

Treating Head and Neck Cancer in the Older Adult



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KEYWORDS

- Older adults (patients) • Comprehensive geriatric assessment • Frailty • Surgery
- Radiotherapy • Systemic therapy

KEY POINTS

- Advanced age alone should not exclude older adults from curative treatment of head and neck cancer.
- Practical geriatric assessment provides valuable insight into functional reserve, cognitive status, and social support, improving decision-making and predicting outcomes beyond chronologic age alone.
- Evidence shows older patients tolerate surgery and radiotherapy well, but chemotherapy raises toxicity risk, requiring careful assessment and personalised treatment planning for safe care.
- Shared decision-making, incorporating patient preferences and life expectancy, is critical in selecting appropriate treatment strategies for older patients with head and neck cancer.

INTRODUCTION

While the management of head and neck squamous cell cancer (HNSCC) in older adults should ideally be individualized, the development of robust, age-specific treatment recommendations remains challenging. Clinical trials have historically underrepresented the oldest age groups and systematically excluded patients with significant comorbidities, limiting the applicability of trial data to the real-world older adult population. In a

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Abbreviations	
5-FU	5-fluorouracil
ACE-27	Adult Comorbidity Evaluation
CARG-HNC	Cancer and Aging Research Group Head and Neck Cancer
CCI	Charlson Comorbidity Index
CGA	comprehensive geriatric assessment
CIT	carbon ion therapy
CPET	cardiopulmonary exercise testing
CRT	Chemoradiotherapy
ERAS	enhanced recovery after surgery
G8	Geriatric 8
GA	geriatric assessment
HDI	human development index
HNC	head and neck cancer
HNSCC	head and neck squamous cell cancer
HPV	human papillomavirus
IMRT	intensity-modulated radiotherapy
LOS	length of stay
OS	overall survival
PBT	proton beam therapy
PGA	practical geriatric assessment
PORT	postoperative radiotherapy
RCTs	randomized controlled trials
RT	radiation therapy
SDM	shared decision-making
TLM	transoral laser microsurgery
TORS	transoral robotic surgery
VES-13	Vulnerable Elders Survey-13

recent meta-analysis¹ of 93 clinical trials, only 4% (692 of 17,346 patients) were aged over 70 years. This exclusion results in a paucity of high-level, age-adjusted evidence to inform practice. In response, various patient-selection algorithms have been proposed to bridge this gap, incorporating factors such as comorbidity burden, functional status, and geriatric assessment (GA) findings. These frameworks aim to optimize treatment intensity, balance oncologic control with quality of life, and guide clinicians in tailoring therapy for a heterogeneous older patient population.

Locally advanced HNSCC often presents at a late (III/IV) stage in older adults requiring multimodality therapy consisting of a combination of surgery, radiation therapy (RT), and systemic therapy. Evidence suggesting no benefit from chemoradiotherapy (CRT) or altered fractionation in patients with head and neck cancer (HNC) aged over 70 years, reference studies over 20 years old. The most likely explanation is the impact of tumor control from these intense regimens is offset by treatment-related toxicities and competing noncancer causes of mortality. Historical studies include predominantly HPV-negative tumours, higher comorbid patients treated with older radiotherapy techniques. However, with the epidemiologic shift of HNSCC (attributable to the rise in HPV-positive disease in higher human development index [HDI] countries), the change in patterns of causative risk factors, potentially fitter aging population in conjunction with modern intensity-modulated radiotherapy (IMRT) the therapeutic balance of intensive treatment may now be more favorable in older adults.

BURDEN OF DISEASE

HNC is regarded as the seventh most common cancer diagnosis worldwide. With 890,000 new cases and 450,000 deaths annually according to the recent GLOBOCAN

2020 estimates.² The overall incidence of HNC continues to rise, with a predicted 30% increase annually by 2030. The *largest growth in cases* will be in *older adults* driven by an aging population and longer life expectancy with approximately 30% of all patients diagnosed over the age of 70 years.³ By 2040, this share could exceed 50% in higher HDI countries.

DEFINITION OF OLDER ADULTS

There is no universal cutoff age that exists for defining older adults. The United Nations defines older adults as 60 years or older to account for shorter life expectancies in low-income countries. The National Institute on Aging at the National Institutes of Health classify older adults into 3 categories: young old (65–74 years), older old (75–85 years), and oldest old (>85 years). ASCO 2018⁴ geriatric guidelines advise GA in patient aged 65 years and over. For this review, 70 years or greater is adopted as the definition of older age (Table 1).

CONSIDERATIONS IN THE OLDER ADULTS

With advancements in systemic anticancer therapy, radiotherapy, surgery, and anesthesia, increasing numbers of older patients are undergoing HNC therapies. Treatment is typically multimodal and carries varying risk.

Aging is associated with multimorbidity, reduced function and reserve across organ systems, with specific geriatric syndromes including dementia, falls and frailty increasingly common making treatment decision-making more complex.

Decision-making requires a comprehensive understanding of an older person's individual characteristics (eg, comorbidities, functional status, and frailty) and their impact and/or interactions with proposed treatment modalities balanced against the potential gains. This can enable appropriate treatment selection, risk estimation, and lever potential to mitigate risks with clinical interventions.

Frailty

Frailty is a distinct syndrome characterized by reduced physiologic reserve across multiple organ systems to maintain hemostasis in the presence of acute stressors and provides a measure of biological age. It is an independent risk factor for worse outcomes (morbidity, mortality, loss of independence, and institutionalization) and predicts worse health-related quality of life in patients with HNC. Frailty increases with age and socioeconomic deprivation, with 1 in 10 people aged over 50 years living with frailty, rising to 50% over the age of 85 years.⁵

HNC accelerates functional decline through dysphagia, malnutrition, pain, and aspiration, precipitating a deterioration in performance status. Definitive CRT may

Age Group (Years)	Description in HNC Context
<65	"Younger" cohort, often HPV-positive OPSCC or fewer comorbidities
65–69	Transitional group, often included in standard protocols
70–74	"Elderly" in most trial reporting. Careful selection for CRT
75–79	"Advanced elderly," higher frailty, often considered for deintensification
≥80	"Oldest old"—often excluded from trials, best supportive care common

compound this due to taste disturbance, mucositis, xerostomia, and weight loss. Compared with other solid malignancies, patients with HNC despite comparable comorbidity burden demonstrate significantly higher frailty (32.6% vs 21.8%; OR 1.74).^{6,7} In HNC, frailty is associated with a more than 2 fold risk of adverse events in patients undergoing surgery and a 2 fold risk with definitive CRT, respectively.⁸

Sarcopenia is the loss of muscle mass and function and a component of frailty. Being sarcopenic does not necessarily mean you will be frail (Table 2). Of note, the evaluation of frailty extends beyond the presence of multiple comorbidities. The comprehensive geriatric assessment (CGA), by incorporating multiple domains of health and function, provides the most thorough characterization of frailty in older adults.

Co-morbidity

Several validated commonly used comorbidity indices exist to define disease burden including the Adult Comorbidity Evaluation (ACE-27, specific to cancer) and the Charlson Comorbidity Index (CCI, general population tool). The CCI consistently predicts less than 1 year mortality, and greater than 1 year mortality. In a Danish⁹ case-control HNC population, it demonstrated a reduction in 10 year overall survival (OS) from 60% (CCI score 0) to 20% (CCI score 4–5).

In addition, the use of life tables (ideally health-adjusted stratifying survival by health status) can support decision-making and sources include the WHO Global Observatory¹⁰ and local/national statistical agencies (eg, ONS and CDC). If mortality prediction tools are to be applied, it is essential to select those validated in the appropriate population (eg, the Lee-Schonberg¹¹ Index, developed in US cohorts, vs the Suemoto¹² Index, which has been globally validated and is more applicable to LMIC settings).

Geriatric Assessment

NCCN Older Adult¹³ guidelines, the ASCO⁴ guideline, and SIOG¹⁴ statements recommend GAs for all older patients aged older than 65 years with cancer to identify health

	Sarcopenia	Frailty
Definition	Loss of skeletal muscle mass and/or function	Multidimensional syndrome of reduced physiologic reserve and vulnerability
Scope	Muscle-specific	Global (physical, nutritional, cognitive, social, and comorbidities)
Assessment	Computed tomography or MRI muscle index (C3/L3), DXA, bioimpedance, and grip strength	Frailty indices (eg, mFI, Fried phenotype, and Rockwood scale), geriatric assessment
Causes in HNC	Dysphagia, malnutrition, cachexia, and treatment toxicity	Age, sarcopenia, comorbidities, cognitive decline, and poor social support
Clinical impact	↑ Surgical complications, poor wound healing, reduced tolerance to CRT, and ↓ survival	↑ Surgical complications, prolonged recovery, functional decline, and ↑ mortality
Relationship	Component of frailty (physical aspect)	Broader construct that may include sarcopenia but extends beyond muscle loss

status issues to prevent treatment-related mortality/morbidity in frail patients while avoiding undertreatment in fit older patients.

Rarely CGA in older patients with HNC is used not only in practice but also in clinical trials. Older adults range from fit patients (without frailty, low comorbidity scores, and preserved performance) who should receive standard of care treatment equivalent to younger counterparts, to frail (unfit) patients who may be suited for best supportive care. However, the intermediate (or pre-fail) patients with significant comorbidities or poor performance status are often the most challenging to manage. This group often require personalized, modified oncologic approaches, including deintensification or supportive care, while remaining eligible for standard therapy when appropriate. Treatment decisions for older patients with HNC should be supported through CGA and multidisciplinary head and neck team consensus, ideally with geriatrician input.

The CGA is a multidimensional, interdisciplinary process that evaluates *frail older adults'* medical, psychological, and functional status to create a coordinated, personalized care plan. It addresses frailty, chronic conditions, polypharmacy, cognitive and physical function, geriatric syndromes (eg, falls and incontinence), mental well-being, and social circumstances (Fig. 1 and Table 3). CGA is a clinical process and combines

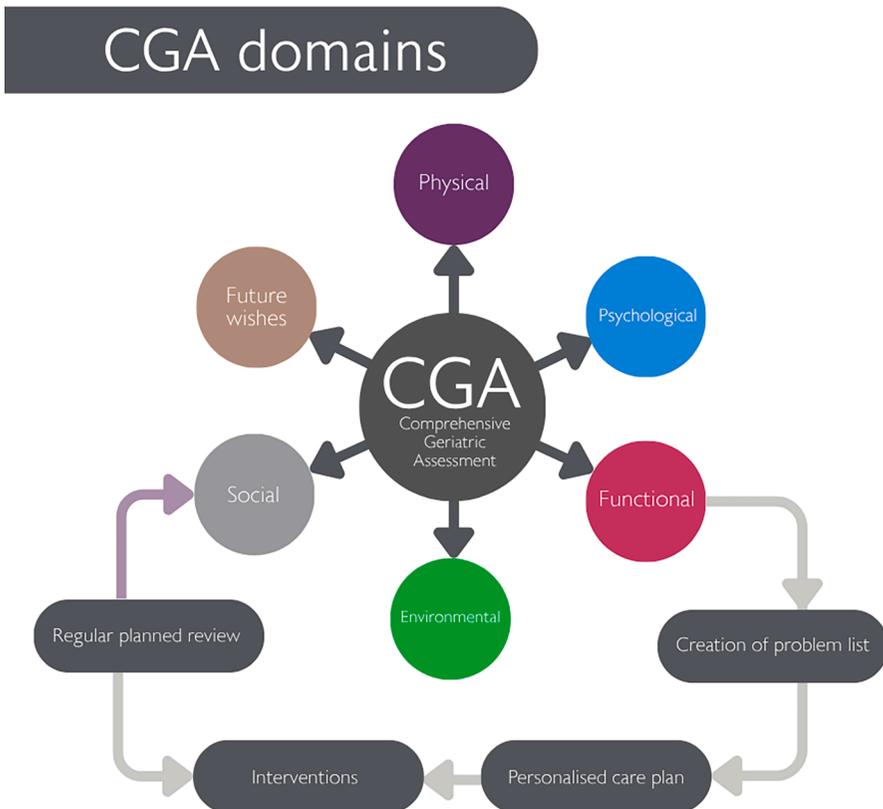


Fig. 1. Comprehensive geriatric assessment. From: British Geriatrics Society, 2025 (Figure taken from Comprehensive Geriatric Assessment (CGA) Hub. British Geriatrics Society (2025). Available at: <https://www.bgs.org.uk/CGA>. Reproduced with permission.).

	Detail of Components	Tools/Interventions
Physical	Medical history, multimorbidity, and long-term condition management, polypharmacy and medication review, nutrition and pain, and frailty	Clinical frailty scale Edmonton frailty scale STOPP/START criteria Malnutrition Universal Screening Tool
Psychological	Mood, mental health, and cognition assessment. Assessment of delirium risk	Hospital anxiety and depression score MoCA 4AT
Functional	Mobility, activities of daily living, and prehabilitation	Nottingham Extended activities of daily living scale Gait speed
Environmental	Home suitability, accessibility, and use of technology	Medication compliance devices Falls risk assessment Mobility aids
Social	Social support (formal and informal), religious beliefs/spirituality, and financial concerns	Social prescribing Voluntary organizations Family support
Future wishes	Treatment preferences, priorities of care, resuscitation, and advance care planning	BRAN tool

screening (clinical questions and/or completion of tools), assessment, intervention through care plans, and follow-through, with support of multidisciplinary team and improves communication, goals-of-care discussions, treatment completion, physical function, and quality of life. Prehabilitation through targeted nutrition, exercise, or psychoeducation before surgery (\pm radiotherapy) improves quality of life, morbidity, and mortality in patients with HNC.¹⁵

GA in older adults with cancer change treatment plans in a median of 31% of patients, with greater impact in multidisciplinary settings, and prompt nononcologic interventions in over 70% of cases.¹⁶ In the ELDERLY study in patients with HNC aged older than 65 years, a CGA resulted in a major therapeutic change (11.8%) and increased supportive care in various domains (nutrition, polypharmacy change, and psychological/psychiatric).¹⁷

Of note, most randomized controlled trials (RCTs) of CGA have been conducted in resource-rich settings in high-income countries and the routine uptake and integration of CGA remains low, only 22% oncology providers in a recent international survey¹⁸ using them regularly primarily due to the perceived concerns about knowledge/training and time resource constraints. To support wider adoption in routine oncological practice in resource-constrained settings, ASCO global¹⁹ guidelines in GA for patients with cancer aged older than 65 years have been published. The guideline recommends the practical geriatric assessment (PGA),²⁰ a more simplified assessment with recommended validated tools against each domain best suited to routine clinical care.

Validated screening tools (which are not decision-making tools) have evolved to screen for at risk/vulnerable patients requiring a CGA and have demonstrated

associations with poorer outcomes. Several validated screening tools exist including the Geriatric 8 (G8), Vulnerable Elders Survey-13 (VES-13), and Groningen Frailty Index. Recent US Delphi consensus of geriatric oncology experts²¹ recommended the VES-13 while the G8 is more widely assessed in Europe. The G8 consists of 8 items, mostly patient-reported and has been reported to correlate better with CGA than VES-13 at baseline,^{22,23} but a cutoff value of 10.5 better predicted survival than the usual cutoff of 14.0.²⁴ In patients with HNC aged older than 65 years, G8 screening has shown to support identification of vulnerable patients with protracted postoperative course specifically length of stay (LOS) and feeding tube dependence²⁵ (Table 4).

Specifically, in HNC the Elan Geriatric Evaluation (EGE) is reported to be more sensitive (95%) and specific (60%) than G8 and can be completed in 20 minutes by non-geriatricians. It has been assessed as part of EGeSOR,²⁶ the first randomized trial to test CGA-driven interventions in older (>65 years, median age 75.3 years) patients with HNC. The 2 year OS was 59.5% with no significant difference between the control and CGA-driven intervention group in 2 year OS, functional status, nutritional decline, or long-term quality of life. However, notably 74% of the intervention arm patients did not receive the full geriatric program, which may have contributed to lack of effect in the trial.

On multivariable analyses, although the overall G8 score was not associated with poor 2 year OS, individual item scores related to weight loss at 3 months ($P = .027$), moderate or severe dementia/depression ($P = .028$), and older age ($P < .001$) were. Several individual components of the EGE in the intervention group emerged as key prognostic factors; low autonomy (an instrumental activities of daily living score <8), poor mobility (a one-leg standing test result <5 seconds), nutritional status (an abnormal Mini Nutritional Assessment score), and cognitive status (a Mini Mental State Examination score <24) were associated with poor 2 year OS.

Treatment risks are raised in older patients due to aging-related decline in organ function, multimorbidity, polypharmacy, and geriatric specific syndromes. Polypharmacy is associated with postoperative complications, chemotherapy toxicity, and poorer function.²⁷ Prediction tools can complement shared decision-making (SDM) conversations, guide appropriate treatment modalities, and inform consent.

The CARG-HNC (Cancer and Aging Research Group Head and Neck Cancer) group have identified specific research gaps and have proposed risk models that are available as online calculators for practicing oncologists to incorporate into their clinical practice. The CARG²⁸ (at http://www.mycarg.org/Chemo_Toxicity_Calculator) and

Table 4	
Considerations in head and neck reconstruction in older adults	
Frailty	Strong Predictor of Complications/Functional Decline (5 Item mFI)
Nutritional status	Impaired wound healing, ↑ infection risk
Comorbidities	Cardiac, pulmonary, diabetes, renal: ↑ risk perioperative and postoperative morbidity/mortality (ACE-27 and Charlson Comorbidity Index)
Duration of surgery	Complexity of reconstruction/flap type: ↑ duration surgery → cardiopulmonary events ↑ flap failure risk (doubles LOS, ↑ complication and mortality rates)
Loss of independence	Weigh functional outcomes (subsite and flap choice) vs operative risk

CRASH or Moffitt score²⁹ (at <https://www.moffitt.org/eforms/crashes> coreform) provide some objective measure of potential risk of severe chemotherapy toxicity. With radiotherapy (± chemotherapy), the Generalized Competing Event (GCE) model, a head and neck-specific tool, stratifies the risk of cancer against noncancer events with radiotherapy.

In the surgical setting, preoperative risk prediction scores such as SORT score (risk of death within 30 days of inpatient surgery) and the ACS NSQIP surgical risk calculator (risk of 19 outcomes within 30 days following surgery) can help guide decision-making but are not validated in complex HNC surgery.^{30,31}

Older patients with HNC can have a high symptom burden related to the tumor location (eg, oral pain and dry mouth), the impact of those symptoms on health and well-being (eg, weight loss, depression, and anemia), or constitutional symptoms due to cancer and/or treatment (eg, fatigue). Multidisciplinary interventions from dietitians, speech and language therapists, psychology, physiotherapy, and occupational therapy are integral supportive resources to managing symptoms and quality of life.

While better assessment with CGA and risk prediction tools can aid an improved understanding of risks, benefits, and mitigations, it is critical to use this information to enable SDM with individuals.³² There is a paucity of literature on older adults' priorities with HNC, scoping reviews suggest patients often prioritize maintaining independence and treatment regret is more common among those with higher depression levels and greater frailty.^{33–35} SDM is a collaborative process where health care professionals support patients to make health care decisions that are right for them. The process is dynamic and incorporates health care professional's expertise (treatment options, evidence risk, and benefits) and patients' priorities (preferences, goals, values, and priorities of care). SDM can lead to realistic expectations of treatment outcomes, lower decisional regret, and reduce the number of patients undergoing major surgical interventions. BRAN,³⁶ an SDM framework, can be used to structure patient and clinician treatment discussions.

SURGERY

Prehabilitation and Enhanced Recovery after Surgery

Prehabilitation is considered a multidisciplinary program initiated before treatment and aims to enhance patients' physical, nutritional, and psychological resilience. Interventions combining swallow exercise, nutrition, and psychoeducation yield greatest benefit in preventing weight loss, reduced LOS, complications, and swallowing outcomes in HNC.³⁷ The University of Calgary trial (NCT04598087) is assessing a multiphase exercise-based program for safety, benefits, and integration for patients undergoing HNC surgery with free flap reconstruction.

Cardiopulmonary exercise testing (CPET) is feasible in older adults providing an objective perioperative risk stratification and predicts cardiopulmonary complications, need of ICU, and LOS. However, lack of data exists for older adults with HNC, but CPET was recently explored in a heterogeneous cohort undergoing major HNC surgery with lower peak Vo_2 values predicting day-5 cardiopulmonary morbidity.³⁸ CPET supports focused prehabilitation and counseling quantifying cardiopulmonary physiologic reserve and is complementary to CGA, which captures nonphysiologic vulnerabilities.

Prehabilitation is not yet standard in enhanced recovery after surgery (ERAS) HNC protocols that primarily focus on perioperative and postoperative optimization. ERAS protocols are variably adopted despite HNC surgery-specific guidelines by the ERAS Society.³⁹

High-quality prospective HNC ERAS trials targeting older adults do not exist, but published HNC ERAS protocols show evidence of some benefit in reduction in LOS, improved pain control, and reduced opioid usage avoiding postoperative complications.⁴⁰ In older adults, this is particularly pertinent to reduce risks of hospital acquired infection, delirium, constipation, and reducing sedation aiding early mobilization and preventing pulmonary complications. Risk-stratified prophylactic tracheostomy insertion and early nutrition are encouraged and have been shown to shorten LOS without compromising outcomes.³⁹

Recent population-based studies suggest the risk of stroke at 30 days after neck dissection is low 0.3% to 0.97% (3–10 per 1000).⁴¹ Ischemic stroke risk is higher in patients aged 75 years or older (OR 1.63), those with diabetes (OR 1.59), hypertension (OR 2.64), prior radiotherapy (OR 2.43), and especially prior stroke with an over a 4 fold increase in odds (OR 4.06).⁴⁰ Severe carotid artery stenosis carries an annual stroke risk of 6.9%, hence preoperative optimization with vascular/stroke teams is recommended if seen on preoperative imaging.⁴² Overall vascular event rates (4.5%) in HNC differ by primary treatment with stroke risk reported to be higher for radiotherapy (6.1%) compared to chemotherapy (5.1%) and surgery (0.9%).⁴³

Head and Neck Reconstructive Surgery

In the context of HNC microvascular free tissue transfer literature, there is no consistent definition of “elderly,” with age cutoffs ranging from 50 to 80 years and most commonly report on cohorts between 65 and 70 years. This in combination with variable use of comorbidity indices and a lack of consensus on complication reporting, makes cross-study comparisons difficult. Despite these limitations, more contemporary evidence suggests that complex reconstruction can generally be performed safely in older adults with caution advised with increasing comorbidity burden and frailty particularly in patients aged over 75 years.

Frailty scores and GAs offer the better predictive value in the assessment of the older patient for surgery. Older patients with HNC are more likely to have cardiovascular and pulmonary comorbidities,⁴⁴ making some poor surgical candidates because of anesthesia risk.

The 5 item Modified Frailty Index based on hypertension requiring medication, COPD, heart failure, diabetes mellitus, and nonindependence, has been validated⁴⁵ as a rapid tool for identifying frailty in surgical patients. Frail patients had significantly higher risks of return to theater (OR 3.47), severe complications (Clavien-Dindo grade IV, OR 6.23), medical complications (respiratory issue OR 2.61 and delirium OR 5.05), and significantly longer hospital stay (+16.46 days on average). Postoperative mortality at 90 days and 1 year was not significantly increased.

A contemporary large multi-institutional cohort⁴⁶ of patients aged 80 years or older undergoing major head and neck surgery with flap reconstruction (free or pedicle) over half-experienced serious complications, with 90 day mortality of 8%. Importantly, 11% of previously independent patients became dependent within 90 days. Frailty and comorbidity (MFI ≥ 0.25 , ACE-27 scores 2–3) predicted worse outcomes rather than age alone, while higher body mass index (≥ 25) was protective. Surgeries of the oral cavity, maxilla, and oropharynx were most strongly associated with functional decline (10%–20% at 90 days). These findings highlight the need for careful risk-benefit assessment, especially regarding postoperative quality of life and subsite specific functional impact in the very old.

Free flap reconstruction itself is not linked to worse outcomes, though surgical complexity resulting in longer operating time and flap failure increase risk. Duration

of surgery has been shown to be an independently associated with early cardiopulmonary morbidity postoperatively.³⁸

National hospital datasets⁴⁷ show that flap failure nearly doubles hospital stay and is strongly linked to complications and in-hospital mortality. Risk is higher with advanced age, comorbidities, social deprivation, emergency surgery, and varies by resection site, being greatest for oropharynx, hypopharynx, and larynx reconstructive failures (OR 4 for death). Outcomes also depend on conduit flap type in circumferential pharyngeal defects: radial forearm and anterolateral thigh flaps carry the lowest mortality, while gastric pull-up has the highest, even when flap failure is accounted for. In older patients, careful flap selection, dual-team surgery, and centralization of complex reconstructions in high-volume centers are recommended.

For older patients undergoing salvage surgery with a clinically N0 neck, superselective or omitted neck dissection may be considered,⁴⁸ with decisions individualized according to tumor site, recurrence pattern, prior treatment, and patient comorbidities, to optimize the balance between oncologic control and surgical morbidity.

Minimally Invasive Surgery

Given the shifting epidemiology of HPV-related OPSCC toward older age groups adults (in North America and Western Europe 70% of new OPSCC is attributable to HPV), there is a pressing need to evaluate the applicability of treatment de-escalation strategies, originally developed for younger, healthier cohorts in older patients. Such consideration must account for age-related comorbidities, functional reserve, and the underrepresentation of older adults in de-escalation trials.

The advent of transoral robotic surgery (TORS) has demonstrated safety in a national database⁴⁹ with no additional mortality risk at 30 and 90 days in patients aged older than 70 years. However, adjuvant therapy is frequently not administered due to patient refusal or comorbidity. Small retrospective TORS cohort studies^{50,51} in patients aged older than 70 years with early stage OPSCC and low comorbid status suggest comparable oncological outcomes, with one study suggesting longer enteric feeding at 3 months and worse functional outcomes in those undergoing adjuvant therapy particularly for tonsil subsite.

Although the phase II E3311⁵² TORS trial had no upper age limit (median 61 years range 57–80 years) definitive number of patients over 70 years is not clear. The study highlights a substantial proportion of patients required adjuvant radiotherapy (57%) or CRT (31%), underscoring the importance of CGA and baseline swallowing evaluation to ensure patients selected can tolerate and complete the full treatment package.

The direct survival benefit of primary TORS versus nonsurgical management in early OPSCC in the older adult remains debated. In a national⁵³ propensity-matched cohort of patients aged older than 70 years, TORS achieved higher 5 year overall survival (81.6% vs 70.7% with RT; $P < .001$), though this may reflect less-intensive chemotherapy regimens and frailty. Despite this, TORS use in the older adult has steadily declined over the last decade in the United States. The reasons remain unclear but likely due to increasing patient complexity and need for swallow rehabilitation, advances in RT techniques, and limited access to surgical expertise.

In the salvage setting, TORS has expanded the eligibility for salvage surgery in appropriately selected older adults with recurrent HNCs. A retrospective international⁵⁴ TORS cohort study (21% >70 years) demonstrated favorable OS (71.8% at 2 years and 49.8% at 5 years) compared to alternate alternative open surgery or reirradiation approaches but caveated with a selection bias toward patients with smaller volume, lower stage, reduced comorbid burden, and lack of reported margin status in

20%. Although subgroup analysis on the functional outcome is not presented for the older patient group, overall, the rates for perioperative tracheostomy and gastrostomy at 1 year were 10.8% and 33.8%.

Retrospective series^{55,56} of patients aged older than 70 years suggest transoral laser microsurgery (TLM) provides effective oncological and functional outcomes, though gastrostomy tube rates are higher in supraglottic than glottic sites, even when elective neck dissection is omitted in radiological N0 early T-stage disease. Age-related presbylarynx further impacts recovery, and a small prospective study⁵⁷ found that voice outcomes in those aged older than 60 years may take up to 12 months to stabilize after TLM despite intensive speech therapy.

RADIOTHERAPY

We saw significant advances in radiotherapy treatment techniques over the last 2 decades with reduced side effects while maintaining the high cure rates.^{58–60} However, radiotherapy research in HNC is primarily focused in people aged younger than 70 years.

We have validated CGA and screening tools from previous studies but their incorporation in clinical practice is not yet standardized. There are also no clear guidelines on whether older patients warrant any adaptation of treatments and how best to modify treatments to achieve the desired outcomes in this population. In this section, we discuss the variation in tolerance of organs to radiation in the older adult, additional side effects to keep in mind, modifications in dose/schedules and personalization of treatments.

Are Older Patients More Prone to Side Effects From Radiotherapy and is the Tolerance of "Organs at Risk" any Different?

Radical RT in HNC is usually associated with side effects including taste changes, mucositis, swallowing problems, dry mouth (xerostomia), effects on skin, soft tissue, teeth, and bone.

Use of IMRT has improved patient-reported xerostomia and the DARS trial showed improvement in swallowing outcomes with optimized radiation dose to pharyngeal constrictors. While the same principles can be extrapolated to the older population, an added factor is age related "impaired recovery of function" following radiation. The rate of xerostomia was higher than predicted even if the QUANTEC criteria for organ tolerance were met in the older patients.⁶¹

The susceptibility of carotid vessels to radiation and potential risk of stroke is higher in the older adults. Close monitoring and management of cerebrovascular risk factors is important in this population.⁶² The feasibility of carotid sparing RT was studied in the context of radical RT to early stage larynx,⁶³ but no conclusive evidence is available thus far.

Evaluation of baseline xerostomia and risk stratification of cerebrovascular disease could help personalize treatments. Further research evidence to establish the need for any adaptations to QUANTEC criteria in older patients may be beneficial.

Importance of Single Modality Treatment in Early Stage Head and Neck Cancer

In early stage disease (T1/2, N0), single modality treatment either surgery or radiotherapy is the preferred choice. The advent of minimal invasive surgery including TORS provides an attractive alternative in selected older patients being a one-off procedure. However, the significant proportion of patients requiring adjuvant radiotherapy is undesirable in this cohort. Careful patient selection including patient priorities,

baseline function and predicted functional impairment with each treatment alongside radiosensitivity of the tumor would help.

Modification in Radiation Dose/Schedule Including Hypofractionated Radiation Therapy and De-Escalation of Treatments

Use of hypofractionated regimes (eg, 55 Gy in 20 fractions) in smaller tumors is preferred in older patients to reduce the overall treatment time and improve compliance. The risk/benefit ratio of elective nodal irradiation should be critically evaluated alongside life expectancy in the older adult population. De-escalation especially in HPV-associated HNSCC in the older adult is of particular interest and being explored in research studies.

In a national database⁶⁴ of just over 7000 patients with advanced OSCC, nearly one-third of patients and over 40% of those aged older than 70 years, did not receive post-operative radiotherapy (PORT) despite NCCN guidelines. This omission increased progressively with each decade from 60 to 90 years with progressively worse OS. Patients aged younger than 65 years and those living within 25 miles of the treatment facility were most likely to receive PORT, with age (OR 1.96) and shorter distance (OR 1.61) being the strongest sociodemographic predictors.

Daily travel for conventional fractionated radiotherapy over 6 to 7 weeks can represent a substantial barrier for older patients. The use of hypofractionated regimens, in which doses greater than 2 Gy per fraction are safely delivered, may significantly reduce overall treatment duration with the potential to improve treatment adherence and patient compliance, particularly advantageous in this population. Hypofractionated radiotherapy was studied in the HYPNO trial testing a hypothesis derived from mathematical modeling of clinical trial data in a large RCT setting and showed noninferiority to both adverse effects and tumor control.^{65,66} However, patients with major comorbidities were excluded, thereby limiting its value in older patients. A prospective randomized trial in older patients would, therefore, be useful to establish safety and effectiveness of this regime.

Proton Beam Therapy and Carbon Ion Therapy

Protons are positively charged particles that deposit at a certain depth by a phenomenon called Bragg peak where the peak is followed by a sharp dose fall-off. The potential to reduce damage to surrounding tissues, and therefore less acute and late radiotherapy side effects, while maintaining cure rates is a particular advance in HNC RT. Proton beam therapy (PBT) is currently commissioned in selected tumors with invasion of skull base where optimization of dose to brain and optical apparatus is beneficial. However, the current evidence is insufficient to support the routine commissioning of PBT for HNC in the United Kingdom. The potential advantages of PBT are currently being explored in several clinical trials. The TORPEDO study⁶⁷ compared photon versus PBT in oropharyngeal cancers, with results awaited. The PROTIS⁶⁸ study, which investigates a similar comparison in sinonasal tumors, is actively recruiting. Specific dosimetric advantages of PBT in lateralized tumors (salivary gland tumors) is being explored in the PRONTO⁶⁹ study.

While advantages are applicable to older adult population too, the accessibility of PBT is a practical concern. Current restricted availability in just few centers and mandatory need for travel makes it a less attractive option for this patient group.

Carbon ion therapy (CIT) is also on the horizon utilizing accelerated carbon ions to deliver a highly focused dose of radiation at a specified depth. The efficacy and safety of CIT in patients aged older than 80 years was explored in early stage lung cancer.⁷⁰

CIT is currently being explored in HNC specifically in tumors that are radioresistant and those in challenging anatomic locations. The hope is for the increased biological effectiveness to potentially overcome radio resistance and tissue hypoxia, which are barriers with standard radiation treatments.⁷¹ The lesser number of fractions is a particular advantage, but safety and efficacy need to be explored further.

Adaptive Radiotherapy in Head and Neck Cancer and Applications

Adaptive radiotherapy has gained a significant interest in HNC treatment. It is a personalized approach where RT is adapted to changes in shape during treatment. Squamous cell cancers especially HPV-associated tumors are usually highly radio-sensitive and can shrink substantially during treatment, rarely some can also continue to progress during treatment. Adaptive radiotherapy involves dynamically adjusting the treatment plan in response to the patients' anatomic changes. It offers opportunity to escalate or de-escalate when clinically indicated with potential to improve overall outcomes of treatment.

Adaptive radiotherapy is particularly important when using hypofractionated regimens (larger dose per fraction) in vulnerable patient groups. Early studies indicate that successful implementation of adaptive radiotherapy techniques can revolutionize HNC radiotherapy.

Palliative Radiotherapy

Due to frailty, comorbidities and preferences, older patients with HNC are often less suitable for radical/curative treatment approaches. Palliative radiotherapy plays an important part under those circumstances. High-dose palliative radiotherapy regimens (eg, 45 Gy in 15 fractions) could be effective in providing good local control and in some patients a sustained benefit.

Several dose fractionation schedules are in use including 20 Gy in 5 fractions, 30 Gy in 10 fractions, 45 Gy in 15 fractions, 24 Gy in 3 fractions over 3 weeks, 40 Gy in 10 fractions over 4 week split course, and 14 Gy in 4 fractions, which can be repeated 2 further times every 4 weeks. Medical management to optimize symptom control alongside RT is essential due to complex needs in older patients.

SYSTEMIC THERAPY

The systemic therapy management of older adults affected by HNSCC requires a pragmatic balance between the goal to maximize disease control and oncologic benefit and the need to minimize toxicity, functional decline, and treatment-related morbidity. Chronologic age alone is not a sufficient determinant of tolerance and contemporary guidelines emphasize the use of GA tools, comorbidity indices, and objective measures of organ function to guide the selection of systemic regimens that can include multiagent combinations or single-agent approaches.⁷² This principle is relevant both in the context of locally advanced disease and in the recurrent/metastatic disease setting, where platinum-based chemotherapy eligibility, immune checkpoint inhibitor suitability, and novel targeted strategies must be carefully considered.

Locally Advanced Setting

Three weekly, bolus (high-dose) cisplatin has remained for decades as the standard radiosensitizer in fit patients, but in older adults, its poor tolerability due to nephrotoxicity, ototoxicity, peripheral neuropathy, and many other adverse effects, has limited its use. Age 70 years or older, poor renal function, baseline hearing loss, peripheral neuropathy, or an ECOG performance status 2 or greater, are widely recognized as

indicators of cisplatin ineligibility.⁷³ For these patients, alternative strategies such as weekly (low-dose) cisplatin, carboplatin-based regimens, or cetuximab-radiotherapy combinations have been explored without any level 1A evidence identified. Systematic reviews of cisplatin-unfit patients with locally advanced disease demonstrated that these regimens may provide reasonable locoregional control (2 year LRC up to 70%–75% with carboplatin-based chemoradiation) while limiting acute and late toxicity but ultimately highlighted the need for clinical studies in this field.^{73–75} Pragmatic adaptation of systemic radiosensitization has therefore become an essential component of tailoring therapy in older populations.

After years of disappointing data with respect to immunotherapy in the locally advanced setting for HNSCC, the perioperative landscape has finally evolved due to the phase 3 KEYNOTE-689 trial results, demonstrating that 2 cycles of neoadjuvant pembrolizumab followed by surgery and adjuvant radiotherapy ± cisplatin, plus adjuvant pembrolizumab, significantly improved event-free survival versus standard care alone in stage III and IV resectable locally advanced HNSCC.⁷⁶ This finding has already prompted regulatory recognition of perioperative pembrolizumab as a new standard option for PDL1-positive resectable, locally advanced HNSCC.

Relevant to geriatric oncology, KEYNOTE-689 enrolled a broad adult population with median age of about 60 years, with reported age ranges extending up to 87 years.⁷⁶ However, efficacy or safety subgroup analysis for patients aged 70 years or older has not been reported and direct trial-level estimates of benefit and toxicity in the 70 years or older cohort remains unknown. Nevertheless, the perioperative data anchor an important shifting paradigm: neoadjuvant immunotherapy can induce early immunologic tumor modulation, may downstage disease at resection, and, when followed by adjuvant treatment, appears to reduce recurrence risk. These are outcomes particularly meaningful for older patients in whom minimizing the need for repeated cytotoxic exposure and hospitalization can preserve function and quality of life. For older adults who are physiologically fit, these results may suggest that, for certain patients, integrating neoadjuvant anti-PD1 into curative-intent pathways is feasible and beneficial. For frailer patients, the lack of age-specific subgroup data leaves clinicians to balance the risks of perioperative immune checkpoint blockade against its potential event-free survival benefits.

In addition, low-dose immunotherapy has been shown in a phase III trial from India to improve survival in advanced HNSCC when added to metronomic chemotherapy, without increasing severe side effects.⁷⁷ Although the study did not specifically focus on older adults (“elderly” defined by local context >60 years [range 28–77 years] 17 patients in treatment arm), the favorable safety profile observed suggests that such a regimen could be relevant for older patients, who often have limited tolerance for intensive treatments.

Recurrent/Metastatic Setting

The introduction of immune checkpoint inhibition has been practice changing. The KEYNOTE-048 trial established pembrolizumab as the backbone of modern first-line treatment. Pembrolizumab monotherapy improved overall survival in PD-L1-positive tumors, while pembrolizumab plus platinum/5-fluorouracil [5-FU] chemotherapy demonstrated superiority over the EXTREME regimen across unselected populations.^{78,79} Subgroup analyses and subsequent systematic reviews confirm that older adults derive similar benefit from immune checkpoint inhibitors, with manageable safety profiles that compare favorably to cytotoxic chemotherapy.⁸⁰ In frail patients, single-agent PD1 blockade can provide durable disease control with minimal incremental toxicity, whereas fit older adults with high tumor burden may derive greater

benefit from immunotherapy to facilitate a rapid tumor shrinkage.^{72,80} The KEYNOTE-B10 trial study demonstrated that combining pembrolizumab with carboplatin and paclitaxel as first-line therapy for recurrent or metastatic HNSCC yielded promising antitumor activity and a manageable safety profile. Its use is in practice in lieu of the EXTREME regimen particularly in North America, as it is not only effective but also feasible for older adults.⁸¹ This patient and risk stratification based on physiologic reserve, tumor biology, and symptom burden represents the principle of tailoring systemic treatment intensity.

Prior to immunotherapy, the EXTREME regimen was used as first-line therapy in the recurrent/metastatic setting. However, its tolerability in older adults was often questioned, particularly given the toxicity of continuous infusion 5-FU. The ELAN-FIT⁸² trial directly addressed this gap by prospectively evaluating an adapted EXTREME regimen of weekly paclitaxel, combined with platinum and cetuximab, instead of 5-FU infusion. The study demonstrated encouraging overall survival and response rates,

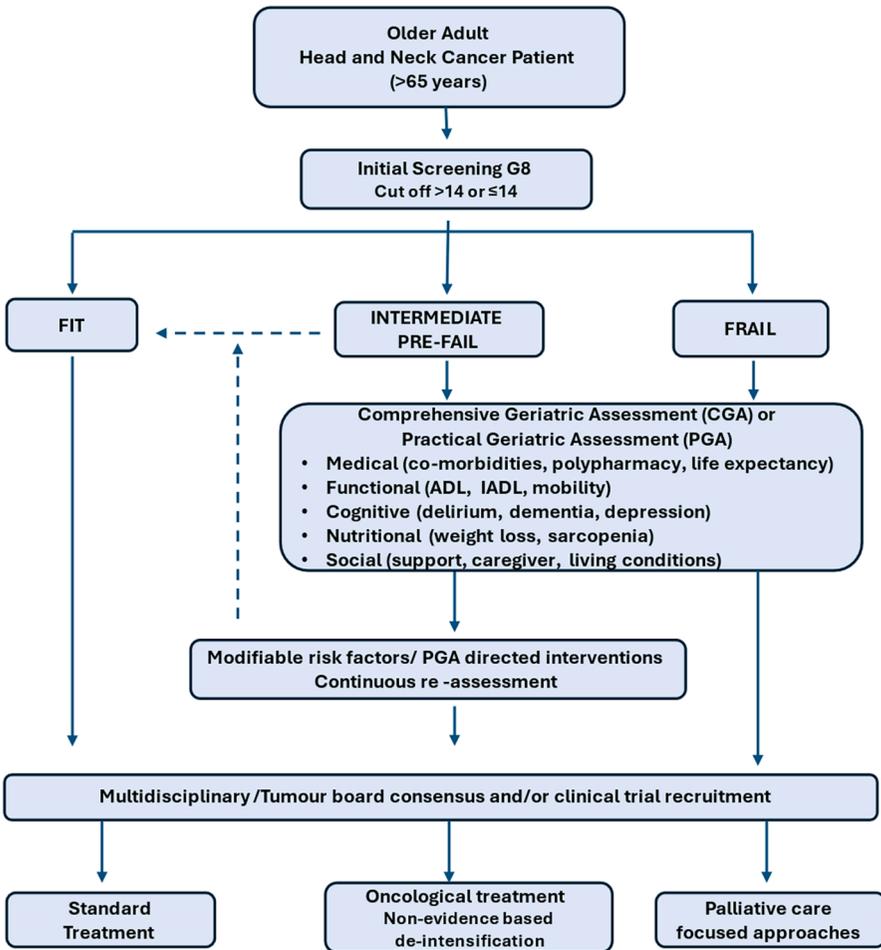


Fig. 2. Suggested algorithm for treatment of HNC in older adults. (ADL, Activities of Daily Living, IADL, Instrumental Activities of Daily Living). Loss of IADLs often comes before loss of ADLs, serving as an early warning of functional decline.

alongside manageable toxicity profiles, reinforcing that “fit older” is a clinically meaningful subgroup and that adapted multiagent regimens can remain viable when supported by rigorous assessment, multidisciplinary care, and proactive toxicity management.

Beyond EGFR inhibition and immunotherapy, ongoing research is expanding the armamentarium of targeted treatments with early phase studies investigating PI3K/AKT/mTOR inhibitors, antibody–drug conjugates, and novel small molecules. These approaches remain highly investigational, with no specific data in the older adult patient population.

Overall, systemic therapy for older patients with HNSCC must be individualized through a framework that balances efficacy and tolerability.⁸³ Cisplatin remains reserved for the exceptionally fit, while alternatives such as carboplatin, or cetuximab-based radiosensitizers may be used in cisplatin-ineligible patients. Single agent anti-PD1 pembrolizumab has transformed the recurrent/metastatic landscape, with evidence supporting both monotherapy and chemoimmunotherapy depending on patient reserve and disease characteristics and its use is now reshaping the curative intent setting with a new neoadjuvant option. The ELAN-FIT trial importantly demonstrates that adapted triplet regimens remain feasible in fit older adults, underscoring that therapeutic opportunities should not be withheld solely based on age. Collectively, these insights support a tailored, multidisciplinary, and patient-centered approach to systemic therapy in older adults with HNSCC.

SUMMARY

Although older patients may have different treatment tolerance than younger individuals, there is no strong evidence that tumor biology or survival outcomes are inherently worse with age. Advanced age alone should not preclude curative treatment.

Decisions should be guided through appropriate screening tools and subsequent CGA/PGA incorporated through routine clinical workflow tailored to local resource and language to ensure equity of care and outcomes (Fig. 2). Use of telemedicine and digital incorporation into electronic medical records to aid compliance and leverage of data analytics for older adults are areas of ongoing research and have shown benefit in HNC.¹⁹

Evidence on less-intensive regimens to improve tolerance is limited. Although digital twins could transform geriatric oncology by modeling frailty, comorbidities, and treatment responses to personalize care and reduce undertreatment currently significant technical, ethical, and equity challenges remain.⁸⁴

Critically, prospective clinical trials targeting older adults, especially those in the “intermediate” or pre-fail category, incorporating GAs are needed to refine management strategies and provide novel strategies to mitigate toxicity burden are desperately needed. Further research is required to validate HNC-specific prognostic scores/screening tools to enable optimal patient selection.

CLINICS CARE POINTS

Clinical Care Pearls

- Balance treatment goals: Decisions should weigh toxicity reduction, efficacy preservation, and patient-specific factors, including curative vs palliative intent.
- Address modifiable risk factors early: Implement nutritional support, physical therapy, and social interventions to reduce complications and improve treatment adherence.

- Reduce toxicity proactively: Use supportive care (eg, G-CSF), select less toxic but effective alternatives (eg, carboplatin/5-FU instead of cisplatin), or modify dosing (weekly instead of 3-weekly, dose ramp-up).

Clinical Care Pitfalls

- Sacrificing efficacy without clear rationale: Adjustments that lower anticancer potency or dose intensity may compromise outcomes, particularly if palliative care is not the intended goal.
- Neglecting postoperative quality of life: Failure to consider surgical sub-site-specific risks, loss of independence, prolonged recovery or permanent functional deficits undermines treatment goals.

DISCLOSURE

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REFERENCES

1. Pignon JP, le Maître A, Maillard E, et al. MACH-NC Collaborative Group. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17,346 patients. *Radiother Oncol* 2009;92(1):4–14.
2. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71(3):209–49.
3. Corry J, Ng WT, Ma SJ, et al. Disadvantaged subgroups within the global head and neck cancer population: how can we optimize care? *Am Soc Clin Oncol Educ Book* 2022;42:1–10.
4. Mohile SG, Dale W, Somerfield MR, et al. Practical assessment and management of vulnerabilities in older patients receiving chemotherapy: ASCO guideline for geriatric oncology. *J Clin Oncol* 2018;36(22):2326–47.
5. Walsh B, Fogg C, Harris S, et al. Frailty transitions and prevalence in an ageing population: longitudinal analysis of primary care data from an open cohort of adults aged 50 and over in England, 2006–2017. *Age Ageing* 2023;52(5):afad058.
6. Bras L, Driessen D, de Vries J, et al. Patients with head and neck cancer: are they frailer than patients with other solid malignancies? *Eur J Cancer Care* 2020;29(1): e13170.
7. de Vries J, Bras L, Sidorenkov G, et al. Frailty is associated with decline in health-related quality of life of patients treated for head and neck cancer. *Oral Oncol* 2020;111:105020.

8. Mascarella MA, Vendra V, Sultanem K, et al. Predicting short-term treatment toxicity in head and neck cancer through a systematic review and meta-analysis. *J Geriatr Oncol* 2024;15(8):102064.
9. Ruud Kjær EK, Jensen JS, Jakobsen KK, et al. The impact of comorbidity on survival in patients with head and neck squamous cell carcinoma: a nationwide case-control study spanning 35 years. *Front Oncol* 2021;10:617184.
10. World Health Organization. Global health observatory data repository. Available at: <https://apps.who.int/gho/data/node.main.LIFECOUNTRY>.
11. Lee SJ, Lindquist K, Segal MR, et al. Development and validation of a prognostic index for 4-year mortality in older adults. *JAMA* 2006;295:801–8.
12. Suemoto CK, Ueda P, Beltran-Sánchez H, et al. Development and validation of a 10-year mortality prediction model: meta-Analysis of individual participant data from five cohorts of older adults in developed and developing countries. *J Gerontol A Biol Sci Med Sci* 2017;72:410–6.
13. Dotan E, Walter LC, Browner IS, et al. NCCN guidelines® insights: older adult oncology, version 1.2021. *J Natl Compr Cancer Netw* 2021;19(9):1006–19.
14. Wildiers H, Heeren P, Puts M, et al. International society of geriatric oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol* 2014;32(24):2595–603.
15. Seghers PALN, Wiersma A, Festen S, et al. Patient preferences for treatment outcomes in oncology with a focus on the older patient—a systematic review. *Cancers (Basel)* 2022;14(5):114.
16. Hamaker M, Lund C, Te Molder M, et al. Geriatric assessment in the management of older patients with cancer - a systematic review (update). *J Geriatr Oncol* 2022;13(6):761–77.
17. Bossi P, Esposito A, Vecchio S, et al. Role of geriatric assessment in tailoring treatment of locally advanced head and neck cancer: the ELDERLY study. *Ann Oncol* 2021;32:S789.
18. Dale W, Williams GR, R MacKenzie A, et al. How is geriatric assessment used in clinical practice for older adults with cancer? A survey of cancer providers by the American society of clinical oncology. *JCO Oncol Pract* 2021;17(6):336–44.
19. Alibh Bergerot CD, Temin S, Verduzco-Aguirre HC, et al. Geriatric assessment: ASCO global guideline. *JCO Glob Oncol* 2025;11:e2500276.
20. ASCO, Cancer and Aging Research Group, International Society of Geriatric Oncology. Practical geriatric assessment. 2023. Available at: <https://cdn.bfldr.com/KOIHB2Q3/as/fr5tbfbs65q37wzqjhnn3fn7/2023-Practical-Geriatric-Assessment>.
21. Mohile SG, Velarde C, Hurria A, et al. Geriatric assessment-guided care processes for older adults: a Delphi consensus of geriatric oncology experts. *J Natl Compr Cancer Netw* 2015;13(9):1120–30.
22. Pottel L, Lycke M, Boterberg T, et al. Serial comprehensive geriatric assessment in elderly head and neck cancer patients undergoing curative radiotherapy identifies evolution of multidimensional health problems and is indicative of quality of life. *Eur J Cancer Care* 2014;23:401–12.
23. Pottel L, Lycke M, Boterberg T, et al. G-8 indicates overall and quality-adjusted survival in older head and neck cancer patients treated with curative radiochemotherapy. *BMC Cancer* 2015;15:875.
24. Ishii R, Ogawa T, Ohkoshi A, et al. Use of the Geriatric-8 screening tool to predict prognosis and complications in older adults with head and neck cancer: a prospective, observational study. *J Geriatr Oncol* 2021;12:1039–43.

25. Palmer AD, Starmer H, Sathe N, et al. Use of the G8 geriatric screening tool in surgical head and neck cancer patients requiring rehabilitation: a multisite investigation. *Ann Otol Rhinol Laryngol* 2024;133(2):158–68.
26. Paillaud E, Brugel L, Bertolus C, et al. Effectiveness of geriatric assessment-driven interventions on survival and functional and nutritional status in older patients with head and neck cancer: a randomized controlled trial (EGeSOR). *Cancers (Basel)* 2022;14(13):3290.
27. Partridge JSL, Ryan J, Dhesei JK, CPOC-BGS perioperative frailty guideline group. New guidelines for the perioperative care of people living with frailty undergoing elective and emergency surgery—a commentary. *Age Ageing* 2022;51(11):afac237.
28. Hurria A, Mohile S, Gajra A, et al. Validation of a prediction tool for chemotherapy toxicity in older adults with cancer. *J Clin Oncol* 2016;34(20):2366–71.
29. Extermann M, Boler I, Reich RR, et al. Predicting the risk of chemotherapy toxicity in older patients: the chemotherapy risk assessment scale for high-age patients (CRASH) score. *Cancer* 2012;118:3377–86.
30. Vosler PS, Orsini M, Enepekides DJ, et al. Predicting complications of major head and neck oncological surgery: an evaluation of the ACS NSQIP surgical risk calculator. *J Otolaryngol-Head Neck Surg Le J d'oto-rhino-laryngologie Chir cervico-faciale* 2018;47:21.
31. Tierney W, Shah J, Clancy K, et al. Predictive value of the ACS NSQIP calculator for head and neck reconstruction free tissue transfer. *Laryngoscope* 2020;130(3):679–84.
32. Kalsi T, Babic-Illman G, Ross P, et al. The impact of comprehensive geriatric assessment interventions on tolerance to chemotherapy in older people. *Br J Cancer* 2015;112:1435–44.
33. van Essen GA, Bakas A, Sewnaik A, et al. Health outcome priorities in older patients with head and neck cancer. *J Geriatr Oncol* 2022;13(5):698–705.
34. Fahy E, Cantwell LA, Patterson JM, et al. Treatment priorities and regret in older adults with head and neck cancer: a systematic review. *Clin Otolaryngol* 2023;48(6):809–19.
35. Seghers PALN, Wiersma A, Festen S, et al. Patient preferences for treatment outcomes in oncology with a focus on the older Patient—A systematic review. *Cancers (Basel)* 2022;14(5):1147.
36. Available at: <https://www.aomrc.org.uk/projects-and-programmes/choosing-wisely/>.
37. Seth I, Bulloch G, Qin KR, et al. Pre-rehabilitation interventions for patients with head and neck cancers: a systematic review and meta-analysis. *Head Neck* 2024;46(1):86–117. Epub 2023 Oct 28. PMID: 37897197.
38. Lalabekyan BB, Tetlow N, Moonesinghe R, et al. Cardiopulmonary exercise testing and cardiopulmonary morbidity in patients undergoing major head and neck surgery. *Br J Oral Maxillofac Surg* 2021;59(3):297–302.
39. Dort JC, Farwell DG, Findlay M, et al. Optimal perioperative care in major head and neck cancer surgery with free flap reconstruction: a consensus review and recommendations from the enhanced recovery after surgery society. *JAMA Otolaryngol Head Neck Surg* 2017;143(3):292–303.
40. Kattar N, Wang SX, Trojan JD, et al. Enhanced recovery after surgery protocols for head and neck cancer: systematic review and meta-analysis. *Otolaryngol Head Neck Surg* 2023;168(4):593–601.

41. MacNeil SD, Liu K, Garg AX, et al. A population-based study of 30-day incidence of ischemic stroke following surgical neck dissection. *Medicine (Baltim)* 2015;94(33):e11106.
42. Melachuri S, Melachuri M, Vallapil B, et al. The incidence of stroke post neck dissection surgery and perioperative management. *Am J Otolaryngol* 2022; 43(2):103360.
43. Monaghan NP, Duckett KA, Nguyen SA, et al. Vascular events in patients with head and neck cancer: a systematic review and meta-analysis. *Head Neck* 2024;46(7): 1557–72.
44. Nouraei SA, Dias A, Kanona H, et al. Impact of the method and success of pharyngeal reconstruction on the outcome of treating laryngeal and hypopharyngeal cancers with pharyngolaryngectomy: a national analysis. *J Plast Reconstr Aesthetic Surg* 2017;70(5):628–38.
45. Cleere EF, Hintze JM, Doherty C, et al. The association of frailty with morbidity and mortality following major mucosal head and neck surgery. *Oral Oncol* 2024;159: 107021.
46. Fancy T, Huang AT, Kass JI, et al. Complications, mortality, and functional decline in patients 80 years or older undergoing major head and neck ablation and reconstruction. *JAMA Otolaryngol Head Neck Surg* 2019;145(12):1150–7.
47. Nouraei SA, Middleton SE, Hudovsky A, et al. Role of reconstructive surgery in the management of head and neck cancer: a national outcomes analysis of 11,841 reconstructions. *J Plast Reconstr Aesthetic Surg* 2015;68(4):469–78.
48. Siddiq S, Dragan A, Dk Gahir, et al. Management of neck metastases in head and neck cancer: United Kingdom national multidisciplinary guidelines, sixth edition. *J Laryngol Otol* 2024;138(S1):S1–224.
49. Costantino A, Haughey B, Alamoudi U, et al. Safety and postoperative outcomes of transoral surgery for oropharyngeal carcinoma in older adults. *JAMA Otolaryngol Head Neck Surg* 2024;150(10):879–86.
50. Parhar HS, Shimunov D, Newman JG, et al. Oncologic outcomes following transoral robotic surgery for human papillomavirus-associated oropharyngeal carcinoma in older patients. *JAMA Otolaryngol Head Neck Surg* 2020;146(12):1167–75.
51. Philips R, Topf MC, Crawley MB, et al. Functional and survival outcomes in elderly patients undergoing transoral robotic surgery. *Oral Oncol* 2020;111:104954.
52. Long-Term Follow-Up of E3311, an ECOG-ACRIN cancer research group phase II trial of transoral surgery and risk-based adjuvant treatment in human papillomavirus-initiated oropharynx. *Cancer. JCO* 2025;43:2559–65.
53. Costantino A, Haughey B, Zhu J, et al. Transoral surgery versus radiotherapy as primary treatment for HPV-related oropharyngeal cancer in the elderly. *Head Neck* 2025;47(7):1867–77.
54. Hardman JC, Holsinger FC, Brady GC, et al. Transoral robotic surgery for recurrent tumors of the upper aerodigestive tract (RECUT): an international cohort study. *J Natl Cancer Inst* 2022;114(10):1400–9.
55. Paderno A, Lancini D, Bosio P, et al. Transoral laser microsurgery for glottic cancer in patients over 75 years old. *Laryngoscope* 2022;132(1):135–41.
56. Valduvicio I, Baste N, Delia Ramírez R, et al. CO₂-TOLMS for laryngeal cancer in the elderly, pushing the boundaries of partial laryngectomy. *Oral Oncol* 2022;134: 106088.
57. Lechien JR, Hans S, Crevier-Buchman L. Influence of age on voice quality after transoral CO₂ laser microsurgery. *J Otolaryngol Head Neck Surg* 2023;52(1):59.
58. Nutting CM, Morden JP, Harrington KJ, et al. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a

- phase 3 multicentre randomised controlled trial. *Lancet Oncol* 2011;12(2):127–36.
59. Grégoire V, Evans M, Le QT, et al. Delineation of the primary tumour clinical target volumes (CTV-P) in laryngeal, hypopharyngeal, oropharyngeal and oral cavity squamous cell carcinoma: AIRO, CACA, DAHANCA, EORTC, GEORCC, GORTEC, HKNPCSG, HNCIG, IAG-KHT, LPRHHT, NCIC CTG, NCRI, NRG Oncology, PHNS, SBRT, SOMERA, SRO, SSHNO, TROG consensus guidelines. *Radiother Oncol* 2018;126(1):3–24.
 60. Royal College of Radiologists. Head and neck cancer RCR consensus statements. 2022. Available at: www.rcr.ac.uk/media/1qnoixei/rcr-publications_head-and-neck-cancer-rcr-consensus-statements_february-2022.pdf.
 61. Beetz I, Steenbakkens RJ, Chouvalova O, et al. The QUANTEC criteria for parotid gland dose and their efficacy to prevent moderate to severe patient-rated xerostomia. *Acta Oncologica* 2013;53(5):597–604.
 62. Smith GL, Smith BD, Buchholz TA, et al. Cerebrovascular disease risk in older head and neck cancer patients after radiotherapy. *J Clin Oncol* 2008;26(31):5119–25.
 63. Gujral DM, Long M, Roe JW, et al. Standardisation of target volume delineation for carotid-sparing intensity-modulated radiotherapy in early glottis cancer. *Clin Oncol* 2017;29(1):42–50.
 64. Awan M, Akakpo KE, Shukla M, et al. The substantial omission of indicated post-operative radiotherapy in patients with advanced-stage oral cancer in the US-A call to action. *JAMA Otolaryngol Head Neck Surg* 2021;147(10):907–9.
 65. Piras A, Boldrini L, Menna S, et al. Hypofractionated radiotherapy in head and neck cancer elderly patients: a feasibility and safety systematic review for the clinician. *Front Oncol* 2021;11:761393.
 66. Bentzen SM, Rosenblatt E, Gupta T, et al. Randomized controlled trial of hypofractionated vs. normo-fractionated accelerated radiation therapy with or without cisplatin for locally advanced head and neck squamous cell carcinoma (HYPNO). *Int J Radiat Oncol Biol Phys* 2023;117(4):e2.
 67. Thomson DJ, Cruickshank C, Baines H, et al. TORPEdO: a phase III trial of intensity-modulated proton beam therapy versus intensity-modulated radiotherapy for multi-toxicity reduction in oropharyngeal cancer. *Clin Transl Radiat Oncol* 2022;38:147–54.
 68. Available at: <https://www.isrctn.com/ISRCTN15983654>.
 69. Available at: <https://clinicaltrials.gov/study/NCT06421649>.
 70. Karube M, Yamamoto N, Nakajima M, et al. Single-fraction carbon-ion radiation therapy for patients 80 years of age and older with stage I non-small cell lung cancer. *Int J Radiat Oncol Biol Phys* 2016;95(Issue 1):542–8.
 71. Rutenberg MS, Beltran C. Future perspective: carbon ion radiotherapy for head and neck and skull base malignancies. *Oral Maxillofac Surg Clin North Am* 2023;35(3):485–92.
 72. Dale W, Klepin HD, Williams GR, et al. Practical assessment and management of vulnerabilities in older patients receiving systemic cancer therapy: ASCO guideline update. *J Clin Oncol* 2023;41(26):4293–312.
 73. Michelon I, Nachtigal GC, Dacoregio MI, et al. Treatment options for cisplatin-ineligible patients with locally advanced head and neck squamous cell carcinoma: a systematic review. *J Cancer Res Clin Oncol* 2024;150(8):379.
 74. Sun L, Candelieri-Surette D, Anglin-Foote T, et al. Cetuximab-based vs carboplatin-based chemoradiotherapy for patients with head and neck cancer. *JAMA Otolaryngol Head Neck Surg* 2022;148(11):1022–8.

75. Rühle A, Marschner S, Haderlein M, et al. Evaluation of concomitant systemic treatment in older adults with head and neck squamous cell carcinoma undergoing definitive radiotherapy. *JAMA Netw Open* 2023;6(2):e230090.
76. Uppaluri R, Haddad RI, Tao Y, et al, KEYNOTE-689 Investigators. Neoadjuvant and adjuvant pembrolizumab in locally advanced head and neck cancer. *N Engl J Med* 2025;393(1):37–50.
77. Patil VM, Noronha V, Menon N, et al. Low-dose immunotherapy in head and neck cancer: a randomized study. *J Clin Oncol* 2023;41(2):222–32.
78. Burtness B, Harrington KJ, Greil R, et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. *Lancet* 2019;394(10212):1915–28.
79. Harrington KJ, Burtness B, Greil R, et al. Pembrolizumab with or without chemotherapy in recurrent or metastatic head and neck squamous cell carcinoma: updated results of the phase III KEYNOTE-048 study. *J Clin Oncol* 2023;41(4):790–802.
80. Salvestrini V, Caini S, Scricciolo M, et al. Immunotherapy in elderly head and neck cancer patients: a systematic review and meta-analysis. *Front Oncol* 2024;14:1395838.
81. Dzienis M, Cundom J, Fuentes CS, et al. Pembrolizumab plus carboplatin and paclitaxel as first-line therapy for recurrent/metastatic head and neck squamous cell carcinoma (KEYNOTE-B10): a single-arm phase IV trial. *J Clin Oncol* 2024;42(25):2989–99.
82. Guigay J, Le Caer H, Ferrand FR, et al, ELAN Group including Gustave Roussy, Unicancer GERICO and H&N groups, and GORTEC. ELAN group including gustave roussy, unicancer GERICO and H&N groups, and GORTEC. Adapted EXTREME regimen in the first-line treatment of fit, older patients with recurrent or metastatic head and neck squamous cell carcinoma (ELAN-FIT): a multicentre, single-arm, phase 2 trial. *Lancet Healthy Longev* 2024;5(6):e392–405.
83. Szturz P, Haddad RI, Posner M, et al. Navigating challenging patient factors in systemic therapy for head and neck cancer. *Oncologist* 2025;30(5):oyaf035.
84. Pilleron S, O'Hanlon S. Digital twins for geriatric oncology: double trouble or twice as nice? *J Geriatr Oncol* 2023;14(5):101524.