Original Article

Effectiveness of Head-and-Neck Molecular Imaging Reporting and Data System Criterion in Head-and-Neck Squamous Cell Carcinoma PostConcurrent Chemoradiotherapy

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Abstract

Purpose: Postconcurrent chemoradiotherapy (CRT) response assessment has been challenging in locally advanced head-and-neck squamous cell carcinoma (LA-HNSCC) due to prevailing postradiation changes. Molecular response methods have been encouraging, although further clarifications and validations were needed. We tested the effectiveness of a proposed semi-quantitative molecular response criterion in these patients. **Materials and Methods:** Two subspecialty-trained physicians evaluated ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography of LA-HNSCC patients (n = 83) post 3 months CRT using a five points Head and Neck Molecular Imaging-Reporting and Data System (HAN-MI-RADS) criterion. Where available, histopathology examination with clinical and imaging interpretation was taken as a reference for the disease. A diagnostic accuracy comparison was done with the existing Hopkins score. Further effectiveness was analyzed with disease-free survival (DFI) and overall survival (OS). **Results:** Metastasis was developed in 11/83 patients at 3 months of evaluation. Of 72 patients, 39, 2, and 31 patients had a complete response, equivocal response, and partial response as per HAN-MI-RADS. Per patient sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for predicting loco-regional disease up to 1 and 2 years was 93.3%, 92.5%, 90.3%, 94.9%, 92.9%, and 84.9%, 91.9%, 90.3%, 87.2%, and 88.6% respectively. One year and two years DFI for each HAN-MI-RADS score showed a statistically significant difference while it was not for OS. The receiver operating characteristic curve analysis showed significantly better outcome predictability of HAN-MI-RADS (area under the curve [AUC] 0.884) than Hopkins (AUC 0.699). **Conclusions:** A five points HAN-MI-RADS criterion was found promising for response assessment with less equivocal results and statistically significant higher AUC than Hopkins for loco-regional recurrence prediction.

Keywords: *Concurrent chemo-radiotherapy, head-and-neck molecular imaging-reporting and data system, head-and-neck squamous cell carcinoma, Hopkins score, molecular response*

Introduction

Two out of three patients with head-and-neck squamous cell carcinoma (HNSCC) presented with locally advanced (LA) cancer and were treated with concurrent chemo radiotherapy (CRT) with a 5-year survival rate of around 50%.[1,2] Response to treatment has been crucial in determining subsequent management.[3] Due to simultaneous postradiation alterations, the standard morphological response approach has been deemed problematic. Consequently, numerous ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT)-based molecular response approaches have been devised and found to be efficient in preventing needless neck dissection.[4,5] Nonetheless, inter-class heterogeneity, a poor positive predictive value (PPV), time dependence, and a lack of validation studies were the most significant issues with these techniques.[6] Consequently, a specialized, well-structured criterion was required in this case. The purpose of this study was to propose and evaluate a semi-quantitative molecular response criterion for these patients.

Materials and Methods

In this retrospective analysis, LA-HNSCC patients treated with CRT during 2011–2018 were screened. Patients with an FDG PET/CT study at 3–4 months post-CRT with a minimum of 2 years of follow-ups were

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included. A baseline PET/CT scan was not a requirement. Patients with a previous history of surgery, chemotherapy, second malignancies, and nonsquamous cell carcinoma histology were excluded. Nasopharyngeal carcinomas, indeterminate lung nodules, and only radiotherapy treatment were the other exclusion criteria. This study was approved by the Hospital Institutional Review Board and has granted a waiver from consenting (IRB-BHR/92/2022, July 28, 2022).

Imaging protocol

A standard protocol was used for performing FDG PET/CT scans.[7] 4–6 h of fasting with a light meal before and adequate hydration were the preparatory instructions. Random blood sugar below 200 mg/dL was used as a cut-off before injecting 3–4 mBq/kg body weight FDG in all the patients. One-liter normal water was permitted during the uptake phase of 1 h (±10 min). A whole-body scan (skull base to mid-thigh) with a regional head and neck sequence was acquired on a dedicated full-ring hybrid PET/CT system (Biograph TruePoint40 Siemens Healthcare with LSO crystal) with 2 min per bed position. A moderate dose (100 mAs and 120 kVp) noncontrast-enhanced CT scan was used for attenuation correction and anatomical localization. An iterative method (two iterations and 12 subsets) was used for PET image reconstruction.

Image interpretation

All PET/CT studies were re-analyzed independently by two >15 years of experienced nuclear medicine physicians in PET/CT on Syngo.via VB30, Siemens workstation. A five-point dedicated Head and Neck Molecular Imaging-Reporting and Data System (HAN-MI-RADS) criterion was formulated for PET/CT interpretation in an inter-departmental consensus meeting among nuclear medicine, radiology, head and neck surgery, radiotherapy, and medical oncology [Table 1]. Degree of uptake above the background (contralateral normal structure in the neck), mediastinal blood pool (arch of the aorta), liver (right lobe), and distribution of tracer activity (diffuse or focal) were the important determinants for the criteria laid down. No size criterion was used for PET interpretation. The highest single voxel maximum standard uptake value normalized to body weight (SUVmax) was recorded for scoring. Briefly, score 1 was no uptake or minimal uptake ≤mediastinal blood pool or contralateral normal activity in the neck. Score 2 was mild uptake ≤liver. Score 3 was diffuse uptake divided into categories of 3A and 3B depending upon moderate diffuse uptake >Liver but ≤2 times of liver (3A) or severe diffuse uptake more than two times of the liver (3B). Score 4 was focal moderate uptake more than the liver. Score 5 was severe focal uptake more than two times of liver or a new focal lesion likely to be disease. The highest score of T (tumor) or N (lymph node) was used to categorize the patients into a standard response group. Complete response (CR) included scores 1, 2, and 3A. Partial response (PR) included scores 4 and 5. Score 3B was considered an equivocal or indeterminate response for HAN-MI-RADS. Metastasis or new lesion was considered a progressive disease (PD). Hopkins scores were also determined for comparison.[8] For that, CR included scores 1 and 2 while the equivocal response was scores 3A and 3B.[9] PR and PD response groups were the same as HAN-MI-RADS.

Statistical analysis

Mean and the range were analyzed for quantitative data, whereas absolute frequencies and percentages were calculated for the categorical data. Where available, histopathology examination (HPE) was considered the gold standard at 3 months for the calculation of sensitivity, specificity, PPV, negative predictive value (NPV), and accuracy. At 1 and 2 years, HPE, or clinical or imaging outcome were taken as standard for disease status assessment. The primary endpoint was the diagnostic accuracy of both criteria for the prediction of loco-regional recurrence. Occurrences of metastasis were separately reported. Disease-free interval (DFI) was calculated from

Table 1: Head-and-neck molecular imaging-reporting and data system response assessment post-3 months of radiotherapy and concurrent chemotherapy in head and neck malignancies

Score	PET/CT findings	Possible interpretation	Proposed suggestion
1	No or minimal uptake (uptake below mediastinum or C/l normal structure) or physiological uptake	No residual disease	Follow up
2	Mild uptake (< liver)	Unlikely disease	Follow up
3	Moderately uptake (> liver but ≤2 times) diffuse with no focal areas	Low chance of disease, likely posttreatment changes	Follow up
	Severe uptake (≥2 times of liver) diffuse with no focal areas	Indeterminate for residual disease (equivocal)	Close follow up
4	Moderate uptake (> liver but ≤2 times) with focal areas at nonphysiological sites	High chance of disease	HPE
5	Severe uptake (>2 times of liver) with focal areas at nonphysiological sites or new lesions likely disease	Likely residual/recurrent disease	HPE

Follow-up: 12–16 weeks, close follow-up: 6–8 weeks. HPE: Histopathological examination, PET: Positron emission tomography, CT: Computed tomography

the end of treatment to the identification of a residual or recurrent disease or death due to any cause. Overall survival (OS) was calculated from the start of treatment to death due to any cause or till the last follow-up. Data were censored in uneventful cases. DFI and OS were calculated by the Kaplan–Meier method and compared with the Log-Rank test. DFI and OS of each score (1, 2, 3A, 3B, 4, and 5) and each response group (CR, PR, Equivocal) for both criteria were calculated. Per-patient diagnostic accuracy for both criteria was compared by receiver operating characteristic (ROC) curve analysis. The type of ROC analysis used was "Comparison of ROC curves" using De Long test. Diagnostic Accuracy has been analyzed with SPSS version 23.0, Chicago, IL, USA while survival analysis was conducted with MedCalc Statistical Software version 20.115, Ostend, Belgium. All the *P* values were two-sided and $P < 0.05$ was considered statistically significant.

Results

Out of screen 314 patients with head-and-neck malignancies, 83 patients were included for final analysis [Figure 1]. Patient characteristics were tabulated [Table 2]. FDG PET/CT scan was done at a mean of 3.2 months post-CRT (range 3.0–3.9 months). Posttreatment mean (range) SUVmax of T, N, background, mediastinum, and liver were 4.3 (16–1.6), 3.0 (26.0–1.0), 2.3 (5.0–1.0), 1.9 (4.0–1.0), and 2.8 (6.0–1.4), respectively. Metastasis was found in 11/83 patients (13.3%) at 3 months. Out of which 7 patients were proven by histopathology. Of remaining 72 patients, 39, 2, and 31 patients had a CR (Scores 1, 2, 3A), equivocal response (score 3B), and PR (Score 4, 5) respectively as per HAN-MI-RADS criterion. At 3 months, 33/72 patients' histopathology was available. Per patient sensitivity, specificity, PPV, NPV, and accuracy at 3 months were 95.8%, 44.4%, 82.1%, 80.0%, and 81.8%. Out of 72, at 1 year 40 and at 2 years 47 patient's histopathology was available. For remaining patients at one and 2 years, clinical and imaging findings were used for disease status. Diagnostic statistics for predicting loco-regional disease up to 1 and 2 years were 93.3%, 92.5%, 90.3%, 94.9%, 92.9%, and 84.9%, 91.9%, 90.3%, 87.2%, and 88.6%, respectively. For the Hopkins score, of 72 patients, 25, 16, and 31 patients had a CR (Score 1, 2), equivocal response (score 3A, 3B), and PR (Score 4, 5) respectively. Indeed, 14 patients of the CR group by HAN-MI-RADS criterion (score 3A) become equivocal in the Hopkins criteria. This was because the Hopkins score 3 category included diffuse uptake more than liver (score 3A, 3B). For Hopkins score, patient-wise sensitivity, specificity, PPV, NPV, and accuracy at 3 months were 95.8%, 28.6%, 82.1%, 66.7%, and 80.7%. Whereas, similar diagnostic statistics for predicting loco-regional disease up to 1 and 2 years were noticed for it and which were 96.5%, 88.9%, 90.3%, 96.0%, and 92.9%. One year and two years of DFI for each HAN-MI-RADS score showed a statistically significant

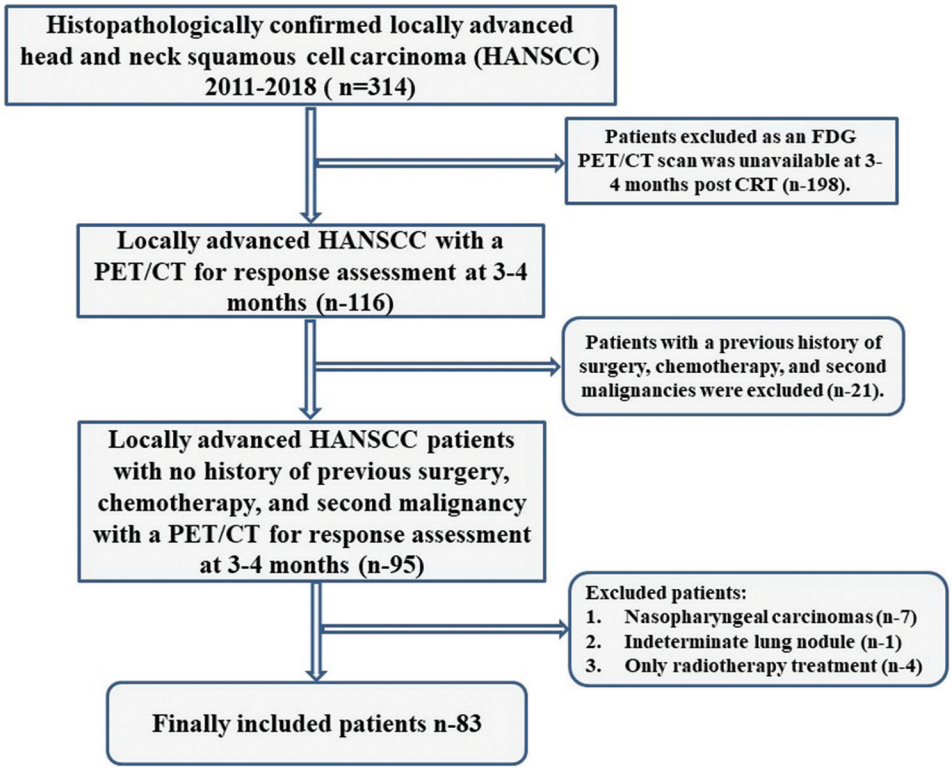

Figure 1: STARD flowchart for patient selection. HNSCC: Head and neck squamous cell carcinoma, FDG: ^{18}F-fluorodeoxyglucose, PET/CT: Positron emission tomography/computed tomography, CRT: Chemo radiotherapy

difference [Table 3]. DFI hazards ratio (HR) for score 3A was near to score 2, while it was near to score 4 for score 3B. Hence, we found that diffuse uptake more than the liver but <2 times, had a lesser risk of harboring disease. One year and two years of OS for each HAN-MI-RADS score showed no statistically significant difference [Table 4]. One year and two years of DFI and OS of each response group (CR, PR, and equivocal) for both HAN-MI-RADS and Hopkins scores were calculated [Tables 5-8]. Statistically, a significant difference was found for DFI but not for OS on intra-comparison for response groups for both. On inter-comparison, by Log-Rank test, the *P* value to compare the DFI of Hopkins and HAN-MI-RADS was 0.5897. It was nonsignificant. The ROC curve analysis showed a statistically significant difference (area under the curve [AUC] difference 0.184, $P = 0.02$, Z statistic 2.327) in the AUC of HAN-MI-RADS (AUC 0.884, 95% confidence interval [CI] 0.785–0.948) and Hopkins (AUC 0.699, 95% CI 0.578–0.803) which suggested better disease outcome predictability of HAN-MI-RADS [Figure 2]. Overall, 2 years recurrence rate was 59.0% (49/83), while 19.3% (16/83) patients developed distant metastasis.

Table 2: Patients characteristics

Characteristics	*n* (%)
Total patients	83
Age (years)	
Mean	55
Range	30–78
Sex	
Male	77 (92.8)
Female	6 (7.2)
Smoker/Gutka	
Yes	74 (89.2)
No	9 (10.8)
Primary site	
Oral cavity	32 (38.6)
Oropharynx	43 (51.8)
Hypopharynx	6 (7.2)
Larynx	1 (1.2)
MUO	1 (1.2)
Grade	
Well differentiated	11 (13.3)
Moderately differentiated	62 (74.7)
Poorly differentiated	9 (10.8)
Undifferentiated	1 (1.2)
T stage	
Tx	6 (7.2)
T1	13 (15.7)
T2	21 (25.3)
T3	42 (50.6)
T4	1 (1.2)
N stage	
N0	9 (10.8)
N1	27 (32.5)
N2a	0
N2b	14 (16.9)
N2c	27 (32.5)
N3	6 (7.2)
Clinical stage	
I	1 (1.2)
II	1 (1.2)
III	15 (18.1)
Iva	58 (69.9)
IVb	8 (9.6)

Discussion

In oncology, the evaluation of a patient's response to initial treatment was crucial for determining the next course of treatment. In clinical practice, RECIST 1.1 was recognized as the gold standard for solid tumors.[10] However, the situation was more difficult in head and neck cancers due to underlying radiation-induced alterations. Recent research has employed a limited number of molecular qualitative response criteria with different degrees of effectiveness.[11] A Deauville score of five points compares tracer activity with mediastinum or Liver.[12] However, it did not account for the type of uptake (diffuse or focal), which is crucial in a postradiation context. Neck imaging reporting and data systems (NI-RADS) was a criterion developed by the American College of Radiology that required validation.[13] The criteria classified the pattern of tracer uptake as mass-like or nonmass-like and the level of tracer uptake as moderate to moderately intense, although neither the mediastinum nor the Liver was included as comparators. This will be essential for a criterion's objectivity and reproducibility. In our criterion, we endeavored to account for all the missing details.

Already, there was a drift of less aggressive management of patients with negative PET/CT post-CRT in HANSCC following the PET-NECK trial.[4] This was a prospective

Table 3: Disease-free interval and hazards ratio for each score

Score (number of patients)	1 year (%)	2 years (%)	*P*	HR	95% CI
1 (*n*=12)	100	91.7	<0.0001	Reference	
2 (*n*=13)	84.6	76.9		2.3616	1.0695–5.2144
3A (*n*=14)	78.6	50		2.4691	1.1082–5.5011
3B (*n*=2)	100	0		6.2154	1.0334–37.3813
4 (*n*=9)	22.2	22.2		7.0666	2.3039–21.6752
5 (*n*=22)	9.09	0		15.752	5.7560–43.1063

HR: Hazard ratio, CI: Confidence interval

Table 4: Overall survival and hazards ratio for each score

Score (number of patients)	1 year (%)	2 years (%)	*P*	HR	95% CI
1 (*n*=12)	100	91.7	0.5926	Reference	
2 (*n*=13)	92.3	84.6		2.3616	1.0695–5.2144
3A (*n*=14)	92.9	85.1		7.0666	2.3039–21.6752
3B (*n*-2)	100	50		15.752	5.7560–43.1063
4 (*n*=9)	100	97.5		2.4691	1.1082–5.5011
5 (*n*=22)	78	66		6.2154	1.0334–37.3813

HR: Hazard ratio, CI: Confidence interval

Table 5: Disease-free interval for each response group of head-and-neck molecular imaging-reporting and data system criteria

Response group (number of patients)	DFI (%)		*P*
	1 year	2 years	
CR (*n*=39)	87.2	71.6	<0.0001
Equivocal (*n*=2)	50	0	
PR (*n*=31)	12.9	8.6	

DFI: Disease-free interval, CR: Complete response, PR: Partial response

Table 6: Disease-free interval for each response group of Hopkin's criteria

Response group (number of patients)	1 year (%)	2 years (%)	*P*
CR (*n*=25)	92	84	<0.0001
Equivocal (*n*=16)	81.3	43.8	
PR (*n*=31)	12.9	8.6	

CR: Complete response, PR: Partial response

Table 7: Overall survival for each response group of head-and-neck molecular imaging-reporting and data system criteria

Response group (number of patients)	1 year (%)	2 years (%)	*P*
CR (*n*=39)	97.4	87	0.1887
Equivocal (*n*=2)	100	50	
PR (*n*=31)	85.3	73.1	

CR: Complete response, PR: Partial response

Table 8: Overall survival for each response group of Hopkin's criteria

Response group (number of patients)	1 year (%)	2 years (%)	*P*
CR (*n*=25)	100	88	0.2283
Equivocal (*n*=16)	93.8	80.4	
PR (*n*=31)	85.3	73.1	

CR: Complete response, PR: Partial response

randomized controlled trial that concluded that PET/CT guided surveillance was noninferior to planned neck dissection, sparing approximately 80% of futile neck dissections with similar survival and more cost-effectiveness. Although, PET/CT response criterion utilized here was qualitative, limited to the neck node,

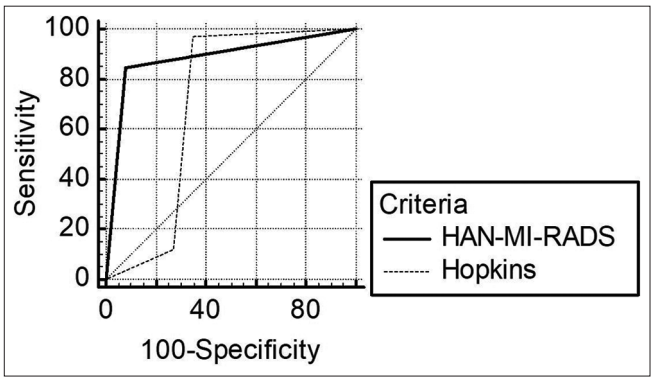

Figure 2: Receiver operating characteristic curves for the two response criteria. HAN-MI-RADS: Head and neck molecular imaging-reporting and data system

and not well elaborated. Normal mucosa in the local disease site shows significant postradiation changes, hence, more clarity on the objective comparator was needed. Hopkins score was the first well-defined criteria for response assessment in this setting.[8] A prospective multicenter "The ECLYPS" study (n = 125) suggested a reliable FDG PET/CT-based surveillance at 12 weeks with sensitivity, specificity, PPV, NPV, and accuracy of 65.2%, 91.2%, 62.5%, 92.15% and 86.4% respectively with a gradual decrease in sensitivity with time.[13] Hence, an additional surveillance scan at 1 year was suggested. Recently, posttreatment FDG-PET/CT Hopkins criteria showed an accuracy of 85% for predicting locoregional recurrence after definitive radiotherapy for oropharyngeal squamous cell carcinoma.[14] In our study, HAN-MI-RADS sensitivity was near similar at 3 months, and 1 year with an accuracy of 88.6% up to 2 years. Hopkins score showed no significant time dependency in our study and a better accuracy of 92.9%.

We used SUVmax measurement rather than purely visual inspection for score interpretation, which may have impacted this differently than the original work done by Marcus *et al*.[8] Further, we used background (contralateral normal structure in the neck), and mediastinal blood pool (arch of the aorta) for scores 1 and 2 allocations, rather than internal jugular vein, However, because the mean liver background was higher than both background and mediastinum, hence this have not made a change in score category. We believed that this newly devised

system will have a better inter-observer agreement. The main difference in HAN-MI-RADS and Hopkins scores was the equivocal response category. In our experience, a diffuse moderate metabolic activity (> liver but ≤2 times of liver) has a low chance of harbouring disease while a severe diffuse metabolic activity (>2 times of liver) needs caution, hence equivocal in nature. Indeed, category 3A was found to have HR close to Category 2. Hence, we found that splitting category 3 into two (3A, 3B) was worth better risk stratifications and planning further strategy of follow-up.

In addition, several shortcomings were observed in our study. Primarily, there was a retrospective character, a small patient population, and heterogeneous main locations. We eliminated nasopharyngeal carcinoma because it behaves differently than other cancers of the head and neck and is related to a different oncovirus.[15] In addition, human papillomavirus has emerged as an important prognostic marker in oropharynx cancers.[16] We did not have access to this information during our data analysis. Only two patients were presented in the ambiguous HAN-MI-RADS group (Score 3B), which was too small to be statistically meaningful and may have impaired the overall picture. The OS HR was greatest for score 3B [Table 4], which we felt was incorrect due to the limited sample size. In this study, the majority of patients belonged to stages T3 and N2, hence additional research is required to determine the applicability of these results to all stages. In addition, we evaluated the data per patient, and diagnostic statistics for T and N separately require additional large-scale research. Not only, HPE was not accessible in all instances, but it was also impractical.

Conclusions

A five points HAN-MI-RADS criterion was found to be promising for response assessment with 88.6% diagnostic accuracy for predicting loco-regional disease recurrence up to 2 years. Comparative analysis showed less equivocal results and statistically significant higher AUC than Hopkins. Further, prospective studies analysis with larger homogeneous patients will provide clinical validity.

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Conflicts of interest

There are no conflicts of interest.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209-49.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016;66:7-30.
3. Goel R, Moore W, Sumer B, Khan S, Sher D, Subramaniam RM. Clinical practice in PET/CT for the management of head and neck squamous cell cancer. AJR Am J Roentgenol 2017;209:289-303.
4. Mehanna H, Wong WL, McConkey CC, Rahman JK, Robinson M, Hartley AG, *et al*. PET-CT surveillance versus neck dissection in advanced head and neck cancer. N Engl J Med 2016;374:1444-54.
5. Werner RA, Bundschuh RA, Bundschuh L, Javadi MS, Higuchi T, Weich A, *et al*. Molecular imaging reporting and data systems (MI-RADS): A generalizable framework for targeted radiotracers with theranostic implications. Ann Nucl Med 2018;32:512-22.
6. Gupta T, Master Z, Kannan S, Agarwal JP, Ghsoh-Laskar S, Rangarajan V, *et al*. Diagnostic performance of post-treatment FDG PET or FDG PET/CT imaging in head and neck cancer: A systematic review and meta-analysis. Eur J Nucl Med Mol Imaging 2011;38:2083-95.
7. Boellaard R, Delgado-Bolton R, Oyen WJ, Giammarile F, Tatsch K, Eschner W, *et al*. FDG PET/CT: EANM procedure guidelines for tumour imaging: Version 2.0. Eur J Nucl Med Mol Imaging 2015;42:328-54.
8. Marcus C, Ciarallo A, Tahari AK, Mena E, Koch W, Wahl RL, *et al*. Head and neck PET/CT: Therapy response interpretation criteria (Hopkins Criteria)-interreader reliability, accuracy, and survival outcomes. J Nucl Med 2014;55:1411-6.
9. Van den Wyngaert T, Helsen N, Carp L, Hakim S, Martens MJ, Hutsebaut I, *et al*. Fluorodeoxyglucose-positron emission tomography/computed tomography after concurrent chemoradiotherapy in locally advanced head-and-neck squamous cell cancer: The ECLYPS study. J Clin Oncol 2017;35:3458-64.
10. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, *et al*. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). Eur J Cancer 2009;45:228-47.
11. Zhong J, Sundersingh M, Dyker K, Currie S, Vaidyanathan S, Prestwich R, *et al*. Post-treatment FDG PET-CT in head and neck carcinoma: Comparative analysis of 4 qualitative interpretative criteria in a large patient cohort. Sci Rep 2020;10:4086.
12. Banks KP, Peacock JG, Gusman M, Clemenshaw MN. It's about quality, not quantity: Qualitative FDG PET/CT criteria for therapy response assessment in clinical practice. AJR Am J Roentgenol 2020;215:313-24.
13. Aiken AH, Rath TJ, Anzai Y, Branstetter BF, Hoang JK, Wiggins RH, *et al*. ACR neck imaging reporting and data systems (NI-RADS): A white paper of the ACR NI-RADS committee. J Am Coll Radiol 2018;15:1097-108.
14. Miller JA, Moradi F, Sundaram V, Liang R, Zhang C, Nguyen NK, *et al*. Posttreatment FDG-PET/CT Hopkins criteria predict locoregional recurrence after definitive radiotherapy for oropharyngeal squamous cell carcinoma. Head Neck 2022;44:2491-504.
15. Chen YP, Chan AT, Le QT, Blanchard P, Sun Y, Ma J. Nasopharyngeal carcinoma. Lancet 2019;394:64-80.
16. Urban R, Godoy T, Olson R, Wu J, Berthelet E, Tran E, *et al*. FDG-PET/CT scan assessment of response 12 weeks post radical radiotherapy in oropharynx head and neck cancer: The impact of p16 status. Radiother Oncol 2020;148:14-20.