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EDITORIAL

On the need for comprehensive assessment of impact of comorbidity in elderly patients with head and neck cancer

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Although a generally accepted definition of "elderly" still does not exist, in a medical context, persons over the age of 65 are often considered to be elderly. As life expectancy rates have increased within the last decades and continuously increase every year by approximately 3 months [1], this segment of the population has increased, particularly in Western countries. Because cancer is a disease of aging, the risk of developing malignant disease including head and neck cancer is highest in this patient population. It also follows that malignancy-related mortality is highest among the elderly.

Younger patients with head and neck cancers have a much better overall prognosis. A comparative survival analysis revealed that patients with head and neck cancer who are aged 40 years or younger at the time of diagnosis show significantly improved 5-year survival when compared to older patients [2]. For all age groups the 5-year survival rate of patients with a newly diagnosed head and neck cancer is approximately 60 % at diagnosis. However, prognosis is a dynamic process that improves after the initial critical years of recurrence-free survival. Conditional relative survival shows clinically relevant variations according to time since diagnosis, type of cancer, and age [3]. Conditional survival rates can better analyze and reflect actual life expectancy. After 3 years of survival, the conditional survival rate improves from 60 % up to 80 %. However, long-term survival rates stagnate at 80 %. Patients cured of and neck cancer face an excess mortality of about 20 % in long-term follow-up [4]. The critical reason for this is attributed to the comorbid burden of head and neck cancer patients, connected with unhealthy habits and general lifestyle choices.

Comorbidities in cancer patients are defined as one or more unrelated diseases present at the time of cancer diagnosis. Particularly in elderly patients, these predominantly consist of reduced organ and cognitive functions, malnutrition, polypharmacy, and socio-economic factors. Most studies show that approximately 60 % of head and neck cancer patients have concurrent illnesses [5]. For better evaluation of comorbidities, weighted assessment systems like Adult Comorbidity Evaluation-27 (ACE-27), and Charlson Comorbidity Index (CCI) include the occurrence of comorbidities as well as their degrees. Comorbidities exist in 46 % of head and neck cancer

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patients evaluated by CCI, with mild forms in 17 % of cases, moderate in 9 %, and severe forms in 10 % [6]. The existence of comorbidities increases with age. However, it declines beyond the age of 70 [7], suggesting that cancer survivors of this age have pursued a more healthy lifestyle or that those with high comorbid burden have already died.

Although most patients with head and neck cancer have curative-intent treatment plans with fair outcomes, the overall survival rate is influenced not only by recurrence but also by non-cancer causes. The overall survival rate declines with age because non-cancer related mortality is directly related to the severity of comorbidities. The cancer-specific mortality rate, however, remains independent of comorbidities [6]. This means that treatment outcomes are adjusted across different age groups for tumor stage, comorbidity burden and treatment intent [8].

As a result of comorbidities, patients who can potentially be cured may receive suboptimal treatment. Information on the disease itself and appropriate treatment modalities are often withheld during education of older patients who are often not sufficiently integrated into the decision making process regarding their treatment plan. Complex and expensive diagnostic tools may not be used, and multimodal therapy and extensive surgical procedures are often not applied. Denial of curative treatment to elderly patients may often produce an adverse effect by prolonging the patient's distress and increasing costs due to the need for long-term palliative care. Progression of suboptimally treated malignant disease can result in poorly controlled symptoms associated with persistent locoregional disease including dyspnea, dysphagia, tumor bleeding and ulcerations, and intractable pain. Abandonment of appropriate and standard curative treatment thus often leads to deterioration of prognosis and quality of life [9, 10].

The greatest challenge in the treatment of elderly head and neck cancer patients is the prediction of post-treatment outcome. It is known that the prediction of postoperative complications or radiotherapy-induced toxicity is much more difficult in the elderly than in the non-elderly population [11, 12]. Comorbidity as measured by different assessment systems does not seem to be sufficient to answer important questions such as expected post-treatment complications and the effects of cancer treatment on quality of life and survival. Such predictions would help in selecting appropriate elderly patients who might benefit from aggressive treatment.

Instead of analyzing only comorbid conditions, the comprehensive geriatric assessment (CGA) has been developed as a new holistic screening tool. The CGA includes, in addition to comorbidity evaluations, several other validated tools for evaluating functional, nutritional, cognitive and psychological status, social support, and physical performance [13]. The CGA has been found beneficial for predicting treatment-related complications as well as preventing hospitalization and geriatric syndromes, recognition of cognitive deficits, and improving survival [14, 15].

Functional status and physical performance can be evaluated by different activity of daily living (ADL) and instrumental ADL (IADL) tests. ADL evaluation focuses on the basic skills to maintain independent activities at home such as bathing, dressing, self feeding, and mobility. IADL tests assess ability to function independently in the community activities, such as shopping, transportation, and housework. CGA studies have demonstrated the predictive value of these ADL/IADL tests with regard to survival, postoperative morbidity and mortality, and chemotherapy toxicity [13]. As an alternative to time-consuming evaluations, some very simple measures have been developed to evaluate functional performance, such as the "Timed Up & Go", which appears to be valuable for predicting postoperative complications after oncologic surgery [16]. Shortened forms of CGA have been proposed, although they require validation in routine clinical settings [17].

Nutritional state at the time of diagnosis of cancer as well as during the treatment process is of high importance. Several validated measurement tools are available for screening feeding status, such as the Nutritional Risk Screening 2002 questionnaire or the Malnutrition Screening Tool (MST) [18]. These tests help clinicians identify high-risk patients who would benefit from active nutritional support such as pre-treatment preventive nasogastric or percutaneous feeding tube placement, as was recently reported in a series of head and neck cancer patients [19].

The importance of evaluation of cognitive state is highlighted in the literature. At initial screening, up to 50 % of elderly cancer patients were found to have cognitive abnormalities that needed further analysis. Impaired cognitive function was related to higher tumor stage at diagnosis, lower chance of curative treatment and significantly worse survival [13]. Another important aspect is the prediction of treatment-related decrease of cognitive function. This consideration seems to significantly influence choice of treatment. Almost 90 % of seriously ill elderly cancer patients would not choose treatment if the outcome was survival with severe cognitive impairment [20]. The most commonly used cognitive state screening tool is the Mini-Mental Status Exam (MMSE).

The most important issues in the analysis of the psychological status of elderly cancer patients are depression and anxiety. A large proportion of elderly cancer patients (up to 40 %) have depression, associated with high clinical and also social impact. A large prospective study showed that depressed patients have a higher risk of postoperative complications and worse survival [12, 21]. Although

several tools, such as the Geriatric Depression Scale, have been developed most studies have employed the psychological domain of different quality of life tests [22]. Beyond clinical relevance, depression has several social implications; thus psychological status is usually evaluated in conjunction with available social support.

CGA is time consuming and, as a result, is often neglected in clinical settings. In the last decade the new concept of frailty has been developed. The term frailty refers to the ease with which a minor stressor can have a major impact on the physical state of a vulnerable patient. It can be explained by the decrease of physiological reserves through the accumulated decline of multiple organ systems [18]. Frailty questionnaires are designed to include somatic, functional, and psychosocial domains which are suitable for quick screening to select patients for thorough analysis by CGA. This two-stepped screening method could save time as it would identify fit patients who do not require CGA. Although several validated frailty screening instruments are in use, the specificity of these tools has been rather disappointing in elderly patients with cancer.

Although several publications have reported experiences with CGA in cancer patients, there has been only a single prospective study reported on surgically treated head and neck cancer patients [23]. A recent review of this topic mainly includes CGA studies performed for sites other than head and neck [14]. Experience with CGA in the non-surgical treatment of head and neck cancer is also limited [24]. A multicenter, prospective study is needed to clarify the value of CGA in head and neck cancer.

Finally, it should be mentioned that a multidisciplinary approach especially among surgeons, oncologists, and radiation oncologists is key to successful treatment of head and neck cancer. Multidisciplinary care in elderly should be an integrated team approach considering all relevant treatment options and develop collaboratively an individual treatment plan for each patient.

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