

Conization as Treatment of Choice for Precancerous Changes and University Cervical Cancer at the Department of Obstetrics and Gynecology of Clinical Center of Sarajevo University in 2009

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PROFESSIONAL PAPER SUMMARY

According to the Public Health Institute of the Federation of Bosnia and Herzegovina there were 132 newly diagnosed patients with cervical cancer in 2008. Aim: The aim of this article is to present the incidence of precancerous changes on the cervix and cervical cancer as well as the incidence of the use of conization as the type of treatment for cervical patients. Methods: The number and type of surgical procedure was analyzed using the protocols from the Clinic of Gynecology and Obstetrics and Clinical Pathology and Cytology. At the Clinic of Gynecology and Obstetrics cold-knife conization with application of Sturmdorf sutures. Results: In 2009 at the Clinic of Gynecology and Obstetrics there were 72 newly diagnosed women with cervical cancer, out of which 16 had in situ carcinoma, 158 CIN I lesions, 64 CIN II lesions, and 46 CIN III lesions. Planocellular carcinoma was diagnosed in 59 patients (82%), cervical adenocarcinoma in 13 patients (18%). 114

patients were treated with conization with the application of Sturmdorf sutures. The most common diagnosis made with pathohistological analysis of the conization was CIN III/CIS, which was found in 48 (29%) patients. CIN II and CIN III were diagnosed in 33 (29%) and 27 (24%) patients, respectively. Conclusion: Surgical method of treatment of precancerous changes as well as cervical cancer using the cold-knife conization with Sturmdorf sutures has shown high efficacy but with certain disadvantages such as the formation of scars, cervical stenosis, postoperative bleeding and others. Therefore, there is a need for the introduction of new protocols and newer methods of treatment. In order to decrease the number of women with precancerous changes, screening program is needed as the required part of women's health care plan as well as the introduction of HPV vaccination program.

Keywords: precancerous changes of the cervix, cancer, conization

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1. INTRODUCTION

Cervical cancer by frequency occupies the second place of all malignant diseases of the female reproductive system, immediately after breast cancer. According to estimates by the World Health Organization from 2009 in the world are recorded 510,000 new cases of cervical cancer, and during the same year are recorded 250,000 deaths from this disease. Eighty percent of new cases are from developing countries

(1). The Federation of Bosnia and Herzegovina, according to data from the 2008 by the report of Federal IPH was 132 new patients (2).

Many studies that were conducted in order to prove association of some infectious agents with cervical cancer confirmed the increased incidence of infection with human papilloma virus in almost 99% of patients suffering from cancer of the cervix (1). Until now is identified over 100 different

types of human papillomavirus (HPV), and about 25 of them infect epithelial cells of the anogenital system causing damages of varying degrees from benign genital warts to cervical cancer (3,4). Strains were divided into three groups according to the prediction of their ability to cause neoplasia. Low-risk strains of HPV are often linked with the development of cell changes described as CIN1, but are rarely associated with the development of high grade dysplasia or invasive cancer. HPV types 6, 11, 42, 43 and 44 have low oncogenic risk. The HPV types that have high oncogenic risk types are: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 68 and they are most common in high grade lesions, especially types of HPV 16 and 18 which carry a very high risk for cervical cancer (4).

Recent epidemiological studies have demonstrated the presence of HPV DNA in almost all CIN lesions of high degree and invasive cancer. Many epidemiological studies have shown a link between sexually transmitted diseases and cervical cancer. Therefore, recent researches are directed towards finding the connection between cervical cancer and infection with Chlamydia, Gonorrhea, Gardnerellom, Mycoplasma, Trichomonas and Herpes simplex virus (HSV) (4). In addition to sexually trans-

mitted diseases, the etiology of cervical cancer is associated with low social status, smoking, early sexual activity, pregnancy before 20 years of age, and the promiscuous habits of the partners (5).

Cervical cancer may arise from squamous epithelial cells as a result of progressive alteration (mostly in the area of transformation zone crossing from the plate in the cylindrical epithelium) and gland cells endocervical glands. Squamous cell carcinoma (carcinoma cervicis uteri planocellulare) is present in 75-85% of all cervical cancer, while cancer of the gland cells (Adenocarcinoma cervicis uteri) is present in 15-25% of all cervical cancers (5). In the treatment of cervical cancer surgery has a major role, especially in patients who are in early stage of the disease (6).

Cervical intraepithelial neoplasia (CIN) is preinvasive change that has the possibility of further progression and deterioration to the invasive carcinoma, but also has the possibility of spontaneous withdrawal. CIN usually occurs in the zone of transformation, and the criteria for the diagnosis of intraepithelial neoplasia are: disorder in distribution and maturation of cells, abnormal nuclei and increased myotic activity. CIN is divided into three stages according to the thickness of the affected epithelium. CIN I represents a change that affects the lower third of epithelial thickness measured from the basement membrane. CIN II is described as the involvement of the lower and middle thirds of the epithelium and CIN III as the involvement of the entire thickness of the epithelium and carcinoma in situ (CIS), which is now classified as CIN III because changes occupy the entire thickness of the epithelium while the basal membrane is intact without changes in stroma beneath (5).

In order to make complete diagnostic evaluation of cervical intraepithelial neoplastic (CIN) it is necessary to implement the following three complementary methods of detection and verification of intraepithelial neoplasia: Papa test, a colposcopy with targeted biopsy and histopathological analysis of biopsy samples. Each tissue sample that is sent to histopathological verification should include the epithelium, basal membrane and part of stroma. Pathologist is the only one to comment on the nature of the final changes, and histopathological diagnosis is consid-

ered the gold standard in diagnostic of preinvasive cervical cancer (5).

The first sign of disease is often small bleeding between menstruations or vaginal discharge with blood. Bleeding is usually painless at the beginning and small in the form of spotting bleeding that occurs occasionally and often after sexual intercourse or bathing. As disease progress hemorrhage become more frequent and more abundant, and there are also bolvi due to pressure on the nerve obturatorius and nerve ishiadicus. As the disease progresses it can lead to edema of the lower limbs, obstructive uropathy, hematuria, and bleeding from the rectum, which occurs in preterminal stage of the disease (5).

Pharmacological treatment of CIN until now has not given the expected results, so only remain the surgical methods of treatment which aims to remove or destroy completely atypical epithelium.

There are two ways of treating precancerosis of the cervix, which are:

- Excision treatment with removing of the sick tissue (knife conization, laser, LETZ, hysterectomy)
- Ablation treatment where is done the destruction only of the altered epithelium without damage to the stroma of the cervix (12).

Recently the method with electrodiathermical loop conization LLETZ (Large Loop excision of the Transformation Zone) gets more and more supporters and is increasingly being used as a method of choice for treating all stages of CIN (5).

Lack of surface locally-destructive methods of treatment is the possibility of the spread of changes in the depth of the cervical canal, simultaneously with the inability to safely destroy them, as glandular crypts are found at a depth of 10 mm, which lies beyond the reach of these techniques. Another disadvantage is the inability of histopathological diagnosis of the treated tissue, since the tissue is destroyed with these methods (5).

2. GOAL

The aim of this research is to show the frequency of precancerous changes and cervical cancer as well as treatment with conization at the G&O CCUS in 2009.

3. MATERIAL AND METHODS

Analysis is done based on the data on the number and type of surgeries

from the protocol of surgeries of the Clinic for Gynecology and Obstetrics, Clinical Centre of Sarajevo University (G&O CCUS) in 2009, and the analysis of data on the histological findings from the protocol of Clinic for Pathology and Cytology, Clinical Centre of Sarajevo University (OJ CCUS CPC) in 2009.

At the G&O in Sarajevo is used conization the cervix with cold knife and plastic surgery of the cervix by Sturmdorf. The procedure is performed under general anesthesia with a shorter postoperative hospitalization at the clinic for several days. Characteristic of this method is that there is no destruction of tissue that is sent to the histopathological verification, the sharp and intact edges of the incision, and it is possible to achieve the desired depth of incision. The main disadvantages of this method are scarring at the site of stitches, cervical stenosis (17%), intraoperative (6%) and postoperative bleeding (up to 8%) and infertility (4%) (5).

4. RESULTS WITH DISCUSSION

At the G&O CCUS in 2009 was diagnosed and surgically treated a total of 72 cervical carcinoma, including 16 carcinomas in situ, 158 CIN I lesions, 64 lesions CIN II and 46 CIN III lesions (Figure 1).

In 2009 at the G&O CCUS in case of 158 patients histologically are verified CIN lesions of type I. The most endangered group of patients aged 41-50 years while the average age of patients was 45 years (Figure 2).

Noticed is a possibility of transition from CIN I to carcinoma in situ in 11% of cases, and the possibility of transition into invasive carcinoma in 1% of case (7). Also is observed that the average time of progression of CIN I in the CIS is 6 years (8). Cytological analysis of Papa smears in adolescents who had CIN I determined that 75.1% of them had their first sexual intercourse by age 16 or earlier (11). Research conducted in Canton Sarajevo has revealed that 60% of patients diagnosed with CIN and cervix cancer have HPV infection. The same study demonstrated that 52% of patients who were HPV positive had 3 or more sexual partners. The same study found that 62% of HPV positive patients are smokers (16).

In 2009 at the G&O CCUS in 64 patients are histologically verified CIN II-type lesions. From the figure we see in-

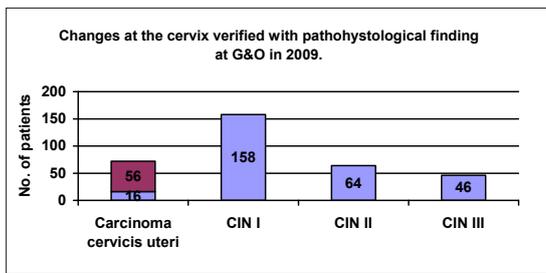


FIGURE 1. Changes at the cervix verified with pathohistological finding at G&O in 2009

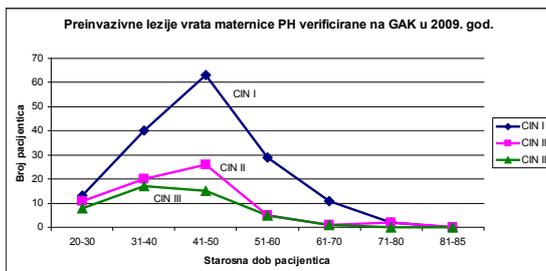


FIGURE 2. Preinvasive lesions of cervix uteri verified by PH analysis in 2009

creased incidence of these lesions from 20 to 50 years of age, and the most vulnerable group of patients is aged 41-50 years. Average age of patients was 40 years (Figure 2). Studies have shown the possibility of transition of the CIN II to carcinoma in situ in 22% of cases, and the possibility of transition into invasive carcinoma in 5% of cases (7). Also noted is an average time of progression from CIN II in the CIS, which is 3.5 years (8). Cytological analysis of cervical swabs in adolescents diagnosed with CIN II found that 92.4% of them had their first sexual intercourse by age 16 or earlier (11). In 2009 the G&O CCUS in 46 patients was histologically verified lesions of the cervix of CIN III type (Figure 2). From the chart we can see that the most vulnerable group of patients is those aged 31-40 years while the average age of patients was 39 years. Studies have pointed to the possibility of transition of the CIN III lesion in invasive carcinoma in more than 12% of cases (7). Also is noted an average time of progression of CIN III in the CIS, which is 1 year (8). Cytological analysis of Papa smears in adolescents who had CIN III found that all had an early start of sexual activity, or first sexual intercourse at age of 16 or ear-

lier (11).

In a study performed at the Department of Gynecology and Obstetrics of Osijek Hospital in the period January 1st 1993 – December 31st 2002 on a sample of 120 patients with histological diagnosis of CIN III, treated with cold coagulation with at least 5 years from start of treatment was found that the pathological cytological findings re-occurred in 25 (20.8%) women in case of CIN I and CIN II in 1 (0.8%) women, CIN I alone in 18 (15%) women while AGCUS occurred in 4 (3.3%), AGCUS and CIN I in 1 (0.8%) and only ASCUS in 1 (0.8%) patient. In the remaining 94 (78.3%) of patients cytological examination was normal (12). This study confirm the effectiveness of cold coagulation which is not inferior to other methods of treatment of CIN III lesions on the cervix, a method which has many advantages such as simplicity and simple training of the staff on the one hand, and treatment in ambulatory conditions without anesthesia and sick leave on the other. At the same time method is compared with other methods of treatment and proves economically more reasonable (12).

Another method that is precise and efficient is laser conization and vapor-

ization PVU whose advantages are high accuracy and efficiency of the procedure and rapid healing with complete epithelization in nearly three weeks. Also this method is characterized by the existence preparation for histopathological analysis, mostly dry operational scope, and almost bloodless and absolutely sterile procedure. Lack of methods is very expensive equipment that requires extensive experience and a high degree of surgical skills (5, 17).

At the G&O clinic in 2009 was diagnosed and histologically verified carcinoma in situ of the cervix in 16 patients, and mostly were affected patient at age 31 to 40 years (Figure 3). These data partially coincide with the data from the Croatian Republic, where they observed increase in CIS at the age 20-24 years, at the beginning of sexual activity, and the highest prevalence is recorded at age 30-34 years. It was noted that the average time of progression of CIS to invasive cancer is 10 years (8).

During 2009 at the G&O clinic was diagnosed and histologically verified invasive cervical cancer in 56 patients, and mostly were affected the patient age 41 to 50 years (Figure 3). Average age of patients with the diagnosis of cervical cancer is 52 years of age.

According to the literature, the average age at diagnosis is 45-47 years of age, although the disease can occur much earlier (5). Commission for Malignomas of the G&O clinic in Sarajevo in the period from January 1st 2009 to August 31st 2009, godine diagnosed cervical cancer in 151 patients, of whom 84 (55.6%) cases were inoperable. The remaining 67 (44.4%) cases were surgically treated at the Clinic of Obstetrics and Gynecology in Sarajevo by conization or hysterectomy. (9)

These figures are very worrying because it indicates that at the time of diagnosis 55.6% of patients was in an advanced stage of disease that cannot be surgically treated, and for the patient remains only oncological treatment with irradiation and chemotherapy.

From a total of 72 cervical cancers, including carcinoma in situ that were diagnosed and treated surgically at G&O CCUS in 2009, histopathological analysis in 59 (82%) cases proved that it was a planocellular carcinoma in 13 (18%) cases was the diagnosis of adenocarcinoma of the cervix (Figure 4). These data were correlated with litera-

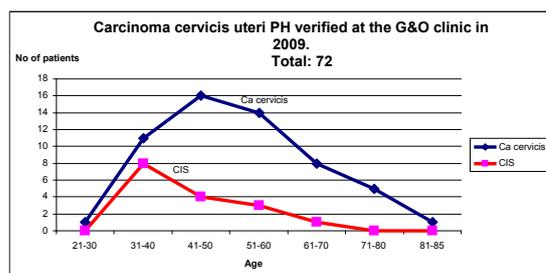


FIGURE 3. Carcinoma cervicis uteri PH verified at the G&O clinic in 2009

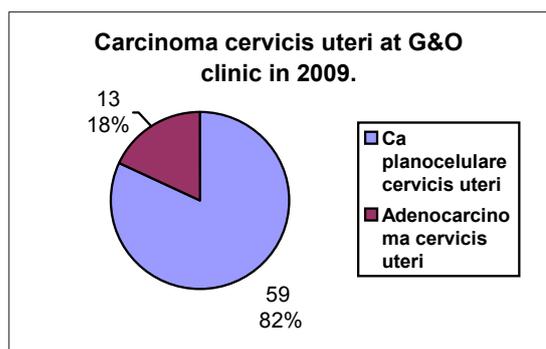


FIGURE 4. Carcinoma cervicis uteri at G&O clinic in 2009

ture data where the recorded incidence of squamous cell carcinoma of the cervix is 75-85% of cases, while the adenocarcinoma of the cervix takes 15-25% of cases. Recent studies show increasing incidence of adenocarcinoma of the cervix (5, 10).

In 2009 at G&O CCUS 114 patients were surgically treated using the cold knife conization of the cervix and plastic surgery according to Sturmdorf. Within each conization was performed and abrasion cavum uteri. The material obtained was analyzed at the CPC CCUS where they confirmed the following diagnoses:

The most common diagnosis was CIN III / CIS and was found in 48 (41%) cases, while immediately after followed milder forms such as CIN II and CIN I in 33 (29%), and in 27 (24%) cases. In 4 (4%) cases is proven carcinoma of the cervix. Preinvasive malignant changes were found in 2 (2%) cases (Figure 5). The mean age of patients undergoing conization was 40.65 years of age.

These data coincide with data obtained from the research conducted in the region, which shows us the studies conducted in the Hospital "Sestre milosrdnice" (Sisters of Mercy) in Zagreb in the period from January 1st 2006 to May 31st 2006 performed on 115 biopsies of the cervix, including 48 (41.7%) of the cone and 67 (58.3%) excisions. In this study, the diagnosis of CIN for 8 (16.6%) cones, CIN II in 11 (22.9%) cones and CIN III in 23 (47.9%) cones. Carcinoma is verified in 2 (4.2%) cones (14). After three months after completed procedures recommended are ordinary cytological, colposcopy and control of HPV testing (13).

5. CONCLUSION

Surgical methods of treatment of precancerous changes and carcinoma of the cervix by conization with knife and plastic surgery according to Sturmdorf proved to be highly effective, but with certain disadvantages such as scar formation at the site of suture, cervical stenosis, postoperative bleeding, etc. Therefore there is a need of introducing new modern method of treatment of precancerous changes in the cervix, such as cold coagulation, electrocauterisation, laser vaporization, laser con-

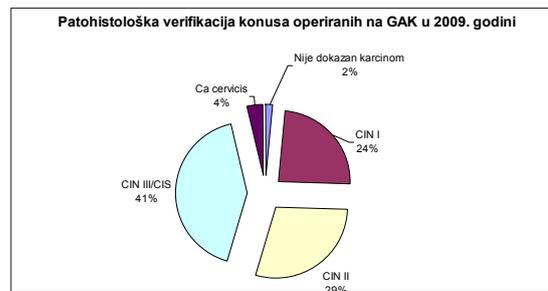


FIGURE 5. Pathohistological verification of conizations treatment at G&O Sarajevo in 2009

ization and loop excision with low voltage diathermic method (LETZ), which is now also most common method for treating CIN. Indicated is the need to introduce treatment protocols of pre-malignant changes and carcinomas of the cervix.

Given the large number of histologically verified cases of CIN I lesions, the patient with evidence of HPV infection with a type of low oncogenic risk can be followed every two years, and those with HPV infection and high oncogenic risk every year as required by protocol to be applied in the Republic of Croatia. According to the same protocol, a patient with CIN II lesions should be resolved within a year, especially if the CIN II and HPV infection persists with high oncogenic risk. CIN III should be immediately treated surgically with the use of some of excision techniques that provide suitable sample for histopathological analysis (18).

To reduce the number of patients with precancerous lesions of the cervix is necessary to make screening program as a mandatory aspect of health care of women. The program would include classic gynecological examination, a review with speculum, VS, taking a Papa smear and colposcopy review. Especially within the population of women aged 30-35 years and over the need exist with a suspicious Papa smear colposcopy and HPV testing because they most vulnerable patients age groups. Due to the risky sexual behavior in recent years indicates the training needs of young people about the risks and consequences of HPV infection, and the possibility of vaccination against HPV to reduce the number of patients with carcinoma of the cervix. Also the promotion of smoking prevention in the future should reduce the number of women with this dangerous cancer.

Today in the 21st century no woman should develop cervical cancer, because the cervix is an organ that is visible dur-

ing gynecological examinations. Statistics shows that reality is different, and that cervical cancer in 2009 at G&O in more than half of all cases is diagnosed too late, or at the stage when the disease cannot be successfully treated surgically.

In the treatment of cervical cancer today in modern centers are increasingly abandoning the surgical treatment with conventional laparotomy approach, and is usually applied laparoscopically assisted vaginal radical hysterectomy (LAVRH). Medicine of the 21st century requires professionals and doctors with the help of modern equipment that can reduce the number of radical procedures that require long term rehabilitation, more frequent occurrence of complications and high cost of treatment, and also gives poorer results than the prevention of disease and treatment of lesions when they are in the initial stage. It is important that for any intervention which will be performed is necessary to discuss, and make indications on the professional meeting such as the Commission on Malignomas of the G&O clinic, whose findings preceded the making of the surgery program.

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The Department of Obstetrics and Gynecology is an important structure in the university hospital being the largest tertiary level referral centre for learning, research and treatment in obstetrics and gynecology in Lithuania. Each year around 350 students from the Lithuanian University of Health Sciences undergo a part of their undergraduate studies in the department. The department also organizes various postgraduate courses for specialists in Obstetrics and Gynecology as a part of CME. It hosts training sessions and courses not only for local doctors, but the clinic is always open for visitors. Clinic for Gynecology, Clinical Center of University of Sarajevo, Bolnicka 25, 71000 Sarajevo, Bosnia and Herzegovina. Unlabelled: According to the Public Health Institute of the Federation of Bosnia and Herzegovina there were 132 newly diagnosed patients with cervical cancer in 2008. Conclusion: Surgical method of treatment of precancerous changes as well as cervical cancer using the cold-knife conization with Sturmdorf sutures has shown high efficacy but with certain disadvantages such as the formation of scars, cervical stenosis, postoperative bleeding and others. Therefore, there is a need for the introduction of new protocols and newer methods of treatment.