

# Therapy Response Assessment and Patient Outcomes in Head and Neck Squamous Cell Carcinoma: FDG PET Hopkins Criteria Versus Residual Neck Node Size and Morphologic Features

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**OBJECTIVE.** This study investigates the prognostic value of <sup>18</sup>F-FDG PET/CT qualitative therapy assessment (Hopkins criteria) in patients with head and neck squamous cell carcinomas (HNSCCs) with residual neck nodes after definitive chemoradiation therapy and compares the Hopkins criteria with anatomic nodal size and morphologic features for prediction of survival outcomes.

**MATERIALS AND METHODS.** A total of 72 patients with HNSCC, with negative primary tumor and positive residual neck nodes (CT criteria > 1 cm short-axis diameter) after the completion of definitive chemoradiation therapy, were included. PET/CT was performed 6–24 weeks after completion of treatment. FDG uptake in residual nodes on PET/CT was interpreted using a structured qualitative 5-point scale (Hopkins criteria). The 5-point scale was dichotomized to negative (scores 1, 2, and 3) or positive (scores 4 and 5) results. Cystic or necrotic nodes were defined as those with central low attenuation with a relatively hyperdense capsule. Kaplan-Meier curve and Cox regression analysis were performed.

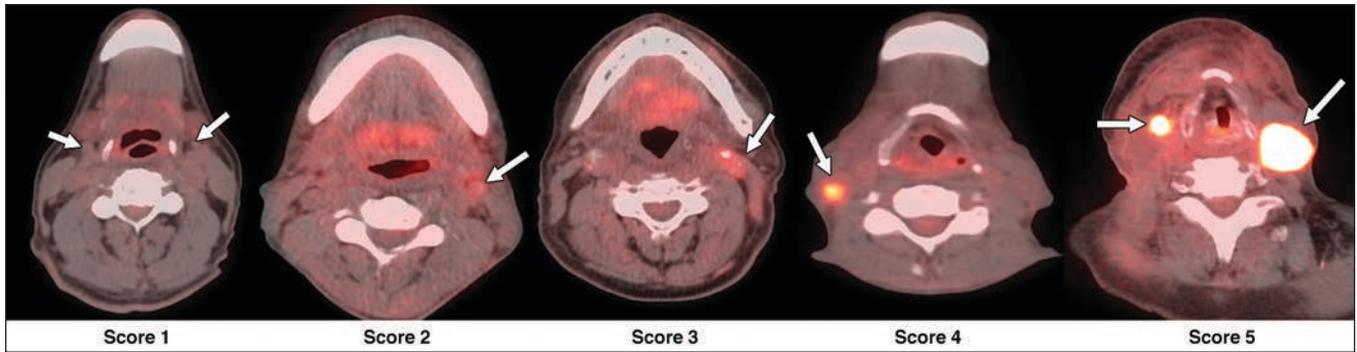
**RESULTS.** On the basis of the Hopkins criteria, 10 (13.9%) patients had positive findings and 62 (86.1%) had negative findings for residual nodal disease. According to CT interpretation, 25 patients (34.7%) had residual cervical lymph nodes greater than or equal to 1.5 cm in diameter, and 41 (56.9%) patients had cystic or necrotic nodes. Patients were followed for a median of 27 months after posttherapy PET/CT. There was a statistically significant difference in overall survival (OS) (hazard ratio, 7.06;  $p < 0.001$ ) and progression-free survival (PFS) (hazard ratio, 6.18;  $p < 0.001$ ) between patients with negative versus positive residual FDG nodal uptake. There was no statistically significant difference in OS and PFS in patients categorized on the basis of nodal size or morphologic features.

**CONCLUSION.** PET-based structured qualitative therapy assessment (Hopkins criteria) can predict survival outcomes of patients with HNSCC with residual neck nodes after definitive chemoradiotherapy.

It has been estimated that there will be 61,760 new cases of cancer of the oral cavity, pharynx, and larynx in the United States in 2016, with 13,190 deaths during the same period [1]. The vast majority of head and neck cancers are squamous cell carcinomas (HNSCC) [2, 3]. Staging is the most important prognostic factor for HNSCC, and 5-year survival rates can be as low as 20–30% for late-stage disease [4]. In spite of surveillance strategies, normal-appearing metastatic nodes remain underevaluated, with recurrence rates as high as 50% even with early diagnosis and definitive treatment [5]. Diagnostic imaging modalities, such as CT and MRI, are the mainstay of staging and monitoring for

disease recurrence, exploiting the size and morphologic characteristics of suspected lesions [6].

Over the past decade, functional imaging with <sup>18</sup>F-FDG PET/CT has been widely suggested to improve the staging and therapy assessment of patients with HNSCC [7, 8]. National Comprehensive Center Network clinical practice guidelines [6] recommend PET/CT in initial staging of some head and neck cancers with stages III and IV. They also consider the use of PET/CT as an option to assess the response and extent of the disease after chemoradiation therapy [6]. Earlier detection of recurrent disease by PET/CT may alter the patient's management and overall outcomes [8, 9]. A previous prospective study showed that patients



**Fig. 1**—Axial fused PET/CT images show Hopkins head and neck therapy assessment criteria scores of 1–5. Scores of 1 (complete metabolic response), 2 (likely complete metabolic response), and 3 (likely postradiation inflammation) were considered negative for residual tumor. Scores of 4 (likely residual tumor) or 5 (residual tumor) were considered positive for residual tumor. Arrows point to where original nodal metastasis was before treatment and degree of FDG uptake in posttherapy scans.

with HNSCC with residual CT-based nodal abnormalities after definitive radiation therapy could be spared neck dissection, if the therapy assessment by PET was negative [10]. Although a number of studies suggested that FDG PET/CT provides better management implications compared with recommended anatomic imaging in therapy assessment of HNSCC [9–11], there still remains controversy as to whether these changes affect the overall survival (OS) outcome in patients.

The objective of this study is to compare the prognostic effectiveness of FDG PET/CT qualitative therapy assessment for residual neck nodes (> 1 cm short-axis diameter) to anatomic size and morphologic features on survival outcome in patients with HNSCC, after definitive radiotherapy with or without chemotherapy.

**Materials and Methods**

*Patient Selection*

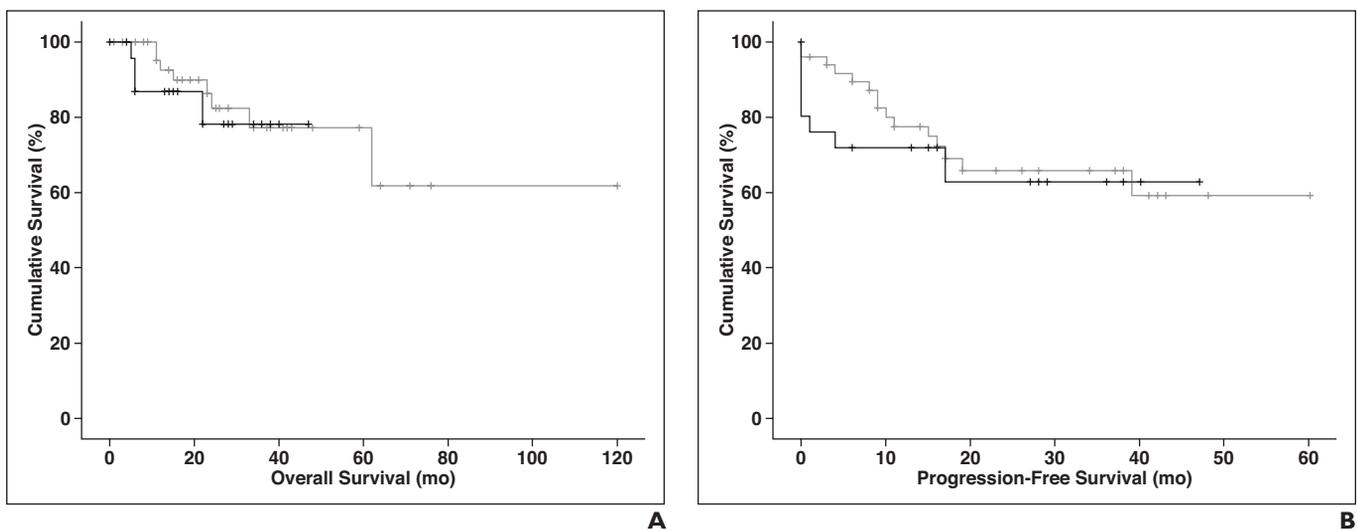
This was a retrospective study performed under a waiver of informed consent approved by the Johns Hopkins Hospital institutional review board. The guidelines of the HIPAA were followed. Patients with histopathology-confirmed primary HNSCC who received evaluation and primary treatment at Johns Hopkins Hospital between 2000 and 2012 were eligible for the study. Seventy-two patients who met the following inclusion criteria were included in the study: FDG PET/CT study performed within 6–24 weeks after definitive treatment with radiation therapy with or without chemotherapy, residual cervical lymph node greater than or equal to 1.0 cm short-axis diameter diagnosed by anatomic imaging at the same time point, and no evidence of residual primary tumor. The posttreatment PET/CT studies were ordered at the treating clinician’s discretion as part of therapy assessment.

*Image Analysis*

FDG PET/CT studies were electronically retrieved on a viewing platform (MIM Vista, version 6.3, Mim Vista Software) and were interpreted by three nuclear medicine physicians (readers 1, 2, and 3). Reader 1 is a current clinical PET/CT fellow with nuclear medicine board certification, reader 2 is a current nuclear medicine resident who has completed radiology residency and neuroradiology fellowship, and reader 3 is an associate professor in radiology who has completed radiology and nuclear medicine board certification with neuroradiology and nuclear radiology fellowships. The scans were analyzed independently by readers 1 and 2. Discordant readings between readers 1 and 2 were resolved by reader 3 independently.

*Residual Neck Node: Anatomic Size*

Each study was analyzed for the size of the largest residual cervical lymph node, which was doc-



**Fig. 2**—Survival differences between patients according to node size. **A** and **B**, Kaplan-Meier plots show overall survival (**A**) and progression-free survival (**B**) of patients with residual node  $\geq 1.5$  cm (black lines) and  $< 1.5$  cm (gray lines) according to CT findings (log-rank Mantel-Cox test,  $p = 0.60$  for overall survival and  $p = 0.54$  for progression-free survival).

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## PET Hopkins Criteria Versus Residual Neck Node Size

umented in the CT interpretation and based on measurements along the shortest axis. Only nodes greater than or equal to 1.0 cm were included in the study (range, 1.0–5.4 cm; mean [ $\pm$  SD], 1.6  $\pm$  0.88 cm). The short-axis diameter of 1.5 cm was used to stratify the patients into two subgroups by size cri-

teria for statistical analysis, because a short-axis cut point of 1.5 cm is used for clinical significance for suspected lymph node involvement.

### Residual Neck Node: Morphologic Appearance

Each study was interpreted for the presence of cystic or necrotic residual cervical lymph nodes. The presence of such lymph nodes was determined by the radiology interpretation of a separate contrast-enhanced CT (CECT) scan of the neck in 52 patients (72.2%), performed either at the time of or within 3 months of the posttherapy FDG PET/CT, and the unenhanced attenuation correction CT evaluation performed as part of the posttherapy FDG PET/CT in 20 patients (27.8%). On the unenhanced attenuation correction CT evaluations, cystic or necrotic nodes were defined as round or ovoid masses with central low attenuation and a relatively hyperdense capsule.

### Residual Neck Node: FDG Uptake

Each study was scored using a qualitative 5-point scale, the Head and Neck PET/CT Interpretation Criteria (i.e., the Hopkins criteria) [12]. The uptake in the internal jugular vein (IJV) was used as background blood pool for reference. Focal FDG uptake in a residual cervical lymph node less than that of the IJV was scored as 1 (i.e., consistent with complete metabolic response). Focal FDG uptake in a residual cervical lymph node greater than that of the IJV but less than that of the liver was scored as 2 (i.e., likely complete metabolic response). Diffuse FDG uptake in a residual cervical lymph node greater than that of the IJV or the liver was scored as 3 (i.e., likely inflammatory changes). Focal FDG uptake in a residual cervical lymph node greater than that of the liver was scored as 4 (i.e., likely residual tumor). Focal and intense FDG uptake in a residual cervical lymph node greater than that of the liver was scored as 5 (i.e., consistent with residual tumor). On the basis of the qualitative 5-point scale, the studies were dichotomized as either positive or negative for recurrent tumor. Scores of 4 or 5, which most likely represent residual tumor involvement, were considered positive. Scores of 1, 2, or 3, which most likely represent complete metabolic response or posttherapy inflammation, were considered negative (Fig. 1).

### Statistical Analyses

Descriptive values are presented as mean ( $\pm$  SD) or median (25th percentile through 75th percentile range) if the data are not in normal distribution. Categorical variables are presented as frequency (percentage). The time to OS was measured from the date of the therapy assessment PET/CT scan until the date of death or last fol-

low-up examination. The time of death was determined using a web-based mortality registry and electronic medical records available at our institution. Survival data for patients who were alive were censored at the last date of follow-up at our institution. Progression-free survival (PFS) was determined from the date of the therapy assessment PET/CT until the date of progression within the 5-year follow-up period. Patients were subgrouped according to the PET result (negative or positive), presence or absence of cystic node, and nodal size (mean cut point, 1.6 cm). Kaplan-Meier curves were generated in each subgroup. Univariate and multivariate Cox regression analyses were performed using death or progression as the end-points, and the hazard ratio (HR) and 95% CI were reported. The statistical significance level was set at  $p < 0.05$ . Statistical analysis was performed using SPSS Statistics (version 22.0, IBM).

## Results

### Patient Characteristics

Seventy-two patients (65 men and seven women) with a mean age of 58  $\pm$  8.5 years were included in the study. The primary site of tumor was classified as oropharynx (68.1%), oral cavity (4.2%), larynx (12.5%), and other sites (15.3%). All patients were followed until death or the last date of visit at our institutions. The median follow-up duration of the patients was 27 months (range, 0–108 months; four patients were censored less than 6 months after the scans) after completion of posttherapy assessment PET/CT. For 24 patients with disease progression, progression was defined histologically after biopsy in eight patients (33.3%), on the basis of imaging findings in 13 patients (54.2%), and on clinical determination in three patients (12.5%). The patient demographics are summarized in Table 1.

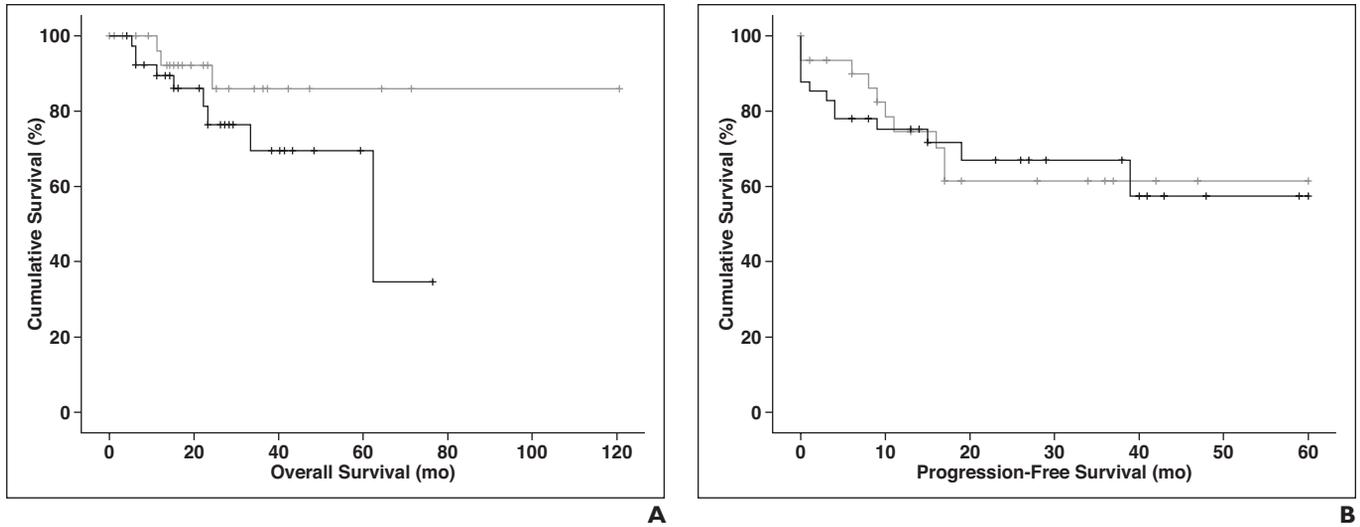
### Time Interval of Posttherapy PET/CT and Contrast-Enhanced CT

All 72 PET/CT studies were performed between 6 and 24 weeks after treatment. The average interval between the date of completion of treatment and the posttreatment FDG PET/CT study was 12.6 weeks. Of the 72 studies, 15 (20.8%) were performed between 6 and 7 weeks, 23 (31.9%) were performed between 8 and 12 weeks, and 34 (47.2%) were performed between 13 and 24 weeks after completion of treatment. CECT scans of the neck were performed for 52 (72.2%) patients at a median of 12 weeks (range, 6–17 weeks) after completion of treatment. Unenhanced attenuation correction CT scans were per-

**TABLE 1: Demographics and Clinical Characteristics of the Study Population**

| Characteristic                       | Value (n = 72)   |
|--------------------------------------|------------------|
| Age (y), mean $\pm$ SD               | 57.96 $\pm$ 8.53 |
| Sex                                  |                  |
| Male                                 | 65 (90.3)        |
| Female                               | 7 (9.7)          |
| Primary tumor site                   |                  |
| Oropharynx                           | 49 (68.1)        |
| Larynx                               | 9 (12.5)         |
| Oral cavity                          | 3 (4.2)          |
| Others                               | 11 (15.3)        |
| Tumor stage                          |                  |
| I and II                             | 33 (45.8)        |
| III and IV                           | 38 (52.8)        |
| Unknown                              | 1 (1.4)          |
| Treatment                            |                  |
| Chemotherapy                         | 67 (93.1)        |
| Radiation therapy                    | 72 (100)         |
| Human papillomavirus positive status | 49 (68.1)        |
| Alcohol                              |                  |
| No                                   | 25 (34.7)        |
| Yes                                  | 45 (62.5)        |
| Unknown                              | 2 (2.8)          |
| Smoking                              |                  |
| No                                   | 23 (31.9)        |
| Yes                                  | 49 (68.1)        |
| Clinically suspicious                |                  |
| No                                   | 69 (95.8)        |
| Yes                                  | 3 (4.2)          |
| Contrast-enhanced CT performed       |                  |
| Yes                                  | 52 (72.2)        |
| No                                   | 20 (27.8)        |
| Cystic node                          |                  |
| Yes                                  | 41 (56.9)        |
| No                                   | 31 (43.1)        |
| Size of node (cm), mean $\pm$ SD     | 1.60 $\pm$ 0.88  |

Note—Except where noted otherwise, data are number (%) of patients. Percentages do not total 100% in all categories because of rounding.



**Fig. 3**—Survival differences according to nodes' morphologic features. **A** and **B**, Kaplan-Meier plots show overall survival (**A**) and progression-free survival (**B**) in patients who had cystic or necrotic residual nodes (*black lines*) versus solid residual nodes (*gray lines*) according to CT findings (log-rank Mantel-Cox test,  $p = 0.13$  for overall survival and  $p = 0.90$  for progression-free survival).

formed for 20 patients as a component of the PET/CT examination.

**PET/CT and Contrast-Enhanced CT Scan Interpretations**

On the basis of the 5-point Hopkins scores, 10 (13.9%) of 72 patients were categorized as positive and 62 (86.1%) were categorized as negative for residual tumor. According to the CT findings, 47 patients (65.3%) had residual cervical lymph nodes smaller than 1.5 cm in diameter, whereas 25 (34.7%) had residual cervical lymph nodes greater than or equal to 1.5 cm. Cystic or necrotic nodes were identified in 41 (56.9%) of patients.

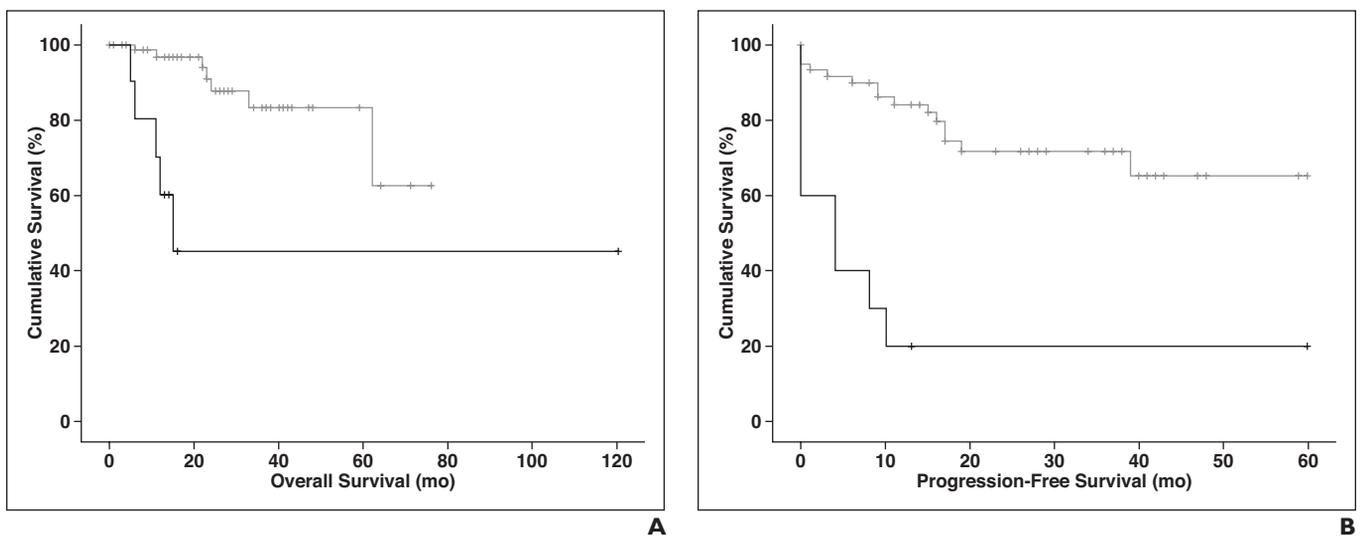
**Nodal Size Criteria and Survival Outcomes**

The median survival duration of the 25 patients with residual nodes greater than or equal to 1.5 cm was 15 months (range, 0–47 months), and four patients within this group died. In contrast, in the 47 patients with residual nodes smaller than 1.5 cm, the median survival duration was 23 months (range, 1–120 months), and eight patients in this group died. The Kaplan-Meier survival analysis did not show a statistically significant difference in the OS (log-rank Mantel-Cox test,  $p = 0.60$ ) and PFS (log-rank Mantel-Cox test,  $p = 0.54$ ) between patients with nodal size greater than or equal to 1.5 cm

and smaller than 1.5 cm (HR, 1.39; 95% CI, 4.04–4.75) (Fig. 2).

**Nodal Morphologic Features and Survival Outcomes**

The median survival duration of the 41 patients with cystic nodes was 16 months (range, 4–76 months), and nine patients in this group died. In contrast, for the 31 patients without cystic nodes, the median survival duration was 23 months (range, 0–120 months), and three patients in this group died. The Kaplan-Meier survival analysis did not show a statistically significant difference in the OS (log-rank Mantel-Cox test,  $p = 0.13$ ) and PFS (log-rank Mantel-Cox



**Fig. 4**—Survival differences according to 5-point posttherapy interpretation criteria. **A** and **B**, Kaplan-Meier plots show overall survival (**A**) and progression-free survival (**B**) in patients who were categorized as positive (*black lines*) or negative (*gray lines*) by 5-point posttherapy interpretation criteria (log-rank Mantel-Cox test,  $p < 0.001$  for overall survival and  $p < 0.001$  for progression-free survival).

## PET Hopkins Criteria Versus Residual Neck Node Size

**TABLE 2: Univariate Cox Regression Analysis**

| Variable             | Overall Survival      |          | Progression-Free Survival |          |
|----------------------|-----------------------|----------|---------------------------|----------|
|                      | Hazard Ratio (95% CI) | <i>p</i> | Hazard Ratio (95% CI)     | <i>p</i> |
| PET/CT               | 7.06 (2.09–23.78)     | <0.001   | 6.18 (2.53–15.05)         | <0.001   |
| Node size            | 1.39 (4.04–4.75)      | 0.60     | 1.30 (0.55–3.09)          | 0.54     |
| Cystic node          | 2.65 (0.71–9.84)      | 0.13     | 1.05 (0.46–2.40)          | 0.90     |
| Age                  | 1.06 (0.99–1.14)      | 0.10     | 1.05 (1.01–1.10)          | 0.02     |
| Sex                  | 0.30 (0.079–1.12)     | 0.07     | 1.10 (0.26–4.07)          | 0.89     |
| Human papillomavirus | 0.19 (0.06–0.65)      | 0.008    | 0.33 (0.14–0.75)          | 0.008    |
| Smoking              | 7.05 (0.90–55.12)     | 0.06     | 6.37 (1.49–27.23)         | 0.01     |
| Alcohol              | 0.70 (0.22–2.24)      | 0.54     | 0.62 (0.26–1.47)          | 0.28     |
| Primary site         | 1.16 (0.75–1.80)      | 0.49     | 1.14 (0.83–1.58)          | 0.42     |
| Disease stage        | 1.27 (0.54–2.97)      | 0.58     | 0.91 (0.48–1.73)          | 0.77     |

test,  $p = 0.90$ ) between patients with cystic nodes versus those without cystic nodes (Fig. 3).

### Hopkins Criteria Score, Survival Outcomes, and Effect on Management

The median survival duration of the 10 PET/CT-positive patients was 13.5 months (range, 5–120 months), and five patients in this group died. In the negative PET/CT group, the median survival duration was 23 months (range, 0–76 months), and seven patients died. The Kaplan-Meier survival analysis showed a statistically significant difference in the OS between patients who were classified as negative for residual tumor by the 5-point scale interpretation, compared with those who were scored as positive for residual tumor (log-rank Mantel-Cox test,  $p < 0.001$ ; HR, 7.06; 95% CI, 2.09–23.78). For PFS, the Kaplan-Meier survival analysis also showed a statistically significant difference between patients who were scored as positive for residual tumor compared with those who were scored as negative for residual tumor (log-rank Mantel-Cox test,  $p < 0.001$ ; HR, 6.18; 95% CI, 2.53–15.05) (Fig. 4). Subgroup analysis according to the nodal size shows that PET/CT could predict OS and PFS both in patients with nodes larger than or equal to 1.5 cm (OS log-rank test,  $p = 0.035$ ; PFS log-rank test,  $p = 0.003$ ) and smaller than 1.5 cm (OS log-rank test,  $p = 0.007$ ; PFS log-rank test,  $p = 0.002$ ).

Of patients with positive PET/CT findings, 60% (6/10) underwent surgery (or direct laryngoscopy) with or without neck dissection and had biopsy specimens obtained for confirmation (five true-positive biopsies), 20% (2/10) started taking systemic chemotherapy, and 20% (2/10) were followed up closely by a clinician who suspected that the FDG

uptake was likely inflammatory (one patient became negative). Most patients (71%; 44/62) with negative PET/CT findings were followed up within 2–3 months, clinically or by further imaging if indicated (one had disease progression and one had a second primary lung tumor identified). Confirmatory biopsy was obtained via direct laryngoscopy or neck dissection for 29% of patients (18/62) and was negative for 16 patients, showing fibrotic nodes or radiation atypia.

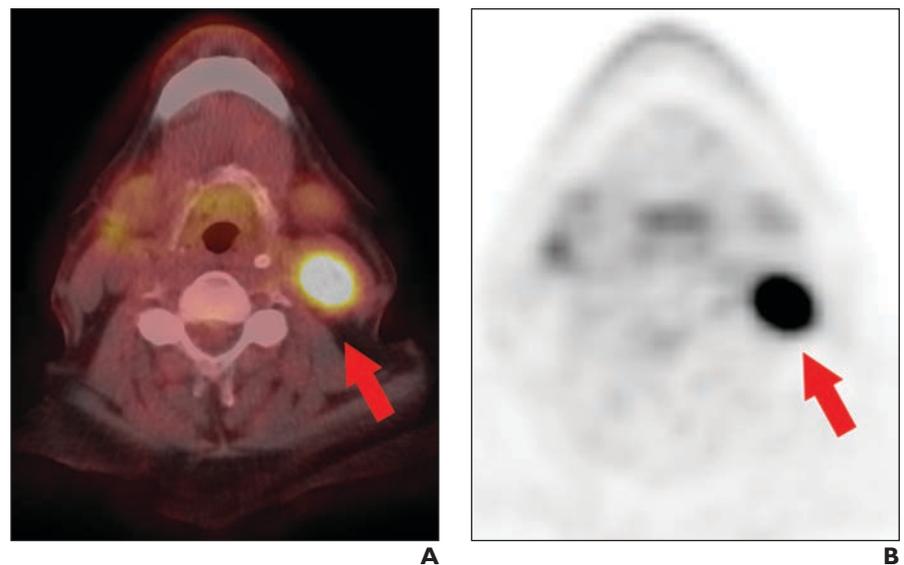
### Cox Regression Analysis and Patient Outcome

Univariate Cox regression analyses, including age, sex, human papillomavirus sta-

tus, smoking, alcohol, primary tumor site, disease stage, node size ( $< 1.5$  or  $\geq 1.5$  cm), cystic node, and PET/CT results, were performed for evaluation of outcome (Table 2). Multivariate Cox regression analysis showed that a positive PET/CT result could significantly predict risk of death (HR, 9.11; 95% CI, 1.61–51.63;  $p = 0.011$ ) independently of potential confounders, including age, sex, human papillomavirus status, and smoking. Positive PET/CT was also associated with PFS within 5 years (HR, 6.73; 95% CI, 2.09–21.70;  $p = 0.001$ ) after adjustment for age, sex, human papillomavirus status, and smoking.

### Discussion

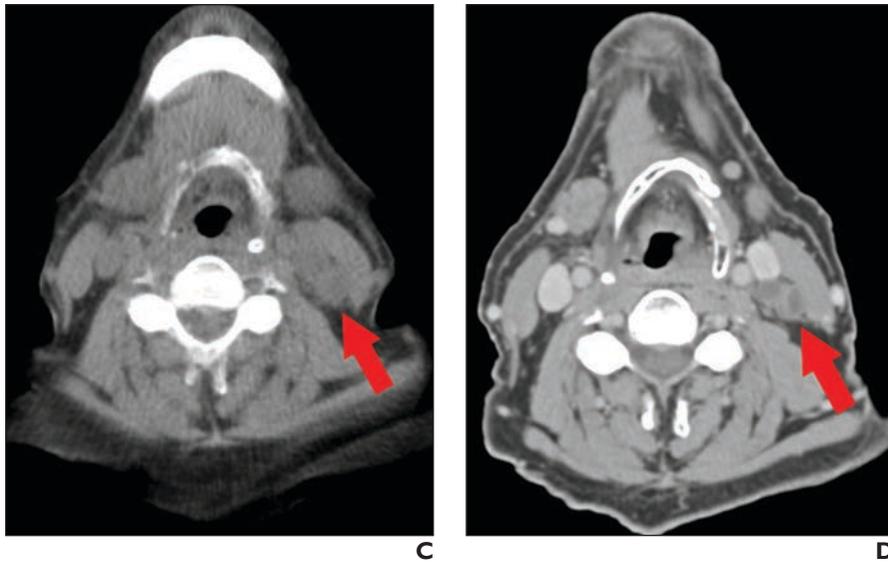
This study investigated the prognostic value of FDG PET/CT qualitative therapy assessment criteria (i.e., the Hopkins criteria) in patients with HNSCC who have residual nodes greater than 1 cm in short-axis diameter, after definitive treatment with radiation therapy with or without chemotherapy. Our study showed that interpretation using the Hopkins criteria for posttherapy response assessment predicts OS and PFS in patients with residual lymph nodes greater than 1 cm. Patients with residual cervical nodes that were negative by the Hopkins criteria had seven times greater OS, compared with those who had positive nodes, and were six times less likely to have progression of disease. This study also showed that size cri-



**Fig. 5—70-year-old man.**

**A–D,** Axial PET/CT and contrast-enhanced CT (CECT) images were obtained. There is focally increased FDG activity localizing to necrotic lymph nodes (arrows) on PET/CT fusion image (A) and PET image (B). CT image for attenuation correction (C) shows hypodense left cervical lymph nodes (arrow). CECT image (D) shows enhancing periphery with central lucency (arrow). These lesions are scored as 5 by Hopkins criteria, with focal uptake that is intense and greater than liver. Patient died 16 months after images were obtained.

(Fig. 5 continues on next page)



**Fig. 5 (continued)**—70-year-old man.

**A–D**, Axial PET/CT and contrast-enhanced CT (CECT) images were obtained. There is focally increased FDG activity localizing to necrotic lymph nodes (*arrows*) on PET/CT fusion image (**A**) and PET image (**B**). CT image for attenuation correction (**C**) shows hypodense left cervical lymph nodes (*arrow*). CECT image (**D**) shows enhancing periphery with central lucency (*arrow*). These lesions are scored as 5 by Hopkins criteria, with focal uptake that is intense and greater than liver. Patient died 16 months after images were obtained.

teria of residual nodes greater than 1.5 cm in the short axis were not associated with increased risk of death or progression of disease. Residual nodes with cystic or necrotic morphologic features on CT examination did not predict OS or PFS (Figs. 5 and 6).

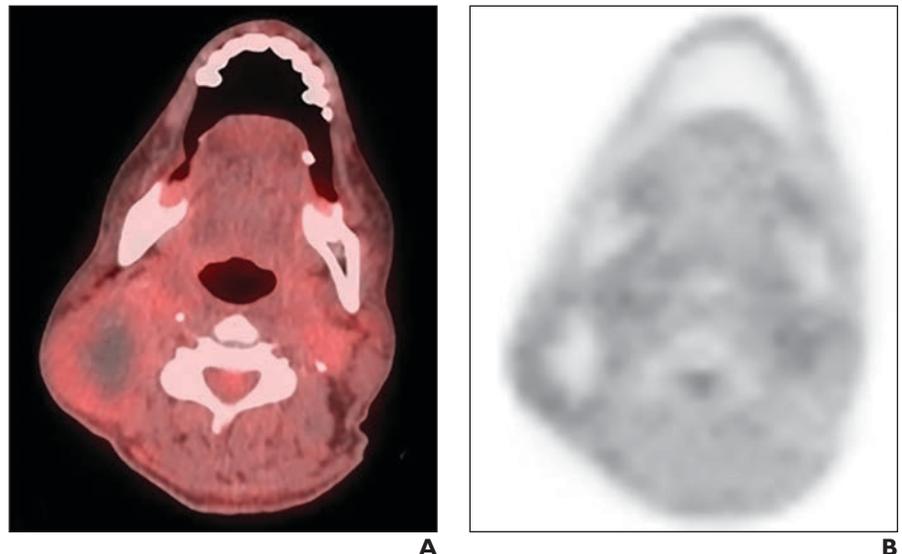
Previous studies have shown the prognostic value of FDG PET/CT in HNSCC after therapy [12–16]. Kim et al. [14] showed that patients with HNSCC treated with postoperative radiation therapy with metabolic tumor volume greater than 41 mL had a 2.4-fold higher recurrence or death rate than did those with a metabolic tumor volume less than or equal to 41 mL. Kikuchi et al. [15] defined an effective response to neoadjuvant chemotherapy as a decrease in standardized uptake value greater than 55.5% and a maximum standardized uptake value less than 3.5 on posttherapy FDG PET/CT scans; these values were associated with a 4.5-fold greater local control rate and 4.9-fold increase in disease-specific survival.

In addition to quantitative parameters, qualitative assessment of FDG PET/CT has been shown to predict outcome. Kao et al. [16] found that qualitative uptake less than that of the surrounding tissue in residual lesions in patients with stages II through IVb HNSCCs treated with radiation therapy was associated with significantly improved 2-year locoregional control, distant control, PFS, and OS. Marcus et al. [12] de-

finer the Hopkins 5-point qualitative therapy response interpretation criteria for head and neck PET/CT in a systematic and reproducible manner to prognosticate HNSCC outcomes on the basis of FDG PET/CT. The criteria have high negative predictive value and substantial interrater reliability. That study also showed a significant difference in OS and PFS between patients with primary HNSCCs who were classified as negative for

residual tumor by the 5-point scale interpretation, compared with those who were scored as positive for residual tumor [12].

Expanding on the findings of Marcus et al. [12], our study substantiates the prognostic value of the Hopkins criteria for residual cervical nodes. Ojiri et al. [17] showed that if residual nodes seen at CT completed 13–64 days after radiotherapy were greater than or equal to 1.5 cm in the largest dimension or had focal low-attenuation defect, this could help predict the likelihood of residual disease in those nodes. Liauw et al. [18] defined a radiographic complete response as the absence of cervical nodes larger than 1.5 cm and no focal lucency; they found that such a complete response had a 94% correlation with neck dissection pathologic findings and that there was no significant difference in 5-year cause-specific survival rates and ultimate neck node control compared with negative postirradiation therapy neck dissection findings. A recent prospective trial by Porceddu et al. [10] evaluated the utility of a policy uniformly omitting neck dissections for patients with node-positive HNSCC with PET-negative CT residual nodal abnormalities. They found that 82% (41/50) of patients with an incomplete response according to CT criteria actually had negative PET findings, were spared a neck dissection, and showed no subsequent nodal failures over time. Essentially, anatomic imaging alone was grossly ineffective in posttherapy evaluation of HNSCC. Our study shows the lack of predictive value for CT size and morphologic criteria while showing a significant correlation with OS

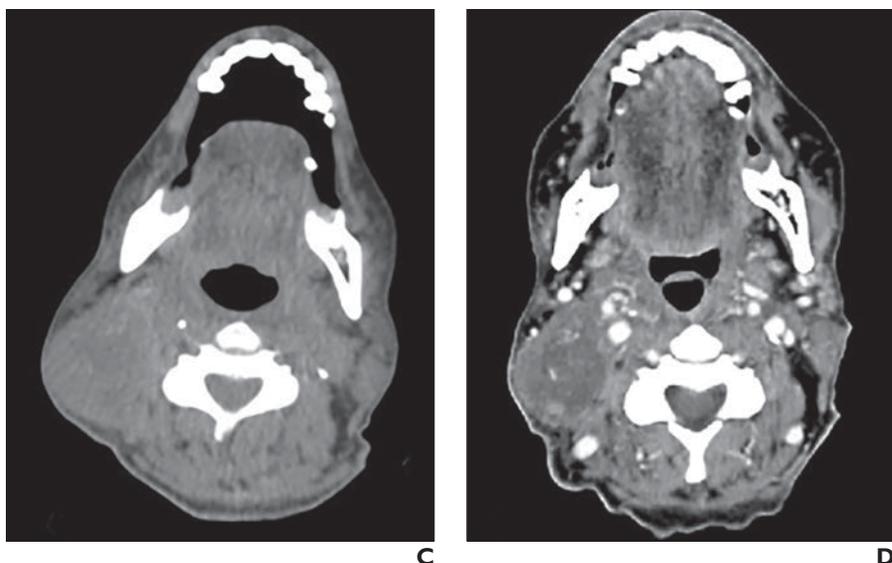


**Fig. 6**—57-year-old woman with residual right stage IIb necrotic node.

**A and B**, Axial PET/CT and contrast-enhanced CT (CECT) images were obtained. There is diffuse FDG activity peripherally on PET/CT fusion image (**A**) and PET image (**B**).

(Fig. 6 continues on next page)

## PET Hopkins Criteria Versus Residual Neck Node Size



**Fig. 6 (continued)**—57-year-old woman with residual right stage IIb necrotic node. **C** and **D**, CT image for attenuation correction (**C**) shows centrally hypodense right cervical lymph node. CECT image (**D**) shows enhancing heterogeneous periphery with central lucency. This lesion is scored as 3 by Hopkins criteria, with diffuse uptake that is less than that of liver.

and PFS based on qualitative therapy assessment criteria (Hopkins criteria).

In assessing the response of HNSCC to therapy, posttreatment changes seen on FDG PET/CT are time dependent. To reduce radiation-induced inflammatory FDG uptake, it has been recommended that the first FDG PET/CT examination to assess therapy response be performed at approximately 12 weeks or more after the completion of radiation therapy [8]. In the current study, about one-fifth of therapy assessment scans were performed less than 8 weeks and half were performed less than 12 weeks after the completion of treatment; this fact is explained by the retrospective enrollment of patients over a long time and by the evolution of clinical practice over time. Other limitations of this study include unavoidable biases in determining clinical suspicion, changes in management due to the retrospective nature of the study, and the use of public registry and electronic medical records to determine the survival endpoints. These limitations may lead to the possibility of confounding errors, lag time effect, and loss of accurate survival data. In addition, only 72.2% of the patients underwent CECT scans to verify size and morphologic features of the residual nodes. The remaining scans were analyzed from unenhanced attenuation correction CT scans obtained during PET/CT acquisition.

### Conclusion

FDG PET/CT qualitative therapy assessment criteria (Hopkins criteria) predicts the OS and PFS outcomes in patients with

HNSCC with residual nodes after radiotherapy, with or without chemotherapy. The size (nodes  $\geq 1.5$  cm in shortest axis) and morphologic (presence of cystic or necrotic nodes) criteria of anatomic imaging do not predict OS and PFS outcomes in the same patients.

### References

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