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ORIGINAL ARTICLE

Acute Toxicities and Advers Events of Chemoradiotherapy in Young and Older Adults

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OBJECTIVE

To evaluate, according to age, the acute toxicity and adverse events, such as interruption or cessation of chemoradiotherapy (CRT) and weight loss, in cancer patients.

METHODS

A total of 813 patients, 67% aged <65 years and 33% aged ≥65 years, were analyzed retrospectively. Toxicities were graded according to the acute radiation morbidity measurement criteria of the Radiation Therapy Oncology Group.

RESULTS

For all patients, 5% of the younger and 12% of the elderly patients (p<0.001) ended CRT, 1% of the younger and 4% of the elderly patients died during treatment (p=0.007). There were differences between the groups treated for brain cancer in terms of performance status (p=0.010), cessation (p=0.001), interruption (p=0.026), and death during treatment (p=0.043). For head and neck cancer, the results showed differences in comorbidity (p<0.001), performance status (p=0.017), and death during CRT (p=0.021). In the thoracic area, differences were found in comorbidity (p=0.015), CRT interruption (p=0.014), grade 1–2 skin toxicity (p=0.025), pharynx/esophagus (p=0.002), upper gastrointestinal tract (p=0.036), and hematocrit (p=0.032). For the abdominal area, differences were observed in comorbidity (p<0.001) and grade 1–2 platelet toxicity (p=0.029). For the pelvis, differences were seen in comorbidity (p<0.001), performance status (p=0.045), and CRT interruption (p=0.032).

CONCLUSION

Cessation, interruption, and death during CRT were observed more frequently in elderly patients.

Keywords: Acute; aged; chemotherapy; radiotherapy; side effect.

INTRODUCTION

The incidence of cancer increases with age, with 50% of newly diagnosed cancer patients being over 65 years of age.[1] According to 2016 data from the United States, it is the leading cause of death between the ages of 60 and 80 and the second most common cause of death above the age of 80.[2] Geriatric (>65 years old) patients are frequently encountered in oncology clinics.

In cancer patients, early side effects due to CRT usually occur during and immediately after treatment. CRT aims to destroy cancer cells using both ionizing radiation and systemic chemotherapy. Essentially, it aims to potentiate the effectiveness of two differ-

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ent treatments. Radiotherapy provides local control, while chemotherapy increases the effectiveness of radiotherapy and prevents the escape of tumor cells into the system. With the cumulative effect of both therapies on the tumor, CRT predisposes normal tissues to an increase in toxicity. The balance between efficacy and toxicity of the treatment is crucial in determining therapeutic success. At this stage, patient selection becomes important. In a treatment that has a profile of increased side effects, selecting a patient group that is generally considered vulnerable is highly undesirable. Elderly patients constitute this vulnerable group due to physiologically aged and generally inadequate organ functions, as well as comorbidities.

In cancer patients, factors such as the patient's age, the presence of other chronic diseases, and the stage of the disease affect the choice of treatment. It has been observed that, in cancer treatment for elderly patients, third and fourth-grade hematological toxicities increase, and some patients require treatment modification due to treatment toxicities.[3,4] Two cohort prospective studies have shown that a geriatric assessment can predict chemotherapy-related toxicity.[5,6] The International Association of Geriatric Oncology[7] recommends conducting a geriatric assessment prior to the treatment of elderly cancer patients. However, the intensity and scope of comprehensive geriatric assessments in oncology practice are still limited due to time constraints. Elderly cancer patients are usually underrepresented in clinical studies, and little data is available on curative radiotherapy in these patients regarding CRT toxicity and compliance.[8,9]

This study aimed to evaluate acute toxicity and adverse events, such as treatment interruption, abandonment, and weight loss, in cancer patients treated with CRT, according to age.

MATERIALS AND METHODS

This study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the ethical committee of Sivas Cumhuriyet University.

Data on 813 cancer patients, who were treated and followed up at the oncology center of Sivas Cumhuriyet University Medical Faculty Hospital between January 2010 and December 2018, were obtained from RTOG's acute toxicities criteria evaluation tables, routinely performed at the center, and analyzed retrospectively. The study included older, nonmetastatic, curative patients who were eligible for CRT. Patients who had received palliative radiotherapy or chemotherapy were excluded from the study. The patients were divided into two groups: over and under the age of 65. The results were analyzed separately for five regions—brain, head and neck, thorax, abdomen, and pelvis.

The performance status of the patients was recorded according to the performance scale of the Eastern Cooperative Oncology Group. Weight loss was defined as the loss of more than 5% of the patient's weight.

Concurrent Chemoradiotherapy Protocols

- **Brain site:** Temozolomide (75 mg/m² daily during radiotherapy) with a total radiation dose of 60 Gy from 2 Gy per day.
- **Head and neck site:** Cisplatin (40 mg/m² weekly) or cisplatin + 5-FU (cisplatin 75 mg/m² D1 and 5-FU 1000 mg/m² D1-5) with a daily radiation dose of 1.8–2.12 Gy and a total radiation dose of 66–72 Gy was applied every 28 days.
- **Thoracic site:** Cisplatin (40 mg/m² weekly) or carboplatin + paclitaxel (carboplatin 2 AUC/m²/week and paclitaxel 50 mg/m²/week) with a total radiation dose of 66.6 Gy from 1.8–2 Gy daily for non-small cell cancers/weekly, or cisplatin + etoposide (cisplatin 50 mg/m² D1, 8 and etoposide 50 mg/m² D1–5 every 28 days).
- **Abdominal site:** Concurrent FUFA (5-FU 400 mg/m² D1–5 and folinic acid 200 mg/m² D1–5 every 28 days) with a total radiation dose of 50.4 Gy from 1.8 Gy daily for stomach, pancreas, and gallbladder cancers.
- **Pelvis site:** Weekly cisplatin (40 mg/m²) was used in cervical cancers with a daily radiation dose of 1.8–2 Gy, totaling 50.4 Gy.

Evaluation of Treatment Side Effects

Acute toxicities were observed within 90 days from the start of CRT. Treatment toxicities were evaluated weekly during treatment and after one and three months following the end of treatment, according to the RTOG acute radiation morbidity criteria. Both hematological and non-hematological toxicities were graded between 0 and 5.[10] Hematological aspects include assessments of white blood cells, neutrophils, platelets, hemoglobin, and hematocrit. Non-hematological areas include the skin, mucous membrane, eye, ear, salivary gland, pharynx/esophagus, larynx, lung, upper gastrointestinal system, lower gastrointestinal system, genitourinary system, and central nervous system. Patients were actively questioned for each of the ten symptoms during each interview. To minimize observer bias, assessment forms detailed the specifics of each grade of

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toxicity, allowing the assessor to directly compare and select the most appropriate grade for the patient. The adverse events examined included weight loss during CRT, deterioration of performance status, cessation of CRT, death during CRT, and interruption of CRT.

Statistical Evaluation

In this study, descriptive tests using the Statistical Package for Social Sciences for Windows (v23.0) were employed, along with the chi-square test, Student's t-test (for data with a near-normal distribution), and the Mann-Whitney U test (also for those with a near-normal distribution) to compare group means. The mean, standard deviation, mean deviation, and median of the data were calculated using descriptive statistical methods. The results were assessed at a 5% level of significance ($p \leq 0.05$).

RESULTS

Of the 813 patients, 542 (67%) were aged <65 years and 271 (33%) were ≥65 years. Weight loss during CRT was observed in 145 (27%) patients aged <65 years and in 63 (23%) patients aged ≥65 years (p=0.153). Deterioration of performance status was noted in 134 (25%) patients aged <65 years and in 63 (23%) patients aged ≥65 years (p=0.145). Non-completion of planned CRT was observed in 27 (5%) patients aged <65 years and in 33 (12%) patients aged ≥65 years (p<0.001). CRT was interrupted in 83 (15%) patients aged <65 years and in 35 (13%) patients aged ≥65 years (p=0.204). The median CRT interruption time was 7 days for patients aged <65 years (range, 1–25) and 7 days for patients aged ≥65 years (range, 1–28) (p=0.543).

A total of 19 (2%) patients died during CRT. Seven (1%) of these patients were aged <65 years, and 12 (4%) were aged ≥65 years (p=0.007). Causes of death included pulmonary embolism (n=4), heart attack (n=3), gastrointestinal bleeding (n=2), cerebral hemorrhage (n=2), and treatment toxicity (n=8). For all patients, three (1%) of the eight who died due to treatment toxicity were younger patients, and five (2%) were elderly (p=0.088).

Data from 82 (10%) brain cancer patients were examined; 62 (76%) were aged <65 years, and 20 (34%) were aged ≥65 years. A comparison is presented in Table 1. The table includes terms for the performance status of the patients (p=0.010), CRT interruption (p=0.001), cessation (p=0.043), and death during treatment (p=0.026). During CRT, one (2%) younger patient had treatment toxicity (febrile neutropenia), while among the elderly patients, one (5%) had a pulmonary embolism, one (5%) had gastrointestinal bleeding, and one (5%) had treatment toxicity (severe thrombocytopenia).

Data from 113 (14%) head and neck cancer patients were analyzed. Of these, 81 (72%) were aged <65 years, and 32 (28%) were aged ≥65. The clinical features of patients with head and neck tumors, the characteristics of treatments, treatment side effects, and the comparison of adverse events by age are given in Table 2. According to Table 2, comorbidity (p<0.001), CRT prior to chemotherapy (p=0.005), death during CRT (p=0.021), grade 1–2 ear toxicity (p=0.006), and grade 1–2 pharynx/esophagus toxicity (p=0.046) showed statistically significant differences between the groups. There were no deaths in the younger cohort, but in the elderly group, one (3%) died of a heart attack, and two (6%) from treatment toxicity (febrile neutropenia, mucositis, malnutrition).

Data from 226 (28%) thoracic cancer patients were analyzed, 144 (64%) aged <65 years, and 82 (36%) aged ≥65. The clinical characteristics of patients with tumors in the thoracic region, the characteristics of their treatment, and a comparison of the side effects and adverse reactions by age are presented in Table 3. Comorbidity (p=0.015), surgery (p=0.031), CRT interruption time (p=0.014), grade 1–2 skin toxicity (p=0.025), grade 1–2 pharynx/esophagus (p=0.002), grade 1–2 upper gastrointestinal toxicity (p=0.036), and grade 1–2 hematocrit toxicity (p=0.032) showed statistically significant differences between the groups. One younger patient (0.4%) died due to gastrointestinal bleeding, and two younger patients (1%) died from treatment toxicity (hematological toxicity with grade 3–4 esophagitis). One elderly patient (1%) died from treatment toxicity (neutropenic fever).

Data from 187 (23%) patients treated for abdominal cancer was examined. Of these, 132 (71%) were aged <65 years, and 55 (29%) were aged ≥65. Table 4 shows the clinical characteristics of patients with tumors in the abdomen, the characteristics of treatment, and a comparison of side effects and adverse reactions by age. According to Table 4, comorbidities (p<0.001) and grade 1–2 platelet toxicity (p=0.029) showed statistically significant differences between the groups. One younger patient (0.7%) died of a heart attack, while in the elderly group, one (2%) died from cranial hemorrhage, one (2%) from a pulmonary embolism, and one (2%) from treatment toxicity (neutropenic fever with gastrointestinal bleeding).

Data from 205 (25%) patients treated for pelvic cancer was analyzed. Of these, 122 (60%) were aged <65 years, and 83 (40%) were aged ≥65. Table 5 presents a comparison of clinical features, treatment characteristics, side

Table 1 Tumors in the brain site by age, clinical features, treatments, adverse events and hematological and non-hematological side effects

Radiotherapy site_brain n=82 (100%)	**<65 age n=62 (76%)**		**≥65 age n=20 (34%)**		**p**
	n	**%**	**n**	**%**	
Gender					
Male	36	58	13	65	0.390
Female	26	42	7	35	
Co-morbidity	13	21	6	30	0.292
ECOG PS					
ECOG 0	32	52	3	15	**0.010**
ECOG 1	26	42	13	65	
ECOG ≥2	4	6	4	20	
Grade					
Grade 3	12	19	4	20	0.590
Grade 4	50	81	16	80	
Treatments					
Surgery	59	95	19	95	0.681
CT after CRT	42	68	9	45	0.061
RT tecniques					
3DCRT	33	53	8	40	0.221
IMRT	29	47	12	60	
RT dose (median, range)	60 (24–60) Gy		60 (40–60) Gy		0.149
Chemotherapy agents					
Temozolamide	62	100	20	100	–
CRT related adverse events					
Weight loss	11	18	2	10	0.332
Performance deterioration	18	29	5	25	0.484
Ending of CRT	2	3	7	35	**0.001**
Exitus during CRT	1	2	3	15	**0.043**
Treatment interruption	12 (19)		–		**0.026**
Mean time to interruption (median, range)	8 (2–25) days		–		–
Non-hematological side effects					
Skin grade 1–2	29	47	10	50	0.502
Mucous membrane grade 1–2	9	15	5	25	0.224
Eye grade 1–2	3	5	1	5	0.681
Ear grade 1–2	5	8	–		0.237
CNS grade 1–2	22	36	9	55	0.307
Hematologic toxicities					
WBC grade 1–2	5	8	–		0.237
WBC grade 3–4	4	7	–		0.319
Platelets grade 1–2	6	10	–		0.179
Platelets grade 3–4	4	7	2	10	0.455
Neutrophils grade 1–2	–	–	–		
Neutrophils grade 3–4	4	7	–		0.319
Hemoglobin grade 1–2	9	15	1	5	0.240
Hematocrit grade 1–2	1	2	1	5	0.435

ECOG: Eastern Cooperative Oncology Group; CT: Computed tomography; CRT: Chemoradiotherapy; 3DCRT: Three-dimensional conformal radiation therapy; IMRT: Intensity-modulated radiation therapy; RT: Radiotheraphy; WBC: White blood cell

effects, and adverse events by age in patients with pelvic tumors. Table 5 shows that comorbidity (p<0.001), performance status (p=0.045), surgery (p=0.011), and CRT interruption (p=0.032) were statistically significant differences between the groups. Among the younger patients, one (0.4%) died from a heart attack, and one

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Table 2 Tumors in the head and neck site by age, clinical features, treatments, adverse events and hematological and non-hematological side effects

Head and neck site n=113 (100%)	**<65 age n=81 (72%)**		**≥65 age n=32 (28%)**		**p**
	n	**%**	**n**	**%**	
Gender					
Male	65	80	24	75	0.353
Female	16	20	8	25	
Co-morbidity	18	22	21	66	**<0.001**
ECOG PS					
ECOG 0	54	67	13	41	**0.017**
ECOG 1	27	33	18	58	
ECOG ≥2	–		1	3	
Cancer					
Nasopharynx	34	42	6	19	0.057
Oral Cavity	12	15	10	31	
Oropharynx / Hypopharynx	6	7	4	12	
Larinyx	29	36	12	38	
Stage					
Stage 1–2	14	17	6	19	0.525
Stage 3–4	67	83	26	81	
Other treatments					
Surgery	23	28	12	38	0.235
CT before CRT	13	16	1	3	**0.005**
CT after CRT	26	32	6	19	0.116
RT Tecniques					
3DCRT	47	58	21	66	0.300
IMRT	34	42	11	34	
RT dose (median, range)	70 (24–72) Gy		70 (19.8–72) Gy		0.412
CT					
Cisplatin (weekly)	73	90	29	91	0.712
Others (except cisplatin)	8	10	3	9	
CRT related adverse events					
Weight loss	48	59	17	53	0.350
Performance deterioration	32	40	16	50	0.210
Ending of CRT	3	4	3	9	0.220
Exitus during CRT	–		3	9	**0.021**
Treatment interruption	8	10	2	6	0.422
Mean time to interruption (median, range)	4 (2–12) days		4 (2–6) days		0.826
Non-hematological side effects					
Skin grade 1–2	61	75	20	63	0.130
Skin grade 3–4	8	10	3	9	0.621
Mucous membrane grade 1–2	49	61	19	60	0.539
Mucous membrane grade 3–4	16	20	4	13	0.268
Ear grade 1–2	–		4	13	**0.006**
Pharynx & Oesophagus grade 1–2	51	63	26	81	**0.046**
Pharynx & Oesophagus grade 3–4	4	5	–		0.258
Salivary gland grade 1–2	39	48	13	41	0.305
Larynx grade 1–2	27	34	12	38	0.452
Hematological side effects					
WBC grade 1–2	24	830	10	31	0.518
WBC grade 3–4	2	3	2	6	0.318
Platelets grade 1–2	3	4	3	9	0.220
Neutrophils grade 1–2	16	20	4	13	0.258
Neutrophils grade 3–4	1	1	2	6	0.193
Hemoglobin grade 1–2	16	20	8	25	0.353
Hematocrit grade 1–2	10	12	4	13	0.602

Table 3 Tumors in the thorax region by age, clinical features, treatments, adverse events and hematological and non-hematological side effects

Thoraks site n=226 (100%)	**<65 age n=144 (64%)**		**≥65 age n=82 (36%)**		**p**
	n	**%**	**n**	**%**	
Gender					
Male	125	87	77	94	0.072
Female	19	13	5	6	
Co-morbidity	46	32	39	48	**0.015**
ECOG PS					
ECOG 0	77	53	38	46	0.191
ECOG 1	66	46	41	50	
ECOG ≥2	1	1	3	4	
Cancer					
Non-small cell lung	104	72	66	80	0.305
Small cell lung	26	18	12	15	
Esophagus	14	10	4	5	
Stage					
Stage 1–2	13	9	9	11	0.398
Stage 3–4	131	91	73	89	
Other treatments					
Surgery	14	10	2	2	**0.031**
CT before CRT	39	27	17	21	0.184
CT after CRT	78	54	35	43	0.064
RT Tecniques					
3DCRT	80	56	35	43	0.191
IMRT	64	44	47	57	
RT dose (median, range)	66 (16.2–68.4) Gy		66 (24–70) Gy		0.614
CT					
Cisplatin weekly	24	17	14	17	0.076
Carboplatin+Paclixaksel	51	35	41	50	
Cisplatin+etoposid	57	40	21	26	
Cisplaitn+docetaxel	5	3	5	6	
Others	7	5	1	1	
CRT related adverse events					
Weight loss	36	25	20	24	0.526
Performance deterioration	39	27	14	17	0.060
Ending of CRT	9	6	10	12	0.098
Exitus during CRT	3	2	1	1	0.540
Treatment interruption	37	26	14	17	0.091
Mean time to interruption (median, range)	7 (2–21) days		12 (5–28) days		**0.014**
Non-hematological side effects					
Skin grade 1–2	25	17	6	7	**0.025**
Pharynx & Oesophagus grade 1–2	96	67	38	46	**0.002**
Pharynx & Oesophagus grade 3–4	4	3	1		0.402
Lung grade 1–2	65	45	40	49	0.348
Upper GIS grade 1–2	70	49	39	35	**0.036**
Upper GIS grade 3–4	2	1		–	0.405
Hematological side effects					
WBC grade 1–2	58	40	26	32	0.127
WBC grade 3–4	38	26	24	29	0.378
Platelets grade 1–2	27	19	13	16	0.360
Platelets grade 3–4	8	6	4	5	0.546
Neutrophils grade 1–2	42	29	26	32	0.400
Neutrophils grade 3–4	28	19	13	16	0.314
Hemoglobin grade 1–2	33	23	26	32	0.099
Hematocrit grade 1–2	14	10	16	20	**0.032**

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Table 4 Tumors in the abdomen region by age, clinical features, treatments, adverse events and hematological and non-hematological side effects

Abdomen site n=187 (100%)	**<65 age n=132 (71%)**		**≥65 age n=55 (29%)**		**p**
	n	**%**	**n**	**%**	
Gender					
Male	98	74	41	74	0.561
Female	34	26	14	26	
Co-morbidity	30	23	32	58	**<0.001**
ECOG PS					
ECOG 0	84	64	31	56	0.488
ECOG 1	46	35	22	40	
ECOG ≥2	2	1	2	4	
Cancer					
Gastric	102	77	47	85	0.182
Pancreas	28	21	6	11	
Gall bladder	2	2	2	4	
Stage					
Stage 1–2	36	27	13	24	0.374
Stage 3–4	96	73	42	76	
Other treatments					
Surgery	124	94	48	87	0.111
CT before CRT	75	57	33	60	0.407
CT after CRT	115	87	42	76	0.057
RT Tecniques					
3DCRT	91	69	32	58	0.107
IMRT	41	31	23	42	
RT dose (median, range)	45 (16.2–59.4) Gy		45 (7.2–59.4) Gy		0.760
Chemotherapy agents					
FUFA	50	38	20	36	0.756
5FU infusional	23	17	11	20	
Capesitabin	49	37	22	40	
Gemsitabin	10	8	2	4	
CRT related adverse events					
Weight loss	38	29	14	26	0.392
Performance deterioration	28	21	13	24	0.426
Ending of CRT	7	5	5	9	0.255
Exitus during CRT	1	1	3	5	0.077
Treatment interruption	19	14	7	13	0.482
Mean time to interruption (median, range)	6 (2–20) days		9 (4–12)		0.364
Non-hematological side effects					
Pharynx & Oesophagus grade 1–2	22	17	8	15	0.452
Upper GIS grade 1–2	75	57	60	33	0.407
Hematological side effects					
WBC grade 1–2	50	38	27	49	0.105
WBC grade 3–4	8	6	5	9	0.324
Platelets grade 1–2	22	17	3	6	**0.029**
Neutrophils grade 1–2	23	17	12	22	0.305
Neutrophils grade 3–4	6	5	5	9	0.171
Hemoglobin grade 1–2	20	15	12	22	0.186
Hematocrit grade 1–2	13	10	3	6	0.251

Table 5 Tumors in the pelvis region by age, clinical features, treatments, adverse events and hematological and non-hematological side effects

Pelvis site n=205 (100%)	**<65 age n=122 (60%)**		**≥65 age n=83 (40%)**		**p**
	n	**%**	**n**	**%**	
Gender					
Male	62	51	52	63	0.063
Female	60	49	31	37	
Co-morbidity	49	40	56	68	**<0.001**
ECOG PS					
ECOG 0	83	68	45	54	**0.045**
ECOG 1	39	32	36	43	
ECOG ≥2	–		2	4	
Cancer					
Anal canal	3	2	2	2	0.054
Rectum	89	73	57	69	
Servix	22	18	9	11	
Bladder	8	7	15	18	
Stage					
Stage 1–2	33	27	26	31	0.305
Stage 3–4	89	73	57	69	
Other treatments					
Surgery	68	56	32	39	0.011
CT before CRT	18	15	6	7	0.151
CT after CRT	65	53	29	35	0.534
RT Tecniques					
3DCRT	80	66	57	69	0.379
IMRT	42	34	28	31	
RT dose (median, range)	50.4 (25.2–66) Gy		50.4 (12.6–64.8) Gy		0.101
Chemotherapy agents					
Cisplatin	26	21	17	21	0.599
FUFA	11	9	12	14	
5FU infusional	37	30	22	26	
Capesitabin	40	33	23	28	
Gemsitabin	6	5	8	10	
Mitomisin C+5FU	2	2	1	1	
CRT related adverse events					
Weight loss	12	10	10	12	0.389
Performance deterioration	17	14	15	18	0.271
Ending of CRT	6	5	8	10	0.151
Exitus during CRT	2	2	2	2	0.534
Treatment interruption	7	6	12	15	**0.032**
Mean time to interruption (median, range)	7 (2–14) days		5 (2–14)		0.249
Non-hematological side effects					
Lower GIS grade 1–2	85	70	58	64	0.215
Lower GIS grade 3–4	2	2	–		0.353
GUS grade 1–2	49	40	40	48	0.160
GUS Grade 3–4	1	8	2	2	0.358
Hematological side effects					
Wbc grade 1–2	42	34	27	33	0.449
Wbc grade 3–4	1	1	3	4	0.183
Platelets grade 1–2	6	5	8	10	0.151
Platelets grade 3–4	–		2	2	0.163
Neutrophils grade 1–2	14	12	9	11	0.518
Neutrophils grade 3–4	2	2	3	4	0.324
Hemoglobin grade 1–2	21	17	19	22	0.324
Hematocrit grade 1–2	8	7	7	8	0.203

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(0.4%) died from a pulmonary embolism. In the elderly group, one (1%) died from a pulmonary embolism, and one (1%) from cranial hemorrhage.

DISCUSSION

This study examined the toxicity of CRT by age and treatment location. The results show that elderly patients had more comorbidities in the brain, head, and neck regions, while poorer performance status was observed in patients undergoing pelvic irradiation. This study also found higher rates of CRT cessation and death during CRT in elderly patients, particularly in the head and neck, brain, and pelvic regions.

For thoracic cancer patients, the rate of CRT interruption was higher among younger patients than older ones, though statistically, this was not significant. No significant differences were detected between the groups in terms of grade 3–4 toxicities. However, grade 1–2 toxicities (e.g., ear, pharynx/esophagus, upper gastrointestinal, platelet, hematocrit) varied between the two groups. Although no significant difference in treatment toxicities was observed between younger and older patients, toxic deaths due to CRT were more common in elderly patients. In elderly patients, 5% of toxic deaths occurred in the brain, 6% in the head and neck, 1% in the thorax, and 2% in the abdomen, while for younger patients, toxic deaths occurred in 2% of brain cases and 1% of thoracic cases. This higher incidence of toxic deaths in elderly patients suggests that CRT-related adverse events may be of greater concern in this age group.

In a trial by Stupp, temozolomide chemotherapy during and after radiotherapy significantly prolonged survival in glioblastoma patients aged 70 or younger at diagnosis.[11] Especially for fit patients over 70, temozolomide with conventional or hypofractionated radiotherapy remains a treatment option.[12,13] Few studies compare CRT-associated toxicity by age in patients with brain tumors. A study conducted by Saito et al.[14] investigated the toxicity of concomitant and adjuvant temozolomide in patients with brain tumors (≥65 years, N=27 vs <65 years, N=49). This study found that thrombocytopenia and grade 4 toxicity rates were higher in the elderly group, but no difference was observed in non-hematological toxicity. Sijben et al.[15] evaluated CRT toxicity in glioblastoma patients over 65 and found no treatment-related deaths, though CRT cessation and death during CRT were more common in elderly patients. However, CRT interruption was more frequent in younger patients. No difference was observed between the groups in terms of hematological and non-hematological toxicity. The higher incidence of adverse events in elderly patients may be attributed to greater comorbidity and poorer performance status. Though temozolomide appears well-tolerated in elderly patients, caution is warranted, given the 5% mortality rate associated with treatment toxicity in this group.

Concurrent CRT has been demonstrated to improve survival compared to radiotherapy alone in locoregionally advanced squamous cell head and neck cancer.[16] However, this approach is associated with significant acute toxicity, such as mucositis, dysphagia, and skin reactions, which can impede patient compliance and disrupt treatment delivery.[17] Merlano et al.[18] investigated the effect of age on acute toxicity caused by CRT in 317 head and neck cancer patients, categorizing them into <65 years (N=224) and ≥65 years (N=93). They evaluated CRT-related acute toxicities and treatment compliance (e.g., delays, non-completion, and death during treatment). Except for a higher frequency of infection and pneumonia in the elderly group, no differences were found between the groups in terms of treatment compliance and hematological or non-hematological side effects. In another retrospective study by Grün et al.,[19] the acute toxicity results of 158 head and neck cancer patients undergoing CRT were examined by age. Grade 3 and higher leukopenia occurred more frequently in elderly patients, though the percentage of patients completing the prescribed chemotherapy was similar between the groups. Non-hematological toxicities such as dermatitis, dysphagia, mucositis, and pain did not differ significantly. Michal et al.[20] compared CRT toxicities between 44 patients ≥70 years and 137 patients <70 years with head and neck cancer, finding comparable rates of acute toxicities, including nausea and vomiting, mucositis, dysphagia, and skin reactions. Toxic death rates were also similar between the groups. Like prior studies, this study found no difference in grade 3–4 hematological and non-hematological complications between the two groups. However, more deaths occurred in elderly patients during CRT, with 6% of deaths in elderly patients attributed to treatment toxicity, indicating that more caution should be exercised during CRT in this population.

Semrau et al.[21] investigated the impact of comorbidity and age on treatment outcomes and acute toxicity in 66 lung cancer patients who underwent CRT. The patients were grouped into those aged under and over 70. Grade 3–4 thrombocytopenia and leukopenia were more common in elderly patients. A prospective study by Servagi-Vernet et al.[22] demonstrated the feasibility

of CRT in selected esophageal cancer patients over 75. A review by Zimmerman et al.[23] found either no or a low incidence of both acute and late high-grade toxicity in elderly patients. Stinchcombe et al.[24] compared treatment-related side effects in elderly and younger patients with non-small cell lung cancer, analyzing 2,768 patients under and over the age of 70. Toxicity rates for all grade 3 and higher, and for both hematological and non-hematological grade 3 and higher, were more frequent in elderly patients. The study also found that elderly patients completed treatment less often (47% vs 57%; p<0.010), ended treatment due to adverse events more frequently (20% vs 13%; p<0.010), refused treatment at higher rates (5.8% vs 3.9%; p=0.020), and died during treatment more frequently (7.8% vs 2.9%; p<0.010). Unlike the current study, no difference was observed in grade 3–4 hematological or non-hematological side effects between younger and elderly patients. However, grade 1–2 hematocrit side effects and treatment interruptions were more common in elderly patients. Younger patients more frequently experienced grade 1–2 skin, upper gastrointestinal, and esophagus toxicities. Deaths due to treatment toxicity occurred at a rate of 1% for both groups. In this study, both young and elderly patients tolerated CRT similarly.

In the abdominal region, CRT may be involved in both adjuvant and definitive therapy for cancers of the stomach, pancreas, and gallbladder. Diarrhea, nausea, vomiting, and hematological side effects, which arise from the rapidly dividing gastrointestinal mucosa, are the most common acute side effects of abdominal CRT. However, external beam radiotherapy in this region is limited by the small intestine's sensitivity to radiation, so doses are relatively lower than in other regions. Few studies have examined CRT toxicity by age in this region. Wilkowski et al.[25] evaluated the toxicity of CRT in 32 patients with inoperable pancreatic cancer, stratifying them by age (≥75 years). They found no difference between groups in terms of grade 3–4 gastrointestinal side effects or grade 3–4 leukopenia and thrombocytopenia. Miyamoto et al.[26] evaluated CRT toxicity in pancreatic cancer patients aged ≥75 years and reported that 7% ended CRT, and 17% were hospitalized, with nausea, pain, and failure to thrive being the most common side effects. Slagter et al.[27] used data from the Critics study to evaluate perioperative treatment results and toxicity in 788 gastric cancer patients by age (<70 vs ≥70). In their study, 79% of younger patients and 63% of elderly patients were able to begin postoperative CRT, with elderly patients initiating CRT at statistically significantly lower rates. However, no difference was observed in grade 3–4 gastrointestinal or hematological toxicities. In this study, as in others, no differences were found between age groups in terms of adverse events or grade 3–4 toxicity. Only grade 1–2 thrombocytopenia rates were higher in younger patients. The findings suggest that young and elderly patients tolerate abdominal CRT similarly, although no treatment-related deaths were observed in younger patients, while elderly patients had a 2% death rate. Thus, more caution is needed when administering abdominal CRT to elderly patients.

CRT is an important treatment modality for cervical, bladder, rectal, and anal canal tumors in the pelvic region. Acute toxicities in this area primarily involve the lower gastrointestinal and genitourinary tracts, as well as hematological side effects. Wang et al.[28] evaluated treatment outcomes and toxicities by age in patients receiving definitive radiotherapy or CRT for cervical cancer. The study compared older (≥70 years, N=70) and younger (<60 years, N=991) patients, finding no difference in acute hematologic toxicity (58% vs 46%, respectively). These results suggest that elderly patients can tolerate definitive CRT well. However, grade 3–4 chronic gastrointestinal side effects were more common in elderly patients. A retrospective analysis compared CRT treatment results in patients with muscle-invasive bladder cancer, aged <75 years (N=106) and ≥75 years (N=61).[29] Comorbidities and impaired performance status were significantly higher in elderly patients. Of the younger patients, 75% completed the planned radiotherapy dose compared to 93% of elderly patients. However, younger patients were more likely to complete four cycles of chemotherapy (19% vs 36%, respectively, p=0.017). Genitourinary and gastrointestinal toxicities were the primary reasons for not completing chemotherapy. Overall, elderly patients tolerated CRT as well as younger patients. Hofheinz et al.[30] investigated the effect of age on oxaliplatin in preoperative CRT and adjuvant chemotherapy for rectal cancer (N=1,232). Dividing the patients into <60 years, 60–70 years, and ≥70 years, they found no difference between the groups in terms of CRT toxicity, morbidity, or treatment completion. Sung et al.[31] investigated the oncological results and morbidity of 1,232 patients with rectal cancer who underwent preoperative CRT and subsequent total mesorectal excision. When patients were grouped by 70 years (<70 years vs. ≥70 years), grade 3–4 acute hematologic toxicity was observed more frequently in the elderly than that in the younger group (9.0% vs 16.1%, p=0.008). However, these differences were not detected in acute non-hematological side effects.

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Limitations

The most important limitation of this study is that it was retrospective.

CONCLUSION

In this study, although it was observed that elderly patients had more comorbid diseases and their performance status was worse, no difference was found between the groups in terms of adverse events and toxicity. It was observed that interruption to CRT was more common in elderly patients. In addition, treatment-related death was not observed in any of the young and old patients in this region of CRT. Elderly patients were able to tolerate CRT applied to the pelvic area similar to younger patients.

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