

Radiotherapy

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Age is the most important risk factor for the vast majority of cancers. More than 50% of tumours arise in patients over 60 years of age. This justifies the increased interest in the topic of 'cancer in the elderly', particularly from therapeutic point of view. As far as radiotherapy is concerned, the issue of tolerance to ionising radiation appears to be the main problem. Elderly patients with cancer are prone to suffer from co-morbid conditions such as diabetes or atherosclerosis, which might alter their ability to support long and sometimes aggressive treatments [1]. Age per se is only indirectly correlated with this lesser tolerance.

Particularly relevant to this topic is the observation that patients sent to receive radiotherapy treatment have often been selected in the past because it was thought their supposedly too advanced age would preclude them coping with radical surgery. Indeed, mortality at 30 days increases with age, but recent advances in anaesthesiology have decreased, to a large extent, the difference between younger and older patients. This is discussed elsewhere in this educational book. It is, however, important to mention that this fact is the cause of much debate between radiation and surgical oncologists since comparative series between the two modalities are invariably biased by large differences in the age structure of the series (mean age usually varies between 5 and 10 years).

Radiobiological experimental data dealing with the age of cells are limited. The survival curve of normal human fibroblasts was found to be similar and independent of the donor's age [2], yet the proliferative potential depended on age [3].

Lung cancer

Patients with lung cancer which is inoperable for medical/technical reasons or because of age are often sent for radiotherapy [4,5]. A radical irradiation, up to doses of 60–65 Gy, achieves usually good palli-

ation and can even be curative for small tumours (less than 4 cm).

A prospective longitudinal study in a group of 45 patients irradiated for breast or lung cancer and whose age varied between 61 and 86 years (mean 69.8 years) showed that radiotherapy was equally well tolerated, independently of age, but not of body weight or performance status. The majority had one or more comorbidities [6], but no one experienced any major change in lung functional status.

Breast cancer

In a series of 2268 patients with breast cancer and aged 55+ years it was found that the stage of the disease was unknown twice as often in the older age group (18%) compared with the younger one (8%) [7].

Patients aged 75+ years are frequently denied access to adjuvant radiotherapy; they are treated by surgery alone or surgery with hormonotherapy. This attitude cannot be recommended since cancer tends to be diagnosed at a more advanced stage in older patients.

A retrospective study (492 patients) has shown in a multivariate analysis that, after correction for stage, younger patients were more often offered a conservative approach than older ones (age varied between 24 and 81 years, mean 54 years). Moreover, axillary dissection was more frequently omitted in older patients and the total dose of radiotherapy, when it was delivered, tended to be lower in this same group. Finally, a compensatory irradiation of the axillary lymph nodes, when a dissection was not performed, was infrequent [8].

The omission of an adequate adjuvant irradiation can have a negative impact on the result of the treatment since local recurrences tend to occur during the first four years of follow-up, i.e. relatively early and therefore before the patient dies from another cause [9]. The substitution of adjuvant radiotherapy

by hormonotherapy must be restricted to women with a clearly short life expectancy. In a group of patients treated in Rochester, there was a preference for conservative surgery without radiotherapy in older women, an attitude which had to be abandoned since local recurrence rates reached 25% vs. 7% only in those who were irradiated [10]. This has been supported by other studies [11]. Whether adjuvant radiotherapy is needed in all conservatively treated cases has been tested in a randomised trial by Veronesi. Between 1987 and 1989, 567 women with small breast tumours (<2.5 cm) were randomised between quadrantectomy alone or surgery followed by radiotherapy. The incidences of local relapse were 8.8% and 0.3%, respectively. However, an age effect was suspected since post-menopausal women had only a 3.8% recurrence rate without radiotherapy [12]. The limited literature does not indicate any difference in early or late tolerance to the treatment in elderly patients [13,9].

A comparison of the local results of free tissue flaps for various localisations (including breast) in older patients previously treated with or without radiotherapy and/or chemotherapy showed that the success rates were high in all cases [55]. In a multivariate analysis, Van Limbergen et al. [14] could not find any influence of age on the cosmetic outcome of conservative breast surgery. Another paper dealing with the risk of developing a plexopathy after radiotherapy for breast cancer found no correlation with age (449 patients aged 18–92 years) [15]. The only predictor of plexus damage was a high dose per fraction.

Since most elderly women wish to keep their breasts, a comprehensive conservative approach including appropriate surgery and adjuvant radiotherapy should be offered to all, as long as the stage permits it [16,17].

Prostate cancer

The controversy regarding the optimal treatment of localised prostate cancer continues. The trend is to prefer radiotherapy in patients aged 70+ years [18]. With the current improvements in irradiation techniques (conformal radiotherapy and brachytherapy), the indication of radiotherapy is chosen more and more. A study from the Metropolitan Detroit Cancer Surveillance System has shown that awareness of radiotherapy as a treatment modality for elderly patients with prostate cancer (75+ years) is increasing. This may be responsible for a migration toward this type of treatment [19]. In a Dutch study, it was sus-

pected that this migration was actually not dependent on age since similar trends were identified in younger age groups [20]. The quality of life after treatment is influenced by urinary or digestive symptoms, the former consecutive to surgery and the latter to radiotherapy. This should be discussed with each patient openly and frankly in order to offer him the possibility to select whichever element of his personal quality of life he would accept to trade for local control of his disease. Regarding patient's choice, a recent Veteran Administration study revealed that elderly patients would rather accept impotence than urinary incontinence as a side-effect. However, older patients seemed less prone to accept impotence as a side-effect than younger, in spite of the rising incidence of impotence with age [21]. Appropriate information regarding treatment consequences is as important in elderly patients as in other age groups. The Pattern of Care Study and the series of the Fox Chase Centre in Philadelphia have shown that treatment results of patients aged 70+ years are similar to those registered in younger patients [22]. This was true for local control as well as for complications. Radiotherapy should therefore not be denied to older patients on the (wrong) basis of a decreased tolerance. In addition, since 3D conformal techniques tend to lower acute effects, it should be offered to all, regardless of age [23].

Gynaecological tumours

Women with cervical or endometrial cancer which are inoperable for medical reasons are usually sent for radiotherapy. There is one randomised trial concluding that radiotherapy offers an equal chance for cure as surgery in cervical cancer [24]. However, radical radiotherapy is not always possible in the presence of co-morbid conditions, indeed similar to those leading to inoperability. Again, age is not an appropriate stratification factor in this case; it is the performance status which must be thoroughly evaluated (and therefore the actual life expectancy) before switching from a curative to a palliative approach.

Daly et al. [25] analysed a group of 188 women irradiated in the pelvis and developing radiation ileitis later on. Age was not a prognostic factor, but women aged 75+ years or who were obese were irradiated with 1.8 Gy per fraction instead of the 2 Gy given to the others. Similar findings have been reported by others [26]. Data regarding the morbidity of brachytherapy have been extracted from a randomised study carried out at Institut Gustave Roussy. Two brachytherapy regimens were compared

in cervical cancer. After correction for tumour size and lymph node status, age had no influence on the prevalence of early or late effects, or on tumour control or overall survival [27,28].

Head and neck cancer

Because of the specific aetiological factors linked with these cancers, their frequency is particularly high in the elderly population. Loco-regional extension of the cancer can bring vital functions into danger: deglutition and phonation/respiration. Simple palliative measures are therefore seldom used. Old or fragile patients are less often treated by surgery alone or in combination with radiotherapy and/or chemotherapy; more often they are offered radical radiotherapy.

In a French retrospective radiotherapy study of 331 elderly patients, 104 had a medical contra-indication for general anaesthesia [29]. Mean age was 75 years (range 70–95 years). Regarding survival, the performance status was a much better predictor than age. Psychological problems (including confusion) did interfere with treatment in 8%, mainly in the group 80+ years. Furthermore, age had no clear influence on mucosal tolerance.

These data are further confirmed in a cohort of 277 patients in which body weight loss was measured weekly during radical radiotherapy and analysed, later on, as function of age. Mean age was 63.3 years (range 29–91 years); mean body weight loss was 4% (max 15%). If any trend could be identified, it was a larger weight loss in younger patients (non-significant). Patient age also had no influence on cancer-specific survival [30]. In contradiction with the former study in which 11 patients died from acute effects of radical irradiation, there was no treatment-related deaths in this series. This might reflect a positive selection of patients with a better performance status. Other groups have confirmed this data [31,32].

A much larger study has been carried out in the European Organization for Research and Treatment of Cancer (EORTC) database of 1589 patients with head and neck cancer included in 5 clinical trials between February 1980 and March 1995. Data regarding local control, survival, early and late tolerance were available in all trials. The mean age was 57 years (range 20–82 years), a relatively young group because of the restriction of eligibility for age (most trials excluded patients aged 70+ years). Twenty percent of patients were 65+ years only and 13% were 70+ years. Age was not a prognostic

factor for loco-regional control, weight loss, acute mucosal reactions as observed by the doctor or late effects. The only statistical significant difference was for subjective discomfort, as assessed by the patients themselves with a worse score in older patients. This discrepancy between objective and subjective scores for acute effects is interesting. Clearly, a similar grade of mucositis was less well tolerated in older patients, although the body weight loss was identical in all age strata [33].

The EORTC experience

The entire EORTC database has been screened to identify those patients who were included in clinical trials where the abdomen and/or pelvis were irradiated [34]; 1619 patients were identified from 9 trials initiated by the radiotherapy co-operative group or the gastro-intestinal group between 1975 and 1991 (rectum, prostate, bladder, uterus and anal canal). Mean age was 61 years (range 47–80 years). All patients were followed according to the strict protocol criteria regarding prospective scoring of treatment side-effects and complications. With respect to nausea and vomiting, young age was associated with a higher incidence if radiation volumes included the upper abdomen. A similar trend was found for mild to severe diarrhoea (grade 2 and 3). In contrast, acute effects on the skin and uro-genital tract, body weight loss, alteration of performance status were similar in all age groups. Regarding late effects, 80% of the patients had no symptoms after 5 years of follow-up. There was no difference in the incidence of small bowel damage, fibrosis or rectal complications.

Discussion

The most important problem for elderly patients treated with radiotherapy is the daily, five days a week, need to travel to the hospital. Inpatient treatment might help, but it creates other problems since the patient is cut from his/her familiar environment, a common cause of disorientation and depression. Accepting interruptions during treatment to cope with these difficulties might impair the chance for success; this cannot be recommended, nor the solution of using fewer but larger fractions in order to shorten the treatment. In this latter case, the risk of late effects might become unacceptable. Such an attitude must be strictly restricted to a palliative setting.

Before each treatment, a thorough analysis of the personal and familial characteristics must take

place and the consequences of the various treatment options should be openly discussed. In this respect, it is a good idea to work hand in hand with a social worker. Ideally, such a professional should be appointed in each radiotherapy department.

Regarding treatment strategy, a central problem is the dilemma between a radical and a palliative approach. Defining in this context what is exactly a palliative approach is a challenging intellectual exercise, but one can put things in the following way. Under given co-morbid circumstances a palliative schedule (with a lesser burden to the patient) will be offered to reduce the tumour burden for a period covering the life expectancy, whereas a radical treatment would be theoretically indicated. This implies that such an attitude should be restricted for the few people with an obviously short life expectancy.

The authors suspect that many retrospective studies in which age had a detrimental effect on the prognosis were biased by one or more of the following: inappropriate staging, unconventional treatment schedule, changing from a curative to a palliative approach, a delay in therapy, etc. It is admitted, for example, that in Hodgkin's disease the prognosis of patients over 60 years is not as good as in younger patients. Two reports, however, indicated that, provided older patients could receive the standard chemotherapy with an appropriate timing, the outcome of treatment was similar in all age groups. Therefore, the supposedly worse prognosis of older patients identified in some trials might reflect alterations in the standard chemotherapy schedule [35,36].

In conclusion, patient with a good performance status tolerate radiotherapy whatever their chronological age. There is no influence of age on loco-regional control, nor on the side-effects and complications. Treatment 'de-escalation' is never a solution, unless the life expectancy of the patient is obviously very short, i.e. the survival time will certainly be shorter than the duration of palliation. This is very seldom the case in potentially curable tumours.

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