Commentary

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Controversy on Prophylactic Oophorectomy

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Abstract: The merits of prophylactic oophorectomy at the time of hysterectomy have been debated for many years. The most compelling argument for prophylactic removal of the ovaries has always been the prevention of ovarian cancer (2). Prophylactic oophorectomy has advantages and disadvantages. The actual incidence of cancer in retained ovaries is difficult to estimate. The advantages of prophylactic oophorectomy include the prevention of ovarian cancer, the alleviation of symptoms from residual ovary syndrome and the elimination of the need for reoperation for adnexal disease (2). Disadvantages include surgical castration, which results in the need for hormone replacement, and changes in self-image (2). In addition, when oophorectomy is performed, the germinal, steroidal and hormonal functions of the ovary are lost, but the nonsteroidal functions continue during natural menopause. Prophylactic oophorectomy in premenopausal women induces surgical menopause, requiring estrogen replacement to prevent symptoms and diseases associated with menopause (2). Consideration should be given to prophylactic oophorectomy in younger women undergoing pelvic surgery if they have high risk factors (3). Although prophylactic oophorectomy may not completely eliminate the potential for intra-abdominal carcinomatosis (4), it remains an effective strategy for the prevention of ovarian cancer. The use of this approach is not limited by age. Advances in medical technology, especially in medical genetics, have led to potentially useful techniques for the early detection of epithelial ovarian cancer and high risk women.

Key Words: Ovarian remnant syndrome, hysterectomy, ovarian cancer, prophylactic oophorectomy, ovarian residual syndrome.

Introduction

Ovarian cancer is the fifth leading cause of cancer death in women and the leading form of fatal gynecologic cancer (1). One simple and effective method of prevention is prophylactic oophorectomy in women undergoing hysterectomy for gynecologic indications (2). However, prophylactic oophorectomy has disadvantages as well.

Menopause is that point in time when permenant cessation of menstruation occurs following the loss of ovarian activity. The median age for the onset of perimenopause is 47.5 years.

Only 0.88 percent of women reach menopause at 40-44 years of age. According to Novak, after 50 years of age, only 23% of women show ovulation histologically.

Consequently, patients who undergo bilateral oophorectomy at 40-45 years age lose 10 years of their ovarian function. The proper decision as to whether to retain or remove normal appearing ovaries during hysterectomy has plagued physicians for many years. The following questions need to be addressed:

• After menopause, do the ovaries continue their functions?

• After menopause, should the ovaries remain?

• After 50 years of age is it necessary to perform prophylactic oophorectomy because of the increased rate of ovarian cancer.

To answer some of the questions, we must also take into consideration nonsteroidal ovarian secretions, including the following:

Growth factors

• Epidermal growth factor

• Transforming growth factors a and b

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	The number of patients	Ages (median)	Standard deviation
Surgical menopause	218	47.2	3.6
Natural Menopause	269	49.2	3.9
Total	468		

Table 1. The distribution of patients.

	Cholesterol	Triglyceride	HDL-c	LDL-c	VLDL-c
Surgical M.	249.6	185.8	45.4	163.3	40.8
Natural M.	228.4*	142.6*	59.1*	141.4*	27.9*

Table 2. Comparison of serum lipid profiles in surgical and natural menopause

*P<0.05

	40-45 years of age	46-50 years f age	>50 years of age
Spinal BMD			
Surgical M	0.8504	0.8860	0.8561
Natural M.	0.8545	0.8589*	0.8927
Femoral BMD			
Surgical M.	0.8140	0.8638	0.8941
Natural M.	0.8853	0.8673	0.8862

Table 2. Comparison of serum lipid profiles in surgical and natural menopause

*P<0.05

- Fibroblast growth factor
- Insulin-like growth factors I and II

Glycoprotein/peptide regulator substances

- Inhibin
- GnRH-like substances
- Follistatin
- Relaxin
- Activin
- Renin and angiotensin

Glycoamynoglycans

- Condroitan sulphate
- Heparan sulphate
- Dermatan sulphate

The disadvantages of performing hysterectomy plus bilateral salpingo-oophorectomy include the following:

1. Psycosomatic disorders
2. Genitourinary disorders
3. Ovarian remnant syndrome
4. Premature serious osteoporosis

5. Increased risk of cardiovascular disease due to the negative effect of oophorectomy on serum lipids (2).

Study Reports

Study 1

At the gynecology clinic at Dr. Zekai Tahir Burak Women's Hospital, Basaran et al. conducted a study on ovarian blood-flow doppler and ovarian hormones in women who had undergone hysterectomies without removal of the ovaries. They performed their study on seventy-three patients, forty-three of whom comprised the study group and thirty the control group.

Ovarian artery blood-flow doppler was evaluated preoperatively, and postoperatively at the third month. Ovarian hormone values were evaluated preoperatively, and postoperatively on the fifth day and at the third month.

Preoperative and the postoperative third-month ovarian artery blood flow measurements in the right and left ovaries were not significantly different.

In forty-three patients, estradiol levels were statistically low for the postoperative fifth day. At the postoperative third month we found no difference between the two groups.

In the hysterectomies where the ovaries were preserved, we saw temporary calmness but at the postoperative third month ovarian blood supply was sometimes seen to return to its normal levels. Naturally in the beginning, the blood supply that comes from ligamentum ovarii proprium is lost, and therefore the functional effect is decreased.

Study 2

Oransay et al. performed a study at the menopause clinic at Dr. Zekai Tahir Burak Women's Hospital. They encountered postmenopausal lipid profiles in patients with surgical menopause and natural menopause. Of the four hundred sixty-eight patients included in the study, two hundred eighteen (aged 47.2±3.6 SD) had cesed menstruating because of hysterectomy and bilateral salphingooophorectomy. Two hundred sixty-nine (aged 49.2±3.9SD) had undergone natural menopause. SD. The distribution of patients is shown in Table 1.

In the group whose ovaries were removed, the serum lipids LDL-c, VLDL-c increased rapidly, and there was increased incidence of cardiovascular disease. Estrogen replacement therapy is an effective treatment for these problems in the majority of women. When estrogen therapy is contraindicated, the decision whether or not to remove the ovaries must be made with great care.

Study 3

Oransay et al. performed another study at the menopause clinic at Dr. Zekai Tahir Burak Women's Hospital on the effect of surgical and natural menopause on spinal and femoral bone mineral density.

In Table 3, spinal and femoral bone mineral density over five years are compared.

In patients aged 46 to 50 who had undergone oophorectomy, spinal bone mineral density was found to have decreased significantly.

Study 4

The menopause clinic at Dr. Zekai Tahir Burak Women's Hospital, a study was conducted on eight hundred seventy-seven premenopausal and four thousand twenty postmenopausal patients.

Loss of libido was found in 56.21% of premenopausal and 6.46% of postmenopausal patients.

A 40-year-old patient who has undergone total abdominal hysterectomy plus bilateral salpingo-oophorectomy has the same vaginal dryness as a 60-year-old. Hysterectomy plus oophorectomy at such an age has a negative effect on a patient's psycological and physiological life.

What are the long-term effects of hysterectomy on the ovaries of normal women?

Much is known about menstrual cyclicity (5, 6) and luteal function. (6, 7, 8, 9) in normal women, but little about the ovarian cycles of women who have no uterus. In normal women, a sudden break in a regular pattern of ovulatory menstrual cycles is often the first sign of the ovarian dysfunction which will eventually lead to menopause (10).

Seidenschnur et al. performed a study on four hundred eighty-eight vaginally or abdominally hysterectomized women involving retrospective questionnaires about preoperative anxieties, postoperative psyhcosomatic complaints and disturbances of their vita sexualis (11). Prior to operation and anesthesia, 48.6% of the patients experienced anxiety. Following hysterectomy, 71.9% of the women reported hot flushes and other psychovegetative complaints. Although hot flushes occurred significantly more frequently in patients with salphingo-oophorectomy, these complaints were also reported in one third of the women whose ovaries had not been removed. Libido, cohabitation, frequency and orgasm ability were significantly lower in the group of women who had undergone salpingo-oophorectomy. This is caused by the reduced blood supply to the ovary via branches of the uterine artery. On no account should a prophylactic extirpation of the adnexa be carried out before the age of 50. Hormonal substituion should be done promptly even with patients whose ovaries have not been removed but who suffer from psychosomatic discomforts (11).

At the University of Kiel Obstetrics and Gynecology clinic, Riedel et al. performed a study on patients between 27 and 42 years of age who had been hysterectomized (12). Of one hundred sixty-four answered questionnaires, 39% typical signs of ovarian failure. The average progesterone and estrogen concentrations in the suspected luteal phases were lower than in healthy women in the same age group.

After hysterectomy, ovarian failure phenomena can be excepted to develop to a considerable degree in 30-50% of patients (12). The primary and secondary complications of hysterectomy, whether abdominal or vaginal, are much more pronounced than after laparoscopic tubal sterilization. Even after hysterectomy with both ovaries left intact, ovarian failure phenomena may follow, and these patients should not undergo psychotherapy but rather hormone therapy (12).

The effects of premenopausal hysterectomy on ovarian endocrine function have so far been insufficently

studied, although menopause is not believed to begin earlier in hysterectomized patients than in healthy women (13). Many hysterectomized patients have climacteric symptoms (hot flushes, vertigo) at a younger age than women with a uterus (12, 14). This suggests that ovarian function may cease earlier after hysterectomy, and hormonal replacement therapy might be indicated for such patients (12). Acute luteal progesterone deficiency after hysterectomy in premenopausal women is common but in most cases reversible (12). The reason for the changes in ovarian function may be surgical stress and perhaps the acute changes in ovarian blood supply compensated for later (15). Anaesthetics may have transient effects on gonadotrophin secretion and on the luteal phase (16).

What is the role of the uterus in the associated etiology of premenstrual syndrome (PSM)?

Hysterectomy has been associated with a 66% reduction in mean premenstrual tension (PMT) severity for both psychological and physical symptoms (17).

There is also evidence that in some women PMT is strongly influenced by factors associated with the ovarian hormone cycle (17). According to present knowledge, hysterectomy is not an appropriate treatment for PMT (17). The only clear indication for hysterectomy would be the demonstration that PMT was strongly influenced by factors associated with the uterus (17).

Hysterectomy is the most common major operative procedure (18). Ovarian cancer continues to be one of the most lethal forms of cancer in women, with a five-year survival rate in no more than 40% of patients in the past 50 years (19).

The aging normal ovary presents a dilemma at the time of hysterectomy. Removal of both ovaries prevents ovarian cancer, but castration without estrogen replacement therapy has adverse effects, particularly in younger women (20, 21).

The proper decision as to whether to retain or remove normal appearing ovaries at hysterectomy has plagued physicians for many years. Past practice was routine removal of normal appearing ovaries in women over 40-44 years of age during hysterectomy (21, 22).

Physicians facing this decision should consider epidemiologic risk factors to determine the likelihood of the patient's developing ovarian cancer or osteoporosis (19). Both patient and physician must be aware, particularly if the patient is from a family prone to ovarian cancer, of the possibility of the future development of an intra-abdominal malignancy, usually

multifocal peritoneal carcinoma, which is almost indistinguishable histopathologically from ovarian cancer (4).

The recognition of risk factors associated with ovarian cancer of the epithelial cell type of osteoporosis should be balanced against the fact that there is a 21% survival rate for a woman undergoing hysterectomy with retention of one or both ovaries who later develops invasive ovarian cancer (18).

Over 50 years of age the risk of ovarian cancer is 0.15%. Randall et al. performed a study on 1000 patients who had undergone hysterectomy plus oophorectomy. Only three were found to have had previous cancers, two of endometrial origin and one adenocarcinoma of the cervix. A dictum as to age for the removal or retension of normal-appearing ovaries during hysterectomy is not always possible, and it may be better to individualize each woman's risk factors (23).

The reported reoperation rate on unremoved ovaries ranges from 0.9 to 5.2% (24).

The second operation is usually indicated for cysts, hydrosalpnx or adhesions. 5.1% of the patients suffered from residual ovarian syndrome. Ten years after hysterectomies in which the ovaries are preserved, the risk of developing a benign ovarian tumor is 1%, while the risk of ovarian cancer is 0.1-0.2%. In a study by from Larry Mc Gowans, 80% of the subjects had had abdominal hysterectomies at an average age of 41, and 20% had had vaginal hysterectomies at an average age of 46. The average interval between hysterectomy and discovery of ovarian cancer was 18 years in the abdominal group and 10 years in the vaginal group (18).

Review of the literature reveals a 4.5-14.1% incidence of prior hysterectomy in women developing ovarian cancer (2). Between 1977-1990, seven hundred fifty-five women were evaluated and treated for ovarian cancer at the University of Miami Jackson Memorial Medical Center (2). One simple and effective method of prevention is prophylactic oophorectomy in women undergoing hysterectomy for gynecologic indications. If all the women treated for ovarian cancer at the University of Miami Jackson Memorial Medical Center (2). One simple and effective method of prevention is prophylactic oophorectomy in women undergoing hysterectomy for gynecologic indications. If all the women treated for ovarian cancer at the University of Miami Medical Center during a 14-year period who underwent hysterectomy after age 40 had had their ovaries removed, 60 cases (7.9%) of ovarian cancer would have been prevented (2).

The value of prophylactic oophorectomy at the time of hysterectomy has been debated for many years (2). The most compelling argument for prophylactic removal of the ovaries has always been the prevention of ovarian cancer (2).

Other advantages include alleviation of symptoms of residual ovary syndrome and elimination of the need for reoperation for adnexal disease (2). The risk of a woman developing ovarian cancer is 1.4% (24), and previous studies have reported an incidence of up to 1.2% in retained ovaries (3).

Conversely, 4.5-14.1% of women with ovarian cancer have undergone a previous hysterectomy with preservation of one or both ovaries (2). Unilateral oopherectomy at the time of hysterectomy does not eliminate the risk of ovarian cancer (23). Disadvantages of routine prophylactic oophorectomy include surgical castration, resulting in the need for hormone replacement, and changes in self-image (2).

Prophylactic oophorectomy in premenopausal women induces surgical menopause, requiring estrogen replacement to prevent symptoms, and diseases associated with menopause (vasomotor instability, atrophic changes of the genital tract, osteoporosis and increased incidence of cardiovascular disease) (2). Sterling et al. recommend routine bilateral prophylactic oophorectomy for all women undergoing hysterectomy after the age of 40 (2). Prophylactic oophorectomy would also prevent the need for reoperation for benign adnexal disease in up to 5% of women (3).

Although prophylactic oophorectomy may not completely eliminate the potential for intra-abdominal carcinomatosis, it remains an effective strategy for the prevention of ovarian caancer (4).

Between 1989-1995, one hundred eighty-six patients were evaluated and treated for ovarian pathology at the oncology at Dr. Zekai Tahir Burak Women's Hospital. Five had had previous hysterectomy or hysterectomy+unilateral oophorectomy. Of these five, two had benign and three had malignant pathology. During the same years at this hospital, 1,020 patients who had previously undergone hysterectomy with preservation of one or both ovaries were evaluated and treated at the gynecology department. The incidence of ovarian tumours among these patients was 0.3%, more than half of which (0.19%) had malignant pathology.

Between 42 and 45 years of age, the indications for removal of functioning ovaries during hysterectomy are as follows (18):

1. Peutz-Jeghers syndrome

2. Never having conceived despite the absence of contraception

3. Inital primary malignancy of the breast endometrium or colon which has a high association with subsequent ovarian cancer.

4. Cervical adenocarcinoma

5. Family history of ovarian cancer (the incidence is 12% (5-19))

6. Ovarian abscess, cyst, endometriozis, tumour, infection

Although the majority of ovarian neoplasms occur in the absence of familial or heritable components, many key observations have been made during the past eight years concerning the genetic alterations associated with this disease (25). Both epidemiology and molecular biology may be used to identify a subset of women who are likely to be at increased risk of developing ovarian cancer (25). A number of genes are known to be involved in inherited susceptibility to breast and/or ovarian cancer. In the context of high-risk families, the most important genes are BRCA1 on chromosome 17q, which is associated with a high penetrance of both breast and ovarian cancer and BRCA2 on chromosome 13q, which is associated with a high risk of breast cancer but a lower risk of ovarian cancer (26).

Ovarian Remnant Syndrome

Ovarian remnant syndrome results from residual ovarian tissue after bilateral oophorectomy (27). The syndrome is associated with chronic pelvic pain and is suspected when premenopausal levels of FSH and LH are present in a patient with documented bilateral oopherectomy (27). Pelvic pain with or without a pelvic mass after hysterectomy plus bilateral salpingo-oophorectomy constitutes a diagnostic dilemma (28). Ovarian remnant syndrome results from the incomplete excision of ovarian cortical tissue and can cause a range of symptoms from constant or cyclic pelvic pain to bowel and ureteral obstruction (28). The preoperative diagnosis of ovarian remnant syndrome is made by history and physical examination, with findings confirmed by ultrasound studies and steroid and gonadotropin hormone assays (28). The syndrome is probably more prevalent than is generally recognized, and it may be misdiagnosed by even experienced clinicians (28). Symptoms may occur 1-5 years after the operation. The most effective treatment for ovarian remnant sydrome is surgical excision of the residuum with adequate margins to insure that all active tissue is removed (28, 29).

Medical therapy is empiric, and hormonal manipulation with newer gonadotropin suppressors and analogs may prove effective in this syndrome (30). Laparoscopy is of little value in the diagnosis or treatment of patients who have already undergone multiple operations for pelvic adhesive disease (28). The best way to prevent this complication is to remove the ovaries entirely during the initial operation as well as the pelvic parietal peritoneum, which may harbor ovarian cortical tissue (28).

Brühwiler and Lüscher presented the second published case of ovarian cancer in ovarian remnant syndrome. Only explorative laparotomy confirms the diagnosis (31).

Ovarian Residual Syndrome

Ovarian residual syndrome appears in some women after hysterectomy in which one or both ovaries remain and is characterized by symptoms of lower abdominal and back pain, deep dyspareunia and disturbance of the urinary tract (32). In most instances, gynecologic examination reveals a fixed tender mass near the vaginal cuff. The frequency of this syndrome is 1-3 percent of all total abdominal hysterectomies in which one or both ovaries remain (32). The syndrome is caused by low grade perioophoritis after surgical treatment prior to hysterectomy (32). In a study by Bukowsky et al., symptoms were found to cease in all patients after oophorectomy or ovariopexy (32). This suggests a role for fixating the adnexa in a high position in younger patients who undergo hysterectomy or fixating the ovary in a high position and performing salpingectomy because of tubal involvement in periadnexal adhesions (32).

During the years 1979 to 1983 at the gynecology department at Assaf Harofe Medical Center, T el-Aviv University, Zerifin, six hundred and one hysterectomies were performed. One or both ovaries were left intact in three hundred twenty-nine of the patients who underwent hysterectomies (abdominal+vaginal). On clinical follow-up examination, six patients (1.8%) complained of lower abdominal and back pain and deep dyspareunia (residual ovarian syndrome) (32). When hysterectomy is performed without removal of both ovaries, there may be disadvantages:

1. Benign ovarian cysts
2. Ovarian residual syndrome
3. Ovarian malignancies
4. Premature menopause (18)

Conclusions

Ovarian cancer is the fifth leading cause of cancer death in women and the leading cause of death from gynecologic cancer (1). One simple and effective method of prevention is prophylactic oophorectomy in women undergoing hysterectomy for gynecologic indications (2). Prophylactic oophorectomy has advantages and disadvantages.

The actual incidence of cancer in retained ovaries is difficult to estimate. The risk of woman developing ovarian cancer is 1.4% and previous studies have reported an incidence (24) of up to 1.2% in retained ovaries (3). Consideration should be given to prophylactic oophorectomy in younger women undergoing pelvic surgery if they have high-risk factors (3). Although prophylactic oopherectomy may not completely eliminate the potential for intra-abdominal carcinomatosis (4), it remains an effective strategy for the prevention of ovarian cancer. This approach is not limited by age.

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