RESEARCH ARTICLE

Lack of Impact of Age on Acute Side Effects and Tolerance of Curative Radiation Therapy

Birsen Yücel[1]*, Yıllar Okur[2], Ebru Atasever Akkaş[3], Mehmet Fuat Eren[1]

Abstract

Aim: The aim of this study was to determine the impact of age on the occurrence, severity, and timing of acute side effects related to radiotherapy. Materials and Methods: We analysed the data of 423 patients. Results: Of the patients, 295 (70%) were under the age of 65 (group 1) and 128 (30%) were over the age of 65 (group 2). The frequencies of radiotherapy-induced side effects were 89% in group 1 and 87% in group 2 (p=0.286). The mean times to occurrence were 2.5±0.1 weeks in group 1 and 2.2±0.1 weeks in group 2 (p=0.013). Treatment was ended in 2% of patients in group 1 and 6% of those in group 2 (p=0.062). Treatment interruption was identified in 18% of patients in group 1 and 23% in group 2 (p=0.142). Changes in performance status were greater in older patients (p=0.013). There were no significant differences according to the frequency or severity of side effects, except skin and genitourinary complications, between the groups. Conclusions: Early normal tissue reactions were not higher in older versus younger patients, though there was a tendency towards an earlier appearance.

Keywords: Radiotherapy - side effects - age - cancer

Asian Pacific J Cancer Prev, **14 (2)**, 969-975

Introduction

Cancer patients have signs and symptoms that are disease- and treatment-related. In particular, many treatment-related signs and symptoms occur due to side effects of the treatment. These may lead to treatment interruption, ending of treatment, and/or have other negative impacts on treatment. The goal of radiation therapy is to provide maximum toxicity in the tumour, with the minimum toxicity to the surrounding normal tissues (Millan, 2009). Curative treatment of a tumour is always associated with a certain risk of side effects, and the dose prescribed in most malignant disease is adjusted according to the tolerance of the surrounding normal tissues. Various tumour and patient factors can affect the radiation sensitivity of normal tissues.

According to the United States National Cancer Institute, approximately one-half of all cancer patients are treated with radiotherapy at some point (National Cancer Institute, 2005). The incidence of most malignancies increases with age. The majority of elderly cancer patients receive radiotherapy. However, aging is also associated with physiological changes that can reduce the functional reserves of multiple organs, co-morbid illnesses, disability in terms of physical condition, and loss of independence; all of these may affect tolerance of radiation. In particular, co-morbidities are associated with reduced life expectancy and increased risk of treatment complications (Extermann, 2007). It is believed that there is a relationship between age and radiation toxicity, and elderly patients can exhibit reduced tolerance of a radical course of radiotherapy; moreover, some treatment complications are more common in older patients. Consequently, elderly patients are more likely to be undertreated by clinicians; e.g. in terms of use of a reduced dose, limited or inadequate margins, or palliative instead of curative treatment.

The aim of this study was to determine the impact of age on the frequency, severity, and timing of acute side effects related to radiotherapy.

Materials and Methods

The investigation was conducted in the Radiation Oncology Department of Cumhuriyet University Hospital in Sivas, Turkey. The Institutional Review Board of Cumhuriyet University approved the study design.

In total, 625 cancer patients admitted to the Radiation Oncology Department, between September 1, 2010 and December 31, 2011 were evaluated retrospectively. Of them, 423 patients treated with curative radiotherapy or chemoradiotherapy were included in this study. During the treatment period, all patients were examined routinely once per week in our clinic by the radiation oncology physician who was caring for the patients. Physical examination findings, vital signs, weights, Eastern Cooperative Oncology Group (ECOG) performance scores, and histopathological, radiological, and laboratory data were routinely recorded in patient files.

*[1]Cumhuriyet University School of Medicine, [3]Department of Radiation Oncology, Sivas Numune State Hospital, Sivas, [2]Department of Radiation Oncology, Ankara Numune Education and Research Hospital, Ankara, Turkey *For correspondence: yucelbirsen@yahoo.com*

Medical records were reviewed and data related to patient characteristics (age and gender), presence of comorbidities, ECOG performance score, cancer, stage of disease, treatment, site of radiotherapy, and dose of radiotherapy were collected and classified. Radiotherapy-related side effects, the frequency and mean time to occurrence of side effects, the frequency of and mean time to treatment interruption, ending of radiotherapy, performance status changes, and weight loss were documented for each individual.

Patient performance status was evaluated according to the ECOG performance scoring system. We evaluated weights and performance changes according to first and last week measurements in the treatment period. Cancers were classified based on system or body site, primary and haematological malignancies: specifically, the central nervous system, head and neck, thorax, breast, gastrointestinal system, genitourinary system, gynaecologic, skin, and soft tissues, as well as lymphomas. Disease stage was determined according to the 2010 UICC/AJCC TNM classification. The site of radiotherapy was classified based on the primary body site involved: the cranium, head and neck, breast, thorax, abdomen, and pelvis.

Radiotherapy was performed using linear accelerators with standard fractionation. Eclipse (ver. 8.6; Varian Medical Systems, Inc. Palo Alto, CA, USA) was used as the three-dimensional conformal radiotherapy planning software program. Radiotherapy-induced side effects were assessed according to the Acute Radiation Morbidity Scoring Criteria (the Radiotherapy Oncology Group (RTOG) criteria) (Radiation Therapy Oncology Group, 2012). This scoring system includes non-haematological side effects (skin, mucous membrane, eye, ear, salivary gland, pharynx, and oesophagus, larynx, lung, upper gastrointestinal tract, lower gastrointestinal tract, and pelvis, genitourinary, heart, and central nervous system) and haematological side effects (white blood cell, platelets, neutrophils, haemoglobin, and haematocrit). Side effects were assessed weekly, starting 1 week after the first radiotherapy session.

Statistical analysis

Patients were categorised in two groups (group 1: under 65 years and group 2: 65 years and older). Statistical analyses were performed using the SPSS software (ver. 15.0 for Windows; SPSS, Chicago, IL, USA). Descriptive statistics are reported, including percentages, and means with standard deviation. Continuous variables were compared statistically using the unpaired t-test or Mann-Whitney U test, depending on whether the data were normally distributed. Categorical data were compared statistically using chi-squared or Fisher's exact tests. A p value≤0.05 was considered to indicate statistical significance.

Results

During the study period, 423 patients were treated with curative radiotherapy (213 cases, 50%) or curative chemoradiotherapy (210 cases, 50%). Table 1 lists the

Table 1. Patients, Cancers, and Treatment Characteristics All Patients (N=423), Group 1 (N=295), and Group 2 (N=128)

			All patients N	Group 1* n %	Group 2# n %
Gender	Male		215 (51)	135 (46)	80 (63)
	Female		208 (49)	160 (54)	48 (37)
Co-morbidity			167 (39)	93 (32)	74 (58)
Diabetes mellitus			56 (13)	34 (12)	22 (17)
Hypertension			118 (28)	67 (23)	51 (40)
Chronic obstructive pulmonary disease			18 (4)	10 (3)	8 (6)
Coronary Artery Disease			34 (8)	13 (4)	21 (16)
Others			12 (3)	8 (3)	4 (3)
Eastern Cooperative Oncology Group		0	335 (80)	261 (88)	74 (58)
		1	62 (15)	25 (9)	37 (29)
		2	26 (6)	9 (3)	17 (13)
Stage	Stage I		46 (11)	30 (12)	16 (14)
	Stage II		128 (30)	85 (33)	43 (38)
	Stage III		151 (36)	114 (45)	37 (33)
	Stage IV (without distant metastases)		43 (10)	26 (10)	17 (15)
Cancer	Head and neck		65 (15)	43 (15)	22 (17)
	Central nervous system		32 (8)	27 (9)	5 (4)
	Breast		107 (25)	91 (31)	16 (13)
	Lung		29 (7)	21 (7)	8 (6)
	Gastrointestinal system		112 (26)	80 (27)	32 (25)
	Genitourinary system		35 (8)	7 (3)	28 (22)
	Gynaecologic		25 (6)	13 (4)	12 (9)
	Skin and soft tissue		7 (2)	4 (1)	3 (2)
	Lymphoma		11 (3)	9 (3)	2 (2)
Treatment	Radiotherapy		213 (50)	144 (49)	69 (54)
	Chemoradiotherapy		210 (50)	151 (51)	59 (46)
Site of Radiotherapy					
	Head and neck		73 (17)	48 (16)	25 (19)
	Cranium		34 (8)	28 (10)	6 (5)
	Breast		106 (25)	**91 (31)**	**15 (12)**
	Thorax		38 (10)	29 (10)	9 (7)
	Abdomen		62 (15)	45 (15)	17 (13)
	Pelvis		110 (26)	**54 (18)**	**56 (44)**
Dose of Radiotherapy		≤ 60 Gy	213 (50)	144 (49)	69 (54)
		> 60 Gy	210 (50)	151 (51)	59 (46)

*Group I: age < 65 years; #Group II: age ≥ 65 years

Table 2. Radiotherapy-induced Side Effects, Treatment Interruption, Cause of Treatment Interruption, Treatment Type Interrupted, Type of Side Effects, Weight Loss and Performance Status Changes in All Patients (N=423), Group 1 (N=295), and Group 2 (N=128) During the Treatment Period

	All patients n %	Group 1 n %	2 n %	p
Radiotherapy-induced side effects				
Occurrence	374 (88)	263 (89)	111 (87)	0.286
Mean time (week)	2.4±0.1	2.5±0.1	2.2±0.1	**0.013**
Treatment interruption				
Occurrence	81 (20)	52 (18)	29 (23)	0.142
Mean time to interruption (day)	5±0.4	6±0.6	4±0.7	0.097
Ending of radiotherapy	13 (3)	6 (2)	7 (6)	0.062
Causes of treatment interruption				
Haematological side effects	36 (9)	25 (9)	11 (9)	0.551
Non-haematological side effects	45 (11)	27 (9)	18 (14)	0.093
Treatment type interrupted				
Radiotherapy	30 (14)	16 (5)	14 (11)	**0.037**
Chemoradiotherapy	51 (24)	36 (12)	15 (12)	0.515
Weight loss (≥5 kg)	52 (12)	38 (13)	14 (11)	0.351
Performance status changes				
None	352 (83)	254 (86)	98 (77)	**0.013**
Recovered	17 (4)	6 (2)	11 (9)	**0.003**
Deteriorated	54 (13)	35 (12)	19 (15)	0.244

Table 3. Frequencies and Mean Occurrence Times of Non-haematological and Haematological Side Effects in All Patients (n=423), Group 1 (n=295), and Group 2 (n=128)

		Frequency of side effects				Mean time to occurrence of side effects (weeks)			
		All patients n (%)	Group 1 n (%)	Group 2 n (%)	p	All patients	Group 1	Group 2	p
Non-haematological side effects									
Skin	**None**	**257 (61)**	**166 (56)**	**91 (71)**					
	Present	**166 (39)**	**129 (44)**	**37 (29)**	**0.011**	3.8±0.1	3.8±0.1	3.8±0.2	0.979
	Grades 1-2	156 (37)	120 (41)	36 (28)					
	Grades 3-4	10 (2)	9 (3)	1 (1)					
Mucous membrane	**None**	**362 (86)**	**250 (84)**	**112 (87)**					
	Present	**61 (14)**	**45 (15)**	**16 (13)**	0.644	3.1±0.1	3.1±0.2	3.1±0.4	0.766
	Grades 1-2	60 (14)	44 (15)	16 (13)					
	Grades 3-4	1 (0.2)	1 (0.3)	-					
Eye	**None**	**417 (99)**	**291 (99)**	**126 (98)**					
	Present	**6 (1)**	**4 (1)**	**2 (2)**	0.587	3.0±0.8	3.7±1.1	1.5±0.5	0.24
	Grades 1-2	6 (1)	4 (1)	2 (2)					
Ear	**None**	**415 (98)**	**290 (98)**	**125 (98)**					
	Present	**8 (2)**	**5 (2)**	**3 (2)**	0.455	3.5±0.6	3.6±0.8	3.3±1.3	0.749
	Grades 1-2	8 (2)	5 (2)	3 (2)					
Salivary gland	**None**	**379 (90)**	**262 (89)**	**117 (91)**					
	Present	**44 (10)**	**33 (11)**	**11 (9)**	0.269	3.0±0.2	3.1±0.3	3.1±0.5	0.955
	Grades 1-2	44 (10)	33 (11)	11 (9)					
Pharynx & Oesophagus									
	None	**323 (76)**	**219 (74)**	**104 (81)**					
	Present	**100 (24)**	**76 (26)**	**24 (19)**	0.258	2.8±0.1	2.9±0.1	3.0±0.3	0.93
	Grades 1-2	99 (24)	75 (25)	24 (19)					
	Grades 3-4	1 (0.2)	1 (1)	-					
Larynx	**None**	**384 (91)**	**266 (90)**	**118 (92)**					
	Present	**39 (9)**	**29 (10)**	**10 (8)**	0.769	3.7±0.2	3.8±0.3	3.6±0.5	0.699
	Grades 1-2	36 (8)	27 (9)	9 (7)					
	Grades 3-4	3 (1)	2 (1)	1 (1)					
Lung	**None**	**395 (93)**	**276 (93)**	**119 (93)**					
	Present	**28 (7)**	**19 (6)**	**9 (7)**	0.378	3.1±0.3	3.1±0.3	3.2±0.5	0.859
	Grades 1-2	25 (6)	18 (6)	7 (5)					
	Grades 3-4	3 (1)	1 (0.3)	2 (2)					
Upper Gastrointestinal system									
	None	**265 (63)**	**181 (61)**	**84 (66)**					
	Present	**158 (37)**	**114 (39)**	**44 (34)**	0.235	2.5±0.1	2.5±0.1	2.5±0.2	0.827
	Grades 1-2	158 (37)	114 (39)	44 (34)					
Lower Gastrointestinal system including pelvis									
	None	**326 (77)**	**234 (79)**	**92 (72)**					
	Present	**97 (23)**	**61 (21)**	**36 (28)**	0.127	3.0±0.1	2.9±0.2	3.3±0.3	0.343
	Grades 1-2	95 (22)	59 (20)	36 (28)					
	Grades 3-4	2 (1)	2 (1)	-					
Genitourinary	**None**	**368 (87)**	**273 (92)**	**95 (75)**					
	Present	**54 (13)**	**22 (8)**	**32 (25)**	**<0.001**	2.6±0.2	2.9±0.3	2.5±0.3	0.308
	Grades 1-2	54 (13)	22 (8)	32 (25)					
Central nervous system	**None**	**402 (95)**	**277 (94)**	**125 (98)**					
	Present	**21 (5)**	**18 (6)**	**3 (2)**	0.076	2.9±0.3	3.2±0.4	2.7±0.3	0.079
	Grades 1-2	21 (5)	18 (6)	3 (2)					
Haematological side effects									
White blood cells	**None**	**337 (80)**	**238 (81)**	**99 (77)**					
	Present	**86 (20)**	**57 (19)**	**29 (23)**	0.56	3.0±0.1	3.2±0.2	2.8±0.3	0.11
	Grades 1-2	77 (18)	52 (17)	25 (20)					
	Grades 3-4	9 (2)	5 (2)	4 (3)					
Platelets	**None**	**380 (90)**	**266 (90)**	**114 (89)**					
	Present	**43 (10)**	**29 (10)**	**14 (11)**	0.143	3.3±0.2	3.4±0.2	3.1±0.3	0.697
	Grades 1-2	39 (9)	28 (9)	11 (9)					
	Grades 3-4	4 (1)	1 (1)	3 (2)					
Neutrophils	**None**	**378 (89)**	**267 (90)**	**111 (87)**					
	Present	**45 (11)**	**28 (10)**	**17 (13)**	0.453	3.2±0.2	3.6±0.3	2.8±0.3	0.087
	Grades 1-2	36 (9)	23 (8)	13 (10)					
	Grades 3-4	9 (2)	5 (2)	4 (3)					
Haemoglobin	**None**	**329 (78)**	**235 (80)**	**94 (73)**					
	Present	**94 (22)**	**60 (20)**	**34 (27)**	0.139	2.6±0.2	2.8±0.2	2.3±0.2	0.096
	Grades 1-2	93 (22)	60 (20)	33 (26)					
	Grades 3-4	1 (0,2)	-	1 (1)					
Haematocrit	**None**	**380 (90)**	**268 (91)**	**112 (87)**					
	Present	**43 (10)**	**27 (9)**	**16 (13)**	0.191	2.7±0.2	3.2±0.3	2.1±0.3	**0.006**
	Grades 1-2	43 (10)	27 (9)	16 (13)					

Table 4. Comparison of Groups 1 and 2 According to Relationships among Radiotherapy Site, Type of Treatment (Radiotherapy vs. Chemoradiotherapy), Occurrence of Side Effects and Mean Time to their Occurrence

Site of radiotherapy and treatment	Frequency of side effects				Mean time to occurrence of side effects (weeks)			
	All patients n (%)	Group 1 n (%)	Group 2 n (%)	p	All patients	Group 1	Group 2	p
Head and neck	67 (93)	45 (94)	22 (92)	0.544	2.3±0.1	2.4±0.2	2.0±0.2	0.181
Cranium	28 (82)	24 (86)	4 (67)	0.281	2.8±0.3	2.9±0.3	2.2±0.6	0.547
Breast	91 (85)	78 (86)	13 (81)	0.442	2.9±0.1	3.0±0.1	2.7±0.3	0.697
Thorax	37 (97)	28 (97)	9 (100)	0.763	2.3±0.2	2.2±0.2	2.7±0.4	0.200
Abdomen	58 (94)	42 (93)	16 (94)	0.7	1.9±0.1	2.0±0.2	1.6±0.1	0.235
Pelvis	93 (85)	46 (85)	47 (84)	0.533	2.1±0.1	2.1±0.2	2.1±0.1	0.747
Radiotherapy	183 (86)	124 (86)	59 (85)	0.529	2.6±0.1	2.8±0.1	2.3±0.2	**0.003**
Chemoradiotherapy	191 (92)	139 (92)	52 (88)	0.261	2.2±0.1	2.3±0.1	2.0±0.1	0.515

characteristics and other case details of the 423 patients. The patients were 215 males (51%) and 208 females (49%), and their ages ranged from 16-86 (median, 58) years. Comorbidities were present in 167 (39%) of the patients. The ECOG performance scores were initially worse in the older patients.

Side effects, treatment interruption, weight loss, and performance status changes in both the two groups and all 423 patients are presented in Table 2. Although there was no significant difference between the groups according to the frequency of side effects, group 2 had a shorter mean time to occurrence of side effects than did group 1 (p=0.013); i.e. treatment-related side effects occurred earlier in older patients than younger. Additionally, there was no significant difference between the groups with respect to the presence of treatment interruption, mean time to treatment interruption, or weight loss. In total, 13 patients ended their treatment: eight patients refused treatment, two had disease progression, and three had haematological side effects. There was no significant difference between groups 1 and 2 with respect to the ending of radiotherapy (p=0.062). The impact of treatment with respect to performance status recovery was better in the older patients than the younger patients (p=0.003), because younger patients' performance status did not reveal significant changes related to treatment (p=0.013).

Table 3 shows the non-haematological side effects. The most common sites were the skin (166 patients, 39%), upper gastrointestinal system (158, 37%), pharynx and oesophagus (100, 24%), and lower gastrointestinal system (97, 23%) in all patients. Moreover, no severe cardiac event was recorded in any patient. The frequency of skin side effects was higher in group 1 (p=0.011), while that of genitourinary system side effects was higher in group 2 (p<0.001). There was no cardiac toxicity from the radiotherapy.

Haematological side effects are presented in Table 4. The most common haematological side effects in all groups were decreased white blood cell counts and haemoglobin values. The mean time of occurrence of decreasing haematocrit values was earlier in older patients (p=0.006).

In all patients who underwent chemoradiotherapy, the mean times to the occurrence of side effects were earlier (p=0.001). There was no significant difference between radiotherapy and chemoradiotherapy according to the occurrence of side effects in groups 1 or 2 (p=0.433 and p=0.071, respectively). Furthermore, the frequency of side effects was higher at doses of ≥60 Gy than at doses <60 Gy in all patients (p=0.019). Although there was no significant difference between a dose of ≥60 Gy and a dose of <60 Gy with regard to the frequency of side effects in group 1 (p=0.154), group 2 showed a higher frequency of side effects at doses ≥60 Gy (p=0.019). There was no significant difference between ECOG performance scores (ECOG 0, and ECOG 1-2 and over) and the frequencies of side effects in groups 1 and 2 (p=0.459 and 0.560, respectively). There was a relationship between the frequency of side effects and co morbidities in group 1 (p=0.040), but not group 2 (p=0.400). Also, there was no relationship between the mean time to occurrence of side effects and co-morbidities in groups 1 or 2 (p=0.743 and p=0.526, respectively).

Table 4 shows a comparison of groups 1 and 2 according to relationships among radiotherapy site, type of treatment (radiotherapy vs. chemoradiotherapy), and the occurrence of side effects and the mean time to the occurrence of side effects.

Discussion

The United States Census Bureau reported that the number of adults aged 65 years or more is expected to be 88.5 million in 2050, more than double the 40.2 million in 2010 (Vincent et al., 2010). Because cancer incidence increases with age, cancer may become a more common problem in an aging population.

The aging process is associated with various physiological effects, such as vascular, gastrointestinal, bone, and pulmonary changes, which may affect the functional reserves of elderly patients. Vascular comorbidities may decrease the tolerance to radiation of the surrounding tissues in an elderly patient (Grenman et al., 2010; Kunkler, 2012). In our study, the most common comorbid disease in both groups was hypertension. Furthermore, hypertension and coronary artery disease are encountered more commonly in older patients. The presence of comorbidities did not significantly affect the frequency of side effects or the mean occurrence time of side effects in our subjects. Interestingly, there was a relationship between comorbid disease and the occurrence of side effects in the younger patients.

Physiological reserve usually decreases with age, so healing may be slower in an older adult population (Landuyt et al., 1991; Rudat et al., 1997; Engeland et al., 2011). Animal and cell models have been used to investigate the relationship between radiation-induced side effects and age (Landuyt et al., 1991; Rudat et al., 1997; Van den Aardwey et al., 2003). These studies showed that early normal tissue reactions in experimental animals did not cause an increase in radiosensitivity with aging. In our study, radiotherapy-induced acute side effects were recorded in 87% of the younger and 89% of the older patient group. Consistent with previous studies, our univariate analyses revealed that age did not affect the frequency of side effects; however, the majority of side effects occurred significantly earlier in older patients.

Zachariah et al. (1997) investigated a total of 191 older patients undergoing radiotherapy for head and neck, breast, thoracic, or pelvic malignancies, and found that 94% completed treatment as planned, without severe acute complications (Zachariah et al., 1997). Margalit et al. reported the results of 36 older patients with rectum cancer undergoing preoperative chemoradiotherapy, 92% of patients completed their treatment (Margalit et al., 2011). Similarly, in our study, 94% of the older patient group completed their treatment as planned; there was no significant difference between the older and younger patient groups. Allal et al. reported in a retrospective study of patients with head and neck cancer, treated with accelerated fractionation, that treatment interruptions were more common in older patients (Allal et al., 2000). In contrast, Huang et al. investigated 1487 patients receiving definitive head and neck irradiation and reported no significant difference in treatment interruption and completion. In addition, no differences were found between the elderly and younger patients undergoing concurrent chemoradiotherapy or hyperfractionated accelerated radiotherapy (n=760) in treatment interruption and completion (Huang et al., 2011). In our results, age also showed no relationship with treatment interruption and completion, consistent with the report of Huang and colleagues. We furthermore found no significant difference in haematological or non-haematological side effects according to age. However, patients who underwent radiotherapy alone experienced a higher rate of treatment interruption and earlier occurrence of side effects.

Pignon et al. investigated the distribution of performance status changes in patients with lung and oesophageal cancer in EORTC trials (Pignon et al., 1998). In this study, changes in performance status during radiotherapy were distributed with no difference according to age. In contrast, Pignon et al. evaluated 840 patients with changes in performance status who had pelvic malignancies (Pignon et al., 1997). In that study, 399 patients showed deterioration, 63 showed improvements, and 419 showed no change. Upon analysis of the deterioration in performance status according to age, they found a significant trend towards more toxicity in the young. In contrast, there was no significant difference between the ages of patients who improved their performance status. In our study, performance status changes both deterioration and recovery were detected more frequently in older patients. These results suggest that older patients have a more vulnerable health status. Hill et al. reported that there were no significant differences in weight changes according to age in gastrointesinal cancer patients (Hill et al., 2011). Also, there was no significant association between age and body weight alterations in our study.

Skin reactions appeared at about the second to third week of radiation therapy and reached a peak at the end or within the first week after the completion of treatment (Hymes et al., 2006; McQuestion, 2006). Hopewell et al. reported that the severity of skin reactions was not associated with age in pigs exposed to a range of radiation doses (Hopewell et al., 1982). Similar results have also been reported in mice (Masuda et al., 1986). Consistent with these previous studies, in the study of Tiefenbacher et al., age was not predictive of early skin reactions in breast cancer patients (Tiefenbacher et al., 2012). Skin toxicity was the most common side effect in our patients, followed by the upper gastrointestinal system, pharynx and oesophagus, and lower gastrointestinal system. Skin complications were also the most common side effect in breast irradiation. A significant tendency towards increased toxicity was seen in younger patients with respect to skin complications, although there was no significant difference in the mean time to occurrence of skin complication between the groups.

The results of 1307 patients with head and neck cancer showed no age-related difference in acute objective mucosal reactions or weight loss (Pignon et al., 1996). Schofield et al. (2003) investigated toxicity in 98 patients with head and neck cancer aged 80 years or older undergoing definitive radiotherapy in a clinical oncology department. Toxicity rates were similar to those of younger patients. In this study, only three patients (3%) developed severe late sequelae (Schofield et al., 2003). Merlano et al. (2012) investigated a total of 317 patients with head and cancer patients. They reported that treatment related side effects were presented similar younger and older patients. However, infections and pneumonias were significantly more represented in elderly patients (Merlano et al., 2012). Our results are consistent with these previous studies.

Pignon and co-workers detected oesophagitis (797 cases, 30%) and dyspnoea (224 cases, 16%) as side effects in patients with chest irradiation (Pignon et al., 1998). They reported no significant difference in the distribution of oesophagitis or dyspnoea according to age. Sgnoi et al. (2007) reported the results of receiving concurrent chemoradiotherapy 203 non-small cell lung carcinoma patients. They found that chemoradiotherapy was associated with higher rates of grade3-4 toxicities (esophagitis, hematologic toxicities and dehydration) in elderly patients (Sgroi et al., 2007). In our study, we found no significant difference between the groups with respect to either the frequency of oesophagitis or dyspnoea, or mean time to occurrence of oesophagitis or dyspnoea.

Liu et al. found that gastrointestinal and genitourinary side effects developed earlier in older patients with prostate cancer, although the overall frequency and severity of symptoms were similar to those in younger patients (Liu et al., 1997). Jani et al. (2005) investigated a total of 527 patients with prostate cancer and found that

patient age did not independently influence gastrointestinal or genitourinary toxicity after radiotherapy for non-metastatic prostate cancer. They suggested that patient age should not be used as an independent factor in treatment decision-making or in patient counselling with regard to gastrointestinal or genitourinary toxicity outcomes after radiotherapy (Jani et al., 2005). Jereczek-Fossa et al. (2010) noted that age ≤65 years correlated significantly with greater acute rectal toxicity (Jereczek-Fossa et al., 2010). Vranova et al. analysed the results of 197 patients with prostate cancer and found an association with increasing age and increasing gastrointestinal or genitourinary acute side effects (Vranova et al., 2011). In our study, a total of 54 patients with cancer in the pelvic region received radiotherapy. Although the frequency and mean time to the occurrence of acute lower gastrointestinal side effects were equal, the frequency of acute genitourinary side effects was higher in older patients. This difference was probably due to the more frequent administration of pelvic region irradiation to older than to younger patients. However, the mean time to occurrence of genitourinary side effects was similar to that in younger patients.

Some studies have suggested that chemoradiotherapy increases the frequency of haematological complications (Schild et al., 2003; Kodaira et al., 2005; Sgroi et al., 2007; Koussis et al., 2008). The most common haematological complications in all patients were altered white blood cell counts and haemoglobin levels, but there was no significant difference between the groups. The mean time to occurrence of haematocrit complications was the only significant difference between older and younger patients; elderly patients suffered earlier from haematocrit complications than did younger patients.

In conclusions, the frequency of early normal tissue reactions was not higher in older than in younger patients, although there was a tendency towards earlier occurrence. Serious acute complications due to radiation therapy occurred in a small group of patients. However, elderly patients exhibited a vulnerable health status, with more frequent performance status alterations and earlier occurrence of side effects. Radiation therapy may be administered safely and effectively to older adults when the treatment is individualised, but precautions should be taken to minimise the occurrence of complications.

References

Allal AS, Maire D, Becker M, Dulguerov P, (2000). Feasibility and early results of accelerated radiotherapy for head and neck carcinoma in the elderly. *Cancer*, **88**, 648-52.

England CG, Gajendrareddy PK, (2011). Wound Healing in the Elderly. Katlic MR (Ed.) Cardiothoracic Surgery in the Elderly, Springer New York, pp: 259-70.

Extermann M (2007). Interactions of cancer and co-morbidity. *Cancer Control*, **14**, 13-22.

Grenman R, Chevalier D, Gregoice V, Myers E, Rogers S, (2010). Treatment of head and neck cancer in the elderly. European Consensus (panel 6) of the EUFOS Congress in Vienna 2007. *Eur Arch Otorhinolaryngol*, **267**, 1619-21.

Hill A, Kiss N, Hodgson B, Crowe TC, Walsh AD, (2011). Associations between nutritional status, weight loss, radiotherapy treatment toxicity and treatment outcome in gastrointestinal cancer patients. *Clinical Nutrition*, **30**, 92-8.

Hopewell JW, Young CM, (1982). The effect of field size on the reaction of pig skin to single doses of X rays. *Br J Radiol*, **55**, 356-61.

Huang SH, O'Sullivan B, Waldron J, et al (2011). Patterns of care in elderly head-and-neck cancer Radiation Oncology patients: A single-center cohort study. *Int J Radiat Oncol Biol Phys*, **79**, 46-51.

Hymes S, Strom E, Fife C (2006). Radiation dermatitis: clinical presentation, pathophysiology, and treatment 2006. *J Am Acad Dermatol*, **54**, 28-46.

Jani AB, Parikh SD, Vijayakumar S, Gratzle J, (2005). Analysis of influence of age on acute and chronic radiotherapy toxocity in treatment of prostate cancer. *Urology*, **65**, 1157-62.

Jereczek-Fossa BA, Zerini D, Fodor C, et al (2010). Correlation Between Acute and Late Toxicity in 973 Prostate Cancer Patients Treated With Three-Dimensional Conformal External Beam Radiotherapy. *Int J Radiation Oncol Biology Physics*, **78**, 26-34.

Kodaira T, Fuwa N, Furutani K, Tachibana H, Yamazaki T (2005). Phase I trial of weekly docetaxel and concurrent radiotherapy for head and neck cancer in elderly patients or patients with complications. *Jpn J Clin Oncol*, **35**, 173-6.

Koussis H, Scola A, Bergamo F, et al (2008). Neoadjuvant carboplatin and vinorelbine followed by chemoradiotherapy in locally advanced head and neck or oesophageal squamous cell carcinoma: A phase II study in elderly patients or patients with poor performance status. *Anticancer Res*, **28**, 1383-8.

Kunkler I (2012). Radiotherapy in Older Adults with Cancer. Bellizzi KM, Gosney MA (Ed.). Cancer and Aging Handbook: Research and Practice. New Jersey, pp:221-37.

Liu L, Glicksman AS, Coachman N, Kuten A (1997). Low acute gastrointestinal and genitourinary toxicities in whole pelvis irradiation of prostate cancer. *Int J Radiat Oncol Biol Phys*, **38**, 65-71.

Landuyt W, van der Schueren E (1991). Effect of age on the radiation-induced repopulation in mouse lip mucosa. Strahlenther. *Onkol*, **167**, 41-5.

Masuda K, Matsuura K, Withers HR, Hunter N, (1986). Age depen-dency of response of the mouse skin to single and multifractionated gamma irradiation. Radiother. *Oncol*, **7**, 147-53.

Margalit DN, Mamon HJ, Ancukiewicz M, et al (2011). Tolerability of combined modality therapy for rectal cancer in elderly patients aged 75 years and older. *Int J Radiat Oncol Biol Phys*, **81**, 735-41.

McQuestion M (2006). Evidence based skin care management in radiation therapy. *Semin Oncol Nurs*, **22**, 163-73.

Merlano MC, Monteverde M, Colantonio I, et al (2012). Impact of age on acute toxicity induced by bio- or chemo-radiotherapy in patients with head and neck cancer. *Oral Oncology*, **48**, 1051-57.

Millan JG, (2009). Radiation therapy in the elderly: More side effects and complications? *Critical Reviews in Oncology/ Hematology*, **71**, 70-8.

National Cancer Institute, 2005. http://cis.nci.nih.gov/fact/7_1.htm. Accessed May 26, 2005.

Pignon T, Gregor A, Schaake Koning C, et al (1998). Age has no impact on acute and late toxicity of curative thoracic radiotherapy. *Radiother Oncol*, **46**, 239-48.

Pignon T, Horiot JC, Bolla M, et al (1997). Age is not a limiting factor for radical radiotherapy in pelvic malignancies. Radiother. *Oncol*, **42**, 107-20.

Pignon T, Horiot JC, Van den Bogaert W, Van Glabbeke M, Scalliet P (1996). No age limit for radical radiotherapy in

head and neck tumours. *Eur J Cancer*, **32**, 2075-81.
Radiation Therapy Oncology Group, 2012. http://www.rtog.org/ResearchAssociates/AdverseEventReporting/AcuteRadiationMorbidityScoringCriteria.aspx
Rudat V, Dietz A, Conradt C,Weber KJ, Flenje M (1997). In vitro radiosensitivity of primary human fibroblasts. Lack of correlation with acute radiation toxicity in patients with head and neck cancer. *Radiother Oncol*, **43**, 181-8.
Schild SE, Stella PJ, Geyer SM, et al (2003). The outcome of combined-modality therapy for stage III non-small-cell lung cancer in the elderly. *J Clin Oncol*, **21**, 3201-6.
Schofield CP, Sykes AJ, Slevin NJ, Rashid NZ (2003). Radiotherapy for head and neck cancer in elderly patients. *Radiother Oncol*, **69**, 37-42.
Sgroi MM, Neubauer M, Ansari R, et al (2007). An analysis of eldelry patients (pts) treated on a phase III trial of cisplatin (P) plus etoposide (E) with concurrent radiotherapy (CRT) followed by docetaxel (D) vs observation (O) in patiens with stage III non-small cell lung cancer (NSCLC). *Proc Am Soc Clin Oncol*, **25**, 9037.
Tiefenbacher UK, Sfintizky A, Welzel G, et al (2012). Factors of influence on acute skin toxicity of breast cancer patients treated with standard external beam radiotherapy (EBRT) after breast conserving surgery (BCS). *Radiation Oncol*, **7**, 217.
Van den Aardwey GJM, Olofsen-van Archt MJJ, van Hooije CMC, Levendag PC (2003). Radiation-induced rectal complications are not influenced by age: a dose fractionation study in the rat. *Radiation Res*, **159**, 642-50.
Vranova J, Vinakurau S, Richter J, et al (2011). The evolution of rectal and urinary toxicity and immune response in prostate cancer patients treated with two three-dimensional conformal radiotherapy techniques. *Radiation Oncology*, **6**, 2-13.
Vincent GK, Velkoff VA, (2010). The next four decades, the older population in the United States 2010-to 2050. Current Population Reports. Washington, DC, US Census Bureau, pp 25-1138.
Zachariah B, Balducci L, Venkattaramanabalaji GV, et al., (1997). Radiotherapy for cancer patients aged 80 and older: a study of effectiveness and side effects. *Int J Radiat Oncol Biol Phys*, **39**, 1125-9.