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Postoperative radiotherapy in the treatment of endometrial cancer: Review of 158 patients

Endometrial kanserin tedavisinde postoperatif radyoterapi: 158 hastanın gözden geçirilmesi

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Abstract

Aim: Endometrial cancer is the most common gynecological cancer in the West. It is the third cancer of women after that of the breast and intestine. It mainly concerns menopausal women. Our aim is to highlight, through a retrospective study and in light of literature data, the role of radiotherapy in the management of this cancer.

Methods: This is a retrospective cohort study concerning patients' records for endometrial in the radiotherapy department at university hospital center of FEZ for a period of 5 years from January 2012 to December 2016.

Results: We collected 158 patients of mean age 64 years (36 to 92 years), all patients had a total hysterectomy with (76% of cases) or without (24% of cases) ganglion dissection. Type 1 was the most common histological type (96% of cases). The myometrial invasion was greater than 50% in 51% of cases, histological grade III in 36% of cases, and cervical invasion was observed in 16% of cases. Therapeutically, 18% of patients received exclusive external radiotherapy at a dose of 50 Gy in conventional fractionation and spreading, a TEN at a dose of 46 Gy followed by a brachytherapy dam in 58% of cases, and 24% of patients received brachytherapy alone. After an average follow-up of 25 months, 91% of the patients are in good locoregional control, 9% of the patients had distant metastases.

Conclusion: Radiotherapy retains an important place in the therapeutic strategy of high endometrial cancers, or with unfavorable histological characters, and thus allows the reduction of locoregional recurrence rates.

Keywords: Endometrium, Cancer, Surgery, Radiotherapy

Öz

Amaç: Endometrial kanser, Batı'da en sık görülen jinekolojik kanserdir. Göğüs ve bağırsaktan sonraki üçüncü kadın kanseridir. Esas olarak menopozdaki kadınlarla ilgilidir. Amacımız, retrospektif bir çalışma ve literatür verileri ışığında, bu kanserin yönetiminde radyoterapinin rolünü vurgulamaktır.

Yöntemler: Ocak 2012 ile Aralık 2016 arasında 5 yıllık bir süre için FEZ'nin üniversite hastanesinde radyoterapi bölümünde hastaların endometriyal kayıtları ile ilgili retrospektif bir kohort çalışmasıdır.

Bulgular: Yaş ortalaması 64 olan (36-92 yaş arası) 158 hasta topladık, tüm hastaların histerektomi (olguların %76'sı) veya (olguların %24'ü) ganglion diseksiyonu yoktu. Tip 1 en sık görülen histolojik tipti (olguların %96'sı). Olguların %51'inde miyometriyal invazyon %50'den, vakaların %36'sında histolojik derece III ve %16'sında servikal invazyon görülmüştür. Terapötik olarak, hastaların %18'i konvansiyonel fraksiyonasyon ve yaymada 50 Gy'lik bir dozda özel eksternal radyoterapi aldı, 46 Gy dozunda bir TEN, %58'inde brakiterapi barajı ve hastaların sadece %24'ü brakiterapi aldı.

Ortalama 25 aylık takipten sonra hastaların %91'i iyi lokal kontrolde, %9'unda uzak metastaz vardı.

Sonuç: Radyoterapi, yüksek endometriyal kanserlerin terapötik stratejisinde veya istenmeyen histolojik karakterlerde önemli bir yer tutmaktadır ve bu nedenle lokal nüks oranlarının azaltılmasına izin vermektedir.

Anahtar kelimeler: Endometrium, Kanser, Cerrahi, Radyoterapi

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Introduction

Endometrial cancer is the most common gynecological cancer in the West [1]. It mainly concerns menopausal women [1]. The majority of endometrial cancers are diagnosed at early stages. Two histological types of endometrial cancer are described: type I and II, with histological, epidemiological and molecular specificities [2]. Surgery is the treatment of reference. It makes it possible to specify the stage according to the classification of the FIGO and thus to guide the indications of the adjuvant treatment [3-5]. Its prognosis remains relatively favorable with a cancer mortality rate that remains the lowest in comparison with other female cancers. The purpose of our work is to report the experience of the radiotherapy department to the National Institute of Oncology in the management of endometrial cancer.

Materials and methods

We conducted a retrospective cohort study through a series of 158 cases followed for endometrial cancer in the radiotherapy department at university hospital center of FEZ during a period of 5 years from January 2012 to December 2016. The data collected from the medical records of our patients, based on a record of exploitation, concerned the epidemiological, clinical, therapeutic and evolutionary aspects of this cancer. The diagnosis was clinical and histological. The tumors were classified according to the FIGO classification; the radiological assessment of the locoregional extension was an abdominopelvic computed tomography (CT); the distance extension assessment was based on the signs of call. The treatment was mainly based on surgery, which allows staging of the tumor and then indicates adjuvant treatment: external radiotherapy and / or brachytherapy of the vaginal fundus. The surgery consisted of a total hysterectomy or even a total colo-hysterectomy with or without an adnexectomy, with or without lymphadenectomy. External radiotherapy was delivered by four beams of high energy X photons (18 to 25 MV). The total dose delivered to the isocenter was 46 Gy in 23 fractions, two Gy per fraction. Brachytherapy was high dose rate (HDR), the total dose delivered varied according to whether it is brachytherapy exclusive or associated with external beam radiotherapy. It was 14 Gy in two weekly fractions, 7 Gy per fraction or 24 Gy in four weekly fractions, 6Gy per fraction.

Results

We collected 158 patients of average age 64 years (36 to 92 years), 87% were menopausal. The average consultation time was 6 months (2-36 months). At the first consultation, 157 of the patients complained of metrorrhagia, a single incidental finding, all patients had a total hysterectomy with (76% of cases) or without (24% of cases) ganglion dissection. Type 1 was the most common histological type (96% of cases). The myometrial invasion was greater than 50% in 51% of cases, histological grade III in 36% of cases, and cervical invasion was observed in 16% of cases. 58% of our patients were classified in the high-risk group, and 42% of the cases in the intermediate risk group. Therapeutically, 18% of patients received exclusive external radiotherapy at a dose of 50 Gy in conventional fractionation and spreading, a TEN at a dose of 46 Gy followed by a brachytherapy dam in 58% of cases, and 24% of patients received brachytherapy alone. After an average follow-up of 25 months, 91% of the patients are in good locoregional control, 9% of the patients had distant metastases.

Discussion

Endometrial cancers are the most common gynecological cancers in the West. More than 75% of patients are postmenopausal at the time of diagnosis and only 3% are under 40 years of age [1], in our series 87% of our patients were menopausal. Among the risk factors for this cancer, treatment with tamoxifen is mainly distinguished between obesity, diabetes and hypertension [1,2]. Hereditary forms represent 2 to 5% of endometrial cancers; they are mainly found in Lynch syndrome (hereditary non-polyposis colorectal cancer, endometrial, stomach, small bowel, pancreatic, ovarian, hepatobiliary cancer) [3], in our series no case of form hereditary has not been reported. Two clinical and prognostic forms are currently described. Endometrioid carcinoma type 1 is slow-moving and has a favorable prognosis. The context is that of a state of hyperestrogenism and overweight. It is most often adenocarcinoma well to moderately differentiated. This form of endometrial cancer is often associated with genetic mutations (K-ras genes, RER genes) [2]. Type 2 carcinoma develops faster than usual risk factors (obesity, diabetes, hyperestrogenism). Histologically, these are low-differentiated serous or clear-cell types. This second form of endometrial cancer is thought to be associated with p53 and/or HER2 gene mutations [2].

The tumor grade represents the degree of differentiation and has a significant influence on the prognosis. It is most often an endometrioid adenocarcinoma. Other histological forms are mucinous carcinoma, clear cell carcinoma, serous papillary carcinoma, sarcoma and carcinosarcoma; in our series Type 1 was the most common histological type (96% of cases). Clear cell carcinoma and serous papillary carcinoma are considered Grade 3 and is aggressive forms. Sarcomas account for about 5% of malignant tumors of the uterus and include mixed mesoderm tumors, leiomyosarcomas and endometrial sarcomas (stroma). Sarcomas are more aggressive, more frequently causing distant metastases [3]. For the circumstances of discovery, it is essentially post-menopausal or peri-menopausal metrorrhagia, usually spontaneous, painless and scanty. Other clinical signs are rare, they can be leucorrhea, heaviness or pelvic pain, urinary disorders. In our series 98% of our patients, the clinical sign of discovery was metrorrhagia. The clinical examination is generally uninformative. Indeed, cervical examination is usually normal except for stages II with cervical extension. The exploration of ganglionic areas, the palpation of the liver, the search for ascites, and the examination is always indicated [2].

The pre-therapeutic extension assessment includes hysteroscopy, abdominopelvic magnetic resonance imaging (MRI), which has now become the best examination for the evaluation of myometrial penetration, and cervical invasion, or failing in pelvic abdomen scan [4]. In our series our patients received a pelvic abdomen scan.

Surgery is the gold standard treatment for endometrial cancer. It consists of a total hysterectomy with bilateral salpingo-

oophorectomy. Additional procedures are lymphadenectomy, omentectomy for clinical stage, histological type and histological grade [5]. Surgery can be used to specify the stage and establish the prognostic factors [3-5].

External radiotherapy is performed according to the conformational modalities and according to the recommendations of the Radiation Therapy oncology group (RTOG), with photons of very high energy (at least equal to 10 MV). The volume of irradiation depends on the tumor extension. It is limited to the pelvis, in the absence of common iliac lymph node involvement or lomboaortic. In the case of lumba-like lymph node involvement, the irradiation volume includes the lumba region. The total dose is 45 to 50 Gy, with 5 weekly fractions of 1.8 to 2 Gy. In case of exclusive irradiation, not preceded by surgery, an overprint of lymph nodes suspected of invasion by imaging can be proposed until 'at a total dose of at least 60 Gy [6,7]. Vaginal brachytherapy is no longer useful at all stages of the disease.

Postoperative vaginal brachytherapy is performed preferentially at high dose rates, avoiding hospitalization and decubitus complications. A dose of 21 to 24 Gy is delivered in 3 sessions of 7 Gy or in 4 sessions of 5 to 6 Gy, calculated at 5 mm of thickness. In case of pulsed brachytherapy or low dose rate, a dose of 50 Gy is delivered, calculated at 5 mm thick. When HDR brachytherapy is performed in addition to external radiotherapy, a dose of 10 Gy is delivered in 2 sessions of 5 Gy, calculated at 5 mm thick. In the case of pulsed or low dose rate brachytherapy, a dose of 15 Gy is delivered, calculated at 5 mm thickness [8,9].

Pelvic radiotherapy improves the rate of local pelvic control of the disease in poorly prognostic forms (stage II, grade 3, myometrial infiltration greater than 50%). It has no impact on metastatic evolution or survival [7].

Management of patients with endometrial cancer is based on surgery, which establishes the stage of the disease according to the FIGO classification and identifies the factors of poor prognosis on which the decision of a treatment the most recognized adjuvant is: stage, histological grade, degree of myometrial infiltration, histological type, age, endocervical infiltration and the presence of intravascular tumor emboli [7]. Thus, for stage I, there are three prognostic groups [10].

The low-risk group includes endometrioid adenocarcinoma without myometrial invasion or with an invasion limited to less than 50% of the grade 1 or 2 myometrium. Retrospective studies and a randomized Swedish trial published in 2009 all confirmed that, although brachytherapy vaginal vault is a well-tolerated therapy, it has no significant impact on local control. No adjuvant treatment can therefore be justified for these patients who have a risk of vaginal recurrence low, estimated at less than 3%, especially since these recurrences are accessible to radiation treatment [10], so for stage IA and grade 1 or 2 cancers, no further treatment is therefore recommended.

The intermediate risk group consists of type I carcinomas without myometrial invasion or with invasion limited to less than 50% of grade 3 myometrial (IA), and carcinomas invading more than 50% of the thickness of the myometrium (IB) of grades 1 and 2. Vaginal brachytherapy is standard adjuvant therapy [10]. Four therapeutic trials demonstrated that in other patients in the group, pelvic radiotherapy improved the rate of local pelvic control of the disease but had no impact on metastatic evolution or survival. This made discuss the interest of this irradiation vis-a-vis brachytherapy only potentially as effective and less toxic. This question was posed by the PORTEC 2 trial (Post-Operative Radiation Therapy in Endometrial Carcinoma) 2. The presentation of the preliminary results at three years suggested that the two therapeutic modalities had similar efficacy in terms of recurrence-free survival and overall survival. [11]. The group at high risk of recurrence includes type I carcinomas with more than 50% invasion of grade 3 myometrial (IB) thickness and type II carcinomas (IA and IB). For these patients, it is recommended to do external pelvic radiotherapy and brachytherapy of the vaginal vault, which does not, however, reduce the risk of recurrence to less than 10%. In these patients, the rate of metastatic progression is also high, which makes discussing concomitant chemoradiotherapy followed by adjuvant chemotherapy [12].

In the case of stage II tumors: the recommended therapeutic course of action is surgery followed by radiotherapy with or without brachytherapy. In the advanced stages (III and IV): the therapies must be more aggressive. Surgery is proposed where possible because, combined with radiotherapy; it provides better results than exclusive irradiation. In advanced forms or at high risk of recurrence, trials including chemotherapy, exclusive or concomitant to irradiation, have been conducted in recent years. The results of these trials have shown the potential value of chemotherapy to decrease [13].

Conclusion

Endometrial cancer is usually of good prognosis whose treatment is based on surgery. Radiotherapy retains an important place in the adjuvant therapeutic strategy in the high-risk group, or with unfavorable histological characters. It thus allows the reduction of locoregional metastases and thus improves the prognosis.

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