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Original article

Intensity-modulated whole pelvic radiotherapy provides effective dosimetric outcomes for cervical cancer treatment with lower toxicities

La dosimétrie de la radiothérapie conformationnelle avec modulation d'intensité pour le cancer du col utérin permet une diminution de la toxicité

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ABSTRACT

Purpose. – To compare the efficacy of intensity-modulated radiotherapy, three-dimensional conformal radiotherapy, and conventional radiotherapy for cervical cancer treatment.
Materials and methods. – Whole pelvis intensity-modulated radiotherapy, three-dimensional conformal radiotherapy, and conventional radiotherapy plans were designed for 16 patients with stage IIB cervical cancer, each using the prescribed dose of 50.4 Gy/28 fractions. Dose–volume histograms of the target volume and organs at risk were evaluated.
Results. – Compared to the 3D conformal and conventional radiotherapy plans, the intensity-modulated radiotherapy plan demonstrated superior conformal treatment. The mean planning target volume dose of all three plans reached the target effective therapeutic dose. The planning target volume dose of the intensity-modulated radiotherapy plan was significantly higher than that of either the three-dimensional conformal radiotherapy or conventional radiotherapy plan ($P < 0.05$). When more than 30 Gy was administered in intensity-modulated radiotherapy, organs at risk including the small intestine, rectum, bladder, and bone marrow received a significantly reduced volume of radiation. In comparison of the average planning target volume doses, significant volume reductions in irradiation of organs at risk were obtained with full bladders.
Conclusions. – An intensity-modulated radiotherapy plan with appropriate margins encompassing the primary tumour and potential microscopic pelvic disease reduces the dose to organs at risk without compromising target coverage. Intensity-modulated radiotherapy is an appropriate definitive treatment for patients with cervical cancer.

Mots clés :
Cancer du col utérin
Radiothérapie conformationnelle avec modulation d'intensité
Remplissage vésical

RÉSUMÉ

Objectif de l'étude. – Comparer l'efficacité de la radiothérapie conformationnelle avec modulation d'intensité, de la radiothérapie conformationnelle tridimensionnelle et de la radiothérapie classique dans le cancer du col utérin.
Matériels et méthodes. – Une radiothérapie pelvienne de 50,4 Gy en 28 fractions a été planifiée pour 16 patientes atteintes d'un cancer du col utérin de stade IIB avec chacune des trois techniques. Les résultats de la dosimétrie ont été comparés avec les histogrammes dose–volume du volume cible et des organes à risque.

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Résultats. – La radiothérapie conformationnelle avec modulation d'intensité a donné les meilleurs résultats, la dose délivrée dans le volume cible prévisionnel étant supérieure à celle atteinte avec les deux autres techniques ($p < 0{,}05$). Dès que la dose dépassait 30 Gy, la dose délivrée par radiothérapie conformationnelle avec modulation d'intensité dans l'intestin grêle, le rectum, la vessie et la moelle osseuse était significativement réduite. Le remplissage vésical aboutissait aussi à une diminution de la dose délivrée dans les organes à risque.
Conclusion. – Une radiothérapie conformationnelle avec modulation d'intensité avec des marges adéquates de la tumeur primaire et des extensions potentielles microscopiques permet une diminution de la dose délivrée dans les organes à risque sans compromettre la couverture de la cible et s'avère un traitement approprié du cancer du col utérin.

1. Introduction

Cervical cancer is the third most commonly diagnosed cancer and was the fourth leading cause of cancer deaths among women worldwide in 2008 [1]. The majority of patients diagnosed with cervical cancer received radiation as a treatment component. The pathological and anatomic characteristics of cervical cancer make it a good target for radiotherapy. First, squamous cell carcinoma and adenocarcinoma are sensitive to radiotherapy. Second, tumours are generally confined to the pelvis during development. Third, the target dose for the tumour can be reached with limited irradiation to the surrounding organs. Finally, the natural cavity of the vagina makes it accessible for brachytherapy.

Conventional radiotherapy for cervical cancer is composed of brachytherapy and external beam radiotherapy. Although brachytherapy boosts the local dose to the tumour, external beam radiotherapy aims to reduce the size of the gross tumour and the presence of microscopic disease in the pelvic area. External beam radiotherapy targets include primary tumours, subclinical lesions (parametrical uterine tissue, and vagina), and regional lymph nodes (common iliac, external and internal iliac, obturator, and presacral nodes) [2]. Because the cervix is localized in the pelvic centre and surrounded by the bladder, rectum, small intestine, and vagina, it is difficult to protect these organs at risk from irradiation using conventional radiotherapy. Grade 3/4 acute radiation proctitis was observed in up to 16.7% of patients and grade 3/4 acute cystitis occurs in up to 18.3% of patients receiving conventional radiotherapy [3]. Multicentre data suggest that complications, including radiation proctitis and cystitis, occur in 5 to 30% of cervical cancer patients after radiotherapy [4]. Three-dimensional conformal radiation therapy was subsequently developed to avoid organs at risk irradiation. Conventional 3D conformal radiotherapy is composed of a set of fixed radiation beams, which are shaped using the projection of the target volume and normally have uniform intensity across the field. When appropriate, conventional fields can be modified using simple devices, such as compensating filters or wedges. With advances in new technologies, including computed tomography (CT), magnetic resonance imaging (MRI), and 3D planning software, radiotherapy techniques have significantly improved. More recently, intensity-modulated radiation therapy has been proposed to treat cervical cancer. The intensity of each beam can be purposely altered by the summation of hundreds of beamlets in order to satisfy clinical target goals and normal tissue doses. In addition, the fluence can be adjusted within individual beamlets, the sum of which represents the entire aperture's contribution [5]. Therefore, when individual contributions from each beam are summed, complex 3D dose clouds can be generated with concave shapes and steep dose gradients. This results in highly conformal treatment, where the high dose regions of the plan are confined to the target only, and doses to organs at risk can be minimized. Intensity-modulated radiotherapy has been shown to reduce normal tissue irradiation [6] and has been associated with reduced acute toxicity compared to conventional 3D conformal radiotherapy [6–11].

One complication in utilizing intensity-modulated radiotherapy for cervical cancers is the interfractional position change of organs near the cervix. Utilizing intensity-modulated radiotherapy in mobile organs not only results in underdose to the target but also presents a high risk of overdose to nearby organs because of the nature of the steep dose gradient. In general, motion of the organs is attributable to variations in bladder filling and rectal filling, and the majority of motion occurs in the anterior–posterior and superior–inferior directions, with mean interfraction movements of 4–7 mm [12–14]. However, it is worth noting that these are the average distances, and in some instances the distance has been reported to be as large as 2.8 cm [14]. To avoid complications of intensity-modulated radiotherapy in cervical cancer patients, effective control of the clinical target volume position and bladder filling status is critical [2,15].

With the aim of addressing the inconsistencies that have arisen based on previous studies, we conducted a dosimetric study to compare conventional radiotherapy, 3D conformal radiotherapy, and intensity-modulated radiotherapy plans. We performed quantitative dosimetric analyses of irradiation on the tumour target and organs at risk, including the bladder, rectum, small intestine, and pelvic bone marrow. In addition, we compared the dosimetric characteristics of targets and organs at risk during different bladder states.

2. Materials and methods

2.1. Patient selection

Approval for this study was obtained from the local ethics review board and all patients provided informed consent for study.

Sixteen patients with stage IIB (FIGO staging) cervical carcinoma that presented to our department from July 2011 to March 2013 were included in the study. All patients were diagnosed by biopsy with cervical squamous cell carcinoma and were untreated before commencing the study. The average age of patients was 52 years (range: 38–79 years). They received written and verbal advice on bladder filling prior to their planning appointment. Patients were advised to "void the bladder and then drink 500 ml of water within the next 15 minutes. After 30 minutes, proceed with the planned radiotherapy. This process should be repeated daily prior to each treatment".

2.2. Methods and protocols

2.2.1. Position

All patients were immobilized using MED-TEC vacuum body bags (Klarity Medical, Guangzhou, China) while they were in a supine position with their hands clasped over their head and their