Original Article

NIRADS-based case assessment of post-treatment head and neck cancer and its clinical correlation: A validation study

ABSTRACT

Introduction: The neck imaging reporting and data system (NIRADS) lexicon is aimed at surveillance of head and neck cancer during post-treatment follow-up using either a CECT or PET-CT scan. These recommendations standardize management, reduce interobserver variability, and standardizes scientific communication.

Objectives: The primary aim of this study was to validate the correlation between the NI-RADS category and disease status on clinical follow-up and histopathological analysis. The other objective was to assess the status of primary as well as nodal site at least 8 to 12 weeks after definitive treatment on first post-treatment imaging as per NI-RADS.

Materials and Methods: We did a retrospective review of maintained a database of patients treated with curative intent radiotherapy or chemoradiotherapy. The diagnostic accuracy of NIRADS was compared with the clinical follow-up and histopathological findings. Data was recorded using the NIRADS lexicon and analyzed using SPSS 25.

Result: In our study, 37 cases were followed with CECT, whereas 111 were followed with PET-CT. We observed no significant difference between CECT and PET-CT for predicting recurrence in any of the NIRADS category. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of NIRADS to predict recurrence for the primary site is 61.54%, 75.21%, 34.8%, 90.1%, and 72.79%, respectively, whereas for the neck, it is 69.54%, 75.41%, 37.5%, 92%, and 74.32%.

Conclusion: NIRADS score is strongly associated with positive disease in as Neck as well as primary. Increased use of NIRADS will lead to a uniform reporting system and improved patient outcome.

Keywords: Chemoradiotherapy, computed tomography scan, head and neck cancer recurrence NIRADS, positron emission tomography

INTRODUCTION

Head and neck cancers form a complex group, and their management ranges from surgery to chemoradiation. Post-treatment follow-up is important to timely diagnose recurrence. Deep recurrences are difficult to diagnose merely by clinical examination, wherein comes the role of post-treatment imaging. The American College of Radiology (ACR) issued a white paper on Neck Imaging Reporting and Data Systems (NI-RADS) in 2018,[1] which intended to reduce ambiguity in radiology reports, improve communication between radiologists and referring clinicians, and provide a consensus regarding the management of suspicious categories.

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NI-RADS is aimed at surveillance using either a contrast-enhanced computed tomography (CECT) scan or an 18 F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET-CT) scan, and provides a standardized lexicon and four-tier classification for consistent reporting of post-treatment head and neck cancer scans. The lexicon provides an objective stratification for subjective interpretation along with management recommendations.[1-5]

In high-volume cancer centers, the need for a standardized reporting system is of utmost significance. This type of reporting system in practice will help clinicians make better decision-making and make way for improved patient outcomes.

OBJECTIVES

The primary aim of this study was to validate the correlation between the NI-RADS category and disease status on clinical follow-up/histopathological analysis. The other objective was to assess the status of the primary as well as nodal sites at least 8 to 12 weeks after definitive treatment on first post-treatment imaging as per NI-RADS.

MATERIALS AND METHODS

General study details

The study was conducted from August 3, 2022 till March 21, 2023 in the Department of Surgical Oncology (head and neck divisional group) in collaboration with the Department of Radiotherapy, Radiodiagnosis, and Nuclear Medicine, at a tertiary care cancer hospital. We strictly followed the ethical guidelines established by the Declaration of Helsinki and other guidelines such as the Good Clinical Practice Guidelines and those established by the Indian Council of Medical Research (ICMR). The study was conducted after clearance from the Institutional review committee of Homi Bhabha Cancer Hospital with reference no 11000557 approved on 3rd August 2022. A waiver of the requirement to obtain informed consent was obtained from the Ethics Committee. Given the retrospective nature of the study, it was not registered in a publicly accessible clinical trials registry. No funding was utilized for the study.

Participants

All diagnosed cases of head and neck squamous cell carcinoma (HNSCC), treated with curative intent by radiation therapy (RT)/concurrent chemo radiotherapy (CTRT), and who underwent post-treatment CECT or FDG PET-CT between January 1, 2020 and December 31, 2021 were included in this study. All patients with palliative intent of treatment, non-squamous histology, and patients who were not on proper follow-up or had inadequate treatment details were excluded.

Study methodology

A retrospective review of the Electronic Medical Record (EMR) database of all the patients undergoing RT or concurrent CTRT for HNSCC with curative intent treatment was done. The post-treatment imaging of patients was studied by the radiologist (blinded to clinical status and histopathology report). The imaging was reviewed and given a category as per the ACR-NIRADS.[1] The diagnostic accuracy of NIRADS was compared with the clinical follow-up and histopathological findings. Disease recurrence was determined either by pathologic confirmation or by clear clinical or imaging disease progression. The same analysis was instituted for the primary site, the lymph node and their combination separately.

Statistical analysis

The presentation of the categorical variables was done in the form of numbers and percentages (%). The quantitative data were presented as the means ± standard deviation and as the median with the 25th and 75th percentiles (interquartile range). The association/comparison of the variables, which were qualitative in nature, were analyzed using the Chi-square test. If any cell had an expected value of less than 5, then Fisher's exact test was used. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for NI-RADS for the primary site, for neck lymph nodes, and combined NIRADS categories for primary and lymph nodes for predicting a positive outcome. The receiver operating characteristic (ROC) curve was used to find cut-off point, sensitivity, specificity, PPV, and NPV of NI-RADS for the primary site and NI-RADS for neck lymph nodes for predicting recurrence. The data entry was done in the Microsoft Excel spreadsheet and the final analysis

was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 25.0. For statistical significance, a *P* value of less than 0.05 was considered statistically significant.

RESULTS

The final data of 148 cases who met the inclusion and exclusion criteria were included in the study. One of these was a case of carcinoma of unknown primary, for which the site of primary could not be ascertained; hence data from 147 primary cases were included against 148 nodal cases.

DISCUSSION

The Neck Imaging Reporting and Data System (NI-RADS) was conceived with the goal of standardizing assessment and reporting in post-treatment surveillance imaging in patients with head and neck squamous cell carcinomas (HNSCC). Standardized reporting for head and neck cancer imaging is essential because the distorted postoperative and post-radiation neck anatomy becomes difficult to interpret. In the absence of a template to provide guidance for post-treatment reporting, radiology reports can become unfocused, inaccurate, and misleading, with little to no guidance for subsequent clinical management. An important role of NI-RADS is to provide guidance for next-imaging decisions, such as time interval and the choice of modality or intervention. NI-RADS helps prevent inordinate biopsies or frequent follow-ups and ensures early detection of recurrent disease.

Radical CTRT, or RT is the primary mode of curative intent treatment for most oropharyngeal, nasopharyngeal, laryngeal cancers, as well as oral cavity cancers which have become inoperable. Follow-up with imaging is important to rule out recurrence, especially in obscure and deep areas of these sub-sites.

NI-RADS originally designed for contrast-enhanced computed tomography (CECT) surveillance imaging in patients with treated head and neck cancer, with or without position emission tomography (PET).[1] This template, however, can be used for magnetic resonance imaging (MRI) as well. In view of superiority of MRI for tumor surveillance in the skull base, sino nasal region, nasopharynx, salivary glands, orbits, and especially for assessing perineural tumor spread, the need of MRI-specific NI-RADS lexicon was felt and under construction.

The two areas that are separately scrutinized in every post-treatment surveillance imaging of a patient with treated head and neck cancer are the primary site of the tumor (to look for local residual or recurrent disease) and the lymph node stations (to look for metastatic adenopathy). The status of each can be designated as belonging to one of the four categories, namely, negative, low suspicion, high suspicion; and definite recurrence. If prior imaging is not available for comparison, the status is considered "incomplete," and assigned a category of 0. The ACR NI-RADS website has all necessary information and additional resources, such as a sample reporting template for a post-treatment neck CT (available at: www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/NI-RADS).

Comparison between CECT and PET–CT

In our study, 37 cases were followed with CECT, whereas 111 were followed with PET-CT. We collated the results of CECT vs PET-CT [Tables 1-5] and observed no significant difference ($P > 0.05$) between CECT and PET-CT for predicting recurrence in any of the NIRADS category. The *sensitivity* of CECT (75% and 87.5%) was more than PET-CT (50% and 61.11%) for primary disease and neck node, respectively, whereas *specificity* of PET-CT (90.22% and 79.57%) was greater than CECT (51.72% and 62.07%) for primary and nodal recurrence.

Kreiger *et al*.,[6] reported no statistically significant difference in predicting recurrence between CECT and PET-CT in the individual NIRADS category. They made an interesting observation, that; for predicting recurrence in NI-RADS 3 category CECT was better than PET-CT and specificity was 91.7% vs 40%, respectively, in CECT and PET-CT. Ong *et al*.[7] in their study that PET-CT can rule out residual lesions at the primary site with a diagnostic accuracy of 92% and a specificity

Table 1: Recurrence rate in CECT and PET in different NIRADS category

Site	NI-RADS	CECT	PET	*P*	Overall recurrence rate
Primary site	NI-RADS 1	0 (0%)	6 (8.57%)	1*	7.89%
	NI-RADS 2	1 (33.33%)	3 (13.64%)	0.422*	16%
	NI-RADS 3	1 (12.50%)	9 (50%)	0.099*	38.46%
	NI-RADS 4	6 (30%)	-	-	30%
	Total	8 (21.62%)	18 (16.36%)	0.468†	
Nodal	NI-RADS 1	1 (5.26%)	7 (8.64%)	1*	8%
	NI-RADS 2	2 (100%)	2 (28.57%)	0.167*	44.44%
	NI-RADS 3	0 (0%)	9 (39.13%)	1*	37.50%
	NI-RADS 4	5 (33.33%)	-	-	33.33%
	Total	8 (21.62%)	18 (16.22%)	0.454†	
Combined primary and nodal	NI-RADS 1	0 (0%)	1 (1.85%)	1*	
	NI-RADS 2	1 (50%)	4 (16%)	0.342*	
	NI-RADS 3	1 (14.29%)	13 (40.63%)	0.386*	
	NI-RADS 4	6 (27.27%)	-	-	
	Total	8 (21.62%)	18 (16.22%)	0.454†	

*Fisher's exact test, †Chi-square test

Table 2: Association of NI-RADS for primary site with outcome in total study subjects

NI-RADS for primary site	Negative (*n*=121)	Positive (*n*=26)	Total	*P*
1	70 (92.11%)	6 (7.89%)	76 (100%)	0.002*
2	21 (84%)	4 (16%)	25 (100%)	
3	16 (61.54%)	10 (38.46%)	26 (100%)	
4	14 (70%)	6 (30%)	20 (100%)	
Total	121 (82.31%)	26 (17.69%)	147 (100%)	

*Fisher's exact test

Table 3: Association of NI-RADS for neck lymph nodes with outcome in total study subjects

NI-RADS for neck lymph nodes	Negative (*n*=122)	Positive (*n*=26)	Total	*P*
1	92 (92%)	8 (8%)	100 (100%)	<.0001*
2	5 (55.56%)	4 (44.44%)	9 (100%)	
3	15 (62.50%)	9 (37.50%)	24 (100%)	
4	10 (66.67%)	5 (33.33%)	15 (100%)	
Total	122 (82.43%)	26 (17.57%)	148 (100%)	

*Fisher's exact test

Table 4: Receiver operating characteristic curve of NI-RADS for primary site and NI-RADS for neck lymph nodes for predicting recurrence in CECT

Variables	NI-RADS for primary site	NI-RADS for neck lymph nodes
Area under the ROC curve (AUC)	0.649	0.711
Standard Error	0.0896	0.0864
95% Confidence interval	0.475 to 0.798	0.539 to 0.848
P	0.0971	0.0146
Cut off	>3	>1
Sensitivity (95% CI)	75% (34.9-96.8%)	87.5% (47.3-99.7%)
Specificity (95% CI)	51.72% (32.5-70.6%)	62.07% (42.3-79.3%)
PPV (95% CI)	30% 11.9-54.3%)	38.9% (17.3-64.3%)
NPV (95% CI)	88.2% (63.6-98.5%)	94.7% (74.0-99.9%)
Diagnostic accuracy	56.76%	67.57%

Table 5: Receiver operating characteristic curve of NI-RADS for primary site and NI-RADS for neck lymph nodes for predicting recurrence in FDG PET CECT

Variables	NI-RADS for primary site	NI-RADS for neck lymph nodes
Area under the ROC curve (AUC)	0.725	0.708
Standard error	0.0687	0.0641
95% Confidence interval	0.631 to 0.806	0.615 to 0.791
P	0.11%	0.11%
Cut off	>2	>1
Sensitivity (95% CI)	50% (26.0-74.0%)	61.11% (35.7-82.7%)
Specificity (95% CI)	90.22% (82.2-95.4%)	79.57% (69.9-87.2%)
PPV (95% CI)	50% (26.0-74.0%)	36.7% (19.9-56.1%)
NPV (95% CI)	90.2% (82.2-95.4%)	91.4% (83.0-96.5%)
Diagnostic accuracy	83.64%	76.58%

of 95%. Kumar *et al*.[8] 2022 reported that CECT alone can be used to predict recurrence with RECIST 1.1, especially if there is no PET available.

Performance of NI-RADS in predicting recurrence

A strong association exist between the NI-RADS score and positive disease both for primary and neck $P < 0.05$ in our study [Tables 2 and 3]. On the first post-treatment scan, we observed a recurrence rate (treatment failure rate) [Table 1] of 7.89%, 16%, 38.46%, and 30%, for the primary site in NIRADS 1, 2, 3, and 4. The nodal site treatment failure rate in NIRADS 1, 2, 3, and 4 is 8%, 44.44%, 37.50%, and 33.33%.

Hameed *et al*.[9] 2019 mentioned the treatment failure rate as 3.9% (NIRADS 1), 17% (2a) and 18.2% (2b) and 76.9% (NIRADS 3) for the primary site whereas for the nodal site, it is 3.8%, 7.1%, and 81.8% in the respective categories 1, 2, and 3. Hsu *et al*.[10] 2019 in their study mentioned a recurrence rate for primary as 6.4%, 11.1%, and 38.5% in NIRADS 1, 2, 3, respectively, whereas for nodal site it is 6.4%, 11.1%, and 38.5% in respective categories 1, 2, and 3. In the studies by Dinkelborg *et al*.,[11] Elsholtz *et al*.,[12] the respective recurrence rate for the primary site are 1% and 5.8% in NIRADS 1, 7.4% and 100% in NIRADS 2, 66.6% and 88.9% NIRADS 3. For NIRADS 4 both studies mentioned 1005 recurrence. For nodal sites, the reported recurrence rate by Dinkelborg *et al.* is 0.5%, 7%, 80%, and 100% in NIRADS 1, 2, 3, and 4 whereas Elsholtz *et al.* observed 2.7%, 10%, 93.8%, and 100% in NIRADS 1, 2, 3, and 4 in their study.[11,12]

For NIRADS 1 and 2, our results are comparable to previous studies, but for NIRADS 4, we had a lower treatment failure rate at both the primary and nodal site. This is because we included only histologically confirmed reports for the analysis. Wangaryattawanich *et al*.[13] 2020 reported 100% patient has treatment failure for NIRADS 4, but 31/65 patients had no

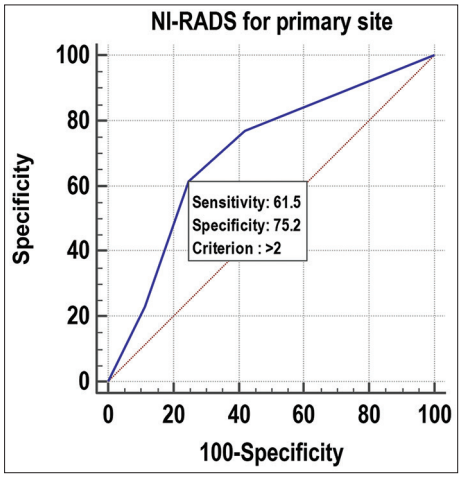

Figure 1: Receiver operating characteristic curve of NI-RADS for primary site for predicting recurrence

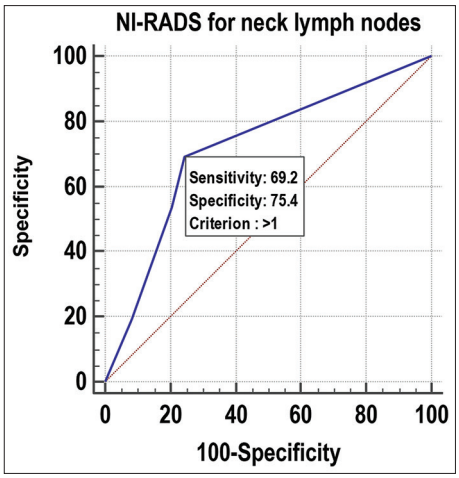

Figure 2: Receiver operating characteristic curve of NI-RADS for neck lymph nodes for predicting recurrence

tissue confirmation, rather only unequivocal treatment failure based on follow-up imaging and clinical examination.

Characteristics of NIRADS to predict recurrence

With the area under ROC curve (AUC) as 0.70 and 0.72 for primary and neck; sensitivity, specificity, PPV, NPV and diagnostic accuracy of NIRADS to predict recurrence for the primary site is 61.54%, 75.21%, 34.8%, 90.1%, and 72.79%, respectively, whereas for the neck, it is 69.54%, 75.41%, 37.5%, 92%, and 74.32% [Figures 1 and 2].

Ong *et al*. in their study on utility of PET-CT to predict recurrence reported a sensitivity of 33%, specificity of 85%, PPV of 14%, NPV 94% with a diagnostic accuracy of 77% for neck.[7] Wangaryattawanich *et al*. mentioned the 56% overall PPV of NIRADS. Koshkareva *et al*.[14] mentioned an 85% NPV and 84% PPV of the first post-treatment PET.[13,14]

Limitations

We have evaluated only the first post-treatment scan in our study; hence we could not compare the usefulness of the NIRADS score in follow-up scans.

CONCLUSION

In our study, a strong association exists between NI-RADS score and positive disease, both for primary and neck ($P < 0.05$). Hence, the introduction and prevalent use of the NI-RADS reporting template will lead to more consistent and accurate radiology reports, improved communication between radiologists and clinicians, and optimizing management strategies, ultimately improving patient outcomes.

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Conflicts of interest

There are no conflicts of interest.

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