk pregnancy due to the risk of miscarriage.

In the terms of oncological safety and the risk of recurrence, the studies have shown no difference between radical hysterectomy and radical trachelectomy in well-selected patients. Several studies suggest that the main objective of RT in early cervical cancer is not only to maintain reproductive fertility but also to achieve a satisfactory recurrence-free survival rate. Since 1994, when fertility preservation through RT was first described, many authors have

suggested the safety of RT, and nowadays more than 1,000 cases (vaginal and abdominal approach) have reported, establishing the oncological outcomes of this procedure²⁵⁻²⁷. It is worth to mention, that the oncological outcome after RT depends on the characteristics of the tumor. Recurrence, is significantly higher in tumors >2 cm (25%-30%), with positive LVSI and stromal invasion >1 cm³. Recent studies²⁵⁻²⁹ have demonstrated that there is no significant difference in five year survival, overall survival and progression free survival rate between RT and RH.

As far as the complications of the two approaches, it seems that RT is superior to RH. It is important to evaluate postoperative aspects as well as quality of life issues after surgery for malignant cervical tumors. Radical hysterectomy is a traditionally used technique for cervical cancer and thus surgeons are familiar with this. Nowadays, with the improvement in skills and an improved familiarity with RT procedure, the incidences of intraoperative complications tend to be eliminated. Blood loss and transfusion rates, nerve or vascular injury, bladder and bowel dysfunction, time to normal urination, fistula formation, lymphedema, sexual dysfunction, stress, depression, and postoperative hospitalization are significantly shorter in the RT compared with RH ^{30,31}.

Finally, in the terms of obstetrical outcomes, there are encouraging data in literature. The development of fertility-sparing surgery has provided patients with early stage cervical carcinoma with the opportunity to pursue conception after the treatment of the disease. The cervical factor is the main cause of infertility after trachelectomy and for this reason some authors support cerclage after trachelectomy³². Individual studies of pregnancy outcomes after RT revealed that the postoperative pregnancy rate was above 70% in women who did attempt to conceive³³.

During the past decade, some investigators have reported the importance of parametrectomy in radical trachelectomy as a prognostic factor for recurrence. Extending the resection of the parametrial tissue in radical hysterectomies and trachelectomies, has been discussed intensively during the past years.

According to authors, parametrial removal in early cervical cancer remains important for several reasons such as to eliminate parametrial spread and indicate further therapy, to prevent local recurrence, and secondary to obtain a clear margin on the cervical primary 34,35 . For patients with tumor size <2 cm, negative pelvic lymph nodes and deph of invasion <10 mm, the risk of parametrial involvement is about $0.6\%^{36}$. In these patients parametrial invasion is also rare (<0.4%) 37 . For the above reason radical procedures (RH, RT) in patients with tumor size <2 cm are considered as overtreatment and less radical surgery such as cone biopsy or simple hysterectomy combined with pelvic lymphadenectomy, consist safe approach 38 .

Conclusion

Due to its radicality, hysterectomy seems to be inappropriate for women with early stage cervical cancer who wish to preserve their fertility. The increased demand for a less radical procedure was satisfied with Radical Trachelectomy. Nowadays, RT is considered as the alternative choice of fertility-sparing surgery, providing the same oncological safety as radical hysterectomy. Careful selection of ideal candidates remains the hallmark of the success.

Conflict of interest

We declare that we have no conflict of interest.

References

- Arbyn M, Autier P, Ferlay J. Burden of cervical cancer in the 27 member states of the European Union: estimates for 2004. Ann Oncol. 2007;18:1423-1425.
- Cubal A, Carvalho J, Costa M, Branco AP. Fertility sparing surgery for early stage cervical cancer – Review Article. Int J of Surgical Oncology. 2012; Article ID 936534.
- Schneider A, Erdemoglu E, Chiantera V, et al. Clinical Recommendation Radical Trachelectomy for fertility preservation in patients with early stage cervical cancer. Int J Gynecol Cancer, 2012; 22:659-666.
- 4. Diaz JP, Sonoda Y, Leitao MM, et al. Oncologic outcome of fertility-sparing radical trachelectomy ver-

- sus radical hysterectomy for stage IB1 cervical carcinoma. *Gynecol Oncol.* 2008 Nov;111(2):255-60.
- 5. Wertheim E. The extended abdominal operations for carcinoma uteri (based on 5000 operative cases). *Am J Obstet Gynecol*, 1921; 66:169.
- 6. Dargent D, Brun JL, Remy I et al. Pregnancies following radical trachelectomy for invasive cervical cancer. *Gynecol Oncol*, 1994; 52(1):105.
- Dargent D, Martin X, Sacchetomi A, et al. Laparoscopic vaginal radical trachelectomy: a treatment to preserve the fertility of cervical carcinoma patients. Cancer, 2000: 88:1877-82.
- Smith JR, Boyle DC, Crless DJ, Ungar L, Lawson AD, Del Priore G, et al. Abdominal radical trachelectomy: a new surgical technique for the conservative management of cervical carcinoma. *Br J Obstet Gynecol*, 1997;104:1196-200.
- 9. Pahisa J, Alonso I, Torne A. Vaginal approaches to fertility sparing surgery in invasive cervical cancer. *Gynecol Oncol*, 2008;110(3Suppl 2):S29-32.
- Burnett AF, Roman LD, O'Meara AT, Morrow CP. Radical vaginal trachelectomy and pelvic lymphadenectomyfor preservation of fertility in early cervical carcinoma. *Gynecol Oncol*, 2003;88:419-23.
- 11. Schlaerth JB, Spirtos NM, Schlaerth AC. Radical trachelectomy and pelvic lymphadenectomy with uterine preservation in the treatment of cervical cancer. *Am J Obstet Gynecol*, 2003;188:29-34.
- 12. Covens A. Preserving fertility in early cervical Ca with radical trachelectomy. *Contemp Ob/Gyn*, 2003;2:46-66.
- Sonoda Y, Chi DS, Carter J, Barakat RR, Abu-Rustum NR. Initial experience with Dargent's operation: the radical vaginal trachelectomy. *Gynecol Oncol*, 2008;108:214-9.
- Thomakos N. Trachana SP, Davidovic-Grigoraki M, Rodolakis A. Less radical surgery for early stage cervical cancer. To what extent do we justify for? our belief. Taiwan J Obstet Gynecol. 2016 Aug;55(4):495-8.
- Thomakos N, Trachana SP, Rodolakis A, et al. Less Radical Surgery for Fertility Preservation in Patients with Early-Stage Invasive Cervical Cancer Contemporary Problematics. Gynecol Obstet 2013; 3:4.
- 16. Beiner ME, Covens A. Surgery insight: Radical vaginal

- trachelectomy as a method of fertility preservation for cervcal cancer. *Nat Clin Pract Oncol*, 2007;4(6):353-61.
- 17. Delgado G, Bundy B, Zaino R, et al. Prospective surgical-pathological study of disease-free interval in patients with stage IB squamous cell carcinoma of the cervix: A Gynecologic Oncology Group study. *Gynecol Oncol*, 1990;38:352-57.
- 18. Plante M. Vaginal radical trachelectomy: An update. *Gynecol. Oncol.* 2008; 111:105-110.
- 19. Roy M, Plante M. Pregnancies after radical vaginal trachelectomy for early stage cervical cancer. *Am J Obstet. Gynecol.* 1998; 179:1491-96.
- Rob L, Charvat M, Robova H, et al. Less radical fertility sparing surgery than radical trachelectomy in early cervical cancer. *Int. J. Gynecol Cancer*, 2007; 17:304-10
- 21. Lakhman Y, Akin O, Park KJ, et al. Stage IB1 cervical cancer, role of preoperative MR imaging in selection of patients for fertility-sparing radical trachelectomy. *Radiology*, 2013;269:149-58.
- 22. Bourgioti C, Koutoulidis V, Chatoupis K, et al. MRI findings before and after abdominal radical trachelectomy (ART) for cervical cancer: A prospective study and review of the literature. *Clin Radiol*. 2014 Jul;69(7):678-86.
- 23. Shepherd JH, Milliken DA. Conservative surgery for carcinoma of the cervix. *Clin Oncol*, 2008; 20:395-400.
- 24. Sepherd JH, Spencer C, Herod J, et al. Radical vaginal trachelectomy as a fertility sparing procedure in women with early stage cervical cancer-cumulative pregnancy rate in a series of 123 women. *Int J of Obstet and Gynecol*, 2006; 113:719-724.
- Beiner ME, Hauspy J, Rosen B, et al. Radical vaginal trachelectomy vs. radical hysterectomy for small early stage cervical cancer: a matched case-control study. *Gynecol Oncol*, 2008;110(2): 168-71.
- Alexander-Sefre F, Chee N, Spencer C, et al. Surgical morbidity associated with radical trachelectomy and radical hysterectomy. *Gynecol Oncol*, 2006; 101(3):450-4.
- 27. Covens A, Shaw P, Murhy 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(11):2273-9.
- 28. Schneider A, Erdemoglu E, Chiantera V, et al. Clinical

- Recommendation Radical Trachelectomy for fertility preservation in patients with early stage cervical cancer. *Int J Gynecol Cancer*, 2012; 22:659-666.
- Marchiole P, Benchaib M, Buenerd A, et al. 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(1):132-41.
- Li X, Fu-Qing S, Zan-Hong W. Radical trachelectomy versus radical hysterectomy for the treatment of early cervical cancer: A systematic review. AOGS, 2011; 90:1200-1209.
- Reade C, Eiriksson L, Covens A. Surgery for early stage cervical cancer: How radical should it be? *Gynecol On*col. 2013;131:222-230.
- 32. Li J, Li Z, Wang H, et al. Radical abdominal trachelectomy for cervical malignancies: Surgical, oncological and fertility outcomes in 62 patients. *Gynecol Oncol*, 2011; 121:565-570.
- 33. Plante M, Renaud MC, Hoskins IA, et al. Radical trachelectomy: a valuable fertility-preserving option in the management of early-stage cervical cancer. A series of 50 pregnancies and review of the literature. *Gynecol Oncol*, 2005; 98(1): 3-10.
- Einstein MH, Park KJ, Sonoda Y, et al. Radical vaginal versus abdominal trachelectomy for stage IB1 cervical cancer: a comparison of surgical and pathologic outcomes. *Gynecol Oncol*, 2009; 112:73-77.
- 35. Covens A, Rosen B, Murphy J, et al. How important is removal of the parametrium at surgery for carcinoma of the cervix? *Gynecol Oncol*, 2002; 84:145-149.
- Stegeman M, Louwen M, van der Velden J, et al. The incidence of parametrial tumor involvement in select patients with early cervix cancer is too low to justify parametrectomy. *Gynecol Oncol*, 2007;105(2):475-80
- Wright JD, Grigsby PW, Brooks R, et al. Utility of parametrectomy for early stage cervical cancer treated with radical hysterectomy. Cancer, 2007;110:1281-6.
- 38. Gemer O, Eitan R, Gdalevich M, et al. Can parametrectomy be avoided in early cervical cancer? An algorithm for the identification of patients at low risk for parametrial involvement. Eur J Surg Oncol, 2013;39(1):76-80.