

MINI-REVIEW

Conservative Treatment in Young Patients with Cervical Cancer: A Review

Mojgan Karimi Zarchi^{1*}, Asamsadat Mousavi², Mona Malekzadeh³, Atefeh Dehghani⁴, Zahra Behnamfar⁴, Arash Godarzi⁴

Abstract

For cervical cancer cases with a low risk of relapse who wish to maintain their fertility, radical trachelectomy is an alternative to radical hysterectomy. Pelvic magnetic resonance imaging is recommended before surgery, with laparoscopic assisted lymphatic dissection required for assessment of lymphatic metastasis. If there is a visible lesion in the cervix, the specimen taken during trachelectomy should be sent for frozen section. The complications of radical trachelectomy are chronic vaginal discharge, irregular vaginal bleeding, dysmenorrhea, ulceration, amenorrhea and cervical stenosis. The probability of cervical cancer recurrence with a lesion of similar size is comparable with radical trachelectomy and radical hysterectomy. Two thirds of pregnancies after trachelectomy lead to live births of which approximately 40% of them are healthy. However, the probability of second trimester abortion and pre-term labor is greater than in the general population. Because of the possibility of uterine arterial injury in short cervix, vaginal delivery should be avoided and a cesarean operation in 37-38th week is recommended. Adjuvant treatment with chemotherapy followed by radical trachelectomy is a suitable option for larger lesions. On the other hand, conization or simple trachelectomy are more proper approaches for very small lesions.

Asian Pacific J Cancer Prev, **11**, 589-594

Introduction

Fertility preservation in women's cancer management is an important point has been discussed recently. Most young women receiving cancer treatment are willing to marriage, so need to preserve their fertility. Considering emotional and sexual problems following therapy of the malignancies is caused to consider this issue (Lee et al., 2006; Carter et al., 2005). Cervical cancer is the most common gynecological cancer following breast cancer in almost always developing countries such as Iran (Ghaemmaghami et al., 2008; Behtash et al., 2009; Karimi Zarchi et al., 2009).

Therefore applying a proper treatment in young women has a significant positive effect on quality of their life and decreases the psychological anxieties (Corney et al., 1993; Mousavi et al., 2008). Radical hysterectomy with pelvic and para-aortic lymphadenectomy is a right technique in cervical cancer management. However, 42% of these patients are younger than 45 years old, so radical trachelectomy can be a suitable option in early stages (IA2, IB1) of these malignancies. Current literature evaluates the prognosis of pregnancy in patients receiving the above surgeries (Dargent et al., 1995).

The objective of this study was to review related

documents to find an ideal approach in Iranian population; a technique with the least side effect on psychosocial coition, but effective on survival.

Radical Vaginal Trachelectomy

Radical trachelectomy is removing cervix, cardinal and uterosacral ligaments (parametria), separating the urethra from round ligaments and cutting the uterus arteries in their origins from internal iliac ligaments followed by Grafting uterus body to vagina. This technique is done through abdomen or vagina. The pioneer of vaginal trachelectomy was Daniel Dargent introduced it in 1980 in France (Plante et al., 2003).

Who are candidates for radical vaginal trachelectomy?

- 1) Patients wish to preserve their fertility.
- 2) Patients younger than 45 years old.
- 3) Clinical stage of disease is an important factor. Patients with stage IA1 with lymphovascular invasion or IA2 and IB1 without lymphovascular invasion are good candidates. (The noticeable point is that in patients with tumor in stage IA1 with no lymphovascular invasion, conization is indicated)
- 4) Cervical lesion less than 2 or 2.5cm on colposcopy

¹Gynecology Oncology Department, Shahid Sadoughi University of Medical Science, ²Gynecologist Oncologist, Tehran University of Medical Sciences, Tehran, Iran, ³Shahid Beheshti University of Medical Science, ⁴Shahid Sadoughi University of Medical Science.
* For correspondence : drkarimi2001@yahoo.com

or MRI.

5) Squamous cell carcinoma or adenocarcinoma forms of the tumor.

6) No diffuse or extensive lymphovascular invasion.

7) No evidence of lymphatic system involvement.

8) Not high risk histopathologic types of the tumor (for example endocrine type) (Dargent et al., 1995; Roy and Plante et al., 1998; Sonoda et al., 2004; Bisseling et al., 2007)

Considering these criteria, about 40% of patients who undergo radical hysterectomy, could be benefit from radical vaginal trachelectomy. On the other hand; the probability of making a mistake in patients' selection for RVT is about 10-12%. In this group, due to extensive endocervix, margin or lymphatic involvement, it is possible that patients lead to definitive radical hysterectomy or adjuvant treatment (radiotherapy) (Marchiole et al., 2007). Up to now, more than 400 reports of vaginal trachelectomy have been published in retrospective studies. Plante et al (2004) reported oncologic outcomes of 72 vaginal trachelectomy of stages IIA, IA2 or IB1 during 1991 to 2006. 5-year survival rate of the patients was 95% and tumor size > 2 cm was associated with higher recurrent rate.

Pre operation assessment

In patients presented with a pelvic mass, pelvic MRI can be so helpful. (Sahdev et al., 2007). Accurate assessment of size and location of the mass, severity of endocervical involvement, cervical canal length and distance between superior edge of the mass to isthmus are important points showed on MIR (Peppercorn et al., 1999). This latter point is very important. If the distance is less than 1cm, RVT will be possible following neoadjuvant chemotherapy.

Technique of radical vaginal trachelectomy (RVT):

Pelvic and Para-aortic lymph nodes are removed laparoscopically to rule out lymphatic system involvement as it is a contraindication for fertility sparing surgery (Hauspy et al., 2007).

There are 6 phases for trachelectomy method (Plante et al., 2003)

1. Preparedness phase: at first vaginal mucosa should be opened in 1 to 2cm of cuff and around the cervix and superior and posterior rim of vaginal mucosa be elevated.

2. Anterior phase: due to dissection of cervix without any injury to bladder, vesicovaginal space in anterior of cervix and also paravesical spaces in both lateral sides should be determine to find the bladder pillars and ureters.

3. Posterior phase: posterior Cole-de- sac should be opened to determine the pararectal space to be able to clamp and cut sacral part and the ligament.

4. Lateral phase: Assessing the ureters, the proximal part of parametria in the level of isthmus is removed. The important point in this phase is exploring main uterus artery that supplies the uterus circulation during pregnancy. For better assessment, ureter stent can be used, but the use of it is limited due to renal failure followed by ureter's edema.

5. Cervix removing phase: approximately 1cm of

isthmus is removed followed by endocervical curettage.

6. The last phase is posterior Cole-de-sac suturing (purse sutures) and carrying out cerclage to close the cervix which leads to proper graft between vaginal mucosa and new endocervix by separated sutures. There isn't any common consensus about the best method of cerclage. Preferably; a polypropylene (number zero) is used (Plante et al., 2004; Abu-Rustum et al., 2006) because of the good stretchy power of polypropylene and its low probability of infection. However; it is noticeable that deep sutures shouldn't be used because it will hurt cervical stroma in endocervical canal. Some surgeons prefer Mersilene sutures (Bernardini et al., 2003), but this kind of string has more infection risk and its stretch isn't proper. It should be noted that Dargent (Saling et al., 1981) used Saling suturing to block cervix completely. (Dargent et al., 2000)

Is there any role for frozen section in RVT procedure?

If a visible lesion is discovered in physical examination, it is better to send a specimen from exocervix to endocervix for longitudinal frozen section (Jolley et al., 2007) to be able to assess the distance of it to endocervical edge which illustrated the margin of the lesion. Observing 8-10mm of normal tissue means that the margin is intact, otherwise, marginal involvement (tumor penetration to endocervical canal) leads to radical hysterectomy.

Complications and morbidity rate of vaginal trachelectomy is less than radical hysterectomy. Peri and post operative complication of this technique is comparable to laparoscopic-assisted vaginal radical hysterectomy (Marchiole et al., 2007). Vaginal narrowing (Tanguay et al., 2004; Plante et al., 2005) is occurred in 10-15% of patients who have undergone RVT operation. This complication is often asymptomatic but sometimes leads to dysmenorrhea, hematuria, hematosalpinx and endometriosis (Sonoda et al., 2008). Cervical stenosis causes more problems if the patient needs assisted fertilization in future (Selo-Ojeme et al., 2002).

Patient's oncologic outcome

Up to now, about 550 cervical cancer cases that underwent RVT have been studied in scientific articles. The probability of recurrence and mortality is less than 5% and 2-3 percent, respectively (Beiner et al., 2007). These results are similar and comparable with radical hysterectomy (Marchiole et al., 2007). The site of about 40% of recurrences is in parametria, pelvic wall, Para-aortic and supra clavicular areas.

Recently, lymph node mapping method (sentinel lymph node) is introduced as an effective procedure for finding the micro metastasis and the style of lymphatic drainage (Lee et al., 2006). It brings about decreasing lymph nodes dissection. In 5 of 550 cases who have experienced RVT, central pelvic recurrence due to multicentric lesions has been reported (Aust et al., 2007). Pathologic type in 4 of them was adenocarcinoma.

What are risk factors for recurrence?

1) Size: Lesions more than 2cm (Klemm et al., 2005; Beiner et al., 2007; Marchiole et al., 2007) are at significant risk for recurrence. The recurrence probability of lesions

more than 2cm is 29% in compare with 1.6% (Marchiole et al., 2007) for lesions less than 2cm. Patients with a mass equal or larger than 2cm aren't proper candidates for RVT unless in a condition that the lesion is completely exophytic with little stromal invasion (Aust et al., 2005).

2) Lymphovascular invasion: It results in increasing recurrent (12% vs. 2%) (Beiner et al., 2007), especially if there is an extensive lymphovascular invasion. Some consider this point as an exclusion criterion for RVT (Hertel et al., 2006).

3) Pathologic type: non squamous cell tumors are associated with higher recurrence, that hasn't been confirmed yet. Neuroendocrine tumors are related with faster invasion and higher probability of recurrence, even with intact margin and no lymph node involvement (Beiner et al., 2007; Marchiole et al., 2007).

When adjuvant therapy following RVT is indicated?

High risk patients for recurrence should receive adjuvant therapy. Risk factors of recurrence are lymph node involvement, positive margin or higher parts involvement. These patients include approximately 10 percent of cases undergo RVT (Beiner et al., 2007).

Even close margin cases (i.e. less than 5mm distance between tumor and rim of the specimen) are proper candidates for adjuvant therapy (Jolley et al., 2007). Adjuvant treatment could be radiotherapy or chemotherapy. In chemotherapy the probability of ovarian failure is less and it's suitable for fertility preservation.

Follow up after RVT

There isn't any proper guideline to follow up these patients. But it colposcopy examination, pap smear with or without endocervical curettage every 3 to 4 months in first 3 years after treatment, every 6 months for next 2 years and then annually is suggested (Mousavi et al., 2008; Ghaemmaghami et al., 2008; Karimi Zarchi et al., 2009). Although, some researchers suggest pelvic MRI in 6, 12 and 24 months after surgery (Burnett et al., 2006) but MRI commentary should be done by an experienced radiologist who could differ between post operation changes and recurrence (Covens et al., 2003). Pap smear after RVT usually shows abnormal results that should be assessed by a proper colposcopy (Shepherd et al., 2006). Due to abnormal endometrial cells, the probability of false positive after RVT is 2% which can be neglected by applying a valuable test such as Pap smear in early detection of recurrence (Marchiolé et al., 2005).

Is hysterectomy necessary after pregnancy?

After termination of pregnancy, hysterectomy can be suggested, but there isn't any large study to answer this question accurately. Even cesarean-hysterectomy isn't suggested, except in limited cases (Plante et al., 2004; Shepherd et al., 2006).

Pregnancy after RVT

It is better to evaluate the patient for fertility before the surgery. After ruling out the infertility problem, the case would be candidate for this operation. Researchers show that RVT doesn't have any side effects on fertility. Even

there is a report of a successful child bearing with using of IVF by a gifted ovule (Plante et al., 2004).

Fertility outcome after VRT

200 cases of pregnancy after VRT have been reported that 66% of them lead to neonate's birth. Entirely 42% has resulted in healthy alive neonates while premature neonate birth before 37th week happened in 27% of the cases. Abortion rate in first trimester hasn't been so different with general population (16-20%) and cerclage hasn't been significantly effective to decrease the abortion rates (Saling et al., 1981; Dargent et al., 2000; ; Tanguay et al., 2004; Plante et al., 2005; Jolley et al., 2007). With the purpose of treatment of neglected abortion, misoprostol, D&C or laminaria could be useful (Singh et al., 2004).

Second trimester abortions after RVT are more than general population (9.5% vs 4%) (Saling et al., 1981). It seems that amnionitis is the reason of starting inflammation, releasing cytokines and preterm rupture of amniotic sac. Even in these cases there's no need to remove cerclage and it is possible to do dilatation and curettage (D&C) after proper dilatation of cervix. It is also possible to remove cerclage and then using misoprostol and remove the pregnancy products.

Preterm delivery is more prevalent than general population. That may be due to the pressure of the enlarged uterus on the short ended cervix and finally preterm dilatation of it. But if at least 1cm of endocervix could be preserved in RVT surgery, the probability of preterm delivery will be significantly decreased. (Carter et al., 2007)

When is the proper time for pregnancy?

Patients with at least 6 to 12 months disease free following RVT can become pregnant. (Dargent et al., 2000) There are some important points should be considered; if these are signs and symptoms of preterm delivery, some procedures are needed as routine screening for genitourinary infection, prophylactic antibiotic therapy, bed rest or decreasing the physical activities, routine prescription of steroids for fetus lung maturation. (Carter et al., 2007) This patients should be informed about possible complications during pregnancy which are more prevalent after RVT. On the other hand; the patients should be supervised by an experienced perinatologist (Kay et al., 2006) Physical activity limitation is recommended in shortened cervical canal. If it's approved in periodic sonography, steroids injection is indicated. (Lavie et al., 2006) Prophylactic antibiotics are only recommended in patients with amniotic sac rupture. In patients with preterm or gestational age 32-34 weeks or more, delivery induction can be done, otherwise; cerclage preservation is better than termination of pregnancy.

Delivery method: vaginal delivery is not recommended because of short cervix and likelihood of uterus artery rupture and massive hemorrhage. Cesarean section in 37th to 38th week of gestational age is preferred. Preferred incision is transverse inferior segment or inferior vertical which not result in uterus artery damage and bleeding (Kobayashi et al., 2006; Hauspy et al., 2007).

Abdominal radical trachelectomy: this method is

similar to abdominal radical hysterectomy which was explained by Smith et al in 1977 (see Plante et al., 2006). Radical abdominal trachelectomy with uterus body preservation was explained by Aburel et al in 1950 (see Aburel, 1981). After a midline incision, bilateral pelvic lymphadenectomy would be done followed by opening of paravesical and pararectal spaces.

Bilateral round ligaments are elevated to explore uterus artery and cutting it in its origin. Infundibulopelvic and paraovarian vessels should be preserved because they are the most important blood source of uterus. Taking the uterus artery, parametrium and Para colpos are separated similar to radical hysterectomy type III. For this procedure it is necessary to dissect the urethras among parametrium tunnel. Also, posterior wall of Cole-de sac should be opened and uretrosacral ligament be taken. Before taking the specimen, the circumference of the vagina should be cut, following taking down the bladder completely.

Cervix should be separated 5mm inferior the internal orifice and specimen is sent for frozen section. If margin was negative and intact, cerclage would be done in isthmus region, although these are controversies about this issue. Uterus fundus and uteroovarian ligament should be assessed for ischemia and then lower segment of uterus is grafted to apex of vagina by 6-8 separated sutures (Abu-Rustum et al., 2006).

The main advantage of abdominal approach is no need of an experienced laparoscopist and change in anatomy of vagina, although it leads to more bleeding and longer hospitalization.

Therefore; you need to clamp bilateral uterus arteries lead to atrophy of endometrium, cervical stenosis and scar which increase probability of low birth weight in later pregnancies. To decrease these complications, a technique with uterus artery preservation will be explained (Kolomainen et al., 2003).

Of course, less cases of recurrence have been reported after ART. For instance, only 2 of 91 patients with large lesion (about 3.8 to 5cm) recurred (Alexopoulos et al., 2002; Petignat et al., 2004; Lee et al., 2007). Normal cycle menstruation and successful pregnancies have been reported in these patients following ART will be normal after this operation and successful pregnancy follow it has been reported and usually fertility outcome is suitable. In young patients in whom vaginal trachelectomy is not possible because of some changes in vagina, ART is applied (Abu-Rustum et al., 2006; Wan; Ungar et al., 2006).

Other methods of fertility preservation in cervical cancer:

Fertility preservation is a proper method for young women who want to maintain fertile, but when we can't apply this method due to size of the lesion, it's replaced by neoadjuvant chemotherapy. When the lesion is so small and radical trachelectomy is considered as an extensive method, it is possible to use a limited local surgery like conization (Naik et al., 2007).

Neoadjuvant chemotherapy:

As lesions bigger than 2cm, have a higher risk of recurrent, neoadjuvant chemotherapy is able to shorten

size of the lesion. Consequently; it leads to better results for fertility preservation surgery. Current experience in neoadjuvant chemotherapy by administration of TIP regimen (consist of Taxol- Ifosfamide and Cisplatin) is reported in 3 patients. Complete pathologic response in 2 patients and dysphasia in another patient was seen. Recurrent has not been found during long term follow up (Maneo et al., 2004).

One of the patients born a baby with cesarean section. The other 2 patients were pregnant and preterm ovarian failure case; respectively. It should be noted that to prevent these complications, a less severe regimen with less effect on ovarian function should be used.

Ultra conservative fertility preservation surgery:

Patients in early stages of cervical cancer (stage IB, with small size lesions), due to low probability of recurrence and involvement of parametria, aren't proper candidates for radical trachelectomy. On the other hand; in 62-67% of patients with margin free specimen after conization, there isn't any tumor residue in pathological report after trachelectomy. Therefore; simple trachelectomy or extensive conization with knife to remove cervical tissue is a more suitable procedure for these patients. Laparoscopic lymphadenectomy or sentinel lymph node mapping is recommended to rule out lymph node involvement. It is noticeable that these two ultraconservative operations will be possible if the tumor volume is less than 500mm, tumor size is less than 2cm and invasion depth of stroma is less than 2mm. in this condition, loop conization with or without laparoscopic lymphadenectomy will be a suitable option. Naturally, large studies should be done to assess safety of operation, oncologic outcome and pregnancy complications.

References

- Abu-Rustum NR, Sonoda Y, Black D, et al (2006). Cystoscopic temporary ureteral catheterization during radical vaginal and abdominal trachelectomy. *Gynecol Oncol*, **103**, 729-31.
- Abu-Rustum NR, Sonoda Y, Black D, et al (2006). Fertility-sparing radical abdominal trachelectomy for cervical carcinoma: technique and review of the literature. *Gynecol Oncol*, **103**, 807-13.
- Alexopoulos E, Efkarpidis S, Fay TN, et al (2002). Pregnancy following radical trachelectomy and pelvic lymphadenectomy for Stage I cervical adenocarcinoma. *Acta Obstet Gynecol Scand*, **81**, 791-2.
- Aust T, Herod J, Macdonald R, et al (2007). Infertility after fertility-preserving surgery for cervical carcinoma: the next challenge for reproductive medicine?. *Hum Fertil (Camb)*, **10**, 21-4.
- Aust TR, Herod JJ, Gazvani R (2005). Placement of a Malecot catheter to enable embryo transfer after radical trachelectomy. *Fertil Steril*, **83**, 1842.
- Bernardini M, Barrett J, Seaward G, Covens A (2003). Pregnancy outcome in patients post radical trachelectomy. *Am J Obstet Gynecol*, **189**, 1378.
- Behtash N, Karimi Zarchi M, Deldar M (2009). Preoperative prognostic factors and effects of adjuvant therapy on outcomes of early stage cervical cancer in Iran. *Asian Pac J Cancer Prev*, **10**, 613-8.
- Beiner, ME, Covens, A (2007). Surgery insight: radical vaginal

- trachelectomy as a method of fertility preservation for cervical cancer. *Nat Clin Pract Oncol*, **4**, 353.
- Bisseling KC, Bekkers RL, Rome RM, et al (2007). Treatment of microinvasive adenocarcinoma of the uterine cervix: a retrospective study and review of the literature. *Gynecol Oncol*, **107**, 424-30.
- Burnett AF (2006). Radical trachelectomy with laparoscopic lymphadenectomy: review of oncologic and obstetrical outcomes. *Curr Opin Obstet Gynecol*, **18**, 8-13.
- Carter, J, Rowland, K, Chi, D, et al (2005). Gynecologic cancer treatment and the impact of cancer-related infertility. *Gynecol Oncol*, **97**, 90-5.
- Carter J, Sonoda Y, Abu-Rustum NR(2007). Reproductive concerns of women treated with radical trachelectomy for cervical cancer. *Gynecol Oncol*, **105**, 13-6.
- Chernofsky MR, Felix JC, Muderspach LI, et al (2006). Influence of quantity of lymph vascular space invasion on time to recurrence in women with early-stage squamous cancer of the cervix. *Gynecol Oncol*, **100**, 288-93.
- Corney RH, Crowther ME, Everett H, et al (1993). Psychosexual dysfunction in women with gynaecological cancer following radical pelvic surgery. *Br J Obstet Gynaecol*, **100**, 73-8.
- Covens A(2003). Preserving fertility in early cervical cancer with radical trachelectomy. *Contemp Ob Gyn*, **2**, 48.
- Covens A, Rosen B, Murphy J, et al (2002). How important is removal of the parametrium at surgery for carcinoma of the cervix?. *Gynecol Oncol*, **84**, 145-9.
- Dargent, D, Brun, JL, Roy, M (1994). La trachélectomie élargie (T.E.). Une alternative à l'hystérectomie radicale dans le traitement des cancers infiltrants développés sur la face externe du col utérin. *J Obstet Gynecol*, **2**, 292.
- Dargent D, Martin X, Sacchetoni A, et al (2000). Laparoscopic vaginal radical trachelectomy: a treatment to preserve the fertility of cervical carcinoma patients. *Cancer*, **88**, 1877-82.
- Ghaemmaghami F, Karimi Zarchi M, Mousavi A, et al (2008). Results of cervical cone excision biopsy in Iran. *Asian Pac J Cancer Prev*, **9**, 45-7.
- Hauspy J, Beiner M, Harley I, et al (2007). Sentinel lymph nodes in early stage cervical cancer. *Gynecol Oncol*, **105**, 285.
- Hertel H, Köhler C, Grund D, et al (2006). Radical vaginal trachelectomy (RVT) combined with laparoscopic pelvic lymphadenectomy: prospective multicenter study of 100 patients with early cervical cancer. *Gynecol Oncol*, **103**, 506-11.
- Jolley JA, Battista L, Wing DA (2007). Management of pregnancy after radical trachelectomy: case reports and systematic review of the literature. *Am J Perinatol*, **24**, 531-9.
- Karimi Zarchi M, Behdash N, Chiti Z, et al (2009). Cervical cancer and HPV vaccines in developing countries. *Asian Pac J Cancer Prev*, **10**, 969-74.
- Kay TA, Renninson JN, Shepherd JH, et al (2006). Successful pregnancy following radical trachelectomy and in vitro fertilisation with ovum donation. *BJOG*, **113**, 965-6.
- Klemm P, Tozzi R, Kohler C, et al (2005). Does radical trachelectomy influence uterine blood supply? *Gynecol Oncol*, **96**, 283-6.
- Kolomainen DF, Herod JJ, Holland N, et al (2003). Actinomyces on a papanicolaou smear following a radical trachelectomy. *BJOG*, **110**, 1036-7.
- Kobayashi Y, Akiyama F, Hasumi K (2006). A case of successful pregnancy after treatment of invasive cervical cancer with systemic chemotherapy and conization. *Gynecol Oncol*, **100**, 213-5.
- Lavie O, Peer G, Sagi S, et al (2006). The management of an early-missed abortion after radical trachelectomy--a case report and a review of the literature. *Int J Gynecol Cancer*, **16**, 1688-90.
- Lee, SJ, Schover, LR, Partridge, AH, et al (2006). American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. *J Clin Oncol* 2006, **24**, 2917.
- Lee KY, Jun HA, Roh JW, et al (2007). Successful twin pregnancy after vaginal radical trachelectomy using transabdominal cervicoisthmic cerclage. *Am J Obstet Gynecol*, **197**, 5-6.
- Marchiolo P, Benchaib M, Buenerd A, et al (2007). 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*, **106**, 132-41.
- Marchiolé P, Buénerd A, Benchaib M, et al (2005). Clinical significance of lymphovascular space involvement and lymph node micrometastases in early-stage cervical cancer: a retrospective case-control surgico-pathological study. *Gynecol Oncol*, **97**, 727-32.
- Maneo A, Landoni F, Caspani G, et al (2004). Chemotherapy and conization for preserving fertility in stage IB1 cervical cancer. 2004 Proceedings International Gynecologic Cancer Society. *Int J Gynecol Cancer*, **14**, 694.
- Mousavi A, Karimi Zarchi M, Gilani MM, et al (2008). Radical hysterectomy in the elderly. *World J Surg Oncol*, **6**, 38.
- Naik R, Cross P, Nayar A, et al (2007). Conservative surgical management of small-volume stage IB1 cervical cancer. *BJOG*, **114**, 958-63.
- Peppercorn PD, Jeyarajah AR, Woolas R, et al (1999). Role of MR imaging in the selection of patients with early cervical carcinoma for fertility-preserving surgery: initial experience. *Radiology*, **212**, 395-9.
- Plante M, Renaud MC, Roy M (2003). In: Atlas of procedures in gynecologic oncology, Levine, DA, Barakat, RR, Hoskins, WJ (Eds), Martin Dunitz.
- Plante M, Renaud MC, Harel F, et al (2004). Vaginal radical trachelectomy: an oncologically safe fertility-preserving surgery. An updated series of 72 cases and review of the literature. *Gynecol Oncol*, **94**, 614-23.
- Plante M, Renaud MC, Hoskins IA, et al (2005). Vaginal 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*, **98**, 3-10.
- Plante M, Roy M (2006). Fertility-preserving options for cervical cancer. *Oncology*, **20**, 479-3.
- Plante M, Lau S, Brydon L, et al (2006). Neoadjuvant chemotherapy followed by vaginal radical trachelectomy in bulky stage IB1 cervical cancer: case report. *Gynecol Oncol*, **101**, 367-70.
- Petignat P, Stan C, Megevand E, et al (2004). Pregnancy after trachelectomy: a high-risk condition of preterm delivery. Report of a case and review of the literature. *Gynecol Oncol*, **94**, 575-7.
- Roy M, Plante M (1998). Pregnancies after radical vaginal trachelectomy for early-stage cervical cancer. *Am J Obstet Gynecol*, **179**, 1491-6.
- Sahdev A, Sohaib SA, Wenaden AE, et al (2007). The performance of magnetic resonance imaging in early cervical carcinoma: a long-term experience. *Int J Gynecol Cancer*, **17**, 629-36.
- Saling, E(1981). Early total occlusion of os uteri prevent habitual abortion and premature deliveries (author's transl). *Z Geburtshilfe Perinatol*, **185**, 259-61.
- Selo-Ojeme DO, Ind T, Shepherd JH (2002). Isthmic stenosis following radical trachelectomy. *J Obstet Gynaecol*, **22**, 327-8.
- Shepherd JH, Spencer C, Herod J, et al (2006). 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* , 113, 719-24.
- Singh N, Titmuss E, Chin Aleong J, et al(2004). A review of post-trachelectomy isthmic and vaginal smear cytology. *Cytopathology*, **15**, 97-103.
- Sonoda Y, Abu-Rustum NR, Gemignani ML, et al (2004). A fertility-sparing alternative to radical hysterectomy: how many patients may be eligible? *Gynecol Oncol*, **95**, 534-8.
- Sonoda Y, Chi DS, Carter J, et al (2008). Initial experience with Dargent's operation: The radical vaginal trachelectomy. *Gynecol Oncol*, **108**, 214-9.
- Tanguay, C, Plante, M, Renaud, MC, et al (2004). Vaginal radical trachelectomy in the treatment of cervical cancer: the role of frozen section. *Int J Gynecol Pathol* , **23**,170.
- Ungar L, Palfalvi L, Smith JR, et al (2006). Update on and long-term follow-up of 91 abdominal radical trachelectomies. *Gynecol Oncol*, **101**, 20.
- Ungar L, Smith JR, Palfalvi L, et al (2006). Abdominal radical trachelectomy during pregnancy to preserve pregnancy and fertility. *Obstet Gynecol*, **108**, 811-4.
- Wan XP, Yan Q, Xi XW, et al (2006). Abdominal radical trachelectomy: two new surgical techniques for the conservation of uterine arteries. *Int J Gynecol Cancer*, **16**, 1698-704.