




A comparison of the MNA-SF, MUST, and NRS-2002 nutritional tools in predicting treatment incompleteness of concurrent chemoradiotherapy in patients with head and neck cancer

Shun-Wen Hsueh¹ · Cheng-Chou Lai² · Chia-Yen Hung^{3,4} · Yu-Ching Lin⁵ · Chang-Hsien Lu⁶ · Kun-Yun Yeh¹ · Ngan-Ming Tsang⁷ · Yu-Shin Hung³ · Pei-Hung Chang¹ · Wen-Chi Chou^{3,8} 

Received: 22 January 2021 / Accepted: 5 March 2021 / Published online: 11 March 2021
© Springer-Verlag GmbH Germany, part of Springer Nature 2021

Abstract

Background Concurrent chemoradiotherapy (CCRT) treatment incompleteness is a known negative prognosticator for patients with head and neck cancer (HNC). Malnutrition is a common phenomenon which leads to treatment interruption in patients with HNC. We aimed to compare the performance of three nutritional tools in predicting treatment incompleteness in patients with HNC undergoing definitive CCRT.

Material and methods Three nutritional assessment tools, Mini Nutritional Assessment-Short Form (MNA-SF), Malnutritional Universal Screening Tool (MUST), and Nutritional Risk Screening 2002 (NRS-2002), were prospectively assessed prior to CCRT for HNC patients. Patients were stratified into either normal nutrition or malnourished groups using different nutrition tools. Treatment incompleteness and treatment-related toxicities associated with CCRT were recorded.

Results A total of 461 patients were included in the study; malnourished rates ranged from 31.0 to 51.0%. The CCRT incompleteness rates were 4.9–6.3% and 14.5–18.2% for normal nutrition patients and malnourished patients, respectively. The tools had significant correlations with each other (Pearson correlation 0.801–0.837, $p < 0.001$ for all) and accurately predicted the incompleteness of CCRT. MNA-SF had the highest performance in predicting treatment-related toxicity, including emergency room visits, need for hospitalization, any grade III or higher hematological adverse events, and critical body weight loss, compared to the other tools.

Conclusions MNA-SF, MUST, and NRS2002 were all shown to be competent tools for prediction of treatment incompleteness and treatment-related toxicity in HNC patients undergoing CCRT. We suggest implementing nutritional assessment prior to treatment to improve the rate of treatment completion and to reduce treatment-related toxicity in HNC patients.

Keywords Nutritional assessment tool · Head and neck cancer · Adverse event · Treatment incompleteness

✉ Wen-Chi Chou
wenchi3992@yahoo.com.tw

¹ Department of Oncology, Chang Gung Memorial Hospital at Keelung, Keelung, Taiwan

² Department of Colon and Rectal Surgery, Chang Gung Memorial Hospital at Linkou and College of Medicine, Chang Gung University, Taoyuan, Taiwan

³ Department of Hematology and Oncology, Chang Gung Memorial Hospital at Linkou and College of Medicine, Chang Gung University, Taoyuan, Taiwan

⁴ Division of Hema-oncology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan

⁵ Department of Medical Imaging and Intervention, Chang Gung Memorial Hospital at Keelung, Keelung, Taiwan

⁶ Department of Oncology, Chang Gung Memorial Hospital at Chiayi, Chiayi, Taiwan

⁷ Department of Radiation Oncology, Chang Gung Memorial Hospital at Linkou and College of Medicine, Chang Gung University, Taoyuan, Taiwan

⁸ Department of Hematology and Oncology, Chang Gung Memorial Hospital, 5 Fu-Hsing Street, Kwei-Shan Shiang, Taoyuan, Taiwan

Introduction

Primary head and neck cancer (HNC), accounting for 4% of all cancers, is a disease with more than 650,000 new cases diagnosed and account for 330,000 deaths annually worldwide [1]. Taiwan is an endemic area of HNC, with one of the highest global incidence rates of 8% [2]. Risk factors for head and neck cancer often involve chronic substance abuse, particularly among lower socioeconomic classes [3–5]. Inevitably, patients with HNC tend to have poor self-care and nutritional deterioration [4, 5]. While the standardized treatment for localized advanced HNC is concurrent chemoradiotherapy (CCRT), the intervention is commonly associated with acute toxicities such as fatigue, nausea, mucositis, xerostomia, dysphagia, and odynophagia, which may worsen malnutrition status [6].

CCRT treatment incompleteness is a well-known negative prognosticator as the premature termination of treatment decreases loco-regional control, increases the risk of distant metastases, and ultimately compromises overall survival [4, 6–8]. Common reasons for treatment incompleteness include treatment-related side effects, limited financial resources, and poor family support [8, 9]. While the reasons for CCRT treatment incompleteness are multifactorial, the reversible causes of treatment incompleteness should be further investigated.

Malnutrition is a reversible cause of treatment incompleteness of CCRT in patients with HNC [10]. Malnutrition is highly prevalent among HNC patients, with approximately 35–60% of patients reported to be malnourished at diagnosis [10–12]. Previous studies have reported that malnutrition is associated with increased treatment-related toxicity and treatment intolerance of CCRT in patients with HNC. Inversely, nutritional intervention has been shown to positively influence CCRT outcomes, with decreased treatment-related toxicity and treatment interruption [13]. However, few studies have used existing nutritional tools to identify malnourished patients and determine their relationship with treatment incompleteness in HNC patients. Thus, to target malnourished patients for improvement of treatment completion, a study to examine the applicable nutritional tools is warranted. This prospective study aimed to (1) determine the prevalence of malnutrition among newly diagnosed HNC patients, (2) assess the correlation among different nutritional tools, and (3) test their accuracy in predicting treatment completion in HNC patients undergoing definitive CCRT.

Material and methods

Patient selection

This multi-center prospective study consecutively recruited HNC patients between August 2016 and December 2017

in Taiwan. Eligibility criteria included patients aged 20 years or older with histologically proven stage II–IVa primary HNC (origin of nasopharynx, oropharynx, hypopharynx, or oral cavity) and patients must have been eligible for definitive CCRT as the antitumor treatment. Patients with the following characteristics were excluded: distant metastatic disease that was unfit for the treatment with definitive CCRT, patients who were unable to provide informed consent for any reason, patients who received other treatments (e.g., surgery or induction chemotherapy) before definitive CCRT, and patients who received bio-radiotherapy (cetuximab) alone. Tumor staging was performed according to the 7th edition American Joint Committee on Cancer (AJCC) staging system. All patients provided written informed consent prior to their inclusion in the study. The study protocol was approved by the Institutional Review Board (No. 1608080002) and was conducted in compliance with the Declaration of Helsinki (1996).

Definitive concurrent chemoradiotherapy

All eligible patients received intensity-modulated or arc technique radiotherapy at a conventional fractionated daily dose of 200 cGy for 5 consecutive days per week, with a total prescribed radiotherapy dose of 7000–7400 cGy over 7 weeks. The chemotherapy regimens, including cisplatin (40 mg/m² every week or 100 mg/m² every 3 weeks), PF regimen (cisplatin 60 mg/m² on day 1 plus continuous infusion of 5-fluorouracil 800 mg/m² on days 1–5, every 2 weeks) [14], and PUL regimen (cisplatin 50 mg/m² on day 1, tegafur-uracil [TTY Biopharm Co. Ltd, Taipei, Taiwan] 300 mg/m²/day, and oral leucovorin 60 mg/day on days 1–14, every 2 weeks) [15], were administered concurrently with radiotherapy according to the treatment guidelines at our institution.

All adverse events, including emergency room visits, need for hospitalization, grade III or higher hematological/non-hematological side effects, and critical body weight loss (defined as $\geq 5\%$ body weight from the pretreatment baseline) due to any reason during the CCRT period, were recorded. CCRT-related toxicity was graded according to the Common Toxicity Criteria (CTC) of the National Cancer Institute (NCI), version 3.

Patients who received less than 90% of the protocol specified radiotherapy dose or a cumulative cisplatin dose of less than 200 mg/m² due to any cause were considered to have incomplete radiotherapy [16] or chemotherapy [17] treatment, respectively. Incomplete CCRT was defined as either incomplete radiotherapy or incomplete chemotherapy. Reasons for treatment incompleteness were documented and included intolerance to side effects, concomitant medical illness, progressive disease, and a patients' will against medical advice.

Nutrition assessment

Three nutritional tools, Mini Nutritional Assessment-Short Form (MNA-SF), Malnutritional Universal Screening Tool (MUST), and Nutritional Risk Screening 2002 (NRS-2002), were synchronously performed within seven days of CCRT initiation. All objective and subjective variables required for nutritional assessment were obtained from the patients.

Mini Nutritional Assessment-Short Form

The MNA-SF tool consists of the following parameters: food intake, weight loss, mobility, psychological stress, neuropsychological problems, and body mass index (BMI). All parameters are scored from 0 to 2 or 3 with a total score of 0–14 [18]. Patients with a total score <12 were classified as malnourished while a total score ≥ 12 was classified as normal nutrition in this study.

Malnutrition Universal Screening Tool

The MUST score is calculated based on the patient's BMI, unplanned weight loss, and acute disease effect [19]. As a score is assigned from each category, the MUST score is the sum of the categorical scores, where a score ≥ 2 is deemed as high risk of malnutrition and patients with such scores were assigned to the malnourished group, and patients with a score <2 were assigned to the normal nutrition group in our study.

Nutritional Risk Screening 2002

The NRS-2002 system is a two-step screening procedure with an initial evaluation of BMI, weight loss, appetite, and severe disease [20]. If further evaluation is indicated, the patient is further scored by two components: nutrition and severity of illnesses. The score is age-adjusted and ranges from 0 to 7. Patients with a value ≥ 3 were assigned to the malnourished group and a value <3 indicated the normal nutrition group in our study.

Statistical analysis

Basic demographic data are summarized as *n* (%) for categorical variables and median with range for continuous variables. All eligible patients were categorized into normal nutrition and malnourished groups according to the definition of each nutritional tool. Univariate logistic regression analyses were used for in-group comparisons of treatment incompleteness and treatment-related toxicity. SPSS software (version 17.0; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. All statistical assessments were two-sided, and a *p*-value <0.05 was considered statistically significant.

Results

A total of 461 patients were recruited in this study, with a median age of 54 years (range, 24–86 years) and 402 (87%) were male (Table 1). Tumors from the oropharynx were the most common (32.8%), followed by the nasopharynx (24.9%), and hypopharynx (24.9%). In terms of staging, 305 (66.2%) patients had stage IV disease, 78 (16.9%) of patients had stage III disease, and the remaining 78 (16.9%) of patients had stage II disease.

Using the nutritional screening tools, malnutrition was recognized in 47.3%, 51.0%, and 31.0% of the cohort using the MNA-SF, MUST, and NRS-2002, respectively (Fig. 1). The Pearson correlation coefficients ranged from 0.801 to 0.837 for the tool-to-tool comparison (*p*<0.001 for all), indicating strong positive correlations among the three tools (Table 2).

Figure 2 shows the percentage of treatment incompleteness between normal nutrition and malnourished patients according to the different tools. The completion rate of CCRT among patients with normal nutrition was 4.9%, 5.3%, and 6.3% as identified by the MNA-SF, MUST, and NRS-2002 tools, respectively, while the incompleteness rate among the malnourished group ranged from 14.5 to 18.2%. Different reasons for CCRT treatment incompleteness were documented (Fig. 3). All tools analyzed showed that patients with normal nutrition had a significantly lower incidence of CCRT incompleteness than the malnourished cohort.

Table 3 shows the ability of the nutritional tools to predict treatment-related toxicities of CCRT. All three nutritional tools performed well in predicting the need for hospitalization, any grade III or higher grade of hematologic adverse events, and critical body weight loss among HNC patients undergoing CCRT. MNA-SF performed better in identifying the risk of emergency room visits than the other two tools, while all three nutritional tools failed to recognize the risk of any grade III or higher non-hematological adverse events in HNC patients undergoing CCRT.

Among the 46 patients with incomplete CCRT, 22 (47.8%) patients were intolerant to treatment-related adverse events, 10 (21.7%) patients had medical advice, 8 (17.4%) had severe concomitant medical illness, and 6 (13.0%) had progressive disease. The reasons for CCRT incompleteness stratified by different nutritional tools are shown in Fig. 4. Malnourished patients had a higher incidence rate of CCRT incompleteness than patients with normal nutrition for all causes. The absolute in-group difference in the percentage of CCRT incompleteness was 4.1–7.0%, 0.8–1.2%, 2.6–2.8%, and 1.2–1.7% due to treatment-related adverse events, medical advice, concomitant medical illness, and progressive disease, respectively, among different nutritional tools.

Table 1 Basic patient's characteristics

| Variable | Category | Overall, n (%) N=461 |
|---------------------|---------------------------------------|-------------------------|
| Gender | Male | 402 (87.2) |
| Age | Median (range) | 54 (24–86) |
| Marital status | Married | 336 (72.9) |
| | Others | 125 (27.1) |
| Education | Less than high school | 91 (19.7) |
| | High school graduate | 290 (62.9) |
| | Associate/bachelor's degree or higher | 80 (17.4) |
| Occupation | Yes | 327 (70.9) |
| | No | 134 (29.1) |
| Main care-giver | Spouse | 269 (58.4) |
| | Child | 66 (14.3) |
| | Others | 126 (27.3) |
| Smoking | Yes | 355 (77.0) |
| Drinking | Yes | 357 (77.4) |
| Betel quid-chewing | Yes | 279 (60.5) |
| ECOG performance | 0 | 237 (51.4) |
| | 1 | 215 (46.6) |
| | ≥2 | 9 (2.0) |
| | CCI | 0 |
| CCI | 1 | 130 (28.2) |
| | ≥2 | 86 (8.7) |
| | Cancer type | Nasopharynx |
| Oropharynx | | 151 (32.8) |
| Oral cavity | | 80 (17.4) |
| Hypopharynx | | 115 (24.9) |
| Tumor stage by AJCC | 2 | 78 (16.9) |
| | 3 | 78 (16.9) |
| | 4 | 305 (66.2) |
| | Chemotherapy regimen | Platinum monotherapy |
| Platinum doublet | | 339 (73.5) |

ECOG, Eastern Cooperative Oncology Group; CCI, Charlson comorbidity index; AJCC, American Joint Committee on Cancer

Discussion

The reversible causes of early termination of CCRT are important issues since incompleteness of treatment is a well-recognized prognostic factor for HNC patients [21].

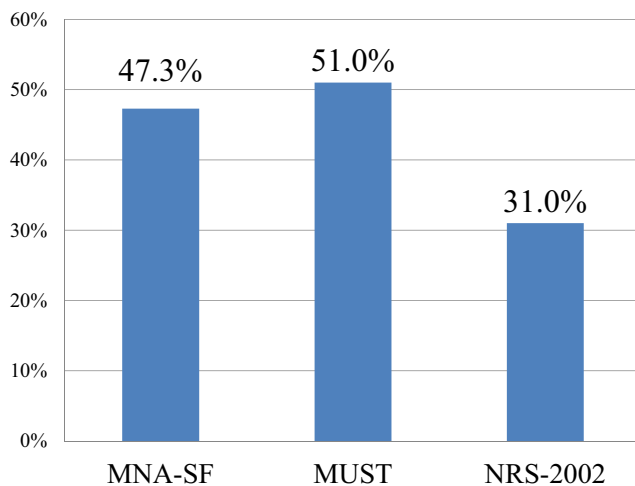


Fig. 1 Prevalence of malnutrition according to the three nutrition assessment tools

While the reasons for premature termination of CCRT are often multifactorial [21], limited literature is available on identifiable possible causes. Malnutrition is frequently associated with poor survival outcomes, poor quality of life, and higher treatment-related toxicities in patients with HNC [22]. Consequently, this study focused on the effect of malnutrition on CCRT completion in patients with HNC. We reported malnutrition as a frequent phenomenon, with a prevalence rate ranging from 31 to 51% by three different nutritional assessment tools, among HNC patients prior to CCRT. The normal nutrition group had a CCRT incompleteness rate of 4.9~6.3%, compared to the malnourished group (15.6~18.2%). Malnourished patients were more susceptible to early treatment termination as

Table 2 Pearson correlation between the nutritional assessment tools according to the MNA-SF, NRS-2002, and the MUST

| | MNA-SF | MUST | NRS-2002 |
|----------|---------------------|---------------------|---------------------|
| MNA-SF | -- | 0.801 ($p<0.001$) | 0.835 ($p<0.001$) |
| MUST | 0.801 ($p<0.001$) | -- | 0.837 ($p<0.001$) |
| NRS-2002 | 0.835 ($p<0.001$) | 0.837 ($p<0.001$) | -- |

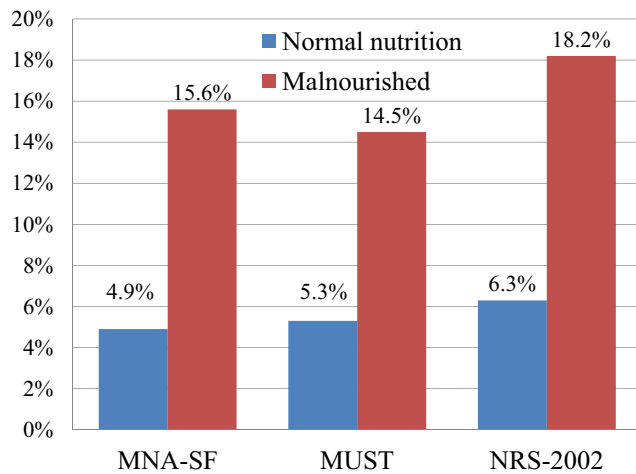


Fig. 2 Treatment incompleteness rate of concurrent chemoradiotherapy in normal nutrition and malnourish patients according to the three nutrition assessment tools

they had a higher rate of adverse events during treatment compared to the normal nutrition patients. The three commonly used nutritional tools, MNA-SF, NRS-2002, and MUST, were well correlated with each other and had a similar performance in the prediction of early treatment termination and treatment-related toxicities. Conclusively, our data showed that recognition of the pretreatment nutritional status, whether by using MNS-SF, NRS-2002, or MUST, is an essential step for HNC patients prior to CCRT.

A previous study reported that the side effects of CCRT or radiotherapy are the main reasons for treatment incompleteness

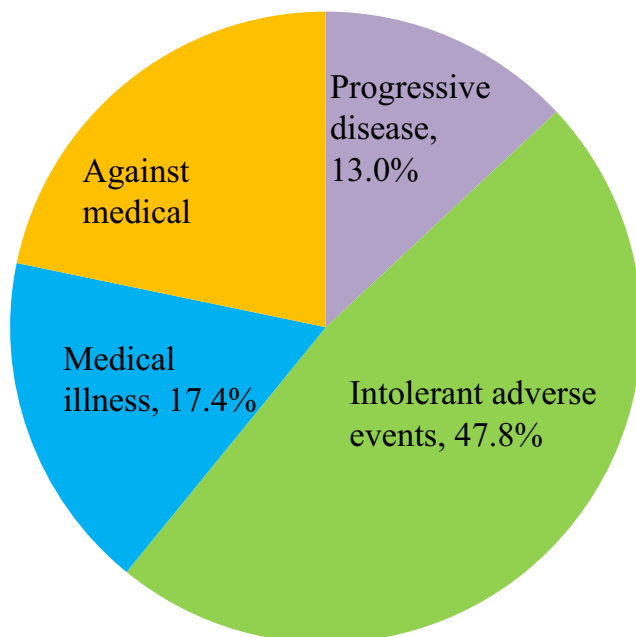


Fig. 3 Causes of treatment incompleteness of concurrent chemoradiotherapy

[23, 24]. In an attempt to identify patients who are more susceptible to adverse events, this study identified that malnourished patients were significantly associated with higher rates of hospitalization, grade III or higher hematological adverse events, and critical body weight loss, compared to those with normal nutrition. Although these treatment-related toxicities are not lethal, they inevitably exacerbate the malnourished patient's physical and psychological functioning; thus, patients are more likely to withdraw from treatment [24]. While previous studies have demonstrated side effects as a common reason for premature treatment termination, our study determined an association between malnutrition and side effects, which eventually led to incomplete treatment.

Our data revealed that while the three nutritional assessment tools, MNA-SF, NRS-2002, and MUST, utilize different parameters for evaluation, a significant correlation is apparent. The correlation among these three tools and their individual prognostic significance suggest that the importance of nutritional screening for malnourished patients is universal. As the most important goal is malnutrition recognition, this result shows that clinicians may use the tools for their convenience in identifying malnutrition. The apparent strength of these tools is their ease of application. While no blood test or image interpretation is needed, tools can be easily applied by all medical staff on the cancer team. As the importance of malnutrition in these patients is recognized, an organized protocol to provide nutritional intervention is essential. The easy accessibility of the tools by all medical staff may facilitate the general use of a potential interventional protocol.

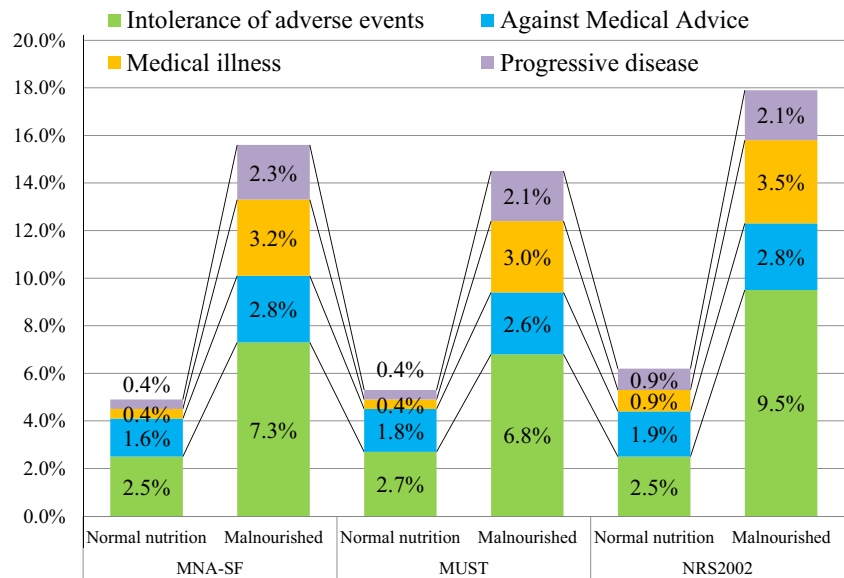
Our study shows that malnourished patients have higher rates of treatment incompleteness, regardless of the reason for termination, compared to patients with normal nutritional status. Lazarea et al. studied the reasons for premature discontinuation of curative radiation at different anatomical sites [8]. Based on 1001 HNC patients treated with curative intent, the treatment incompleteness rate among this population was 5.8% and the main reason for early termination was discontinuation of medical advice [8] while medical advice ranked 2nd in the most common reasons in our study, accounting for 10 of 461 (2.2%) patients for CCRT incompleteness. The apparent difference (0.8–1.2%) of CCRT incompleteness rate between the two groups with respect to medical advice highlighted that malnourished patients were more vulnerable to treatment-related toxicity, deterioration of concomitant illness, and progression of cancer, compared to the normal nutrition population. On the other hand, patients will against medical advice is often multifactorial, involving concerns such as family support and socioeconomic issues [22]. As self-care is pertinent to any medical treatment [25, 26], malnutrition may also help to identify patients who need social support.

The strength of this study lies in the large number of patients from multiple institutes, allowing the objective examination of the association between malnutrition and CCRT

Table 3 The relationship of the nutritional assessment tools and CCRT outcomes

| Outcome | MNA-SF | MUST | NRS-2002 |
|--|--------|-------|----------|
| Incompletion of CCRT | <0.001 | 0.001 | <0.001 |
| Incompletion of radiotherapy | 0.001 | 0.003 | 0.02 |
| Incompletion of chemotherapy | 0.004 | 0.013 | <0.001 |
| Emergency room visiting | 0.004 | 0.370 | 0.330 |
| Hospitalization | <0.001 | 0.020 | 0.030 |
| Any grade III or higher hematological adverse events | <0.001 | 0.009 | 0.043 |
| Any grade III or higher non-hematological adverse events | 0.09 | 0.11 | 0.088 |
| Critical body weight loss | 0.001 | 0.025 | 0.001 |

Critical body weight loss: indicated a body weight loss $\geq 5\%$ from pretreatment

Fig. 4 Causes of concurrent chemoradiotherapy incompletion stratified by the three nutritional assessment tools

treatment completion in HNC patients. Nevertheless, this study had several limitations. Firstly, this study did not investigate other commonly used nutritional assessment tools, such as the Glasgow prognostic score, Patient Generated Subjective Global Assessment, and prognostic nutritional index. Since the initiative of the study was to discover a convenient tool for nutrition evaluation, tools that require blood work or professional evaluation by the medical staff were excluded. However, these may also play a contributory role in nutritional evaluation. Secondly, nutrition is a dynamic status that may fluctuate prior to and during treatment. This raises two important issues among HNC patients undergoing CCRT. The first issue is whether the predefined timing for nutritional assessment is representative of a patient's nutritional status throughout the treatment trajectory. The second issue is whether malnutrition is an irreversible or reversible condition in patients with HNC. While both issues cannot be answered directly by this study, our data emphasizes the importance of nutritional assessment in patients with HNC prior to CCRT. Further studies to examine the effect of

aggressive nutritional intervention for patients with recognized malnutrition are warranted.

Conclusion

Malnutrition is prevalent among patients with HNC. The pretreatment nutritional status of HNC patients is related to the possibility of treatment incompletion and treatment-related toxicity. Nutritional tools such as MNA-SF, MUST, and NRS2002 are all competent tools for malnutrition recognition. We suggest that clinicians implement nutritional assessment prior to treatment to improve the chances of treatment completion for HNC patients with malnutrition.

Acknowledgements The authors gratefully acknowledge Miss Vengi Ho and the support from the Cancer Center of Chang Gung Memorial Hospital, Taoyuan, Taiwan.

Availability of data The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability Not applicable

Author contribution Conception and design of study: HSW, LCC, YKY, CHL, and WCC; Acquisition of data: TNM, SWH, HYS, and CPH; Analysis and interpretation of data: HCY, LYC, WCC, and TNM; Drafting of the manuscript: HSW, LCC, HCY, HYS, LCH, and WCC.

Declarations

Ethics approval This study was approved by the institutional review board of Chang Gung Memorial Hospital in August 2017 (ethic code: 1608080002) and has been conducted in compliance with the Helsinki Declaration (1996).

Consent to participate All patients provided written informed consent prior to inclusion.

Consent for publication Not applicable.

Competing interest The authors declare no competing interests.

References

- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 68:394–424
- Lai YC, Tang PL, Chu CH, Kuo TJ (2018) Effects of income and residential area on survival of patients with head and neck cancers following radiotherapy: working age individuals in Taiwan. *PeerJ* 6:e5591
- Dhull AK, Atri R, Dhankhar R, Chauhan AK, Kaushal V (2018) Major risk factors in head and neck cancer: a retrospective analysis of 12-year experiences. *World J Oncol* 9:80–84
- Thomas K, Martin T, Gao A, Ahn C, Wilhelm H, Schwartz DL (2017) Interruptions of head and neck radiotherapy across insured and indigent patient populations. *J Oncol Pract* 13:e319–e328
- Patel UA, Thakkar KH, Holloway N (2008) Patient compliance to radiation for advanced head and neck cancer at a tertiary care county hospital. *Laryngoscope* 118:428–432
- Rosenthal DI (2007) Consequences of mucositis-induced treatment breaks and dose reductions on head and neck cancer treatment outcomes. *J Support Oncol* 5:23–31
- Nguyen-Tan PF, Zhang Q, Ang KK, Weber RS, Rosenthal DI, Soulieres D, Kim H, Silverman C, Raben A, Galloway TJ, Fortin A, Gore E, Westra WH, Chung CH, Jordan RC, Gillison ML, List M, le QT (2014) Randomized phase III trial to test accelerated versus standard fractionation in combination with concurrent cisplatin for head and neck carcinomas in the Radiation Therapy Oncology Group 0129 trial: long-term report of efficacy and toxicity. *J Clin Oncol* 32:3858–3866
- Lazarev S, Gupta V, Ghiassi-Nejad Z, Miles B, Scarborough B, Misiukiewicz KJ, Reckson B, Sheu RD, Bakst RL (2018) Premature discontinuation of curative radiation therapy: insights from head and neck irradiation. *Adv Radiat Oncol* 3:62–69
- Sharma A, Madan R, Kumar R, Sagar P, Kamal VK, Thakar A, Sharma A, Mohanti BK (2014) Compliance to therapy-elderly head and neck carcinoma patients. *Can Geriatr J* 17:83–87
- Jager-Wittenaar H, Dijkstra PU, Vissink A, Langendijk JA, van der Laan BF, Pruim J et al (2011) Changes in nutritional status and dietary intake during and after head and neck cancer treatment. *Head Neck* 33:863–870
- Dechaphunkul T, Martin L, Alberda C, Olson K, Baracos V, Gramlich L (2013) Malnutrition assessment in patients with cancers of the head and neck: a call to action and consensus. *Crit Rev Oncol Hematol* 88:459–476
- Bossola M (2015) Nutritional interventions in head and neck cancer patients undergoing chemoradiotherapy: a narrative review. *Nutrients* 7:265–276
- Yanni A, Dequanter D, Lechien JR, Loeb I, Rodriguez A, Javadian R, van Gossum M (2019) Malnutrition in head and neck cancer patients: impacts and indications of a prophylactic percutaneous endoscopic gastrostomy. *Eur Ann Otorhinolaryngol Head Neck Dis* 136:S27–S33
- Taylor SG, Murthy AK, Vannetzel JM, Colin P, Dray M, Caldarelli DD et al (1994) Randomized comparison of neoadjuvant cisplatin and fluorouracil infusion followed by radiation versus concomitant treatment in advanced head and neck cancer. *J Clin Oncol* 12:385–395
- Huang PW, Lin CY, Hsieh CH, Hsu CL, Fan KH, Huang SF, Liao CT, Ng SK, Yen TC, Chang JTC, Wang HM (2018) A phase II randomized trial comparing neoadjuvant chemotherapy followed by concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in advanced squamous cell carcinoma of the pharynx or larynx. *Biom J* 41:129–136
- Garden AS, Harris J, Vokes EE, Forastiere AA, Ridge JA, Jones C, Horwitz EM, Glisson BS, Nabell L, Cooper JS, Demas W, Gore E (2004) Preliminary results of Radiation Therapy Oncology Group 97-03: a randomized phase ii trial of concurrent radiation and chemotherapy for advanced squamous cell carcinomas of the head and neck. *J Clin Oncol* 22:2856–2864
- Loong HH, Ma BB, Leung SF, Mo F, Hui EP, Kam MK et al (2012) Prognostic significance of the total dose of cisplatin administered during concurrent chemoradiotherapy in patients with locoregionally advanced nasopharyngeal carcinoma. *Radiother Oncol* 104:300–304
- Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B (2001) Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). *J Gerontol A Biol Sci Med Sci* 56:M366–M372
- Stratton RJ, Hackston A, Longmore D, Dixon R, Price S, Stroud M, King C, Elia M (2004) Malnutrition in hospital outpatients and inpatients: prevalence, concurrent validity and ease of use of the ‘malnutrition universal screening tool’ (‘MUST’) for adults. *Br J Nutr* 92:799–808
- Kondrup J, Rasmussen HH, Hamberg O, Stanga Z (2003) Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin Nutr* 22:321–336
- Dronkers EA, Mes SW, Wieringa MH, van der Schroeff MP, Baatenburg de Jong RJ (2015) Noncompliance to guidelines in head and neck cancer treatment; associated factors for both patient and physician. *BMC Cancer* 15:515
- Isenring EA, Capra S, Bauer JD (2004) Nutrition intervention is beneficial in oncology outpatients receiving radiotherapy to the gastrointestinal or head and neck area. *Br J Cancer* 91:447–452
- Yeh SA (2010) Radiotherapy for head and neck cancer. *Semin Plast Surg* 24:127–136

24. Riley P, Glenny AM, Worthington HV, Littlewood A, Clarkson JE, McCabe MG. (2015) Interventions for preventing oral mucositis in patients with cancer receiving treatment: oral cryotherapy. *Cochrane Database Syst Rev* CD011552. <https://doi.org/10.1002/14651858>
25. Knight TG, Deal AM, Dusetzina SB, Muss HB, Choi SK, Bensen JT et al (2018) Financial toxicity in adults with cancer: adverse outcomes and noncompliance. *J Oncol Pract*. <https://doi.org/10.1200/JOP.18.00120>
26. Dodd MJ, Miaskowski C (2000) The PRO-SELF Program: a self-care intervention program for patients receiving cancer treatment. *Semin Oncol Nurs* 16:300–308 discussion 308-16

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.