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# Managing older patients with head and neck cancer: The non-surgical curative approach

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ABSTRACT

Managing older patients with head and neck cancers poses a challenge due to the often reduced levels of physiological reserve, the frequent comorbidities and treatment related toxicity. These factors have implications on speech, breathing and swallowing functions. Treatment management plans in these patients may result in de-intensification strategies and as a result of this, use of non-standard treatments is increasing. There have been published reports that indicate the addition of concurrent systemic therapy to radiation in selected older patients is feasible, and produces outcomes comparable with younger patients. However, some other studies including meta-analyses suggest a lack of real survival benefit with the addition of chemotherapy. So, the key point appears to be the optimal patient selection. Appropriate geriatric and frailty assessments are required to help determine the optimal treatment for older patients with head and neck cancer. Treatment for this population still needs to be well defined and optimized in both modality and intensity.

Qualitative studies are also required to address short and long-term post-treatment quality-of-life and survivorship issues in this specific patient population. This review summarizes the evidence available regarding the non-surgical management of older patients with head and neck cancers.



## 1. Introduction

Primary Head and Neck Cancer (HNC) constitutes the sixth most common malignancy worldwide, representing approximately 6% of all new cancer cases [1]. Although the majority of HNC occur during the fifth and sixth decades of life, approximately 25–40% of the patients are over 70 years old, with this figure expecting to rise due to increased life expectancy in general [1,2]. There is evidence that older patients with HNC might receive less aggressive and suboptimal treatment when compared to younger patients with the same disease status [3,4]. However, it is not clear whether older patients might really benefit from more aggressive therapies. In the meta-analysis evaluating the impact of adding concurrent chemotherapy to radiation or employing altered fractionation regimens, no advantage was shown for patients >70 years old [5,6]. Other retrospective series suggested that with careful selection, older patients may achieve similar outcomes to younger patients with combined treatments, although with a higher burden of toxicities. The lack of solid data comes from the fact that older patients with HNC are less likely to be enrolled in prospective clinical trials, accounting for only around 5% of trial participants according to a meta-analysis of 93 studies [5].

Age related biological changes cause a decline in multiple physiological functions. Due to this, treatment decision making in older patients requires vigorous evaluation and risk assessment. Older patients are potentially at increased risk of treatment related toxicities due to the alterations in pharmacokinetics and pharmacodynamics resulting from age-related physiological changes [7].

The objective of this current review is to discuss and summarize the evidence available for the non-surgical treatment of older patients with HNC.

## 2. Geriatric Assessment of the Older Patients With Head and Neck Cancer

### 2.1. Definition of "Old"

There is no universal agreed definition of old and many synonyms are frequently used such as older patients, geriatric, senior adults, advanced age. Pallis et al. in his European Organization for the Research and Treatment of Cancer (EORTC) older patient task force position

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paper took 70 years as the cut-off for old age, [8] while Porceddu and Haddad, in their recent review, defined old as 65 years or above [9]. European Medicines Agency considers 65 years of age as the cut-off for the definition of "old" patients [10]. The National Institute of Health and the National Institute of Aging use three categories of age cut-off to define old; they consider 65–74 years old as "young old", 75–84 years as "older old" and 85 years and above as "oldest old" [11,7]. Patients with HNC often suffer from multiple comorbidities and are more at risk of complications because of disease related malnutrition. In addition, these patients are more at risk of complications due to alcohol or smoking addictions. Therefore the age limit of 65 years may be more appropriate for this specific patient population with HNC.

### 2.2. Definition of Frailty

Frailty is a syndrome of advancing age characterised by immune dysregulation, chronic inflammation, sarcopenia, increased cellular senescence and loss of resilience. Fried et al. described frailty as a clinical syndrome in which at least three of the following criteria are present: unintentional weight loss (≥10 lb in past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity [12]. Frail older adults have chronic conditions, difficulty maintaining independence and geriatric syndromes. Therefore, they may be more vulnerable to therapy related toxicities. They may also have less substantial lasting benefit because of comorbidities and related earlier mortality.

### 2.3. Role of Geriatric Assessment

The geriatric assessment is a multidimensional, inter-disciplinary evaluation to determine the physiological age rather than the chronological age of a patient. It is particularly challenging for the treating clinicians/multidisciplinary team (MDT) to differentiate between the "fit" or "unfit" older patients for aggressive or gentle management strategy, respectively. Fit older patients have been shown to tolerate aggressive cancer treatments just as well as their younger counterparts with similar outcomes [13–15]. Adequate assessment of the older patient group to see if they are fit enough for radical treatment is the key. Failure to adequately assess these patients can lead to either under-treatment or over-treatment with radical aggressive therapy which may add problems to their existing symptoms, thus affecting their quality of life [2].

The comprehensive geriatric assessment (CGA) is a systematic and holistic method to assess physiological age rather than the chronological age of a patient per se [16]. The CGA is a validated tool through which the evaluation of different parameters such as cognition, functioning, physical and emotional status, nutrition, and co-morbidities. It also predicts morbidity and mortality in community-dwelling older adults. The components of the CGA have also been shown to influence clinical decision-making and predict outcomes in older patients with cancer. The combined data from the CGA can be used to stratify patients into risk categories to better predict their tolerance to treatment and risk for chemotherapy toxicity. The CGA is now considered the "gold standard" method to assess older patients individually and there is evidence that it can significantly change outcomes in up to 21–49% of older patients with solid malignancies [17]. There is also strong evidence that the CGA improves function and reduces hospitalization in older patients [18]. However, there is little data on the use of the CGA in prospective HNC trials. The CGA is a comprehensive tool requiring significant time and training to perform. Implementation of the CGA for every patient above 65 or 70 years old is laborious and resource-intensive in a busy clinical practice. Therefore, there is a role for pre-CGA screening, to identify those who may potentially benefit from a CGA assessment. There are many validated geriatric assessment tools available; one commonly used is the Geriatric 8 (G8) [19]. Pottel et al. compared the G8, the Vulnerable Elders Survey-13 (VES 13) and the "gold standard" CGA at baseline prior to radio chemotherapy. The G8 appeared to correlate better than the VES-13 and was thought to be a good way to distinguish fit from vulnerable patients as a "screening tool" [16]. The result was validated in their subsequent study which showed that dividing patients into fit and vulnerable groups based on G-8, the vulnerable patient group experienced significantly lower quality-adjusted survival, and overall survival as compared to the fit patient group [20].

## 3. Patient Selection to Define Tailored Treatment Intensity

There are no specific guidelines offering firm recommendations about the most adequate therapeutic strategy for older patients with HNC. Moreover, the lack of older patients with cancer recruited into clinical trials causes a huge problem in building evidence based treatments. This lack of older patients with cancer in clinical trials has been highlighted by geriatric societies, which recommend performing older patient-specific clinical trials with a comprehensive geriatric assessment and predictive models for treatment choice.

A comprehensive assessment of an older patient's comorbidities, functional status, functional reserves and their susceptibility to toxicity needs to be carried out in order to tailor their treatment and supportive care. In older patients with HNC, the potential benefit from potentially toxic treatments on patient outcomes could be outweighed by treatment related morbidity. This risk of harm should be clearly assessed in the shared decision making process [21].

In light of recent therapeutic improvements, managing comorbidities is becoming an increasing issue in HNC which deserves attention [22]. For instance, dysphagia after curative treatment may lead to an increased risk of pneumonitis, which is often under-recognized due to silent aspiration, causing an increased mortality risk persisting even several months/years after treatment ends [23].

Cardiovascular toxicity has been reported as a major source of morbidity and cause of death in older patients; the interaction of risk factors (smoking, comorbidities, etc.) and treatment toxicities may contribute to an increased risk in the older HNC population [24]. For these reasons, the selection of optimal treatment options is vital. It is also necessary to address the need of allocating supportive and rehabilitative resources when patients undergo intensive treatment.

Patient selection through the CGA can improve functional status and survival. In addition, patient selection through the CGA can reduce hospitalizations and nursing home stays. Moreover, it may detect unsuspected conditions and unaddressed problems. In addition, the CGA improves function, outcomes, and possibly patient survival.

However, data reviewing appropriate patient selection, optimal time of intervention and which treatment modality to be used is limited and heterogeneous in HNC. Recently, the first set of data about the ELAN-ONCOVAL (ELderly heAd and Neck cancer-Oncology eValuation) study has been presented [25]. The trial enrolled patients older than 70 years who were not amenable to surgery and stratified those patients using a geriatric assessment to deem patients fit or unfit. They found that the geriatric assessment changed the treatment planned after oncological evaluation alone in 8% of cases, due to the addition or deletion of systemic therapy. In addition, the rate of patients requiring multidisciplinary interventions was significantly higher when the assessment was performed by geriatricians (71% vs 51%). These results showed the importance of cooperation with geriatricians in the decision-making process and the integration of the geriatric assessment into a patient's evaluation. Other trials are ongoing in this field and they will help find the right place for the geriatric assessment in the definition of a tailored treatment approach. A large randomized trial, Comprehensive Geriatric Assessment and Head and Neck Elderly Cancer Patients (EGéSOR) is enrolling patients with HNC who are 65 and older. The patients are randomized to the standard of care group or the CGA group to assess the impact of the geriatric evaluation and to follow-up on the overall survival, the functional status, and the nutritional status of