

SYSTEMATIC REVIEW

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Oophorosalingectomy during hysterectomy in patients with benign uterine pathology

Ooforosalingectomía durante la histerectomía en pacientes con patología uterina benigna

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ABSTRACT

Hysterectomy is the most common surgical procedure in gynecological practice. During the operation, surgeons are faced with the decision whether or not to preserve the Fallopian tube and ovaries. In many cases, oophorosalingectomy is performed simultaneously with hysterectomy in order to prevent the development of ovarian neoplasms, especially high-grade serous ovarian carcinoma. This decision is important in view of the benefits and risks associated with resection of ovaries that may retain some hormonal activity after natural menopause. The risk of developing malignancies is low in the general population, while potential effects of ovarian cessation include increased cardiovascular, psychological and bone complications. Patients with BRCA1 and BRCA2 mutations may benefit from oophorosalingectomy. However, the oncologic safety of this approach is still under evaluation and is not recommended outside the current protocol. The objective of this review was to evaluate the controversies surrounding oophorosalingectomy during hysterectomy in patients with benign uterine pathology.

Key words: Hysterectomy, Ovarian neoplasms/prevention & control.

RESUMEN

La histerectomía es la intervención quirúrgica más común en la práctica ginecológica. Durante la intervención, los cirujanos enfrentan la decisión de conservar o no las trompas de Falopio y los ovarios. En muchos casos se realiza la ooforosalingectomía en forma simultánea a la histerectomía con el propósito de prevenir la aparición de neoplasias malignas, en especial el carcinoma ovárico seroso de alto grado. Esta decisión es importante ante los beneficios y los riesgos asociados a la resección de los ovarios que pueden conservar alguna actividad hormonal luego de la menopausia natural. El riesgo del desarrollo de neoplasias malignas es bajo en la población general, mientras que los efectos potenciales del cese de la función ovárica incluyen aumento de complicaciones cardiovasculares, psicológicas y óseas. Las pacientes con mutaciones BRCA1 y BRCA2 pueden beneficiarse de la ooforosalingectomía. No obstante, la seguridad de este enfoque está todavía en evaluación y no se recomienda fuera del protocolo actual. El objetivo de esta revisión fue evaluar las controversias sobre la ooforosalingectomía durante la histerectomía en pacientes con patología uterina benigna.

Palabras clave. Histerectomía, Neoplasias ováricas/prevención y control.

INTRODUCTION

Despite the knowledge acquired on the treatment of benign diseases of the female genital organs, surgery continues to play a fundamental role. Progress in the development of conservative treatment of genital and uterine pathologies has led to a decrease in the number of hysterectomies. Nevertheless, it is still a frequent procedure. The frequency varies from 10 surgeries / 10,000 patients in Denmark to 55 interventions / 10,000 patients in the United States. Factors related to the increased frequency are race, educational level, socioeconomic status, medical practice and skill of the treating physicians⁽¹⁾.

The most common indications for hysterectomy are benign pathologies, including benign tumors such as leiomyomas, severe abnormal uterine bleeding unresponsive to minimally invasive pharmacological or surgical treatment. Other indications include postmenopausal bleeding, malignant cervical pathologies, endometriosis and genital prolapse^(2,3).



During surgery, the patient and the surgeons are faced with the difficult decision as to whether or not to preserve the uterine adnexa (ovaries and Fallopian tubes). Until recently, the patient's age was the deciding factor. A large proportion of women over 40 years of age who underwent hysterectomy were eligible for simultaneous oophorosalingectomy⁽²⁾. Today, this decision is made after careful analysis of additional factors that are key to the future of the woman's life and health. These factors include, in addition to the patient's age, the surgical approach (transabdominal or transvaginal) and the macroscopic evaluation of the ovaries during surgery^(2,4).

Hysterectomy with bilateral oophorosalingectomy is performed in about 40% of patients aged 40 to 44 years, in 60% of those aged 45 to 50 years and in 78% of cases older than 50 years^(3,4). The decision to perform oophorosalingectomy has gained interest since the effects of adnexal preservation on some organ and system functions after women reach menopause have become known. These functions cannot be replaced by hormone replacement therapy. Moreover, given the complications and adverse effects of this treatment, the decision whether or not to conserve the ovaries should be made with caution⁽⁴⁾.

During menopause, the ovaries continue to be active endocrine glands that produce small amounts of estrogens and androgens, which are converted to estrone in adipose tissue. Estrone is the main estrogen in women after cessation of reproductive function⁽⁵⁾. In patients undergoing bilateral oophorosalingectomy, androstenedione, testosterone and estrone concentrations are significantly lower than in patients with at least one ovary^(5,6). Exogenous estrogens do not replace the action of endogenous hormones in their entirety⁽¹⁾.

The aim of this review was to evaluate the controversies surrounding the performance of oophorosalingectomy during hysterectomy in patients with benign uterine pathology.

METHODOLOGY OF THE INFORMATION SEARCH

A search of electronic databases of biomedical scientific literature (UpToDate, OvidSP, ScienceDirect, SciELO, and PubMed) was conducted between March and July 2021 to investigate eligi-

ble articles in the last 30 years (1991 to 2021). Database search terms used were: "prophylactic oophorectomy", "oophorosalingectomy", "hysterectomy", "ovarian cancer", "menopause" and "prevention". Case-control studies, cohort studies and systemic reviews in English and Spanish conducted in humans were included. The potential benefits and risks associated with the decision whether or not to preserve uterine adnexa during hysterectomy in patients with benign pathologies were included in this review.

BENEFITS OF OOPHOROSALPINGECTOMY DURING HYSTERECTOMY

There are several arguments in favor of bilateral oophorosalingectomy during hysterectomy, which have been known for several decades and are accepted by most gynecologists and oncologists. The main reported benefit is the decreased risk of developing future ovarian malignancies, although the likelihood of this occurring is generally low⁽⁷⁾. Despite advances in treatment, ovarian cancer continues to be the fifth leading cause of death in women from malignant neoplasms, with no evidence of significant improvement in survival rate over the past 30 years⁽⁸⁾. Each year between 14,000 and 16,000 women die from this disease in the United States alone^(9,10).

Due to the absence of symptomatology in early stages of the disease, it has not been possible to develop a sufficiently effective screening strategy. Ovarian cancer diagnostic methods that include clinical questionnaires of symptomatology, periodic gynecological check-ups, annual ultrasound evaluation, determination of tumor markers, as well as any combination of these methods, do not achieve effective diagnostic and prognostic capacity to establish the risk of developing malignant ovarian neoplasms. On the other hand, they also do not increase the survival rate, which for diagnosed cases only reaches 42% to 44% at 5 years, which is the lowest of all gynecological malignancies⁽¹⁰⁾.

The possibility of developing ovarian malignant neoplasms during a woman's lifetime is only 1.4%. One study showed that, in patients with ovarian cancer, between 4.5% and 18.2% had a history of hysterectomy, so that, from an oncologic point of view, oophorosalingectomy would only protect this group of pa-



tients. On the other hand, some investigators have proposed that only 12% of new cases of ovarian cancer per year could be prevented by bilateral oophorosalingectomy in women over 40 years of age⁽⁹⁾. However, risk factors that may complicate the decision to resect the uterine adnexa should be taken into account. These factors associated with increased risk include early menarche, late menopause, nulliparity, white race, endometriosis, dysmenorrhea, body mass index greater than 30 kg/m² and/or diagnosis of polycystic ovarian syndrome⁽¹¹⁾.

Bilateral oophorosalingectomy also decreases the risk of developing breast cancer, as well as the overall risk of developing malignant tumors, especially in patients operated on before the age of 45. But it increases the risk of developing lung cancer. The causes of this association are not known so far^(2,9).

About 10% of ovarian cancer cases are hereditary⁽¹²⁾. Women at greatest risk are those with a family history or carriers of BRCA-1 and BRCA-2 mutations, who may benefit from oophorosalingectomy. This procedure is recommended for this group of patients, as it reduces the risk of ovarian cancer by 80% to 98% and of death from 10% to 3%. In these cases, it also reduces the risk of developing breast cancer (50%) and death (in case of BRCA-1, 85%, and BRCA-2, 72%)⁽¹³⁻¹⁵⁾. The evidence suggests the need to develop questionnaires that evaluate the risk of ovarian, breast or colorectal cancer in patients undergoing hysterectomy for benign causes, which would facilitate decision-making in patients at risk of cancer⁽¹¹⁾.

Malignant Fallopian tube tumors were considered extremely rare until recently. In recent years several studies have been published that have changed the view of the process of tubal carcinogenesis. There is some evidence that, depending on the histopathological type of cancer, the primary malignant process would begin in the distal portion of the fallopian tubes and not in the ovarian tissue. This is key in the development of the most common type of ovarian cancer: high-grade serous carcinoma, as well as other less common types such as endometrioid and clear cell^(14,15). In view of the above, salpingectomy would reduce the risk of developing ovarian, fallopian tube and peritoneal cancer⁽¹⁶⁾.

There is evidence showing that the risk of ovarian cancer also decreases after unilateral oophorosalingectomy, leaving a functional ovary. This would make it possible to avoid the complications of premature menopause and the abrupt drop in the concentration of ovarian hormones⁽¹⁴⁾. However, the decision to perform this type of procedure remains controversial and more studies are needed to evaluate its benefits and safety.

Hysterectomy also reduces the risk of adnexal malignancies by 36% and this effect lasts for about 15 years⁽¹⁶⁾. This may be due to the decrease in ovarian reserve which accelerates the cessation of gonadal activity, decreases the potential number of ovulations and the transit of potential carcinogens⁽⁹⁾.

In most cases, oophorosalingectomy during hysterectomy does not significantly prolong surgical time (it only requires an additional 10 minutes regardless of the approach) and does not increase the rate of surgical complications (need for reoperation and transfusion of blood products)^(8,17). However, there is evidence that complementing hysterectomy with adnexal resection is associated with an increased risk of intestinal and neighboring organ injury, as well as a higher frequency of infection and cardiac/respiratory complications, compared to adnexal preservation⁽¹⁰⁾.

In patients with endometriosis, chronic pelvic pain and a history of pelvic inflammatory disease, oophorosalingectomy can significantly reduce the likelihood of repeat surgery, which may be associated with extensive and complicated surgical procedures, with increased risk of perioperative complications. The general risk of repeat surgery due to untreated anomalies is 2% to 7% and increases in cases of endometriosis: 13% after 5 years and 23% after 7 years of surgery^(10,18). In these cases, the recommendation would be to perform conservative surgery only in patients under 40 years of age, although each case should be evaluated individually (Figure 1).

RISKS OF OOPHOROSALPINGECTOMY DURING HYSTERECTOMY

The arguments against oophorosalingectomy during hysterectomy are partially supported by evidence indicating a potential increase in overall mortality. This increased mortality is



associated with increased risk of cardiovascular disease, coronary heart disease, and myocardial infarction⁽¹⁹⁾. Cardiovascular disease is the leading cause of death in elderly patients and its occurrence depends on the time since menopause. It has been proposed that it may be a consequence of lipid disorders secondary to endocrine changes related to the cessation of ovarian function.

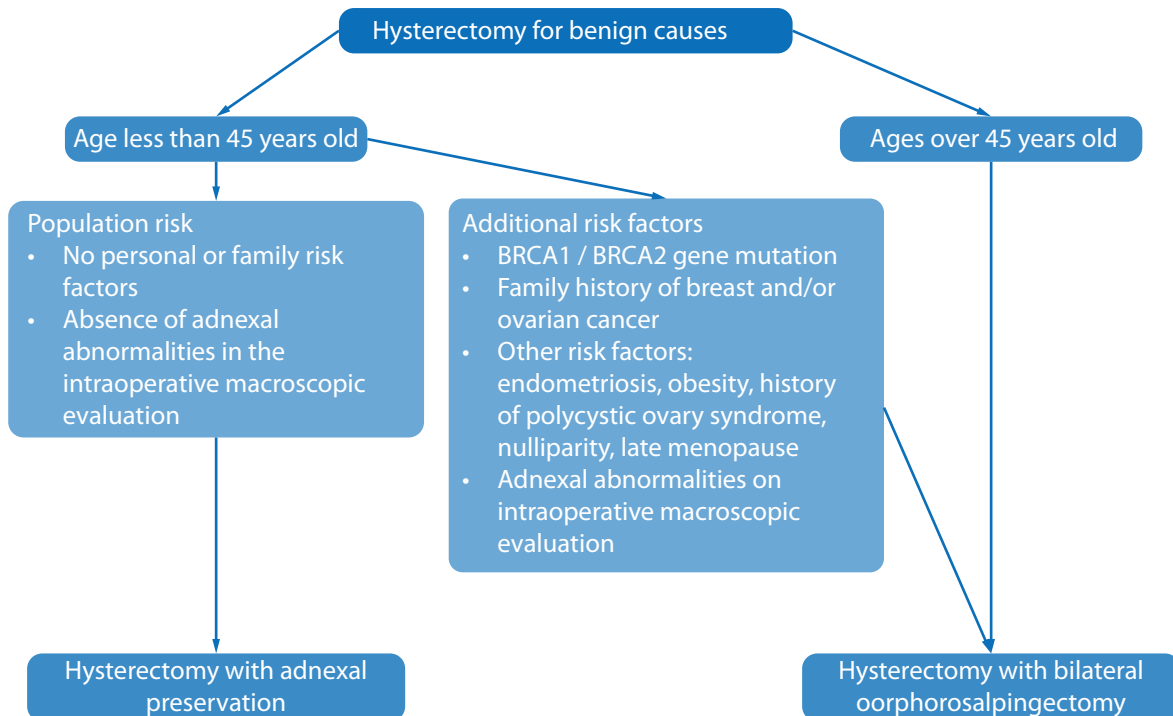
Until now, there has been controversy about the effects of hormone replacement therapy in reversing the consequences of the absence of endogenous hormones. The results of several studies have shown that natural menopause in women over 50 years of age does not increase the risk of cardiovascular disease, atherosclerosis and metabolic syndrome. The increased incidence of these diseases is associated with surgical castration and the risk is inversely proportional to the age at which the procedure was performed⁽¹⁹⁾. The situation is similar in the case of oophorosalingectomy in menopausal women up to 65 years of age, since there is an increased risk of cardiovascular disease in this group of patients⁽¹⁹⁻²¹⁾.

The use of hormone replacement therapy in the 5 years following surgery may reduce or even

eliminate the adverse effects of oophorosalingectomy, independently of other risk factors for cardiovascular disease, including coronary artery disease⁽²²⁾. These results differ from those obtained by other studies that found increased risk of hypertension and coronary artery disease in oophorosalingectomized patients, but with the same number of cardiovascular events. This study also did not confirm an increase in the frequency of osteoporotic fractures or mortality in the group of patients with oophorosalingectomy. However, it is necessary to take into account that the study included younger patients (51 years compared to 63 years) and that the follow-up period was shorter (8 years compared to 24 years), which could produce biases in the results⁽³⁾.

Another undesirable effect of oophorosalingectomy during hysterectomy in premenopausal women is the symptomatology resulting from the abrupt deficiency of ovarian hormones. The symptoms of surgical menopause are more severe, bothersome and of longer duration (8 to 12 years) when compared to those women with natural cessation of gonadal activity. The recommendation in these cases is hormone replacement therapy until 51 years of age to prevent/decrease symptoms⁽²³⁾. Among the symptoms, in addition

FIGURE 1. DIAGRAM OF THE PROCEDURE DURING HYSTERECTOMY FOR THE DECISION OF THE TYPE OF PROCEDURE.





to vasomotor symptoms, are cognitive disorders -dementia, depression and anxiety disorders-, whose severity is related to the age at which the surgery was performed and may not improve with hormone treatment. These symptoms may worsen and affect quality of life for years, even in the case of unilateral oophorosalingectomy⁽⁸⁾. The frequency of occurrence of these symptoms in menopausal women is not well defined⁽²⁴⁾.

Osteoporosis is another disease associated with menopause that increases the risk of fractures, leading to severe disability, impaired mobility and even death. The risk is age-related, but the process accelerates significantly after menopause. In women with early cessation of gonadal function or after surgical menopause, bone mass at older age is lower compared to those with later onset of menopause⁽⁹⁾. After menopause, the persistence of gonadal hormonal activity (production of androgenic hormones with anabolic and bone-forming effects) may reduce the risk of osteoporotic fractures, although the data are contradictory⁽²⁵⁾.

Data from studies on quality of life and sexual function in women undergoing oophorosalingectomy are limited. Some investigators suggest that reduced serum testosterone and androstenedione concentrations lead to decreased libido. Androgens are peripherally converted to estrogens, which has an impact on urogenital tissue maintenance and hydration, atrophy, and incidence of urogenital tract infections^(6,8). However, other reports do not provide conclusive evidence for the association between surgical menopause and decreased quality of life/sexual function^(8,26). Some women report a negative impact on the frequency and quality of sexual intercourse after surgery⁽⁸⁾. Currently, this group of patients is considered as potential candidates for treatment with testosterone combined with estrogen or androgen-only therapy for short periods of time⁽²⁶⁾. However, some research in menopausal women shows deterioration in the quality of sexual life as a consequence of oophorosalingectomy, which persists despite estrogen replacement therapy⁽²⁷⁾.

The most severe effect in women undergoing oophorosalingectomy is cardiovascular disease, which is the most important cause of death in menopausal women, accounting for more than 400,000 deaths per year in the United

States, compared to about 15,000 deaths per year caused by ovarian cancer⁽²⁸⁾. Also important are the neurological effects of premature menopause, such as possible dementia disorders or decreased self-esteem in this group of patients.

CONCLUSIONS

When deciding whether to perform oophorosalingectomy during hysterectomy, it is necessary to carefully evaluate the patient's data and estimate the risk of developing ovarian cancer, as well as the potential risk of cardiovascular, neurological and bone complications in each case. However, in women younger than 65 years, without additional risk factors, the benefits of ovarian preservation appear to outweigh the risks associated with the potential development of malignancies. Therefore, women in this age group, undergoing hysterectomy for benign causes, need further evaluation for possible oophorosalingectomy during hysterectomy. This decision is controversial and needs careful consideration, particularly when discussing with the patient the risks of ovarian conservation and the possible consequences of surgical menopause.

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