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Original Paper

No Age Limit for Radical Radiotherapy in Head and Neck Tumours

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The elderly are often treated less aggressively in an attempt to preserve their quality of life with regards to toxicity. However, there are few data regarding the acute and late toxicity of radiotherapy (RT) in elderly patients. From February 1980 to March 1995, 1589 patients with head and neck cancers who enrolled in EORTC trials received RT and were available for analysis on RT toxicity. Patients over 65 years of age were in excess of 20%. Data regarding age and acute objective mucosal reactions were available for 1307 patients and 1288 had toxicity $\geqslant$ grade 1. Age and acute functional mucosal reactions were registered for 838 patients and 824 patients had toxicity $\geqslant$ grade 1. Body-weight alteration during treatment was available in 1252 patients; it increased in 153 patients and decreased in 1099 patients. Late toxicities were examined only if they occurred before an eventual tumour failure in order to avoid confusion between effects of first- and second-line treatments. 749 patients were available for analysis of which 646 had late toxicity grade $\geqslant$ 1. Survival and toxicity were examined in different age ranges from 50 to 75 years and over. There was no significant difference in survival between each age group. A trend test was performed to assess any correlation between age and the acute occurring toxicity. There was no significant difference in acute objective mucosal reactions ($P = 0.1$) and in weight loss >10% ($P = 0.441$). In contrast, older patients had more severe (grade 3 and 4) functional acute toxicity ($P < 0.001$) than younger patients. We evaluated the probability of late toxicity occurrence in relation to time with the Kaplan–Meier method and the logrank test in each age group. Eighteen per cent of patients were free of late effects at 5 years, the logrank test showing no significant difference between ages ($P = 0.84$). In conclusion, chronological age is irrelevant for therapeutic decisions.

Key words: age, elderly, head and neck tumours, radiotherapy, acute toxicity, late toxicity

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INTRODUCTION

AGE IS an essential risk factor for the majority of cancers. Half of all tumours become clinically detectable in people over 70 years of age. In spite of this frequency, few data are available on the tolerance to treatment in this patient population. This is particularly true for radiotherapy, although this lack of data might reflect the fact that previous attempts to relate age to a different side-effect pattern were not conclusive and hence not published [1]. A frequent attitude of physicians about cancer in elderly patients is to give substandard treatment. This attitude is not supported by clinical evidence, but stems rather from a lack of specific knowledge regarding the prognosis and the treatment of the disease in the elderly [2, 4], together with the belief that tolerance to radical treatments, including radiotherapy, might be compromised in older patients.

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Table 1. EORTC trials

EORTC group	Trial number	Tumour sites	Trial type	Patient number	Acute effects	Late effects
Radiotherapy	22791	1	phase III	356	omr,fmr	b,ly,m,mu,o,p,sk,sp,t
	22811	1,2,3,4	phase III	523	omr	ly,mu,o,x
	22843	1,2,3,4	phase II	61	omr,fmr	b,d,la,ly,m,mu,o,p,sk,sp,t,x
	22851	1,3,4,5,6	phase III	510	omr,fmr	b,m,mu,o,sp
Head and Neck	24844	1,3	phase III	139	omr,fmr	b,d,la,ly,m,mu,o,p,sk,sp,t,x

1, oropharynx; 2, hypopharynx; 3, oral cavity; 4, larynx; 5, nasopharynx; 6, paranasal sinus; omr, objective mucosal reaction; fmr, functional mucosal reaction; b, bone; d, dysphagia; la, larynx; ly, lymphatic drainage; m, mucosis; mu, muscular fibrosis; o, other; p, pain; sp, spinal cord; t, trismus; x, xerostomy; sk, skin.

Head and neck cancer represents approximately 3% of all sites of cancer [5]; it classically peaks in the sixth decade of life, with a wide spread from the third to the ninth. With the rapid ageing of the western population, these tumours will become more frequent in the future, especially in elderly population groups [6]. Radiation therapy has an established role in the management of head and neck malignancies. Applied as single modality or combined with surgery, it is an essential part of the curative treatment of patients. The classical protocol on the European continent consists of fractionated irradiation, delivering 66–70 Gy in 33–35 fractions of 2 Gy, 5 fractions per week, with megavoltage equipment, i.e. a cobalt unit or, more frequently, a linear accelerator. The treatment is protracted over a period from 6.5 to 7 weeks. The main acute side-effect of radiotherapy is painful mucositis, i.e. severe inflammation of the upper aerodigestive mucosa, often with patchy or confluent desquamation. Mucosal reactions are often responsible for a decrease in food intake which can result in a dramatic weight loss. Active supportive care during irradiation (analgesics, semi-liquid diet, etc) helps the patient to reach the last session without treatment interruption. Late side-effects of radiotherapy include various symptoms such as pain and dryness in the mouth, skin and subcutaneous fibrosis, and ultimately to radiomyelitis and osteoradionecrosis [7]. All these tissue alterations have an impact on the quality of life and may lead to various degrees of disability and/or social isolation.

The present study aimed to evaluate whether or not a limit of age could be identified beyond which acute and late toxicity in patients receiving radiotherapy for head and neck cancer were more frequent or more severe. Locoregional control and survival were also analysed in relation to the age of the patients. The study was based on the total number of patients enrolled in five trials of the European Organization for Research and Treatment of Cancer (EORTC) carried out from 1980 to 1995. The originality of this database is that side-effects and complications were registered prospectively as an integral part of the trial protocols.

PATIENTS AND METHODS

1589 patients with head and neck cancer were enrolled from February 1980 to March 1995 in 5 trials initiated by the Radiotherapy cooperative group or in collaboration with the Head and Neck cooperative group of the EORTC. The characteristics of these trials are shown in Table 1. Details of eligibility have been previously reported [8–10]. Four studies compared conventional fractionation to multifractionation (protocol numbers 22.791, 22.811, 22.843 and 22.851) and one compared the association of chemotherapy with surgery-radiotherapy versus surgery-radiotherapy alone (protocol number 24.844). Protocol 22.843 was a phase II feasibility study; all the others were phase III randomised trials. All patients received radiotherapy (there was no control treatment arm without radiotherapy) and were taken into consideration in this analysis.

Approximately half the patients were irradiated according to the standard protocol described in the introduction as the control arm of the various phase III studies. The other half were treated with investigational schedules, e.g. two fractions of 1.15 Gy per day up to a total of 80.5 Gy in 7 weeks (protocol 22.791), three fractions of 1.6 Gy per day up to a total of 72 Gy in 5 weeks (protocol 22.851), approximately the same schedule with or without concomitant cisplatin (protocol 22.843), or 67.2–72 Gy in fractions of 1.6 Gy with misonidazole as radiosensitiser, three fractions per day but with a different split during treatment (protocol 22.811). Patients included in trial 24.844 were all irradiated with the standard schedule.

There were 1310 males and 150 females, the information being unavailable in 129 cases. Diseases originating from maxillary antrum were staged according to the AJCC staging system [11], and tumours from ethmoid according to the University of Florida staging system [12]. Other tumours were staged or re-staged according to the 1987 UICC-TNM staging system. The tumour stages are shown in Table 2. 57 of these 1589 patients were metastatic (1 T2, 16 T3 and 40 T4). The mean age was 57 years (range 20–82). The maximum follow-up was 12 years and the mean follow-up for living patients was 3.6 years.

The epidemiological structure of the present series (Table 3) was compared with the overall age distribution of head and neck tumours in the general population [5, 13]. Patients older than 70 accounted for 12% of the trial patients versus 24% in the general population (1.9 versus 19.2% for patients over 75). However, although the percentage of patients over 65 and 70 were under-represented, the absolute number of such patients was suffficient to perform the analysis.

Table 2. Distribution of patients according to tumour stage

	N0	N1	N2	N3	ns	Total
T1	1	1		11	1	14
T2	235	90	23	34	0	382
T3	286	230	67	203	0	786
T4	65	68	54	83	1	271
ns	2	0	0	4	130	136
Total	589	389	144	335	132	1589

ns = not specified.

Table 3. Age-groups

Age-group (years)	<50	50–54	55–59	60–64	65–69	70–75	>75	ns	Total
Patients									
Number	281	237	279	297	223	155	30	87	1589
(%)	(17.7)	(14.9)	(17.6)	(18.7)	(14)	(9.8)	(1.9)	(5.5)	

ns = not specified.

The grading of toxicity was standardised in a such manner that it was possible to encompass all data in the analysis. However, the registration of some toxicities was not required in some studies so that the number of evaluable patients was different for each type of side-effect. Patients were examined weekly during treatment and one month after the end of treatment. Modalities of follow-up changed with trials, but the main directive was to examine patients every 2 months up to 8 months and then twice yearly until the off-study date. As the data of this paper were gained from multicentre studies, the possible bias coming from the assessment of the symptoms and severity of the side-effects were most probably minimised by the design of the original trial.

Three separate acute reactions were analysed: acute objective mucosal reaction, acute functional mucosal reaction and body weight loss. Objective mucosal reactions corresponded to tissue modification as assessed by the examiner; it was scored as absent (grade 0), mild erythema (grade 1), patchy desquamation (grade 2) or diffuse desquamation (grade 3). Functional mucosal reactions corresponded to symptoms as experienced by the patient, directly related to pain as a result of the mucositis; these subjective reactions were scored as absent (grade 0), mild irritation (grade 1), moderate irritation (grade 2), liquid diet only (grade 3) and oral alimentation impossible (grade 4). Body weight loss ensuing from difficulties in food intake was taken as an objective index of acute mucosal reaction to irradiation and expressed in per cent of the body weight at diagnosis. Performance status (WHO/ECOG scale) was evaluated before and after treatment. Late toxicity was evaluated according to the EORTC/RTOG toxicity scale. However, an adaptation of the scoring system was necessary because of differences in scoring methods between some trials. For some effects, only their presence or absence were scored. These different scales are summarised in Table 4.

Table 4. Grading of late toxicities

Toxicity	Grade	Definition
Pain	0	none
	1	mild
	2	moderate
	3	severe
	4	intractable
Dysphagia	0	none
	1	mild
	2	moderate
	3	severe = dilatation
	4	total obstruction
Larynx	0	none
	1	mild oedema
	2	moderate oedema
	3	severe oedema = tracheostomy
	4	chondritis = laryngectomy
Mucositis/fibrosis/skin	0	none
	1	mild
	2	moderate
	3	severe
Bone	0	none
	1	periosteal exposure
	2	moderate lysis
	3	necrosis
Spinal cord	0	none
	1	L'Hermitte's syndrome
	2	myelitis
Xerostomy	0	none
	1	moderate
	2	severe
Trismus	0	none
	1	yes
Other	0	none
	1	yes

Survival was evaluated from the date of randomisation to the date of death or most recent follow-up date. Locoregional control was evaluated from the date of randomisation to the date of recurrence or last follow-up. In analysing time to development of recurrent disease, the interval was measured from when complete remission was achieved to the time when either disease recurred or the patient was most recently evaluated disease free. Survival and locoregional control were calculated using the product limit method of Kaplan and Meier [14]. The logrank test was used for comparison of survival curves. Survival and toxicities according to age were analysed after splitting the database in seven classes of age (<50, 50–54, 55–64, 65–69, 70–75, >75). The patients and treatment characteristics were compared by chi-square test for contingency tables. Acute toxicity and body weight alteration were also examined in seven different age ranges from 50 years to 75 years and over; the chi-square test was performed to assess any difference in occurring toxicity and a trend test (χ^2) was used to examine if chronological age had an impact on difference.

Late radiation effects were considered only if they occurred before a recurrence in order to avoid confusion between first- and second-line treatment side-effects. The probability of late toxicity occurrence with regards to time was calculated with the Kaplan–Meier method which also eliminated the bias of differences in disease-free follow-up time. Time to a late effect was measured from the start of radiation to first occurrence of toxicity post-90 days or to the date of the last follow-up. To minimise actuarial bias, only patients surviving more than 90 days were analysed for late effect risks. The logrank test was performed to compare toxicity in the same seven age ranges.

RESULTS

The two groups of patients with and without toxicity were similar with respect to age, sex, WHO performance

Table 5. Acute and late toxicity according to age group

Side-effect	Age-groups (y) < 50 *n*	50–54 *n*	55–59 *n*	60–64 *n*	65–69 *n*	70–75 *n*	>75 *n*	Total
Acute reaction								
Objective mucosal reaction								
0	5	5	3	3	1	1	1	19
1	44	31	48	41	20	13	0	197
2	93	70	86	78	59	29	3	418
3	140	131	142	115	81	60	4	673
Functional mucosal reaction								
0	4	3	5	1	1	0	0	14
1	24	12	12	22	5	3	0	78
2	78	57	74	54	45	18	1	327
3	74	59	59	57	39	18	4	310
4	15	13	17	25	19	11	9	109
Late reaction								
Pain								
0	44	39	45	46	41	28	10	253
1	5	4	3	5	6	0	1	24
2	2	3	2	1	2	1	0	11
3	2	3	3	2	1	1	0	12
4	1	0	0	1	0	0	0	2
Dysphagia								
0	20	18	21	22	19	11	9	120
1	2	3	4	2	3	3	1	18
2	2	3	3	1	1	1	0	11
3	0	0	1	0	0	0	0	1
4	0	0	1	1	0	0	0	2
Larynx								
0	19	17	15	22	18	10	6	107
1	2	1	1	2	2	2	1	11
2	1	1	1	2	0	1	0	6
3	0	0	0	0	1	0	0	1
4	0	0	0	0	0	0	0	0
Mucositis								
0	73	75	79	80	77	60	10	454
1	22	20	26	32	30	22	6	158
2	13	15	12	10	18	16	0	84
3	5	8	4	9	7	3	1	37
Fibrosis								
0	51	50	55	59	49	22	20	306
1	52	54	38	50	20	7	2	223
2	22	26	27	24	14	6	1	120
3	2	3	1	5	13	6	4	34
Skin								
0	42	49	52	57	53	20	17	290
1	1	0	0	0	0	0	0	1
2	0	1	0	1	0	0	0	2
3	0	0	0	0	1	0	0	1
Bone								
0	73	69	70	76	65	42	22	417
1	2	5	4	3	0	0	0	14
2	2	1	3	3	0	1	0	10
3	2	3	5	3	1	0	0	14
Spinal cord								
0	86	85	88	95	84	65	15	518
1	1	0	2	0	0	1	0	4
2	1	2	1	0	1	0	0	5
Xerostomy								
0	36	35	28	31	26	15	9	180
1	5	6	6	10	14	8	3	52
2	0	0	0	0	11	6	1	18
Trismus								
No	66	57	56	53	45	23	19	319
Yes	39	43	35	45	18	12	10	202
Others								
No	103	107	101	105	104	89	9	618
Yes	20	21	20	18	22	20	0	121

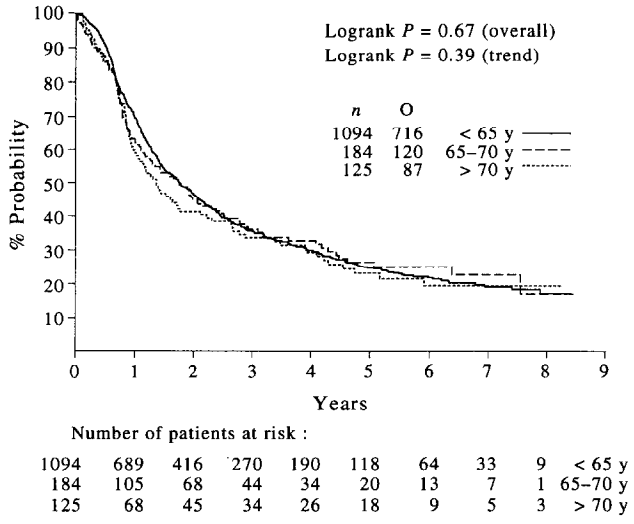

Figure 1. Overall survival by age group.

status, site of primary, extent of the tumour and the type of treatment. Neither survival nor locoregional control was affected by age. The actuarial curves of the different age groups were nearly superimposable, as shown in Figures 1 and 2. Since the patients included in the initial trials were strongly selected regarding their general condition (WHO performance status 0-1-2), we adjusted survival on WHO performance status. The difference was not significant indicating that survival was independent of age. Although calculations have been initially performed on seven age groups, data were further pooled in three for the sake of graphical clarity. All acute and late toxicities are shown in Table 5.

Acute side-effects

1307 patients were evaluable for objective acute mucosal reactions, 838 for functional acute mucosal reactions, 1252 for body weight alteration and 1452 for WHO performance status alteration. Objective mucosal reactions were present in 1288 patients (98.5%). The difference in distribution over age was not significant ($P = 0.69$). Distribution of severe side-effects (grade 2 and 3) was not affected by age

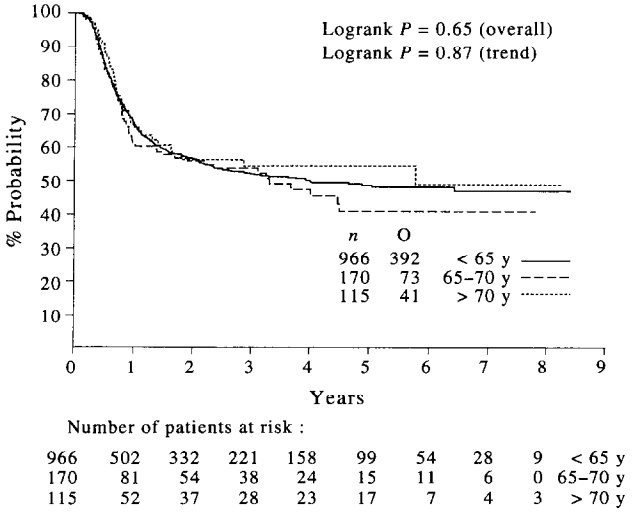

Figure 2. Locoregional control by age group.

($P = 0.1$). There was also no statistical difference in grade 0 and grade 1 toxicities in each age group ($P = 0.45$ for the trend test). The distribution of toxicity was quite similar in all the age ranges investigated: grade 1 accounted for between 12.4 and 17.3%, grade 2 for between 28.2 and 36.6% and grade 3 for between 48.5 and 58.2% (excluding <>75 years due to small numbers).

Functional mucosal reaction affected 824 out of 838 patients (98.3%). There was a statistical difference in distribution of these toxicities with regards to age ($P = 0.001$). a trend test showed that this difference also existed for severe side-effects (grades 3 and 4) ($P < 0.001$) but not for grade 1 and 2 toxicities ($P = 0.278$). The percentage of grade 1–2 toxicities was similar in each age range. Grade 3 side-effects were more frequent in the age range 55–59 and the percentage of grade 4 increased regularly with age, being 7.7% for patients under 50 and 31.25% for patients over 70.

1099 patients experienced body weight loss and 153 weight gain. No difference was observed in body weight alteration between age groups ($P = 0.739$ and $P = 0.653$, respectively) nor in weight loss >10% between age groups ($P = 0.441$). Moderate weight loss (<10%) occurred in approximately 80% of patients in each age range. However, there seemed to be a trend towards more frequent severe weight loss (10–14%) in patients aged 60 and over. Weight loss greater than 14% did not affect patients over 75 years of age.

Before treatment, there was a significant difference in the distribution of patients according to WHO performance status, elderly patients scoring on average higher ($P < 0.05$). However, at the end of radiotherapy, no difference was found. After this treatment, 54 patients had an amelioration in their performance status and there was no change for 1198 patients. After adjustment on performance status, the occurrence of objective and functional mucosal reactions were quite similar.

Late side-effects

Of the 1589 patients, late side-effects were scored in 981 patients. 751 patients had sufficient follow-up to experience late side-effects, but since age was not registered in 2, only 749 could be included in the analysis. The mean follow-up for living patients was 3.7 years for the < 65 years age group, 3.5 years for the 65–70 years age group and 3.7 years for the > 70 years age group. The median follow-up times were, respectively, 3.2 years, 3.1 years and 3.2 years. There were 670 males and 80 females, the gender being unspecified in 1 case. Data on local control were available for 735 patients. 646 patients experienced late toxicity, accounting for a total of 1199 events since several events occurred in individual patients. The mean delay of appearance of the late effect was 24 months with a median of 19 months. The difference in delay did not statistically differ from one age group to another.

The evaluation of late toxicity for all complications and grades performed, using the Kaplan–Meier method, showed that the actuarial curve deteriorated with time of observation, with approximately 18% of patients being free of complication at 5 years (Figure 3). The comparison of late toxicity for all complications and all grades in each age group was undertaken with the logrank test, showing that there was no significant difference in the actuarial incidence

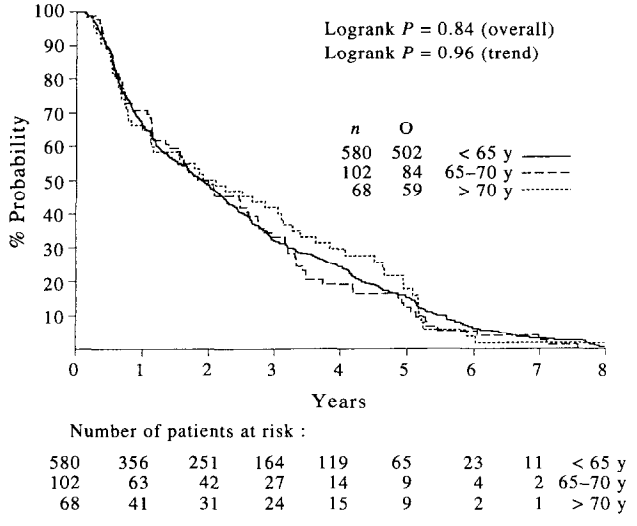

Figure 3. Free of late toxicity by age group.

of late effect between age groups (logrank $P = 0.84$). When the logrank test was adjusted for performance status, there was still no difference in the occurrence of late effects. As was already observed, this fact confirmed that the occurrence of late toxicity was independent of age.

DISCUSSION

Clinical trials usually prescribe an age limit in their inclusion criteria, often 65 or 70 years of age. Treatment guidelines validated through clinical research in younger age groups are, therefore, of unknown relevance to patients over this age limit. Several reasons can be evoked for the use of an age limit. Investigators are concerned that the effects of treatment might be masked by deaths from intercurrent disease. Also, it is unethical to expose a patient to a treatment which will significantly impact on their quality of life, if their individual life expectation does not allow them to benefit from the therapy. Finally, there is concern regarding the ability of elderly people, beyond a given age, to sustain radical treatments without increased morbidity [15, 16]. Data supporting this last argument are, however, surprisingly scarce.

Considering that a women aged 70 has a further life expectation of 15 years and a man of 70 can expect to live a further 8–10 years [4], the pertinence of an age limit around 65 or 70 can be seriously questioned. About 60% of all patients referred for radiotherapy are already over the age of 60 and 25% over the age of 70, both proportions rapidly increasing with time [17]. Moreover, the proportion of the ten commonest cancers in the European Community arising in patients over 70 years of age varies between 22 and 70% [15].

There is thus a clear and urgent need for more clinical research, unrestricted toward patients older than 65 or 70 years. However, before removing all age limits from future clinical trials in radiotherapy, it is necessary to gather sufficient clinical evidence from existing data regarding both cancer prognosis and treatment tolerance in relation to age at diagnosis.

The EORTC Database gives a large representation of patients treated with radiotherapy in a relatively wide age range and for a large scale of tumour locations. The present analysis was restricted to patients receiving radiotherapy for head and neck cancer since, in contrast with breast [20], gynaecological [19] or prostate cancer [20], few data are available regarding head and neck tumours in the elderly [21]. This is probably due to the low incidence of head and neck cancer as well as to the fact that radiation oncologists have always treated these patients, for whom the majority are old, without major problems. Four important aspects have been addressed in this study: acute tolerance, late tolerance, locoregional control and survival.

With respect to acute tolerance, there was no statistical difference in the occurrence of objective acute mucosal reactions among the different age groups. The distribution of the patients among the four grades of severity was also independent of age. However, if acute damages were similar for all patients, it seems that older patients tolerated less acute toxicity than younger patients. It was particularly true for severe functional (grade 3 and 4) reactions for which a significant trend with age was observed. Given the absence of a difference in objective toxicity, we acknowledge that similar grades of mucositis had a larger functional impact on older patients. However, it must be stressed that differences observed in the functional scoring, although significant, are probably of only limited clinical relevance, as suggested by the absence of a trend with age toward more severe body weight loss and performance status deterioration. In order to rule out any confounding factor bound to the treatment itself, an analysis adjusted for the total dose and the total treatment time confirmed that all patients were treated according to the prescribed protocol, independently of age. A subgroup of 15% of patients gained weight during treatment. A gain in body weight during radical radiotherapy for head and neck tumour seems paradoxical. It is explained by the peculiar epidemiology, and particularly by the severe ethylism associated with these tumours. A not inconsiderable proportion of patients are diagnosed after years of alcohol abuse and, therefore, in a deep state of denutrition. Coming into contact with a medical team is often a good occasion for them to improve their food intake, both in quantity and in quality. Severe acute functional side-effects in older patients can be prevented with appropriate care since notable improvements in pain control and in oral intake during the course of radiation therapy are observed with aggressive clinical management [22]. New preventive treatments are emerging which provide measures to improve the quality of life during radiotherapy for head and neck tumours [23]. All patients, including elderly patients, will certainly benefit from such treatments.

Approximately 40% of patients in the present study survived at least 5 years. The fact that the age groups over 65 are under-represented decreased the number of patients available for late effect examination, leading to possible less reliable results than for acute toxicity. However, it represents, as far as statistics is concerned, a sufficient proportion of patients at risk from developing late complications. A low overall actuarial late complication-free survival rate of 18% at 5 years was found. There was no difference between the various age groups, which is why all data were pooled in a single curve (Figure 3). This is a less favourable figure than the one published earlier on a subgroup of this patient population (protocol 22.811), which reported on a 50% complication-free survival at 5 years [9]. The difference is provided by the fact that we chose to encompass all side-effects in analysis whereas, in the ma-

jority of studies, grade 1 late effects were ignored. It is well known by radiotherapists that, after some years, all patients irradiated in head and neck area develop some degree of fibrosis or xerostomy that can be scored as grade 1. We judge it is a misconception not to know about these mild complications, as even a grade 1 xerostomy or pain can cause nutritional problems or discomforts.

With respect to local-control and overall survival, there was, again, no difference between the various age groups (Figures 1 and 2). An identical local control throughout the entire lifespan covered in this study indicates that, within these age limits, the prognosis was not influenced by age. The frequent belief that older patients suffer from less aggressive tumours [24] is thus not supported by the present data. In addition, since all patients within each treatment protocol received the same irradiation, it can be inferred that the tumours were of equal radiocurability, i.e. the tumour proliferation rate, the tumour growth fraction, the level of tumour oxygenation etc. were not dependent on the age of the patient.

The absence of difference in 5 year overall survival between the various age groups reinforces the previous conclusion as it indicates that further disease dissemination beyond the locoregional level was both uncommon which is not unexpected for head and neck tumours—and similar in all age groups. Intercurrent death was also not a frequent event because of the selection bias introduced by the trial protocols. In an unselected population, overall survival would have been worse in older patients due to a higher intercurrent death rate. This is further supported by the finding of a trend toward a better performance status in the patients over 65 years of age included in these EORTC trials.

These considerations can, therefore, not be straightforwardly applied to the general population. One difficulty in treating older patients is determining where on the very broad spectrum of biological age a particular patient fits [25]. The present data indicate that independently of age, patients aged up to 75 and with a good performance status (0 to 2) can benefit from curative radiotherapy. The probability of local-control, of 5 year survival and the toxicity profile are similar in all age groups of patients.

Issues, such as 5 year survival, are of growing importance to large numbers of elderly cancer patients, and achieving extended quantity of life, as well as enhanced quality of life, has become a primary clinical research goal [26]. The definition of reliable selection criteria for discriminating among elderly patients those who will benefit from radical treatments and those which would better be treated with less aggressive, palliative modalities is, therefore, a priority [27]. The use of an age limit as a guide for head and neck cancer therapy is not a good strategy.

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