

A specific approach for elderly patients with head and neck cancer

Cécile Ortholan^a, Karen Benezery^b, Olivier Dassonville^c, Gilles Poissonnet^c, Alexandre Bozec^c, Nicole Guiochet^a and Yazid Belkacemi^{a,d}

Approximately 10% of head and neck (HN) tumors occur in patients aged more than or equal to 80 years. In this population, the main challenge for physicians is to deal with the benefit/risk ratio of treatments and tumor-related symptoms. As elderly patients are generally excluded from clinical trials, there is a lack of evidence-based data with regard to the most appropriate multidisciplinary management. The prevalence of frailty and the pattern of comorbidities in this specific population are still unknown. The management of these tumors in a geriatric context is complex due to the high risk of toxicity of locoregional treatments. Thus, physicians often have to adapt to the treatment schedule to decrease potential adverse effects even with a risk of undertreatment. A retrospective series reported that the treatment delivered to elderly patients presenting with HN tumor complies with an institution's policy in less than 50% of cases, emphasizing the need to assess the outcome of personalized/adapted treatment in geriatric patients. The major issue is to determine which adaptation could be carried out, and then, what could be the respective individual benefit/risk ratio of each adaptation. In this review, we will focus on the locoregional

management of elderly patients, and develop the issue of adapted local treatment. We will discuss the feasibility of adapted surgery and radiotherapy and provide current evidence-based data that may allow physicians involved in locoregional treatment of elderly patients with HN cancers to be acquainted with practical guidelines. Then, we will highlight the importance of nutritional support in this population in which the prevalence of malnutrition is high. *Anti-Cancer Drugs* 22:647–655 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Anti-Cancer Drugs 2011, 22:647–655

Keywords: geriatric oncology, head and neck cancer, old patients radiotherapy, surgery

^aDepartment of Radiation Oncology, Centre Hospitalier Princesse Grace, Monaco, Departments of ^bRadiation Oncology, ^cHead and Neck Surgery, Centre Antoine Lacassagne, Nice, France and ^dAssociation of Radiotherapy and Oncology of the Mediterranean arEa (Arome; www.aromecancer.org)

Correspondence to Cécile Ortholan, MD, PhD, Department of Radiation Oncology, Centre Hospitalier Princesse Grace, 98000 Monaco
Tel: +377 97 98 84 19; fax: +377 97 98 84 20;
e-mail: c.ortholan@wanadoo.fr

Received 28 December 2010 Revised form accepted 28 December 2010

Introduction

Head and neck (HN) cancers represent the sixth most common malignancy. Approximately 650 000 new HN cancer cases and 350 000 cancer-related deaths are reported worldwide every year [1], and approximately 10% of HN cancers are diagnosed in patients aged more than 80 years (<http://www-dep.iarc.fr>). Thus, physicians often have to manage the treatment of patients aged more than or equal to 75 years.

HN cancers represent a heterogeneous group of tumors requiring multimodality approaches. The management of these tumors in a geriatric context is complex due to the high toxicity of locoregional treatments, and physicians often have to adapt to the treatment schedule to decrease potential adverse effects in these frail patients. Moreover, elderly patients are generally excluded from prospective clinical trials resulting in a lack of evidence-based data with regard to the most appropriate treatment. Thus, data on the management and outcome of elderly patients with HN cancer are limited and mainly based on small retrospective series that included patients with a median age of approximately 70–75 years [2–11]. In the literature, a few series have focused on treatment modalities in

patients aged more than or equal to 75 years [12–14]. This review aims to provide practical recommendations for HN treatment in elderly patients, and is based on a complete review of the literature.

Epidemiology of head and neck cancers in elderly patients

Patients' characteristics and risk factors

The clinical presentation of HN cancers in the elderly has some specific features compared with younger patients, with a high prevalence of oral cavity cancers. In a recent single institution study of 316 patients aged more than or equal to 80 years, from southern France, Italiano *et al.* [14] found 46% of oral cavity, 23% of laryngeal, 19% of oropharyngeal, and 4% of hypopharyngeal cancers. In 8% of the patients, another site was involved. As a comparison, in the meta-analysis of chemotherapy in head and neck cancer involving 17 346 patients from 93 randomized trials, the most represented location was the oropharynx with 36% of cases, followed by the larynx and oral cavity (21% each) and the hypopharynx (16%) [15]. Between 70 and 75 years of age, data on the type of tumor sites seem to be similar: Kruse *et al.* [16] have described in a recent epidemiological study of

99 patients (aged ≥ 70 years) a significant prevalence of oral cavity cancer, whereas in another study of 273 patients (aged ≥ 74 years), Sarini *et al.* [7] showed that hypopharyngeal cancer occurred less frequently in this population.

The usual male-to-female ratio in the HN squamous cell carcinoma population varies between 8 and 15. Many studies reported that women are over-represented in the elderly HN cancer population, with a sex ratio close to 1 [13–16]. In addition, a history of alcohol or tobacco intoxication is reported in more than 70% of the patients [17–19]. However, the elderly patients had a significantly lower degree of alcohol and tobacco exposure [4,13,16] compared with the rest of the younger populations that developed HN cancers. In a French series of 270 patients aged more than or equal to 80 years and treated for oral cavity cancer, risk factors were different between men and women. For example, tobacco or alcohol intoxication was the main risk factor for more than half of the male population, whereas an earlier chronic oral traumatic or a history of lichen planus (or leukoplakia) was found in half of the women [13]. In this study, as in the other reports on elderly patients, we did not specifically investigate the role of human papilloma virus (HPV). However, it seems that HPV-positive tumors are more likely to occur in younger than in older patients suggesting that HPV infection could play a marginal role in HN carcinogenesis of elderly patients [20].

Tumor stage

Several reports in this population have pointed out the high incidence of locally advanced tumors (T3, T4) with, however, less nodal involvement compared with younger patients [4,11]. In the French series of patients including only patients aged more than or equal to 80 years, and in the study reported by Italiano *et al.* [13,14] only one-third of the population have been treated for stage I/II whereas two-thirds were treated for stage III/IV. Tumor stage is widely reported as a prognostic factor for survival of several malignancies. In elderly patients, the delay between first symptoms and diagnosis could be shortened by patients and doctors education.

Molecular profile

Some biological markers, such as Ki-67, p53, EGFR expression, and Bcl2, have been shown to have an impact on the locoregional control in the general population [21,22]. Epidemiological data showing that HN cancers in the elderly have a specific epidemiological profile compared with younger patients suggest that the molecular profile of these tumors could be specific. To date, no data assessing the molecular profile of HN cancers in elderly patients have been reported. Future studies comparing the molecular profile of HN tumor in elderly and young patients could be relevant.

Geriatric evaluation for head and neck cancers in elderly patients

During the past years, the European Organisation for Research and Treatment of Cancer used the borderline of 65 years to define the middle and old age. Currently, this age limit is no longer valid [23]. Comorbidities, disabilities, frailty, and functional reserve issue are considered to be more relevant criteria than civil age for decision making [23]. In addition, elderly patients represent a heterogeneous population in which decisions for diagnosis and treatment are often complex and have to be discussed in the frame of a multidisciplinary approach including onco-geriatric evaluation. Thus, numerous geriatric indexes have been developed during the recent years to assess the degree of frailty of patients.

The comprehensive geriatric assessment

The comprehensive geriatric assessment (CGA) is a multidimensional, interdisciplinary diagnostic process to determine the medical, psychological, and functional capabilities of elderly patients to develop a coordinated and integrated treatment schedule and follow-up [24]. The CGA uses standardized instruments to evaluate aspects of patient functioning, impairment, and social support. This assessment aims to identify frail patients that are with the highest risk of adverse outcome. In cancer treatment, a recent study shows that CGA influences treatment decision in approximately 80% of cases [25]. The CGA and multidisciplinary approach is widely recommended in HN cancers [26–28]. Unfortunately, to our knowledge, no specific prospective studies assessed the value of geriatric scores in elderly patients with HN cancer, and the prevalence of frailty in this specific population is unknown.

Vulnerable elders survey-13

As CGA is time consuming, new tools have been established to screen patient candidates for CGA. The vulnerable elders survey-13 (VES-13) is a simple function-based tool for screening community-dwelling populations to identify older persons at risk of health deterioration. The VES-13 considers age, self-rated health, limitations in physical function, and functional disabilities. Its usefulness as preliminary means of assessing older patients before undertaking CGA is now recognized and has been adopted by several practitioners involved in cancer care of elderly patients in general [29]. Relevance of VES-13 in HN cancers needs to be investigated in future studies.

Balducci classification

Balducci and Extermann [30] proposed classifying patients presenting with cancer in three groups: group 1 = patients who are totally independent without serious comorbidities and who should receive full-dose treatment (as long as their average life expectancy is longer than the life expectancy from cancer); group 2 = patients

dependent on one or more instrumental activities of daily living or with some comorbidities that should be subjected to some precaution; group 3 = frail patients that are mainly candidates for supportive care. Although this classification is widely used in several types of patients with cancer, it could not be fully applied to HN cancer treatment for the following reasons:

- (1) First, the prevalence of malnutrition is dramatically high in patients with HN cancer [31]. Therefore, the greatest number of elderly patients would be in 'group 2' or 'group 3' and only a small subset of patients would be potential candidates for standard local treatment. However, in the literature, clinical data showed that standard local treatment is feasible in about half of elderly patients with HN cancer [11,13,14] contradicting the value of the Balducci classification in this population. Thus, in the geriatric evaluation, it seems that nutritional status should be considered separately for these patients.
- (2) Second, as HN cancers are highly symptomatic they induce a rapid functional decline that could be reversible with intensive nutritional support and local treatment of the tumor. Some patients, classified in 'group 3', could reintegrate 'group 2' after multi-disciplinary team intervention. Therefore, not all patients from 'group 3' should be systematically denied for curative local treatment.
- (3) HN tumor could be painful, induces dyspnea, discomfort, and strongly alters the quality of life in patients from 'group 3'. Although these patients are candidates for palliative treatment, some of them would probably benefit from local treatment, with adequate adaptations.

Notion of adapted treatment for head and neck cancers in elderly patients

Management of HN cancer is complex. In general, local HN treatments are associated with significant acute iatrogenic morbidities in elderly patients, with a high risk of functional deterioration even in patients in good general condition before the treatment. However, a natural history of nontreated HN cancers could induce severe symptoms (related to locoregional invasion), leading to rapid deterioration of functional status. These facts explain why treatment of geriatric patients with HN cancer needs to make compromises, and physicians sometimes propose suboptimal treatment: less toxic than standard treatment, but less efficient. Thus, the border between adapted treatment and palliative treatment is usually very thin. Although 'standard treatment' could be considered as the same treatment that is given to younger patients, palliative treatment should be defined as any local treatment that could not ensure local control but could decrease local symptoms. Conversely, adapted treatment should be defined as any treatment that could control the disease, but with a higher risk of either local recurrence or toxicity [13,14].

Three studies reported that therapeutic strategy complies with institution's policies in approximately 50% of cases in older patients with HN cancer [11,13,14]. This emphasizes the need to assess the outcome of adapted treatment in geriatric patients. The major issue is to determine which adaptations could be carried out, and then, what could be the respective individual benefit/risk ratio of each adaptation. Interestingly, 'adapted treatment' does not necessarily mean a loss of chance for survival in elderly patients. In the French series of oral cavity cancer in patients, the distinction was clearly made between palliative and adapted treatment, according to the definition mentioned above. Overall survival and disease-free survival were similar between 'standard' and 'adapted' treatments. In contrast, survival of patients treated with palliative intent was very poor [14].

To propose the best-tailored treatment, physicians have to determine the primary goal of local treatment: to cure or to relieve/prevent tumor symptoms. Whatever the goal of the treatment, it should not have high acute toxicity, to avoid post-treatment major functional decline. Thus, the first objective of treatment's adaptation should be to decrease acute adverse events to improve compliance [13,14]. In the next section we will review the respective adaptation feasible for surgery and radiotherapy.

Adapted surgery in elderly patients with head and neck cancers

Indications according to tumor stage

Early stage of head and neck cancers

For early disease (T1, T2, N0), resection of the primary tumor is often limited, with good functional results [32,33]. Adaptation of surgical technique for elderly patients with early HN cancers could consist of omitting neck dissection. Indeed, in T1–T2 N0 oral cavity cancers, prophylactic neck dissection is considered a standard of care in younger patients [34–36], whereas it is often omitted in the elderly. In the French series, for example, neck dissections were omitted in 69% of patients [13]. This undertreatment adaptation does not seem to benefit elderly patients, as the neck node recurrence rate was significantly increased (40% vs. only 6% in patients who had node dissection) [13]. These data clearly showed that adaptation of surgery for elderly patients with early stage of HN tumors should be carefully evaluated in routine practice and included in prospective clinical trials that investigate the balance of the benefit/risk ratio of each adaptation. Careful geriatric evaluation of life expectancy, comorbidities, and predictive toxicity of the surgical procedure should be carried out in a multi-disciplinary team, and physicians should propose optimal surgical procedure as far as possible in this population.

Locally advanced head and neck cancers

For locally advanced disease, surgical procedure is more complex (longer operative time, higher risk of

post-operative complications, and major functional deterioration of HN). In the postoperative setting, the prognostic factors for increased risk of complications after wide HN surgery are: age [37], preoperative comorbidities evaluated with Charlson index or with Adult Comorbidity Evaluation-27 index [37–39], and duration of anesthesia [37–39]. In a retrospective analysis of 24 patients aged ≥ 70 years who underwent a wide HN surgery, Zabrodsky *et al.* [39] reported a significant rate of surgical or medical complication (54%). The investigators recommended reducing the surgical stress in elderly patients with important preoperative comorbidities. For patient candidates for large surgical resection, careful preoperative staging and evaluation of associated comorbidities, as well as skilful perioperative and postoperative management, are essential for reducing postoperative morbidity and mortality. Successful outcome depends on appropriate surgical management, treatment of concurrent illnesses, and minimization of postoperative complications.

When patients are unsuitable for the standard surgical procedure, two approaches could be proposed. The first one is to adapt the surgical procedure to minimize the operative time and the risk of postoperative complications. For example, surgeons could omit reconstruction (such as hemimandibulectomy without reconstructive surgery), could deny patients for a conservative surgery that would require a long postoperative functional rehabilitation (such as transform a partial laryngectomy in total laryngectomy), and could tailor the extension of the resection (such as a selective radical dissection rather than a radical neck dissection). All these adaptations are acceptable as long as the procedure ensures both complete removal of the tumor and a satisfactory postoperative function with minimal comorbidity. However, clinical data showing the outcome and the functional results in patients who underwent these adaptations are lacking.

When standard surgery is not feasible, the second approach is to propose definitive radiotherapy as an alternative treatment. In our study including only oral cavity cancers in patients aged more than or equal to 80 years, we compared the outcome of patients presenting with resectable stage III/IV tumors who received surgery versus those who were denied surgery and who received radiotherapy. The disease-free survival and the overall survival were significantly better in the surgical group [13]. In another recent study comparing toxicity of radiotherapy versus laryngectomy in patients aged 65 years or less or patients ≥ 75 years, radiotherapy was more toxic than surgery irrespective of the age of the patients [40]. Altogether, these data suggest that definitive radiotherapy could not always be a better option than surgery in advanced-stage HN cancer. The balance of efficacy/toxicity of surgery and radiotherapy should be discussed in a frame of a multidisciplinary meeting.

Morbidity after surgery in elderly patients with head and neck cancers

Surgery is less often used for elderly patients compared with younger patients [7]. However, some studies suggest that age alone should not be a contraindication to adequate oncologic surgery and, thus, recommend aggressive surgical approach for this population [12,41,42]. This is supported by some reports. A series of 43 patients suggested that older patients undergoing HN cancer surgical procedures have the same rate of postoperative complications as younger patients [12]. Another series of 810 patients with HN cancer aged ≥ 65 years, reported a postoperative mortality rate of 3.5%, similar to what is reported in younger patients [43]. In the French series, 61% of the patients who were amenable to be cured by surgery underwent surgical resection. In that study, the postoperative 30-day death rate was 3% [14]. In elderly patients (> 80), surgery was performed in 82% of patients treated with a curative intent. This has clearly indicated that HN surgery is feasible even in older patients.

In collaboration with a geriatric oncologist, careful selection of patients suitable for surgery is recommended. Indeed, there is a wide range of surgical techniques for HN cancer (from limited excision under local anesthesia to extensive resection requiring reconstruction) with specific complications and functional impairments. For elderly patients, the decision of appropriate surgical procedure should take into account the duration of operative time, the need of reconstruction with bone or soft tissue transfer, the need of postoperative functional rehabilitation, and the need of postoperative irradiation that could compromise functional results. Furthermore, CGA is useful to help the oncologist to tailor the surgical procedure in elderly patients. A prospective study including 460 elderly patients with cancer showed that instrumental activities of daily living and an abnormal performance status were independent predictors of post-surgical complication for moderate/severe fatigue [44].

Adapted radiotherapy in elderly patients with head and neck cancers

Radiotherapy is delivered as a definitive treatment for patients with inoperable locally advanced cancers or for patients presenting with early cancers not suitable for surgery. Adjuvant radiotherapy is indicated in case of poor prognostic factors. The most widely used fractionation in patients with HN is conventional fractionation of 2.0 Gy/fraction, 5 days a week for more than 7 weeks up to a total dose of 66–70 Gy for macroscopic disease and 50–60 Gy for prophylactic treatment.

Adapted schedule of radiotherapy or combined radiochemotherapy

Adaptation of fractionation

Accelerated fractionated radiotherapy, which aims to shorten the total duration of treatment, could be attractive for elderly patients. However, protocols of

accelerated radiotherapy associated with hyperfractionation (more fraction during a short time, reduction of overall treatment time) are proven to induce more acute mucositis than standard treatment and should not be proposed to elderly patients [45]. Some other accelerated protocols called 'split course' propose a planned radiation break, which have the potential benefit of improving radiation tolerance and increasing the quality of life by reducing mucositis and its consequences. On the opposite to achieve unplanned interruption in the standard treatment, data from the Danish Head and Neck group randomized trial showed that the combination of accelerated radiotherapy with a break does not affect local control of the tumor [46].

Hypofractionated treatments (increased dose per fraction and decrease total number of fraction) seem to have many advantages in the geriatric field. To limit acute toxicity, these protocols are delivered in a split-course manner: typically, protocols propose to deliver two series of 30 Gy in 10 fractions for more than 2 weeks with a planned interruption of 2 or 3 weeks between the series or three series of 20 Gy in five fractions with the same planned interruption [11,13,14]. In addition, split course helps in wound healing of mucositis and could limit pain, malnutrition, and functional deterioration. Such adapted irradiation regimens may represent a good compromise between a biologically effective dose and an acceptable tolerance in elderly patients. In the French series, 56% of patients received split-course hypofractionated radiotherapy, the compliance was acceptable with a 81% rate of treatment completion, indicating that definitive radiotherapy is feasible with adaptation for selected patients [14]. However, a word of caution should be given on late toxicity when patients are treated using a hypofractionated schedule, because large doses per fraction may increase late toxicity [47]. Late toxicity of HN radiotherapy, which is a major concern in younger patients, should also be considered in patients with early-stage tumors, as the overall probability of survival is high in this population (median overall survival of patients aged ≥ 80 years with stage I/II tumors is approximately 42 months) [14]. Any adaptation of the treatment that could induce late adverse effects in patients with HN stage I/II tumors should be decided in the frame of a multidisciplinary approach, taking into account the life expectancy of the patient. Conversely, in patients with advanced tumors, late complications are unlikely to occur, as median survival is less than 1 year [13,14]. Therefore, in this population, any adaptation of the treatment that could improve compliance but increases late toxicity should be considered.

Adaptation of volume

Delineation of the irradiation volume is a complex task in HN radiotherapy. The definition and selection of microscopic extensions of the tumor, known as clinical

target volume (CTV), are ruled by guidelines [48]. In elderly patients, an open question is whether the reduction of the volume of the CTV (to minimize adverse events) is safe. We have reported that the omission of node treatment for T1–T2 N0 oral cavity cancer in patients aged ≥ 80 years induces a high risk of node recurrence [13]. These data suggest that physicians should be very careful when reducing the volume of the CTV. More clinical data on the outcome of radiotherapy with adapted volume are required in elderly patients.

Use of concurrent chemotherapy with radiotherapy

To date, in locally advanced HN cancer, the standard treatment is concurrent radiochemotherapy. Some series reported that concurrent radiochemotherapy is feasible in patients aged ≥ 70 years [49]. However, a worldwide meta-analysis showed that concurrent radiochemotherapy did not provide any benefit after 71 years [15]. Prospective data are needed to assess the real benefit of radiochemotherapy in elderly patients.

Palliative radiotherapy

Many hypofractionated palliative schedules for HN cancers have been reported in the literature: 20 Gy in five fractions [50], 30 Gy in five fractions [51], 14 Gy in four fractions [52], and 50 Gy in 16 fractions [53]. All these series have reported a good compliance, and resulted in high response rate and symptom relief. Palliative radiotherapy should be proposed for patients unsuitable for standard treatment. The border between palliative and curative radiotherapy is thin. Indeed, when patients experience a significant clinical improvement after palliative radiotherapy, a treatment option could be to complete the radiotherapy course with additional series (such as split-course regimen), to achieve local control.

Morbidity of standard radiotherapy in the elderly

When considering all primary tumor sites (prostate, breast, lung), a retrospective study on 183 patients aged ≥ 80 years has shown that 80% of patients completed their treatment. Treatment breaks were noted in 36% of patients [54]. All those data showing a good tolerance of radiotherapy in the elderly population are not always transposable to HN radiotherapy, in which unplanned treatment breaks are frequent irrespective of the age of the patients [55,56]. These treatment breaks are particularly of concern in HN tumors, as they could compromise the local control of the disease [57].

The major issue of HN radiotherapy in the elderly is acute toxicity. HN radiotherapy could induce severe mucositis, dermatitis, dysphagia, weight loss, pain, malnutrition, and functional deterioration. Oral confluent mucositis is the most debilitating side effect reported by patients [56]. In standard HN treatment, the confluent mucositis starts 2 weeks after the beginning of the treatment and lasts for 10 weeks, with a maximum intensity of

symptoms at 6 weeks [58]. The first factor associated with the risk of oral mucositis is the percentage of oral and oropharyngeal mucosa included in the radiation fields. For example, irradiation of T1 tumor of the larynx is performed by small fields of radiotherapy encompassing only the larynx, and induces little toxicity [59]. Conversely, irradiation of the oral cavity requires treating the whole oral mucosa, which rapidly induces severe oral mucositis, pain, dysphagia, denutrition, hospitalization, and deterioration of quality of life [56]. Other factors associated with the incidence of oral mucositis are altered fractionation schedules (hyperfractionation and/or accelerated fractionation), use of concurrent chemotherapy [55], and age. Pignon *et al.* [60] reported the tolerance of radiotherapy in 1589 patients included in the European Organisation for Research and Treatment of Cancer trials between 1980 and 1995. In this series, 20% of patients were aged more than or equal to 65 years and 2% aged more than or equal to 75 years. Acute functional mucosal reaction increased with age of the patients, with 8% of grade 4 in patients aged less than 50 years and 31% in patients aged more than 70 years. Therefore, in frail patients, tolerance of HN could be a major problem, as all these adverse events could induce rapid functional deterioration and dependence.

Another issue is the number of daily transportations required for HN radiotherapy, which is a major problem. In standard fractionation, the schedule necessitates approximately 35 daily transportations for more than 7 weeks, inducing fatigue [61]. Thus, standard fractionation could be difficult to deliver and treatment interruption due to fatigue is frequent in elderly patients [54].

Primary surgery of HN tumor could also compromise the compliance to adjuvant radiotherapy. In the adjuvant setting, the French series of oral cavity cancer in patients aged ≥ 80 years showed that only 50% of the eligible patients according to standard guidelines were submitted to adjuvant irradiation, and the treatment could only be completed in 75% of the cases [13]. This means that radiotherapy may be difficult to be carried out, as the risk of toxicity remains high in elderly patients.

Thus, all these specific constraints of radiotherapy in HN tumors of elderly patients should encourage physicians to propose relevant adaptations to decrease acute toxicity and to reduce daily transportation and overall treatment duration. The final goal of adaptation should ensure good compliance to treatment and minimize the risk on functional decline after radiotherapy.

Importance of nutritional support

Prevalence of protein/caloric malnutrition is high in elderly patients. A retrospective study conducted on 2076 older patients (mean age of the population study = 80 years) showed that 33% of patients were classified as

malnourished and 51% were at nutritional risk, according to the mini-nutritional assessment score [62]. Malnutrition in the aged population has multiple causes, including decreased taste, decreased gastric secretion, depression, forgetfulness, limited mobility, decreased ability to feed oneself, and poverty. In the presence of cancer, the prevalence and risk of malnutrition are higher, especially in HN cancer [31]. Malnutrition is associated with a number of complications, including enhanced toxicity of surgery [63] and of radiotherapy [64–66].

With timely intervention, malnutrition may be prevented or reversed in older patients with cancer. Many prospective studies assessed the benefit of early nutrition intervention in patients who receive HN radiotherapy on quality of life, treatment break, and risk of unplanned admissions to hospital [64–66]. Options for the re-nutrition of elderly patients are placement of feeding [67] and/or oral re-nutrition supplementation [68]. Careful evaluation of nutritional support when needed should be fully integrated in the management of elderly patients with HN cancer.

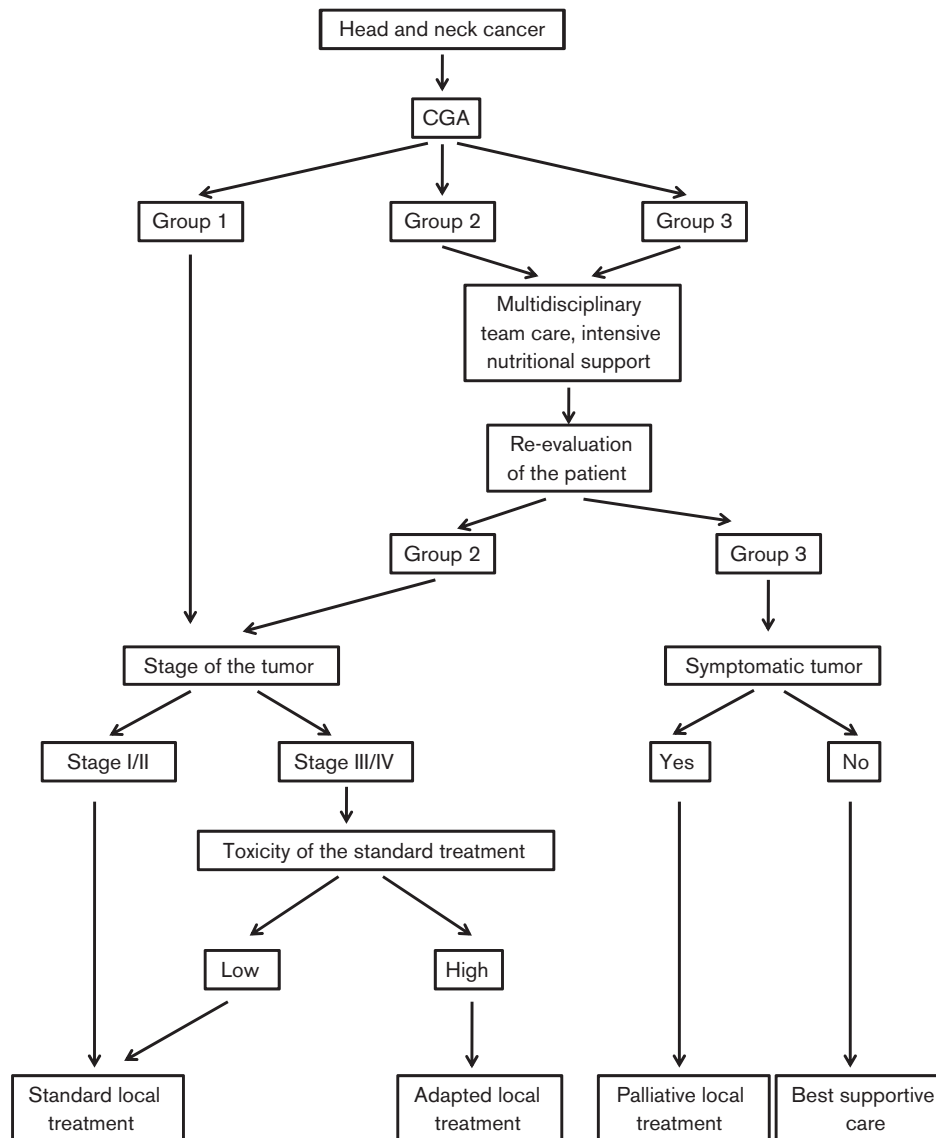
Conclusion and clinical recommendation

In the elderly population, surgery and radiotherapy of HN cancer may induce high acute and chronic toxicities. Therapeutic strategies with potentially high adverse effects should be adapted. We propose in Fig. 1 a flow chart for HN treatment approach in elderly patients.

We also emphasize the need for more clinical data in elderly patients with HN cancer. Standard and adapted schedules should be evaluated in collaboration with geriatric oncologists in prospective studies. For this issue, we propose the following guidelines for HN cancer treatment in elderly patients:

- (1) CGA could be very useful, but the predictive toxicity of the local treatment should be integrated in the geriatric evaluation (Fig. 1).
- (2) Multiple interventions should be proposed to improve treatment tolerance and compliance. Intensive nutritional support should be fully integrated in the treatment.
- (3) Three types of treatment could be proposed: 'standard', 'adapted', or 'palliative'. Patients should not be denied 'standard treatment' without geriatric evaluation. The proposed treatment of the patients could be reappraised after intensive nutrition and multidisciplinary care.
- (4) Elderly patients with early-stage tumors have the same prognostic value as younger patients. Therefore, optimal 'standard treatment' should be proposed to patients with long life expectancy.
- (5) Patients with advanced tumor have a poor prognostic value. If standard treatment is considered as highly toxic and could induce functional decline in these patients, 'adapted treatment' should be proposed.

Fig. 1



Flow chart for treatment approach in elderly patients with head and neck cancers. CGA, comprehensive geriatric assessment.

(6) Patients unsuitable for standard or ‘adapted treatment’ should not be systematically denied local treatment when the tumor is symptomatic. ‘Palliative treatment’ such as hypofractionated schemes of radiotherapy are shown to be efficient and should be proposed whenever possible.

References

- Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005; **55**:74–108.
- Jun MY, Strong EW, Saltzman EI, Gerold FP. Head and neck cancer in the elderly. *Head Neck Surg* 1983; **5**:376–382.
- Lampe HB, Lampe KM, Skillings J. Head and neck cancer in the elderly. *J Otolaryngol* 1986; **15**:235–238.
- Koch WM, Patel H, Brennan J, Boyle JO, Sidransky D. Squamous cell carcinoma of the head and neck in the elderly. *Arch Otolaryngol Head Neck Surg* 1995; **121**:262–265.
- Chin R, Fisher RJ, Smees RI, Barton MB. Oropharyngeal cancer in the elderly. *Int J Radiat Oncol Biol Phys* 1995; **32**:1007–1016.
- Reid BC, Alberg AJ, Klassen AC, Samet JM, Rozier RG, Garcia I, Winn DM. Comorbidity and survival of elderly head and neck carcinoma patients. *Cancer* 2001; **92**:2109–2116.
- Sarini J, Fournier C, Lefebvre JL, Bonafos G, Van JT, Coche-Dequéant B. Head and neck squamous cell carcinoma in elderly patients: a long-term retrospective review of 273 cases. *Arch Otolaryngol Head Neck Surg* 2001; **127**:1089–1092.
- Vaccher E, Talamini R, Franchin G, Tirelli U, Barzan L. Elderly head and neck (HN) cancer patients: a monoinstitutional series. *Tumori* 2002; **88**:63–66.
- Sesterhenn AM, Teymoortash A, Folz BJ, Werner JA. Head and neck cancer in the elderly: a cohort study in 40 patients. *Acta Oncol* 2005; **44**:59–64.
- Cinamon U, Hier MP, Black MJ. Age as a prognostic factor for head and neck squamous cell carcinoma: should older patients be treated differently? *J Otolaryngol* 2006; **35**:8–12.
- Lusinchi A, Bourhis J, Wibault P, Le Ridant AM, Eschwege F. Radiation therapy for head and neck cancers in the elderly. *Int J Radiat Oncol Biol Phys* 1990; **18**:819–823.

- 12 Clayman GL, Eicher SA, Sicard MW, Razmpa E, Goepfert H. Surgical outcomes in head and neck cancer patients 80 years of age and older. *Head Neck* 1998; **20**:216–223.
- 13 Ortholan C, Lusinchi A, Italiano A, Bensadoun RJ, Auperin A, Poissonnet G, et al. Oral cavity squamous cell carcinoma in 260 patients aged 80 years or more. *Radiother Oncol* 2009; **93**:516–523.
- 14 Italiano A, Ortholan C, Dassonville O, Poissonnet G, Thariat J, Benezyer K, et al. Head and neck squamous cell carcinoma in patients aged ≥ 80 years: patterns of care and survival. *Cancer* 2008; **113**:3160–3168.
- 15 Pignon JP, le Maître A, Maillard E, Bourhis J; MACH-NC Collaborative Group. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17346 patients. *Radiother Oncol* 2009; **92**:4–14.
- 16 Kruse AL, Bredell M, Luebbbers HT, Grätz KW. Head and neck cancer in the elderly: a retrospective study over 10 years (1999–2008). *Head Neck Oncol* 2010; **2**:25.
- 17 Jovanovic A, Schulten EA, Kostense PJ, Snow GB, Van der Waal I. Squamous cell carcinoma of the lip and oral cavity in The Netherlands: an epidemiological study of 740 patients. *J Craniomaxillofac Surg* 1993; **21**:149–152.
- 18 Jovanovic A, Schulten EA, Kostense PJ, Snow GB, Van der Waal I. Tobacco and alcohol related to the anatomical site of oral squamous cell carcinoma. *J Oral Pathol Med* 1993; **22**:459–462.
- 19 Carvalho AL, Singh B, Spiro RH, Kowalski LP, Shah JP. Cancer of the oral cavity: a comparison between institutions in a developing and a developed nation. *Head Neck* 2004; **26**:31–38.
- 20 Ang KK, Harris J, Wheeler R, Weber R, Rosenthal DI, Nguyen-Tân PF, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med* 2010; **363**:24–35.
- 21 Buffa FM, Bentzen SM, Daley FM, Dische S, Saunders MI, Richman PI, et al. Molecular marker profiles predict locoregional control of head and neck squamous cell carcinoma in a randomized trial of continuous hyperfractionated accelerated radiotherapy. *Clin Cancer Res* 2004; **10**:3745–3754.
- 22 Suwinski R, Jaworska M, Nikiel B, Grzegorz W, Bankowska-Wozniak M, Wojciech M, et al. Predicting the effect of accelerated fractionation in postoperative radiotherapy for head and neck cancer based on molecular marker profiles: data from a randomized clinical trial. *Int J Radiat Oncol Biol Phys* 2010; **77**:438–446.
- 23 Extermann M, Aapro M, Bernabei R, Cohen HJ, Droz JP, Lichtman S, et al.; Task Force on CGA of the International Society of Geriatric Oncology. Use of comprehensive geriatric assessment in older cancer patients: recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). *Crit Rev Oncol Hematol* 2005; **55**:241–252.
- 24 Bernabei R, Venturiero V, Tarsitani P, Gambassi G. The comprehensive geriatric assessment: when, where, how. *Crit Rev Oncol Hematol* 2000; **33**:45–56.
- 25 Chaïbi P, Magné N, Breton S, Chebib A, Watson S, Duron JJ, et al. Influence of geriatric consultation with comprehensive geriatric assessment on final therapeutic decision in elderly cancer patients. *Crit Rev Oncol Hematol* 2010 [Epub ahead of print].
- 26 Syrigos KN, Karachalios D, Karapanagiotou EM, Nutting CM, Manolopoulos L, Harrington KJ. Head and neck cancer in the elderly: an overview on the treatment modalities. *Cancer Treat Rev* 2009; **35**:237–245.
- 27 Metges JP, Eschwege F, de Crevoisier R, Lusinchi A, Bourhis J, Wibault P. Radiotherapy in head and neck cancer in the elderly: a challenge. *Crit Rev Oncol Hematol* 2000; **34**:195–203.
- 28 Lalami Y, de Castro G Jr, Bernard-Marty C, Awada A. Management of head and neck cancer in elderly patients. *Drugs Aging* 2009; **26**:571–583.
- 29 Luciani A, Ascione G, Bertuzzi C, Marussi D, Codecà C, Di Maria G, et al. Detecting disabilities in older patients with cancer: comparison between comprehensive geriatric assessment and vulnerable elders survey-13. *J Clin Oncol* 2010; **28**:2046–2050.
- 30 Balducci L, Extermann M. Management of cancer in the older person: a practical approach. *Oncologist* 2000; **5**:224–237.
- 31 Pressoir M, Desné S, Berchery D, Rossignol G, Poiree B, Meslier M, et al. Prevalence, risk factors and clinical implications of malnutrition in French Comprehensive Cancer Centres. *Br J Cancer* 2010; **102**:966–971.
- 32 Roh JL, Kim DH, Kim SY, Park KI. Quality of life and voice in patients after laser cordectomy for Tis and T1 glottic carcinomas. *Head Neck* 2007; **29**:1010–1016.
- 33 Cosmidis A, Rame JP, Dassonville O, Temam S, Massip F, Poissonnet G, et al. T1-T2 NO oropharyngeal cancers treated with surgery alone: a GETTEC study. *Eur Arch Otorhinolaryngol* 2004; **261**:276–281.
- 34 Haddadin KJ, Soutar DS, Oliver RJ, Webster MH, Robertson AG, MacDonald DG. Improved survival for patients with clinically T1/T2, NO tongue tumors undergoing a prophylactic neck dissection. *Head Neck* 1999; **21**:517–525.
- 35 Keski-Säntti H, Atula T, Törnwall J, Koivunen P, Mäkitie A. Elective neck treatment versus observation in patients with T1/T2 NO squamous cell carcinoma of oral tongue. *Oral Oncol* 2006; **42**:96–101.
- 36 Pernot M, Verhaeghe JL, Guillemin F, Carolus JM, Hoffstetter S, Peiffert D. Evaluation of the importance of systematic neck dissection in carcinoma of the oral cavity treated by brachytherapy alone for the primary lesion (apropos of a series of 346 patients). *Bull Cancer Radiother* 1995; **82**:311–317.
- 37 Boruk M, Chernobilsky B, Rosenfeld RM, Har-El G. Age as a prognostic factor for complications of major head and neck surgery. *Arch Otolaryngol Head Neck Surg* 2005; **131**:605–609.
- 38 Ferrier MB, Spuesens EB, Le Cessie S, Baatenburg de Jong RJ. Comorbidity as a major risk factor for mortality and complications in head and neck surgery. *Arch Otolaryngol Head Neck Surg* 2005; **131**:27–32.
- 39 Zabrodsky M, Calabrese L, Tosoni A, Ansarin M, Giugliano G, Bruschini R, et al. Major surgery in elderly head and neck cancer patients: immediate and long-term surgical results and complication rates. *Surg Oncol* 2004; **13**:249–255.
- 40 Peters TT, Van der Laan BF, Plaat BE, Wedman J, Langendijk JA, Halmos GB. The impact of comorbidity on treatment-related side effects in older patients with laryngeal cancer. *Oral Oncol* 2010; **47**:56–61.
- 41 Teymoortash A, Wulf H, Werner JA. Head and neck cancer surgery in the elderly. *Laryngorhinootologie* 2002; **81**:293–298.
- 42 Laccourreye O, Brasnu D, Perie S, Muscatello L, Menard M, Weinstein G. Supracricoid partial laryngectomies in the elderly: mortality, complications, and functional outcome. *Laryngoscope* 1998; **108**:237–242.
- 43 Morgan RF, Hirata RM, Jaques DA, Hoopes JE. Head and neck surgery in the aged. *Am J Surg* 1982; **144**:449–451.
- 44 Audisio RA, Pope D, Ramesh HS, Gennari R, Van Leeuwen BL, West C, et al.; PACE Participants. Shall we operate? Preoperative assessment in elderly cancer patients (PACE) can help: a SIOG surgical task force prospective study. *Crit Rev Oncol Hematol* 2008; **65**:156–163.
- 45 Fu KK, Pajak TF, Trotti A, Jones CU, Spencer SA, Phillips TL, et al. A Radiation Therapy Oncology Group (RTOG) phase III randomized study to compare hyperfractionation and two variants of accelerated fractionation to standard fractionation radiotherapy for head and neck squamous cell carcinomas: first report of RTOG 9003. *Int J Radiat Oncol Biol Phys* 2000; **48**:7–16.
- 46 Hansen O, Overgaard J, Hansen HS, Overgaard M, Höyer M, Jörgensen KE, et al. Importance of overall treatment time for the outcome of radiotherapy of advanced head and neck carcinoma: dependency on tumor differentiation. *Radiother Oncol* 1997; **43**:47–51.
- 47 Glatstein E. Hypofractionation, long-term effects, and the alpha/beta ratio. *Int J Radiat Oncol Biol Phys* 2008; **72**:11–12.
- 48 Grégoire V, Eisbruch A, Hamoir M, Levendag P. Proposal for the delineation of the nodal CTV in the node-positive and the post-operative neck. *Radiother Oncol* 2006; **79**:15–20.
- 49 Patel S, Wolff PB, Lin B, Karnad AB. Concurrent chemotherapy plus radiation therapy (CRT) in elderly patients (E): a retrospective analysis (abstract e19660). *J Clin Oncol* 2010; **28**S.
- 50 Mohanti BK, Umapathy H, Bahadur S, Thakar A, Pathy S. Short-course palliative radiotherapy of 20 Gy in 5 fractions for advanced and incurable head and neck cancer: AIIMS study. *Radiother Oncol* 2004; **71**:275–280.
- 51 Porceddu SV, Rosser B, Burmeister BH, Jones M, Hickey B, Baumann K, et al. Hypofractionated radiotherapy for the palliation of advanced head and neck cancer in patients unsuitable for curative treatment: 'hypo trial'. *Radiother Oncol* 2007; **85**:456–462.
- 52 Corry J, Peters LJ, Costa ID, Milner AD, Fawns H, Rischin D, et al. The 'QUAD SHOT': a phase II study of palliative radiotherapy for incurable head and neck cancer. *Radiother Oncol* 2005; **77**:137–142.
- 53 Al-mangani A, Tans L, Van rooij PH, Noever I, Baatenburg de jong RJ, Levendag PC. Hypofractionated radiotherapy denoted as the 'Christie scheme': an effective means of palliating patients with head and neck cancers not suitable for curative treatment. *Acta Oncol* 2009; **48**:562–570.
- 54 Wasil T, Lichtman SM, Gupta V, Rush S. Radiation therapy in cancer patients 80 years of age and older. *Am J Clin Oncol* 2000; **23**:526–530.
- 55 Russo G, Haddad R, Posner M, Machtay M. Radiation treatment breaks and ulcerative mucositis in head and neck cancer. *Oncologist* 2008; **13**:886–898.
- 56 Trotti A, Bellm LA, Epstein JB, Frame D, Fuchs HJ, Gwede CK, et al. Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: a systematic literature review. *Radiother Oncol* 2003; **66**:253–262.

- 57 Robertson C, Robertson AG, Hendry JH, Roberts SA, Slevin NJ, Duncan WB, *et al.* Similar decreases in local tumor control are calculated for treatment protraction and for interruptions in the radiotherapy of carcinoma of the larynx in four centers. *Int J Radiat Oncol Biol Phys* 1998; **40**:319–329.
- 58 Overgaard J, Hansen HS, Specht L, Overgaard M, Grau C, Andersen E, *et al.* Five compared with six fractions per week of conventional radiotherapy of squamous-cell carcinoma of head and neck: DAHANCA 6 and 7 randomised controlled trial. *Lancet* 2003; **362**:933–940.
- 59 Cellai E, Frata P, Magrini SM, Paiar F, Barca R, Fondelli S, *et al.* Radical radiotherapy for early glottic cancer: results in a series of 1087 patients from two Italian radiation oncology centers. I. The case of T1N0 disease. *Int J Radiat Oncol Biol Phys* 2005; **63**:1378–1386.
- 60 Pignon T, Horiot JC, Van den Bogaert W, Van Glabbeke M, Scalliet P. No age limit for radical radiotherapy in head and neck tumours. *Eur J Cancer* 1996; **32**:2075–2081.
- 61 Junor EJ, Macbeth FR, Barrett A. An audit of travel and waiting times for outpatient radiotherapy. *Clin Oncol (R Coll Radiol)* 1992; **4**:174–176.
- 62 Charlton KE, Nichols C, Bowden S, Lambert K, Barone L, Mason M, *et al.* Older rehabilitation patients are at high risk of malnutrition: evidence from a large Australian database. *J Nutr Health Aging* 2010; **14**:622–628.
- 63 Guo CB, Ma DQ, Zhang KH, Hu XH. Relation between nutritional state and postoperative complications in patients with oral and maxillofacial malignancy. *Br J Oral Maxillofac Surg* 2007; **45**:467–470.
- 64 Ravasco P, Monteiro-Grillo I, Marques Vidal P, Camilo ME. Impact of nutrition on outcome: a prospective randomized controlled trial in patients with head and neck cancer undergoing radiotherapy. *Head Neck* 2005; **27**:659–668.
- 65 Paccagnella A, Morello M, Da Mosto MC, Baruffi C, Marcon ML, Gava A, *et al.* Early nutritional intervention improves treatment tolerance and outcomes in head and neck cancer patients undergoing concurrent chemoradiotherapy. *Support Care Cancer* 2010; **18**:837–845.
- 66 Salas S, Baumstarck-Barrau K, Alfonsi M, Digue L, Bagarry D, Feham N, *et al.* Impact of the prophylactic gastrostomy for unresectable squamous cell head and neck carcinomas treated with radio-chemotherapy on quality of life: prospective randomized trial. *Radiother Oncol* 2009; **93**:503–509.
- 67 Chen AM, Li BQ, Lau DH, Farwell DG, Luu Q, Stuart K, *et al.* Evaluating the role of prophylactic gastrostomy tube placement prior to definitive chemoradiotherapy for head and neck cancer. *Int J Radiat Oncol Biol Phys* 2010; **78**:1026–1032.
- 68 Lee H, Havrila C, Bravo V, Shantz K, Diaz K, Lamer J, *et al.* Effect of oral nutritional supplementation on weight loss and percutaneous endoscopic gastrostomy tube rates in patients treated with radiotherapy for oropharyngeal carcinoma. *Support Care Cancer* 2008; **16**:285–289.