ROLE OF NECK IMAGING REPORTING AND DATA SYSTEM (NI-RADS) IN THE PREDICTION OF LOCAL AND REGIONAL RECURRENCE OF HEAD AND NECK SQUAMOUS CELL CARCINOMA BY CROSS SECTIONAL IMAGING MODALITIES

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ABSTRACT:

Background: Detection of residual, recurrent, or second primary malignancies in head and neck cancers treated patients can be challenging. Soft tissue changes and anatomical disfigurement seen after surgery, radiotherapy, and chemotherapy can distort the anatomy of the head and neck and make post treatment imaging reporting very complex.

Aim of work: To evaluate the performance of the Neck imaging, and reporting data system template recently created by the American College of Radiology (ACR) Committee in the prediction of local and regional disease recurrence or persistence of head and neck squamous cell carcinoma after treatment by using CE MRI/ CT, and PET-CT in inconclusive cases.

Patients and Methods: 116 scans for 55patients with head and neck squamous cell cancerswere included after finishing their treatment, reporting done using the ACR NI-RADS reporting template and lexicon and NI-RADS category was assigned to each scan, the accuracy of this categorization was done by correlation with our gold standard: tissue pathological examination and/ or three months interval follow up scan.

Results: Out of the 116 scans included in our study, we had 232 targets for primary tumour sites and lymph nodes, the overall tumour recurrence have occurred in 53 targets out of the total of 232, with a total tumour recurrence rate of 22.8%, the recurrence rates for each NI-RADS category for the primary tumour site were: 3.9% (2/51) for NI-RADS 1 category, 17.6% (3/17) for NI-RADS 2a category, 18.2% (4/22) for NI-RADS 2b category , and 76.9% (20/26) for NI-RADS 3 category. Regarding the lymph nodes, the recurrence rates for the different NI-RADS categories were: 3.8% (3/80) for NI-RADS 1 category, 7.1% (1/14) for NI-RADS 2 category, and 81.8% (18/22) for NI-RADS 3 category. The recurrence rates for combined NI-RADS categories for both the primary tumour site and lymph nodes were (Table 7): 3.8% (5/131) for NI-RADS 1 category, 19.6% (10/51) for NI-RADS 2 category, and 76.2% (38/48) for NI-RADS 3 category.

Conclusion: The performance of the ACR NI-RADS reporting system and its linked management recommendations is excellent, with statistically significant discrimination in between the different NI-RADS categories for either the primary tumour site, lymph nodes and for both combined. The use of NI-RADS can help to direct the management plans towards more proper options.

INTRODUCTION:

Head and neck (H&N) cancers represent the sixth most common form of cancers reported worldwide. More than 90% of them are squamous cell carcinomas. Head and neck squamous cell carcinoma (HNSCC) can arise from mucosal surface of the oral cavity, oropharynx, hypopharynx, larynx, and nasopharynx[1].

A wide variety of management options for HNSCC exists including Surgery, radiation, and chemotherapy in various combinations; this depends on the TNM stage, primary site, the functional outcome and the patient's clinical condition[2].

Despite the recent advances in the treatment options offered for H&N cancers; locoregional recurrence occurs in about 20–50% of patients during the first two years after treatment[3].

Disease recurrence is the main obstacle to long-term survival in HNSCC, so post treatment surveillance should be concerned for tumour recurrence detection at an early stage in order to provide a salvage procedure[4].

The complexity of head and neck anatomy added to the post treatment soft tissue changes and anatomical distortion are making the detection of residual, recurrent, or second primary malignancies in treated patients a complex process[5].

The ACR Intersociety Committee Summer Conference recommended the universal standardized use of report templates. A multidisciplinary team created a standardized template for surveillance of post-treatment H &N cancers with linked management options, and so the Head and Neck Imaging Reporting and Data System (NIRADS) was developed for surveillance of patients with treated H&N cancers[6].

AIM OF WORK:

To assess the performance of the NI-RADS system template recently created by the ACR Committee in the prediction of local and regional disease recurrence or persistence of head and neck squamous cell carcinoma after treatment by using different cross-sectional imaging modalities.

PATIENTS AND METHODS:

A total of 55 patients who finished their treatment for HNSCC were referred from Ain Shams university hospital oncology hospital, 116 follow up scans done to them in Ain Shams University Hospital, Radiology Department, these scans included 50 CE MRI scans, 48 CE CT scans and 18 PET CT scans, and follow up done up to 12 months to them, from the period between November 2017 and April 2019.

Exclusion Criteria:

- Cases of H&N cancers other than squamous cell carcinoma.

- Patients with renal impairment (Gadolinium can't be given with estimated glomerular filtration rate < 30 ml/min/1.73 m2, and serum creatinine above 2.0 mg for iodinated contrast material should not be administered).

- Patients known to have allergy to contrast mediumand patients with

contraindications for MRI, e.g. ferromagnetic implants as pacemakers.

Ethical Considerations;

- An informed consent was obtained explaining the procedure details, and possible complications.
- Risks and complications:

For CE MRI: the hazards of the contrast agent include; coldness, warmth, or pain at the injection site, nausea, vomiting, headache, paraesthesia, and the rare nephrogenic systemic fibrosis (NSF) which is a disease of fibrosis of the skin and internal organs caused by gadolinium injection in patients who have renal insufficiency.

For CE CT and PET CT: the serious uncommon side effects of the iodinated contrast agent include; allergic anaphylactic or non-allergic anaphylactic, contrast induced acute kidney injury, and arrhythmia.

For PET CT: Radiation can be hazardous to foetuses. The administered 18F-FDG might be excreted in breast milk, and the scan should be delayed unless needed urgently.

Study Tools:

- Full history taking and full dedicated clinical examination.
- Patients scanned at 8-week baseline after treatment, re scanning three months later done in case of negative findings and a third scan done six months later in case of negative findings.
- CE MRI/ CT or PET- CT scanning were done; the choice of the modality tailored according to each patient's condition and tolerance, considering the primary tumour site, and questions need to be answered by the clinicians.
- NI-RADS template: Findings were categorized into one of four categories followed by further action (biopsy) or follow up according to the template

recommendations (Table 1).

- Criteria for tumour recurrence included the following:[7]

  1) Biopsy positive for squamous cell carcinoma,

  2) Evidence of disease progression on subsequent imaging (per Response Evaluation Criteria in Solid Tumours Criteria),

  3) Obvious tumour on clinical examination.

- To confirm the lack of tumour recurrence, the following must have been fulfilled:

  1. Negative findings on follow-up imaging at least 6 months after the index scan with,

  2. No evidence of recurrence on clinical follow-up for at least 6 months, or

  3. Biopsy of an abnormality detected on an imaging scan with pathology results negative for tumour.

- Study Procedures:

- Patient Preparation:

For all modalities informed consent was obtained after detailed explanation and renal functions checked before the procedure, one ante-cubital wide bore intravenous cannula was inserted.

For patients underwent CE MR scan:

- Exclusion of any hazards like pacemaker implantation done first.

For patients underwent CE CT scan:

- Patients got well hydration and were screened for history of iodinated contrast material allergy, metformin use, and renal disease (Intravenous contrast material should not be administered when the serum creatinine level is above 2.0 mg/dl).

For patients underwent PET CT:

- Before the procedure the patients were fasting for 4–6 hours except for water. The patient has been seated in a quiet and dimly lit room before the administration of 18F-FDG, and blood glucose level checked and must have been less than 200 mg/dl.

Scanning parameters and imaging acquisition:

Some modifications with limited sequences were done depending on the disease presentation and the patient's condition to reduce scan times in case of patient's discomfort or distress.

CE MRI:

- Machine: MRI scans were performed on a 1.5 T MRI Philips Achieva scanner.

- The patient was positioned supine, and a special dedicated coil was used. Scan time was 18- 25 minutes, field of view: AP 230, and slice thickness:4 mm

- Morphological sequences included pre-contrast axial T1 WIs (TE =21 ms, TR = 633 ms), coronal T1 (TE = 14, TR = 555), axial T2 WIs (TE =110 ms, TR =7039 ms), and sagittal T2 drive WI (TE = 100, TR =3196.7), All these sequences are single shot spin echo, and also coronal T2 STIR (TR/TI = 3500/150, TE = 80 ms) and axial echo-planner DWI study performed with 3 b-values.

- A dose of 0.1 mmol/kg gadolinium was administered by injector at a flow rate 2-3 ml/sec followed by post-contrast dynamic sequences, and T1 WIs in axial, sagittal, and coronal.

CE CT:

- Machine: 128-row MDCT scanner (GE 128, Optima 660, USA).

- The patient positioned with arms down. FOV: 28 cm. 100 ml of iodinated contrast agent was injected; at a rate of 1-1.5 ml/sec and scanning done 80-100 sec after the start of the contrast agent injection.

- Axial images from the frontal sinuses through the mediastinum at 1.25-mm section thickness; pitch, 0.984:1; gantry rotation, 0.7 seconds; 120 kv (peak). The native CT-images acquired with a slice thickness of 0.6-0.75 mm, and reformatted for display with a slice thickness of 3 mm

PET CT:

- Machine: GE Discover 600 and 690 PET/CT scanners

- Combined PET/CT from the skull vertex to mid-thigh was obtained 1 hour after intravenous administration of 10–14 mCi of FDG.

After the procedure:

- Patient's adequate hydration and follow up done, the patients underwent PET CT were instructed to limit the contact with pregnant women and children for 24 hours post procedure.

Image analysis:

CT and MR data were transferred to workstations (AW volume share 7 and 3D synapse, Fujifilm). Imaging findings analysis done using the ACR NI-RADS lexicon and reporting templates for PET-CT; CT and MRI scans. NI-RADS category assigned to each scan according to the template; one for primary site and one for lymph-nodes, management done according to the linked management recommendations. Confirmation of the findings and NI-RADS category was done by our gold standard which was pathological examination or follow up scan.

Imaging Reporting and Data System lexicon (8):

- **Non-mass-like soft tissue:**

  - Non-enhancing or minimally enhancing distortion of soft tissue and fat planes {1}

- **Masses:**

  - Morphology: ill-defined{2} versus discrete {3}

  - Enhancement: mild {2} versus intense {3}

  - FDG avidity: mild {2} versus intense {3}

- **Mucosal abnormality:**

  - Low density submucosal edema{1}

  - Diffuse linear enhancement: benign radiation mucositis {1}

  - Focal or mass-like mucosal enhancement or FDG uptake {2a}

- **Lymph nodes:**

  - Residual nodal tissue plus no FDG {1}

  - Residual nodal tissue plus mild FDG {2}

  - Residual nodal tissue plus intense FDG {3}

  - Lymph node, increasing size, without definite morphologically abnormal features, along with expected nodal drainage {2}

  - Lymph node, increasing size, with morphologically abnormal features {3}.

  - Lymph node of increasing size plus intense FDG {3}.

Table (1) NI-RADS reporting template and linked management recommendations (8):

| Category	Category	Imaging findings	Management
	0	New baseline study without any prior imaging available and knowledge that primary imaging exists and will become available	Assign score in addendum after prior imaging examinations become available
No evidence of recurrence	1	-Expected post treatment changes -Non mass like tissue distortion -Low density mucosal edema (Figure 1) -No abnormal FDG uptake -Diffuse linear mucosal enhancement after radiation	Routine surveillance
Low suspicion	2a	-Focal mucosal enhancement but not mass like -Focal mild to moderate mucosal FDG uptake	Direct visual inspection
	2b	-Deep ill-defined soft tissue, not discrete -Little to no differential enhancement -Mild to moderate FDG uptake	Short interval follow up (3 months), repeat PET
High suspicion	3	-New or enlarging primary mass or lymph-node -Discrete nodule or mass with differential enhancement (Figure 2) -Intense focal FDG uptake	Image guided or clinical biopsy
Definitive recurrence	4	-Pathologically proven or definite radiologic and clinical progression	Clinical management
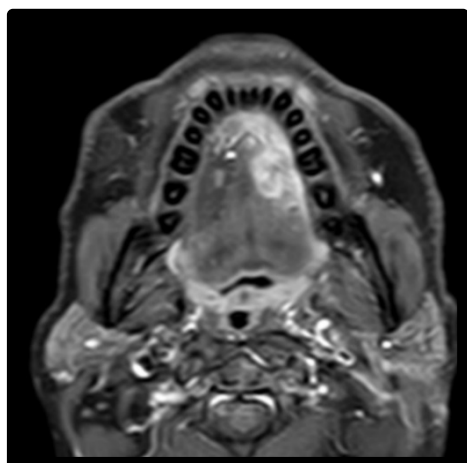
Figure 1: axial CE-CT neck at the level of the supraglottis showing predominant diffuse mucoid edema of the supraglottis in a patient underwent conservative surgery for supraglottic cancer and received RTH, keeping with NI-RADS (1) category.

Figure 2: axial CE CT neck at the level of the tongue showing discrete enhancing mass lesion at the left anterior oral tongue, keeping with NI-RADS (3) category which was confirmed by tissue pathological examination to be residual tumorous tissue.
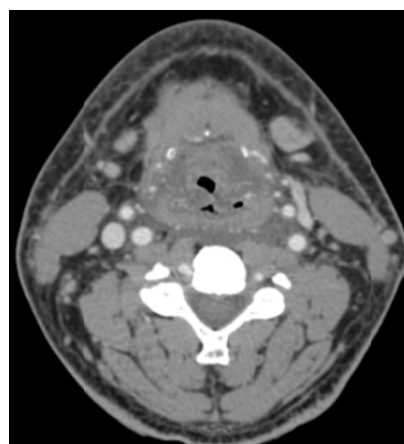
We followed up the patients according to our oncology hospital follow up programs for treated H&N cancers patients by an initial scan eight weeks after finishing therapy, then after additional three months in case of negative findings and a third follow up six months later if the findings are still negative. If the study was positive which is representing NI-RADS 3 category, further action done either by biopsy and tissue diagnosis or close follow up in cases refused biopsy or the general condition was not permitting it in proper timing. Clinical and radiological follow up interval for negative cases extended for 12 months interval post treatment.

Statistical methods:

IBM SPSS statistics (V. 25.0, IBM Corp., USA, 2017-2018) was used for data analysis. Date were expressed as median and percentiles for quantitative non-parametric measures in addition to both number and percentage for categorized data.

RESULTS

The study cohortincluded116 scans done for 55 patients; population demographics are shown in (Table 2).There were 50CE CT scans (43.1%), 48CE MRI scans (41.3%) and 18 PET CT (15.5%).58 (50%) scans were initial baseline follow up scan done eight weeks after finishing treatment; 33 (28.4%) scans were second follow up examinations, and 25 (21.5%) scans were third follow up examinations (Table 3). The pathological grading is shown in (Table 4):

Table (2) population demographics:

Age	18-89	
Patients number	55	
Gender	Male	73.6 %
	Female	26.4 %

Table (3) scans types and number:

Total scans number	116	
Scan type	MRI	48 (41.3%)
	CT	50 (43.1%)
	PET CT	18 (15.5%)
Scan order	First follow up	55 (47.5%)
	Second follow up	36 (31%)
	Third follow up	25 (21.5%)

Table (4) tumour pathological grading:

Tumour grade	Low	Count	18
		%	15.5%
	Moderate	Count	71
		%	61.2%
	High	Count	27
		%	23.2%

Out of the 116 scans included in our study, we had 232 targets for primary tumour site and lymph nodes which have been followed up to twelve months duration post treatment. Overall tumour recurrence occurred in 53 targets out of total of 232, with a recurrence rate of 22.8%, the recurrence rate for each NI-RADS category for the primary tumour site (Table 4) was: 3.9% (2/51) for NI-RADS 1 category, 17.6% (3/17) for NI-RADS 2a category, 18.2% (4/22) for NI-RADS 2b category, and 76.9% (20/26) for NI-RADS 3 category.

Regarding the lymph nodes, the recurrence rates (Table 5) were: 3.8% (3/80) for NI-RADS 1 category, 7.1% (1/14) for NI-RADS 2 category, and 81.8% (18/22) for NI-RADS 3 category.

The recurrence rates for the NI-RADS categories combined for both the primary tumour site and lymph nodes were (Table 6): 3.8% (5/131) for NI-RADS 1 category, 19.6% (10/51) for NI-RADS 2 category, and 76.2% (38/48) for NI-RADS 3 category.

Table (5) Tumour recurrence for primary tumour site among NI-RADS categories correlated to the gold standard:

			Outcome for primary site		Total
			Neg.	Pos.	
NI-RADS for Primary site	NI RADS 1	Count	49	2	51
		%	96.1%	3.9%	100.0%
	NI RADS 2a	Count	14	3	17
		%	82.4%	17.6%	100.0%
	NI RADS 2b	Count	18	4	22
		%	81.8%	18.2%	100.0%
	NI RADS 3	Count	6	20	26
		%	23.1%	76.9%	100.0%
Total		Count	87	29	116
		%	75.0%	25.0%	100.0%

Table (6): Tumour recurrence for neck lymph-nodes among NI-RADS categories correlated to the gold standard:

			Outcome for LNs		Total
			Neg.	Pos.	
NI-RADS for neck lymph nodes	NI-RADS 1	Count	77	3	80
		%	96.3%	3.8%	100.0%
	NI-RADS 2	Count	13	1	14
		%	92.9%	7.1%	100.0%
	NI-RADS 3	Count	4	18	22
		%	18.2%	81.8%	100.0%
Total		Count	94	22	116
		%	81.0%	19.0%	100.0%

Table (7): Tumour recurrence for both primary tumour site and neck lymph-nodes among combined NI-RADS categories to the gold standard correlated to the gold standard:

			Merged Outcome for primary and LNs		Total
			Neg.	Pos.	
Combined NI-RADS categories for primary and lymphnodes	NI RADS 1	Count	126	5	131
		%	96.2%	3.8%	100.0%
	NI RADS 2	Count	43	10	51
		%	84.4%	19.6%	100.0%
	NI RADS 3	Count	10	38	48
		%	20.8%	79.2%	100.0%
Total		Count	179	53	232
		%	77.1%	22.8%	100.0%

DISCUSSION:

The core of the ACR NI-RADS system is simplifying the complexity of the post-operative imaging findings in treated cases of head and neck cancers and summarizing these findings into four categories for the primary tumour site and for lymph nodes, with linked management recommendations for each category depending on the degree of suspicion for tumour residual/ recurrence. By this categorization we can obtain worldwide standardized reporting and follow up system for head and neck cancers treated patients and we can avoid unnecessary biopsies, or too close follow up for low risk cases, on the other hand close follow up/ assessment by PET CT or biopsy would be done at proper timing for early detection of recurrence in suspicious cases, avoiding unwarranted delays.

The performance of NI-RADS in our study showed significant discrimination between its different categories, with disease recurrence/persistence rates of 4% for NI-RADS 1, 25% for NI-RADS 2, and 76.9% for NI-RADS 3. A strong association between score and positive disease was found for primary site, lymph nodes, and all targets combined.

We compared our study with the initial study that evaluated the performance of NI-RADS conducted by Kreiger et al., 2017which demonstrated significant discrimination between groups, with disease recurrence/persistence rates of 3.8% for NI-RADS 1, 17.2% for NI-RADS 2, and 59.4% for NI-RADS 3.In our study we also had significant discrimination in-between different categories, yet we had higher rate of recurrence for NI-RADS 3 category. In our study we also had small erintervalin between the recurrence rates for NI-RADS 2a and 2b categories, than the difference found by Kreiger et al., 2017 and this could be attributed to a lesser number of scans in our study.

NI-RADS 1 and 2 in general are considered negative studies, while NI-RADS 3 considered as a positive disease study, NI-RADS 4 is pathologically proven cases or definitely progressing and these cases in our point of view in no need for statistical assessment, we focused on assessing NI-RADS categories 1, 2 and 3 as these what represent the complexity of imaging interpretation and the patient management is significantly altered according to them.

Limitations of this study include a relatively low number of the population.

Conclusion

The performance of the ACR NI-RADS reporting system and its linked management recommendations is excellent, with

statistically significant discrimination in between the different NI-RADS categories for either the primary tumour site, lymph nodes and for both combined. The use of NI-RADS can help to direct the management plans towards more proper options.

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دور نظام البيانات و التقارير الخاص بتصوير الرقبة في التنبؤ بعودة ظهور سرطانات الخلايا الحرشفية في الوجه و الرقبة باستخدام طرق التصوير المقطعي

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المقدمة: تُمَثِّل سرطانات الخلايا الحرشفية أكثر من ٩٠٪ سرطانات الرأس والرقبة. يرتبط فشل العلاج في المقام الأول بظهور الورم من جديد في نفس مكانه او مكان مجاور له. وقد أنشأ فريق متعدد التخصصات نموذجاً موحدا لمتابعة سرطانات الرأس و الرقبة بعد العلاج يعرف بإسم نظام البيانات و التقارير الخاص بتصوير الرقبة يختص بتصنيف الفحوصات لمراحل طبقاً لدرجة التنبؤ لعودة ظهور الورم.

الهدف: تقييم أداء نظام التصوير و التقارير الخاص بالرقبة المعد من قبل الجمعية الأمريكية للأشعة في التنبؤ بعودة ظهور أو استمرار سرطانات الخلايا الحرشفية المحلية والمنطقية في الوجه و الرقبة بعد العلاج.

المرضى والطرق: تضمنت الدراسة ١١٦ فحص تصويري لـ٥٣مريض تم علاجهم من سرطانات الخلايا الحرشفية في الرأس و الرقبة.تم تصنيف هذه الفحوصات طبقاً لنظام التصوير و التقارير الخاص بالرقبة المعد من قبل الجمعية الأمريكية للأشعة و تم اثبات صحة أو خطأ نتائج الحالات التصنيف بالمقارنة مع نتائج فحوصات الأنسجة أو بفحص متابعة بعد ثلاثة شهور.

النتائج: من بين الـ ١١٦ الفحص اللتي شملتها دراستنا، تكرار ظهور الورم حدث في ٥٣ هدفًا من إجمالي عدد ٢٣٢، بمعدل تكرار (٢٢,٨٪)معدل التكرار للفئة ١ من نظام التصوير و التقارير الخاص بالرقبةلموقع الورم الرئيسي ٣,٩٪ (٥١/٢)، ١٧,٦٪(١٧/٣) للفئة٢أ،١٨,٢٪ (٢٢/٤) للفئة٢ب، و٧٦,٩٪ (٢٦/٢٠) للفئة ٣. بالنسبة للعقد اللمفاوية ، كان معدل التكرار كالتالي: ٣,٨٪ (٨٠/٣) للفئة ١ من نظام التصوير و التقارير الخاص بالرقبة، ٧,١٪(١٤/١)للفئة ٢، و ٨١,١ ٪ (٢٢/١٨) للفئة ٣.

الخاتمة:أداء نظام التصوير و التقارير الخاص بالرقبة والتوصيات المرتبطة به ممتاز، مع وجود تمييز ذي دلالة إحصائية بين مختلف فئات هذا النظام.