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Latest news and trends in what concerns the risk factors of endometrial cancer

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Abstract

Endometrial cancer is the most common neoplasms in the gynaecological sphere, occupying, according to the World Health Organization, the fifth position the world in women's malignant pathology after breast, colon, lung and cervical cancer. The present study aims to present the most essential data appeared so far in the literature on the risk factors involved in the occurrence of endometrial cancer as well as emphasising the particular aspects regarding their reporting in the clinical evaluation. By discovering new methods to prevent risk factors and their implementation at the population level, we can hope for better quality and hope for the survival of endometrial cancer survivors.

Introduction

Endometrial cancer is the most common neoplasms in the gynaecological sphere, occupying, according to the World Health Organization, the fifth position the world in women's malignant pathology after breast, colon, lung and cervical cancer.

At the European level, there is a difference in incidence between the western/central and eastern regions, so that in Western Europe endometrium cancer occupies the fourth position, exceeding the rate of cervical cancer, while in the East European area, it holds the third position after breast and colorectal cancer. The risk of developing endometrial cancer over the lifetime is estimated to be between 1-3%, higher in developed countries from North America and Europe. The explanation for maintaining an increased incidence consists of the multifactorial etiological substrate, with a central element in a continuous epidemic expansion being obesity.

The present study aims to present the most essential data appeared so far in the literature on the risk factors involved in the occurrence of endometrial cancer as well as emphasising the particular aspects regarding their reporting in the clinical evaluation.

Materials and Methods

The research was conducted on the PubMed, ScienceDirect -Scopus and Web of Knowledge platforms using the following search words: ((risk factor) OR epidemiology) AND ((endometrial cancer) OR (endometrial neoplasia) without additional filters, including both reviews as well as original papers.

Results

Histopathological features

There are two types of endometrial neoplasms described (BOOKMAN & al [1]). Type I is encountered in young women in perimenopause, where exposure to estrogen, exogenous or endogenous, the absence of the protective effect of progestins, and conditions such as obesity, nullity, insulin resistance can be documented. Endometrial carcinomas are better differentiated and commonly diagnosed in the early stages, showing a better prognosis. Considered more common (about 80%), they are associated with endometrial hyperplasia and express mutations in the PTEN suppressor tumour gene, oncogene K ras, genes involved in DNA repair (mismatch repair genes) and are frequently positive for the estrogen receptor and progesterone (MATIAS-GUIU & al [2]) (see Table 1).

Type II endometrial cancer has an unfavourable prognosis and is encountered in older ages. It is less differentiated, unrelated to estrogen stimulation, and diagnosis is made in more advanced stages. It has also been observed that from a histopathological point of view adenocarcinomas or cystadenocarcinomas are frequent, severe, papillary or glandular as well as clear, mucous, or other types (BOOKMAN & al [1]). At a molecular level, mutations of the p53 tumour suppressor gene and the HER2 / neu gene were recorded (RISINGER & al [3]) (see Table 1).

Table 1 - Percentage of endometrial cancer types depending on the immunohistochemical profile

Immunohistochemical profile	**Type I Endometrial Cancer**	**Type II Endometrial Cancer**
DNA repairing genes anomalies	*7%–25%*	*rare*
K ras Oncogene	26%	*2%*
HER2/neu		*9%–30%*
PTEN	*34%-83%*	
p53	*16%-40%*	*71%–85%*

Risk factors. In what concerns the occurrence of endometrial cancer, some risk factors in a continuous change regarding incidence are cited in the literature (VOICULESCU & al [4]). Although most endometrial cancers are associated with prolonged exposure to estrogen stimuli in the absence of a progestative balancing, an important role in oncogenesis is played by the interaction between various other environmental factors and the individual predisposition (ANTONOVICI & al [5]) (see Table 2).

Table 2 – Risk factors for endometrial cancer

Modified after RA et al. American Cancer Society Guidelines for Early Endometrial Cancer Detection: Update 2001 (SMITH & al [6])

Risk factors	Relative Risk
Obesity	2-11
Nulliparity	2-3
Tardive Menopause	2.4 (above 52 years)
Unbalanced Estrogen by Progestatives	1.6-2
Tamoxifen	1.7-2.5
Diabetes Mellitus	1.3-2.7
Arterial Hypertension	1.2-2.1
High-fat diet	1.1-2
Non-polyposis hereditary colorectal cancer	39-60% throughout life.

Metabolic cancer and endometrial cancer. The metabolic syndrome comprises a group of potential risk factors in various types of cancer(including endometrial cancer) such as obesity, hypertension, insulin resistance, diabetes and dyslipidemia (SMITH & al [6]; NICOLAE & al [7]). The pathophysiological link between metabolic syndrome and endometrial cancer is primarily associated with abdominal obesity, especially white adipose tissue. Adipose tissue is a complex endocrine organ that secretes a variety of adipokines including adiponectin, leptin, resistin, and visfatin, which are essential in tissue processes, namely insulin resistance, fatty acid oxidation, inflammation and immunity.

Obesity. Obesity (defined by a BMI over 30 kg / m2) is considered a standard risk factor associated with endometrial cancer (FRIEDENREICH & al [8]) and may contribute to an increase up to 40% in its incidence. So far it is uncertain if linear distribution exists between different degrees of obesity and the risk of developing endometrial cancer. Some studies consider that obesity is associated with endometrial cancers of favourable prognosis and a high degree of differentiation. Also, obesity is related to the presence of early forms of malignancy, but not all of this can be documented (RENEHAN & al [9]).

Most studies that tracked this topic note that anthropometric measurements were made at or near the diagnosis so that the risk-sickness-obesity-endometrial cancer relationship cannot be established as one-way. Also, obesity has been defined as only the body mass index, but central obesity can be an essential component because abdominal fat is considered to be more metabolically active compared to that distributed in other areas (BARRETT & al [10]). Also, are differences in the distribution of adipose tissue that may vary between populations or ethnicities, as well as between risk factors that participate alongside obesity in the development of endometrial cancer in premenopausal women as compared to menopausal women (ZHANG& al [11]).

In the postmenopausal period, the ovarian production of estrogen stops, while in the adipose tissue there is a permanent conversion of androgen into estrogen. An increased level of unprocessed endogenous estrogen unbalanced by progesterone induces endometrial changes. Also, serum levels of sex hormone binding proteins decrease, the amount of endogenous estrogen available being higher. Thus, the proliferation of endometrial tissue increases and numerous somatic mutations and DNA replication errors occur with the development of endometrial cancer. Unlike this mechanism, in premenopausal women, obesity may increase the risk of endometrial cancer by inducing anovulatory cycles and progesterone deficits (IARC WORKING GROUP [12]).

Insulin resistance. Obesity, type II diabetes and polycystic ovary syndrome can be grouped in pathologies associated with insulin resistance and are an important risk factor for endometrial cancer. Insulin resistance, defined by the decrease in tissue sensitivity to insulin, causes an increase in serum glucose levels. Counteracting this change, pancreatic beta cells secrete insulin with the appearance of hyperinsulinism. This prediabetic status plays an essential role in the development and progression of certain types of cancers, including endometrial cancer and breast, colorectal, prostate and pancreatic cancer . Some studies consider hyperinsulinism a risk factor independent of estrogen (AKHMEDKHANIV & al [13]). Another study highlights that hyperinsulinism has been implicated in the development of endometrial cancer in normoponderal women. Also, insulin resistance appears to correlate directly with the stage of the disease as well as local and regional endometrial cancer dissemination (GUNTER & al [14]).

The increased insulin level secondary to insulin resistance is a risk factor for endometrial cancer through multiple mechanisms. Insulin is defined as a growth factor that exerts its effects on different types of cells by attaching to specific or non-specific receptors. Malignant endometrial cells express surface-specific insulin receptors, favouring attachment of insulin proliferation and inhibiting cellular apoptosis in a dose and time-dependent manner. The insulin-specific receptor and the IGF 1 receptor (Insulin Growth Factor 1) are mostly similar, insulin being attached to both receptors (BERSTEIN & al [15]). In vitro studies demonstrate that insulin, by attaching itself to the IGF1 receptor increases the circulating IGF1 level with a mitogenic role in the development of endometrial cancer. An analysis of 17 in vivo prospective studies suggest a positive association between increased circulating levels of IGF1 in breast cancer, but not in the case of endometrial cancer (KATO& al [16]). On this line, studies are showing an inverse association, no association or even a positive association (LACEY & al [17]). To accurately determine the correlation between increased levels of circulating IGF 1 and endometrial cancer, further studies are needed.

The mechanism by which insulin resistance favours the development of endometrial cancer is mediated by some molecules, such as inflammatory agents, adipokines, and excess of androgenic hormones.Inflammation induces insulin resistance by inhibiting the insulin-mediated signalling pathway and favouring the release of free fatty acids from adipose tissue. In this process, the macrophages recruited into the adipose tissue of monocyte chemoattractant protein (MCP-1) (WAKASMANSKI & al [18]) or hypoxia are secreting tumour necrosis factor (TNF alpha), which induces lipolysis and inhibits insulin-mediated signalling (XU & al [19]). Increasing the level of free fatty acids in the adipose tissue, as the occurrence of reactive oxygen species, inhibits the insulin-mediated signalling pathway, with the tendency for self-perpetuation of insulin resistance. In response to the release of TNF alpha, macrophages from IL-6 secreting adipose tissue appear to contribute to maintaining insulin resistance through an insufficiently

known mechanism. It has been observed that TNF alpha and IL-6 increase estrogen production in both healthy cells and cancer cells, as shown in breast cancer (HOTAMISIGIL & al [20]). A prospective study, including postmenopausal women without hormone replacement therapy, showed that the reactive C protein level, an IL-6 induced biomarker, was a risk factor for endometrial cancer. The risk can be partly explained by hyperinsulinemic status and increased estradiol levels. Also, inflammation characterised by increased levels of TNF alpha, estradiol and hyperinsulinemia may be involved in the association between obesity and endometrial cancer. At present, there is no association between endometrial cancer and TNF alpha or IL-6, suggesting that these proinflammatory cytokines interfere with local action (PUROHIT & al [21]).

Adipose tissue, the insulin-susceptible head of inflammation, is also an important source of aromatase, the enzyme involved in androgen conversion to estrogen (WANG & al [22]). By increasing the level of circulating estrogens unbalanced by progesterone, the development of endometrial cancer is favoured, according to the above-stated theories. Adipokines, like adiponectin, leptin and plasminogen 1 activator inhibitor (PAI-1) play an important role in the occurrence of insulin resistance and endometrial cancer. Adiponectin reduces the serum glucose concentration by activating kinases (AMP-kinase, PPAR alpha) and favouring hyperinsulinemic status. Some studies suggest a robust correlation between adiponectin and endometrial cancer, the two adiponectin receptor adiponectin, adipo-R1 and adipo-R2 being expressed in normal and stromal endometrial and stromal endometrial cells (LONGSCOPE & al [23]). Moreover, adiponectin treatment induces apoptosis of specific receptors in the endometrial tumour test, highlighting the protective effect of adiponectin in endometrial cancer (TAKEMURA & al [24]). Insulin favours the development of endometrial cancer in less direct ways, also. It inhibits the synthesis of sex hormone binding globulin, which generally interferes with the regulation of sex hormone activity. Thus, the increase in insulin level secondary to insulin resistance is associated with the rise in serum sex hormones. It is important to underline that insulin favours the synthesis of androgenic hormones in the ovary. Studies show that obese women have elevated levels of estradiol and testosterone and low sex hormone binding proteins. Androgenic hormone growth provides a substrate for peripheral conversion to estrogen, potentially harmful mechanism especially in postmenopausal women. In premenopausal women, elevation of androgenic hormone levels induces anovulation and insufficient progesterone to counterbalance estrogen-induced proliferation of endometrial levels. In the same way, women with the polycystic ovarian syndrome have a high risk of developing endometrial cancer (CONG & al [25]). Prolactin is a peptide with many effects in the body, including regulation of sex hormone levels, while thyroid stimulating hormone (TSH) is essential in achieving the daily metabolic functions of any human body. Hyperprolactinemia and thyroid disease can cause menstrual disorders. Also, prolactin and TSH can play an important role in endometrial cancer. A study that followed serum biomarkers in endometrial cancer patients revealed that of 64 of the biomarkers followed, prolactin was significantly different between cancer patients and healthy patients with a 98.3% and 98% specificity (NAVARATNARAJAH & al [26]).

Treatment of insulin resistance and endometrial cancer

In the treatment of type II diabetes various antiglycemic agents, including Metformin, are used. Metformin is an antiglicemic biguanide that lowers glucose production, reduces glucose uptake and increases muscle glucose metabolism through an insulin-mediated mechanism. Therefore, less insulin is required to regulate glucose levels, and insulin resistance is improved by a mechanism involving Mitogen-Activated Protein Kinase (AMPK) kinase (YURKOVETSKY &

al [27]). In addition to the effects of Type II diabetes, more and more studies have shown that metformin has anti-cancer results (SCHIMMACK & al [28]). A review conducted in 2010 by Gonzalez-Angulo et al., shows that metformin is a beneficial option in the treatment of breast cancer (GONZALEZ-ANGULO & al [29]), but evidence of its usefulness in endometrial cancer is limited (CANTRELL & al [30]). On the same line, a case reported in 2003 of a 37-year-old patient diagnosed with endometrial hyperplasia, a precancerous lesion of endometrial cancer, revealed the regression of lesions after only one month of treatment with metformin. In another series of cases, metformin was used together with estriol, progesterone, and ergocryptine in the treatment of endometrial cancer (stage IA, type I) in 5 other women diagnosed with this disease. After six months of treatment and two years of follow-up, the results of the histopathological examination revealed a normal aspect of the endometrium (STANOSZ & al [31]). Although metformin was not the only drug used in these cases, it should be considered to have at least a partial role in the result and require further studies.

Exogenous insulin administration is another way of treatment in patients with type II diabetes. Several studies associate insulin administration with an increased risk of insulin resistance associated colorectal cancer (CHUNG & al [32]). Consider these aspects, and it is necessary to study the relationship between exogenous insulin and endometrial cancer.

Diet. Among food habits, it is considered that a high-fat diet increases the risk of endometrial cancer by favouring the pathologies involved in the above-mentioned metabolic syndrome, while the consumption of vegetals and fish decreases this risk. Some prospective studies consider that there is a definite association between sugar consumption and endometrial cancer and a reverse one regarding coffee consumption (GAVRILYUK & al [33]). On the other hand, another risk factor, regarding diet, is the consumption of products of animal origin, especially the consumption of red meat in excess. The use of dairy products is also incriminated in the occurrence of endometrial cancer due to the content of estrogens that these products contain (GOODMAN & al [34]). The results of these studies are not statistically significant for parameters to be considered or not as risk factors.

Particular attention should be paid to vitamin D deficiency. Endometrial cancer is one of 19 types of cancer that has increased sensitivity for this vitamin-hormone. In several studies, the relationship between exposure to UVB and low risk of endometrial cancer (indirectly correlated with an increased level of vitamin D) was established. These studies compared the risk of endometrial cancer in women with vitamin D levels between 40-60 ng/ml and those with low levels below 20 ng/ml. It was found that the risk of developing breast, colon and rectum cancer decreased between 15-25% and endometrial by 20-40% (EPSTEIN & al [35]). Dairy products consumed in excess would have a negative impact on the risk of endometrial cancer. However, the association of supplementation with vitamin D and calcium appears to be beneficial, so at least suggests the Lappe study, where it is recommended to supplement with at least 1000 mg of calcium daily (LAPPE & al [36]).

Family history. Approximately 10% of endometrial cancers are considered to be familial and occur most frequently as an extracolonic manifestation of non-polyposis hereditary colorectal cancer (HNPCC). Non-polyposis hereditary colorectal cancer is a syndrome determined by a germinal line abnormality encountered in one of five DNA repair genes, with the occurrence of the instability in chromosomal microsatellites. Women with HNPCC have a ten times higher risk of life-threatening endometrial cancer compared to the general population, the risk being even higher than that of colorectal cancer (42% endometrial cancer versus 30% colorectal cancer risk)

(NELSON & al [37]). In most cases, endometrial cancer occurs sporadically (90%). Also, endometrial cancer may be secondary neoplasia, especially after breast, ovarian, colon cancer (PETTERSSON & al [38]).

Early Menarha and Late Menopause. In 1986, Pettersson et al. was the first researcher to note that the onset of menstruation, or the number of ovulatory cycles, are significant risk factors for endometrial cancer (KEY & al [39]). Menarha, the first menstruation, is associated with the initiation of ovulation, respectively with elevated levels of endogenous and lowered progesterone estrogen, as well as the onset of hormonal changes in puberty. There is a relationship of inverse proportionality between the more advanced age of menarche and the risk of endometrial cancer, based on the theory that estrogen exposure in the absence of progesterone causes increased mitotic activity, DNA replication and somatic mutations of endometrial cells associated with malignant transformation. Thus, as menstrual cycles are fewer, the ovulation, which is characterised by endogenous estrogen exposure under progesterone deficiency, are less likely to endanger the lower endometrial cancer (DOSSUS & al [40]). The same mechanism in the development of endometrial cancer, namely endogenous estrogen exposure over an extended period, highlights another risk factor, namely, late menopause, usually after 50 years (HENDERSON & al [41]). The extended period between menarha and menopause is also an important risk factor, even for the same pathogenic considerations.

Parity. Multiparous women are considered to have a 20-40% lower risk of developing endometrial cancer than nulliparous ones (GHEORGHISAN-GALATEANU & al [42]). The mechanism is not fully known, but are some hypotheses that have been proposed for this. Increased progesterone levels during pregnancy can inhibit estrogen-dependent endometrial proliferation and favour differentiation and apoptosis of endometrial cells (JENSEN & al [43]). Also, vaginal birth or involution of the uterus postpartum facilitates the transport of precancerous and cancerous cells into the superficial layers of the endometrium and their subsequent elimination. In uniparous women, the 20-49 age group finds a significant decrease in the risk of endometrial cancer as the pregnancy is at a more advanced age, while the same results have not been recorded in patients over 50 years. As for multiparous women, there is no association between the age of first birth and the risk of endometrial cancer, but as the age of last birth is more advanced, the risk of endometrial cancer decreases. In the same manner, some causes of primary infertility can also contribute to the increased risk of developing endometrial cancer in nulliparous women (SPEERT & al [44]).
These mechanisms, supposed to have a protective role for multiparous patients, take place during the fertile period, but most endometrial cancers manifest later on with the onset of menopause. Therefore, multiparity can contribute to lowering the risk of endometrial cancer, especially in premenopause, and then by associating with other risk factors such as the use of oral contraceptives, menopause, obesity and postmenopausal hormone replacement therapy (ROTTERDAN ESHRE & al [45]).

Infertility. Endometrial cancer was associated with infertility in various studies (PILLARY & al [46]). Among the most common causes of infertility, we can find ovulatory dysfunction, such as polycystic ovary syndrome and its association with endometrial cancer has been reported in several studies. The polycystic ovarian syndrome is characterised according to the Rotterdam criteria (2003) by the presence of two or more anovulatory cycles, clinical signs of hyperandrogenism and polychronic ovaries highlighted ultrasound (MIANNAY& al [47];

MODAN & al [48]). Periods accompanied by anovulatory cycles involve a release of unbalanced progesterone estrogen, resulting in changes in the structure of endometrial cells, particularly in young women. Luteinized hormone hypersecretion, chronic hyperinsulinemia and elevated levels of IGF 1 insulin growth factor are additional risk factors for endometrial cancer (CHEGINI & al [49]).

The association between polycystic ovary syndrome and endometrial cancer has been appreciated since 1949 by Speert et al. (SPEERT & al [44]). Currently, this association is not statistically supported by sufficient data. A longitudinal study involving 750 women with the polycystic ovarian syndrome has shown no higher mortality due to endometrial cancer and they had a better prognostic, based on the higher degree of tumour differentiation. There is also data that contradicts the previous premise, so a recent Pillar et al. 2006 study highlights the presence of the Cyclin D1 proto-oncogene, particularly in endometrial cancers that associate polycystic ovary syndrome (SOPER & al [50]). In the same survey, Polycystic Ovary Syndrome is present in similar fashion in the two compared groups: women with endometrial cancer and women with other benign pathologies. In the age group below 50 years, polycystic ovary syndrome is more commonly associated with endometrial cancer (ZUCCHETTO & al [51]).

Ovarian stimulation. Ovarian stimulation treatment includes drugs that promote the release of pituitary gonadotrophins (FSH / LH) to promote ovulation. In 1994, Miannay et al. first reported the occurrence of 3 endometrial adenomatous hyperplasias in patients treated with fertility stimulants (BERGFELDT & al [52]). Other studies have not demonstrated this association for a follow-up period of up to 10 years. Modan et al. (in 1998) studied the effects of ovarian stimulation medication on the endometrium. Following treatment with Clomiphene, a selective estrogen receptor modulator, or Clomiphene and menopausal menopause (menotropin) over a period of 10 years, five times more endometrial cancers have been described than expected. The authors also report that neoplasia occurred in patients with normal estrogen levels but having a progesterone deficiency (CGP [53]).
Studies published to date suggest an increase in the risk of endometrial cancer in infertile women with ovarian stimulation treatment, and medication may speed up the onset of neoplasia. The lack of statistically significant information on other cofactors associated with ovarian stimulation (infertility, parity) and the short follow-up of studies limits the consideration of ovarian stimulation as a risk factor for endometrial cancer.

Other gynaecological pathologies. Leiomyomas (polyphibromatos uterus) and endometriosis are gynaecological pathologies that may increase the risk of developing endometrial cancer by associating with pelvic inflammation (CGP [53]) and estrogen excess (ZUCCHETTO & al [51]). In spite of some 17 studies that followed this correlation, information from the literature does not provide sufficient arguments for characterising the relationship between endometriosis, uterine fibroids and endometrial cancer. Most studies were conducted on a small number of cases, without the possibility of excluding other cofactors, and the follow-up period was a short one. While the history of endometriosis increases the risk of endometrial cancer or clear cells cancer, the endometriosis-endometrial cancer relationship is imprecisely defined (CGP [53]). In the literature, single cases of concomitant association of endometrial cancer and endometriosis are presented, without being able to establish the chronology of pathology or to exclude other risk factors. Concerning uterine fibroids, the most reliable association with endometrial cancer

belongs to one case of a woman diagnosed with a fibroma uterus one year before endometrial neoplasia.

Also, although cystic ovarian pathology and pelvic inflammatory disease have been correlated with the risk of ovarian cancer, there is little data to support the association with the endometrial (BARAKAT & al [54]).

Tamoxifen therapy. Tamoxifen, a non-steroidal anti-estrogen-selective estrogen receptor modulator (SERM), is widely used in the adjuvant treatment of breast cancer, metastatic breast cancer treatment, and reduction of breast cancer incidence in high-risk women. Although the primary therapeutic effect derives from the anti-estrogenic properties, Tamoxifen also has modest estrogenic activity. In standard doses, Tamoxifen may be associated with endometrial proliferation, hyperplasia, endometrial polyps, invasive carcinoma and uterine sarcoma (BARAKAT & al [54]).
Most studies consider that the risk of endometrial cancer in patients receiving Tamoxifen is 2-3 times higher than in the general population. The risk is dependent on the dose and duration of treatment. Studies suggest that the tumour stage, differentiation, histology and tumour biology that develop in Tamoxifen-treated patients (20 mg/dl) do not differ from the reported cases in the general population. However, some studies indicate the emergence of aggressive tumours at high doses of Tamoxifen (40 mg/dl) (WEISS & al [55]).. The current recommendations of the international guidelines consider the administration of Tamoxifen at doses of 20 mg/dl, even in the long term (up to 10 years), and periodic monitoring of patients (clinically and paraclinical) to decontaminate the endometrial changes in an incipient stage and then stop treatment.

Hormonal replacement therapy. Since the 1960s, estrogen replacement therapy has begun to be administered to relieve menopausal symptoms and was subsequently routinely administered for postmenopausal prevention of osteoporosis and cardiovascular disease (GREEN & al [56]). In the 1970s, the first cases of endometrial cancer occurred in patients undergoing substitution treatment; the studies conducted confirming the increase in the risk of endometrial cancer by 2 to 10 times the overall population, depending on the duration of administration. The highest risk was associated with an over ten year administration period, but it is uncertain if this risk continues to increase after 15 years of use. In most studies, the risk is manifested after at least 2-3 years of administration. A significant part of studies have shown that stopping hormone replacement therapy is associated with a rapid decrease in risk, although some studies believe that there is a significant risk of endometrial cancer that persists for a period of 10 or even longer many years after (GREEN & al [56]).
To counteract the possible effects of estrogen therapy on the endometrium, synthetic progesterone administered continuously (over 25 days/month) or sequentially (under 25 days/month) is added to the treatment. It observed that the risk of endometrial cancer remains as high when progesterone is administered less than ten days/month, as it does not deliver . It is not known to date whether this form of treatment completely removes the risk of endometrial cancer. Short-term and long-term follow-up studies indicate the possibility of endometrial cancer in association with other risk factors, particularly obesity (CROSBIE & al [57]).

Conclusions

Endometrial cancer maintains a high incidence in the entire world, with risk factors being continually expanding. Obesity, with an epidemic evolution, requires the implementation of measures to combat at the population level, representing not only a significant factor in the development of endometrial cancer but also many other comorbidities that decrease the quality of life. Prevention strategies and early detection of endometrial cancer can significantly reduce the incidence and mortality of the disease. By discovering new methods to prevent risk factors and their implementation at the population level, we can hope for better quality and hope for the survival of endometrial cancer survivors.

Conflict of interest. The authors declare that they have no competing interests. All data can be accessed by e-mailing the correspondence author.

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