Advances in Radiation Oncology (2022) 8, 101096

advances in radiation oncology

www.advancesradonc.org

Scientific Article

Correlation of an Electronic Geriatric Assessment With Receipt of Adjuvant Radiation and Chemotherapy in Older Adults With Head and Neck Cancer

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Received June 12, 2022; accepted September 25, 2022

Abstract

Purpose: Treatment patterns for head and neck squamous cell carcinoma (HNSCC) vary among older adults because of concerns about their health status. Geriatric assessment may guide treatment for older adults with HNSCC by assessing their health status.

Methods and Materials: We conducted a retrospective review of adjuvant treatment received by older patients with HNSCC who completed a novel geriatric assessment, the electronic Rapid Fitness Assessment, before treatment. The electronic Rapid Fitness Assessment yields an accumulated geriatric deficits (AGD) score. Higher AGD score indicates greater frailty. Comparators were age and performance status. The Wilcoxon rank sum test compared differences between those who did and did not receive adjuvant radiation therapy and chemotherapy.

Results: The cohort included 73 patients, of whom 56 (77%) had oral cavity cancer. The most common geriatric deficits were major distress, social activity limitation, depression, and impaired activities of daily living. AGD score, age, and performance status were not associated with receipt of adjuvant radiation. Patients who received adjuvant chemotherapy had a significantly lower median AGD score than those who did not (3 vs 6; $P = .044$), but there was no association with age and performance status. Of the 17 patients with newly diagnosed disease and either positive margins or extranodal extension, only 9 received adjuvant radiation and only 3 received systemic therapy. Most often, systemic therapy was omitted because of patient preference or comorbidities and poor performance status. There was a nonstatistically significant lower AGD score between patients who did and did not receive standard fractionated radiation therapy (median, 4 vs 6.5; $P = .13$).

Conclusions: Receipt of adjuvant chemotherapy was associated with frailty. Rates of chemotherapy utilization were very low, indicating the need for novel strategies to mitigate the toxicity burden in this patient population. Receipt of adjuvant radiation therapy was not associated with frailty; however, there was a trend toward lower frailty among those who did receive radiation therapy.

Sources of support: This research was funded by a Cancer Center support grant to Memorial Sloan Kettering Cancer Center (P30 CA008748).

Disclosures: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data sharing statement: Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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https://doi.org/10.1016/j.adro.2022.101096

Introduction

The management of head and neck squamous cell cancer (HNSCC) in older adults is challenging because of the higher incidence of both treatment toxicity and competing mortality, narrowing the therapeutic index of intensive treatment.[1,2] Meta-analyses have shown that older patients and those with poor performance status do not benefit from the addition of chemotherapy to radiation therapy.[3-6] Thus, the use of chemotherapy among older patients with HNSCC is controversial and treatment patterns vary between institutions.[7-10]

Older patients with cancer should not be excluded from intensive curative therapy on the basis of age alone.[5,7,8] Rather, treatment decisions should consider a patient's overall health status because a patient's chronological age can differ from their biological age.[5,11] The health status of older adults with cancer can be appraised with a geriatric assessment (GA), which measures a patient's comorbidities, functional status, cognitive status, psychological status, nutritional status, medication use, and social support.[12,13] GA can predict which patients can tolerate oncologic treatment or might benefit from additional supportive care during treatment.[12-14] The electronic Rapid Fitness Assessment (eRFA) is a novel GA that provides a fast and convenient overall measure of health status.[15]

The goal of this study was to determine whether receipt of adjuvant chemotherapy and radiation therapy for older adults with HNSCC varies according to frailty as defined by GA. We hypothesize that GA will provide an objective measure of frailty that is associated with receipt of adjuvant chemotherapy and radiation treatment.

Methods and Materials

Sample

The study sample consisted of 77 consecutive patients aged 75 and older with HNSCC who were referred to the Geriatrics Service at [Memorial Sloan Kettering Cancer Center] for preoperative evaluation before undergoing surgery from 2015 to 2019. Since the development of the eRFA in 2015, all patients referred to the Geriatrics Service at [Anonymized for review] complete the eRFA within 60 days before surgery. Whether patients over 75 years old are referred to the Geriatrics Service is dependent on surgeon and patient preference. We excluded patients (n = 4) who did not have at least 3 months of follow-up after the date of their surgery. Patients with squamous cell cancers of the oral cavity, oropharynx, hypopharynx, and larynx were included, and tumor staging was determined according to the seventh edition of the American Joint Committee on Cancer system. This study sample includes patients with both newly diagnosed and recurrent disease, which was determined through chart review. This study was a retrospective analysis approved by the [Anonymized for review] institutional review board.

GA

The eRFA was created by the Geriatrics Service at [Anonymized for review].[15] Most of the eRFA can be completed on an electronic tablet in clinic or at home via the Internet by the patient or a caregiver. Two components of the eRFA are assessed by nursing in clinic: Mini-Cog and Timed Up and Go. The eRFA yields an accumulated geriatric deficit (AGD) score, which ranges from 0 to 13. Patients receive 1 point toward their AGD score for a deficit in any of the following 13 domains: patient-rated Karnofsky performance scale (KPS), activities of daily living, instrumental activities of daily living, history of fall(s) in the past year, Timed Up and Go, Mini-Cog, major distress, depression, social activity limitation, poor social support, medications, weight loss in the past 6 months, and comorbidities.[13]

Adjuvant radiation therapy and chemotherapy

Outcomes of this study were the type and receipt of adjuvant radiation therapy and chemotherapy within 3 months of surgery. Radiation therapy and chemoradiation utilization were assessed separately because chemoradiation is harder to tolerate for older and frail adults. Details on receipt and types of radiation and systemic therapy were obtained from the electronic medical record. We examined surgical pathology reports to determine whether patients received adjuvant chemotherapy according to traditional indications for adding adjuvant chemotherapy to radiation, which include positive surgical margins or extranodal extension. Other potential indications for chemotherapy were also considered, including close surgical margins of less than 1 mm or extensive adenopathy (10 or more lymph nodes). For patients presenting with newly diagnosed HNSCC we performed chart review to determine why patients with indications for chemotherapy did not receive chemotherapy.

Types of adjuvant radiation therapy treatment included standard fractionated radiation therapy and palliative quad shot radiation therapy. Palliative quad shot radiation therapy consists of a shorter course of radiation therapy intended to reduce symptom burden.[16] Types of adjuvant systemic therapy included chemotherapy

regimens that included platinum and/or taxane. Some patients received systemic therapy that included cetuximab, which was used alone or in combination with platinum and/or taxane chemotherapies.

Statistical analysis

All statistical analysis was performed in R software (version 4.0). Wilcoxon rank sum test was used to test for differences between AGD score, age, and KPS with receipt of adjuvant radiation and chemotherapy.

Results

The cohort included 73 patients who had at least 3 months of follow-up after surgery for HNSCC, and 55 had newly diagnosed invasive disease. The mean patient age was 80 years old, and most patients were female (53%). The median AGD score was 6.0 in patients with newly diagnosed invasive disease and in patients with recurrent disease. The most common geriatric deficits in descending order were major distress, social activity limitation, depression, impaired activities of daily living, and poor social support (Table 1). The most common subsite was oral cavity cancer (77%) followed by larynx cancer (9.6%) (Table 2).

Most patients (n = 44, 60%) did not receive adjuvant therapy. The remaining 25 (34%) patients all received adjuvant radiation therapy, while only 9 (12%) patients additionally received adjuvant systemic therapy (Table 3). Radiation was mostly delivered with standard fractionation (n = 21), and only a minority of patients received palliative fractionation or intraoperative radiation therapy. Three patients received palliative radiation therapy: 2 patients received palliative quad shot radiation therapy because of recurrence soon after surgery and 1 patient received palliative quad shot radiation therapy in the absence of recurrence because of poor performance status and comorbidities. Additionally, 3 patients who started standard fractionation switched to palliative quad shot radiation therapy because of intolerance or development of metastatic disease.

Among the 9 patients who received systemic therapy (ie, including cetuximab), 6 received chemotherapy regimens that included platinum and/or taxane. There were 3 patients who received cetuximab alone without chemotherapy. Among the 9 patients who received systemic therapy, 8 received standard fractionated radiation therapy and 1 received quad shot radiation therapy. Cisplatin alone was the most common regimen used (4 patients) followed by cetuximab alone (3 patients) (Table 3).

Patients who received chemotherapy had a statistically significant lower median AGD score, indicating lower frailty, compared with those who did not receive

Table 1 Sample demographics and components of eRFA (n = 73)

Characteristics	Value
Sex	
Female	39 (53%)
Male	34 (47%)
Age, mean (SD)	82 (5.0)
KPS	
≥90	40 (55%)
≤80	33 (45%)
ADL score (higher is better)	
≥14	33 (45%)
≤13	40 (55%)
iADL score (higher is better)	
≥16	39 (53%)
≤15	34 (47%)
Fall in the past year	
No	46 (66%)
Yes	24 (34%)
Missing	3
TUG score (lower is better)	
<10 s	46 (66%)
≥10 s	24 (34%)
Missing	3
Mini-Cog score (higher is better)	
≥3	52 (75%)
≤2	17 (25%)
Missing	4
Social support score (higher is better)	
≥17	38 (52%)
≤16	35 (48%)
Social activity limitation score (lower is better)	
≤7	24 (33%)
≥8	49 (67%)
Weight loss of 10 pounds or more	
No	52 (74%)
Yes	18 (26%)
Missing	3
Distress thermometer score (lower is better)	
≤3	23 (32%)
≥4	50 (68%)
Depression based on geriatric depression score (lower is better)	

(*continued on next page*)

Table 1 (*Continued*)

Characteristics	Value
No	28 (38%)
Yes	45 (62%)
Number of medications	
≤4	35 (56%)
≥5	28 (44%)
Missing	10
Accumulated geriatric deficit, mean (SD)	6.0 (2.9)
Accumulated geriatric deficit score (lower is better)	
≤4	32 (44%)
≥5	41 (56%)

Abbreviations: ADL = activities of daily living; eRFA = electronic Rapid Fitness Assessment; iADL = instrumental activities of daily living; KPS = Karnofsky performance scale; TUG = Timed Up and Go.
Data are presented as frequency (%) unless otherwise indicated.

chemotherapy; (3 vs 6; P = .044). There was nonstatistically significant lower AGD score between patients who did and did not receive standard fractionated radiation therapy (median, 4 vs 6.5; P = .13). Similarly, there was nonstatistically significant lower AGD score between patients receiving any systemic therapy compared with those who did not (median, 3 vs 6; P = .13). KPS and age were not statistically different between those who did and did not receive adjuvant chemotherapy or radiation therapy (Table 4).

Of the 55 patients with newly diagnosed invasive disease, 17 (30%) had positive margins and/or extranodal extension, which are typical indications for adjuvant radiation and systemic therapy. Of these 17 patients, 7 received standard fractionated radiation therapy (including the 3 patients receiving concurrent chemotherapy or systemic therapy), 2 received quad shot radiation, and the remaining 8 received no radiation therapy. Of the 3 patients receiving both adjuvant radiation and systemic therapy, 2 patients received chemotherapy regimens that included platinum and/or taxane and 1 patient received systemic therapy with cetuximab.

Most commonly, systemic therapy was omitted in patients with positive margins and/or extranodal extension because of patient preference (n = 6) and comorbidities or poor performance status (n = 5) (Table 5). "Patient preference" indicates that the treating physicians either recommended or offered systemic therapy, but the patient refused. "Comorbidities or poor performance status" indicates that treating physicians did not recommend systemic therapy because of the patient's overall medical condition.

Table 2 Tumor characteristics (n = 73)

Characteristic Subsite	Frequency (%)
Oral cavity	56 (77%)
Oropharynx	5 (7%)
Larynx	7 (9%)
Hypopharynx	5 (7%)
T stage	
1	13 (18%)
2	17 (23.3%)
3	7 (10%)
4	18 (25%)
Metastatic	1 (1%)
Tumor in situ	1 (1%)
Recurrent	16 (22%)
N stage	
0	39 (53%)
1	10 (14%)
2	7 (10%)
Recurrent	16 (22%)
Positive margins*	
No	46 (84%)
Yes	9 (16%)
Extranodal extension*	
No	45 (82%)
Yes	10 (18%)
Extensive adenopathy*	
No	55 (100%)
Close margins (<1 mm)*	
No	36 (65%)
Yes	19 (35%)

* Applies only to patients without a recurrence (n = 55).

Discussion

In our small sample of older adults with HNSCC who underwent surgery, we found that receipt of adjuvant chemotherapy was associated with AGD score, while age and KPS were not. Receipt of adjuvant radiation and systemic therapy was not associated with AGD score, age, and KPS. However, we saw evidence that patients who received adjuvant radiation therapy and systemic therapy had lower median AGD scores compared with those who did not, though the differences did not meet conventional levels of significance. Because we had a small heterogenous cohort, further research should determine whether these associations can be substantiated in a larger sample.

Table 3 Radiation therapy and chemotherapy details within 6 months of surgery (n = 73)

Treatment characteristics Systemic therapy regimen	Frequency (%)
Carboplatin, paclitaxel, and cetuximab	1 (1%)
Cetuximab	3 (4%)
Cetuximab, docetaxel	1 (1%)
Cisplatin	4 (5%)
None	64 (88%)
Radiation therapy	
No	48 (66%)
Yes	25 (34%)
Treatment patterns	
Systemic therapy and radiation	9 (12%)
Radiation only	16 (22%)
Neither	48 (66%)
Type of radiation therapy	
None	48 (66%)
Standard fractionation	21 (29%)
Palliative quad shot	2 (3%)
Intraoperative	2 (3%)

Surprisingly, only 3 of 17 (18%) patients with positive margins and/or extranodal extension received adjuvant radiation and systemic therapy in the setting of a newly diagnosed HNSCC. For patients with an indication for chemotherapy (ie, positive margins and/or extranodal extension) but who did not receive adjuvant systemic therapy, the most common reasons were patient preference or comorbidities and poor performance status. Similarly, national databases show a substantial proportion of older adults with HNSCC do not receive indicated adjuvant radiation or chemotherapy.[9,17] Clearly, new strategies are needed to reduce the burden of toxicity and better support older adults through adjuvant radiation and chemoradiation therapy. Palliative quad shot radiation therapy could potentially reduce treatment toxicity and increase the proportion of patients who receive radiation, though the efficacy of this approach relative to standard fractionation remains unclear.

GA can aid in identifying opportunities to better manage geriatric syndromes that might otherwise interfere with receipt and tolerability of radiation therapy and systemic therapy.[14,18] GA can help clinicians identify which older adults are vulnerable and can facilitate interventions to optimize comorbidities and supportive care needs before radiation or chemoradiation.[19] Additionally, information on frailty can help clinicians tailor the intensity of therapy

Table 4 Adjuvant therapy among all patients according to median AGD, KPS, and age

	Did not receive chemotherapy n = 67	Received chemotherapy n = 6	*P* value
AGD	6	3	.044
KPS	90	90	.3
Age	80	81	.9
	Did not receive standard fractionated radiation therapy	Received standard fractionated radiation therapy	*P* value
	n = 52	n = 21	
AGD	6.5	4	.13
KPS	90	90	.7
Age	81	80	.3

Abbreviations: AGD = accumulated geriatric deficits; KPS = Karnofsky performance scale.
Patients included as "received chemotherapy" were those whose treatment regimen included platinum or taxane chemotherapies.

Table 5 Reasons systemic therapy was omitted in patients with newly diagnosed head and neck cancer and positive margins and/or extranodal extension (n = 14)

Reason	Number of patients (%)
Patient preference	6 (43%)
Comorbidities/poor performance status	5 (36%)
Poor swallowing function in setting of prior head and neck radiation therapy*	1 (7%)
Unknown	2 (14%)

* This patient did not receive adjuvant radiation, while the remaining 13 patients did receive adjuvant radiation.

according to each patient's expected treatment tolerance and predict quality of life outcomes among older adults with HNSCC receiving definitive treatment.[20,21]

Strengths of this study include use of a novel electronic GA to determine whether adjuvant treatment of older adults with HNSCC is associated with frailty. We were also able to compare frailty as determined by GA to age and performance status. Additionally, detailed information from patient charts allowed us to document reasons for omission of adjuvant systemic therapy. These details are not available in population-based data sets and revealed that patient preference is a leading cause of omitting indicated adjuvant systemic treatment.

This study has several limitations, including the single-institution retrospective design and a limited number of patients receiving adjuvant chemotherapy, which reduces statistical power. Furthermore, AGD was determined before surgery and patients may have experienced greater frailty after surgery, which may have precluded them from receiving adjuvant treatment. Alternatively, patients may have experienced an improvement in their frailty, resulting from supportive interventions (eg, feeding tubes, swallowing therapy, and physical therapy) in the perioperative period. Another limitation of this study is the lack of information on indications for adjuvant radiation therapy. We chose to focus on indications for adjuvant chemoradiation as our primary hypothesis because these indications (positive margins and/or extranodal extension) are widely accepted in practice. Finally, a lack of standardization for referral to the [Anonymized for review] Geriatric Service may contribute to selection bias in our sample.

Conclusion

We found that AGD score was associated with receipt of adjuvant chemotherapy in a small cohort of patients with various types of HNSCC. Although patients who received adjuvant radiation therapy and systemic therapy had lower median AGD scores than those who did not, these differences did not meet conventional levels of significance. Given our small sample, further research in larger data sets and prospective studies are needed to determine how GA can help to guide delivery of adjuvant chemotherapy. The overall utilization of adjuvant chemoradiation was very low, even among patients with positive margins and/or extranodal extension, highlighting the challenge of delivering adjuvant chemoradiation to older and frail adults with HNSCC. Future research should examine how GA can be incorporated into clinical practice to allow oncologists to manage older adults with head and neck cancer as well as assess the overall health status of patients and determine whether supportive care interventions could reduce the toxicity burden of adjuvant therapy. Assessing how AGD score correlates to treatment may help guide multidisciplinary teams to select better treatment options and provide appropriate counseling.

Acknowledgments

We thank biostatistician Amy Tin for her review and commentary on this article.

References

1. Siddiqui F, Gwede CK. Head and neck cancer in the elderly population. *Semin Radiat Oncol*. 2012;22:321-333.
2. Machtay M, Moughan J, Trotti A, et al. Factors associated with severe late toxicity after concurrent chemoradiation for locally advanced head and neck cancer: An RTOG analysis. *J Clin Oncol*. 2008;26:3582-3589.
3. Pignon JP, le Maître A, Maillard E, Bourhis J. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 93 randomised trials and 17,346 patients. *Radiother Oncol*. 2009;92:4-14.
4. Pignon JP, Bourhis J, Domenge C, Designé L. Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: Three meta-analyses of updated individual data. MACH-NC Collaborative Group. Meta-analysis of chemotherapy on head and neck cancer. *Lancet Lond Engl*. 2000;355:949-955.
5. Porceddu SV, Haddad RI. Management of elderly patients with locoregionally confined head and neck cancer. *Lancet Oncol*. 2017;18:e274-e283.
6. Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for locoregionally advanced head and neck cancer: 5-year survival data from a phase 3 randomised trial, and relation between cetuximab-induced rash and survival. *Lancet Oncol*. 2010;11:21-28.
7. Amini A, Jones BL, McDermott JD, et al. Survival outcomes with concurrent chemoradiation for elderly patients with locally advanced head and neck cancer according to the National Cancer Data Base. *Cancer*. 2016;122:1533-1543.
8. Juarez JE, Choi J, St John M, Abemayor E, TenNapel M, Chen AM. Patterns of care for elderly patients with locally advanced head and neck cancer. *Int J Radiat Oncol Biol Phys*. 2017;98:767-774.
9. VanderWalde NA, Meyer AM, Liu H, et al. Patterns of care in older patients with squamous cell carcinoma of the head and neck: A surveillance, epidemiology, and end results-medicare analysis. *J Geriatr Oncol*. 2013;4:262-270.
10. VanderWalde NA, Meyer AM, Deal AM, et al. Effectiveness of chemoradiation for head and neck cancer in an older patient population. *Int J Radiat Oncol Biol Phys*. 2014;89:30-37.
11. Shahrokni A, Alexander K. The age of talking about age alone is over. *Ann Surg Oncol*. 2019;26:12-14.
12. Extermann M, Aapro M, Bernabei R, et al. 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.
13. Rodin MB, Mohile SG. A practical approach to geriatric assessment in oncology. *J Clin Oncol*. 2007;25:1936-1944.
14. 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;36:2326-2347.

15. Shahrokni A, Tin A, Downey RJ, et al. Electronic rapid fitness assessment: A novel tool for preoperative evaluation of the geriatric oncology patient. *J Natl Compr Cancer Netw*. 2017;15:172-179.
16. Grewal AS, Jones J, Lin A. Palliative radiation therapy for head and neck cancers. *Int J Radiat Oncol Biol Phys*. 2019;105:254-266.
17. Awan M, Akakpo KE, Shukla M, et al. The substantial omission of indicated postoperative radiotherapy in patients with advanced-stage oral cancer in the US-A call to action. *JAMA Otolaryngol Head Neck Surg*. 2021;147:907-909.
18. Kalsi T, Babic-Illman G, Ross PJ, et al. The impact of comprehensive geriatric assessment interventions on tolerance to chemotherapy in older people. *Br J Cancer*. 2015;112:1435-1444.
19. Neve M, Jameson MB, Govender S, Hartopeanu C. Impact of geriatric assessment on the management of older adults with head and neck cancer: A pilot study. *J Geriatr Oncol*. 2016;7:457-462.
20. VanderWalde NA, Deal AM, Comitz E, et al. Geriatric assessment as a predictor of tolerance, quality of life, and outcomes in older patients with head and neck cancers and lung cancers receiving radiation therapy. *Int J Radiat Oncol Biol Phys*. 2017;98:850-857.
21. Bossi P, Esposito A, Vecchio S, et al. 864MO Role of geriatric assessment in tailoring treatment of locally advanced head and neck cancer: The ELDERLY study. *Annal Oncol*. 2021;32(suppl 5):S786-S817.