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NOVELTIES IN REVISED FIGO CERVICAL CANCER CLASSIFICATION FROM 2018. WHAT RADIOLOGIST SHOULD KNOW?

NOVINE U REVIDIRANOJ FIGO KLASIFIKACIJI KARCINOMA GRLIĆA MATERICE IZ 2018. GODINE. ŠTA RADIOLOZI TREBA DA ZNAJU?

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Abstract

Cancer of the cervix uteri represents major socioeconomic problem, given the incidence which, regardless of prevention measures, remains at high level, particularly in countries of lower socioeconomic status. Cervical cancer is the fourth most common cause of cancer incidence in women. Accurate assessment of disease stage is a prerequisite for a selection of adequate therapeutic modality.Used for many years, the International Federation of Gynecology and Obstetrics (FIGO) classification did not meet criteria of the spread of the disease and thus it became insufficient. Compared to the previous classification, which was based on clinical evaluation of the stage of disease based on gynecological examination and other diagnostic methods, revised FIGO classification includes radiologic imaging modalities and pathological assessment, as a supplement to clinical evaluation, in determination of the stage of cervical cancer for all stages of cervical cancer.Diagnostics and treatment of patients with cervical cancer is based on multidisciplinary approach.

INTRODUCTION

Cancer of the cervix uteri still represents major socioeconomic problem, given the incidence which, regardless of prevention measures, remains at high level, particularly in countries of lower socioeconomic status. Cervical cancer is the fourth most common cause of cancer incidence in women, with estimated 570 000 new cases in the world in 2018, which represents in total 6.6% of all cases in the female population. (1) Both on the list of causes of diseases and the list of causes of deaths, cervical cancer is on the fifth place. (2) According to the World Health Organisation, cancer of the cervix uteri in most cases is caused by Human Papilloma Virus (HPV), of which more than 70% are caused by highly oncogenic HPV types 16, 18, 31, 35 (3), although other factors contributing to development of this type of cancer cannot be completely ruled out. Predisposing factors are immaturity of the cervical epithelium, early sexual intercourse, a large number of partners, promiscuity, lower socioeconomic status, smoking.

Accurate assessment of disease stage is a prerequisite for a selection of adequate therapeutic modality. For many years therapy of cervical cancer is primarily based on surgical treatment and as adjuvant therapy is used preoperative or postoperative radiation therapy. The aim of chemotherapy is significant in recurrent disease, however newer non-standard form of treatment has found its place in application of preoperative chemotherapy, based on platinum derivatives, and in order to reduce the size of primary tumor and consequent surgical treatment. In order to undertake adequate treatment of patients it is necessary to accurately determine the degree of spread of disease. As well as cancers of other localizations, cervical cancer is divided into four stages - stages I, II, III, IV of disease. Stages of cervical cancer are determined clinically, with speculum and bimanual examination, digital rectal examination, with additional imaging diagnostics such as MRI of the pelvis, MRI of the abdomen, cystoscopy, rectoscopy, X-ray of the chest, CT of the thorax, and as a newer method in assessment of the stage of disease

it is used PET/CT. Clinical stage of the disease remains as such, and does not change.

Used for many years, the FIGO classification (The International Federation of Gynecology and Obsetetrics), even though it was revised for several times, did not meet criteria of the spread of the disease and thus it became insufficient. The insufficiency of the old classification is reflected in the lack of evidence of spread of disease to the pelvic lymph nodes, primarily on paraaortic lymph nodes, and also does not provide adequate evaluation of the volume of the tumor.

With the latest revised FIGO classification for 2018 some novelties are introduced in staging of cervical cancer. Compared to the previous classification, which was based on clinical evaluation of the stage of disease based on gynecological examination and other diagnostic methods (hysteroscopy, cystoscopy, proctoscopy, colposcopy and biopsy), revised FIGO classification includes radiologic imaging modalities and pathological assessment, as a supplement to clinical evaluation, in determination of the stage of cervical cancer for all stages of cervical cancer. [4-6] Any available imaging modality can be used for assessment of the stage of cervical cancer including ultrasound, computed tomography (CT), positron emission tomography (PET), magnetic resonance imaging (MRI), and rarely hybrid imaging (PET/CT, PET/MRI). [7] Transvaginal ultrasound can measure tumor size and assess infiltration of the stroma of the cervix or parametria, and transabdominal ultrasound is used to diagnose hydronephrosis in case of advanced cancer.[8] Amongst these radiological modalities the most superior is MRI because of its high resolution and tissue characterization, as well as because of its exact tumor measurement, assessment of local extension and assessment of pathological lymph node enlargement.[9] Carcinoma in situ are too small in size and usually cannot be detected on any imaging modality.

Exact diagnosis is set up based on pathohistological finding, biopsy of the cervix or endovaginal curettage. In rare cases, lymph node biopsy is used - fine needle biopsy, while postoperative or postradiationpathohistological verification in case of rest or recidive of the disease is used very rarely.

Revised FIGO classification form 2018 (table 1) has introduced changes in cervical cancer staging. Key changes are:

Use of any available imaging modality and/or pathological finding which complement and enable precise evaluation of the volume of cervical tumor [7]

Change in the first stage of disease where now exist three subgroups IB in regard to size of lesion [10]

Assessment of retroperitoneal pelvic and paraaortic lymph nodes, and in accordance with this stage IIIC is introduced. If pathologically enlarged lymph nodes are observed in pelvis or paraaortally, regardless of the tumor size, stage of disease is classified as IIIC. [7]

In order to preserve fertility of young patients which have stage IA cancer as a therapeutic method conization of the cervix can be used, and in early stage IB1 radical trachelectomy, simple trachelectomy. [5, 7, 11]

Table 1 *FIGO classification of the cervical cancer from 2018 (https://obgyn.onlinelibrary.wiley.com/doi/full/10.1002/ijgo.12749)*

STAGE I	Cancer is strictly limited to the cervix uteri (extension on the body of the uterus is negligible)
IA	Microscopically diagnosed invasive cancer with the deepest invasion ≤5mm
IA1	Stromal inasion ≤3mm in depth
IA2	Stromal invasion between 3 and 5 mm in depth
IB	Clinically visible lesion limited on the cervix uteri and preclinical cancer bigger than stage IA; the deepest invasion ≥5mm
IB1	Clinically visible lesion <2cm in the biggest diameter
IB2	Clinically visible lesion ≥2cm and <4cm in the biggest diameter
IB3	Clinicallu visible lesion ≥4cm in the biggest diameter
STAGE II	Cancer is spread beyond the cervix uteri but does not involve pelvic wall and the lower third of vagina
IIA	Without parametrial invasion
IIA1	Clinically visible lesion <4cm in the biggest diameter
IIA2	Clinicallu visible lesion ≥4cm in the biggest diameter
IIB	Cancer infiltrates parametria
STAGE III	Tumor is spread to the pelvic wall and/or involves the lower third of vagina and/or causes hydronephrosis or nonfunctioning kidney; pelvic and/or paraaortic lymph nodes can be involved
IIIA	Tumor involves the lower part of vagina with spread to the pelvic wall; pelvic and/or paraaortic lymph nodes are not infiltrated
IIIB	Pelvic wall infiltration and/or hydronephrosis or nonfunctioning kidney; pelvic and/or paraaortic lymph nodes are not infiltrated
IIIC	Lymph nodes involvment
IIIC1r	Pelvic lymph nodes, seen with imaging, which are suspected to metastaticaly changed lymph nodes
IIIC1p	Pathologically confirmed metastatically changed paraaortic lymph nodes
IIIC2r	Paraaortic lymph nodes, seen with imaging, which are suspected to metastaticaly changed lymph nodes
IIIC2p	Pathologically confirmed metastatically changed paraaortic lymph nodes
STAGE IV	Cancer is spread beyond pelvis and involves the mucose of a urinary bledder or rectum (biopsy proven); bullous edema does not allow the case to be classified as stage IV
IVA	Cancer is spread to the surrounding organs
IVB	Cancer is spread to a distant organs

FIGO CLASSIFICATION

STAGE I

Cervical cancer which is limited exclusively on the cervix, and in size up to 5mm, is classified as stage I of disease. This stage, depending on the size, is divided into stage IA and IB. If there is a microscopic invasion less than 5mm stage is classified as IA, which is further divided into IA1 and IA2, depending on whether is a tumor smaller or bigger than 3mm.

Stage IB refers to a tumor bigger than 4mm. Novelty in FIGO classification from 2018 is that now there are 3 instead of earlier 2 substages IB. Actually, revised FIGO classification divides earlier stage IB1 (tumor <4sm) into IB1, where the tumor is ≥5mm and <2cm, and stage IB2, in which tumor is ≥2cm and <4cm. Stage IB3 remains the same, tumor is ≥4cm in the biggest diameter. In revised classification lateral tumor spread is no longer considered. (7)

New division of stage IB enables the use of limited surgery, cervical conization and radical trachelectomy, in order to preserve fertility of patients whohave not given birth or want to give birth again. The possibility of preserving fertility of young patients was not considered in earlier FIGO classifications. (5) The use of cervical conization is reserved for patients with stage IA, while radical trachelectomy is possible if tumor is <2cm, which corresponds to stage IB1. (12)

Matusoet al. have shown that there is a significant difference between substages IB at the survival rate. Mortality is twice as large in stage IB2 as in stage IB1. (10)

Another novelty in revised FIGO classification from 2018 is assessment of paraaortic and pelvic lymph nodes. Patients with metastases in pelvic and/or paraaortic lymph nodes, regardless of tumor size, are classified automatically as stage IIIC of disease. (5, 7)

STAGE II

If the cancer is spread outside of cervical borders, but does not reachthe lower third of vagina and pelvic wall, is classified as stage II. This stage is divided into stage IIA, when the tumor is spread to upper two thirds of vagina but does not extend to parametria, and in regard to tumor size IIA1 (<2cm) and IIA2 (≥2cm), and IIB, when the tumor besides upper two thirds also extends to parametria. (7)

STAGE III

Tumor that spreads to the lower third of vagina, reaches and extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney and/or involves retroperitoneal or pelvic lymph nodes is classified as stage III. Earlier FIGO classification has divided stage III in 2 substages, IIIA and IIIB, while the novelty in revised FIGO classification is existence of substage IIIC. Stage IIIA involves tumor which is spread on the lower third of vagina but is not extended to pelvic wall, while tumor in stage IIIB also involves pelvic wall and/or causes hydronephrosis or nonfunctioning kidney. New substage IIIC, as stated above, implies the presence of metastasis in retroperitoneal and/or pelvic lymph nodes regardless on tumor size. This stage is further determined with an appendix r or p depending on which way metastases in lymph nodes were identified, with imaging modalities or pathologically, subsequently. (7) Survival rate in stage III differs and it is interesting that substage IIIC has better prognosis than stages IIIA and IIIB. Five-year survival rate in stage IIIC primarily depends on local extend of a tumor. (10)

STAGE IV

New revised FIGO classification does not bring any novelties in stage IV. Stage IV involves tumor which is spread beyond small pelvis or has spread to mucose of a urinary bladder or rectum, which has to be proven by biopsy. It is divided in two substages: IVA, tumor inflitrates surrounding organs, and IVB, dissemination of the tumor to distant organs. (7)

CONCLUSION

The need for a change in FIGO stages of cervical cancer has originated precisely from clinical practice. Correct selection of the patients for a certain type of treatment of patients with this cancer is based on precisely defined stage of disease. The primary principle of medicine *primun non nocere*is also used in case of treatment of cervical cancer, as in other diseases. Patient selection for operative treatment implies a selected group of patients who will not receive postoperative therapy, thus avoiding duplication of therapy, as well as possibility of complications and satisfying cost benefits. Special entity represents fertility spearingprocedures of treatment of cervical cancer in young patients who have not given birth or who are motivated to give birth, and adequate assessment of stage of disease with the use of all available imaging techniques will provide better assessment in preoperative selection of such patients and thus confirmation of indication for conservative treatment.

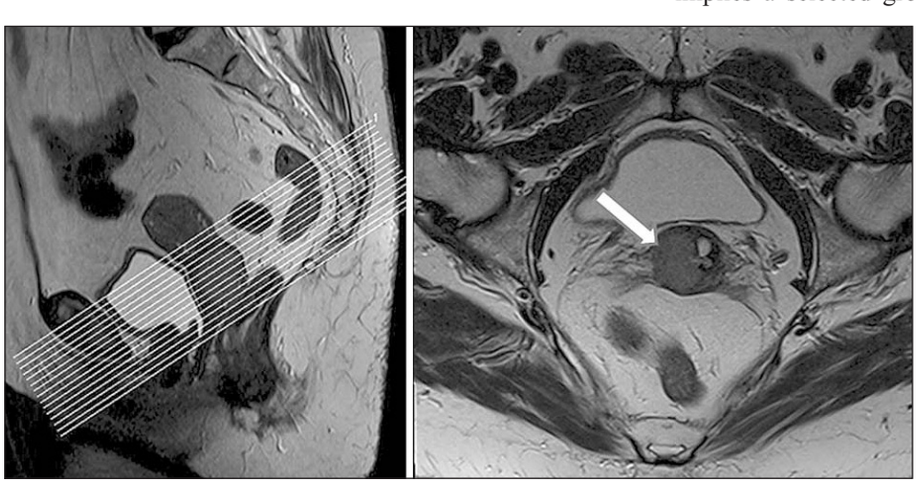

Image 1. *Pelvic MRI T2W sagittal and paraaxial plane (3T, Trio, Siemens) – Infiltration of the cervix uteri, the largest dimension of the lesion is 22 mm. Cervical stromal ring is intact. According to revised classification FIGO IB2.*

Although it is a well-known fact that primary prognostic factor in order to monitor prognosis of

patients is a stage of disease, as additional prognostic factor involvement of lymphatic glands is important as well as parametrial invasion. In early stage IA the question of the histological grading of the tumor, presence or absence of lymphovascular invasion as well as prognostic parameters which are not included in classification of early stage of disease still remain undefined.

Taking into consideration above mentioned, diagnostics and treatment of patients with cervical cancer is based on multidisciplinary approach.

Sažetak

Karcinom grlića materice i dalje predstavlja veliki socioekonomski problem, obzirom na incidencu cervikalnog carcinoma koja se i pored mera prevencije i dalje održava na visokom nivou, naročito u zemljama nižeg socioekonomskog razvoja. Karcinom grlića materice četvrti je karcinom po učestalosti kod žena. Precizna procena stadijuma bolesti preduslov je za izbor adekvatnog terapijskog modaliteta.Dugo godina upotrebljavana FIGO klasifikacija nije zadovoljavala kriterijume proširenosti bolesti i samim tim postala je insuficijentna. U odnosu na prethodnu FIGO klasifikaciju, koja je bila bazirana na kliničkom procenjivanju stadijuma bolesti na osnovu ginekološkog pregleda i pomoću drugih dijagnostičkih metoda, revidirana FIGO klasifikacija uključuje radiološke imidžing metode i patološku procenu u određivanju stadijuma karcinoma grlića materice i to za sve stadijume bolesti, kao dopuna kliničkoj proceni kada su radiološke metode dostupne. Dijagnostika i lečenje pacijentkinja obolelih od karcinoma grlića materice zasniva se na multidisciplinarnom pristupu.

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