

Review Article

Preservation of Ovarian Function in Young Women with Gynecologic Cancer Desiring Future Pregnancy: A Review

Nader Husseinzadeh, MD*

Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, University of Cincinnati, 231 Albert Sabin Way, Cincinnati, Ohio 45267 United States

Abstract

Objective: The aim of this paper is to present an overview of available published methods for preservation of ovarian function and fertility in young patients with gynecologic malignancies who desire to maintain their child-bearing capacity or ovarian function.

Methods: A Medline search was conducted and published articles from American and European studies from 1984 to present were reviewed. The effect of cancer treatment on reproductive capacity and different methods of fertility preservation with their reproductive outcomes and ovarian function and long term side effects are presented.

Results: The pregnancy rate in patients with gynecologic malignancies varies according to the type of the malignancy, stage of disease, treatment modalities, and other factors such as patient's age and reproductive capacity, status of sexual partner, and potential for surrogacy. The highest success rates of pregnancy have been reported in patients who had fertility-sparing surgery and utilized assisted reproduction technology.

Conclusion: Today, higher cure rates and longer survival are a result of early cancer detection and treatment. In conjunction with the advances in assisted reproduction and fertility, the preservation of ovarian function and fertility has become a major part of contemporary patient care and should be offered to any young patient with gynecologic cancer. These alternative options are appropriate only in highly selective patients with good prognoses. A multidisciplinary approach and collaboration between other related disciplines might optimize a successful outcome in these patients.

Keywords: Fertility; ovarian function; gynecologic cancer

Peer Reviewers: Chih-Yen Chien, MD, Department of Otolaryngology, Kaohsiung Chang Gung Memorial Hospital, Taiwan; Ciro Isidoro, MD, PhD, Laboratory of Molecular Pathology and Nanobioimaging, "A. Avogadro" University of Novara, Italy

Received: March 6, 2013; **Accepted:** May 17, 2013; **Published:** June 30, 2013

Competing Interests: The authors have declared that no competing interests exist.

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*Correspondence to: Nader Husseinzadeh, Department of Obstetrics and Gynecology, University of Cincinnati.

Email: nader.husseinzadeh@uc.edu

Introduction

It is estimated that approximately 88,750 new cases of gynecologic malignancies were diagnosed in 2012 with approximately 32,500 deaths (1). Fifteen to 21% of these women will be less than 40 years of age at the time of diagnosis (2).

With the continuous trend in delayed childbearing

age, some patients have a strong desire for future child bearing, and others may wish to preserve their ovarian function only and have the option for adoption as well. Unfortunately preservation of reproductive function cannot be offered to every eligible patient for various reasons including unfamiliarity, lack of knowledge, financial and psychosocial constraints.

An increasing number of patients, particularly

those younger than 40 years old, are confronted with the consequences of cancer treatment, particularly radiation and chemotherapy, which can have significant impact not only on the ovarian function and fertility, but also long term deleterious effects of menopause (3-5).

Several strategies have been explored for preservation of ovarian function and fertility. Recently, there has been a tendency towards less radical approaches for treatment of cervical cancer in young women. Loop excision technique or cervical conization are increasingly being recommended for very early stage cervical cancer and more recently radical trachelectomy which is a less radical procedure and the uterus can be preserved for future fertility (6, 7).

Ovarian transposition has been utilized in patients with locally advanced cervical cancer. The aim is to surgically remove the ovaries from the direct field of radiation. Most ovarian transpositions currently are carried out laparoscopically, and there have been suggestions that lateral transposition may be more protective than median transposition of ovaries (8, 9).

Endometrial cancer is usually a disease of the postmenopausal group and is rare in women under the age of 40 (www.cancer.org). The treatment commonly involves total hysterectomy and bilateral oophorectomy. Although the standard treatment for women with complex atypical endometrial hyperplasia is hysterectomy, hormonal therapy may be recommended for young patients who have not completed their family and have a desire for future childbearing (10).

Epithelial ovarian cancer continues to be treated radically with loss of reproductive organs. Germ cell ovarian tumors, sex cord-stromal tumors, borderline tumors of the ovary (low malignant potential) and stage IA invasive epithelial ovarian cancer can be treated with more conservative (fertility-sparing) surgeries. These types of surgical procedures include, ovarian cystectomy or unilateral salpingo-oophorectomy, with or without hysterectomy, are often adequate treatment (11-14).

Cervical cancer

The standard treatment for patients with early, locally invasive cervical cancer had been some form

of radical hysterectomy and bilateral pelvic with or without paraaortic lymphadenectomy. Radiation or chemo-radiation has been utilized for those with locally advanced or metastatic disease. However, there are several alternative options for young patients with early stage disease who desire to preserve their ovarian function and fertility without compromising their cure.

Conization Cervical Conization is recommended for young patients with stage IA1 (stromal invasion ≤ 3 mm and extension < 7 mm) with no lympho-vascular invasion in whom the risk of nodal metastasis or recurrence is minimal. The reported survival at 5 years was 98% (95% CI 96-99%) for patients who had hysterectomy and 99% (95% CI 97-99%) for those who had Conization (15).

Simple Trachelectomy

In recent years several retrospective studies have shown a low incidence ($< 1\%$) of parametrial involvement in patients with early stage (IA2, IB1) cervical cancer with favorable pathologic characteristics. In addition, in approximately 60% of patients undergoing radical trachelectomy, the final pathologic specimen after a diagnostic cone did not have any residual disease (16-19).

Currently, a prospective, multi-center, international cohort study is being conducted evaluating the outcome of performing pelvic lymphadenectomy with conservative surgery (simple hysterectomy or conization) in patients with favorable pathologic characteristics. The inclusion criteria includes patients with stage IA2 or IB1 disease; tumor size ≤ 2 cm; and squamous or adenocarcinoma histology without lymphovascular invasion (20).

Radical Trachelectomy. This procedure can be performed vaginally, abdominally or robotically with pelvic with or without para aortic lymphadenectomy (21). Radical trachelectomy may be recommended in stage IA1 disease with lymphovascular invasion, stage IA2, or stage IB1 with small tumor size (< 2 cm) in the absence of high risk histological features (e.g. clear cell, small cell neuroendocrine type, and glassy cell tumors) and no evidence of nodal metastasis (22). Successful pregnancies have

been reported following radical trachelectomy (Table 1). There were 77 fetal losses and 181 births among cumulative of 258 patients who underwent radical trachelectomy (23-28). Shepherd et al (29) reported on a total of 123 radical vaginal trachelectomies, of which a 5 year cumulative pregnancy rate was 52.8%. Rate of pregnancy loss and premature birth was 12.7% and 25%, respectively. Jolly et al (30), in a literature review, reported an overall conception rate of 40% following radical trachelectomy, with rates of preterm and term deliveries of 25% and 42% respectively. In cases of pregnancy loss, the overall rate of first trimester pregnancy loss was 19% comparable to that of general population. The rate of second trimester loss was 9.5% and elective termination rate of 3.5%. These findings were in agreement to those reported by Plante et al (31) and Alexander-Sefre et al (32).

In a more recent review article, Schneider et al (33), reported, the overall recurrence rate after vaginal trachelectomy was 3% to 6% and the death rate was 2% to 5% when the tumor size was no larger than 2 cm in diameter. The fertility did not decrease, but the risk for premature delivery was 2 to 3 times higher compared to women with an intact cervix. In this cohort 50% of women delivered beyond 37 weeks, whereas 21%-28% delivered prematurely before 37 weeks and 12% of patients delivered before 32 weeks. Long term morbidity associated with radical trachelectomy includes vaginal discharge, dysmenorrhea, irregular bleeding, and complication of cervical suture such as isthmic stenosis, and prolonged amenorrhea. Recent reviews of radical vaginal trachelectomy reported, over all tumor recurrence rate of < 5% (4.2-5.3%) and a death rate of <3% (2.5-3.2%) (34,35). These results are comparable to those of radical hysterectomy for similar size lesions (36).

Neo-adjuvant chemotherapy has been used to reduce the tumor size in patient with >2cm lesion prior to fertility- sparing surgery.

Maneo et al (37) reported their experience with 21 stage IB1 cervical cancer patients. Median tumor size was 1.5 cm (1.0-3.0 cm) and patients were treated with neo-adjuvant chemotherapy followed by

cold knife conization and pelvic lymphadenectomy. Complete pathologic response was observed in 5(24%), and residual in situ or microinvasive disease was present in 12(14%) patients. Nine patients (43%) had stromal invasion between 1-3 mm, and 4 patients (19%) had more than 3 mm invasion. No disease relapse was observed after median follow up of 69 months. Nine women attempted to conceive; and 10 pregnancies occurred in 6 of these patients. There were 9 live infants and one miscarriage.

There are no specific guidelines for follow up surveillance after radical trachelectomy. In general, it is recommended to obtain cervical cytology, every 3 or 4 months for the first 3 years and every 6 months for the next 2 years. Colposcopy with or without endocervical curettage is recommended when cytology is abnormal. Singh et al (38) reviewed 197 cytological specimens' from 32 patients and reported false positive result in 2% of smears, was most often due to presence of atypical endometrial cells. However, in 2 of these cases, cytology identified recurrences long before they were clinically apparent. Follow up cytology can be truly normal but frequently reported as abnormal, so good communication with an experienced cytopathologists becomes very important and critical to avoid an unnecessary surgery. The decision to perform definite hysterectomy in patients once they have completed their family plan should be done on an individual basis.

Transposition of the Ovary Ovarian transposition is a procedure in which the ovaries and their blood supply are detached from the uterus and transposed to an area above the pelvis in the paracolic area. Retro uterine bilateral ovarian transposition has been performed in patients with hematologic malignancies i.e. lymphoma or Hodgkin disease (39, 40).

The rationale of this procedure is to protect the ovaries from direct radiation exposure, hereby preserving ovarian function for future surrogate pregnancy by in vitro fertilization. Only a few cases of occult metastatic cervical cancer to ovaries have been reported, most involving non-squamous lesions

(41). Ovarian transposition can be performed in high risk early stage cervical cancer patients treated with radical hysterectomy that will require post-operative radiation or chemoradiation. Potential risks include direct injury to ovarian vessels, torsion, cystic changes, and mid-cycle extra pelvic (abdominal) pain. Unfortunately, some of the published papers lack detailed descriptions of the surgical procedures

and precautions taken to protect ovaries from scattered radiation. Several studies (41-48) demonstrated that 50-70% of patients who undergo ovarian transposition retain their ovarian function after radiation therapy at a median follow up of 35 months (Table 2). Successful surrogate pregnancies involving patients who had hysterectomy and pelvic radiation have also been reported (49, 50).

Table 1 Reported pregnancy out come from radical trachelectomy

Authors	No of Pregnancies	Fetal losses	Birth Rate
Covens A, et al (23).	5	2 (40%)	3 (60%)
Dargent D, et al (24).	25*	12 (48%)	13 (52%)
Shepherd J, et al (25).	14	5 (36%)	9 (64%)
Burnett AF, et al (26).	3 (1 twin)	1 (33.3)	3 (66.7%)
Plante M, et al (27).	50*	10 (20%)	36 (72%)
Boss FA, et al (28).	161	47(29%)	107 (70%)
Total	258	77	181

* Include cases that were pregnant at the time of procedure

Table 2 Ovarian transposition in cervical cancer patients treated with pelvic radiation

Authors	No of Patients	Stage of disease	Preservation of Ovarian Function
Morice, et al (41).	25	IB-IIA**	60%
Hodel, et al (42).	7	IB-IIIB	57%
Husseinzadeh, et al	18	IB-IIIB	63%
Chambers, et al (44)	14	IB**	71%
Anderson, et al (45)	24	IB	17%
Husseinzadeh, et al (46)	15	IB-IIIB	64%
Feeny, et al (47)	28	IA-IIB	50%
Buekers, et al (48)	24	IA-IIB	41%

**No information was given regarding ovarian shielding and dosimetry

Endometrial Hyperplasia and Adenocarcinoma

Approximately 5% of women with endometrial cancer are younger than 40 years of age. Endometrial adenocarcinoma is preceded by

complex endometrial hyperplasia with or without atypia. The risk of concomitant complex atypical endometrial hyperplasia and endometrial cancer has been reported to be 25% (51). Currently, the standard treatment of early stage endometrial

adenocarcinoma is total abdominal hysterectomy and bilateral salpingo-oophorectomy. However there is no specific fertility-sparing surgery for young women with this disease, although the survival for patients with stage IA is reported to be near 100% (52). Therefore, those patients with complex atypical hyperplasia or stage IAG1 endometrial adenocarcinoma are optimal candidates for hormonal therapy using progestational agents. In fact, successful pregnancies have been reported in patients who were treated with progestin therapy. Ushijima et al (53) reported the result of a multicenter study in Japan. Twenty-eight patients having endometrial cancer (EC), presumed at stage IA, and 17 patients with atypical hyperplasia (AH) younger than 40 years of age were given an oral daily dose of 600 mg of medroxy progesterone acetate (MPA). Complete response was found in 55% of EC patients and 82% of AH patients (overall CR=67%). During a 3 year follow up period, 12 pregnancies and 7 normal deliveries were achieved.

Gallos et al (54) reported the result of thirty-four observational studies evaluating the rate of regression, relapse, and live birth in 408 women with early-stage endometrial cancer and 151 women with atypical endometrial hyperplasia that received fertility-sparing treatment. In patients with EC there was a 76.2% regression rate, the relapse rate was 40.6%, and live birth rate was 28%. For patients with ACH, the regression rate was 85.6%, a relapse rate of 26%, and a live birth rate of 26.3%. Twenty women were diagnosed with ovarian cancer (concurrent or metastatic) during follow-up (3.6%) and 10 progressed to higher than stage I EC (1.9%), from which 2 women died.

Options for fertility preservation in young patients with endometrial cancer without myometrial invasion are limited to hormonal therapy. DeCruz et al. (55) reported the result of five randomized and 29 phase II studies of hormone interventions in previously untreated patients with grade 1 (G1) or G2 endometrial cancer. The response rate for progestogens and the progression-free survival was in the range of 11-56% and 2.5-14 months,

respectively. Higher response rates were seen in progesterone receptor-positive cases.

In a review of the literature, Ramirez et al (56) reported that in 81 patients with G1 endometrial adenocarcinoma, 76% responded to hormonal treatment with a 12 week median time to response. The recurrence rate was 24% with median time to recurrence of 19 months.

The intrauterine progesterone device has been used in patients with endometrial hyperplasia and early stage endometrial cancer with some success. Levonorgestrel-releasing intrauterine system (LNG-IUS) has been used in the treatment of endometrial hyperplasia. LNG-IUS achieved endometrial regression in 90% of patients by 2 years and 96% within one year. Regression occurred in 92% of non-atypical and 67% of atypical hyperplasia (57, 58).

In a study by Montz et al (59), using a different intrauterine device, complete regression in 75% of patients with stage I G1 endometrial cancer was reported. Within endometrial cancer, well differentiated tumors with positive progesterone receptors are most likely to respond to the treatment with progesterone. However there is some concern that intrauterine progesterone devices may not deliver a uniform dose to the total endometrial cavity or, undetected myometrial invasion becomes sanctuary of this tumor in patients with persistent disease (60).

Ovarian Cancer

Ovarian cancer commonly occurs in postmenopausal women with the vast majority having advanced disease at the time of diagnosis. Ovarian cancer also occurs in young women and there are some patients who might be more appropriate for fertility-sparing surgery. Those include stage IA epithelial ovarian cancers and tumors of low malignant potential, germ cell and sex-cord tumors. These tumors are frequently limited to one ovary and generally present at a very early stage without extra-ovarian metastasis. Although conservative surgery with comprehensive

staging is required, this should not result in sterility of the patient. Types of fertility-sparing surgery may include ovarian cystectomy or unilateral salpingo-oophorectomy with or without hysterectomy, and bilateral salpingo-oophorectomy without hysterectomy. In some patients with high grade immature teratomas, embryonal carcinomas, endodermal sinus tumors, and stage IA grade 3 epithelial ovarian cancers, combination chemotherapy is recommended. Zanetta et al (61) reported reproductive function in 138 of 169 (81%) patients with malignant germ cell tumors in whom fertility-sparing surgery was performed. Of these 81 patients (77%) received chemotherapy. During follow up, 12 untreated and 20 treated patients had total of a 55 pregnancies. Of those, 40 had term pregnancies, 6 had pregnancy termination, and 9 had pregnancy loss. Four fetal malformations were reported: one in a patient who did not receive chemotherapy and 3 in those who did. Tangir et al (62) also reported the reproductive function in patients with malignant germ cell tumors after conservative surgery and chemotherapy. Of 86 patients, fertility-sparing surgery was performed on 64 of them. Of these, 38 patients attempted pregnancy and 29 achieved at least one pregnancy (76%). There was no significant difference between those treated with surgery combined with chemotherapy versus surgery alone. Gershenson et al (63) reported in a series of 132 survivors of malignant germ cell tumors, seventy one patients (53.8%) had fertility-sparing surgery, and 24 patients reported 37 children after cancer treatment was complete.

Ovarian tumors of low malignant potential (LMP) or border line tumors are often diagnosed by incident after ovarian cystectomy or oophorectomy for a suspected benign ovarian tumor. These tumors account for 10-15% of all epithelial ovarian cancer. These patients commonly have a longer survival and very low recurrences rates compared to their invasive counterparts. The 5 year survival of patients with stage I tumors exceeds 95% and makes them excellent candidates for fertility-sparing surgery, as many of them will become pregnant and

carry normal deliveries (64). Morris et al (65) reported the result of their study in 43 patients with borderline ovarian tumors. Recurrence was more frequent in patients who had ovarian cystectomy compared to those treated with oophorectomy alone (58% compared with 23%). After treatment, 29 of 36 patients (81%) retained normal menstrual cycles, and 12 of 24 patients (50%) attempting pregnancy conceived 25 pregnancies. In another study reported by Morice et al (66), 44 patients were treated with conservative management. There were 17 pregnancies, of which 13 occurred in patients with stage I disease and 4 occurred in patients with stage III disease.

A French multi-center study (67) on fertility after conservative treatment of borderline ovarian tumors revealed that among the 360 women, 162 (45%) underwent conservative treatment. Regarding fertility after conservative treatment, 21 of the 65 conservatively treated women (32.3%) became pregnant and had a total of 30 pregnancies.

Patients with stage IA epithelial ovarian cancers who wish to preserve fertility could have conservative surgery because of reported a 5-year survival approaching 90% (68). Patients with a strong family history for ovarian and breast cancer or carry BRCA1, BRCA2 mutations require counseling regarding fertility-sparing surgery and my instead consider prophylactic mastectomy or salpingo-oophorectomy with or without hysterectomy when childbearing is completed. Successful pregnancies have been reported in patients with early stage invasive epithelial ovarian cancer who underwent fertility sparing surgery. Schilder et al (69) reported reproductive outcome on 52 patients with stage I epithelial ovarian cancer: 24 patients attempted pregnancy and 17 (71%) conceived. These 17 patients had 26 term deliveries and 5 had spontaneous pregnancy loss. The estimated survival was 98% at 5 years and 93% at 10 years.

Morice et al (70) published the result of a retrospective multicenter study by two French groups on clinical outcome and fertility-sparing surgery. Of 34 eligible patients with invasive

epithelial ovarian cancer, 30 patients had stage IA disease, 3 had stage IC and one had stage IIA disease. Eleven patients had recurrence: 10 patients had invasive and one had borderline. Adjuvant platinum-based chemotherapy was given to 10 patients (7 stage IA, 3 with stage >IA). Of 24 patients without recurrences, 10 pregnancies occurred in 9 patients. The authors concluded that conservative management could safely be proposed in patients with stage I G1 disease.

Malignant gestational trophoblastic tumors (GTDs)

Malignant GTDs can occur after any type of pregnancy and commonly are treated with chemotherapy for GTD. Oral contraception pills are preferred method over intra uterine device because of increased risk of uterine perforation with IUD (71).

Matsui H et.al (72) reported the overall pregnancy outcome in the first pregnancies of 137 women treated with chemotherapy. There was an increased risk of spontaneous abortion and still birth and repeat mole in pregnancies occurring within 6 months of completing chemotherapy compared to those conceived >12 months (37.5% vs. 10.5%). Similar findings were reported by Braga, et al (73).

Other methods of fertility –preservation

Cryopreservation of oocyte, embryo or ovarian tissue is available for patients who lose complete use of their reproductive organs due to surgery, radiation or chemotherapy.

In oocyte cryopreservation, eggs are harvested for future fertilization and implantation. Initial results with this method were disappointing due to poor oocyte survival, low fertilization and successful pregnancy rates (74). Sonmezer et al (75) reviewed data from 21 studies and found a mean oocyte survival rate of 47%, a mean fertilization rate of 52.5%, and a mean pregnancy rate per thawed oocyte of 1.5%.

However advances in freezing and thawing techniques over the years have resulted in improved oocyte survival rate. For example use of intracytoplasmic sperm injection (ICSI) overcomes zona hardening (76), a frequent cause of implantation failure. Vitrification (ultra-rapid IVF) for embryo freezing that uses high concentration of a cryoprotectant that does not result in ice formation. Not only does this technique produce superior results, but it is easier and less expensive. Yoon et al (77) reported a survival rate of $85.1 \pm 2.9\%$ (320/364,) a fertilization rate of $74.4 \pm 3.5\%$ (168/218), an implantation rate of 14.2% (17/120), and a pregnancy rate of 43.3% (13/30), with vitrification using slush nitrogen.

Cao et al (78) also reported that vitrification was superior to the traditional slow-freezing method, leading to improve oocyte survival rates, fertilization rates and in vitro embryonic development.

Grifo et al (79) reported the result of their study on 22 women who presented for IVF. Patients underwent 23 embryo transfer procedures using thawed, fertilized oocytes. Collected oocytes were cryopreserved either by the slow-freezing or vitrification method. Fourteen women became pregnant; one miscarried and 10 delivered 13 viable infants (9 singleton and 4 twins), for a cumulative delivered /pregnancy rate of 57%. In this cohort ,the oocyte survival rate was 92% with fertility rate of 72%.These result was not significantly different from in age-matched controls using fresh, nonfrozen autologous or donor oocytes during a similar time period.

Rienzi et al (80) conducted an observational longitudinal cohort multicentric study to investigate the efficacy and reproducibility of oocyte cryopreservation outcomes in IVF/ICSI cycles. Oocyte survival from cryopreservation was 84.7%.The rate of fertilization and subsequent development to top-quality embryos of oocytes subjected to ICSI was 75.2 and 48.1%, respectively. In 450 patients there were a total of 128 deliveries (28.4%) with 147 live infants from 929 transferred embryos (15.8%). They concluded that oocyte vitrification was an efficient and reliable approach,

with consistent results.

Embryo cryopreservation is the most established and among the most widely available options for fertility preservation. It is also commonly used in conjunction with in vitro fertilization (IVF) which requires ovarian stimulation, oocyte retrieval, and fertilization.

Embryo cryopreservation has some advantages for those who are interested in preserving fertility. It provides reassurance that the patient will have some potential to conceive and have a child. It also provides some assurance that it has no adverse effect on implantation of embryo or the outcome of pregnancy (81).

The greatest concern of using this method is the high estrogen level required for ovarian stimulation particularly in patients with hormone-sensitive tumors such as endometrial and breast cancer. Another major concern is delay in the initiation of cancer treatment (82). Recent studies showed a successful ovarian stimulation using letrozole and gonadotropins which is associated with reduced estrogen level in patients with endometrial and breast cancer (83)

Oktay et al (84) reported the results of a prospective controlled study comparing ovarian stimulation with tamoxifen and letrozole. Cancer recurrence rate was similar in both groups and did not appear to be increased, regardless of stage of the cancer. The study concluded that the Letrozole-IVF protocol was preferable for ovarian stimulation in those with breast and endometrial cancers because of lower peak estrogen (E2) level.

Due to the large number of primordial follicles ovarian cortical tissue, cryopreservation can be performed without requiring ovarian stimulation and delaying the initiation of cancer treatment. At present, cryopreservation of ovarian tissue is a promising option for the female cancer patient that also offers an excellent chance of fertility preservation. Cryopreservation of ovarian cortical strips has emerged in recent years as an easy, fast, and inexpensive technique (85). In particular it is the preferred method for prepubertal and premenarcheal

patients receiving chemotherapy or pelvic radiation (86, 87).

Orthotopic and heterotopic ovarian transplantation is an additional option in the hands of an experienced surgeon. However major concern of ovarian transplantation is the potential risk transplanted tissue to harbor malignant cells leading to disease recurrence (88, 89).

Additionally, transplantation of ovarian tissue to a different microenvironment may raise concern that the oocyte quality might be compromised due to temperature differences on those sites that may interfere with follicular development and IVF for pregnancy (90).

Natural pregnancy and live birth have been achieved by orthotopic transplantation of both fresh and frozen ovarian tissue where the fallopian tubes are present and patent. As a site of transplantation, peritoneal tissue appears to be superior to subcutaneous tissue due to more effective neovascularization and less follicular loss in the peritoneal tissue. Heterotopic autotransplantation is less invasive; it permits easy access to the transplanted tissue for monitoring follicular development in the event of reoperation and costs less than orthotopic transplantation (91, 92).

Conclusion

Earlier detection and more effective treatment strategies have significantly improved survival in patients with gynecologic cancer. As a result, there has been increasing attention toward patients' quality of Life, including preservation of childbearing potential for young women. Traditionally, the surgical treatment of cervical, endometrial and ovarian cancers had involved the removal of reproductive organs, despite of its impact on fertility regardless of patient's desire. Today, one can offer conservative surgery to a selected young patients affected by early stage gynecologic cancer, not only for planning in future pregnancies but also to maintain psychosexual wellbeing.

Patients should be informed that fertility-sparing

surgery may not always be the right choice for their disease and could significantly impact the rate of disease control or remission. Other fertility preservation options such as oocyte or embryo cryopreservation and ovarian transplantation are also available. As a last resort they might choose adoption as an alternative option.

To maximize patients' understanding about their treatment and future fertility, a multidisciplinary approach and close collaboration between other related disciplines such as gynecologic oncology, maternal-fetal medicine, infertility and reproductive endocrinology, psychology, and social worker is required to ensure a successful outcome in these patients.

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