22 Feasibility of Combined Chemo- and Radiation Treatment in Elderly/Comorbid Patients

Hans Geinitz

CONTENTS

22.1 Introduction

There is growing evidence from retrospective studies that radiation therapy in elderly patients is effective and well tolerated (Geinitz et al. 2005; Baumann 1998; Pignon et al. 1996, 1997, 1998). Most of the patients treated within these studies received radiation therapy either as the sole anti tumour agent or in conjunction with surgery in a neoadjuvant or adjuvant fashion. Only a few analyses deal with combined chemo- and radiation treatment in elderly patients. Large prospectively conducted studies assessing the safety and effectiveness of combined radio-chemotherapy in elderly patients are lacking. On the other hand, the evidence for the superiority of radio-chemotherapy over radiation therapy alone in the elderly is limited since many study protocols either definitively exclude patients above the age of 70 years from participation or the contributing physicians are not willing to enter these patients on the trial. The underrepresentation of elderly patients in cancer-treatment trials is still an unsolved problem (Hutchins et al. 1999).

Older patients tend to be less often screened and subsequently more often present with advanced disease (Clark et al. 2004; Berkman et al. 1994). Disease staging is often carried out less accurately than in younger patients with malignant diseases (Wylie et al. 1998; Yancik and Ries 1994). Lastly, elderly patients are more often treated inadequately or not treated at all (Merchant et al. 1996; Berkman et al. 1994; Samet et al. 1986). The reasons for these age-related variations are not entirely clear. Patient's preferences and physician's attitudes play a major role and are influenced by the fear of excessive treatment toxicity as well as the common belief that cancer in the aged is in general less aggressive than in their younger counterparts (Berkman et al. 1994). Recent advances in supportive cancer therapy may not have been acknowledged by elderly persons as well as their primary care physicians.

22.2 Demographics

In the next decades oncologists will be confronted more and more with cancer in the elderly. Life expectancy has steadily increased in industrial countries over the past 100 years. With advancing age, cancer incidence and cancer death arise in a near exponential fashion (Geinitz et al. 1999). In the United States the total number of newly diagnosed cancer in persons aged 75 years or older is expected to increase nearly threefold from 389,000 in the year 2000 to 1,102,000 in the year 2050, a rise from 30 to 42% of the cancer population aged 75 years or older (Edwards et al. 2002). The further life expectancy of a 70-year-old woman in Germany is still 15.7 years, and that of a 70-year-old man is 12.8 years (Federal Statistical Office of Germany, life

H. Geinitz, MD
Department of Radiation Oncology, Klinikum rechts der Isar der Technischen Universität München, Ismaninger Strasse 22, 81675 Munich, Germany

table 2002/2004; www.destatis.de). These time spans are too long to a priori choose a palliative therapy regime in patients whose malignant tumours are potentially curable with radio- or radio-chemotherapy. Most cancer recurrences occur within 2–5 years after treatment. Since there is no unequivocal data that malignant tumours are per se less aggressive with advanced age, recurrences will be experienced also by the elderly patient with all the negative consequences on the patient's quality of life.

22.3 Comorbidity and Organ Function

Comorbidity and organ function are important cofactors that must be taken into account when assessing the indication for radio-chemotherapy. The prevalence of comorbid disease increases with age and organ capacity (renal, pulmonary and liver function) usually decreases with age (Ogle et al. 2000). The influence of concomitant disease on acute or late radiation toxicity has not yet been studied in great detail, but some investigators report that diabetes mellitus or hypertension have a negative impact on radiation side effects (Herold et al. 1999; Boehler et al. 1992). There is evidence that decreased pulmonary function limits the tolerated radiation dose to the lung (Mehta 2005). Concomitant disease as well as decreased organ capacity could impair the clearance of chemotherapeutic substances and consequently lead to toxic plasma- and/or tissue concentrations. Furthermore, concomitant disease might be more important to the overall prognosis of the patient than the malignant disease itself. Comorbidity- and organ-functioning scores might further help assigning the indication to radio-chemotherapy in elderly patients (Charlson et al. 1987).

22.4 Clinical Studies of Radio-chemotherapy in the Elderly

Clinical studies of radio-chemotherapy in the elderly are rare. Since the effects of radio-chemotherapy on the elderly are not very well known, study protocols often include lower radiation doses and/or less toxic chemotherapy protocols in this population than in younger patients (Jeremic et al. 1999a; Allal et al. 1999).

22.4.1 Head and Neck Cancer

Kodaira et al. (2005) carried out a phase-I trial in 15 elderly (≥70 years) or medically unfit patients with head and neck cancer that were treated with combined radio-chemotherapy. Patients had to have an Eastern Cooperative Oncology Group (ECOG) performance status of 0–2 and adequate organ function. In previously untreated patients radiation therapy was applied to a total dose of 60–66 Gy to the primary tumour and 66–70 Gy to involved cervical lymph nodes in 2-Gy fractions. Patients who had received radiation therapy to the neck before (n=5) were treated to doses of at least 39.4 Gy to the primary lesion in 1.8-Gy fractions with the cumulative dose of both radiation schedules not exceeding 100 Gy. Docetaxel was administered concomitantly once weekly over five consecutive weeks. The starting dose was 10 mg/m^2 which was escalated by 2 mg/m^2 following the treatment of at least three consecutive patients until a grade-3 toxicity occurred (with the exception of side effects concerning mucosa, skin and nausea which had to be at least grade 4). No patient experienced any grade-3 or higher haematological toxicity. Six patients developed grade-3 mucositis and 3 patients grade-4 mucositis, all of them in the 14-mg/m^2 dose group; thus, the recommended docetaxel dose was 12 mg/m^2 weekly over five consecutive weeks.

An Italian group prospectively evaluated postoperative radio-chemotherapy in 40 elderly patients with head and neck cancer and a high risk for loco-regional recurrence (Airoldi et al. 2004). Patients 70 years or older with an ECOG performance status of 0–2 who have had curative resection for squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx or larynx were entered on this trial. A total dose of 54 Gy was applied to regions at risk of microscopic disease and a dose of 64.8 Gy was given for positive margins or extracapsular nodal extension. Carboplatin was administered 45–60 min prior to irradiation at a dose of 30 mg/m^2 on days 1–5 of weeks 1, 3, and 5. Treatment was administered on an outpatient basis and 80% of the patients received all three cycles of chemotherapy. Grade-3 toxicity was observed for mucositis (25%), neutropaenia (15%), dermatitis (5%), and thrombocytopaenia (2.5%). No grade-4 toxicity occurred. One case of moderate osteoradionecrosis occurred as a late side effect. The 3-year local control rate was 79% and 3-year overall survival was 64%. These data compared favourably to matched controls 70 years or older who received postoperative radio-