Analele Științifice ale Universității „Alexandru Ioan Cuza”, Secțiunea Genetică și Biologie Moleculară
TOM XVIII, Fascicula 1, 2017

A RETROSPECTIVE SEQUENTIAL STUDY OF THE RISK FACTORS AND THE INCIDENCE OF THE ENDOMETRIAL CANCER

MIHAI-VLAD VĂLU[1*], OVIDIU TOMA[1]

Received: 23 November 2016 / Revised: 05 December 2016 / Accepted: 08 March 2017 / Published: 4 April 2017

Keywords: endometrial cancer, age at diagnosis, risk factors, tamoxifen, demographic data
Abstract: Uterine body cancer represents the uncontrolled and chaotic growth of some abnormal cells from the womb lining, being thus included in the category of gynaecologic cancers. The main risk factors for endometrial cancer are: ageing, nutritional imbalances that lead to obesity, diabetes, high blood pressure, nulliparity. This article is made up of a retrospective study for 5 months, including the patients diagnosed with endometrium cancer.

INTRODUCTION

Endometrial cancer is a type of cancer that begins in the uterus. The uterus is the hollow, pear-shaped pelvic organ in women where fetal development occurs. Endometrial cancer begins in the layer of cells that form the lining (endometrium) of the uterus. Endometrial cancer is sometimes called uterine cancer. Other types of cancer can form in the uterus, including uterine sarcoma, but they are much less common than endometrial cancer (Jan V. Bokhman., 2004).

Endometrial cancer is often detected at an early stage because it frequently produces abnormal vaginal bleeding, which prompts women to see their doctors. If endometrial cancer is discovered early, removing the uterus surgically often cures endometrial cancer. Each year, endometrial cancer develops in about 142 000 women worldwide, and an estimated 42 000 women die from this cancer. Worldwide, endometrial cancer is the seventh most common malignant disorder, but incidence varies among regions (Parkin DM et al., 1999). In less developed countries, risk factors are less common and endometrial cancer is rare, although specific mortality is higher. The incidence is ten times higher in North America and Europe than in less developed countries; in these regions, this cancer is the commonest of the female genital tract and the fourth commonest site after breast, lung, and colorectal cancers. The incidence is rising as life expectancy increases. Age-adjusted incidence is increasing even when corrected for hysterectomy (Frederic Amant et al., 2005). The rise has been associated with an epidemic of obesity and physical inactivity. As an example, in the year 2000 in the Flemish region of Belgium, with a female population of just over 3 million, 743 women were diagnosed as having endometrial cancer (Smith RA et al., 2003; Parkin DM et al., 1999).

In Flanders, this cancer is the third commonest in the female population, after breast and colon cancers. The incidence of 24·7 per 100 000 women in this region is much the same as that in other western European countries. The incidences per 100 000 women in the same region for cervical, ovarian, and breast cancers were 13·6, 20·8, and 161·9 (Jemal A et al., 2005) The cumulative risk of endometrial cancer up to age 75 years has been estimated as 1·7%. In North America, endometrial cancer is the eighth commonest cause of death from cancer in the female population (Van Eycken E et al., 2003). Each year, in Europe, an estimated 9000 women die of endometrial cancer. Substantial decreases in the incidence and mortality of endometrial cancer are unlikely in the next few years, because early detection and treatment modalities have not had a major influence on mortality (Smith RA et al., 2003).

The typical age-incidence curve for endometrial cancer shows that most cases are diagnosed after the menopause, with the highest incidence around the seventh decade of life (Frederic Amant et al., 2005). The mean age at diagnosis is 61 years; however, 5-30% of women are aged younger than 50 years at the time of diagnosis (Soliman PT et al., 2005).

The etiology of the endometrial carcinoma is not fully understood. Most cases appear sporadically whereas about 10% are hereditary. Chief among the latter is the autosomal dominantly inherited hereditary non-polyposis colorectal cancer (HNPCC). The risk of developing endometrial cancer is believed to be ten times higher for women carrying the gene compared to the general population (Dunlop MG et al., 1997). The likelihood of a synchronous or metachronous development of endometrial carcinomas is, however, higher for patients with breast, ovarian, and non-hereditary colorectal cancer (Baufeld K et al., 2000).

Within the current concept of multi-step progression of normal cells to malignancy, recent molecular work has identified several gene alterations important for tumor development. In summary, mutations and amplifications of oncogenes K-ras and HER2/neu, mutations or deletions of tumor suppressor genes p53, p21, p16, and pTEN/MMAC1 as well as impaired DNA repair functions through mutations of hMLH1, hMSH2, and hMSH6 have been connected with the development of endometrial carcinomas (Salvesen HB et al., 2002).

Environmental, dietary and hormonal factors as well as an aging female population have been attributed to an observed increase of endometrial carcinomas over the past few years. Epidemiologic studies have observed correlations between the incidence of endometrial cancer and the usage of estrogens, especially when applied to alleviate perimenopausal and postmenopausal symptoms. Therefore, it appears that estrogen plays a key role in the development and progression of endometrial carcinomas (Karsten Münsted et al., 2004).

MATERIAL AND METHODS

This article is made up of a retrospective study for 5 months, including the patients diagnosed with endometrium cancer, hospitalized in the Radiotherapy Clinic from within the Regional Institute of Oncology – Iasi, during the period 01.07.2015 – 01.12.2015, in which I assessed the incidence of different risk factors. The data collection was done based on the medical record available in the hospital's archive. There were taken into consideration the patients from whom there could be extracted from the medical record the following information: personal data (age, environment, risk factors).

There were excluded the cases insufficiently researched, and the incomplete consultation sheets. After the selection process, resulted a lot of 60 cases who were present at the Oncology Regional Institute from Iasi (IRO Iasi), with an observation of endometrial cancer All the patients agreed upon studying the consultation sheets, and using them in an academic and scientific purpose.

Results and discussions

Demographic data

The distribution according to the residence

The origin environment of the female patients with uterine body cancer (CCU) hospitalized in the clinic is predominantly urban, most likely, because of the different lifestyle of the female patients from the two lifestyles (Figure 1). For example, nutrition represents a factor after which we can make certain distinctions between the two environments. Nutrition in urban environment is much more diversified in comparison to that of the rural area thus favouring the appearance of obesity. Also, a sedentary life can be another cause of obesity appearance, much more representative for urban environment than for the rural one.

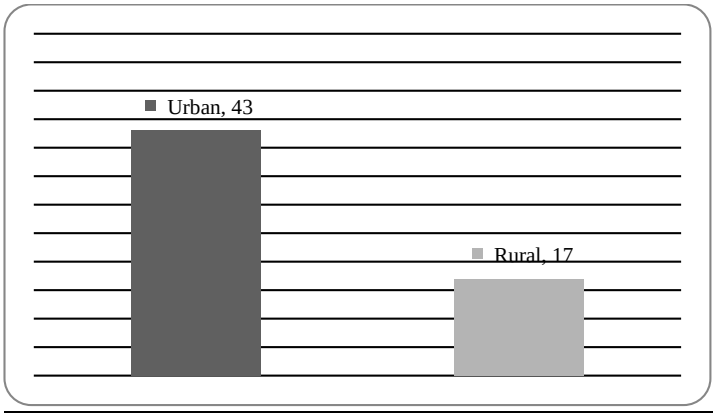

Figure 1. CCU Distribution according to the residence.

Distribution on age groups

Uterine body cancer is characteristic for the elderly woman, with a peak frequency between the ages of 55-65 years old. In the analysed lot of patients, the age distribution was carried out in 4 groups (Figure 2), the peak frequency being in the range of 50-60 years old (44%), followed by the range of 61-70 years old (38%). From the analysed lot we find

out that the average age at which the maximum rate of endometrial cancer is registered, is of 57 years old. An interesting aspect is the appearance of endometrial cancer at young ages. Thus, in the studied lot, it was found out that 8% of the female patients had the age under 50 years old. The minimum age in the analysed lot was of 39 years old, from which results the necessity of clinic and biological investigations as invariable as possible.

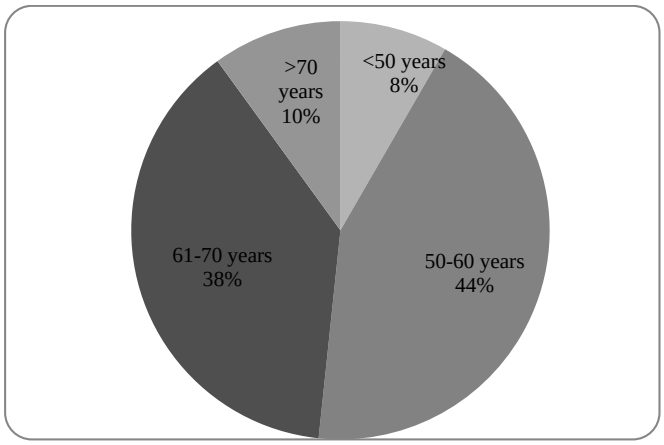

Figure 2. Distribution on age groups.

Risk factors

In the appearance of uterine body cancer many risk factors are involved, out of which, the most frequently met are the diabetes (DM), high blood pressure (HTN) and obesity (Figure 3).
Out of those 60 female patients who were included in the study, associations of these risk factors were met, the most frequently, (45%), followed by HTN in a percentage of 27%. There were also patients who didn’t show any risk factor, but who, developed the disease (22%).

This thing highlights the fact that the triggering of the uterine body cancer does not correlate with these risk factors in a percentage of 100%, but we observe the weight of some diseases with aggravating potential.

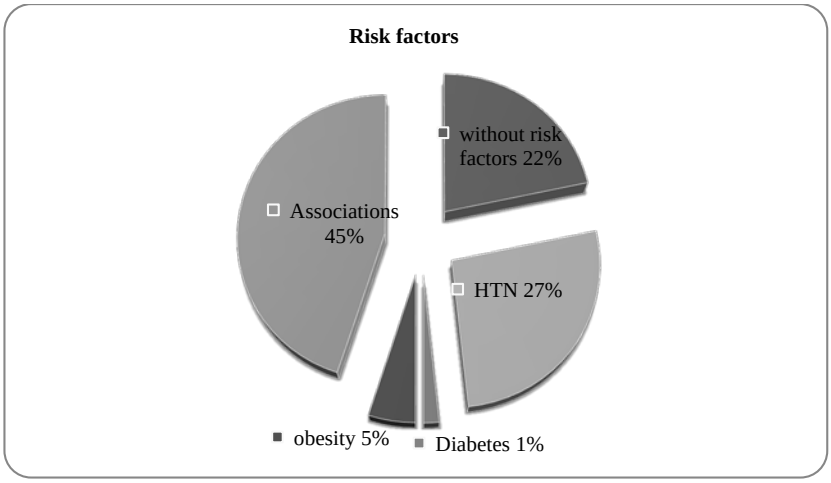

Figure 3. CCU distribution according to the risk factors

Among those 27 cases, in which there were associations between the risk factors, the majority of the cases were represented by the association between the obesity and high blood pressure (66%), while the association between diabetes and obesity presented the least number of cases. (4%).

When analysing carefully the above tables, we find out that the maximum frequency of the endometrial cancer develops on a private field, in which the obesity, diabetes, HTN, are frequently signalled.

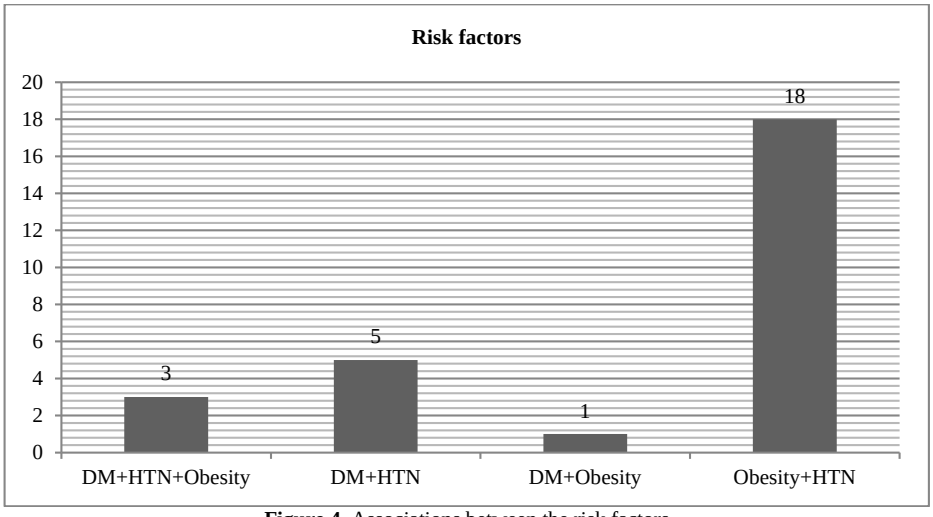

Figure 4. Associations between the risk factors

Also, it was discovered the association of uterine body cancer with the breast cancer, ovarian cancer, and the treatment with tamoxifen (Figure 5). In the studied lot, there were two cases of ovarian cancer before, 1 case in which the treatment with tamoxifen was followed, and 2 cases of breast cancer, out of which, 1 was synchronic with endometrial cancer.

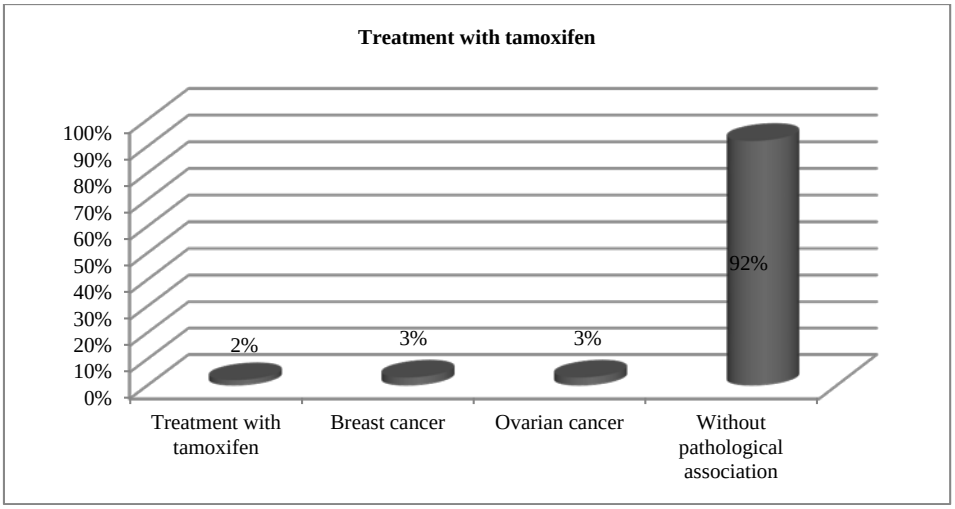

Figure 5. Treatment with tamoxifen and breast cancer, ovarian cancer**.**

CONCLUSIONS

Endometrial cancer usually appears at elderly women, the peak frequency being at ages of 55-65 years old, but it can be met at the young woman (<40 years old). In Romania, endometrial cancer is on the fourth place, among gynaecologic cancers, and seventh place, as a number of deaths through cancer. Endometrial cancer is a disease characteristic for the postmenopausal period, the majority of the female patients of the studied lot, having the age between 51-60 years old.

The reason for the medical check-up, was in the majority of cases metrorrhagia (uterine bleeding). The interval between the appearance of bleeding and the medical check-up is very important, the more this period is extended, the more endometrial cancer can advance, and it can be identified in a more advanced phase.

Among the risk factors of endometrial cancer, the most frequently met were high blood pressure, obesity and diabetes, frequently met in associations. After the accomplished study, we found out that the appearance of endometrial cancer does not correlate in a percentage of 100% with the existence of these risk factors.

REFERENCES

Baufeld K.,Kullmer U.,Kalder M.,Vahrson H.,Münstedt K. (2000). *Zur Nachsorge des Endometriumkarzinoms*. Geburtsh Frauenheilk. 60: 423-428.

Dunlop MG.,Farrington SM.,Carothers AD.,Wyllie AH.,Sharp L. Burn J.,Liu B.,Kinzler KW.,Vogelstein. (1997). *Cancer risk associated with germline DNA mismatch repair gene mutations.* Hum Mol Genet. 6:105-110.

Frederic Amant.,Philippe Moerman.,Patrick Neven.,Dirk Timmerman.,Erik Van Limbergen.,Ignace Vergote. (2005). *Endometrial cancer*. The Lancet Seminars. Volume 366, No. 9484, p491-505.

Jan V. Bokhman. (2004). *Two pathogenetic types of endometrial carcinoma*. Department of Gynecology, N. N. Petrov Research Institute of Oncology, USSR Ministry of Health, Leningrad, USSR; p6-10

Jemal A.,Murray T.,Ward E. (2005). *Cancer statistics*. CA Cancer J Clin 2005; 10-30.

Karsten Münsted.,Phillip Grant.,Joachim Woenckhaus.,Gabriele Roth.,Hans-Rudolf Tinneberg. (2004). *Cancer of the endometrium: current aspects of diagnostics and treatment.* World Journal of Surgical Oncology; 04 July 2004. p2-24.

Parkin DM.,Pisani P.,Ferlay J. (1999). *Global cancer statistics*. CA Cancer J Clin 1999; 49: 33–64.
Salvesen HB.,Akslen LA. (2002). *Molecular pathogenesis and prognostic factors in endometrial carcinoma*. APMIS. 110: 673-689
Smith RA.,Cokkinides V.,Eyre HJ. (2003). *American Cancer Society guidelines for the early detection of cancer*. CA Cancer J Clin 2003; 53: 27–43.
Soliman PT.,Oh JC.,Schmeler KM.,Sun CC.,Slomovitz BM.,Gershenson DM.,Burke TW.,Lu KH. (2005). *Risk factors for young premenopausal women with endometrial cancer*. Department of Gynecologic Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas, USA. Obstet Gynecol. 2005 Mar;105(3):575-80
Van Eycken.,E. Kankerincidentie in Vlaanderen (2000). Available at http://www.tegenkanker.net/. (accessed November 1, 2016).

The institutional affiliation of authors:

1 "Alexandru Ioan Cuza" University Iași, Faculty of Biology, Carol I 20A, 700605 Iasi, Romania.
* corresponding author: mihai.vlad@student.uaic.ro