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Treatment in elderly patients with head and neck cancer

A challenging dilemma

The elderly constitute the fastest growing segment of the population of Western countries. Despite an increasing number of human papilloma virus (HPV)-related cancers that affect young patients in particular, most head and neck cancers still occur mainly in patients over the age of 50 [1]. Because we lack a precise definition of "elderly" we cannot state the exact portion of such patients [2]. According to the literature, about 20–25 % of the head and neck cancer population is over the age of 65 [3]. Another problem is that chronological age does not coincide with biological "age." Head and neck cancer patients are often frail and frequently have multiple comorbidities due to their unhealthy lifestyle [4].

Prognostic factors and treatment decisions

Although age is not an independent negative prognostic factor in head and neck cancer treatment [5], nonstandard treatment is more frequently applied in elderly patients [6]. It is a common experience that patients who can potentially be cured may receive suboptimal treatment. It is very likely that the more frequent comorbidities, the obviously shorter life expectancy, and physician prejudices play a role in the decision-making process. In the study of Derks et al. [7], the following parameters were identified as significant prognostic factors for nonstandard treatment: marital status, cancer stage (IV), comorbidity, pain, patient considers length of life less important than quality of life, and age. Extended surgery is less frequently offered to elderly patients, and single-modality, nonsurgical treatment – preferably radiotherapy – is often preferred. In order to prevent treatment-related morbidity or mortality in this population, many patients may be undertreated. Therefore, abandonment of appropriate and standard curative treatment often leads to a deterioration in the prognosis and quality of life of these patients [8, 9]. Decisions about the treatment of elderly patients with head and neck cancer are often influenced by the challenge of predicting their treatment outcomes with respect to treatment tolerance, complications, quality of life, and survival. It is essential to find a balance between aggressive therapy and therapeutic nihilism in elderly patients [10]. Patients' preferences must also be considered. Elderly patients often prefer quality of life to life extension.

Current state of the literature

Based on these facts, there is a need for special attention to the treatment of elderly patients with head and neck cancer. However, the present literature does not provide enough firm recommendations. One should be aware that older people are underrepresented in the available studies. Patients over the age of 70 are often excluded from clinical trials because of multiple comorbidities requiring complex management that disqualify them. In this respect, however, it is important to mention that the willingness to participate in studies is not reduced in elderly patients [11]. Conversely, younger patients in terms of biological age are often overtreated when chronologic age assumes inappropriate importance. The next problem with the hitherto published studies is their limited significance. Elderly patients recruited for studies reported in the literature are often a selected small group. Studies are often of retrospective nature with heterogeneous therapy patterns lacking data on comorbidities, causes of death, and therapy-related toxicities. Therefore, currently, there are only limited valid data on elderly patients with head and neck cancer. The aim of this review is to identify and clarify the deficiencies of these studies.

Surgical treatment

Most retrospective studies analyzing the outcomes of surgical treatment in the elderly are biased by the selection of patients eligible for aggressive treatment. A comparison of data in these studies is very limited since the decision for surgical treatment is often not based on objective measures to assess patients' eligibility for surgery. Previous results have shown that patients of advanced age can be can-

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Abstract

Despite the increasing number of elderly patients requiring treatment for head and neck cancer, there is insufficient available evidence about the oncological results of treatment and its tolerability in such patients. Owing to comorbidities, elderly patients often need complex evaluation and pretreatment management, which often results in their exclusion from clinical trials. The question of which patients constitute the highest-risk groups regarding treatment-related morbidity and mortality, and who can tolerate and benefit from aggressive treatment, has not been adequately studied. Biologic rather than chronologic age should be a more important factor in treatment protocols. Age-specific prospective clinical studies are needed on the treatment of head and neck cancer in elderly patients.

Keywords

Head and neck cancer · Elderly · Comorbidity · Treatment · Survival

Behandlung der Patienten mit einem Kopf-Hals-Karzinom im fortgeschrittenen Lebensalter. Ein herausforderndes Dilemma

Zusammenfassung

Trotz zunehmender Häufigkeit der „älteren" Patienten mit Karzinomen im Kopf-Hals-Bereich ist insgesamt wenig über die onkologischen Resultate und Verträglichkeit der Therapie bei diesen Patienten bekannt. In klinischen Studien stellt fortgeschrittenes Lebensalter oft ein Ausschlusskriterium dar, weil für ältere Patienten aufgrund ihrer Komorbiditäten häufig eine aufwendigere Untersuchung und prätherapeutische Versorgung benötigt werden. Die Fragen, welche Patienten das höchste Risiko bezüglich therapiebedingter Morbidität und Mortalität aufweisen und welche Patienten von einer aggressiven Therapie profitieren und diese vertragen, sind nicht adäquat untersucht worden. Für Therapieentscheidungen sollte eher das biologische Alter als das chronologische Alter Berücksichtigung finden. Altersspezifische prospektive klinische Studien zur Behandlung von Patienten mit einem Kopf-Hals-Karzinom im fortgeschrittenen Lebensalter sind erforderlich.

Schlüsselwörter

Kopf-Hals-Karzinom · Alter · Komorbidität · Therapie · Überleben

didates for extensive surgical treatment. Some authors argue against extensive surgical treatment in this patient population, especially with regard to the application of microvascular free flap reconstructive methods [12]. However, reports show equal success rates in flap surgery between elderly people and younger patients. Most studies have shown that extensive surgical treatment in the form of laryngectomies, neck dissections, and myocutaneous flap reconstructions did not produce a higher incidence of mortality and was associated with acceptable incidences of complications [13–15]. The role of comorbidity as a predictive factor for postoperative complications in elderly head and neck cancer patients is not obvious [6, 16]. Some studies find a positive correlation between comorbidity and complications in elderly [17], while others do not [18]. The correct conclusion drawn from these studies should be that, with proper selection, elderly head and neck cancer patients may be eligible for extensive surgical treatment.

Radiotherapy and chemotherapy

There are only a few studies available to directly compare outcomes among different age groups after radiotherapy. The value of therapy in the elderly was evaluated in an analysis of five prospective European Organisation for Research and Treatment of Cancer (EORTC) studies with over 1,500 patients with head and neck cancer receiving curative radiotherapy [19]. About 20 % of the patients were older than 65 years. The locoregional control rate was independent of age. There were no significant differences found in early and late toxicity or weight loss in different age groups. However, older patients experienced mucositis-related symptoms more frequently than did younger ones. The authors concluded that there is no age limit for radiotherapy for head and neck cancer. One major shortcoming of this study is the inclusion of patients only up to the age of 75. That study suffers from a selection bias, as only patients with a good performance status were analyzed, thus very likely accounting for an equal overall survival rate of all included patients. Furthermore, radiotherapy-related toxicities were not adequately analyzed, and in two out of five studies chemotherapy was administered in addition to irradiation. In another retrospective study of 2312 patients, tolerance of radiotherapy was compared between patients over 75 years of age (20 %) and a younger cohort [20]. No differences were found in both age groups regarding unplanned radiotherapy interruptions, non-completion of radiotherapy, and treatment-related death as indicators of treatment tolerance. In this study there were no data available on comorbidity and performance status of the patients. In the meta-analysis of 15 randomized studies by Bourhis et al., which included more than 6500 patients, conventional radiotherapy was compared with radiotherapy with altered fractionation [21]. The absolute survival benefit after 5 years for patients receiving fractionated radiotherapy was 3.4 % (hazard ratio [HR], 0.92). Patients over 70 years did not benefit from hyperfractionated compared with conventional radiotherapy (HR 1.08). The study lacks data on radiotherapy-related toxicities and comorbidities. Non-cancer- related deaths were also not considered.

In the well-known meta-analysis by Pignon et al. of 93 randomized trials including more than 17,000 patients, the effects of chemotherapy in combination with radiotherapy in head and

neck cancer were analyzed [22]. The absolute survival benefit after 5 years in patients receiving chemotherapy was 4.5 % (HR, 0.88) and in patients receiving concomitant chemotherapy 6.5 % (HR, 0.81). In patients over the age of 71, no survival benefit from chemotherapy was observed (HR, 0.97). The results of this meta-analysis became the basis for treatment recommendations in elderly in many centers. However, underlying studies of this meta-analysis reveal relevant deficiencies. Comorbidities were not considered in 30 % of the pooled studies. Causes of death are only reported on in more recent studies. Non-cancer-related causes of death were not considered; more importantly, chemotherapy-related deaths were not analyzed. It remains unknown whether the lack of benefit in the elderly is caused by their chronological age or by other characteristics, such as frailty, performance status, comorbidities, etc. In addition, only 4 % of the patients were older than 71 years in this meta-analysis. It is not certain if the results for the entire cohort of studied patients are applicable to this small subgroup of patients older than 71 years.

Cetuximab has gained an increasing role as a molecular targeting agent in the treatment of head and neck cancer. Better survival and locoregional control rates have been reported for cetuximab in young patients with good performance status in combination with radiotherapy versus radiotherapy alone [23]. These results were demonstrated to some degree for cetuximab in combination with platinum-based chemotherapy versus chemotherapy alone [24]. However, these trials are not able to determine the efficacy and safety of cetuximab in elderly head and neck cancer patients. To date, no age-specific trials exist that clarify the value of cetuximab in elderly patients.

Conclusion

Despite limited availability of data, it can be concluded that chronological age alone should not preclude the use of a curative protocol by surgery or radiotherapy in patients with head and neck cancer. The efficacy and safety of chemotherapy in the aged population need to be further investigated. Patients with advanced age can benefit from standard therapeutic options. The question of which subgroup of patients presents the highest risk of treatment-related morbidity and mortality, and which can tolerate aggressive treatment and benefit from it, cannot be answered.

In the future, age-specific prospective clinical studies are needed considering elderly patients independently from their performance status. The decision-making process for planning treatment of elderly patients should consider the patients' biological age, which should take several factors into account, such as comorbidities, functional, nutritional, cognitive, psychological, and performance state. The patient's preferences should be regarded before the prejudices of caregivers. The implementation of geriatric tools, as part of a comprehensive assessment, in the clinical management of elderly head and neck cancer patients might assist in making individualized treatment decisions, although their value in head and cancer has yet to be clarified [25].

Brief summary

- **There are only limited valid data on elderly patients with head and neck cancer available.**
- **Despite the limited availability of data, it can be concluded that chronological age alone should not preclude the use of aggressive treatment in elderly patients with head and neck cancer.**
- **Comorbidities, disabilities, frailty, and impaired functional status are considered to be more relevant criteria than chronological age for decision making in elderly patients with head and neck cancer.**
- **Abandonment of appropriate and standard curative treatment of elderly head and neck cancer patients often leads to a deterioration of their prognosis and quality of life.**

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Compliance with ethical guidelines

Conflict of interest. A. Teymoortash, A. Ferlito, and G. B. Halmos state that there are no conflicts of interest.

The accompanying manuscript does not include studies on humans or animals.

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Buchbesprechung

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Patientenverfügungen

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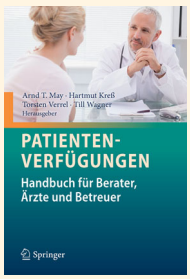

Wenn 4 namhafte Herausgeber mit 46 weiteren Autoren sich in 45 Beiträgen auf 441 Seiten mit ethischen, weltanschaulichen, rechtlichen und medizinischen Aspekten von Patientenverfügungen befassen und auch den beratenden Aspekt dazu sowie zu weiteren Themen (Kinderwunschbehandlung, genetische Beratung, Organ-Lebendspende, Suizidgefährdung, Bestattungsregelungen) aufgreifen, dann darf der Leser erwarten, dass nun tatsächlich alle denkbaren Facetten zum Umgang mit Patientenverfügungen berücksichtigt werden. Der Leser wird nicht enttäuscht. Selbst die Sichtweise muslimischer Patienten und buddhistischer Traditionen finden Beachtung neben der christlichen Sicht. Juristisch fundiert von den verfassungsrechtlichen Grundlagen über das Betreuungsrecht bis zur Vorsorgevollmacht finden sich Beiträge ebenso wie zu medizinischen Fragen, nicht nur seitens der Intensiv- und Notfallmedizin oder der Problematik der künstlichen Ernährung, auch zur Schmerztherapie, der Hirntoddiagnostik und der Organspende. Die Rolle der Palliativmedizin wird thematisiert mit u.a. Angeboten und Formen der spezialisierten ambulanten Palliativversorgung (SAPV), beispielhaft auch der Umgang mit dem Krankheitsbild der amyotrophen Lateralsklerose. Auf dem Markt befindliche Broschüren und Muster für Vorsorgedokumente werden betrachtet. Das Buch wird dem Anspruch eines Handbuches für Berater, Ärzte und Betreuer umfassend gerecht und kann ohne Einschränkung allen Interessierten wärmstens empfohlen werden.

R. Dettmeyer (Gießen)