

RETROSPECTIVE EVALUATION OF THE INCIDENCE AND TREATMENT OF CERVICAL CANCER

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Abstract: *The second leading cause of death in women worldwide is the cervical cancer, being an important public health issue. The aim of the paper was to evaluate the prevalence of cervical neoplasia and the treatment used for this pathology. We included a total of 111 cases diagnosed with cervical neoplasia. The cervical cancers are found more frequently in women on perimenopause and menopause. In our study, the stage I or the carcinoma in situ were treated by conization or hysterectomy. The type of interventions for the other stages (I B, II A and II B) were radical hysterectomy and bilateral adnexectomy. In 79 (71.17%) cases the intervention was radical Wertheim hysterectomy (with pelvic lymphadenectomy). We also identified 3 (2.70%) cases of stage IIIA, IIIB or IV where it was performed an exploratory laparotomy. Cervical cancer can be detected relatively easily by screening, indicated especially at the women at high risk, through a gynecological examination, vaginal cytology and HPV genotyping. The prognosis is favorable in cases detected in the early stages, and unfavorable in the advanced ones, so, it is dependent on the breakthrough stage, the woman's age, histopathological form and the combination of therapeutic approach to the task.*

Key words: *HPV, cervical neoplasia, Radical Wertheim hysterectomy.*

1. Introduction

The second leading cause of death in women worldwide is the cervical cancer, being an important public health issue [10]. Cervical cancer incidence and mortality decreased since the introduction and widespread use of the Babes-Papanicolaou test [12], [19]. According to the World Health organization, in a report from 2014, Romania remains the first country in Europe regarding the incidence of cervical cancer, the mortality rate being

2-2.7 times higher in our country than in Eastern and Central Europe and 6.3 times higher than in the EU countries, mainly because of the late diagnosis, when the disease is in invasive forms [9]. In addition to the known risk factors for developing cervical cancer, recent screening recommendations include: identification of the infection with human papillomavirus (HPV) (the detection of oncogenic HPV types associated with cervical cancers) along with the PAP test among women aged 30–65 years [13].

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Among populations with limited access to health care, the incidence and mortality rates because of cervical cancer remain increased, despite the evidence that cervical cancer screening saves lives.

2. Objectives

The aim of the paper was to evaluate the prevalence of cervical neoplasia and the treatment used for this pathology in the Clinical Hospital of Obstetrics and Gynecology „Dr. I.A. Sbarcea” Brasov.

3. Material and Method

The retrospective study was carried out in the Clinical Hospital of Obstetrics and Gynecology “Dr. I.A. Sbârcea” Brasov,

conducted over a period of six years. The study included a total of 111 cases diagnosed with cervical neoplasia in the period January 2010 to December 2015. Data was obtained from the medical records. Statistical and graphical data processing was performed using MS Excel 2016 and MedCalc program.

4. Results

In the studied period, we identified 111 cases diagnosed with cervical cancer aged between 25 and 79 years (Figure 1). There is an increased incidence between 55-59 years (27.92%), lowest risk has had patients under 29 years (0.90%) and over 70 years (5.40%).

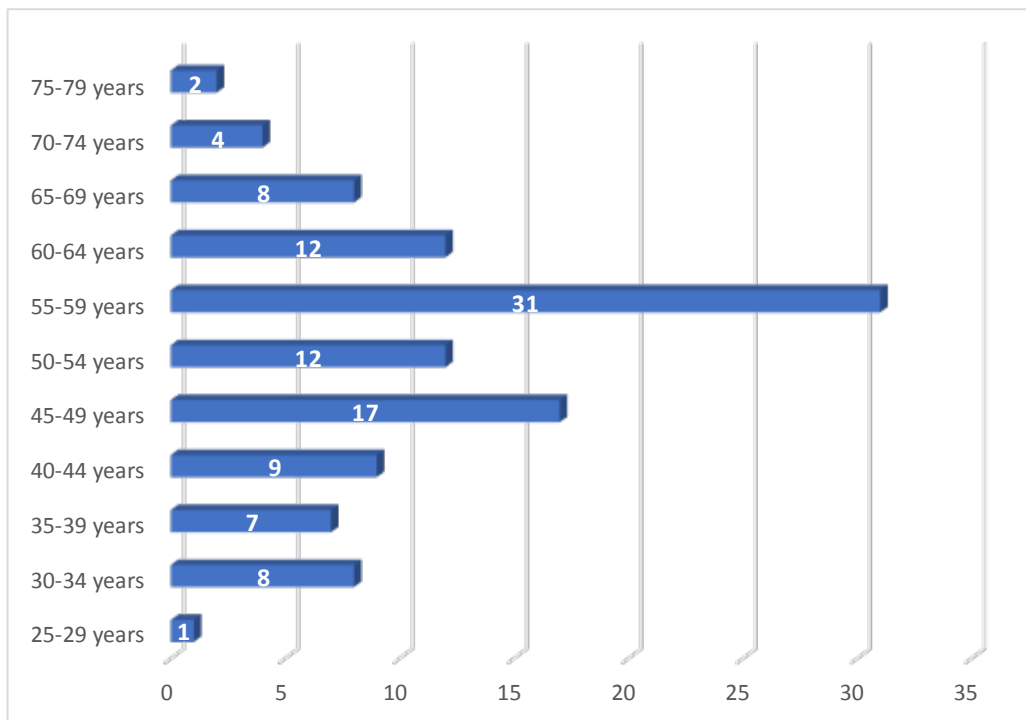


Fig.1. *Distribution of patients diagnosed with cervical cancer by age*

The sociodemographic characteristics of the study population are summarized in Table 1. The residence areas were mainly urban (85.25%), possibly due to early

presentation to the hospital and multiple risk factors present in the environment, (food, sexual behavior, smoking).

Table 1

<i>Sociodemographic characteristics of the study group</i>			
<i>Residence area</i>	Urban	86	77.47 %
	Rural	25	22.52 %
<i>Education status</i>	Without studies	1	0.90 %
	Less the high school graduated	27	24.32 %
	High school	36	32.43 %
	Vocational school	33	29.72 %
	Superior studies	14	12.61 %
	Unemployed	29	26.12 %
	Employees	44	39.63 %
	Retired	38	34.23 %

We also observed that patients with higher levels of education and employed presented earlier at the hospital for screening of cervical cancer.

The symptoms of the patients with cervical cancer were also investigated in

our study. 51.35% had abnormal vaginal bleeding, 25.22% were enrolled in the screening program for cervical cancer, 14.41% presented with modified leucorrhea and 9.01% for abdominal pain, as showed in figure 2.

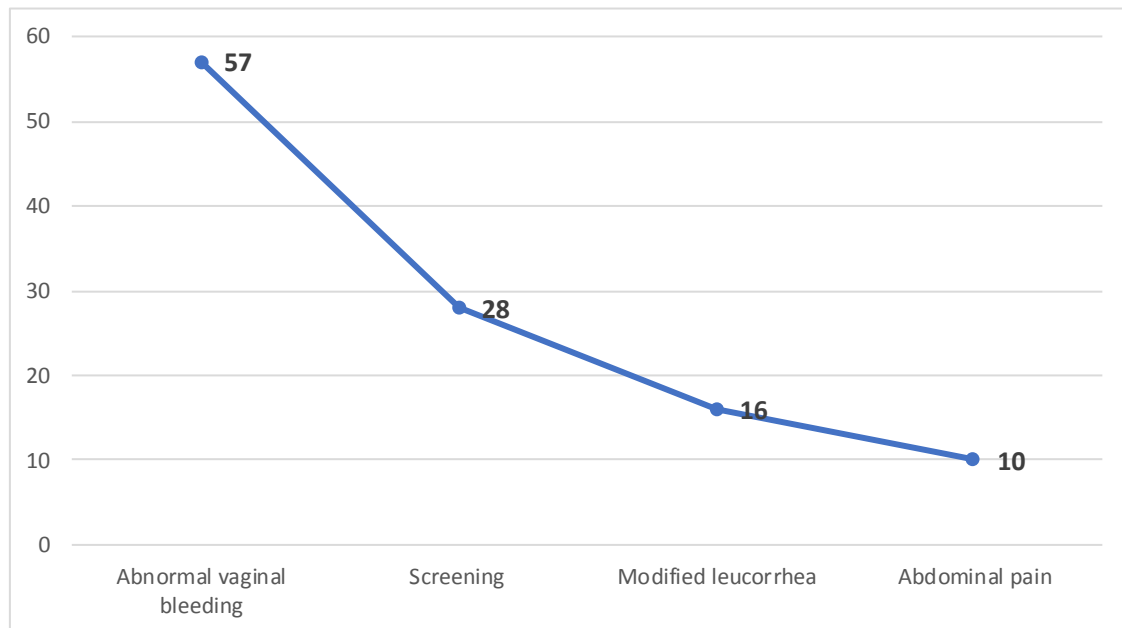


Fig. 2. Distribution of the patients according to the symptomatology

As seen in figure 3, 23 (20.72%) cases were diagnosed at the stage carcinoma in situ in, stage IB1 in 29 (26.12%) cases, stage IIB in 26 (23.42%) cases, mostly because of the delayed appearance of

symptoms and lack of instruction for the cervical cancer screening programs.

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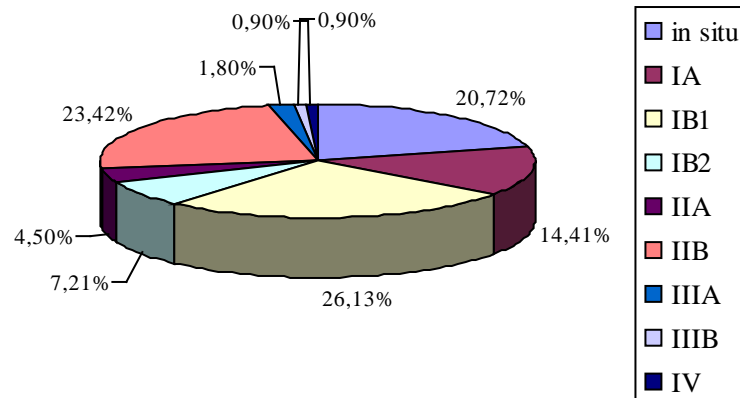


Fig. 3. *Distribution of patients diagnosed with cervical cancer by stage*

The treatment applied for the patients included in the study are showed in figure 4. The choice of surgery was taken according to the clinical examination, the patient's age and desire of preserving the fertility, histopathological results of cervical biopsies.

In our hospital, there were performed radical Wertheim hysterectomy in 71.17% of cases, total hysterectomy with bilateral adnexectomy in 17.11% cases, hysterec-

tomy with preservation of ovaries in 3.60% of cases, in 2.70% of cases of cervical neoplasia stage IIIA, IIIB and IV it was performed exploratory laparotomy, followed by hypogastric artery ligation. Cold knife conization followed by endocervical curettage was the choose type of treatment in 5.40% cases staged as carcinoma in situ, because of the desire of the patient to preserve the fertility.

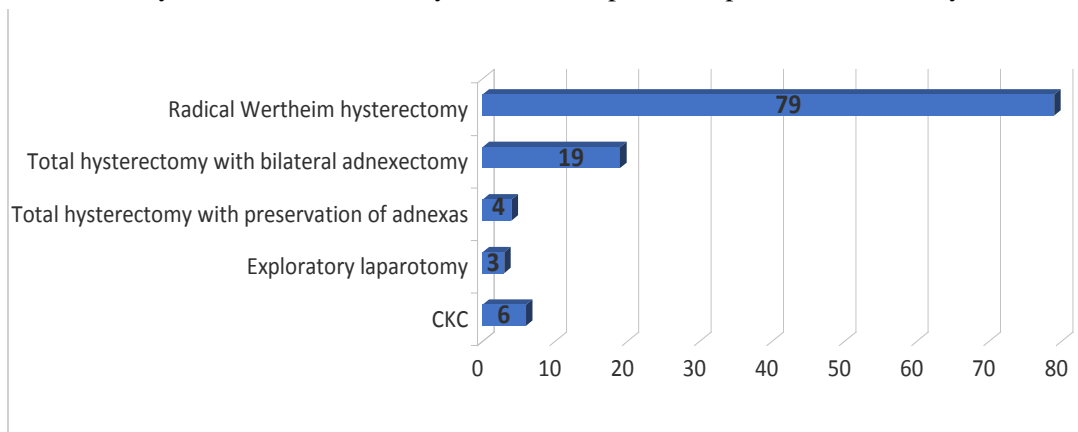


Fig. 4. *Treatment applied for patients with cervical neoplasia*

5. Discussion

The cervical cancers are found more frequently in women on perimenopause and menopause, with an increased incidence between 48-55 years, with two peaks: one between 35-39 and another between 60-64 years. Nowadays, cervical cancer is diagnosed at younger ages, mostly because of the well-known carcinogenic effect of the HPV infection (in the present study it was identified only one case under 29 years). The gap between low developed countries and developed ones is enormous, screening being crucial in the detection of this disease [5].

Addressability to health care is higher in educated patients, as evidenced in this study. Genotyping of HPV effective, and in association with the Pap smear, is used to prevent invasive cervical cancer by detecting earlier persistent high-grade lesions and providing a lower risk of developing cancer [23].

A study from 2015, conducted on the women population from Brasov city, observed that the prevalence of the HR-HPV infections among the women with positive cytological examination was 28.64%. The indication for HPV genotyping at all women aged 18-45 years old and pap test every 6 months in patients with high-risk HPV could decrease the mortality by cervical cancer through early diagnosis of this pathology [17]. Cervical cancer is identified most common at women with cytology with atypical glandular cells and HSIL. HPV-positive women remain at a high risk of cervical cancer at all ages compared to HPV negative cytological categories. It has been determined that the HPV infections last longer if Chlamydia is present. The increased incidence of cervical cancer in middle age is observed also in breast, ovary and endometrium cancer [5].

Bello et al concluded in their study from 2009 that in women infected with multiple HPV genotypes, the risk for developing precancerous lesions is increased [4].

A meta-analysis from 2017 observed that the HPV infection rate was slightly higher in the cases of squamous cell carcinoma compared to the cases with HSIL lesions, identifying HPV 16 as the most common type, being more prevalent in the neoplasia cases. They concluded that an HSIL lesion with HPV 16,18 or 45 infection have a higher rate to progress to SCC than HSIL infected with other high risk HPC types [7].

There is a hypothesis that cervical cancer has the same incidence, because the cervix is also a hormone-dependent tissue. A strong effect of estrogen in cervical carcinogenesis in mice was demonstrated experimentally 70 years ago. Human cervix is strongly modified by hormonal fluctuations and the incidence is increased with use of oral contraceptives. With the decrease in circulating hormone levels in perimenopause would explain the increased incidence of cancer. Although there are many similarities with other hormone-dependent cancers, there are some differences. The first term pregnancies at a young age and parity numbers are associated with a decreased risk of breast, ovarian and endometrial cancer, but cervical cancer is increased. It is expected that early menopause might be associated with a decreased risk of cervical and breast cancer [8], [23]. A longitudinal study of the incidence rate of HPV infection in young women has found that the infection rate reduced at first intercourse close to menarche, suggesting that immature cervix is less easily infected than adults. Another explanation is that the rate of infection in young women is low because their partners tend to be young, still uninfected with HPV [8], [23].

Several recent studies have investigated the possible role of the diet in the

prevention of cervical cancer. A study from 2016 concluded that polyphenols have multiple cellular effects, such as carcinogens can prevent the achievement of the target, reactive molecules claim detoxification, improving the elimination of transformed cells, influence cell proliferation and inhibit tumor suppression, interfering in carcinogenesis. More specifically, HPV inhibit cell proliferation by inducing apoptosis, halting the growth and inhibition of DNA synthesis [18].

Women with cervical cancer diagnosed following a Pap test have a better prognosis than women whose cancer is detected based on symptoms and so a much better healing rate [1,24]. The prognosis is favorable in cases detected in early stages, falling as they become advanced stages; so it is dependent on the discovered stage, the woman's age, pathological form, histopathological type (which will make the radiosensitivity of the tumor cells), therapeutic approach to the task and association with pregnancy.

In our study, the stage I or carcinoma in situ were treated by conization (those patients who desired to preserve their fertility), or hysterectomy (in case of the patients in menopause). In most interventions for the other stages (I B, II A and II B) radical hysterectomy and bilateral adnexectomy was preferred. In 79 cases was preferred radical Wertheim hysterectomy (with pelvic lymphadenectomy). We also identified 3 cases of stage IIIA, IIIB or IV where it was performed an exploratory laparotomy (for hypogastric artery ligation).

In numerous studies, it is concluded that preoperative radio-chemotherapy treatment in the incipient stages would help reduce tumor size and then it is possible a simple conization [15], [25]. The disadvantage of preoperative chemotherapy it is the delay until the surgery, that is increasing the

possibility of surgery in chemo resistant cells. However, these drawbacks may be offset by a high dose regimen in a brief period before surgery [16]. In surgery after chemotherapy, it is observed dense fibrosis and adhesions and an increase need for blood transfusions caused by tumor necrosis.

A Korean study states that there is no long-term benefit of preoperative chemotherapy treatment, or even pre- and postoperative treatment hasn't major benefits [6]. Another study comparing hysterectomy with radiation therapy, reached the following conclusions: in women with cervical lesions <6 cm radical hysterectomy is superior to radiation therapy, but in the tumors >6 cm survival is equal between the two ways of treatment [2], [22]. Patients who received radiation with concurrent chemotherapy had a survival rate at 5 years of 90% compared with those who received only radiation therapy, with a percentage of 76%. For high-risk patients with cervical cancer who underwent radical hysterectomy and pelvic lymphadenectomy, adjuvant use of chemoradiotherapy resulted in better survival rate than radiotherapy only. It is recommended weekly cisplatin in addition to radiation therapy [14]. For the incipient stages, to preserve fertility in women, it is recommended to perform vaginal trachelectomy than radical hysterectomy, both treatments with a 5-year survival rate of approximately 100% [3]. A comparison of laparoscopic or laparotomy radical hysterectomy in the incipient stages would be in favor of the laparoscopy with decreased postoperative recovery time, intraoperative hemorrhage and infectious morbidity, although an increase in the time of surgery [11], [20].

Nezhat et al compared the laparoscopic and robotic assisted radical hysterectomy and concluded that there are no significant differences between these methods, the only advantages of robotic technology is a

more efficient, higher flexibility and dexterity of laparoscopy [21].

The limitations of the study were the lack of information regarding the HPV genotyping at the patients included in the study, mostly because this investigation is not included in the screening program, being performed only in the private practice.

6. Conclusions

Cervical cancer can be detected relatively easily by screening the adult female population, especially those at high risk, through a gynecological examination, vaginal cytology and HPV genotyping at least once a year for women aged 35-50 years and every two years to the rest of the female population.

The prognosis is favorable in cases detected in the early stages, falling as they become advanced, so the outcomes are dependent on the breakthrough stage, the woman's age, pathological form, histopathological type (which will make the radiosensitivity of the tumor cells) and also the combination of therapeutic approach to the task.

To preserve female fertility, it is recommended to effectuate vaginal trachelectomy than radical hysterectomy. As a method of choice of surgery, it is preferable laparoscopy, it brings multiple benefits, and if possible, robotic assisted intervention with a degree of accuracy superior to other methods.

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