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Frailty in Non-geriatric Patients With Head and Neck cancer

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Abstract

Objective. Patients with head and neck cancer (HNC) are characterized by a poor lifestyle and comorbidity. The Geriatric 8 (G8) is an established screening tool to identify frail older patients with cancer. However, studies evaluating frailty in younger HNC patients are lacking. The aim of this study is to evaluate if the G8 can identify frailty and if it is related to mortality in younger HNC patients.

Study Design. Case-control study design.

Setting. Tertiary cancer center.

Methods. We studied patients <70 years with HNC. Patients with G8 ≤ 14 were considered frail. Patients were matched to nonfrail (G8 > 14) control patients. Patients were matched according to sex, age, smoking, tumor location, and period of first consultation. Baseline health characteristics were compared between frail patients and nonfrail controls. Second, the treatment plan and adverse outcomes were compared.

Results. Forty-five patients with G8 ≤ 14 were included and matched to 90 nonfrail controls. The median follow-up time was 357 days. Frail patients had a significantly lower body mass index and level of education, a worse World Health Organization performance status, and reported lower experienced overall health. 28.9% of the frail patients died after 1 year versus 10% of the nonfrail control patients (hazard ratio: 3.87 [95% confidence interval: 1.32-11.36], $p = 0.014$).

Conclusion. The G8 is a valid screening tool to identify frail patients in younger HNC patients.

Keywords

Comprehensive Geriatric Assessment, frailty, G8, head and neck cancer

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Head and neck cancer (HNC) is 1 of the 6 most common cancers in the world with approximately more than 900,000 new cases and 500,000 deaths per year.[1] It mostly affects older adults. The typical HNC patient is older, exposed to smoking and alcohol intake, and has comorbidity.[2,3] Frailty, a syndrome defined as "a state of vulnerability to poor resolution of homeostasis following stress," is increasingly present with older age and is strongly associated with adverse outcomes.[4] Nonetheless, frailty can also be present in younger patients aged <70, in case they have been exposed to risk factors such as smoking and alcohol intake. Frailty is often accompanied by multiple (geriatric) impairments such as malnutrition, which can lead to an overall decreased condition of the patient. The HNC population is considered to be more frail compared to other solid organ malignancies.[5] Thus, a patient's biological age rather than the chronological age should be taken into account when making treatment decisions. The presence of frailty in HNC patients is increasingly getting attention.[6]

The gold standard to assess frailty is the Comprehensive Geriatric Assessment (CGA).[7,8] The CGA is applied for patients aged ≥70 years after it was recommended in 2015 by the International Society of Geriatric Oncology.[8] In the HNC population the Geriatric 8 (G8) is often used as screening instrument.[9,10] The G8 predicts (postoperative) complications,[11,12] longer postoperative stay,[13] decline in health related quality of life,[14] and mortality.[12,14] However, studies evaluating the G8 and a subsequent CGA in younger patients, that is, <70 years, are currently lacking. Therefore,

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the aim of this study is to evaluate whether the G8 can be used as a screening tool to identify frailty, and whether the G8 is associated with mortality in HNC patients aged <70 years. Using a case-control design, we aimed to compare baseline health characteristics, treatment decisions, and treatment outcomes of frail versus nonfrail patients according to the G8. Furthermore, we explored in a subgroup analysis geriatric impairments in the young HNC patients who received a CGA.

Methods

Study Design and Patients

This study is a single-center observational case-control study conducted at the Erasmus MC University Medical Center Rotterdam from November 2019 to August 2021. All patients aged <70 years with pathologically confirmed HNC were screened with the G8. The G8 contains 8 questions on the following subjects: food intake in the past 3 months, weight loss in the past 3 months, mobility, neuropsychological problems, body mass index (BMI), number of medications, perceived health compared to peers, and an age <80 years. The G8 score ranges from 0 to 17, with a higher score indicating better health status.[9]

The G-8 questionnaire with the possible score at every section is provided in Supplemental Table S1, available online

Patients classified as frail (a score ≤14) according to the G8 were referred to the Geriatrics Department for a CGA. After giving informed consent, they were included in the patient group. These frail patients were matched to controls in a 1:2 ratio. Controls were extracted from the cohort of patients with HNC who were screened as nonfrail according to the G8, aged <70 years. Matching of the control patients was based on sex, age, smoking, tumor location, and when the first visit took place with a range between 2 months before or after the first visit. The study was approved by the Ethics Committee of the Erasmus Medical Center.

Demographic and Health Characteristics

Patient characteristics were assessed at study entry and retrieved from the patients' medical history. HNC was categorized into the following categories: skin, oral cavity, nasal cavity, sinonasal, salivary glands, oropharynx, nasopharynx, hypopharynx, larynx, and unknown primary. Tumors were classified and defined according to the 7th edition of the Union for International Cancer Control TNM classification.[15] The World Health Organization (WHO) performance status is defined as follows: grade 0 is defined as no restriction and fully mobilized, grade 1 is restricted only in strenuous activity, grade 2 is capable of self-care and more than 50% of the time mobilized, grade 3 is limited self-care and more than 50% of the time immobilized, and grade 4 is completely immobilized and not able to carry out any self-care.[16] Level of education was classified conform the International Standard Classification of Education (ISCED 2011) and subdivided into 5 levels of education; early childhood and primary education (level 1, ISCED 0-1), lower secondary education (level 2, ISCED 2), upper secondary education (level 3, ISCED 3), postsecondary nontertiary and short-cycle tertiary education (level 4, ISCED 4-5), and bachelor's, master's, or doctoral level (level 5, ISCED 6-8).[17]

Cancer was defined as a history of all forms of cancer except the current HNC. BMI was calculated as weight (kg) divided by height-squared (m^2). Myocardial infarction was defined as a history of a myocardial infarction or coronary artery bypass graft. Heart failure was defined as a left ventricular ejection fraction <40% or medication use for heart failure. Vascular disease was defined as a history of peripheral artery disease, aneurysms or a vascular intervention. Cerebrovascular accident was defined as a history of cerebral infarction or hemorrhage or transient ischemic attack. Pulmonary disease included a history of chronic obstructive pulmonary disease, asthma or obstructive sleep apnea syndrome. The Cumulative Illness Rating Scale-Comorbidity Index was perceived by calculating the mean score of 13 comorbidity systems, each of which was rated as mild, moderate or severe.[18]

CGA

Patients with a G8 score ≤14 were referred to the Geriatrics Department for a CGA. The CGA is used to get a holistic view of a patient's health in order to give preventive medical advices, treatment advices or advices to optimize a patient's condition. It entails (1) a thorough review of the medical history and social history, medication, intoxications (smoking and alcohol intake), physical, cognitive, functional, and social anamnesis, (2) a physical examination including measurements of the length, weight, blood pressure (orthostatic hypotension), heart rate, physical tests of the handgrip strength and gait speed, and Timed Up and Go Test (TUGT),[19,20] (3) additional tests such as laboratory research and electrocardiogram, and (4) various scoring lists such as the Mini-Mental State Examination (MMSE) to test the cognitive functioning,[21] Katz' index activities of daily living (ADL),[22] Lawton's instrumental activities of daily living (IADL),[23] the Mini Nutritional Assessment-Short Form in order to evaluate the nutritional status, the Exton Smith Scale to evaluate the risk for development of pressure sores[24] and the Outcome Prioritization Tool, which is an instrument to prioritize a patient's health outcome preferences.[25]

Handgrip strength was measured using a digital strip dynamometer. The patient was positioned upright in a chair in neutral position with the elbow in 90°. The instructions were given to squeeze as hard as possible. The measurement was performed twice, for both the left as the right hand. Of the 2 measurements, the highest score was used in the analysis. Gait speed was measured as the time

a patient needed to walk 5 m from a standstill position in a comfortable pace. The measurements were performed twice and the fastest time was used in the analysis. Handgrip strength and gait speed were classified according to percentile categories which were based on normative reference values.[19] The TUGT was measured as the time a patient needed to go from a seated position, stand up (without using the arms), walk 3 m comfortably, turn around, walk back, and sit down in the chair. The use of a walking aid was allowed. Orthostatic hypotension was defined as a decrease in systolic blood pressure of ≥20 mm Hg and or a decrease in diastolic blood pressure of ≥10 mm Hg within 3 minutes after standing up. The Multidimensional Prognostic Index (MPI) was calculated based on the results of the CGA, which is categorized in MPI-stages 1 (score ≤0.33), 2 (score 0.34-0.66), and 3 (≥0.67), indicating, respectively, a low, moderate-to-high 1-year mortality risk.[26]

Treatment Intention and Treatment Outcome

All patients with a pathologically proven HNC were discussed by a multidisciplinary team of various physicians including otolaryngologists, maxillofacial and plastic surgeons, an oncologist, a radiation therapist, a radiologist, and a geriatrician. The multidisciplinary team discussed the most adequate type of treatment and treatment intention. In consultation with the patient, the treatment was chosen, and if necessary, deviated from standard protocol and or advice. Mortality for all patients is assessed on the same date October 22, 2021. The cause of death of the deceased patients was determined by the patient's record and classified into 5 categories: palliative care, palliative sedation, refusing treatment, tumor recurrence, and complications.

Statistical Analysis

Continuous variables were expressed as mean with standard deviation or as median with the interquartile range. Categorical variables were expressed as absolute numbers with percentages (%). Continuous variables were compared between the frail patient group and the nonfrail control group using the independent t test or the Mann-Whitney U test (in case of a nonnormal distribution). For categorical variables, the χ^2 test and Fisher's exact test (if applicable) were used. A Kaplan-Meier curve was used to assess differences in survival between the frail patient and

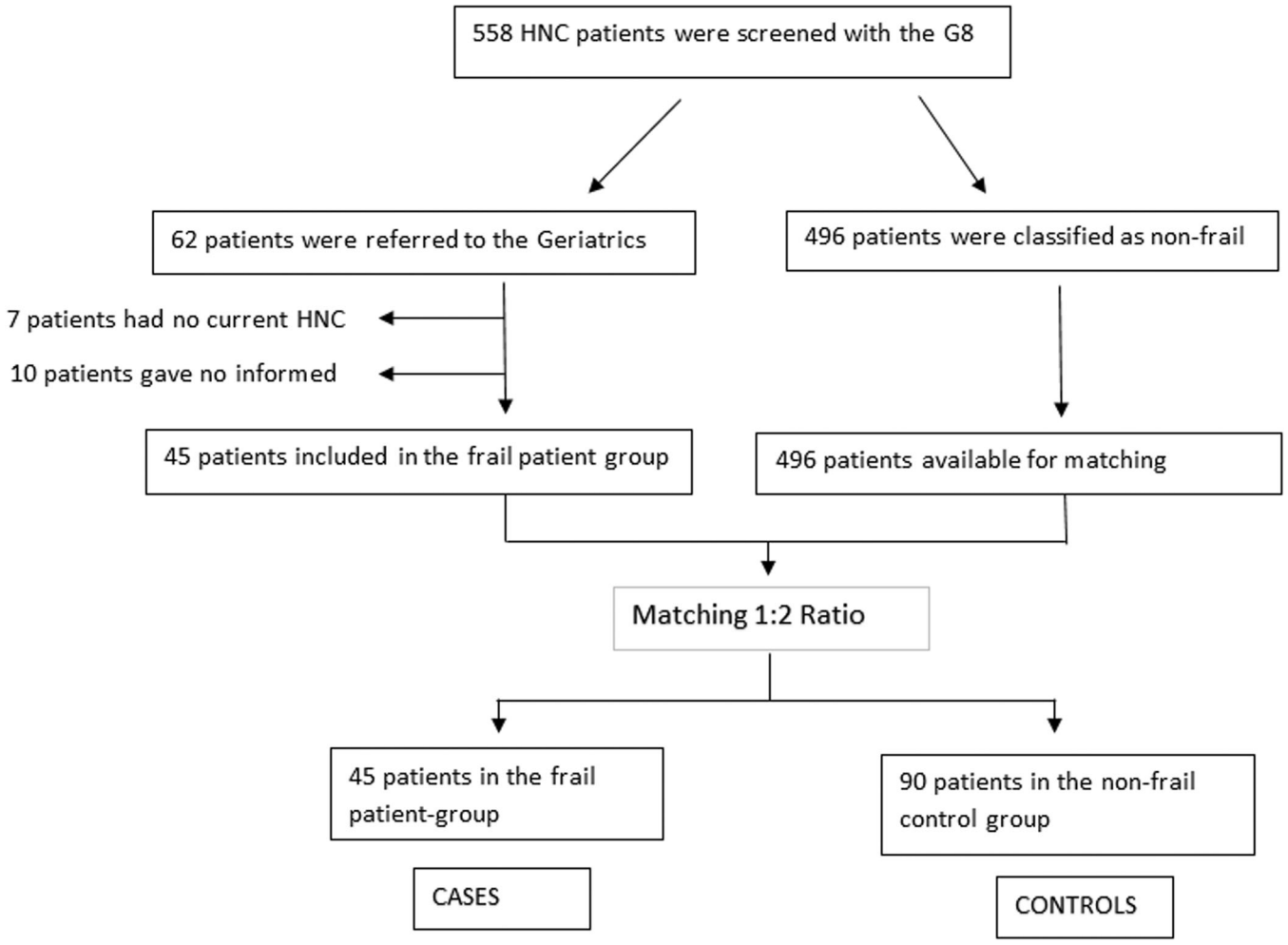

Figure 1. Flowchart of the patient enrollment and the matching. HNC, head and neck cancer.

Table 1. Baseline Characteristics of Patients With Head and Neck Cancer

Characteristics	Frail patient group (n = 45)	Nonfrail control group (n = 90)	*p* Value
Demographics			
Age, y, median [IQR]	62 [58–67]	62 [58–65]	0.5
Male, n (%)	31 (68,9)	62 (68.9)	1.0
BMI, median [IQR]	21.0 [18.5-24.5]	25.1 ± 5.09	<0.001
Marital status, n (%)			0.7
Married or living with a partner	27 (60.0)	61 (67.8)	
In a relationship, but living apart	1 (2.2)	3 (3.3)	
Divorced	7 (15.6)	11 (12.2)	
Widow or widower	4 (8.9)	3 (3.3)	
No partner and has never been married	6 (13.3)	11 (12.2)	
Level of education, n (%)			0.012
Level 1 (ISCED 0-1)	8 (17.8)	8 (8.9)	
Level 2 (ISCED 2)	15 (33.3)	42 (46.7)	
Level 3 (ISCED 3)	12 (26.7)	24 (26.7)	
Level 4 (ISCED 4 + 5)	0 (0)	0 (0)	
Level 5 (ISCED 6-8)	5 (11.1)	15 (16.7)	
Unknown	5 (11.1)	1 (1)	
ACE comorbidity, n (%)			0.6
Grade 0: No comorbidity	7 (15.6)	21 (23.3)	
Grade 1: Mild comorbidity	9 (20.0)	18 (20.0)	
Grade 2: Moderate comorbidity	8 (17.8)	10 (11.1)	
Grade 3: Severe comorbidity	21 (46.7)	41 (45.6)	
WHO performance status, n (%)			<0.001
Grade 0	10 (22.2)	60 (66.7)	
Grade 1	16 (35.6)	25 (27.8)	
Grade 2	15 (33.3)	3 (3.3)	
Grade 3[a]	4 (8.9)	2 (2.2)	
Smoking, n (%)			0.3
No	6 (13.3)	22 (24.4)	
Yes	29 (64.4)	52 (57.8)	
Ex-smoker (<3 mo)	10 (22.2)	16 (17.8)	
Alcohol use, n (%)			0.042
No	4 (8.9)	19 (21.1)	
Yes < 7 units per week	6 (13.3)	16 (17.8)	
Yes ≥ 7 units per week	20 (44.4)	42 (46.7)	
Stopped after abuse	15 (31.1)	13 (14.4)	
Tumor-related characteristics			
Tumor location, n (%)			1.0
Oral cavity	12 (26.7)	17 (18.9)	
Skin	0 (0)	1 (1.1)	
Salivary glands	0 (0)	2 (2.2)	
Sinonasal	1 (2.2)	2 (2.2)	
Oropharynx	15 (33.3)	34 (37.8)	
Nasopharynx	1 (2.2)	2 (2.2)	
Hypopharynx	5 (11.1)	10 (11.1)	
Larynx	11 (24.4)	22 (24.4)	
Tumor stage, n (%)			0.5
T0	1 (2.2)	2 (2.2)	
Tis	2 (4.4)	7 (7.8)	
Tx	1 (2.2)	1 (1.1)	
T1	4 (8.9)	13 (14.4)	

(*continued*)

Table 1. (continued)

Characteristics	Frail patient group (n = 45)	Nonfrail control group (n = 90)	*p* Value
T1a	0 (0)	6 (6.7)	
T1b	0 (0)	1 (1.1)	
T2	12 (26.7)	22 (24.4)	
T3	13 (28.9)	20 (22.2)	
T4	5 (11.1)	3 (3.3)	
T4a	6 (13.3)	14 (15.6)	
T4b	1 (2.2)	1 (1.1)	
Regional lymph nodes, n (%)			0.3
N0	23 (51.1)	57 (63.3)	
NI-III	22 (48.9)	32 (35.6)	
Nx	0 (0)	1 (1.1)	
Distant metastasis, n (%)			1.0
M0	44 (97.8)	87 (96.7)	
M1	1 (2.2)	3 (3.3)	

Comparison of the baseline characteristics between the patient and the control group. Data are presented as means ± SD, median (IQR), or number and percentages (%). The level of education is classified according to the ISCED.
Abbreviations: ACE, Adult Comorbidity Evaluation; BMI, body mass index; IQR, interquartile range; ISCED, International Standard Classification of Education; WHO, World Health Organization.
[a]No patients were categorized as WHO performance status grade 4. Data were incomplete for: Marital status (n = 134).

the nonfrail control group and to calculate median survival. Cox-regression modeling was used to evaluate the effect of covariates on mortality and to calculate the hazard ratio (HR). Because the patients were successfully matched on age, gender, comorbidity, marital status, smoking, tumor location, and tumor stage, we adjusted for alcohol and comorbidity according to the Adult Comorbidity Evaluation-27 in the multivariable model. A p value of <0.05 was considered as statistically significant. SPSS version 25 (SPSS Inc IBM company) was used for the analyses.

Results

Enrollment and Patient Characteristics

During the study period, 558 patients aged <70 years were screened using the G8. Of those patients, 62 (11%) were categorized as frail and referred for a CGA. Of the 62 patients, 7 had no pathologically-proven HNC, and 10 did not give informed consent. Thus, a total of 45 patients were included in this study and were matched to 90 nonfrail control patients (**Figure 1**).

Demographic and Health Characteristics in Frail Patients Versus Nonfrail Patients

Demographic and health characteristics of the frail patient group and the nonfrail control group are presented in **Table 1**. In both groups, the majority of the patients were male and the median age was 62 years.

Table 2. Treatment-Related Characteristics and Outcome

	Patient group (n = 45)	Control group (n = 90)	*p* Value
Advice treatment, n (%)			0.5
Surgery	17 (37.8)	30 (33.3)	
Radiotherapy	7 (15.6)	22 (24.4)	
Chemoradiotherapy	15 (33.3)	26 (28.9)	
Palliative radiotherapy	2 (4.4)	1 (1.1)	
Palliative chemotherapy	0 (0)	2 (2.2)	
Palliative symptomatic treatment	4 (8.9)	6 (6.7)	
Other	0 (0)	3 (3.3)	
Palliative treatment intention, n (%)	6 (13.3)	9 (10.0)	0.6
Treatment according to protocol, n (%)	40 (88.9)	84 (93.3)	0.5
Follow-up, d, median [IQR]	336 [252-420]	371 [315-427]	0.2
Overall mortality	13 (28.9)	9 (10.0)	0.005
Cause of death, n (%)			0.176
Palliative care	7 (53.8)	2 (22.2)	
Palliative sedation	4 (30.8)	6 (66.7)	
Refusing treatment	1 (7.7)	0 (0)	
Tumor recurrence	1 (7.7)	0 (0)	
Complications	0 (0)	1 (11.1)	

Comparison of treatment-related characteristics and outcomes between the patient and the control group. Data are presented as median (IQR) or number and percentages (%).
Abbreviation: IQR, interquartile range.

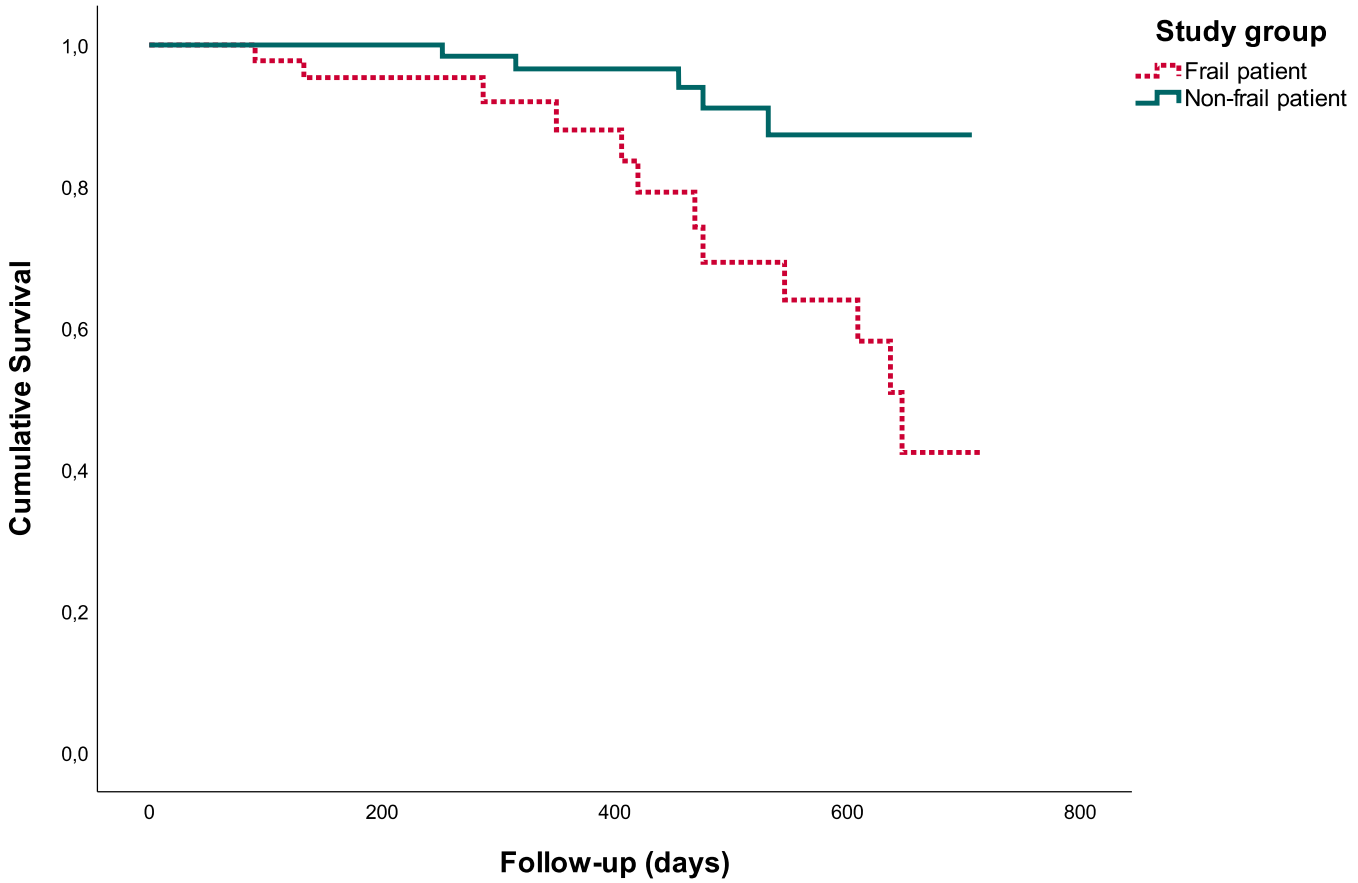

Figure 2. Kaplan-Meier of the cumulative survival, showing the follow-up time in days on the *x*-axis. Mean survival of both groups: 580 days in the frail patient group, and 672 days in the nonfrail control group (log-rank test, $p = 0.003$).

BMI was significantly higher in the nonfrail control patients compared to the frail patients (25.2 vs 21.0 kg/m^3, $p < 0.001$). Frail patients had a significantly lower level of education and a worse WHO performance status, a higher percentage of psychiatric disease. Furthermore, frail patients had a higher alcohol consumption compared to the nonfrail controls.

G8 Score

The frail patient group had a median G8 score of 12 compared to 15 in the nonfrail control group. All questions of the G8, except for question 3 regarding mobility, were significantly different between the 2 groups (**Table 2**).

Treatment Outcomes

Treatment outcomes of the frail patient group and the nonfrail control group are presented in **Table 2**. No differences were observed in treatment intention, curative versus palliative intention, and treatment according to protocol versus deviations from the protocol. Median follow-up time was 357 days for the total of all patients and there was no significant difference between both groups. However, 1-year mortality was significantly higher in the frail patient group since 28.9% of the frail patients died compared to 10.0% in the control patients $p = 0.005$ (**Figure 2**). Frail patients had an almost 4 times higher mortality risk compared to nonfrail controls (HR: 3.87 [95% confidence interval: 1.32-11.36], $p = 0.014$), after adjustment for alcohol use and comorbidities. Mortality rates start to differ between the 2 groups after about 100 days posttreatment in our study. Exploring causes of death in both frail patients and nonfrail controls, we did not find any significant differences since all deaths were HNC-related. The majority of patients died either during palliative care or after palliative sedation. One frail patient died after the refusal of curative treatment. Furthermore, 1 control patient died after a severe hemorrhage from the trachea cannula.

Geriatric Impairments in the Frail Patients

Several comorbidities were especially present in frail patients: hypertension (40%), vascular disease (27%), cancer other than HNC (24%), diabetes mellitus (22%), and pulmonary disease (22%) (**Table 3**). Twenty percent of the frail patients were ADL dependent and 36% were IADL dependent. Almost 50% of the patients were at risk for malnutrition, and 27% were malnourished. Handgrip strength was below the 10th percentile in 20%, and gait speed was below the 10th percentile in almost 30% of the patients.

Table 3. Markers of Physical and Cognitive Functioning in the Subgroup Who Received a CGA

Results	Patient group (n = 45)
Housing situation, n (%)	
Living at home-independent	44 (97.8)
Nursing home	1 (2.2)
Comorbidities, n (%)	
Hypertension	18 (40)
Diabetes mellitus	10 (22.2)
Cancer	11 (24.4)
Myocardial infarction	4 (8.9)
Heart failure	1 (2.2)
Vascular disease	12 (26.7)
Cerebrovascular accident	8 (17.8)
Chronic kidney disease	4 (8.9)
Pulmonary disease	10 (22.2)
Dementia	2 (4.4)
Psychiatric disease	9 (20)
Liver disease	2 (4.4)
Bowel disease	1 (2.2)
Musculoskeletal problems	9 (20)
CIRS-CI, median [IQR]	4 (3-6)
CIRS total score, median [IQR]	13 [9-17.5]
Handgrip strength, n (%)	
<p10	9 (20)
P10-p90	34 (75.6)
>p90	2 (4.4)
Gait speed, n (%)	
<p10	12 (28.6)
P10-p90	26 (61.9)
>p90	4 (9.5)
TUGT, s, median (IQR)	8.7 (7.8-12.0)
Orthostatic hypotension, n (%)	12 (31.6)
Exton Smith Scale, median [IQR]	19 [18-20]
Nutritional status according to MNA-SF, n (%)	
Sufficient: 12-14	12 (26.7)
At risk for malnutrition: 8-11	21 (46.7)
Malnutrition: 0-7	12 (26.7)
Use of walking aid, n (%)	12 (26.7)
MMSE (N = 39)	
Total, median [IQR]	27 [26-29]
<24, n (%)	3 (7.7)
ADL dependent (Katz ≥ 1), n (%)	9 (20.0)
IADL Dependent (Lawton ≥ 4), n (%)	16 (35.6)
First priority on OpTool, N = 39, n (%)	
Life extension	15 (38.5)
Maintaining independence	17 (43.6)
Reducing pain	4 (10.3)
Reducing other symptoms	3 (7.7)
Number of medications, n (%)	
0-3	18 (40.0)
4-6	11 (24.4)
>6	16 (35.6)
MPI score	0.31 [0.25-0.44]
MPI stages, n (%)	
MPI-stage 1, score ≤0.33	23 (51.1)
MPI-stage 2, score 0.34-0.66	20 (44.4)
MPI-stage 3, score ≥0.67	2 (4.4)

Characteristics and physical and cognitive markers of the patients who were referred to the geriatrician for a CGA. Data are presented as median (IQR) or number and percentages (%). Data are incomplete for: Gait speed (n = 42), TUGT (n = 39), orthostatic hypotension (n = 38), MMSE (n = 39), and first priority on OPTool (n = 39).

Abbreviations: ADL, activities of daily living; CGA, Comprehensive Geriatric Assessment; CIRS-CI, Cumulative Illness Rating Scale-Comorbidity Index; IADL, instrumental activities of daily livings; IQR, interquartile range; MMSE, Minimal Mental State Examination; MNA-SF, Mini Nutritional Assessment-Short Form; MPI, Multidimensional Prognostic Index; OPTool, Outcome Prioritization Tool; TUGT, Timed Up and Go Test.

Discussion

Eleven percent of the patients with HNC aged <70 years are considered frail and have higher mortality using the G8 as a screening tool. In this case-control study, we found significant differences in health characteristics between frail and nonfrail patients classified according to the G8. Frail patients had a high prevalence of geriatric impairments, lower BMI and level of education, a worse WHO performance status, and a higher alcohol intake compared to nonfrail controls. Treatment intention was not different between the 2 groups. However, mortality was almost 4 times higher in the frail patient group.

There's a growing interest in identifying frail patients in the oncological setting.[27] Several screening tools have been studied. Compared to other screening tools such as the Vulnerable Elders Survey-13 and the Groningen Frailty Indicator, the G8 was reported as the best screening tool for older patients with the highest sensitivity (76.5%) and acceptable specificity (64.4%).[10,28] A study by Neve et al[13] showed that in patients with HNC in their cohort with a median age of 75 years, the G8 is a better tool to identify frail patients compared to a multidisciplinary team. The G8 tool identified twice the number of frail patients compared to the multidisciplinary team. In the HNC patients, a study by Bras et al[29] found in a study population with a median age of 67.4 years, that a G8 ≤ 14 was significantly associated with postoperative complications within 30 days after surgery. Second, 30-day mortality and all-complications rate were found to be correlating with an abnormal G8, in HNC patients with a median age of 79 years.[12] Current studies do not describe the use of the G8 screening tool for patients <70. As the G8 was developed for older patients. The highlight of the present study is that it examined the clinical significance of the G8 screening tool for patients <70 with HNC.

We identified many geriatric impairments in frail patients. The distribution of comorbidities is consistent

with findings in a study performed by Eytan et al,[30] performed in 10,524 HNC patients but with a higher mean age of 74.8 years. Importantly, we found a higher percentage of frailty in patients with psychiatric disease: 20% in comparison with 8% in the older cohort of Eytan et al without psychiatric disease. An explanation could be that patients with psychiatric diseases have lower quality of life and are often care avoiders. Furthermore, we found that 20% and 2.6% scored below the 10th percentile of, respectively, handgrip strength, and gait speed. 31.6% of the frail patients suffered from orthostatic hypotension, which is high compared to other studies: 5% in HNC patients with a median age of 76 years.[31] In the general population, the prevalence of orthostatic hypotension is 6%, increasing to 30% >70 years.[32] 73.4% of the frail patients were either at risk for malnutrition or malnourished, which is almost double the percentages found in other studies.[31,33,34] For ADL and IADL dependence, our frail patient group appeared to be more dependent compared to other findings in HNC patients 35.6% versus 9.9%.[31,33] About half of the patient has MPI-stage 2 or MPI-stage 3, meaning moderate-to-severe frailty and subsequent higher 1-year mortality risk. Surprisingly, looking at the MMSE score, only 7.7% scored <24, which is low compared to other studies.[34,35] However, we know that cognitive function declines with older age,[36] and our population is younger compared to the previously mentioned studies.

An important finding in our study is that, despite similar tumor stages and treatment in both groups, the mortality rate was almost 4 times higher in the frail patient group. One explanation could be that the geriatric impairments of frail patients are independently associated with mortality.[33,37] Second, treatment might be too intensive for those frail patients, and they might not be able to recover after the intensive treatment anymore. This will cause higher long-term mortality, which could explain why mortality rates start to differ between the 2 groups in long-term follow-up. This suggests that we are still treating frail patients too intensively, or that we may need to focus more on optimizing the patient's health condition before treatment.

A strength of this study is that it is, to our knowledge, the first study that assesses the G8 tool in HNC patients <70 years. Second, the case-control study design allowed us to compare frail patients with nonfrail patients. This gives us a lot of information about the differences in health characteristics. Third, a thorough CGA was performed yielding detailed and extensive geriatric determinants to characterize the frail patients.

A limitation needs to be mentioned. Our population was of limited size because we only included patients <70 years.

In a future study, we will also evaluate other treatment outcomes such as complications and length of hospital stay.

Our study shows the importance of frailty screening in younger HNC patients. The G8 is a tool to identify frail patients with adverse health outcomes in the younger HNC population. Frail HNC patients aged <70 years were treated similarly to nonfrail patients but showed higher mortality. Thus, more attention is needed on whether treatment strategies are probably too intensive for frail young HNC patients and whether prehabilitation might improve survival in frail young HNC patients.

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Authors Contributions

Ajay T. Bakas, study design, acquisition of data, analysis, presentation; **Harmke A. Polinder-Bos**, study design, presentation; **Fleur Streng**, acquisition of data, analysis; **Francesco U.S. Mattace-Raso**, presentation; **Gijsbertus Ziere**, study design; **Robert J. Baatenburg de Jong**, presentation; **Aniel Sewnaik**, study design, analysis, presentation.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author on request.

Supplemental Material

Additional supporting information is available in the online version of the article.

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