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Evaluation of pelvic lymph node coverage of conventional radiotherapy fields based on bony landmarks in Chinese cervical cancer patients using CT simulation

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Abstract: Objective: To evaluate the pelvic lymph node coverage of conventional pelvic fields based on bony landmarks in Chinese patients with cervical cancer by using computed tomography (CT) simulation images to contour pelvic vessels as substitutes for lymph nodes location. Methods: A retrospective review of CT simulation images and conventional pelvic radiation planning data sets was performed in 100 patients with cervical cancer at the International Federation of Gynecology and Obstetrics (FIGO) Stage IIB to IIIB in our hospital. Pelvic arteries were contoured on CT simulation images, and the outlines of conventional pelvic fields were drawn as defined by the gynecologic oncology group (GOG) after hiding the contours. The distances between the following vessel contours and field borders were measured: D_1, the superior border of the anterior/posterior (AP) field and the bifurcation of abdominal aorta; D_2, the ipsilateral border of the AP field and the distal end of external iliac artery; and D_3, the anterior border of the lateral (LAT) field and the distal end of the external iliac artery. The distances were recorded as positive values if the measuring point was within the conventional pelvic fields, or they were recorded as negative values. Lymph nodes coverage was considered adequate when $D_1 \geq 0$ mm, $D_2 \geq 17$ mm or $D_3 \geq 7$ mm. Results: All patients had at least 1 inadequate margin, 97 patients (97.0%) had 2, and 22 patients (22.0%) had all the 3. On the AP field, 95 patients (95%) had the measuring point, the bifurcation of the abdominal aorta, out of the field ($D_1 < 0$ mm), and all the patients had a distance less than 17.0 mm between the distal end of the external iliac artery and ipsilateral border ($D_2 < 17.0$ mm). On the LAT field, 24 patients (24%) had a distance less than 7.0 mm between the distal end of the external iliac artery and anterior border ($D_3 < 7.0$ mm). Conclusion: We observed that conventional pelvic fields based on bony landmarks provided inadequate coverage of pelvic lymph nodes in our patients with cervical cancer. CT simulation may be a feasible technique for planning pelvic fields optimally and individually.

Key words: Cervical cancer, Radiotherapy planning, Computed tomography (CT) simulation, Lymph nodes
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INTRODUCTION

Radiotherapy is an important and promising modality for the treatment of cervical cancer. Effective therapy needs covering an adequate area of the tissues at risk for metastasis (Tewari and Monk, 2009). Pelvic lymph nodes were involved in 15%~30% of patients with the International Federation of Gynecology and Obstetrics (FIGO) Stage IB/II cervical cancer and 45%~60% with Stage III (Bonin *et al*., 1996). Optimal treatment requires a combined approach including intracavitary radiation for in situ tumor and external radiation for parametrial tissue and pelvic draining lymph nodes.

Theoretically, a dose of 50 Gy can get 90% probability for local control, even if there are microscopic diseases in pelvic lymph nodes (Withers *et al*., 1995). However, approximately 5%~50% of patients with radiotherapy would relapse ultimately in their pelves (Perez *et al*., 1988). This locoregional failure may be caused by inadequate pelvic radiation coverage for the draining lymph nodes.

Presently, pelvic radiation fields are still planned based on conventional bony landmarks in both western

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countries and China. In the past twenty years, lymphangiograms, surgical techniques, and placement of surgical clips were used to assess pelvic coverage of the conventional fields, and were applied as new precise methods for setting radiation field parameters by several western researchers (Greer *et al*., 1990; Bonin *et al*., 1996; Zunino *et al*., 1999; McAlpine *et al*., 2004). Although these techniques have confirmed the inadequate coverage of conventional pelvic radiation fields, they could not be prevalently applied due to several practical reasons.

Computed tomography (CT) simulation can contour the pelvic blood vessels in image to locate the corresponding lymphatic vessels and lymph nodes. It has been widely used in the developed countries nowadays, but only in a few tertiary care centers in China. Recently, CT simulation has been used to assess the coverage of conventional pelvic fields in 43 patients with cervical cancer at FIGO Stages I~III in a Canadian study (Finlay *et al*., 2006). They found that 95.4% patients had at least 1 inadequate margin, and the majority of the inadequate margins were located superiorly. They suggested that noninvasive CT stimulation would offer a more precise radiation planning than bony landmarks (Finlay *et al*., 2006).

Cervical cancer is the second leading cause of cancer death in Chinese women (Parkin *et al*., 2001), so it is urgently needed to develop or improve all possible therapies. Although it is known that in western women the conventional pelvic fields based on bony landmarks provided inadequate coverage for pelvic lymph nodes in cervical cancer (Finlay *et al*., 2006), it remains unclear in Chinese patients because of the pelvic anatomic discrepancies between occidental and oriental women. In the present study, we evaluated the pelvic lymph node coverage of conventional pelvic fields based on bony landmarks in Chinese patients with cervical cancer for the first time by using CT simulation images to contour pelvic vessels as substitutes for lymph nodes location.

MATERIALS AND METHODS

Patients

100 patients with advanced cervical cancer (from FIGO Stages IIB to IIIB, aged 29 to 82 years), treated at Zhejiang Cancer Hospital between January of 2007 and June of 2008, were involved in this study. Among them, 56 patients were diagnosed as cervical cancer at FIGO Stage II and the remainders at Stage III.

CT simulation

CT simulation was performed by GE LightSpeed® RT16 CT simulation system (Healthcare of General Electric Company, UK). Iobitridol was used as intravenous contrast in all patients except for those hypersusceptible to iodine. CT simulation images were obtained every 5 mm for all patients and transferred to treatment planning system (TPS).

Setting of conventional pelvic fields

The outline of conventional pelvic fields was drawn on TPS. On the anterior/posterior (AP) field, L4-L5 interspace was identified as the superior border, and the inferior aspect of the obturator foramen was labeled as the inferior border. The lateral border was allocated at 1.5 cm beyond the widest part of the pelvic brim. On the lateral (LAT) field, the most anterior part of the symphysis pubis was identified as the anterior border, and S2-S3 interspace was labeled as the posterior border. The superior and inferior borders were identical to those on the AP fields. These borders were outlined on coronal and sagittal digitally reconstructed radiograph images as suggested by Finlay *et al*.(2006).

Measurements for pelvic lymph node coverage assessment

Pelvic vessels were contoured and also demonstrated on coronal and sagittal digitally reconstructed radiograph images. Then distances between the following parts were measured (Fig.1): D_1, the bifurcation of the abdominal aorta and superior border of the AP field; D_2, the distal end of the external iliac artery and ipsilateral border of the AP field; and D_3, the distal end of the external iliac artery and anterior border of the LAT field. The distances were recorded as positive values if the measuring point (the bifurcation of the abdominal aorta and the distal end of the external iliac artery) was within the conventional pelvic fields, or they were recorded as negative values. According to Taylor *et al*.(2005), the adequate coverage of lymph nodes was defined as $D_1 \geq 0$ mm, $D_2 \geq 17$ mm, and $D_3 \geq 7$ mm.

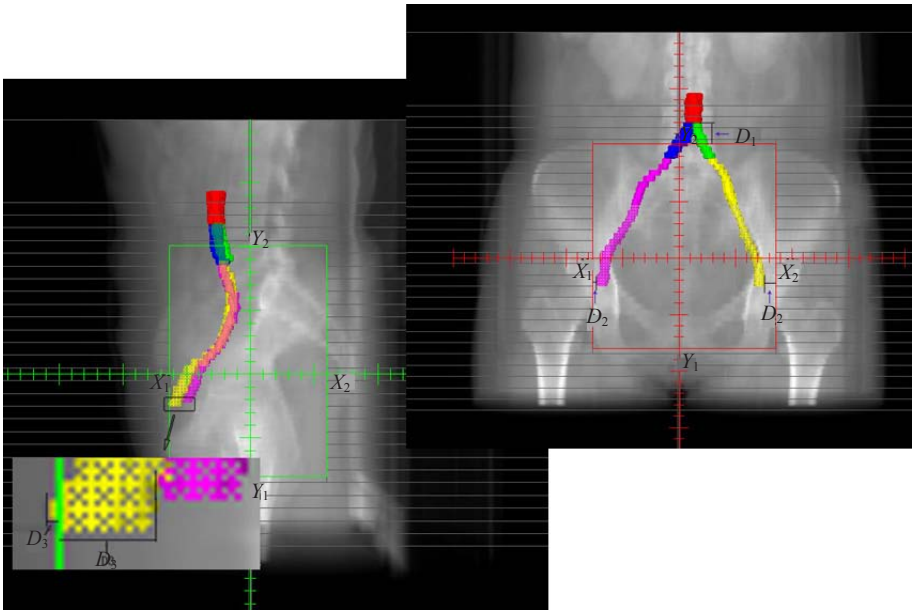

Fig.1 Location of measurements taken with contoured vessels and pelvic fields in place

Red: aorta; Blue: right common iliac artery; Green: left common iliac artery; Pink: right external iliac artery; Yellow: left external iliac artery. D_1: distance between the bifurcation of abdominal aorta and the superior border of the AP field; D_2: distance between the distal end of external iliac vessels and the ipsilateral border of the AP field; D_3: distance between the distal end of external iliac vessels and the anterior border of the LAT field. The distances were recorded as positive values if the measuring point (the bifurcation of abdominal aorta and the distal end of external iliac artery) was within the conventional pelvic fields, or they were recorded as negative values

RESULTS

Superior border of AP field

At the superior border of the AP field, only 5 patients (5.0%) had sufficient distance between the bifurcation of the abdominal aorta and the superior border ($D_1 \geq 0$ mm) to supply adequate radiation coverage for common iliac lymph nodes. At least part of the common iliac artery in 95 patients (95.0%) was not included in the conventional pelvic field ($D_1 <$ 0 mm), which indicates inadequate radiation coverage by our definition. Meantime, 5 patients (5.0%) even had single or both common iliac artery bifurcations entirely out of the field. The average D_1 was (–17.0±13.1) mm, ranging from –50.0 to 10.0 mm.

Lateral border of AP field

At the lateral field border, the average distance between the distal end of left external iliac vessels and ipsilateral field edge (D_2) was (–22.0±7.5) mm, with a range of –22.0 to 10.5 mm, while the average distance for the right side was (–8.4±5.3) mm, ranging from –19.5 to 3.0 mm. Seven patients (7%) had at least 1 distal end of the external iliac artery out of the conventional pelvic field. Less than 17.0 mm between the distal end of the external iliac vessels (single or both) and the ipsilateral border of the AP field was observed in all patients.

Anterior border of LAT field

At the same time, the average value of D_3 in the left side (between the left distal end of external iliac vessels and the anterior border of the LAT field) was (–10.1±6.0) mm, ranging from –23.0 to 0 mm, while in the right side it was (–11.6±5.8) mm, ranging from –27.0 to –4.0 mm. Less than 7.0 mm between the distal end of external iliac vessels (single or both) and the anterior border of the LAT field was observed in 24 patients (24%).

Overall, all patients had at least 1 inadequate margin, 97 patients (97.0%) had 2, and 22 patients (22.0%) had all the 3, with the majority being located at the superior and lateral borders of AP field (Table 1).

Table 1 Adequacy of field boarders

	Average (mm)	Adequate margin*	Inadequate margin*
D_1	–17.0±13.1	5 (5%)	95 (95%)
D_2	–22.0±7.5 (L) –8.4±5.3 (R)	0	100 (100%)
D_3	–10.1±6.0 (L) –11.6±5.8 (R)	76 (76%)	24 (24%)

L: left; R: right. *Data expressed as *n* (%)

DISCUSSION

In the current study, CT simulation was demonstrated as a feasible method to contour pelvic vessels and to evaluate the pelvic coverage of radiotherapy for cervical cancers. The radiotherapeutic fields of patients with advanced cervical cancer in China are mostly planned by bony landmarks. By using CT simulation, we confirmed that the conventional radiation fields usually did not have adequate coverage of pelvic lymph nodes, and the majority of the inadequate coverages were located at common iliac lymph nodes and the distal end of external iliac lymph nodes on the AP field. In the present study, we found that the relationship between conventional pelvic fields and the location of pelvic lymph nodes in Chinese patients was not only similar to that observed in other populations, but the inadequate coverage was even more notable.

Radiotherapy is used as primary treatment for locally advanced cervical cancer and adjuvant therapy for early disease in many countries. Conventional pelvic fields planned on bony landmarks as indication of lymph node location have been used for several decades. Although the concurrent chemoradiotherapy has recently improved their curative effect to a certain extent, locoregional relapse rates still remain high, especially in pelvic lymph node regions (Pearcey *et al*., 2002; Eifel *et al*., 2004). Optimization of radiation field parameters to improve the cure is crucial. It is especially important in China, because approximately 131 500 new patients with advanced cervical cancer, occupying 28.8% of the patients worldwide, were diagnosed every year (Parkin *et al*., 2001).

It was found that an optimal external irradiation to prevent the locoregional relapse required an adequate coverage of pelvic lymph nodes (Bonin *et al*., 1996). However, in most cases conventional pelvic fields based on bony landmarks could not provide adequate radiation area. In Chinese women, the relationship between conventional pelvic fields and pelvic lymph node coverage has not been demonstrated. It is indispensable due to the pelvic anatomic discrepancies between occidental and oriental woman. In this study, we found for the first time that Chinese patients also have inadequate coverage by conventional pelvic fields. Most inadequate coverages of lymph nodes were found at common iliac lymph nodes on the AP field and the distal end of external iliac lymph nodes on both the AP and LAT fields.

Lymphangiograms, surgical techniques and CT/MRI imaging (Bonin *et al*., 1996; Zunino *et al*., 1999; McAlpine *et al*., 2004) were used to identify the adequacy of pelvic lymph node coverage in the past few years. Pendlebury *et al*.(1993) examined 87 patients with cervical cancer at Stage II or III by bipedal lymphangiogram, and only 50 patients were successfully dyed bilaterally. Nearly two-thirds (62%) of the 50 patients had their conventional pelvic fields altered. They also found that, in 90% of these cases, additional 2.5 cm for the lateral margins of the AP field and 0.5 cm for the anterior border of the LAT field were recommended to cover the pelvic lymph nodes. Lymph nodes are located along the vessels, especially arteries, so McAlpine *et al*.(2004) placed clips at the bifurcation of the common iliac arteries and the junctions of the deep circumflex vein and the external iliac vein by surgery in 100 patients. They performed an abdominal X-ray exam for each patient postoperatively, and compared the conventional pelvic fields with the position of the clips shown on these films. It was demonstrated that a part of common iliac lymph nodes in 39 patients (39%) were out of the radiation fields, and 26% of the patients had inadequate coverage of one or both of the lateral boundaries of pelvic radiation. Greer *et al*.(1990) carried out retroperitoneal measurements of 100 patients to examine anatomic basis during radical surgery. As a conclusion of their study, a superior border at the L4-L5 interspace covered lymphatic pathways to the mid-common iliac nodal level. McAlpine *et al*.(2004) and Greer *et al*.(1990) recommended that surgical techniques would be useful for pelvic field design when noninvasive CT or magnetic resonance imaging (MRI) was unavailable. However, for practical reasons, neither lymphangiograms nor surgical techniques can be feasible presently.

With the progress of imaging techniques, CT and MRI have become prevalent methods for examination of pelvic lymph nodes. By using diagnostic MRI, Thomas *et al*.(1997) found that conventional pelvic field allowed adequate coverage of superior boarder or lateral boarder for few patients. Marnitz *et al*. (2006) evaluated pretreatment CT images of 42 patients, and found that in 26 patients (62%) conventional pelvic fields encompassed the common iliac lymph nodes insufficiently at the superior boarder of the AP field. They recommended that individualized fields including the whole common iliac vessels should be planned on MRI or CT images.

In the present study, we also confirmed that conventional pelvic fields failed to cover all of pelvic lymph nodes in Chinese women. Notably, all the patients in our study had at least 1 inadequate margin, and 97 patients (97.0%) had 2 inadequate margins. This ratio is much higher than any other studies for western women. This means that the situation of missing therapy for pelvic lymph nodes in cervical cancer patients might be much severer in Chinese women. The majority of inadequate coverage was located at common iliac lymph nodes and the distal end of external iliac lymph nodes on the AP field. Based on these observations, we recommended that a new pelvic radiation planning model adapting to Chinese women should be founded, in which the superior boarder should be elevated to cover common iliac lymph nodes, and the lateral boarder should be extended to cover external iliac lymph nodes.

It should be mentioned that in our study we adopted $D_1 \geq 0$ mm, $D_2 \geq 17$ mm and $D_3 \geq 7$ mm as adequate coverage markers based on the viewpoint of Taylor *et al*.(2005). In their study, by using MRI with administration of iron oxide particles, they demonstrated that blood vessels with a 7-mm margin offered a good surrogate target for pelvic lymph nodes and a 17-mm margin for lateral external iliac lymph nodes. Compared to the standards setting undifferentiated 15 mm as adequate marker for all the three margins used by Finlay *et al*.(2006), our standard strengthened the ipsilateral border of the AP field distal to provide better coverage for the lateral external iliac lymph nodes, and weakened the anterior border of the LAT field to minimize normal-tissue irradiation without cutting off the coverage for pelvic lymph nodes.

CONCLUSION

In summary, conventional pelvic fields based on bony landmarks provided inadequate coverage of pelvic lymph nodes. Pelvic fields should be planned individually. CT simulation may be a feasible technique for planning pelvic fields optimally. Diagnostic CT and MRI may be suggested to be referenced to plan pelvic fields precisely when CT simulation is not available.

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