

Pelvic Nodal CTV from L4–L5 or Aortic Bifurcation?—An Audit of the Patterns of Regional Failures in Cervical Cancer Patients Treated with Pelvic Radiotherapy

Bhavana Rai*, Anshuma Bansal, Firuza Patel, Abhishek Gulia, Rakesh Kapoor and Suresh C. Sharma

Department of Radiotherapy and Oncology and Regional Cancer Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India

*For reprints and all correspondence: Bhavana Rai, Department of Radiotherapy and Oncology, Regional Cancer Centre, Post Graduate Institute of Medical Education and Research, Chandigarh, UT 160012, India.
E-mail: bhavana1035@gmail.com

Received April 28, 2014; accepted July 15, 2014

Objective: To assess the patterns of recurrence in cervical cancer patients treated with pelvic nodal clinical target volume at L4–L5 junction instead of aortic bifurcation.

Methods: Records of patients with locally advanced cervical cancer treated with chemo-radiation were reviewed. Patients treated with standard pelvic fields (superior border of the field at L4/L5 junction), without any radiological evidence of regional lymphadenopathy (<10 mm) were included in the study. The level of aortic bifurcation was retrospectively documented on computed tomography. Patterns of recurrences were correlated to the aortic bifurcation and the superior border of the radiation fields (L4/L5).

Results: Aortic bifurcation was above the radiation fields (above L4/5) in 82 of 116 (70.7%) patients. Of the nine patients that recurred above the radiation field, 5 (55%) were above L4/5 failures, i.e. between aortic bifurcation and L4/5, and 4 (45%) had para-aortic failures. On retrospective analysis, 16 patients were found to have subcentimeter lymph nodes and higher nodal failures (7/16) were observed in patients with subcentimeter regional lymph nodes at diagnosis.

Conclusions: Superior border of nodal clinical target volume should ideally include the aortic bifurcation instead of L4–L5 inter space in patients with locally advanced cervical cancer. Radiotherapy fields need to be defined cautiously in patients with subcentimeter pelvic lymph nodes.

Key words: aortic bifurcation – nodal CTV – L4–5 – cervical cancer – subcentimeter nodes

INTRODUCTION

Cervical cancer is one of the most common cancers in women worldwide (1). The standard treatment in these patients is external beam radiotherapy (EBRT) with concurrent weekly cisplatin and brachytherapy. EBRT can be delivered using conventional four-field box fields, three-dimensional conformal radiotherapy (3D CRT) or intensity modulated radiotherapy (IMRT).

With the improvement in technology and availability of imaging techniques, 3D CRT and IMRT have become the

standard of care. The use of these techniques enables us to tailor the radiation fields individually and thus reduces the risk of geographical miss. Of the various guidelines proposed, the most commonly used consensus guidelines for clinical target volume (CTV) delineation for pelvic IMRT in cervical cancer by Lim *et al.* (2) state that the common iliac lymph nodes along with the other relevant pelvic nodal groups must be included in the nodal CTV. However, no definite conclusion regarding the delineation of the superior border of the nodal CTV can be drawn from the same and the authors refer to the

guidelines by Taylor and Small *et al.* (3,4). Whereas, Taylor *et al.* suggest the contouring of the common iliac vessels starting from the aortic bifurcation, Small *et al.* recommend the contouring of the common iliac vessels starting from 7 mm below the L4–L5 inter-space. In another guideline, Toita *et al.* (5) recommend the superior borders at either the aortic bifurcation or the L4–L5 inter-space. Studies in the past have shown that aortic bifurcation may often occur above the L4–L5 junction and placing the superior borders of the radiation fields at L4–L5 junction may result in a ‘marginal miss’ in a significant number of patients. (6,7). However, clinical outcomes and validation of these guidelines with respect to the adequacy of lymph node coverage of the common iliac lymph nodes is yet to be ascertained. The present audit was carried out to assess the patterns of failure with respect to the superior borders of the radiation fields at L4–L5 and aortic bifurcation in patients with locally advanced cervical cancer.

PATIENTS AND METHODS

The medical records of patients with cervical cancer treated radically with concurrent chemo-radiation with conventional four-field box or 3D-CRT technique and brachytherapy, from 2001–10 were reviewed. Only patients with International Federation of Gynecology and Obstetrics (FIGO) Stages II and III with radiologically and morphologically negative lymph nodes, i.e. lymph nodes < 10 mm in short-axis dimension, on initial diagnostic computed tomography (CT) were included in the study (8). Thus, there were 116 evaluable patients.

RADIOTHERAPY PLANNING

Before the installation of a CT simulator in 2004 in our department, patients had a diagnostic CT scan done. For the diagnostic CT, a contrast enhanced scan was performed on a light speed plus four-slice spiral CT (GE Health Care Ltd, Waukesha, WI, USA). Volumetric data were acquired and reconstructions were performed at 10 mm slice thickness. Two-dimensional (2D) X-ray based planning was performed on a simulator and the patients were treated with conventional four-field box technique delineated according to bony landmarks. For anterior posterior fields, the superior border was taken at L4–L5 inter vertebral space and the inferior border was kept at lower border of the obturator foramen or lower in the case of vaginal extension. The lateral borders were marked 2 cm on either side of the widest part of the pelvic brim. For the lateral fields, the superior and inferior borders were same as that of the anterior posterior fields. The anterior border was marked along the anterior edge of pubic symphysis. The posterior border included the sacral hollow.

For patients treated after year 2007, all the patients underwent a planning CT and treatment was delivered using 3D conformal radiotherapy. For the treatment planning, a CT was acquired on the CT simulator light speed VFX-16 (GE Health Care Ltd). Sections were taken at 3.75 mm intervals starting

from T12–L1 superiorly up to the level of the lesser trochanter of the femur inferiorly. Prior to the planning CT, patients were kept fasting for minimum 4 h. Oral and rectal contrast was administered for delineating the critical structures. For the oral contrast 20 ml urografin dissolved in 1 litre water given over 1 h, prior to CT. Rectal contrast was given by dissolving 20 ml urografin in 50 ml normal saline. Patients were asked to void urine 15 min prior to CT. Similar fluid intake and bladder voiding instructions were followed even during treatment. For intravenous contrast, 100 ml of omnipaque was used. These images were then transferred to the treatment planning system (9). The contouring was done on Advantage Sim Workstation 4.3 (GE Health care Ltd). The guidelines by Taylor *et al.* (3) and by Small *et al.* (4) were followed for the delineation of pelvic nodal CTV. The CTV primary included gross tumor volume of the primary tumor (GTV primary), the whole uterus, cervix, parametrium, vagina and ovaries. The nodal CTV included the obturator, presacral, external iliac, internal iliac and common iliac lymph nodal groups. For the external iliac vessels, the RTOG guidelines by Small *et al.* (4) were followed and no additional margin was given around the external iliac vessels anterolaterally along the iliopsoas muscle. Nodal CTV was delineated starting from the aortic bifurcation as recommended by Taylor *et al.* (3). However, although the aortic bifurcation was often observed to occur higher than L4–L5, the upper border of the field was kept at L4–L5 junction. This was done because at that time we did not want to deviate radically from the standard conventional 2D practice. Moreover, since all the patients received concurrent chemo-radiation, we felt that extending the superior border to include the aortic bifurcation would lead to an increase in the irradiated volume and thus an increase in treatment related toxicity. Target volume was defined as CTV total (CTV primary + CTV nodal). An additional margin, the internal target volume (ITV uterus) was defined to account for uterine mobility. An expansion of 15 mm was given anterior, posterior, superior, inferior and 7 mm laterally to the uterus, cervix and upper vagina (10). Planning target volume included ITV uterus and margin to the total CTV. The organs at risk including bladder, rectum and small bowel were delineated accordingly. Three-dimensional conformal planning was done on the Eclipse treatment planning system (v.8.6, Varian Medical Systems, Paolo Alto, CA, USA) and all the patients were treated with conformal four-field plan on a linear accelerator with 15 MV energy. A dose of 46 Gy in 23 fractions was delivered over 4.5 weeks. All the patients received weekly concurrent cisplatin (40 mg/m²) during the period of external radiotherapy followed by brachytherapy. The patients were treated with high dose rate brachytherapy and a dose of 9 Gy per fraction in two fractions was delivered at an interval of 1 week. Prior to year 2007, 2D brachytherapy planning was performed using orthogonal X-rays and thereafter, all the patients underwent CT-based planning. The dose was prescribed to point A and the doses to the bladder and the rectum were reported in accordance with the International Commission on Radiation Units and measurements recommendations.

The patients were followed up regularly and a detailed clinical examination along with a pelvic examination was done at each visit. A CT scan of the chest abdomen and pelvis was done in the case a recurrence was suspected.

For the study, the diagnostic and the planning CT scans of all the patients were retrospectively evaluated and the level of aortic bifurcation was documented. Patterns of failure were then analyzed and correlated with the pre-treatment CT scan findings and the radiotherapy fields used. The failures were broadly classified as loco-regional failures (with or without evidence of simultaneous distant metastasis) and distant failures. The loco-regional failures were further categorized based on the radiotherapy fields used. The failures occurring within the radiation field, i.e. below L4–L5 (with or without evidence of simultaneous distant relapse) were labeled as ‘in-field failures’, those above L4–L5 but below or starting below the aortic bifurcation as ‘above L4/5 failures’. The distant failures were classified as ‘Para-aortic failures’, i.e. those occurring above the aortic bifurcation, in the para-aortic nodes (without evidence of in-field failure) and as distant metastasis. The disease free survival (DFS) and overall survival (OS) were compared for patients in whom the aortic bifurcation was included in the radiation field versus those in whom the aortic bifurcation was above the radiation field (i.e. above the L4/5). All events were reported from the date of diagnosis to death or occurrence of the event.

STATISTICAL ANALYSIS

The statistical package SPSS version 12 was used for computations. *P* values < 0.05 were considered significant. The comparison of survivals was done using the χ^2 test. Survival rates were calculated using the Kaplan–Meier method (11).

RESULTS

One hundred and sixteen patients were eligible for this study. The mean age of the patients was 49 years (range, 28–67 years). Only the patients with locally advanced cervical cancer were included in the study. Sixty (51.8%) had Stage II disease and 56 (48.3%) had Stage III disease. The median follow-up was 44 months (range, 3–122 months). The baseline patient and tumor related characteristics are shown in Table 1.

FAILURES WITH RESPECT TO LYMPH NODE FINDINGS

On retrospective evaluation of the CT scans closely, it was observed that 16 (13.8%) patients had subcentimeter lymph nodes measuring 5–8 mm in short-axis dimension. Since the presence of these subcentimeter lymph nodes was concerning and given the limited sensitivity of CT scans in detecting lymph node metastasis, these were further evaluated. In 13 (81.3%) of the 16 patients with subcentimeter lymph nodes, the subcentimeter regional nodes were adequately covered with the superior border level of L4–L5 vertebra and in 3 (18.7%) patients these lymph nodes were above the radiation

Table 1. Patient characteristics

Total no. of patients (<i>n</i>)	116
Histology	
Squamous	111 (95.68%)
Adenocarcinoma	5 (4.31%)
FIGO stage	<i>n</i> (%)
IIa	1 (0.9%)
IIb	59 (50.9%)
IIIB	56 (48.3%)
Node status on computed tomography scan	
No nodes	100 (86.20%)
Subcentimeter lymph nodes (<10 mm)	16 (13.79%)
Level of AB	
L3 upper	3 (2.5%)
L3 mid	8 (6.9%)
L3 lower	1 (0.9%)
L3–L4 junction	6 (5.2%)
L4 upper	36 (31.0%)
L4 mid	20 (17.4%)
L4 lower	8 (6.9%)
L4–5 junction	20 (17.2%)
L5 upper	8 (6.9%)
L5 mid	5 (4.3%)
L5 lower	–
L5–S1 junction	1 (0.9%)
Field border with respect to aortic bifurcation	
AB included in radiation field	34 (29.3%)
AB above radiation field	82 (70.7%)

FIGO, International Federation of Gynecology and Obstetrics; AB, aortic bifurcation

portals. Of the 13 patients in whom these subcentimeter lymph nodes were adequately covered, 6 (46.1%) patients were disease free at last follow-up, 4 (30.7%) patients had a component of in-field failure, 2 (15.4%) had above L4/5 failures and 1 (7.6%) patient recurred in the para-aortic nodes. All the three patients in whom the subcentimeter lymph nodes were not included in the radiation fields failed. While two patients failed at the respective nodal sites (1 above L4/5 failure, 1 para-aortic failure), one patient had evidence of in-field recurrence along with the nodal failure at the same site. Thus, of the 16 patients with subcentimeter lymph nodes, 6 (37.5%) were disease free, 5 (31.25%) had evidence of in-field failure, 3 (18.7%) had above L4/5 failures and 2 (12.5%) had para-aortic failures.

Of the 100 patients without subcentimeter nodes, 85 (85%) had no evidence of disease at last follow-up, 6 (6%) had in-field failures, 2 (2%) had above L4/5 failures and 1 (1%) failed in the para-aortic nodes. Six (6%) patients had distant metastasis alone without any evidence of loco-regional or para-aortic failures.

FAILURES WITH RESPECT TO AORTIC BIFURCATION

Aortic bifurcation occurred above the L4–L5 junction, i.e. aortic bifurcation was not included in the radiation fields in 82 (70.7%) of the 116 patients. In 43 of the 59 (72.9%) patients with Stage IIB and 39 of the 56 (69.6%) with Stage IIIB disease, the aortic bifurcation was above the radiation fields (Table 2). Of the patients in whom the aortic bifurcation was not included in the radiation fields, 14 (19.5%) patients had loco-regional failures and 5 (6.1%) developed distant metastasis and the rest were disease free. Of the 14 loco-regional failures, in-field failures occurred in 8 (9.8%) patients and 5 (6.1%) patients had above L4/5 failures. Para-aortic failures occurred in 3 (3.7%) patients. Of the 34 patients treated with aortic bifurcation within the radiation field, 1 (2.9%) patient had in-field failure while 1 (2.9%) patient failed in the high para-aortic lymph nodes. Distant metastasis occurred in two (5.8%) patients and the remaining were disease free (Table 3).

ABOVE L4/5 FAILURES

Five (4.3%) of 116 patients treated had above L4/5 failures (Table 3). The time to recurrence ranged from 6 to 72 months.

Table 2. Aortic bifurcation and FIGO stage

	Stage IIa (n = 1)	Stage IIB (n = 59)	Stage IIIB (n = 56)
Aortic bifurcation included in radiation field (n = 34)	1 (2.9%)	16 (47.1%)	17 (50%)
Aortic bifurcation above radiation field (n = 82)	–	43 (52.4%)	39 (47.6%)

FIGO, International Federation of Gynecology and Obstetrics

Table 3. Patterns of failure according to radiation field and aortic bifurcation

	Total (n = 116)	Aortic bifurcation included in radiation field (n = 34)	Aortic bifurcation above the radiation field (n = 82)
Total loco-regional failures	14 (12.0%)	1 (2.9%)	12 (14.6%)
In-field failures			
Local	3 (2.6%)	–	3 (3.7%)
Local + pelvic nodes	3 (2.6%)	–	3 (3.7%)
Local + para-aortic + distant metastasis	3 (2.6%)	1 (2.9%)	2 (2.4%)
Above L4/5 failures	5 (4.3%)	–	5 (6.1%)
Total distant failures	11 (9.5%)	3 (8.8%)	8 (9.7%)
Para-aortic failures			
Para-aortic	2 (1.7%)	–	2 (2.4%)
Para-aortic + distant metastasis	2 (1.7%)	1 (2.9%)	1 (1.2%)
Distant metastasis	7 (6.0%)	2 (5.9%)	5 (6.1%)

One patient recurred at the aortic bifurcation (L4 upper border). On retrospection evaluation of the pre-treatment CT, there was a subcentimeter lymph node at the aortic bifurcation. The second patient recurred in the lymph nodes at the level of the bifurcation of the common iliac artery. The aortic bifurcation was at L3–L4 junction and the bifurcation of the common iliac artery was just above the L4–L5 junction and was not included in the radiation field. The third recurred just below the aortic bifurcation and presented with nodal recurrence starting from above L4–L5 but below the aortic bifurcation up to the para-aortic nodes and with distant metastasis. The aortic bifurcation was at L4 upper border and the patients had a subcentimeter external iliac lymph node that was included in the radiation field. The fifth patient recurred in the L3–L4 region and the aortic bifurcation was at mid L3 (Table 4).

Thus, of the 116 patients evaluated, 14 (12.0%) patients had loco-regional failures and 11 (9.5%) had distant failures. Of the loco-regional failures, 9 (50%) had in-field failures and above L4/5 failures occurred in 5 (27.7%) patients. Four (22.2%) patients had para-aortic failures (Fig. 1).

SURVIVAL RATES

At a median follow-up of 44 months, the DFS in 116 patients was 79.9% in whom the aortic bifurcation was above the radiation field compared with 90.9% in those with aortic bifurcation within the radiation field ($P = 0.08$) (Fig. 2). The DFS for Stage II with aortic bifurcation above the radiation fields versus those with aortic bifurcation included in the radiation fields was 88.9 and 76.2% ($P = 0.29$), respectively, and OS was 83.3 and 76.2% ($P = 0.45$), respectively. Similarly, for Stage III the DFS for patients with aortic bifurcation above the field and aortic bifurcation within the radiation field was 93.8 and 75% ($P = 0.14$), respectively, and the OS was 93.8 and 77.5% ($P = 0.14$), respectively. On comparing the patients with respect to subcentimeter lymph nodes, the DFS in patients with and without subcentimeter lymph nodes was 37.5 and 88% ($P = 0.00$) (Fig. 3) and the OS was 37.5 and 86% ($P = 0.00$), respectively.

DISCUSSION

The literature fails to give us a clear definition of where the upper border of the pelvic radiation field should be for treating cervix cancer patients. Hence, the focus of this study was to evaluate the regional failures at the superior border of the radiation fields with respect to the L4–L5 junction and aortic bifurcation. Of the total failures above the radiation fields, 55% (5/9) were above L4/5 failures and 44% (4/9) failed in the para-aortic lymph nodes. Beadle *et al.* studied the patterns of recurrence in 198 cervical cancer patients with regional failures. Of the 68 patients with above the field recurrences in whom regional imaging at diagnosis was available, 43 (63%) had no regional lymph nodes, 22 (32%) had positive lymph

Table 4. Above L4-5 failures

Patient	FIGO stage	Pre-treatment lymph nodes	Level of aortic bifurcation	Region of 'Above L4-5 failure'	Time after treatment completion
1	IIIb	Subcentimeter lymph node at aortic bifurcation (not included in radiation field)	L4 upper border	At aortic bifurcation	6 months
2	I Ib	No lymph nodes	L3 lower	L4 upper	33 months
3	I Ib	Subcentimeter right external iliac lymph node (included in radiation field)	L4 upper border	Retroperitoneal lymphadenopathy from just below aortic bifurcation to renal hilum	11 months
4	I Ib	Subcentimeter external iliac lymph node (included in radiation field)	L4 mid	Starting from above L4–L5, mediastinal lymphadenopathy, supraclavicular lymph node metastasis	72 months
5	IIIb	No lymph nodes	L3 mid	L4 mid	13 months

FIGO, International Federation of Gynecology and Obstetrics

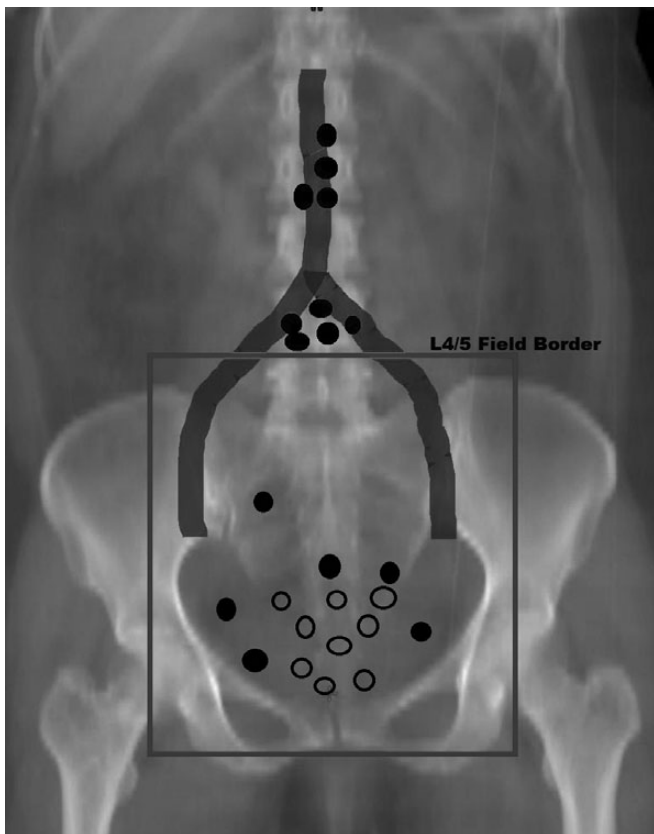


Figure 1. Figure showing the patterns of regional failures. (The black circles represent the nodal failures and the empty circles represent the local failures).

nodes and 3 (4%) had equivocal lymph nodes. The superior borders of radiation field varied from S2/3 to T12–L1 (or higher), depending on the extent of lymph node involvement and majority of patient received radiation only. The authors attributed the failures to inadequate estimation of regional disease and inadequacy of the treatment volumes (12). The higher incidence of ‘above field’ failures reported by Beadle *et al.* as compared with our study could be because in 30 of the 198 patients the superior border of the fields were

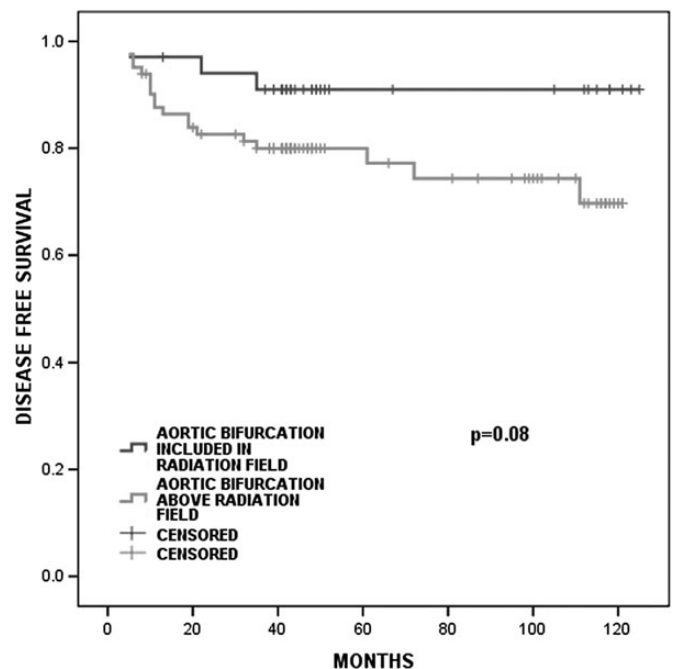


Figure 2. Graph showing the disease free survival (DFS) for patients with aortic bifurcation within the radiation field and those with aortic bifurcation above the radiation field.

kept at or below the L4–L5 junction. In addition, 42% patients already had enlarged lymph nodes at diagnosis and these failures were reported based on distance of nodal recurrence from the superior border of the fields rather than the aortic bifurcation. Contrary to Beadle *et al.*, our study comprised of a selected group of patients with radiological negative lymph nodes treated with concurrent chemo-radiation and superior border of the fields were placed at L4–L5 junction.

Regional lymph node involvement is an important prognostic factor in determining the clinical outcome in patients with cervical cancer. Hence, adequate coverage of the draining pelvic lymph nodal regions is essential as grossly unenlarged nodes on imaging may still harbor micrometastasis. Although,

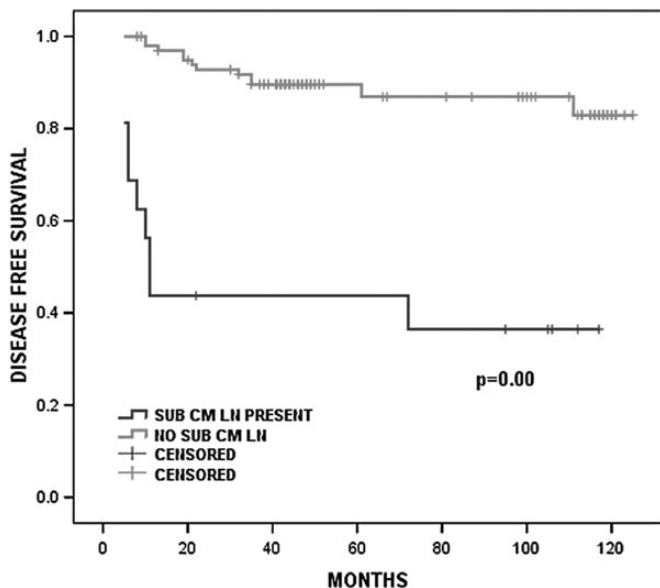


Figure 3. Graph showing the DFS for patients with subcentimeter lymph nodes compared with no lymph nodes on CT.

obturator and the external iliac nodes are thought to be the most commonly involved lymph node regions, involvement of the internal iliac and the common iliac lymph nodes is not uncommon. Kasuya *et al.* studied the patterns of distribution of lymph nodes in 114 cervical cancer patients with clinically metastatic lymph nodes on CT or magnetic resonance imaging (MRI) (>10 mm in greatest dimension). Of the 273 enlarged lymph nodes assessed, incidence of positive lymph nodes was 91% for the obturator group of nodes, 27% for the external iliac, 14% for the internal iliac, 19% for the common iliac and 5% for the presacral lymph nodes. Although solitary involvement of the internal iliac or the common iliac lymph nodes were not seen, the rate of involvement of these nodal groups was not low (13). In our study also, even though only clinically node negative (<10 mm on CT) patients were included, maximum failures were observed in the common iliac region indicating that even in the absence of gross pelvic lymphadenopathy in the obturator and the external iliac lymph nodes, micrometastasis may still be present in the less frequently involved common iliac region.

On retrospective evaluation, 16 patients in our study had subcentimeter regional lymph nodes. Studies have shown that conventional imaging techniques like CT and MRI have limited sensitivity in detection of lymph node metastasis as they rely on lymph node enlargement or distorted nodal architecture (14). Grigsby *et al.* compared CT lymph node staging to whole body positron emission tomography (PET) in 101 cervical cancer patients. PET was positive for para-aortic node metastasis in 14 additional patients as compared with CT and led to a modification of treatment fields in 14% patients (15). Sironi *et al.* compared the accuracy of PET-CT in detection of lymph node metastasis with histopathological results in patients with early stage cervical cancer. Although, PET-CT was accurate in 13 of the 18 histology proved

metastasis measuring >0.5 cm in short-axis diameter, all the five lymph nodes missed with PET-CT measured >0.5 cm (16). Thus, PET-CT is important in detection of lymph node metastasis in patients with doubtful findings on conventional imaging so that the treatment fields and protocols can be modified accordingly. However, adequate coverage of relevant draining lymph node regions is imperative even in the absence of PET-CT positive pelvic lymph nodes.

Though inadequacy of radiation portals have been documented in various dosimetric studies (17,18), very few studies have tried to correlate these failures to the radiation field borders (12,19,20). In the present study, deficiency in radiation fields with respect to the superior border of the nodal CTV was observed in 70.7% patients. Of the total nodal failures occurring above the radiation field, 55% (5/9) were solely 'above L4/5' failures and 40% (2/5) of above L4/5 failures occurred in patients without any evidence of subcentimeter lymph nodes. In these two patients with above L4/5 failures without obvious subcentimeter lymph nodes, the aortic bifurcation occurred at a higher level, i.e. at L3 level as compared with the other patients in whom the bifurcation was at a lower level. In fact, the bifurcation of the common iliac into the external and internal iliac vessels occurred superior to the L4–5 border in one patient and was just at L4–5 junction in the second patient.

Although in the present audit, it is difficult to draw a definitive conclusion regarding the superior border of the radiation field, to our knowledge, this is the first study where we have reported the regional failures that occur between the aortic bifurcation and the conventionally defined radiation field starting at L4–L5 junction. One of the reasons why failures at the common iliac region have not been separately documented so far could be possibly because common iliac lymph nodes have been traditionally assumed to be included in conventional radiation portals and thus these failures may often be reported as pelvic lymph node recurrences and hence assumed to be 'in-field' regional failures (11).

The drawback of our study is its retrospective nature and the fact that CT imaging was not routinely performed at follow-up and was done only when a recurrence was suspected. This could have resulted in a potential bias and underreporting of our results. The actual incidence of the 'above L4/5 failures' could possibly be higher than that reported in our study. A higher DFS was observed in patients with aortic bifurcation included in the radiation field compared with those with aortic bifurcation above the radiation fields. However, the difference between the two arms was not statistically significant although there was a trend towards significance. This could be probably due to the relatively small patient cohort in our study. Secondly, patients with subcentimeter lymph had an inferior outcome and the worst outcomes were observed in patients who had subcentimeter lymph nodes and the aortic bifurcation was above the radiation fields. Thus, although not yet tested in randomized trials, patients with subcentimeter lymph nodes may define a distinct prognostic subgroup where field borders need to be defined cautiously and additional chemotherapy may be

of benefit (21). Even in the absence of subcentimeter lymph nodes on CT, the level of aortic bifurcation may be another factor to be looked into as in patients with higher level of aortic bifurcation, the conventional superior field border may be insufficient in even adequately covering the external and internal iliac group of lymph nodes. Although, a small number of recurrences were demonstrated in the present study, given the magnitude of cervical cancer worldwide, this may extrapolate to a statistically significant number. Since in many centers especially those in the developing countries, it is difficult to perform a PET-CT routinely, adequate coverage of the target volume by including the common iliac group of nodes starting from aortic bifurcation may be an ideal practice to be followed in patients with locally advanced cervical cancer especially in those with subcentimeter pelvic lymph nodes. PET-CT may be reserved for a selective group of patients with doubtful imaging findings with conventional imaging techniques. Whereas on one hand it seems important to adequately include the common iliac lymph nodes, on the other hand, extending the fields higher could result in an increased treatment related toxicity. Hence, its advantage needs to be weighed against the treatment related toxicity that may be expected with the use of non-IMRT techniques.

CONCLUSION

Our retrospective analysis suggests the need for including the aortic bifurcation in the pelvic nodal CTV for patients with locally advanced cervical cancer especially in those with subcentimeter lymph nodes. Radiation fields need to be carefully defined in patients with subcentimeter lymph nodes especially in a resource constrained setting where facilities for further evaluation of lymph nodes are lacking. Since a randomized prospective study may be ethically difficult to justify, multi institutional retrospective studies with a similar patient cohort are required in order to validate our observations.

Conflict of interest statement

None declared.

References

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010;127:2893–917.
2. Lim K, Small W, Jr, Portelance L, et al. Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic

- radiotherapy for the definitive treatment of cervix cancer. *Int J Radiat Oncol Biol Phys* 2011;79:348–55.
3. Taylor A, Rockall AG, Powell MEB. An atlas of the pelvic lymph node regions to aid radiotherapy target volume definition. *Clin Oncol* 2007;19:542–50.
4. Small W, Mell LK, Anderson P, et al. Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy in postoperative treatment of endometrial and cervical cancer. *Int J Radiat Oncol Biol Phys* 2008;71:428–34.
5. Toita T, Ohno T, Kaneyasu Y, et al. A consensus-based guideline defining the clinical target volume for pelvic lymph nodes in external beam radiotherapy for uterine cervical cancer. *Jpn J Clin Oncol* 2010;40:456–63.
6. Finlay MH, Ackerman I, Tirona RG, Hamilton P, Barbera L, et al. Use of CT simulation for treatment of cervical cancer to assess the adequacy of lymph node coverage of conventional pelvic fields based on bony landmarks. *Int J Radiat Oncol Biol Phys* 2006;64:205–9.
7. Gulia A, Patel FD, Rai B, Bansal A, Sharma SC. Conventional four field radiotherapy versus CT based treatment planning in cancer cervix: a dosimetric study. *South Asian J Cancer* 2013;3:132–5.
8. McMahon CJ, Rofsky NM, Pedrosa I. Lymphatic metastases from pelvic tumors: anatomic classification, characterization, and staging. *Radiology* 2010;254:31–46.
9. Bansal A, Patel FD, Rai B, Gulia A, Dhanireddy B, Sharma SC. Literature review with PGI guidelines for delineation of clinical target volume for intact carcinoma cervix. *J Cancer Res Ther* 2013;9:574–82.
10. Taylor A, Powell MEB. An assessment of interfraction uterine and cervical motion: implications for radiotherapy target volume definition in gynaecological cancer. *Radiother Oncol* 2008;88:250–57.
11. Kaplan E, Meier P. Nonparametric estimation from incomplete observations. *J Stat Assoc* 1958;53:457–81.
12. Beadle BM, Jhingran A, Yom SS, Ramirez PT, Eifel PJ. Patterns of regional recurrence after definitive radiotherapy for cervical cancer. *Int J Radiat Oncology Biol Phys* 2010;76:1396–403.
13. Kasuya G, Toita T, Furutani K, et al. Distribution patterns of metastatic pelvic lymph nodes assessed by CT/MRI in patients with uterine cervical cancer. *Radiat Oncol* 2013;8:139.
14. Bellomi M, Bonomo G, Landoni F, et al. Accuracy of computed tomography and magnetic resonance imaging in the detection of lymph node involvement in cervix carcinoma. *Eur Radiol* 2005;15:2469–74.
15. Grigsby PW, Siegel BA, Dehdashti F. Lymph node staging by positron emission tomography in patients with carcinoma of the cervix. *J Clin Oncol* 2001;19:3745–9.
16. Sironi S, Buda A, Picchio M, et al. Lymph node metastasis in patients with clinical early-stage cervical cancer: detection with integrated FDG PET/CT. *Radiology* 2006;238:272–9.
17. Russel AH, Walter J, Anderson M, Zukowski CL. Sagittal magnetic resonance imaging in the design of lateral radiation treatment portals for patients with locally advanced squamous cancer of the cervix. *Int J Radiat Oncol Biol Phys* 1992;23:449–55.
18. Zunino S, Rosato O, Lucino S, et al. Anatomic study of the pelvis in carcinoma of the uterine cervix as related to the box technique. *Int J Radiat Oncol Biol Phys* 1999;44:53–9.
19. Kim RY, McGinnis LS, Spencer SA, Meredith RF, Jennelle RL, Salter MM. Conventional four-field pelvic radiotherapy technique without computed tomography-treatment planning in cancer of the cervix: potential geographic miss and its impact on pelvic control. *Int J Radiat Oncol Biol Phys* 1995;31:109–12.
20. Uno T, Isobe K, Ueno N, et al. Vessel-contouring-based pelvic radiotherapy in patients with uterine cervical cancer. *Jpn J Clin Oncol* 2009;39:376–80.
21. Chemoradiotherapy for Cervical Cancer Meta-Analysis Collaboration. Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: a systematic review and meta-analysis of individual patient data from 18 randomized trials. *J Clin Oncol* 2008;26:5802–12.