ORIGINAL ARTICLE

Efficacy and toxicity of intensity-modulated radiation therapy for prostate cancer in Chinese patients

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Objective To report the treatment efficacy and toxicity profile of intensity-modulated radiation therapy in Chinese patients with clinically localised prostate cancer.

Design Historical cohort study.

Setting Oncology unit in a university teaching hospital in Hong Kong.

Patients Patients with clinically localised prostate cancer undergoing intensity-modulated radiation therapy in our institution between May 2001 and November 2009 were reviewed.

Main outcome measures The 5-year biochemical failure–free survival, 5-year overall survival, as well as acute/late gastro-intestinal toxicities and genito-urinary toxicities.

Results A total of 182 patients were treated with prostate intensity-modulated radiation therapy with or without whole-pelvic radiotherapy. The median follow-up was 44 months. The median patient age was 72 years. Overall survival of the cohort was 92% after 5 years. The favourable, intermediate, and unfavourable risk category distributions of the National Comprehensive Cancer Network were 21 (12%), 42 (23%), and 119 (65%), respectively. The 5-year actuarial biochemical failure–free survival rates for patients in these categories were 95%, 82%, and 80%, respectively. Multivariate analysis identified early tumour stage, low pre-treatment prostate-specific antigen levels, and the use of adjuvant androgen deprivation as independent prognostic factors for better biochemical failure–free survival. Grade 2 and 3 late gastro-intestinal/genito-urinary toxicities occurred in 8%/3% and 4%/3% of the patients, respectively.

Conclusion Intensity-modulated radiation therapy for prostate cancer is feasible and safe in the Chinese population. These data are consistent with the results of other series in Caucasian populations.

Key words
Prostate neoplasms; Radiotherapy, intensity-modulated; Treatment outcome

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New knowledge added by this study

- Intensity-modulated radiation therapy is effective and safe in the Chinese population.

Implications for clinical practice or policy

- Intensity-modulated radiation therapy should be considered as one of the effective treatment options for clinically localised prostate cancer.

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Introduction

The incidence of prostate cancer is mounting in both the United States and the United Kingdom, the annual rate being 32 per 100 000 person-years.[1] Similar to the western world, the widespread use of prostate-specific antigen (PSA) screening in Asia has also resulted in a surge in the number of patients diagnosed with early-stage prostate cancer. In China, it has been estimated that more than 200 000 cases of prostate cancer are diagnosed annually.[2] For patients with locally confined prostate cancer, radiation therapy is one of the most commonly used treatment modalities. The aim of radiotherapy is to deliver an effective dose of radiation to the prostatic tumour while minimising the injury to surrounding normal tissues. Four randomised controlled trials demonstrated benefits in terms of biochemical control with escalation of radiotherapy dose.[3-6] However, dose

前列腺癌華籍患者接受強度調控放射治療後的療效和毒性

目的 報告非擴散性前列腺癌的華籍患者接受強度調控放射治療後之療效和毒性。

設計 歷史性隊列研究。

安排 香港一所大學教學醫院中的腫瘤科。

患者 在2001年5月至2009年11月期間，在上述機構接受強度調控放射治療之非擴散性前列腺癌的病人。

主要結果測量 五年無生化失敗存活率、五年存活率以及急性及晚期之腸道系統和泌尿系統的毒性。

結果 共182位前列腺癌病人接受強度調控放射治療，其中部份病人接受盆腔放射治療。跟進時間的中位數為44個月。病人平均年齡72歲；總五年存活率為92%。分別有21位（12%）、42位（23%）和119位（65%）病人屬於美國癌症中心聯盟分類中的低、中和高風險類別。本研究之五年精算無生化失敗存活率在低、中和高風險類別的病患者分別為95%、82%和80%。多變量分析確認早期腫瘤、低治療前前列腺特定抗原水平，以及使用輔助去雄激素治療為較佳無生化失敗存活率的獨立預後因素。二級和三級晚期腸道系統/泌尿系統之併發症發生在8%/3%及4%/3%的患者。

結論 強度調控放射治療在前列腺癌的華籍患者中是可行和安全的。本研究之數據與西方國家同等系列之研究結果一致。

escalation of radiotherapy runs an increased risk of late complications, whenever treatment is delivered by conventional external beam techniques[7,8] or three-dimensional conformal radiotherapy.[9,10]

Recent advances in intensity-modulated radiation therapy (IMRT) have led to an improved efficacy/toxicity profile in the treatment of prostate cancer. Several reports on prostate cancer IMRT demonstrated encouraging biochemical control and favourable treatment-related toxicities compared to conventional techniques.[11-16] However, those studies enrolled predominantly Caucasian subjects. As there are differences in stage distribution, risk categories, and pre-treatment PSA levels in Asian patients undergoing radiotherapy,[17,18] it appeared valuable to evaluate the treatment efficacy and toxicity of prostate cancer IMRT in Asian populations.

From May 2001 to November 2009, our centre has treated a cohort of Chinese patients with localised prostate cancer using IMRT. Based on this patient cohort, our current study primarily aimed to evaluate the efficacy and treatment toxicities of IMRT for prostate cancer. The association between clinical factors and toxicities endured was also studied, as was the impact of dose-volume dosimetrics on critical organs at risk (OAR).

Methods

Study population

Between May 2001 and November 2009, 182 consecutive patients with histologically proven clinically localised (T1-4N0M0) prostate cancer were treated at the Prince of Wales Hospital, which is one of the tertiary oncology centres in Hong Kong. The tumour (T) stage was determined by digital rectal examination and supplemented by computed tomography (CT) and/or magnetic resonance imaging. The 2002 version of the American Joint Commission on Cancer staging was used for this purpose.[19] The recurrence risk was determined according to the National Comprehensive Cancer Network guidelines.[20] The study was approved by the institutional review board of the Chinese University of Hong Kong, and conducted in accordance with the Helsinki Declaration of 1975.

Radiotherapy planning

The treatment schemes were determined by the risk of pelvic nodal metastasis. Patients with a lower-than-15% risk, as calculated by the Roach formula,[21] received prostate IMRT alone. On the other hand, those with a higher risk received prior whole-pelvic radiotherapy (WPRT) in addition to a prostate IMRT boost.

All patients underwent CT simulation in the supine position, with immobilisation by vaclock or easyfoam; the slices were taken at 3-mm intervals. To reduce discrepancies in bladder volume between simulation and treatment, patients were instructed to drink 300 mL of water 30 minutes before both the CT simulation and the actual treatment. The planning CT data were then transferred to the Cadplan planning system before 2002, and to the Varian Eclipse planning system (Palo Alto, US) thereafter. The clinical target volume (CTV), planning target volume (PTV), bladder, rectum, and bilateral femoral heads were contoured. The whole prostate gland was included in the CTV, as were the proximal two thirds of the seminal vesicles in those at intermediate or high risk. The PTV was the 3-dimensional expansion of the CTV with a 1-cm margin, except at the posterior border where a 6-mm margin was applied.

For the prostate IMRT–alone group, six static fields with equal-spacing field angles were used to deliver 70-76 Gy (2 Gy per fraction) to the PTV. Optimisation was performed with an inverse-planning iterative algorithm, based on a standard template of dose-volume constraint parameters for both the targets and the OARs. To fulfil the planned

acceptance criteria, no more than 5% of the PTV would entail less than the prescribed dose, and none of the PTV would entail more than 110% of that dose. The dose limits and parameters for each critical organ were similar to those described in other IMRT reports. All patients were treated with a sliding window technique using 10-20 MV Varian linear accelerators. For WPRT, a conventional 4-field box technique, which encompassed the regional pelvic lymphatics, and the PTV was used to deliver 44 Gy in 22 daily fractions. This was then followed by the prostate IMRT boost, which delivered a further radiation dose to a total dose of 70-76 Gy; the exact dose was determined/limited by the cumulative dose to the OARs.

Hormonal therapy

A course of 3 to 4 months of neoadjuvant androgen deprivation (hormone) therapy (NHT) was recommended for patients with a more-than-15% risk of pelvic nodal metastases.[22] Such NHT was also used when the prostate gland was considered too bulky for upfront prostate radiotherapy alone. A total of 3 years of adjuvant androgen deprivation (AHT) was recommended for high-risk patients or those within the intermediate risk group, which was at the discretion of individual clinicians. However, not all patients received AHT as recommended because a proportion of them were unable to afford the drug (a self-paid item according to local policy). The typical regimen for both NHT and AHT entailed 3-monthly injections of luteinising hormone-releasing hormone (LHRH) agonist with 2 weeks of flutamide before the first injection.

Dosimetric analysis

The conformity index (CI) and homogeneity index (HI) were calculated for the PTV; the former was calculated using the method described by Paddick.[23] This evaluates the dose-fitting of the PTVs, relative to the volume covered by the prescribed dose:

$$CI = V_{PTV} * TV / TV_{PTV}^2$$

where TV is the volume covered by the prescription isodose lines, V_{PTV} is the volume of the PTV, and TV_{PTV} is the volume of the PTV within TV

$$HI = D_5\% / D_{95}\%$$

where $D_X\%$ is the minimum dose delivered to X% of the PTV[24]

Values of CI and HI approaching unity were normally regarded as ideal indications of the plan's quality. The following parameters including maximum dose (D_{max}), mean dose (D_{mean}), V_{50}, V_{60}, V_{65}, V_{70} and V_{75} of the rectum, and D_{max}, D_{mean}, V_{65}, V_{70}, V_{75} of the urinary bladder were studied. The mean values of the dose-volume parameters in patients with and without grade 2 or above toxicities were compared.

Follow-up

Patients were reviewed every week during radiotherapy to monitor them for acute toxicities. Follow-up evaluations after completion of radiotherapy were performed at intervals of 3 to 6 months for at least 5 years; the PSA was determined at every visit. Both acute and late toxicities were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) 4.02 toxicity scale. Genito-urinary (GU) toxicities included urinary frequency, cystitis, and urinary incontinence, whereas gastro-intestinal (GI) toxicities included proctitis, diarrhoea, abdominal cramps, and faecal incontinence. Post-radiotherapy biochemical failure was defined according to the Phoenix definition (ie elevation of PSA by 2 ng/mL above the nadir).[25]

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (Windows version 17.0.1.80; SPSS Inc, Chicago [IL], US). Continuous variables were expressed as means with standard deviations. Baseline continuous variables were compared using Student's *t* test and categorical variables by the Chi squared test. The database was frozen on 16 September 2010. Survival curves were constructed using the Kaplan-Meier method and differences were compared using the log-rank test. Clinical factors related to toxicities were examined with the Cox proportional hazards model in the multivariate analysis. The hazard ratio (HR) and the corresponding 95% confidence interval were calculated.

Results

Patients' characteristics

The baseline characteristics of the patient cohort are shown in Table 1. The median follow-up duration was 44 (range, 7-146) months. The median age at the commencement of treatment was 72 (range, 45-82) years. The median pre-treatment PSA level was 20 (range, 3-440) ng/mL; before treatment 50% of the patients had PSA levels of >20 ng/mL. In our cohort, 12%, 23%, and 65% of the patients belonged to the favourable, intermediate, and unfavourable risk groups, respectively. The median prescribed dose to the prostate PTV was 72 (range, 70-76) Gy. Thirty-six (86%) of the intermediate risk patients received 76 Gy while 43 (36%) of the unfavourable risk patients received a PTV of 76 Gy (Table 1). A total of 128 (70%) of the patients underwent NHT; the median duration of therapy being 101 (range, 89-132) days. The apparently wide range of NHT therapy durations (11-3660 days) was due to two outliers—the 11-day duration was as a result of one patient who refused subsequent LHRH injections after 11 days of flutamide, while the 3660-

TABLE 1. Patient characteristics and treatment*

Characteristic	No. (%) of patients
Age (years)	
≥65	157 (86)
<65	25 (14)
T stage	
T1-T2a	79 (43)
T2b-T2c	56 (31)
T3-4	47 (26)
Gleason score	
≤6	77 (42)
7	58 (32)
≥8	47 (26)
Pre-treatment PSA level (ng/mL)	
<10	39 (21)
10-20	53 (29)
>20	90 (49)
Risk group (NCCN classification)	
Favourable	21 (12)
Intermediate	42 (23)
Unfavourable	119 (65)
Radiation dose to planning target volume (Gy)	
<76	93 (51)
76	89 (49)
Patients who had 76 Gy to planning target volume	
Favourable (n=21)	10 (48)
Intermediate (n=42)	36 (86)
Unfavourable (n=119)	43 (36)
Patients who received WPRT	
No	106 (58)
Yes	76 (42)
Patients who received WPRT in respective subgroup	
Intermediate (n=42)	4 (10)
High (n=119)	72 (61)
Patients who received neoadjuvant androgen deprivation	
Overall	128 (70)
Favourable (n=21)	4 (19)
Intermediate (n=42)	13 (31)
Unfavourable (n=119)	111 (93)
Patients who received adjuvant androgen deprivation	
Overall	106 (58)
Favourable (n=21)	3 (14)
Intermediate (n=42)	6 (14)
Unfavourable (n=119)	97 (82)

* T denotes tumour, PSA prostate-specific antigen, NCCN National Comprehensive Cancer Network, and WPRT whole-pelvic radiotherapy

day duration was because one patient with localised disease was given 10 years of NHT by doctors from other departments before referral to our clinic.

Treatment efficacy

The median time to the post-radiotherapy PSA nadir was 9.7 months, and the overall survival of the cohort at 5 years was 92%. The 5-year biochemical failure–free survival (BFFS) rates were 95%, 82%, 80% for the favourable, intermediate, and unfavourable risk groups, respectively (P=0.4616; Fig). Use of AHT in the unfavourable subgroup significantly improved biochemical control as inferred from the univariate analysis (P=0.0094). In the multivariate analysis, early clinical T stage, low pre-treatment PSA level, and the use of AHT were significant prognostic factors for better BFFS (Table 2). In contrast, the radiotherapy dose (76 Gy vs <76 Gy) and the use of WPRT were not prognostic factors for BFFS in the univariate or multivariate analyses.

Treatment toxicity

Gastro-intestinal toxicity

Three (2%) of the patients suffered from grade 3 acute GI complications during radiotherapy; none had grade 4 acute GI complications. Eight (4%) patients developed grade 3 late GI complications that manifested as symptomatic rectal bleeding for which they received blood transfusions (Table 3). There were no grade 4 late GI complications. Both WPRT and a history of bowel disease were associated with grade 2 or higher acute GI complications (Table 4). In the multivariate analysis, the occurrence of acute GI complications was associated with late GI complications (HR=4.497; P=0.026) [Table 4].

Genito-urinary toxicity

In all, 120 (66%) of the patients had grade 1 or 2 acute GU toxicity; none had grade 3 or higher acute GU complications (Table 3). Grade 3 late GU complications developed in five (3%) patients, two of whom had gross haematuria treated endoscopically and blood transfusions, and another three underwent urethral dilatation for stricture. In the univariate analysis, WPRT was associated with an increased likelihood of developing acute GU toxicities with borderline significance (P=0.0457) [Table 4].

Dosimetric analysis

The mean CI and HI were 1.22 and 1.07, respectively. With respect to OARs, the mean D_{max}, D_{mean}, V_{50}, V_{60}, V_{65}, V_{70} and V_{75} of the rectum in our cohort were: 75.5

Gy, 45.8 Gy, 49.0%, 25.0%, 17.0%, 10.4%, and 3.7%, respectively. The mean D_{max}, D_{mean}, V_{65}, V_{70} and V_{75} of the bladder were: 76.0 Gy, 48.0 Gy, 27.0%, 19.0%, and 7.5%, respectively. The values for V_{50} (53.9% vs 48.0%) and D_{mean} (49.1 Gy vs 45.1 Gy) of the rectum were higher in patients who had acute GI complications that were grade 2 or higher (Table 5). The D_{mean} of the bladder was significantly higher in patients who had acute GU complications that were grade 2 or higher (52.0 Gy vs 46.8 Gy) [Table 5]. For the late GI or GU complications, there were no significant differences in dosimetric parameters in those with and without grade 2 or higher late complications.

Discussion

In the current study, we demonstrated that prostate IMRT could achieve good biochemical control in a cohort of Chinese patients. The 5-year BFFS rates were 95%, 82%, 80% for the favourable, intermediate, and unfavourable risk groups, respectively. These data were consistent with the results of IMRT series in Caucasians (Table 6).[11-16] Our study also concurred with previous reports that Asian patients with prostate cancer tended to present with more advanced or high-risk disease, as evidenced by 88% of the patients having intermediate- or unfavourable-risk disease. Nevertheless, it was evident that ethnicity differences did not influence treatment outcomes. To the best of our knowledge, the current study is the first to demonstrate that IMRT for prostate cancer is effective in Chinese patients.

Our cohort also showed that the IMRT for prostate cancer is generally well tolerated by Chinese patients. In general, the rates of severe acute toxicities

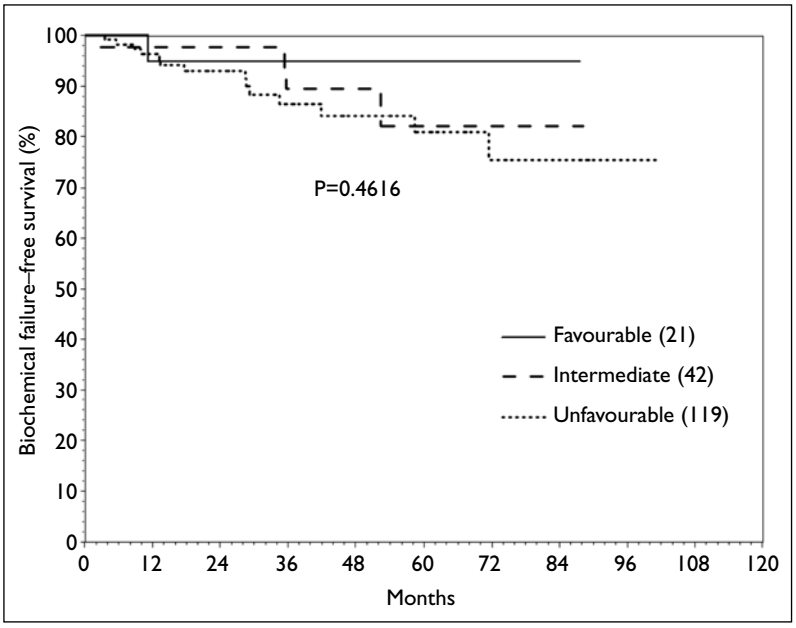

FIG. The Kaplan-Meier curve for the biochemical failure–free survival stratified by risk group

TABLE 2. Multivariate analysis on biochemical failure–free survival*†

Prognostic factor	P value	Hazard ratio	95% Confidence interval
Age (<70 vs ≥70 years)	0.2384	NS	NS
Clinical T stage (T1-2 vs T3-4)	0.0232	2.531	1.341-4.779
Gleason score (≤7 vs >7)	0.2502	NS	NS
Pre-treatment PSA (≤20 vs >20 ng/mL)	0.0342	2.169	1.046-4.498
Dose (prescription dose to prostate PTV: 76 vs <76 Gy)	0.7714	NS	NS
WPRT	0.5706	NS	NS
NHT	0.8208	NS	NS
AHT	0.0081	0.148	0.049-0.443

* T denotes tumour, PSA prostate-specific antigen, PTV planning target volume, WPRT whole-pelvic radiotherapy, NHT neoadjuvant androgen deprivation, AHT adjuvant androgen deprivation, and NS not significant

† Cox regression analysis

TABLE 3. Acute and late treatment-related complications

Complication	No. (%) of patients (n=182)		
	Grade 1	Grade 2	Grade 3
Gastro-intestinal complications			
Acute	71 (39)	31 (17)	3 (2)
Late	6 (3)	14 (8)	8 (4)
Genito-urinary complications			
Acute	93 (51)	27 (15)	0
Late	8 (4)	5 (3)	5 (3)

TABLE 4. Univariate analysis for acute gastro-intestinal (GI) and genito-urinary (GU) complications and multivariate analysis for late GI complications*

Variable	G2 or higher acute GI complications	G2 or higher acute GU complications	G2 or higher late GI complications		
	P value	P value	P value	Hazard ratio	95% Confidence interval
Dose (prescription dose to prostate PTV: 76 Gy vs <76 Gy)	0.5361	0.3580	0.6137	NS	NS
WPRT	0.0026‡	0.0457‡	0.9654	NS	NS
NHT	0.0888	0.1693	0.1988	NS	NS
T stage	0.1618	0.0550	0.9271	NS	NS
Age (<70 vs ≥70 years)	0.2941	0.6745	0.4099	NS	NS
DM	0.1688	0.8000	0.4029	NS	NS
Bowel disease†	0.0459§	0.5563	0.6577	NS	NS
G2 or higher acute GI complications	N/A	N/A	0.026	4.497	1.059-19.142

* T denotes tumour, PTV planning target volume, WPRT whole-pelvic radiotherapy, NHT neoadjuvant androgen deprivation, DM diabetes mellitus, G2 grade 2, N/A not applicable, and NS not significant
† Including a history of haemorrhoids, rectal polyps, and previous pelvic surgery
‡ Chi squared test
§ Fisher's exact test

TABLE 5. Comparison of the mean values of dosimetric parameters in patients who did or did not develop acute gastro-intestinal (GI) and genito-urinary (GU) complications*

Rectum	Grade 2 or higher acute GI complications			Bladder	Grade 2 or higher acute GU complications		
	With complication	No complication	P value		With complication	No complication	P value
D_{mean}	49.1 Gy	45.1 Gy	0.0208†	D_{mean}	52.0 Gy	46.8 Gy	0.0161†
D_{max}	75.0 Gy	75.6 Gy	0.4904	D_{max}	75.5 Gy	76.2 Gy	0.4917
V_{50}	53.9%	48.0%	0.0253†	V_{65}	31.2%	26.3%	0.1966
V_{60}	26.6%	24.2%	0.9030	V_{70}	21.5%	18.3%	0.6040
V_{65}	18.3%	17.2%	0.9433	V_{75}	8.8%	7.3%	0.4993
V_{70}	10.3%	10.4%	0.3665	-	-	-	-
V_{75}	3.1%	3.8%	0.4999	-	-	-	-

* D_{mean} denotes mean dose, and D_{max} maximum dose
† Student's *t* test

TABLE 6. Efficacy and toxicity of intensity-modulated radiation therapy for prostate cancer in published studies*

Study	No. of patients	Median follow-up (months)	Dose (Gy)	5-Year biochemical control (%)†			Complications			
				Favourable	Intermediate	Unfavourable	GI (%)		GU (%)	
							G3	G4	G3	G4
Zelefsky et al[11]	561	84	81	89	78	67	<1	0	3	0
De Meerleer et al[12]	133	36	74-76	100	94	74	1	0	3	0
Liauw et al[13]	130	53	76	97	94	87	2	0	2	0
Vora et al[14]	160	60	75.6	88	73	60	1	0	6	0
Kupelian et al[15]	770	45	70 (2.5 Gy/Fr)	94	83	72	1	<1	<1	0
Cahlon et al[16]	478	53	86.4	98	85	70	2.5	0	<1	0
Present study	182	44	72	95	82	80	4.4	0	2.7	0

* GI denotes gastro-intestinal, GU genito-urinary, PSA prostate-specific antigen, G3 grade 3, and G4 grade 4
† Zelefsky et al[11]: 8-year PSA relapse-free survival rates by Phoenix definition;
De Meerleer et al[12]: 5-year biochemical relapse-free survival rates by the American Society for Therapeutic Radiology and Oncology (ASTRO) definition;
Liauw et al[13]: 4-year biochemical control rates by Phoenix definition;
Vora et al[14]: 5-year biochemical control rates by ASTRO definition;
Kupelian et al[15]: 5-year biochemical failure–free survival by Phoenix definition;
Cahlon et al[16]: 5-year PSA relapse-free survival by Phoenix definition

(grade 3 or above according to CTCAE) were lower than 2%. The most frequent were acute GU toxicities, but most were grade 1 to 2 (51 and 15%, respectively) only. Notably, in this study, WPRT was associated with both acute GI and GU toxicities. A possible reason was that the conventional WPRT (4-field box technique) used in our cohort was inefficient in shielding the bowel or bladder. Apart from WPRT, a history of bowel disease was associated with acute GI toxicities, which was also consistent with previous reports.[26,27] This highlights the importance of a history of bowel disease and cautious planning of radiotherapy so as to minimise acute toxicities.

In the current series, the risk of grade 3 late complications was <5%. However, the proportion of patients experiencing grade 3 late GI complications (4%) was slightly higher than that in other relevant reports.[11-16] We therefore conducted a comprehensive multivariate analysis to identify clinical factors associated with late GI complications, and found that having an acute GI complication was an independent predictor of late GI complications. This finding was also consistent with previous reports.[28,29] On the other hand, in the current study, WPRT was not associated with late GI toxicities. Although WPRT could lead to a higher rate of acute GI toxicities, treating them aggressively is the most effective strategy to minimise late GI toxicities.

In the multivariate analysis, AHT was the most significant prognosticator of biochemical control. This finding is compatible with the EORTC study which showed that 3 years of androgen deprivation after external radiation could improve treatment outcomes, especially in patients with an unfavourable risk.[30] In this cohort, 65% of the patients belonged to an unfavourable group. Despite financial limitations, a high proportion (82%) of the patients in the unfavourable group received AHT. Therefore, the association of AHT and better BFFS was less likely to be a chance finding. On the other hand, neither the radiotherapy dose level (76 Gy vs 70 Gy) nor WPRT were prognostic indicators of biochemical control. This was in contrast to the findings of the RTOG 94-13[22] and other dose-escalation studies.[3-6] While the individual effects of AHT, WPRT, and dose escalation are widely acknowledged, the interaction between the three treatment modalities in contributing to the benefits is less well defined in the literature. Further prospective randomised studies are needed to elucidate the interaction of these different treatment modalities used in combination.

We have demonstrated that the V_{50} of the rectum is an important parameter in predicting the development of grade 2 or higher acute GI complications. The Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) report and others have emphasised the importance of parameters such as V_{70} and V_{75} in relation to the probability of complications, but this may pertain more specifically to the situation of the prostate IMRT alone.[31,32] With the incorporation of WPRT, however, the intermediate dose-volume parameters such as the D_{mean} and V_{50} become more relevant in predicting the chance of developing complications. Having saturated the rectum and bladder with almost full tolerance dosing, conventional WPRT becomes a hindrance to dose escalation within the prostate. To overcome this, WPRT delivered by conformal techniques such as the use of IMRT is currently being investigated in many institutions. Ashman et al[33] reported that IMRT-WPRT could significantly reduce irradiation to the small bowel and rectum dosimetrically. Several clinical reports revealed that IMRT-WPRT could significantly reduce treatment-related toxicity in prostate cancer.[34,35] The previously mentioned limitation in dose escalation after conventional WPRT may be disentangled by improvements in normal tissue sparing with IMRT-WPRT. Furthermore, IMRT-WPRT could potentially reduce the risk of geographically missing pelvic lymph nodes, which was common with conventional WPRT.[36] While the merits of WPRT over prostate-alone radiotherapy are still under debate, intensity-modulated WPRT is no doubt the optimal mode of pelvic irradiation from a dosimetric standpoint.[22,37-39]

One limitation of our study was that it was retrospective, as any attempt to measure the contributory effect of IMRT might be limited by the presence of known or unknown confounders. We therefore tried to conduct a multivariate analysis to evaluate a comprehensive list of putative confounding factors to explore such influences. Secondly, this was a single institution study in a public hospital, so the patient population might be biased towards high-risk disease. However, because of local hospital policies and low recourse to health care insurance in Hong Kong, more than 90% of cancer patients are treated in public hospitals. Thirdly, the multivariate analysis apparently yielded benefit from AHT. Three years of androgen deprivation was shown to be better than 6 months, but the role of extended AHT use beyond 3 years is still unclear.[40] As our follow-up time was relatively short, we were unable to comment on the possibility of late relapse upon withdrawal of AHT.

Conclusion

We demonstrated that IMRT for prostate cancer in Chinese patients can achieve satisfactory biochemical control, while the risk of developing treatment-related complications is within an acceptable range. More conformal treatment delivery for WPRT is recommended for safe dose escalation in the course of treating prostate cancer.

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