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Post-therapeutic aspects of cervical cancer: Different evolutionary profiles and MRI results

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Abstract

Cervical cancer is a major cause of morbidity and mortality in women, with squamous cell carcinoma being the most common histological type. Imaging, and more specifically MRI, plays a key role in its diagnostic and prognostic management as well as its post-therapeutic follow-up. Treatment with concomitant radio-chemotherapy followed by brachytherapy has changed the prognosis of these cancers, particularly in the advanced stages of these tumors.

The objective of our work is to review through our series, an illustration of the different radiological aspects of post-therapeutic states of the cervix, to expose the place of MRI in the post-therapeutic monitoring of cervical cancer thanks to the evaluation of the therapeutic response, the detection of tumor residues and recurrences, as well as the exposure of the different types of post-therapeutic complications, in particular those related to radiotherapy.

Keywords: Cervical cancer; Radio-chemotherapy; Brachytherapy; Recurrence; MRI; Post-therapeutic changes

1. Introduction

Cervical cancer is the third most common female cancer in the world (after breast and endometrial cancer), squamous cell carcinoma is by far the most common histological type. Imaging, particularly MRI, plays a major role in its positive diagnosis, staging assessment, and post-therapeutic evaluation. The current therapeutic strategy has become more effective than before thanks to the introduction of concomitant chemotherapy and radiotherapy in advanced stages.

2. Method

We conducted a retrospective study including 113 patients with cervical cancer collected in the gynecology and mother and child radiology departments at the Hassan II University Hospital in FES, spread over a period of four years from January 2020 to December 2023.

All our patients underwent pelvic MRI, biopsy and histological confirmation.

3. Results

The age range was between 28 and 81 years with an average of 53 years. The most affected age group was between 42 and 64 years.

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The most common presenting sign was genital hemorrhage, which was found in 106 patients (93%). It was either isolated or associated with leukorrhea and/or pelvic pain.

The histological type found was squamous cell carcinoma in 98 cases (89%), adenocarcinoma in 11 cases (7.7%), carcinoma in situ in 2 cases (1.4%), endometrioid carcinoma in 1 case (0.7%), and small cell carcinoma in 1 case (0.7%).

The classification stage FIGO (International Federation of gynecology and obstetrics) in MRI was:

Table 1 Distribution of cases in our series according to the FIGO classification stage

Number of cases (percentage)	FIGO Stadium
82 cases (72.5%)	IIB
10 cases (8.84%)	IIIB
7 cases (6.19%)	IIA
7 cases (6.19%)	IVA
3 cases (2.6%)	IVB
2 cases (1.76%)	IIIA
2 cases (1.76%)	IIIC

The series note cases listed in the previous table were divided into two FIGO categories IB-IIA and IIB-IVB of which 13.4% were in the (IB-IIA) category and 86.6% in the (IIB-IVB) category.

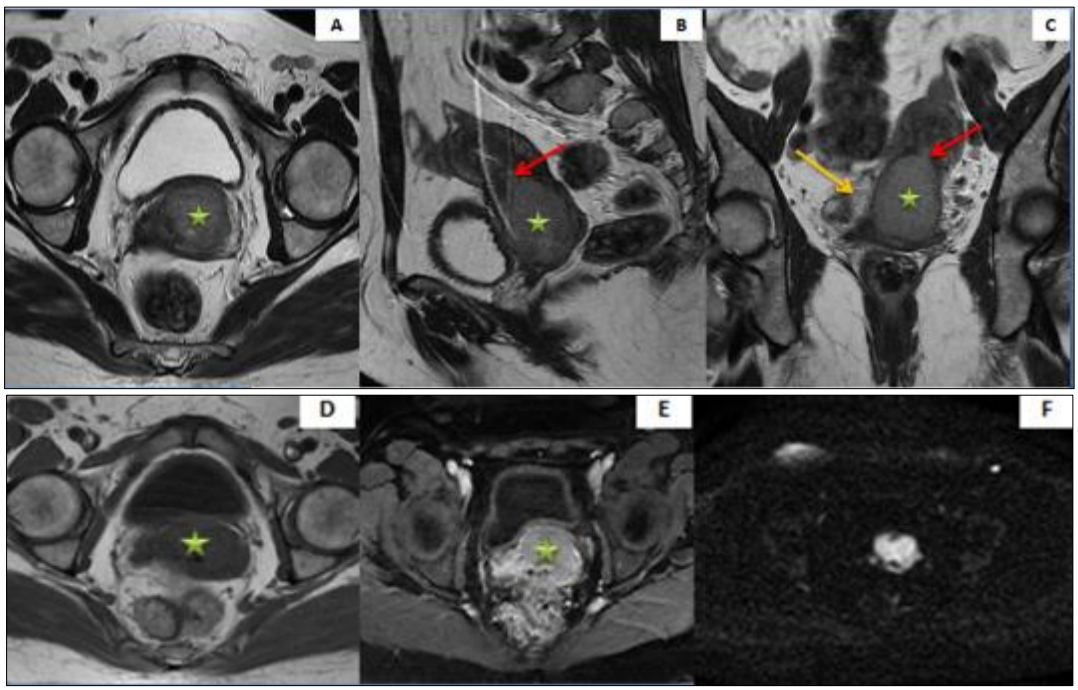

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Figure 1 Pelvic MRI in T2 sequence: axial (A), sagittal (B) and coronal (C), axial T1 without and after injection of Gadolinium (D and E), and in diffusion (F), showing a voluminous tumor process of the uterine cervix (green star), described in isosignal T1, intermediate signal T2, heterogeneously enhanced after injection of Gadolinium. This process infiltrates the proximal parametrial fat especially on the right (yellow arrow), and extends to the uterine isthmus above (red arrow), (A and C),

Only 6 (5.4%) cases in our series benefited from a surgical procedure (including a conization in one patient and a Wertheim-type procedure (extended colpohysterectomy) in the other 5 cases. Among these patients, 2 cases benefited from

The therapeutic strategy was concomitant radio-chemotherapy (CRT) + utero-vaginal brachytherapy in 105 cases (97.3%), external radiotherapy + brachytherapy in 5 cases (exclusive in 1 case and in addition to surgery in 4 other cases), exclusive surgery in 2 cases, and palliative chemotherapy in 1 case,

The total dose of external radiotherapy received in our patients (alone or in combination with concomitant chemotherapy) was greater than or equal to 46 Gray in 93% of cases, described in the following table:

Table 2 Total doses of external radiotherapy and brachytherapy used in the cases in our series

Type of radiotherapy	**Total dose received in Gray (Gy)**	**Average total dose**
External radiotherapy	It varied between 38Gy at a rate of 3Gy/fraction in 10 sessions (on the pelvis) followed by 4 sessions of 2 Gy (on the pelvis) and 70Gy in two series of 35 fractions of 2Gy each,	47.8 Gy
Uterovaginal brachytherapy	It varied between 10Gy at a rate of 5Gy/fraction in 2 sessions and 28Gy in 4 fractions of 7Gy each,	26 Gy

Post-treatment follow-up was based on pelvic MRI and thoraco-abdomino-pelvic CT in all cases in our series, which revealed a complete therapeutic response in 79 cases (66.1%), tumor residue was found in 8 cases (8%), and tumor recurrence was observed in 15 cases (15%) (including 6 cases of lymph node recurrence and 7 cases of local recurrence), and 11 cases (10.9%) of metastatic relapse.

Among cases with complete response to concomitant radiochemotherapy treatment with or without surgery, 67% were classified in the FIGO category (IIB-IVB) and 33% in the category (IB-IIA) with a non-significant difference (p=0.59).

Among the cases that responded completely to concomitant radio-chemotherapy treatment with or without surgery, 69% had squamous cell carcinoma as histological type, and 41% of the other cases had another histological type, either adenocarcinoma, small cell carcinoma, or squamous cell carcinoma, with a non-significant difference in complete therapeutic response between the two cases (p=0.1).

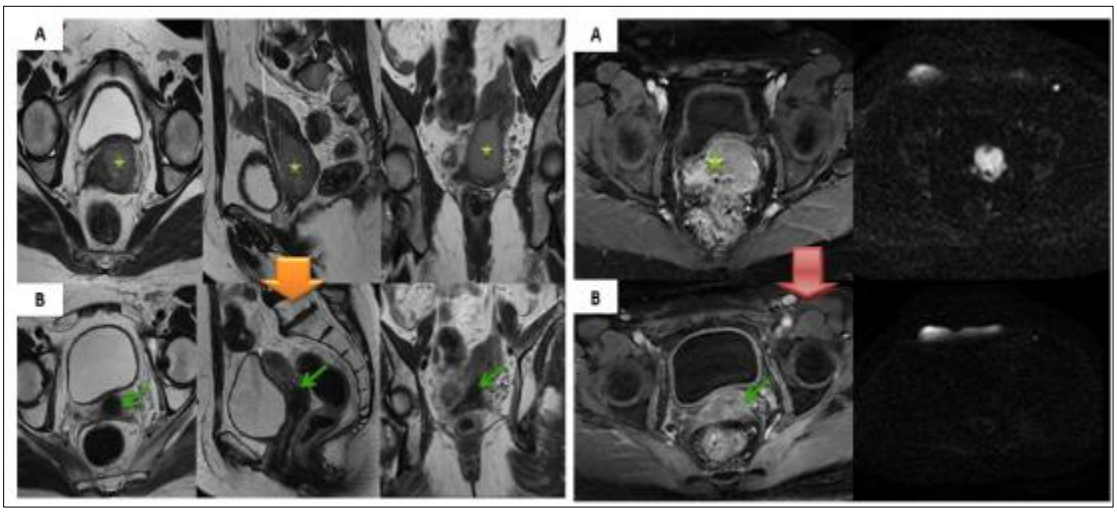

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Figure 2 (A=MRI pre-concomitant radio-chemotherapy (CRT) + brachytherapy, B= post-therapeutic MRI): Pelvic MRI in T2 sequence (axial, sagittal and coronal) (right of the image), in axial T1 after injection of Gadolinium and in diffusion (left of the image), performed on a 50-year-old patient followed for FIGO stage IIB cervical cancer, showing complete regression of the bulky tumor process of the uterine cervix (green star), giving way to an atrophic profile of the uterine cervix described in T2 hypointense (green arrow), non-restrictive in diffusion, and without suspicious enhancement after injection of Gadolinium

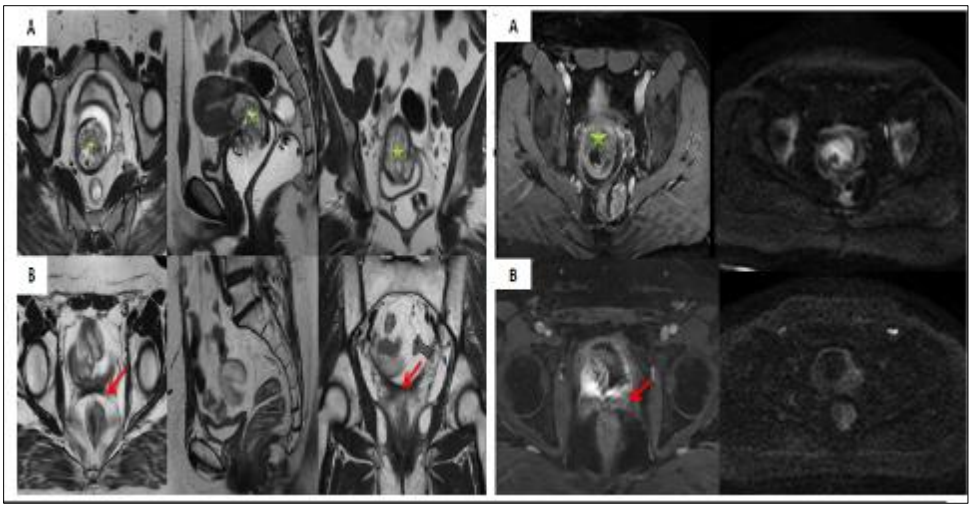

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Figure 3 (A=pre-therapeutic MRI, B= MRI after Wertheim-type surgery with RCC+ brachytherapy: Pelvic MRI in T2 sequence (axial, sagittal and coronal) (right of the image), in axial T1 after injection of Gadolinium and in diffusion (left of the image), performed on a 42-year-old patient followed for FIGO stage IIA cervical cancer, showing fibrous changes in T2 hypointense (red arrow), non-restrictive in diffusion, and without suspicious enhancement after injection of Gadolinium.

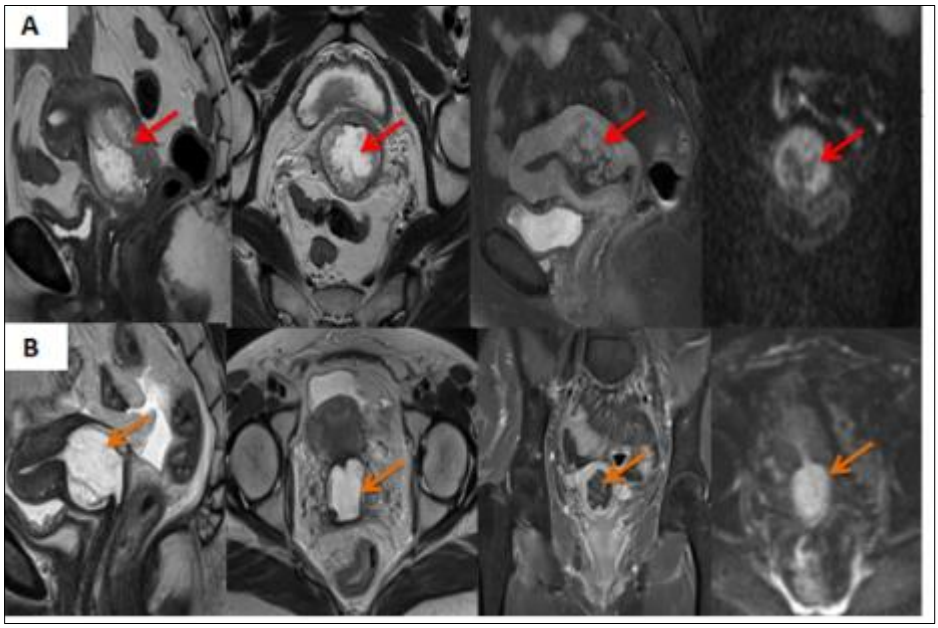

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Figure 4 (A=pre-therapeutic MRI, B= MRI 4 weeks after the end of concomitant radio-chemotherapy+ brachytherapy: Pelvic MRI in T2 sequence (axial and sagittal), in axial T1 after injection of Gadolinium (sagittal (A) and coronal (B)), and in diffusion, carried out in a 47-year-old patient followed for FIGO stage IIB cervical cancer (red arrow), showing tumor residue of the uterine cervix in heterogeneous hypersignal T2, restrictive in diffusion, and heterogeneously enhanced after injection of Gadolinium (yellow arrow)

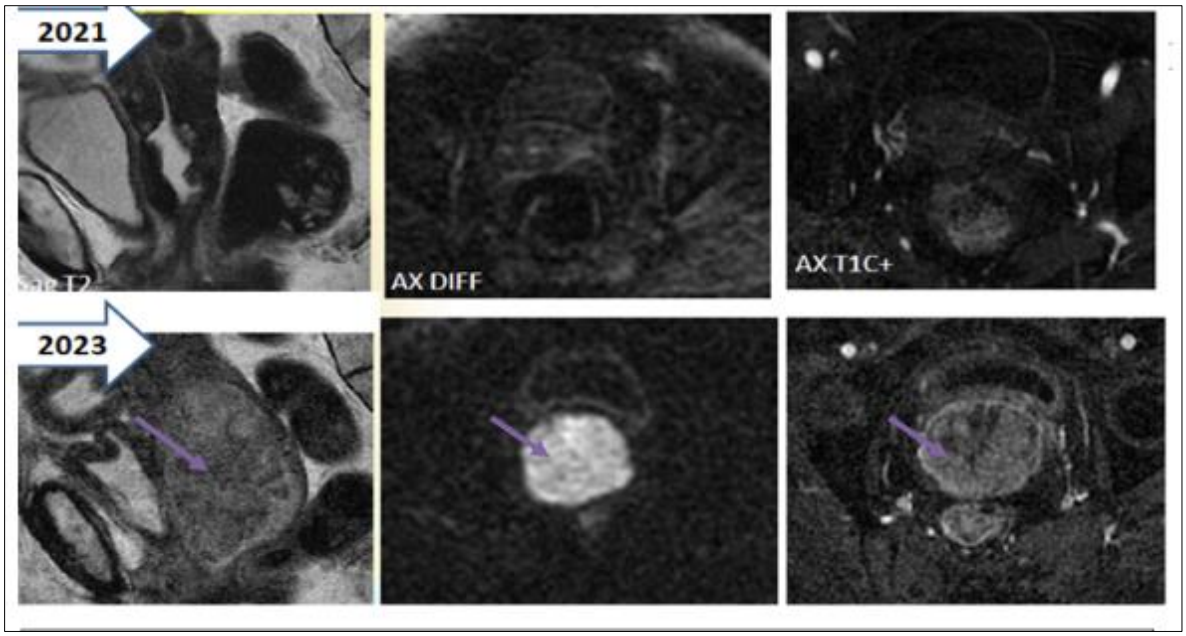

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Figure 5 Pelvic MRI performed in 2021 on a 42-year-old patient followed for cervical cancer treated with CCR (the images at the top show post-radiation changes of the cervix), the control MRI in 2023 (the images at the bottom) shows a local tumor recurrence of the cervix in heterogeneous intermediate T2 signal, restrictive in diffusion, and heterogeneously enhanced after injection of Gadolinium (yellow arrow).

Post-therapeutic complications in our series were mainly related to radiotherapy, found in 13 patients (9.8%), including 5 cases of symptomatic proctitis, 5 cases of cystitis, 2 cases of vaginitis, and 1 case of rectovaginal fistula.

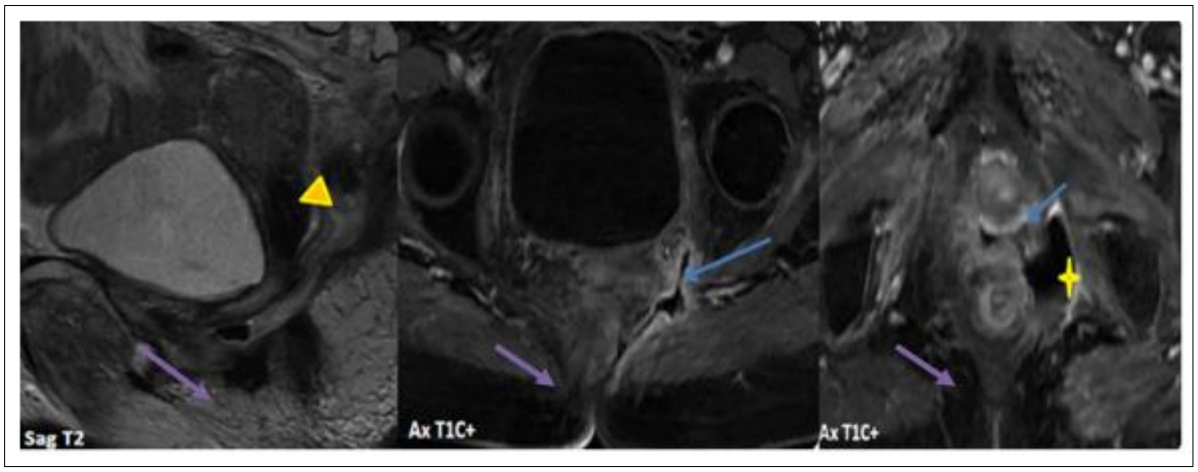

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Figure 6 Pelvic MRI performed on a 68-year-old patient, treated for squamous cell carcinoma of the cervix who had received radiochemotherapy, consulted for fecaloid leukorrhea: The MRI shows a cervix with a very hypointensity T2 fibrous signal (arrowhead), with a large rectovaginal fistula (arrow blue) with loss of substance of the left ischio-anal fossa (star)

4. Discussion

Cervical cancer is the third most common gynecological cancer and mainly affects young women under 45 years of age. Today, its therapeutic management is more effective than before thanks to the introduction of concomitant chemotherapy and radiotherapy, particularly in advanced stages. The main prognostic factors are: tumor size, stage, and the existence of pelvic and/or lumboaortic lymph node invasion. Therapeutic management is discussed in a multidisciplinary consultation meeting and is based on the FIGO stage. At stage IA, a diagnostic conization is performed.

Additional hysterectomy, without adnexectomy, is indicated in the event of emboli, involvement of the section slices, and/or the desire for non-conservative treatment. Trachelectomy is a therapeutic option in the event of a desire to preserve fertility. Pelvic lymph node dissection is recommended in the event of lymph emboli on the initial histological sample. Postoperative pelvic radiochemotherapy is indicated in cases of high risk of relapse [1]. At stages IB1 and IIA1, two therapeutic options are possible [2]. Extended colpohysterectomy with bilateral adnexectomy and pelvic lymph node dissection, which may be preceded by uterovaginal brachytherapy. Adjuvant pelvic radiochemotherapy is given in the event of pelvic lymph node invasion. Pelvic radiotherapy followed by uterovaginal brachytherapy is an alternative in the event of surgical contraindication and/or the patient's wishes. From stage IB2, pelvic radiotherapy (extended to the lumbo-aortic bar if the lymph nodes are affected) with concomitant chemotherapy based on platinum salts and closure uterovaginal brachytherapy has been the first-line therapeutic reference since 2000. [3, 4]. Radiotherapy is delivered at a total dose of 45 Gy with weekly concomitant chemotherapy (cisplatin 40 mg/m2 in the absence of contraindications), with a spread that must be less than 49 days. Dose supplements can be delivered to macroscopically affected lymph nodes, taking into account the dose contribution of brachytherapy. The place of closure surgery after pelvic radio-chemotherapy can be discussed in selected patients.[5].

The evaluation of tumor response after radio-chemotherapy is based on pelvic MRI, in addition to the gynecological examination, which is essential. Pelvic MRI allows the initial tumor stage to be determined, by evaluating tumor size, local extension (vagina, parameters), and looking for pelvic lymph node involvement. It is also an essential examination for uterovaginal brachytherapy guided by three-dimensional imaging. [6, 7]. During follow-up after exclusive pelvic irradiation, pelvic MRI assesses the partial or complete regression of the hyperintensity in T2 sequence and the reduction in tumor size. The objective of this early examination, performed 6 to 8 weeks after the end of pelvic radio-chemotherapy, is to detect a tumor residue potentially accessible to salvage surgery (hysterectomy)[8]Sensitivity was 80% while specificity was only 55% in a retrospective study conducted on 44 patients after pelvic radio-chemotherapy of 45 Gy and uterovaginal brachytherapy of 15 Gy, followed by surgery, for FIGO stage IB2-II cervical cancer between 2003 and 2006.[9]. Evaluation MRI showed residual tumor in 16 patients (36.5%), among these patients only eight (50%) remnants were confirmed histologically on the surgical specimen, which reflects a high risk of false positive. Analysis of the apparent diffusion coefficient in diffusion sequence as a biomarker of tumor response seems promising in order to refine the radiological interpretation during the initial follow-up.[10].

In our study, tumor residue was found in 8 patients, or 7%.

Tumor relapses occur mostly within 24 months after initial treatment and rarely after the first 5 years of follow-up in old retrospective series.[11]. Relapse rates increase with initial FIGO stage: 11–22% at stages IB-IIA and 28–64% at IIB-IVA [12]. Local pelvic relapses are said to be central (cervix, vagina or parametrium) or lateral (pelvic wall).

In our series, the relapse rate was observed in 15 patients, wich means 13% (6% cases of lymph node recurrence and 7% cases of local recurrence), among these patients only 2 cases had a FIGO stage IB-IIA (14%) the other 13 cases had a stage IIB-IVA (86%).

The most frequent sites of distant relapse are pulmonary and lumbar-aortic lymph nodes. After pelvic radiochemotherapy and image-guided MRI uterovaginal brachytherapy, the rate of metastatic relapse was 25.9% in a series of 189 patients treated between 1998 and 2008[13].

In our series, metastatic relapses were observed in 11 patients or 9.7%, the metastatic sites were, in decreasing order, pulmonary, lymph node, and hepatic.

5. Conclusion

Concomitant radio-chemotherapy and brachytherapy are essential therapeutic strategies in the management of advanced cervical tumors. Post-therapeutic monitoring is based mainly on MRI, it allows early detection of relapses, locoregional and distant, as well as a rigorous prospective collection of post-therapeutic complications in the medium and long term that can impact on quality of life.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

'The present research work does not contain any studies performed on animals/humans subjects by any of the authors'.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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