

Laparoscopic ovarian transposition in patients with pelvic cancer

Kastytis Žilinskas¹,

Živilė Sabonytė-Balšaitienė²,

Narimantas Evaldas

Samalavičius¹

¹ Clinic of Oncosurgery,
Institute of Oncology,
Vilnius University,
Lithuania

² Faculty of Medicine,
Vilnius University

Background. The aim of this study was to evaluate the feasibility of laparoscopic ovarian transposition prior to radiation therapy on the preservation of hormonal function in the treatment of pelvic cancer.

Materials and methods. A chart review of premenopausal women diagnosed with pelvic cancer, who underwent laparoscopic ovarian transposition to paracolic gutters, then received preoperative radiotherapy at the Center of Oncosurgery, Oncology Institute of Vilnius, from January 2010 to July 2013.

Results. A total of 14 patients underwent laparoscopic ovarian transposition. Patients were divided into two groups by localisation of cancer: 2 (14.29%) patients diagnosed with rectal cancer and 12 (85.71%) with cervical cancer. Patients' age was from 24 to 42 years with a mean age of 33.71 (SD ± 5.22) years. The average age of the patients in the first group was 26 (SD ± 2.83) years. In the second group women, aged 29 and 42 years with a mean age of 35 (SD ± 4.35) years, were analyzed. Rectal cancer of stage III was diagnosed in both women of the first group. Tumor stage distribution in the second group, respectively: stage I – 2 cases (16.67%), stage II – 3 cases (25%), stage III – 7 cases (58.33%). Seven (58.33%) patients of the second group underwent complete endoscopic staging. In these groups of 14 patients there were 2 (14.3%) complications (injury of the inferior vena cava and postoperative abnormal vaginal bleeding). No postoperative exitus occurred. The mean duration of the operation was 2 hours 26 minutes ± 55 minutes (60–245 minutes), respectively, 2 hours 40 minutes ± 49 minutes (95–245 minutes) when laparoscopic staging and ovarian transposition was performed and 2 hours 12 minutes ± 1 hour 1 minute (60–245 minutes) when only ovarian transposition was performed. The hospitalization period ranged from 5 to 52 days (average 12 days).

Conclusions. Laparoscopic ovarian transposition is a relatively safe and effective procedure for preserving ovarian function. This procedure should be considered in all reproductive age female patients who need to undergo pelvic irradiation as part of pelvic cancer treatment.

Key words: ovarian transposition, laparoscopy, rectal cancer, cervical cancer, radiation

INTRODUCTION

The preservation of hormonal function of ovaries in the treatment of cancer in young women is one of the critical issues. Anticancer drugs and radiation therapy are the most common of the known ovarian toxins, and have become one of the main causes of ovarian failure. It is known that oocytes are uniquely sensitive to radiation injury: a mathematical model predicted 16 gray (Gy) of radiation would deplete the ovarian oocyte pool at the age of 20 years and 10 Gy of radiation would deplete the ovarian oocyte pool at the age of 45 years (1). Moreover, radiation doses received by the ovaries ranging from 3.2 to 20 Gy have been found to induce menopause so complete ovarian failure occurs with a dose of 20 Gy in women under 40 years of age and with a dose of only 6 Gy in older women (2, 3). Surgical transposition of the ovaries is performed to prevent early menopause and tries to preserve fertility in premenopausal women who are undergoing pelvic or low abdominal radiation therapy. This method involves moving the ovaries outside the predictable irradiation field so that the direct effects of ionizing radiation are avoided while retaining ovarian circulation by preserving ovarian vessels. Ovarian transposition reduces the radiation dose to approximately 5% to 10% of the dose to the ovaries in their normal position (3, 4).

Historically, ovarian transposition was typically performed for premenopausal patients undergoing pelvic irradiation for Hodgkin's disease at the time of staging laparotomy (5). As an effective method to maintain ovarian function in patients irradiated for cervical carcinoma it was introduced by Mc Call in 1957 (6). In the beginning of using this method, the ovaries were relocated medially by suturing them to the posterior uterus, and protected during radiation therapy with a lead shield placed centrally on the abdomen (7). However, medially placed ovaries still absorb radiation from scatter and some transmission through the shield, reducing the efficacy of the procedure (8). Literature reviews suggest multiple techniques for ovarian transposition. Contemporary procedures transpose the ovaries above the pelvic brim and as lateral as possible, which minimizes the ovarian dose of radiation and improves efficacy compared with medial approaches. Various lateral locations have been used: the base of the round ligament (9),

the level of lower kidney pole (10), and the paracolic gutters (first introduced by Larue-Chalus S. in 1987) (6, 11, 12). Historically, exploratory laparotomy performed for staging or debulking procedures for these malignancies provided an opportunity to perform ovarian transposition. As laparoscopic procedures became more widespread, surgical procedures dedicated to ovarian transposition alone became more common (2). In recent years, a laparoscopic approach is favoured because it allows the patient to return to normal function faster, prolonged hospital stay is avoided. The procedure is safe and gives the opportunity not to delay the proposed treatment for the malignancy.

The purpose of this procedure is placing the ovaries above the pelvic brim and as lateral as possible in order to avoid the radiation field. Transposition to this level can be achieved easily without separating the fallopian tubes from their uterine origin. When laparoscopy is utilized, three or four port incisions are made and the trocars are introduced into the peritoneal cavity at the umbilicus, both lower quadrants, and / or the suprapubic region (2). To facilitate mobilization of the ovaries, the ovarian ligament should be divided because, unlike the fallopian tube, the ovarian ligament is not stretchable. The peritoneum is incised under and lateral to the ovarian vessels. The transposed ovaries and tubes are fixed as high as possible in the paracolic gutters below the spleen and the liver. They are sutured in 3 points to prevent torsion and returning back to the pelvic cavity (2, 16). Good blood supply to the ovaries is confirmed. The ovaries are marked inferiorly with metal clips to ensure they are out of the radiation portals on radiation verification films (5). This ensures the minimal radiation dose given to the ovaries.

Surgical transposition of ovaries can be offered to premenopausal patients (younger than 40–45 years) presenting with malignant disease requiring pelvic irradiation. Malignant disease indications for ovarian transposition are broad. The indications for the procedure include cervical cancer, upper vaginal cancer, lymphoma, anal cancer, unilateral ovarian dysgerminoma (2, 13). However, this method is no longer used in the treatment of Hodgkin's disease because radiation therapy is no longer applied systemically. Nevertheless, with various new disease managements and the proliferation of laparoscopic surgical techniques,

ovarian transposition can now take place in other clinical settings, including gastrointestinal cancers that require pre-operative radiation (2, 5, 14). In children, Hodgkin or non-Hodgkin lymphoma, vaginal or uterine tumors, pelvic Ewing's sarcoma, and spinal tumors are more common reasons for referral for the procedure (15).

The procedure may have some specific complications, particularly ovarian insufficiency, increased frequency of functional ovarian cysts after transposition, and recurring malignancy in the form of ovarian metastasis (2, 6, 13). One case of isolated tubal torsion after adnexal transposition and one case of small bowel obstruction from adhesions at the site of transposed ovary have been described in the literature (2, 13). The most common complication is functional ovarian cysts which can be found in 1.8–5.2% of cases (6). A history of endometriosis or pelvic inflammatory disease increased these risks. Metastasis from cervical cancer to the transposed ovary is rare in early stage disease, but has been reported to occur in 5% of patients with bulky, stage IIB tumors (2).

MATERIALS AND METHODS

This was a retrospective chart review study. We systematically evaluated the medical charts of patients who underwent laparoscopic ovarian transposition to paracolic gutters, then received preoperative radiotherapy at the Center of Oncosurgery, Oncology Institute of Vilnius, from January 2010 to July 2013. Charts were reviewed for patient's age, diagnosis, type and duration of the operation, duration of hospitalisation and possible complications. The inclusion criteria were premenopausal age, primary diagnosed minor pelvic cancer, good physical and mental condition, not diagnosed cancer of other localization, signed Patient Information and Agreement forms. The exclusion criteria were postmenopausal age, poor physical or mental condition, a history of previous hysterectomy or salpingo-oophorectomy, cancer of other localizations or not signed Patient Information and Agreement forms. For all patients magnetic resonance imaging (MRI) or / and computed tomography, as well as abdominal ultrasound and chest X-ray for the disease extension evaluation have been done. The charts of the patient were divided into two groups by localisation of the cancer:

the first group consisted of women diagnosed with rectal cancer and the second group consisted of women diagnosed with cervical cancer. The diagnosis of cancer was confirmed histologically at the State Pathology Center (Vilnius, Lithuania).

All statistical analysis was performed using the Statistical Package for Social Sciences for Windows Version 17.0 (SPSS 17.0). Age is presented as the mean and standard deviation (SD). Categorical data are presented as percentage. Statistical significance was considered as $p < 0.05$.

RESULTS

A total of 14 patients underwent laparoscopic ovarian transposition at the Center of Oncosurgery, Oncology Institute of Vilnius, from January 2010 to July 2013: in 2010 – 1 operation, in 2011 – 3, in 2012 – 6 and in 2013 – 4 operations. Charts of fourteen women, aged 24 and 42 years with a mean age of 33.71 (SD \pm 5.22) years, were analyzed. The charts of the patients were divided into two groups: the first group consisted of 2 (14.29%) women diagnosed with rectal cancer, the second group consisted of 12 (85.71%) women with cervical cancer. The average age of the patients in the first group was 26 (SD \pm 2.83) years. In the second group women, aged 29 and 42 years with a mean age of 35 (SD \pm 4.35) years, were analyzed. Rectal cancer of stage III by Figo classification was diagnosed in both women of the first group. Tumor stage distribution in the second group, respectively: stage I – 2 cases (16.67%), stage II – 3 cases (25%) and stage III – 7 cases (58.33%). In the first group one patient underwent unilateral and one bilateral transposition of the ovaries. Bilateral laparoscopic ovarian transposition to paracolic gutters has been performed to 9 (75.75%) patients of the second group. Seven (58.33%) patients of the second group underwent complete endoscopic staging. In these series of 14 patients there were only 2 (14.3%) complications – 1 intraoperative complication and 1 early postoperative complication. In the first case the inferior vena cava injury has been made during the laparoscopic staging of cervical cancer. While performing paracaval lymph node dissection a 1 mm diameter inferior vena cava wall defect has been made that led to laparotomy. In the second case abnormal vaginal bleeding occurred one day after ovarian transposition. Embolisation of left

and right iliac arteries has been made. No deaths occurred. The mean duration of the operation was 2 hours 26 minutes \pm 55 minutes (60–245 minutes), respectively, 2 hours 40 minutes \pm 49 minutes (95–245 minutes) when laparoscopic staging and ovarian transposition was performed and 2 hours 12 minutes \pm 1 hour 1 minute (60–245 minutes) when only ovarian transposition was performed. The postoperative period ranged from 3 to 41 day (average 8 days). The hospitalization period ranged from 5 to 52 days (average 12 days). All patients were offered adjuvant radiotherapy, and all underwent it.

DISCUSSION

Cervical cancer is the second biggest cause of female cancer mortality worldwide and the most common cancer in women in Lithuania (17). Moreover, increasingly younger patients are reported to suffer from cervical cancer. Pelvic radiotherapy or chemoradiation are included in all cervical cancer treatment protocols (18). One of the main difficulties of treatment for invasive cervical cancer is early menopause and the loss of fertility due to radiation therapy-induced function ablation. The same issues remain in the treatment of other pelvic cancers, for example, rectal cancer. Results of cancer registry data by Meyer showed that the incidence of rectal and rectosigmoid cancer appeared to be increasing in patients aged less than 40 years (5). Although the survival rates of colorectal cancer improve because of the improved adjuvant therapy a problem of ovary function preservation remains. A typical course of neoadjuvant radiotherapy for rectal cancer would involve a total dose of 45 Gy over 5 weeks to the pelvis, which would result in complete ovarian failure unless other measures are taken (5). In recent years, a laparoscopic procedure for ovarian transposition has been reported and the technique may become standard in the future, providing a minimally invasive means of preserving ovarian function (3).

Laparoscopic ovarian transposition in women younger than 40 years preserves ovarian function in 88.6% of cases (16). Morice and colleagues reported a series of 24 patients who underwent ovarian transposition to the paracolic gutters before radiation for gynecologic malignancies. The authors concluded that this procedure was a safe and effective method of preserving ovarian

function. Complications in both of these reports were rare (5). In another report by Morice et al. 15 out of 19 (79%) patients who received postoperative irradiation exhibited preserved ovarian function. Moreover, Morice et al. found an 83% ovarian function preservation rate among the 107 patients who underwent ovarian transposition during surgical treatment for cervical cancer at the Institute Gustave Roussy from 1985 to 1998 (2).

Success depends on the dose of radiation delivered to the ovaries and on the patient's age. Haie-Mederet et al. reported that ovarian transposition success is influenced by two factors: the patient's age at the time of treatment and the radiation dose administered to the ovaries (2). It is important to mention that the authors used the cut-off of the age of 25 years old as the measure of successful preservation of ovarian function and the median age in their study was younger than those encountered in cervical cancer because patient in their cohort were treated for Hodgkin's disease or dysgerminoma.

The advantage of ovarian transposition is that it prevents premature menopause and preserves fertility. Another important benefit is that radiation therapy can be initiated immediately. Nevertheless, the primary benefit of ovarian transposition is prevention or delay of premature menopause, not preservation of fertility. In fact, with "curative" doses in the range of 8500 cGy with external beam plus intracavitary brachytherapy, the resultant endometrial damage essentially precludes successful pregnancy, either spontaneously or with in vitro technique (5). Based on studies of radiotherapy effects to uterus when childhood cancers were treated, it is believed that the uterus is extremely vulnerable to irradiation and it is likely that radiation damage to the uterine musculature and vasculature adversely affects prospects for pregnancy. A recent retrospective study published by Sudour et al. evaluated fertility after abdominal or pelvic irradiation in long-term female childhood cancer survivors and found that the dose of radiation delivered to the ovaries and uterus was the most important risk factor for future fertility. In the case of rectal cancer with doses in the range of 45 to 50 Gy administered over a 6-week course, the resultant endometrial damage makes it highly unlikely for a woman to have a successful pregnancy although there are some isolated case reports of

successful spontaneous pregnancy in patients with rectal cancer after radiotherapy (3, 5, 16).

CONCLUSIONS

Ovarian transposition is a highly effective surgical procedure used to preserve ovarian function in patients who are at risk of iatrogenic ovarian failure as a result of radiation therapy-induced function ablation. Using laparoscopic techniques, the ovaries can be moved to a position outside of the direct radiation portal with virtually no postoperative complications. The laparoscopic approach is favoured. This procedure should be considered in all reproductive aged female patients who need to undergo pelvic irradiation as part of pelvic cancer treatment.

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**Kastytis Žilinskas, Živilė Sabonytė-Balšaitienė,
Narimantas Evaldas Samalavičius**

**LAPAROSKOPINĖS KIAUŠIDŽIŲ
TRANSPOZICIJOS VAIDMUO GYDANT
MAŽOJO DUBENS PIKTYBINIUS NAVIKUS**

Santrauka

Tyrimo tikslas – ištirti laparoskopinės laterokolinės kiaušidžių transpozicijos metodo prieš spindulinės terapijos taikymą tinkamumą išsaugant kiaušidžių funkciją ir gydant mažojo dubens piktybinius navikus.

Pacientai ir metodai. Atlikta retrospektyvinė VUOI Onkochirurgijos centre nuo 2010 m. sausio mėnesio iki 2013 m. liepos mėnesio gydytų pacienčių ligos istorijų analizė. Įtraukimo kriterijai – vaisingo amžiaus ligonės, kurioms diagnozuotas mažojo dubens piktybinis navikas, atlikta laparoskopinė laterokolinė kiaušidžių transpozicija bei taikytas spindulinis pooperacinis gydymas.

Rezultatai. Laparoskopinė kiaušidžių transpozicija atlikta 14-ai pacienčių. Ligonės išskirtos į dvi grupes: pirmos grupės 2 (14, 29 %) ligonės, kurioms diagnozuotas tiesiosios žarnos vėžys, ir antros grupės 12 (85, 71 %) ligonių, kurioms nustatytas gimdos kaklelio vėžys. Vidutinis tiriamųjų amžius buvo 33, 71 m. (SD ± 5, 22; 24–42 m.). Pirmos grupės ligonių vidutinis amžius 26 ± 2, 83 m. (24–28 m.), o antrosios – 35 ± 4,35 m. (29–42 m.). Abiem pirmos grupės ligonėms buvo nustatyta III naviko stadija. Antroje grupėje naviko stadijos pasiskirstė atitinkamai: I ligos stadija – 2 atvejai (16, 67 %), II stadija – 3 atvejai (25 %), III stadija – 7 atvejai (58, 33 %). Laparoskopinė limfonodektomija atlikta 7 (53,9 %) ligonėms. Septynioms pacientėms (58,33 %) iš antrosios grupės atlikta tik kiaušidžių transpozicija. Iš operuotų 14-os pacienčių operacinė ir pooperacinė eiga komplikavosi 2 (14, 3 %) pacientėms (intraoperacinė komplikacija – apatinės tuščiosios venos pažeidimas, pooperacinė komplikacija – kraujavimas). Mirčių nebuvo. Vidutinė operacijos trukmė – 2 valandos ir 26 minutės ± 55 minutės (60 – 245 minutės); atitinkamai 2 valandos ir 40 minučių ± 49 minutės (95 – 245 minutės), kai buvo atlikta kiaušidžių transpozicija ir limfonodektomija, bei 2 valandos ir 12 minučių ± 1 valanda ir 1 minutė (60 – 245 minutės), kai buvo atlikta tik kiaušidžių transpozicija. Hospitalizacijos trukmė – nuo 5 iki 52 dienų (vidutiniškai 12 dienų).

Išvados. Laparoskopinė laterokolinė kiaušidžių transpozicija yra pakankamai saugi bei efektyvi pro-

cedūra, padedanti išsaugoti kiaušidžių funkciją. Vertėtų apžvelgti šios procedūros pritaikymo galimybes visoms reprodukcinio amžiaus pacientėms, kurioms diagnozuotas mažojo dubens piktybinis navikas ir numatoma taikyti spindulinę terapiją.

Raktažodžiai: kiaušidžių transpozicija, laparoskopija, tiesiosios žarnos vėžys, gimdos kaklelio vėžys, radioterapija