Ovarian transposition for the preservation of ovarian function in young patients with cervical carcinoma

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Summary

Radiotherapy with or without surgery for the treatment of pelvic malignancies irreversibly destroys the hormonal activity and reproductive capacity of ovaries in young women. On the other hand, menopausal symptoms associated with estrogen deficiency is an important contributor to the poor quality of life scores in gynecologic cancer survivors. Transposing of the ovaries into the paracolic gutters (ovarian transposition) was described in 1958 with the aim of protecting gonadal functions in reproductive-aged women treated by pelvic radiotherapy and/or surgery. Although the laparatomic approach has been used as a parallel to development in endoscopic surgery, today it is generally performed laparoscopically. However, there is ongoing debate about the effectiveness of ovarian tranposition with respect to protecting gonadal functions. Moreover, metastasis to the transposed ovaries and port sites is another concern about this procedure. In this short review, indications, techniques and functional outcomes of ovarian transposition have been summarized.

Key words: Ovarian transposition; Cervical carcinoma; Radical hysterectomy; Fertility saving surgery; Pelvic malignancy; Laparoscopy.

Introduction

Menopausal symptoms associated with estrogen deficiency is one of the important contributors to the poor quality of life scores in gynecologic cancer survivors [1]. It is well known that removal of the ovaries in young women may increase the risk of osteoporosis and the development of coronary heart diseases. On the other hand, there is ongoing debate about the risk and benefits of hormone replacement therapy in menopausal women. Therefore, the idea of protecting the ovaries in appropriate candidates is an attactive suggestion both for patients and physicians [2-4].

Ovarian transposition (OT) has been used to limit ovarian damage from radiation for pelvic malignancies in women. It was first described by McCall *et al.* in 1958 in order to maintain ovarian function in patients irradiated for cervical carcinoma [2]. Today, it is generally used for the protection of gonadal functions of reproductive-aged women treated by combined radiotherapy and surgery for pelvic malignancies, but mainly it is used for women with cervical carcinoma [3]. As a parallel to the increasing use of laparoscopy for the primary treatment of cervical carcinoma, transposing the ovaries into the paracolic gutters by "pediculisation" of the ovarian vessels by laparoscopy has been progressively accepted in order to improve the quality of life and preserve fertility potential in reproductive-aged patients. Today, it is well established that preservation of the ovaries in early-stage cervical cancer does not negatively affect survival, allowing these women to retain hormonal function by preserving oocytes, as well as potential future fertility [4].

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In this short review, indications, techniques and results of ovarian transposition are summarized.

Indications for ovarian transposition

Ovarian transposition was first described by McCall *et al.* during radical hysterectomy and they reported that hormonal activity may continue up to nine years after surgery. They also stated that women with preserved ovaries had a better quality of life compared with the irradiated group of women [2, 5]. In 1975, Webb reported that 5-year survival was no different in women with preserved ovaries compared to women with removed ovaries in cervical carcinoma [6]. After these preliminary studies, gynecologic oncologists tend to not remove ovaries in reproductive-aged women with cervical carcinoma. Today the main indication for ovarian transposition is cervical carcinoma but ovarian transposition can also be performed in vaginal carcinoma, pelvic sarcoma, ovarian dysgerminoma, rectal carcinoma, ependymoma of the cauda equina, and Hodgkin's disease [7].

In 2001, Yamamoto *et al.* [8, 9] suggested some criteria for the preservation and transposition of the ovaries in patients with cervical carcinoma. These can be summarized as follows:

1. Women, 44 years old or younger, with normal preoperative ovarian function
2. No morphological abnormalities of the ovaries
3. Stage IB-II squamous cell carcinoma of the cervix
4. Candidate for postoperative radiotherapy
5. No history of breast cancer and familial ovarian cancer
6. Strong desire for fertility preservation

In contrast, some authors have suggested that ovarian transposition should not be performed in women over 40 years old when adenocarcinoma is present, and when there is lymphovascular space involvement [7].

Ovarian transpositon techniques

It is believed that the dose of radiation exposure can be reduced to 10% of the administered dose by transposing the ovaries as high and lateral as possible in the paracolic gutters [4]. Initial attempts of ovarian transposition (OT) were performed by laparatomic approaches. As a parallel to the increasing usage of laparoscopy in gynecology practice, laparoscopic OT has become a current standard. Laparoscopic OT has been extensively described by Morrice *et al.* [7]. In this technique, the uteroovarian ligaments are cauterized using bipolar forceps. The fallopian tubes separate from the ovaries through the mesovarium. The peritoneum incises along the infundibulopelvic ligament to mobilize the ovaries completely. Then, dissection of the ovarian vessels is perform up to the level of the aortic bifurcation. The ovaries are transposed laterally to the paracolic gutters and fixed securely with the use of two *trans-aponeurotic* sutures. Metal clips can be used for each transposed ovary to guide subsequent roentgenographic localization.

Recently, Huang *et al.* [10] described their own technique. In this technique the middle point between the umbilicus and xyphoid process was used for the Veress needle insertion and the ovaries were mobilized as in other techniques. However salpingo-oophorectomy was performed in all cases and the ovaries were transposed to the anterolateral abdominal wall. The sites of ovariopexy were at the tip of the triangle with the base between the umbilicus and the point at the level of 3 to 4 cm above the umbilicus.

Ovarian functions after transposition

Although the main aim of ovarian transposition is to maintain hormonal activity of the preserved ovaries, reports of different investigators on the functional outcome of transposed ovaries have had conflicting results. Feeney *et al.* reported that lateral ovarian transposition could preserve normal ovarian function in only 50% of the patients undergoing pelvic radiotherapy following radical hysterectomy [11]. On the other hand, Morice *et al.* reported the functional outcomes of 24 laparoscopic ovarian transpositions for pelvic malignancies. In this study, mean follow-up was 31 months and ovarian preservation was achieved in 79% of the patients and also three pregnancies were obtained in the patients who had uteri in place. In this study, 16.6% of the patients who underwent ovarian transposition developed menopause after the procedure. These authors attributed the cause of menopause to both surgery and radiation therapy in these cases. In their discussion, Morice *et al.* suggested that successful OT is strictly dependent on the dose of radiation to the ovaries and age of the patient [7].

On the contrary, Buekers *et al.* reported the long-term results of 80 OT cases with a mean of 87 months of follow-up. After OT without radiotherapy, 98% of the patients retained ovarian function for a mean of 126 months with menopause at a mean of 45.8 years. However, if ovarian transposition and postoperative adjuvant radiotherapy were added 41% of the patients retained ovarian function for a mean of 43 months and mean age at menopause of 36.6 years. These authors concluded that radical hysterectomy with bilateral ovarian preservation without ovarian transposition does not significantly reduce the age of menopause. However, the addition of ovarian transposition to radical hysterectomy reduces ovarian function markedly. Furthermore, the addition of adjuvant radiotherapy after ovarian transposition dramatically lessens ovarian function. Therefore, these authors emphasized that patients should be extensively informed that ovarian function could be preserved in less than half of the patients who underwent this procedure, and that early menopause might be expected ten years prior to the population [5].

In contrast, Kier and Chambers reported the imaging findings of 14 patients with OT. They pointed out that transposed ovaries can easily be found because of the surgical clips which are used during the transposition. Cysts detected in the transposed ovaries did not correlate with pain or hormonal dysfunction. However, they misinterpreted one ovarian physiologic cyst as a mucosele of the appendix and one ovarian cyst as tumor recurrence or a lymphocele. Therefore, they concluded that the appearance of the ovaries does not predict the development of complications [12]. Moreover, Chambers *et al.* reported the long-term sequelae of lateral OT in unirradiated patients with cervical carcinoma. They compared 59 patients with radical hysterectomy to 25 patients who had radical hysterectomy plus OT. In this study, the incidence of a symptomatic ovarian cyst was 24% in the OT group compared with 7.4% in the radical hysterectomy without transposition group. Symptomatic ovarian cysts were significantly higher in the transposition group ($p = 0.048$) [13].

Although the primary aim of OT is to protect ovarian hormone synthesis and to improve the of quality of life secondary to the prevention of early menopause and atherosclerotic heart disease, some authours reported spontaneous or assisted pregnancies after OT in patients who had undergone pelvic irradiation with or without hysterectomy. Morice *et al.* reported 18 pregnancies in 12 of the 27 patients treated by ovarian transposition plus external irradiation or brachytherapy for pelvic malignancies. In this study, the pregnancy rate was 15% for patients with cervical or vaginal carcinoma whereas this rate was 80% for patients with dysgerminomas and soft tissue sarcomas. They concluded that fertility was excellent after OT in irradiated patients with morphologically normal genital tracts. The prognosis is not as good for patients treated for clear cell adenocarcinoma of the vagina and/or the cervix who may have morphological and/or functional anomalies of the genital tract. They also stated that repositioning of the ovary is not essential to achieve pregnancy [7].

Recently, surrogate pregnancies have also been reported in patients who had a radical hysterectomy plus chemoradiotherapy with OT. Giacalone *et al.* and Steigrad *et al.* reported that ovulation induction and

oocyte retrieval can be succesfully performed on transposed ovaries [14, 15]. Recently, Oktay *et al.* suggested the forearm as an alternative site for OT in order to maintain ovarian function [16]. Later on, Falcone *et al.* suggested different recipient areas including the breast, thigh, neck and abdomen for ovarian transplantation [17]. Therefore, ovarian transplantation into different areas of the body might be suggested to candidates for ovarian transposition.

Metastases to the transposed ovaries

The probability of ovarian metastasis from primary tumors or other primary tumors should always be taken into consideration and patients should be informed about the possible risks. Recently some reports describing metastasis to the transposed ovaries in cervical carcinoma have been reported. Although Tabata *et al.* reported 28.6% of ovarian metastases in Stage IB-III cervical adenocarcinoma compared with 17.4% in squamous cell carcinoma in an autopsy series [18]. Morice *et al.* suggested that histological type was not an important risk factor for the development of ovarian metastasis after tranposition in patients with early-stage cervical carcinoma and macroscopically normal ovaries. However, they suggested that bulky tumors and uterine corpus involvement as risk factors for the development of ovarian metastasis to the transposed ovaries [2]. On the contrary, Yamamoto *et al.* found that histological type and blood vessel invasion were significant independent risk factors for the development of ovarian metastases in multivariate analysis [7]. However further studies are needed to determine the exact risk factors for metastasis to transposed ovaries. Port site metastasis after laparoscopic OT has been reported in a few cases and patients should also be informed about the risk of this rare complication [19].

Conclusion

Ovarian transposition can be suggested in reproductive-aged women with pelvic malignancies to reduce ovarian damage from radiation therapy. Ovarian function may be preserved in more than half of the patients who undergo OT. Furthermore, spontaneous or assisted pregnancies can be achieved after OT. However, patients should be informed about the possible risks of the transposition, i.e., early menopause and the possibility of metastasis to the transposed ovaries and port sites, etc.

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