RADIATION ONCOLOGY—ORIGINAL ARTICLE

Stage IB cervix cancer with nodal involvement treated with primary surgery or primary radiotherapy: Patterns of failure and outcomes in a contemporary population

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Abstract

Introduction: The purpose of this study is to evaluate patterns of failure, overall survival (OS), disease-free survival (DFS), prognostic factors and late toxicities in node positive International Federation of Gynaecology and Obstetrics (FIGO) stage IB cervix cancer treated with curative intent.
Methods: Patients with FIGO stage IB cervix cancer and positive nodes were identified from the Peter MacCallum Cancer Centre prospective gynaecology database. Patients were treated with primary surgery and adjuvant radiotherapy (S + RT) or primary radiotherapy (primary RT). Prognostic factors examined were tumour size, histology, grade, lymphovascular invasion or corpus uterine invasion, MRI tumour volume, number of nodes involved, highest site of nodal involvement, treatment modality, age and smoking.
Results: Of the 103 eligible patients, 43 patients had S + RT and 60 patients had primary RT. Tumours were significantly smaller in the S + RT group (mean 3.0 cm vs. 4.5 cm, $P < 0.001$). Five-year OS (95% confidence interval) and DFS (95% confidence interval) for the whole cohort was 67.6% (56.5–76.4%) and 66.1% (55.7–74.6%), respectively. Tumour diameter and number of positive nodes were significant prognostic factors for OS and DFS and smoking was related to DFS. Treatment modality was not a significant prognostic factor in OS and DFS. Of 33 patients that relapsed, 32 patients relapsed outside the pelvis. One patient failed in the pelvis only.
Conclusions: Early stage cervix cancer with nodal involvement is associated with excellent pelvic disease control following curative intent treatment. Almost all relapses occurred beyond the pelvis and therefore more aggressive local treatment is unlikely to improve survival in these patients.

Key words: cervix cancer; chemoradiation; node positive; radiotherapy; stage IB; surgery.

Introduction

International Federation of Gynaecology and Obstetrics (FIGO) stage IB cervix cancer can be treated equally effectively with either primary surgery or primary radiotherapy (RT)[1] and the choice depends on many factors including patient and tumour characteristics, treatment-related morbidity, available resources, and patient and clinician preferences. Lymph node status is an important factor to consider when selecting primary therapy. Nodal involvement is associated with an increased risk of disease recurrence and decreased survival.[2] Therefore, traditionally, adjuvant RT is given after surgery to improve tumour outcomes. However, Landoni *et al.* showed that combined modality treatment with primary surgery and adjuvant RT (S + RT) is associated with increased morbidity compared with primary RT.[1] The authors recommended primary RT in patients with unfa-

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vourable risk factors such as nodal involvement, reserving primary surgery for patients who would not be anticipated to need adjuvant therapy.

Since this study was published, multiple phase III studies have shown the superiority of concurrent chemoradiation (CRT) over RT alone in the definitive and adjuvant settings, changing standard practice.[3–7]

The purpose of this study was to evaluate the patterns of failure, survival outcomes and treatment-related toxicities in patients with FIGO Stage IB lymph node positive cervix cancer treated with either S + RT or primary RT in a contemporary population.

Methods

All patients referred to Peter MacCallum Cancer Centre (PMCC) with a diagnosis of cervix cancer were prospectively entered into an ethics-approved tumour registry.

Selection criteria

Patients were eligible for this study if they had previously untreated cervix cancer and presented to PMCC between January 1996 and December 2010. Selection criteria included (i) FIGO Stage IB1 or IB2 disease, (ii) squamous cell carcinoma or adenocarcinoma histologies (endometrioid or mucinous), (iii) positive nodes on histology, positron emission tomography (PET) or magnetic resonance imaging (MRI) if PET was not available, and (4) treatment with either S + RT or primary RT with curative intent. Following the publication of the concurrent CRT trials demonstrating the superiority of CRT over RT in the radical and adjuvant settings in 1999 and 2000,[3–7] patients received concurrent cisplatin with RT unless there was a contraindication, as determined by the treating clinician.

Staging

All patients were staged according to FIGO protocol,[8] and most had MRI of the pelvis. Positive nodal involvement was confirmed by PET scanning (or MRI if PET was not available) or surgical nodal staging or both. The number of positive nodes on PET scan was based on the number of foci of fludeoxyglucose uptake present in nodal sites, excluding ovarian or other normal tissue uptake if present. The information on lymph node status obtained from imaging and surgical staging was used to determine the treatment fields and radiation boost dose to nodal sites.

Treatment policy

Surgery

Patients with FIGO 1B1 disease underwent type II or type III hysterectomy and pelvic lymphadenectomy. In three patients, the scheduled hysterectomy was abandoned in favour of primary RT when lymphadenectomy revealed gross positive nodes. The other patients found to have histological nodal involvement following radical hysterectomy were treated with post-operative RT/CRT.

Post-operative RT

External beam RT (EBRT) was delivered to a dose of 45–50.4 Gy in 25–28 fractions using a four field technique with 18 MV photons. Concurrent chemotherapy was given with weekly cisplatin (40 mg/m^2) during the course of RT unless contraindicated. In these cases, carboplatin was used (four patients).

Radical RT

Patients with FIGO 1B1 or IB2 disease with positive nodes confirmed on staging investigations were treated with definitive EBRT using a four-field technique with 18 MV photons followed by intracavitary brachytherapy. If pelvic nodes alone were involved, EBRT was delivered to the pelvis to a dose of 40Gy in 2Gy fractions or 45Gy in 1.8Gy fractions with an involved nodal boost to 50.4–54Gy. If patients had common iliac or para-aortic (PA) nodal involvement, extended field RT was used to 45 Gy in 25 fractions, and the positive nodes received a boost to a total dose of 50.4–54 Gy in 28–30 fractions. Brachytherapy consisted of 28–30 Gy in 3–5 fractions using high dose rate brachytherapy or 40–45 Gy in two fractions using low dose rate brachytherapy. Nodal boost, if required, was delivered in between brachytherapy fractions. Concurrent weekly cisplatin (40 mg/m^2) was used during the EBRT component, except in two patients where carboplatin was used due to contraindications.

Follow-up

All patients were reviewed 4–6 weeks post RT and thereafter every 3–4 months for the first 3 years, every 6 months for the fourth and fifth years and annually until 10 years. A post-treatment PET was performed 6 months after completion of RT to assess response to treatment. At each visit, clinical history was taken, physical examination was performed and a form recording disease status and late complications was completed prospectively. If history or examination warranted further investigations, then additional tests such as PET, computed tomography (CT) scan and/or MRI were performed at the discretion of the treating clinician.

Criteria for assessing outcomes

Failure was defined as persistent or recurrent disease following RT. Sites of failure were defined as local (resid-

ual or recurrent disease at cervix or vaginal vault), pelvic (vaginal, parametrial or nodal disease below L5–S1 level), PA (nodal disease above L5–S1), and distant. Distant sites include supraclavicular nodes, inguinal nodes, lung, liver, bone, brain and subcutaneous tissue metastases.

Prognostic factors assessed were tumour size, histology, grade, lymphovascular invasion or corpus uterine invasion, MRI tumour volume, number of positive nodes involved, highest site of nodal involvement, treatment modality, age, and smoking. For tumour size, pathological tumour size was considered in S + RT patients whereas the longest diameter based on MRI measurements was considered as tumour size for primary RT patients. In seven patients treated with primary RT where MRI was not available, the clinical diameter determined at EUA was used.

The late toxicities were recorded according to a modified World Health Organisation/Radiation Therapy Oncology Group (WHO/RTOG) toxicity criteria and defined as any toxicity developing at least 3 months after RT.[9] The highest toxicity scores for bowel, bladder, vagina and lymphoedema were recorded.

Statistical analysis

Descriptive statistics were used to describe the characteristics of participants. Overall survival (OS) was measured as the time difference between the date of diagnosis and date of death from any cause. Disease-free survival (DFS) was measured as the time difference between the date of diagnosis and date of failure or death. Kaplan–Meier curves were calculated for OS and DFS. Prognostic factors for OS and DFS were evaluated using univariate and multivariate Cox regression models. Toxicities were expressed as proportions using descriptive statistics.

Results

Patient characteristics

Of the 103 patients included in this study, 43 patients were treated with S + RT and 60 patients were treated with primary RT. Patient and tumour-related characteristics are described in Table 1.

Median patient age was 45 years (range: 21–86). Nodal involvement was diagnosed by PET in 26 patients (25.2%), by surgical staging in 40 patients (38.8%), by both PET and surgery in 36 patients (35.0%) and by MRI in one patient (1.0%). Six patients in the S + RT group had preoperative PET and five of these patients had false negative nodes. The patient with node positive disease on preoperative PET was pregnant, elected to terminate the pregnancy and had a radical hysterectomy with pelvic lymphadenectomy.

The median number of nodes involved was 2 (range: 1–12). PA nodes were the highest echelon of nodal involvement in 10 patients (16.7%) treated with primary RT, whereas only two patients (4.7%) had involved PA nodes in the S + RT group. The mean (standard deviation) number of nodes removed at surgery was 14.4 (8.4). Concurrent CRT was used in 56 patients (93.3%) receiving primary RT. Thirty-four patients (79.1%) received adjuvant CRT following surgery. Tumour size was the only characteristic that was significantly different between the S + RT and primary RT groups and was significantly smaller in the S + RT group ($P < 0.001$). MRI tumour volume was available in 62 patients (nine S + RT patients and 53 primary RT patients), and there was no significant difference between the groups ($P = 0.0677$).

OS, DFS

Median (interquartile range) follow-up was 3.9 (1.4–7.7) years. Eleven patients were lost to follow-up. Thirty-four patients died. Five-year OS was 67.6% (95% confidence interval (CI) 56.5–76.4%) for all patients. Five-year OS was 77% for the S + RT group and 61% for the primary RT group, which was not significantly different between groups ($P = 0.079$) (Fig. 1). Five-year DFS was 66.1% (95% CI 55.7–74.6%) for all patients, and was 73% for S + RT and 62% for primary RT, which was not significantly different ($P = 0.181$) (Fig. 2).

Prognostic factor analysis

Univariate analysis showed that number of positive nodes and tumour size were significant prognostic factors for OS. These factors remained significant on multivariate analysis (Table 2). Prognostic factors statistically significant for DFS were smoking status, number of positive nodes involved and tumour size on both univariate and multivariate analysis. Treatment modality was not a significant prognostic factor for OS or DFS. PA nodal involvement was a significant prognostic factor for OS and DFS on univariate analysis but was no longer significant on multivariate analysis ($P = 0.132$).

Patterns of failure

Overall, 33 patients (32.0%) developed a failure at either local, pelvic, PA or distant sites, 10 in the S + RT group and 23 in the primary RT group (Table 3). There were 10 local relapses, all in the primary RT group. However, nine of these 10 patients also relapsed at more distal sites (one patient had PA recurrence as the most distal site of relapse, and eight patients had distant metastases). For three of these patients, primary and distant relapses occurred at the same time and for one patient, primary and PA relapses occurred at the same time. For one patient, distant relapse occurred 7 months before relapse at the primary site. Four patients relapsed at the primary site first, before relapsing at distant sites

Table 1. Patient and tumour characteristics

Variable	All patients		S + RT		Primary RT		*P* value
	No.	%	No.	%	No.	%	
Total number	103	100	43	41.7	60	58.3	
Age:							0.752†
Median (range)	45 (21–86)		44 (24–81)		46 (21–86)		
<40 years	35	34.0	16	37.2	19	31.7	
≥40 years	68	66.0	27	62.8	41	68.3	
Smoking status:							0.413
Ever smoked	51	49.5	22	51.2	29	48.3	
Never smoked	42	40.8	15	34.9	27	45.0	
Unknown	10	9.7	6	14.0	4	6.7	
Tumour size:							<0.001†
Mean (range)	3.9 (0.5–11.5)		3.0 (1.0–5.0)		4.5 (0.5–11.5)		
Histology:							0.125
Squamous cell carcinoma	77	74.8	30	69.8	47	78.3	
Adenocarcinoma	23	22.3	13	30.2	10	16.7	
Adenosquamous	3	2.9	0	0.0	3	5.0	
Grade:							0.742
1	7	6.8	3	7.0	4	6.7	
2	37	35.9	14	32.6	23	38.3	
3	58	56.3	25	58.1	33	55.0	
Unknown	1	1.0	1	2.3	0	0.0	
LVSI/corpus invasion:							0.041
Negative	28	27.2	8	18.6	20	33.3	
Positive	71	68.9	35	81.4	36	60.0	
Unknown	4	3.9	0	0.0	4	6.7	
Number of positive nodes:							0.789
Median (range)	2 (1–12)		2 (1–12)		2 (1–11)		
1	44	42.7	21	48.8	23	38.3	
2	24	23.3	9	20.9	15	25.0	
3	14	13.6	5	11.6	9	15.0	
≥4	21	20.4	8	18.6	13	21.7	
Highest site of nodal involvement:							0.136
Pelvic	77	74.8	37	86.0	40	66.7	
Common iliac	14	13.6	4	9.3	10	16.7	
Lower PA	10	9.7	2	4.7	8	13.3	
Upper PA	2	1.9	0	0.0	2	3.3	

†Test for median difference. LVSI, lymphovascular space invasion; No., number; PA, para-aortic; RT, radiotherapy; S + RT, primary surgery and adjuvant radiotherapy.

2, 2, 5 and 7 months later. Only one patient failed at the local site alone, and her recurrent disease was salvaged by surgery. There were no relapses in the pelvis alone. Thirty-two of the 33 patients (97.0%) relapsed at PA or distant sites. The PA region was the most distal site of failure in seven patients. There were 25 (75.8%) distant failures overall, eight in the S + RT group (18.6% of S + RT patients) and 17 in the primary RT group (28.3% of primary RT patients). Seventeen patients had distant relapses without local relapse, eight in the S + RT group and nine in the primary RT group.

Treatment-related late toxicities

For the entire cohort, there were 22 patients (21.4%) with grade 1–2 bladder toxicities, 23 patients (22.3%) with grade 1–2 bowel toxicities, 33 patients (32.0%) with grade 1–2 vaginal toxicities and seven patients (6.8%) with grade 1–2 lymphoedema. Eight patients developed grade 3 toxicities, summarised in Table 4. There were no grade 4 or 5 toxicities. There were no significant differences in the late toxicities of the bladder ($P = 0.227$), bowel ($P = 0.786$), vagina ($P = 0.701$) or lymphoedema ($P = 0.859$) between treatment modalities.

Discussion

Nodal involvement is an important negative prognostic factor in cervix cancer,[2] although it is not part of FIGO staging. Stage IB cervix cancer is associated with favourable prognosis with 5-year overall survival rates of

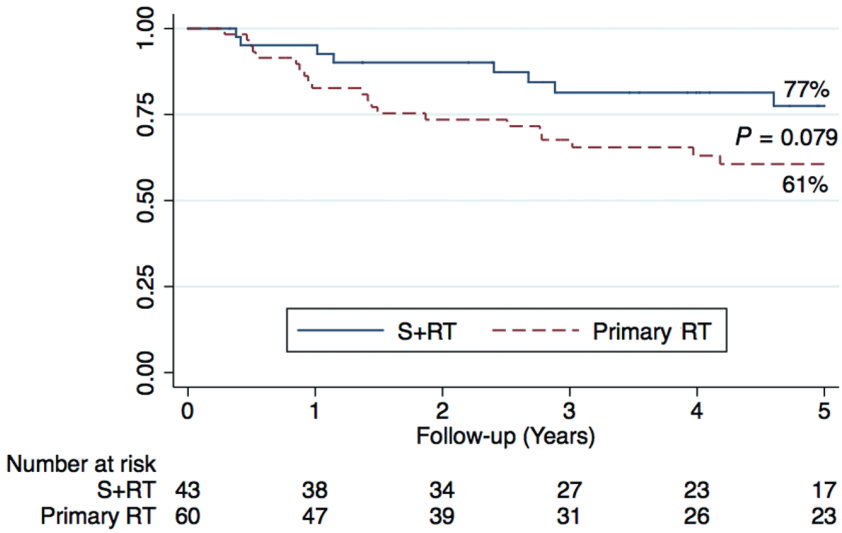

Fig. 1. Kaplan–Meier curves for overall survival by treatment modality.

80–90% in node negative patients; however, this falls to 30–60% with positive nodes.[2,10–12] This study describes the outcomes following treatment of FIGO stage IB cervix cancer with positive nodes over a 15-year period at a single institution.

The 5-year OS for the entire study population was 68%. The 5-year OS in the S + RT group (77%) was higher compared with the primary RT group (61%), but this difference in OS was not statistically significant. This is despite the primary RT group having more advanced disease at the outset. Patients in the primary RT group had significantly larger tumours with mean tumour size of 4.5 cm compared with 3.0 cm in the S + RT group. In addition, 10 patients (17%) in the primary RT group had PA nodal involvement compared with only two patients (5%) in the S + RT group. DFS was not significantly different between the treatment modalities either. These results are consistent with previously published studies comparing survival outcomes with primary surgery versus primary RT including a randomised trial[1,12] but in contrast to a retrospective study comparing radical hysterectomy and tailored adjuvant therapy with primary CRT.[13]

The most significant prognostic factors affecting OS and DFS in this study were the number of nodes involved and tumour size. There are conflicting reports regarding the prognostic significance of number of positive nodes. Tinga *et al.*[14] demonstrated significantly better survival rates of patients with single nodal metastasis compared with patients with multiple nodal metastases and/or

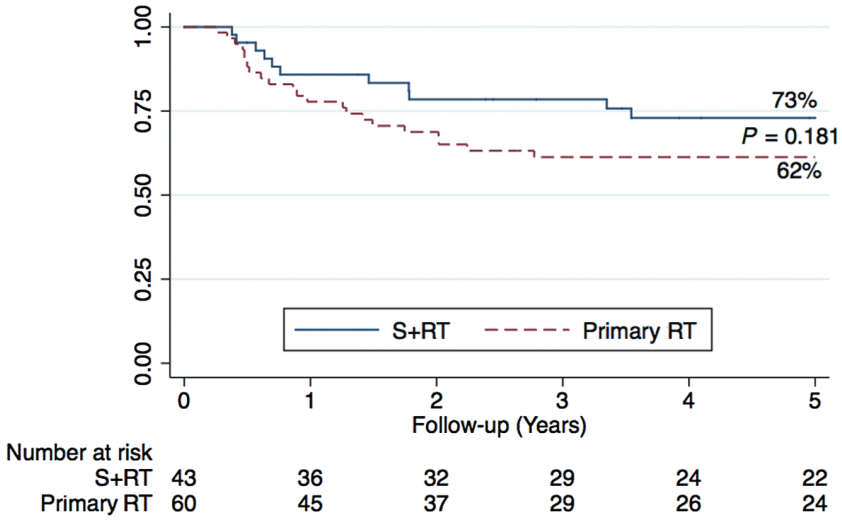

Fig. 2. Kaplan–Meier curves for disease free survival by treatment modality.

Table 2. Multivariate Cox proportional hazard models predicting overall survival and disease free survival

	Odds ratio (95% CI)	*P* value
OS		
Primary RT versus S + RT	1.29 (0.51–3.26)	0.592
Tumour size	1.29 (1.06–1.57)	0.012
Number of positive nodes	1.19 (1.04–1.36)	0.012
Extrapelvic nodal involvement	1.82 (0.83–3.99)	0.132
DFS		
Primary RT versus S + RT	1.04 (0.45–2.40)	0.931
Tumour size	1.29 (1.05–1.59)	0.017
Number of positive nodes	1.17 (1.03–1.33)	0.017
Smoking status	3.15 (1.38–7.19)	0.006
Extrapelvic nodal involvement	1.81 (0.86–3.83)	0.119

CI, confidence interval; DFS, disease free survival; OS, overall survival; RT, radiotherapy; S + RT, primary surgery and adjuvant radiotherapy.

single nodes with extranodal tumour infiltration (85% versus 24%, $P < 0.001$). Alvarez *et al.*[15] showed that number of nodal metastases was a significant prognostic factor for survival ($P = 0.004$) in an analysis of 185 patients found to have nodal metastasis at the time of radical hysterectomy. Hopkins *et al.*[12] showed that when three or fewer lymph nodes were involved in patients with stage IB cervix cancer, survival was 79% compared with 33% when four or more lymph nodes were positive. Aoki *et al.*[16] demonstrated number of positive nodes was associated with decreased disease specific survival.

On the other hand, in a Gynecologic Oncology Group (GOG) study evaluating patients with stage I squamous cell carcinoma of the cervix who were treated with radical hysterectomy with pelvic lymphadenectomy, Delgado *et al.* suggested number of positive pelvic nodes did not correlate with poor prognosis.[17] Of the 645 patients analysed, 100 patients had microscopic pelvic nodal involvement with 3-year disease-free interval of 74.4%, compared with 85% in node negative patients. However, 98 patients were removed from this analysis, because they were found to have extrauterine nodal disease at the time of surgery and hysterectomy was abandoned. A subsequent evaluation of the outcomes of these omitted patients showed a much shorter median recurrence free interval (19 months versus 84 months) and median OS (22 months versus 113 months) than those who completed radical surgery.[18]

Tumour size has been identified as prognostically significant in multiple studies. Hopkins *et al.*,[12] in a study of 341 patients with Stage IB cervix cancer, demonstrated that patients with tumour size less than 3 cm had 5-year survival of 91% compared with 76% in patients with tumour size greater than 3 cm. Alvarez *et al.*[15] also found tumour diameter to be a significant prognostic factor in overall survival. Delgado *et al.*[17] demonstrated disease-free interval (DFI) correlated significantly with clinical tumour size with 3-year DFI of 85.5% in tumours smaller than 3 cm but was 68.4% for tumours 3 cm or greater. Perez *et al.*[19] showed that 5-year DFS for stage IB tumours was 90% for tumours less than or equal to 3 cm and 67% for tumours more than 3 cm ($P = 0.01$).

In this study, smoking was identified as a significant negative prognostic factor for DFS. Smoking is a risk factor for the development of cervix cancer[20] and has been associated with increased risk of disease relapse and poorer survival following treatment. In a GOG study (GOG165) consisting of patients with locally advanced cervix cancer, Waggoner *et al.*[21] showed a significant difference between smokers and non-smokers in progression free survival (median 28 months versus 64 months) and OS (median 49 months versus 64 months). Mileshkin *et al.*[22] demonstrated similar findings with 5-year relapse-free survival of 53% versus 68% and 5-year OS of 51% and 65% in ever-smokers and never-smokers, respectively.

PA nodal involvement is associated with greater risk of disease recurrence and decreased survival. Stehman *et al.*,[23] in a multivariate analysis of 626 patients entered into prospective GOG trials of definitive RT, showed that PA nodal involvement was the most important prognostic factor for relapse and survival. Pelvic nodal involvement and tumour size retained significance, only if PA nodes

Table 3. Patterns of failure

Site(s) of failure	All patients		S + RT		Primary RT	
	No.	%	No.	%	No.	%
Local only	1	1.0	0	0.0	1	1.7
Pelvic only	0	0.0	0	0.0	0	0.0
PA only	2	1.9	1	2.3	1	1.7
Pelvic, PA	4	3.9	1	2.3	3	5.0
Local, pelvic, PA	1	1.0	0	0.0	1	1.7
Distant only	7	6.8	4	9.3	3	5.0
PA, distant	10	9.7	4	9.3	6	10.0
Local, pelvic, distant	2	1.9	0	0.0	2	3.3
Local, PA, distant	1	1.0	0	0.0	1	1.7
Local, pelvic, PA, distant	5	4.9	0	0.0	5	8.3
Total	33	32.0	10	23.3	23	38.3

No., number; PA, para-aortic; RT, radiotherapy; S + RT, primary surgery and adjuvant radiotherapy.

Table 4. Grade 3 treatment-related late toxicities.

Toxicity	All patients		S + RT		Primary RT	
	No.	%	No.	%	No.	%
Bladder	2	1.9	0	0.0	2	3.3
Bowel	5	4.9	1	2.3	4	6.7
Vagina	0	0.0	0	0.0	0	0.0
Lymphoedema	1	1.0	0	0.0	1	1.7

No., number; RT, radiotherapy; S + RT, primary surgery and adjuvant radiotherapy.

were negative. However, PA nodal involvement was not a significant prognostic factor in our study, due to the small number of patients (12 patients) with metastases to this region.

In a systematic review of follow-up procedures for women treated with cervix cancer, Elit *et al.*[24] found recurrence rates ranged from 8% to 49%, although there was a wide variation in the patient populations of the studies included. A range of 15% to 61% of patients had recurrences that were distant or detected at multiple sites. Recurrent disease was seen in 32% of our study patients. Most of these patients (97%) either failed distantly (76%) or in the PA region (21%). This higher rate of distant metastases can be explained by nodal involvement in all our study patients at diagnosis. Patients with nodal involvement at initial diagnosis have a higher risk of distant failure than patients with negative lymph nodes.[2,25] In the S + RT group, 19% developed distant relapse, whereas in the primary RT group, 28% developed distant relapse. This higher relapse rate is likely related to the primary RT group having more advanced disease. However, the difference in distant relapse rates was not statistically significant.

Isolated local or pelvic failures (i.e. within the radiation fields) were rare. Ten patients developed local relapses; however, nine of the 10 patients had disease elsewhere, with distant disease in eight patients (80%). Four of these patients were found to have distant relapse at the same time or prior to developing local relapse. For the four patients that recurred at the primary site first, distant relapse occurred within a short time frame (2–7 months), and perhaps distant tumour dissemination was already present that was not detectable on early investigations. In addition, 23 (70%) of the 33 patients that relapsed had no evidence of local relapse and of these, 17 (74%) failed at distant sites. As the incidence of distant metastases was not significantly different between primary RT and S + RT groups, it is unlikely that control of the primary would have improved survival in these node-positive patients. A French group attempted to augment control at the primary site in cervix cancer by incorporating routine hysterectomy after CRT with no impact on survival outcomes.[26] An Austrian group used interstitial brachytherapy to supplement MRI-guided intracavitary brachytherapy and showed marginal improvement in local control.[27] However, survival figures were no better than in patients treated without the routine use of interstitial implants.[28]

The one patient in the primary RT group who developed primary only failure was salvaged with surgery. There were no patients that had pelvis only failures and no patients died of uncontrolled disease in the pelvis alone. Thus, the available treatment options for node positive Stage IB cervix cancer provide excellent pelvic control.

Because primary surgery and primary RT are equally effective in early stage cervix cancer, treatment-related morbidities are a major consideration in the selection of primary therapy. Landoni *et al.*[1] showed that morbidity was greater in surgery patients that required adjuvant RT than those treated with primary RT. In the current study, however, there were no differences in treatment-related late toxicities. This may be related to the small number of patients and imbalance of patient numbers between treatment groups. Since the publication of the study by Landoni *et al.*, when nodes are known to be involved, patients with early stage cervix cancer are treated with primary RT/CRT rather than primary surgery to avoid potential greater morbidity associated with combined modality treatment.

The main weaknesses of this study are the retrospective nature and small patient numbers, thereby limiting the conclusions that can be drawn and generalisability to a larger population. In addition, sacral insufficiency fractures, a commonly observed complication following pelvic radiotherapy,[29] were not recorded. However, it provides valuable information regarding patterns of failure and survival in a specific patient subgroup with nodal involvement to help guide treatment decision making in patients with FIGO stage IB cervix cancer. Larger multi-institution prospective studies are required for further clarification of outcomes in this group of cervix cancer patients. Ideally, with the availability of non-invasive diagnostic tests such as MRI to look at a primary tumour's characteristics and PET/CT to evaluate nodal status, it may be possible to devise appropriate treatment protocols for FIGO stage IB patients such that combined modality treatment can be avoided, thereby limiting long-term treatment-related toxicities without compromising cure.

Conclusions

Node positive stage IB cervix cancer, whether treated with S + RT or primary RT, results in excellent disease control in the pelvis. Almost all patients who subsequently failed developed relapse outside the pelvis and most without relapse at the primary site. More aggressive local treatment is unlikely to play an important role in improving survival in this group of patients.

Multi-institution prospective studies are required to refine subgroups in FIGO stage I cervix cancer to allow appropriate patient selection for either primary surgery or primary CRT.

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