Effects of Treatment of Uterine Cervical Carcinoma Monitored by Magnetic Resonance Imaging - Sarajevo Experience

Amela Sofic[1], Azra Husic-Selimovic[2], Nermina Beslic[3], Azra Rasic[4], Dzenana Begic[4], Anja Tomic-Cica[5], Nejira Imsirevic[2]

[1]Clinic of Radiology, Clinical center University of Sarajevo, Sarajevo, Bosnia and Herzegovina
[2]Institute of Gastroenterohepatology, Clinical center University of Sarajevo, Sarajevo, Bosnia and Herzegovina
[3]Clinic of Nuclear medicine, Clinical center University of Sarajevo, Sarajevo, Bosnia and Herzegovina
[4]Oncology Clinic, Clinical center University of Sarajevo, Sarajevo, Bosnia and Herzegovina
[5]Clinic of obstetrics and gynecology, Clinical center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

Corresponding author: prof Amela Sofic, MD, PhD. Clinic of Radiology, Clinical center University of Sarajevo, Sarajevo, Bosnia and Herzegovina.

doi: 10.5455/aim.2017.25.39-43
ACTA INFORM MED. 2017 MAR; 25(1): 39-43
Received: Dec 27, 2016 • Accepted: Feb 17, 2017

ABSTRACT

Goal: The goal of this study was the determination of the effects in treatment of early stage (<IIB) and locally advanced stages (≥IIB) of uterine cervical carcinoma by using MRI. Material and Methods: The study was a prospective, comparative, analytical, and observational and included 74 patients with cervical cancer (PH confirmed). All 74 patients have initially gone through the pre-therapeutic MRI to determine the tumour FIGO stage. At a renewal of the initial MRI findings, patients were divided into two study groups: group A and group B. Group A consisted from 39 patients with early-stage cervical carcinoma (<IIB) and group B comprised from 35 patients with locally advanced stage (≥IIB). Postterapeutic MRI control, were perfomed in both group (A and B). Further MRI examinations were set for the patients from both groups. Results: An analysis of treatment outcomes in group A showed that most patients had no local recurrence or residuum disease in 89.7%, while local recurrence was observed in only 10.3% cases. An analysis of treatment outcomes in group B showed that most patients had complete regression after local chemoradiotherapy in 68.8%, while 25.7% of patients had local progression of the disease, while the 5.7% cases recorded partial local tumour regression($p<0.05$). It has been shown that a complete local regression was more frequent in the case of squamous cell carcinoma in 74.2% vs 25% in adenocarcinoma cases. Also local and partial regression was observed more frequently in the case of squamous cell carcinoma in 6.5% compared to 0% in adenocarcinoma, while progression was more common in adenocarcinoma at 75% compared to 19.4% for squamous cell ($p<0.05$). MRI results showed positive outcome of treatment group A and B in our study, showed a statistically significant difference in favour of group A (89.7%) compared to group B 68.8% ($p<0.05$). Conclusion: The results obtained from our studies show that early stage cervical cancer (<IIB) shows a better outcome in treatment of advanced stages (≥IIB). In the treatment of advanced stages (≥IIB), concomitant radio chemotherapy shows significant results in terms of complete tumour regression, especially in squamous cell type of cervical cancer.

Keywords: cervical cancer, MRI, FIGO stage, surgical treatment, oncology treatment.

1. INTRODUCTION

Invasive cervical cancer is the fourth most common malignancy of women in the world and it holds a fourth place of death caused by cancer in women (1). It develops from precursor lesions, dysplasia, which may be cervical intraepithelial neoplasia (CIN) or adenocarcinoma in situ. The diagnosis of invasive cervical cancer is set using any of the following procedures: history and physical examination, gynaecological speculum and recto-vaginal palpation examination, the cervix cytology (Pap smear), HPV typing, colposcopy, biopsy, endocervical curettage. Regular gynaecological examinations and Pap smear screening test can greatly reduce the incidence rate of cervical cancer. Staging of the tumour can be evaluated using: ultrasound (US), magnetic resonance (MR), computer tomography (CT), positron emission tomography (PET) and bone scintigraphy. Determining the correct tumour stage is an important step in the treatment process, because it directly affects the choice of therapy and prognosis. Retrospective studies have shown that the disease is most often repeated within the first 2 years (2). As a result, most of the guide suggests routine monitoring of patients every 3-4 months during the first two years, after which the inspections are required every 6 months.

It is known that magnetic resonance

is a "state of the art" method to estimate FIGO stage, treatment planning, monitoring after therapeutic treatment and monitoring survival (3, 4, 5). MRI is the method of choice in the evaluation of cervical cancer because it shows better results when determining the local extent of the tumour compared with physical examination and other imaging techniques (6, 7). Also, MRI is sovereign in determining the tumour response to treatment after chemoradiotherapy cycle, and in determining the after-effects on normal tissue (8, 9). The superiority of MRI is proven in comparison to all other procedures because through a single act of scanning it gives a complete insight into tumour staging, it enables a large FOV, good spatial and contrast-resolution and thus good characterization of soft tissue.

2. GOALS

The goal of the study focused at determination of the effects of treatment of early stage (<IIB) and locally advanced stages (≥IIB) of uterine cervical carcinoma using magnetic resonance imaging.

3. MATERIALS AND METHODS

The study was a prospective, comparative, analytical, and observational and was made in the Clinical centre University of Sarajevo (KCUS) during 2013 through the year 2016. The study included 74 patients with cervical cancer, which were diagnosed using PH received from biopsy material. All patients (n = 74) have initially gone through the pre-therapeutic MRI to determine the tumour FIGO stage. The selection was made for the therapeutic treatment of patients. At a renewal of the initial MRI findings, patients were divided into two study groups, group A and group B. Group A consisted a 39 patients with early-stage cervical carcinoma (<IIB) who were candidates for surgical treatment. Group B is comprised of 35 patients with locally advanced stage of cervical cancer of the uterus (≥IIB), which were not candidate for surgical treatment. Their FIGO stage demanded a chemoradiotherapy treatment.

After appropriate therapeutic treatment, all patients in both groups underwent through a second MRI control, in order to assess therapeutic effects. Further MRI examinations were set for the patients from both groups, and as per the oncological protocol were defined to be undertaken every four months, during the next three years.

Positive outcome of treatment in the group A is considered the tumour remission, while a negative treatment outcome was defined through a presence of recurrence or residuum.

Positive outcome of treatment in group B was considered a complete regression after radiochemo therapy, a negative outcome was defined as a partial regression or progression.

Outcomes of both groups were compared with the following parameters: patients age, FIGO stage of cancer, tumour size, PH tumour findings, the degree of differentiation of the tumour, the type of therapeutic treatment. The patients were examined by MRI apparatus Siemens (Germany) of 1.5T and GE (USA) of 1.5T. Gel was applied to vagina using T2 bright a contrast medium in order to reach dilatation and better resolution of detail. The patients were given intravenous contrast medium based on gadolinium (Gadovist).

Protocols for MRI

For all the patients (group A and B) the same MRI protocol applied. Basic protocol included: T2 without suppression of fat tissue, min 3 sections of anatomical details view; T1W without suppression of fat tissue or opposite phases; T1W with suppression of fat tissue; PDW or T1W extended to the upper abdomen; T1W with suppression of fat tissue adding Gadolinium contrast DWI Extended protocol was used when there was a need to obtain more information and it contained the following added sequences: T2W inclined or orthogonal towards cervix; FOV variations; larger FOV in order to cover a complete surface of pelvis, smaller FOV centrally positioned towards uterus, T1 post-contrast images in 3 planes.

Statistical analysis

The differences observed between the groups were tested using the CHI square, Student's test and one-way analysis of Variance (ANOVA), depending on the data type, with the level of significance of p <0.05, or at the level of 95%. The analysis was conducted using statistical package IBM SPSS Statistics in 21.0.

4. RESULTS

In our total sample (groups A and B), mostly consisted of six decades, in 37.8% of cases, while the average age of patients was 56.6 ± 12.3 years. There was no statistically significant difference (p> 0.05) in the average age among the group A of 58.4 ± 10.98 and group B of 54.4 ± 13.4. Table1 Looking at the entire sample (group A and B) we can observe that more squamous carcinoma type were present with n = 61 (82.4%) cases, in comparison to adenocarcinoma of the present n = 13 (17.6%) cases (p < 0.05). This proportion is retained in both study groups without statistically significant difference (p> 0.05). Squamous cell cancer of the group was present in 76.9%

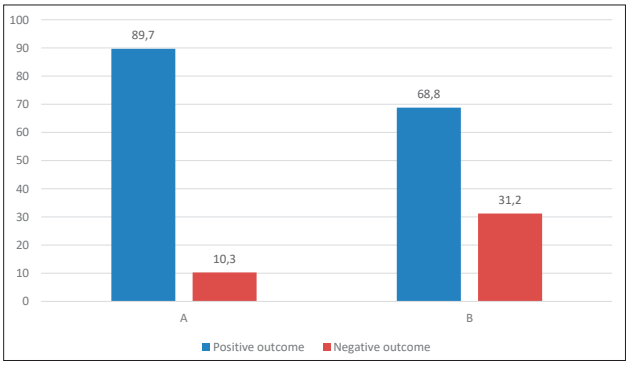

Figure 1. Analysis of treatment results of group A with early stage of cervical carcinoma

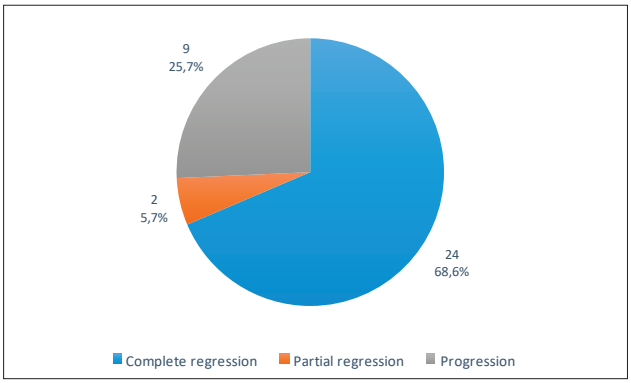

Figure 2. Analysis of treatment results of group A with advanced stage of cervical carcinoma

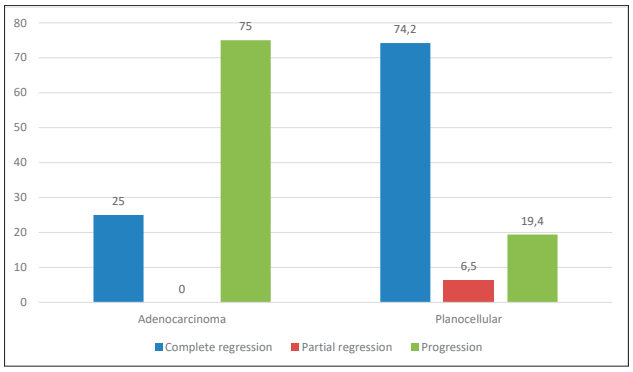

Figure 3. Distribution of results of treatment -patohistological type group B

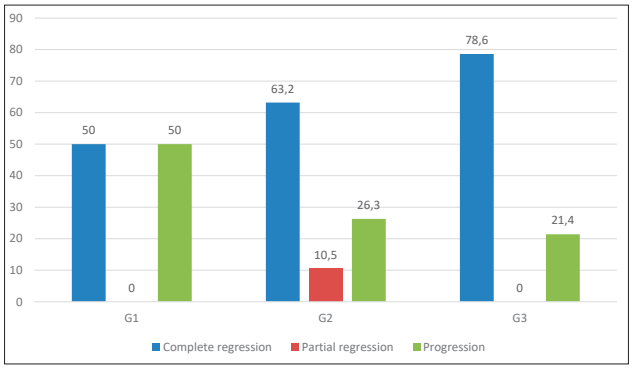

Figure 4. Distribution of results of treatment – the degree of differentiation of tumours within the group B

of A, the group B of 88.6%, and adenocarcinoma of the group A of 23%, the group B of 11.4%.

Comparison of representation of squamous cell in comparison to adenocarcinoma its pointing to statistically significant difference in relation to the expected distribution both in the total sample ($\chi 2$ = 31.135, p = 0.000) and in certain groups, group A ($\chi 2$ = 11.308, p = 0.001) and group B ($\chi 2$ = 20.829, p = 0.000). Viewing grade shows that in the total sample (groups A and B) was the most represented G2 with n = 41 (55.4%) cases, followed by G3 with n = 27 (36.5%) cases, and at least G1 n = 6 (8.1%) cases. This relationship is maintained and in between the two groups with no statistically significant differences (p> 0.05). In group A represented by G2 of 56.4%; G3 33.3% and 10.3% of G1. In group B represented by 54.3% of G2 stage, G3 of 40%, and the G1 stage in 5.7% patients. Average length of tumours in group B was 53.9 ± 13.3 mm, with a minimum value of 10 mm, and the highest 76 mm, with a slightly greater length in the tumour and the stage IIB was 56.6 ± 15.2 mm (40-76 mm) according to the stage IIIB tumours with an average length of 53, 5 ± 13.2 mm (10-70 mm) with no statistically significant difference (p> 0.05). An analysis of treatment outcomes in group A showed that most patients had no local recurrence or residuum disease n = 35 (89.7%), while local recurrence was observed in only n = 4 (10.3%) cases.

Statistical analysis by chi-square test shows that there is a statistical discrepancy in statistical significance of the expected distribution in favour of representation of patients without recurrence (p <0.05). An analysis of treatment outcomes in group B showed that most patients had complete regression after local chemoradiotherapy n = 24 (68.8%), while n = 9 (25.7%) patients had local progression of the disease,

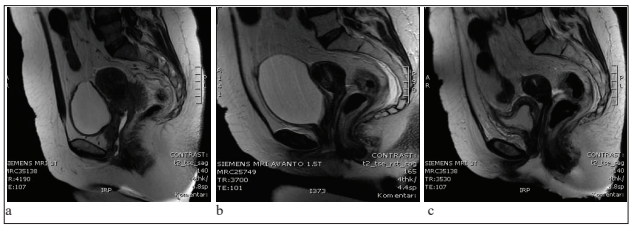

Figure 5. MRI-T2 sag: Regression of cervical carcinoma FIGO IIIB: a.before, b.after, c. a year after radio/chemo treatment

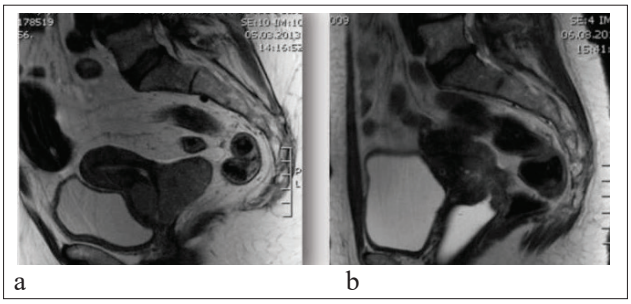

Figure 6. MRI-T2w sag: a. FIGO IIB b. FIGO IVA

while the un = 2 (5.7%) cases recorded partial local tumour regression (Figure 1).

Statistical analysis by chi-square test shows that there is a statistical discrepancy in statistical significance of the expected distribution for the benefit of complete regressions (p <0.05). It has been shown that a complete local regression was more frequent in the case of squamous cell carcinoma in 74.2% compared to 25% in adenocarcinoma cases. Also local and partial regression was observed more frequently in the case of squamous cell carcinoma in 6.5% compared to 0% in adenocarcinoma, while progression was more common in adenocarcinoma at 75% compared to 19.4% for squamous cell (Figure 2).

These differences are statistically significant (p <0.05). An analysis of treatment outcomes in relation to the age of patients in the group were not proven to be statistically significant. Analysis of treatment outcome in respect to the average size of the tumour, demonstrates the highest value of 55.9 ± 18.9 mm in the case of the progression, over 53.9 ± 11 mm in the case of total regression, and to 42.5 ± 14.8 mm in the case of partial regression, no statistically significant differences (p> 0.05). Analysing the outcome of group B, compared to the G stage, complete regression was observed in 1 patient (50%) in the group G1, 12 (63.2%) patients in group G2 and 11 (78.6%) patients in the group with the G3, with no statistically significant difference (p> 0.05). Progression occurred in 1 patient (50%) in the group G1, and 5 (26.3%) patients in the group G 2 and the n = 3 (21.4%) patients in the group G 3, no statistically significant difference (p > 0.05). Partly regression was observed only in the group with the G2 and in 2 patients, which amounts to 10.5% of the cases with the PC grade (Figure 3).

Comparing the MRI results positive outcome of treatment group A and B in our sample, showed a statistically significant difference (p <0.05) in favour of group A (89.7%) compared to group B (68.8%) (Figure 4).

5. DISCUSSION

It is imperative to make the proper MRI FIGO selection of patients with cervical cancer in order to receive appropriate therapeutic treatment.

Infiltration parametric (IIB) is the main diagnostic marker, because patients with lower FIGO stage, without infiltration parametric should be successfully operated, with no signs of recurrence of the tumour resection margin. (Figure 5, 6). For negative women with early-stage cervical cancer (<IIB), MRI helps determine the suitability of surgical treatment compared to primary chemo radiation treatment. (10, 11). Several studies, using preoperative MRI examination showed that in patients with early-stage cervical cancer MRI has a 94% precision and 95% negative predictive value for determining invasion parametric in the time of diagnosis. Multiplan T2 sequences at MRI plays an important role in making a selection for therapeutic treatments among patients (12, 13, 14). Surgical treatment and radiation therapy are equally effective in the early stages of the disease, although for tumours of small volume (15). Younger patients may benefit from surgery for ovarian preservation and avoidance of vaginal atrophy and stenosis. Surgical treatment is indicated for most patients with stage IB and IIA cervical cancer. The classic surgical approach involves Wertheim-Meigs operation. It includes a total abdominal hysterectomy, resection of the upper third of the vagina, and excision parametria paravaginal sakrouterine tissues including ligament and pelvic dissection paraaortic lymph nodes (16). Concomitant radiooncological treatment of cervical cancer varies depending on the stage of the disease, radiation dose and schedule of administration of Cisplatin and radiation, but shows significant benefit in survival when combined approach to therapy. Five randomized trials (GOG-85, RTOG-9001, GOG-120, GOG-123 and SWOG -8797) showed an overall survival advantage for Cisplatin therapy given concurrently with radiation therapy, and one study shows that this mode of therapy has no benefit (17, 18, 19). The risk of death from cervical cancer has declined from 30% to 50% when using chemoradiation in the total sample of our study (<IIB and (≥IIB). Mostly consisted of six decades, in 37.8% of cases, and when the average age of patients was 56.6 ± 12.3 years, with no significant differences between early and advanced stages. A similar survey of French population states that top the incidence was between 40 and 49 years of age, with a mean age of 52 ± 16.4 years (20). The total sample was significantly more common squamous (82.4%) compared to adenocarcinoma no statistically significant differences between early and advanced stages. Dominated the G2 was in 55.4%, G3 in 36.5% and G1 in 8.1% of cases, with no significant difference. The average length of tumor was 53.9 ± 13, 3 mm, with a minimum value of 10 and maximum of 76 mm. Elmarjany Research shows that the median size of tumors in their patients was 48 ± 16 mm from the domination of squamous cell with 86.2% (21).

The results indicate that there is no statistically significant difference in length compared to the tumours in advanced stages of the stages of cervical cancer, although it was slightly higher in stage IIIB and was 56.6 ± 15.2 mm (40-76 mm) as compared to stage IIIb with an average length of tumours from 53.5 ± 13.2 mm (10-70 mm).

When it comes to the early stages of cervical cancer (<IIB) in our study, there was a statistically and significantly more patients with the absence of tumours after treatment in the OP 89.7%, while the relapse was recorded only in 10.3% of cases. A survey conducted in Serbia showed that relapse after surgical treatment with radical hysterectomy occurred in 12.5% of patients (22).

In advanced stages of cervical cancer (≥IIB), after radio/chemo treatments in our study, a complete tumour was achieved regression in 68.8%, indicating a statistically significant difference with respect to progression (25.7%) and partial regression (5.7%). Study Naghi and his associates is showing nearly identical results for the same period of monitoring (23). Our studies, as well as Zhang and associates from China showed statistically significant better response to radio/chemo therapy from squamocellular tumours of the cervix of 74% compared to 25% of adenocarcinomas, with statistically no significant difference in the tumour size (24).

After radio/chemo therapy we had complete regression of 50.0% in the group with G1, over 63.2% in the group with G2 to 78.6% in the group with the G3, but no statistically significant difference. In a similar study, conducted by Heller and his associates in Croatia, the statistically significant difference has not been proven in radio sensitivity between poorly and well-differentiated tumours (25). There were no statistically significant differences between the patient's age and tumour successfully treated through radio/chemo therapy. Our results show that the complete regression was more frequent in stage IIB (80%) compared to stage IIIB (66.7%). West and his associates haven't reached statistically significant differences in results when it comes to a comparison of success in radio/chemo therapy in relation to a tumour stage (26). The Elmarjany study shows small percentage differences to better treatment outcomes in stages IIB.

In relation to the outcome of stage IIIB, which are also not statistically significant (21). These results suggest that in patients with advanced tumour stage (≥IIB), its height tumour stage, tumour grade, tumour length and age of the patient are not independent factors to the success of treatment and different influence on the individual therapeutic result radio/chemo therapy. In contrast, PH type of cervical cancer significantly affects the therapeutic response. Squamous cell type compared to adenocarcinoma shows better treatment outcome and prognosis. Comparison of our results in a three-year study, a total sample of n = 74 patients showed that significantly better outcome of treatment in terms of the absence of tumours in the early stages of 89.7% (<IIB) in relation to the locally advanced cervical carcinoma from 68, 8% (≥IIB).

6. CONCLUSION

The results obtained from our studies show that early stage cervical cancer (<IIB) shows a better outcome of treatment of advanced stages (≥IIB). In the treatment of advanced stages (≥IIB), concomitant radio chemotherapy shows significant results in terms of complete tumour regression, especially in squamous cell type of cervical cancer.

- **Author's contribution:** Amela Sofić: substantial contribution to conception and design, acquisition of data, final approval of the version to be published. Azra Rasic, Dzenana Begic and Anja Tomić: colection of data, substantial contribution to acquisition

of data, substantial contribution to analysis and interpretation of data. Azra Husic-Selimovic: substantial contribution to analysis and interpretation of data, drafting the article. Nejira Imsirevic:- substantial contribution to acquisition of data. Nermina Beslic: substantial contribution to analysis and interpretation of data.

- **Conflict of interest:** There is no conflict of interest of any of listed authors.

REFERENCES

1. Fact Sheets by Cancer [Internet]. Globocan.iarc.fr. 2016 [citirano maj, 2016]. Dostupno na: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx
2. Ansink A, de Barros Lopes A, Naik R. Recurrent stage IB cervical carcinoma: evaluation of the effectiveness of routine follow up surveillance. Br J Obstet Gynaecol. 1996; 103(11): 1156-8.
3. Balleyguier C, Sala E, Da Cunha T, Bergman A, Brkljacic B, Danza F. Staging of uterine cervical cancer with MRI: guidelines of the European Society of Urogenital Radiology. European radiology. 2011; 21(5):1102-10.
4. Paulson ES, Erickson B, Schultz C, Li AX. Comprehensive MRI simulation methodology using a dedicated MRI scanner in radiation oncology for external beam radiation treatment planning. Med Phys. 2015; 42(1): 28-39.
5. Hricak H, Swift PS, Campos Z, Quivey JM, Gildengorin V, Goranson H. Irradiation of the cervix uteri: value of unenhanced and contrast-enhanced MR imaging. Radiology. 1993; 189(2): 381-8.
6. Hricak H, Gatsonis C, Coakley FV, Snyder B, Reinhold C, Schwartz LH. Early invasive cervical cancer: CT and MR imaging in preoperative evaluation - ACRIN/GOG comparative study of diagnostic performance and interobserver variability. Radiology. 2007; 245(2): 491-8.
7. Mitchell DG, Snyder B, Coakley F, Reinhold C, Thomas G, Amendola M. Early invasive cervical cancer: tumor delineation by magnetic resonance imaging, computed tomography, and clinical examination, verified by pathologic results, in the ACRIN 6651/GOG 183 Intergroup Study. J Clin Oncol. 2006; 24(36): 5687-94.
8. Hatano K, Sekiya Y, Araki H, Sakai M, Togawa T, Narita Y. Evaluation of the therapeutic effect of radiotherapy on cervical cancer using magnetic resonance imaging. Int J Radiat Oncol Biol Phys. 1999; 45(3): 639-44.
9. Vandecasteele K, Delrue L, Lambert B, Makar A, Lambein K, Denys H. Value of magnetic resonance and (1)(8)FDG PET-CT in predicting tumor response and resectability of primary locally advanced cervical cancer after treatment with intensity-modulated arc therapy: a prospective pathology-matched study. Int J Gynecol Cancer. 2012; 22(4): 630-37.
10. Mitchell DG, Snyder B, Coakley F, Reinhold C, Thomas G, Amendola M. Early invasive cervical cancer: tumor delineation by magnetic resonance imaging, computed tomography, and clinical examination, verified by pathologic results, in the ACRIN 6651/GOG 183 Intergroup Study. J Clin Oncol. 2006; 24(36): 5687-94.
11. Hricak H, Gatsonis C, Coakley FV, Snyder B, Reinhold C, Schwartz LH. Early invasive cervical cancer: CT and MR imaging in preoperative evaluation - ACRIN/GOG comparative study of diagnostic performance and interobserver variability. Radiology.2007; 245(2): 491-8,
12. Sironi S, Villa G, Rossi S, Bocciolone L, Maggioni A, Sonzogni A. Magnetic resonance imaging in the evaluation of parametrial invasion of carcinoma of the cervix uteri: optimization of the study protocol. La Radiologia medica. 2001; 101(6): 477-84.
13. Sironi S, Bellomi M, Villa G, Rossi S, Del Maschio A. Clinical stage I carcinoma of the uterine cervix value of preoperative magnetic resonance imaging in assessing parametrial invasion. Tumori. 2002; 88(4): 291-5.
14. Iwata S, Joja I, Okuno K, Miyagi Y, Sakaguchi Y, Kudo T. Cervical carcinoma with full-thickness stromal invasion: efficacy of dynamic MR imaging in the assessment of parametrial involvement. Radiation medicine. 2002; 20(5): 247-55.
15. Eifel PJ, Burke TW, Delclos L, et al. Early stage I adenocarcinoma of the uterine cervix: treatment results in patients with tumors less than or equal to 4 cm in diameter. Gynecol Oncol. 1991; 41(3): 199-205.
16. DiSaia PJ, Creasman WT. Clinical gynecologic oncology 6th ed. St Louis, Mo: Mosby, 2002; 53-95.
17. Whitney CW, Sause W, Bundy BN. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. J Clin Oncol. 1999; 17(5): 1339-48.
18. Peters WA 3rd, Liu PY, Barrett RJ 2nd. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. J Clin Oncol. 2000; 18(8): 1606-13.
19. Pearcey R, Brundage M, Drouin P, et al. Phase III trial comparing radical radiotherapy with and without cisplatin chemotherapy in patients with advanced squamous cell cancer of the cervix. J Clin Oncol. 2002; 20(4): 966-72.
20. Lorin L, Bertaut A, Hudry D, Beltjens F, Roignot P. About invasive cervical cancer: a French population based study between 1998 and 2010. Eur J Obstet Gynecol Reprod Biol. 2015; 191: 1-6.
21. Elmarjany M, Maghous A, Razine R. Diagnostic, therapeutic and evolutionary characteristics of cervical cancer in Department of Radiotherapy. Gynecologic Oncology Research and Practice. 2015; 2: 2. doi 10.1186/s40661-015-0009-y.
22. Đurđević S, Stojanović S, Pantelić M, Nikolić D. Radikalna histerektomija u hirurškom lečenju invazivnog karcinoma grlića materice na Novosadskoj ginekološko-akušerskoj klinici u periodu 1993-2013. godine. Medicinski pregled. 2015; 68(7-8): 227-33.
23. Negi RR, Gupta M, Kumar M, Gupta MK. Concurrent chemoradiation in locally advanced carcinoma cervix patients. J Cancer Res Ther. 2010; 6(2): 159-66.
24. Zhang M1, Cai S, Shi D. The comparison of radiosensitivity between uterine cervical squamous carcinoma and adenocarcinoma. Zhonghua Fu Chan Ke Za Zhi. 1998; 33(10): 611-3.
25. Heller H, Rupić S, Kraljević M. Original scientific paper Treatment of Invasive Cervical Cancer: Rijeka Experience. Antropol. 2007: 31(2): 139-46.
26. West CM, Davidson SE, Burt PA, Hunter RD. The intrinsic radiosensitivity of cervical carcinoma: correlations with clinical data. Int J Radiat Oncol Biol Phys. 1995; 31(4): 841-6.