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Unidimensional Measurement May Evaluate Target Lymph Nodal Response After Induction Chemotherapy for Nasopharyngeal Carcinoma

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Abstract: The aim of the study was to evaluate whether short axis and long axis on axial and coronal magnetic resonance imaging planes would reflect the tumor burden or alteration in size after induction chemotherapy in nasopharyngeal carcinoma.

Patients with pathologically confirmed nasopharyngeal carcinoma (n = 37) with at least 1 positive cervical lymph node (axial short axis ≥15 mm) were consecutively enrolled in this prospective study. Lymph nodal measurements were performed along its short axis and long axis in both axial and coronal magnetic resonance imaging planes at diagnosis and after 2 cycles of induction chemotherapy. In addition, lymph nodal volumes were automatically calculated in 3D treatment-planning system, which were used as reference standard. Student's *t* test or nonparametric Mann–Whitney *U* test was used to compare the continuous quantitative variables. Meanwhile, the κ statistic and McNemar's test were used to evaluate the degree of agreement and discordance in response categorization among different measurements.

Axial short axis was significantly associated with volumes at diagnosis ($P < 0.001$). A good agreement (κ=0.583) was found between axial short axis and volumetric criteria. However, the inconsistent lymph nodal shrinkage in 4 directions was observed. Axial short-axis shrinking was more rapid than the other 3 parameters. Interestingly, when utilizing the alternative planes for unidimensional measurements to assess tumor response, coronal short-axis showed the best concordance (κ=0.792) to the volumes.

Axial short axis may effectively reflect tumor burden or change in tumor size in the assessment of target lymph nodal response after induction chemotherapy for nasopharyngeal carcinoma. However, it should be noted that axial short axis may amplify the therapeutic response. In addition, the role of coronal short axis in the assessment of tumor response needs further evaluation.

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Abbreviations: Ax-long = long axial axis, Ax-short = short axial axis, Cor-long = long coronal axis, Cor-short = short coronal axis, CR = complete response, ICC = intraclass correlation coefficient, IQR = interquartile range, MRI = magnetic resonance imaging, NACT = neoadjuvant chemotherapy, NPC = nasopharyngeal carcinoma, OR = overall response, PD = disease progression, PR = partial response, RECIST = response evaluation criteria in solid tumors, RLN = retropharyngeal lymph node, SD = stable disease, VM = volume.

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is characterized by high prevalence of lymph nodal spread at initial diagnosis.[1] Neoadjuvant chemotherapy (NACT) has been regarded as an effective treatment for local-regional advanced NPC as it may not only reduce the micrometastatic foci, but also help to shrink the large tumors before radiotherapy to achieve better loco-regional control.[2,3] Hence, accurate assessment of lymph nodal responses after induction chemotherapy is beneficial with regard to treatment evaluation, micrometastatic eradication, and survival prognosis.[4] At present, Response Evaluation Criteria In Solid Tumors (RECIST) Version 1.1 guideline has been used to assess the tumor response. The lymph nodes with a short axis of ≥15 mm are considered measurable and assessable as target lesions, and short axis measurement should be included in calculating total lesions to reflect tumor response.[5] However, the short-axis measurement of tumor lesions to evaluate the outcome of induction chemotherapy for NPC has not been fully elucidated, especially in volumetric (three-dimensional [3D]) measurement (VM) era.

In 2000, the RECIST Working Group advocated the unidimensional measurement to simplify and clarify the tumor response criteria (RECIST 1.0). However, a number of issues and questions concerning the number of target lesions, the size of lymph nodes to be measured, and the application of new imaging technologies were not well established. In 2009, the guideline was revised (RECIST 1.1), mainly based on the analyses of the database of ~6500 patients with >18,000 target lesions from 16 clinical trials, in order to overcome the limitations of version 1.0.[5] Later, many studies were emerged to validate RECIST 1.1 criteria. An et al conducted a study to compare the accuracy of VMs with unidimensional measurements in patients with breast cancer after induction

chemotherapy. The study results had shown a good consensus between the one-dimensional (1D) and 3D measurements for the tumor response.[6] However, a retrospective analysis of treatment response in breast cancer showed poor agreement between 1D and 3D measurements.[7] Several investigations comparing the 1D and 3D methods for metastatic lymph nodes, pulmonary metastasis, and gliomas have reported contradicting results.[8–10] However, the assessment of tumor response comparing the 1D and 3D measurements for solid tumor remains controversial.

To our knowledge, King et al conducted the only study, comparing the cross-sectional magnetic resonance imaging (MRI) with unidimensional measurement on tumor burden and assessed the treatment response based on VMs as the reference standard in NPC.[11] It was found that the unidimensional measurement of RECIST 1.1 might not be applicable to the primary, morphologically irregular NPCs. However, it is unknown whether the RECIST 1.1 criteria can be applicable to relatively regular cervical lymph nodes in NPC. Furthermore, the technologies are no longer limited to the cross-sectional images of tumor lesions because of the widespread use of MRI. The plane of acquisition may be axial, sagittal, or coronal. There is a pressing need to explore a feasible method that uses an alternative plane for the unidimensional measurement of metastatic cervical lymph nodes in NPC.

The purpose of the present study was to use MRI to verify whether short axial axis (Ax-short) in the RECIST 1.1 criteria would reflect tumor burden or alteration in size after induction chemotherapy for NPC. New measurements such as the long axial axis (Ax-long) and the long and short coronal axis (Cor-long and Cor-short) were also evaluated with respect to tumor burden and alteration in size with chemotherapy. VM was automatically acquired from the 3D image-based treatment-planning system, which was used as the reference standard.

MATERIAL AND METHODS

Patients

The present study was approved by the Institutional Ethics Committee of Fujian Provincial Cancer Hospital, China (the reference number was FJCH-09911). All the patients signed an informed consent form before participating in the study. All patients who met the following inclusive criteria were enrolled in this prospective study: (1) patients with newly diagnosed, histologically proven, stage III or IV NPC with no gross evidence of distant metastasis, according to the 7th edition of American Joint Committee on Cancer staging system;[12,13] (2) patients with at least 1 positive metastatic cervical lymph node, and the smallest axial short-axis of cervical lymph node by the RECIST 1.1 had to be ≥15 mm; (3) patients with a satisfactory Karnofsky performance status (≥70) and adequate blood counts (white blood cell count of ≥4000/μL and platelets count of ≥100,000/μL), as well as renal function (creatinine clearance of ≥60 mL/minute). The study exclusion criteria included age ≥70 years or < 18 years, pregnancy, and a prior or synchronous malignancy. In the present study, patients were enrolled consecutively to avoid any kind of selection bias. Finally, a total of 37 patients were enrolled in this study from September 2013 to June 2014.

Chemotherapy

With the reference to clinical stage and patient tolerance, all the patients received 2 or 3 cycles of NACT. The NACT protocol was as follows: 10 patients received cisplatin (100 mg/m^2 intravenously from day 1 to 3) and paclitaxel (135 mg/m^2 intravenously on day 1), whereas remaining 27 patients received cisplatin (100 mg/m^2 intravenously from day 1 to 3) and gemcitabine (1000 mg/m^2 intravenously on day 1 and 8).

MRI Scanning

MR images were obtained by MultiTransmit Whole Body scanner (Achieva 3.0T TX, Philips Healthcare, Best, The Netherlands), using16-channel head and neck array coils. The MRI images for each patient were obtained before treatment and after 2 cycles of NACT. The following 4 sequential images from the neck to the thoracic outlet were obtained: axial and oblique coronal fast-spin echo (FSE) T2-weightedimaging (T2WI) with short tau inversion recovery technique and contrast-enhanced (CE) FS axial T1 and CE FS coronal T1-weighted images. The parameters of scanning sequences were as follows: (1) axial FSE T2WI: a repetition time/echo time (TR/TE) of 6526/60, a 230 × 230 mm field of view (FOV), a 5 mm thick section and a 1-mm gap, number of slices = 36, number of signal averages (NSA) = 2, and scan time = 2:23 (min); (2) coronal FSE T2WI: a TR/TE of 2327/64, a 200 × 260 mm FOV, a 5 mm thick section and a 1-mm gap, number of slices = 15, NSA = 2, and scan time = 1:58 (min); (3) CE FS axial T1-weighted images: a TR/TE of 1215/8.1, a 230 × 230 mm FOV, a 5 mm thick section and a 1-mm gap, number of slices = 36, NSA = 2, and scan time = 1:54 (min); and (4) CE FS coronal T1-weighted images: a TR/TE of 500/8.1, a 200 × 260 mm FOV, a 5 mm thick section and a 1-mm gap, number of slices = 15, NSA = 2, and scan time = 1:24 (min). A rapid bolus injection of gadolinium with diethylenetriaminepentacetate (0.1 mmol/kg body weight) (Magnevist, Schering AG, Berlin, Germany) was administered for the postgadolinium sequences.

Imaging Analysis

Two radiologists with >8 years' of diagnostic experience in NPC performed the lymph nodal measurements using the picture archiving and communicating system (PACS). Lymph nodal measurements were performed along its short axis and long axis in both axial and coronal planes. The long axis of the node was defined to be the length of that rectangle with the largest length of all slices. The short axis was defined to be the perpendicular axis to the long axis in the slice (Figure 1). All the lymph nodes at diagnosis with a short-axis of ≥15 mm were marked as target lesions. If the target lymph nodes were split into separate segments on the post-NACT MRI, the sum of the segments was regarded as the post-NACT long axis, and the short axis of the relatively bigger one was defined as the post-NACT short axis. If nodes coalesced into a single one, the longest diameter and perpendicular short-axis of the integration lesion were measured (Figure 1). All the measurements were conducted on T2-weighted MR images.

Lymph nodal VM

Pretreatment and post-NACT image data were submitted to the 3D treatment-planning system, and the target lesions were manually outlined by 2 clinicians (with >5 years' of experience) using the 3D treatment-planning software. The system can automatically reconstruct a 3D image and calculate the lymph nodal volume.

Definition of Tumor Response

Tumor response was categorized according to RECIST 1.1 and volumetric criteria[5,11](5.11: complete response [CR]: all
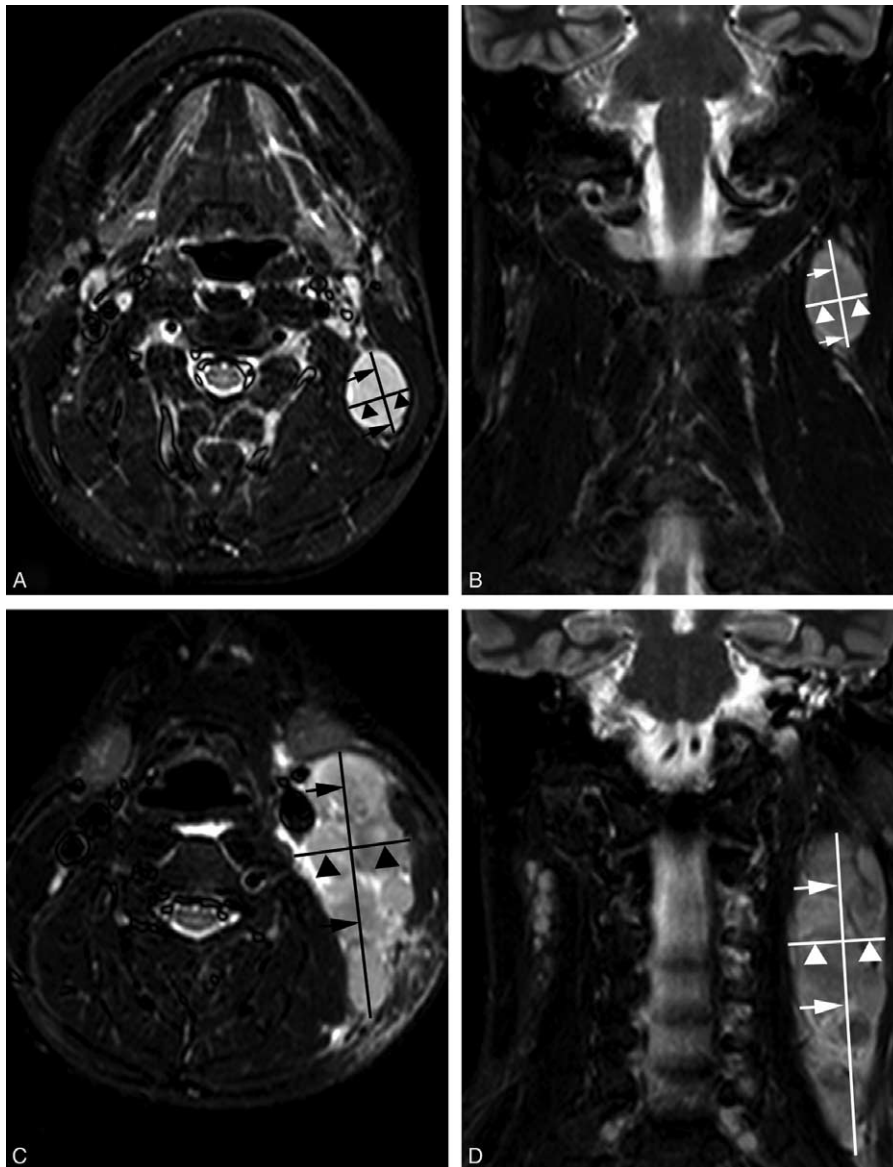
FIGURE 1. The unidimensional measurements in axial and coronal T2-weighted MR images. (A) The Ax-long (arrows) of the node was obtained by measuring the maximum length of that rectangle with the largest axial slice. The Ax-short (arrowhead) was obtained by measuring the perpendicular axis to Ax-long in the slice. (B) The Cor-long (arrows) and Cor-short (arrowhead) of the node were obtained by the same measurements in the largest coronal slice. (C) The Ax-long (arrows) and Ax-short (arrowhead) of the coalesced node were obtained by measuring the maximum length and greatest perpendicular axis in the largest axial slice. (D) The Cor-long (arrows) and Cor-short (arrowhead) of the coalesced node were obtained by the same measurements in the largest coronal slice. Ax-long = long axial axis, Ax-short = short axial axis, Cor-long = long coronal axis, Cor-short = short coronal axis, MR = magnetic resonance.

pathological lymph nodes [target or nontarget lymph nodes] must reduce to < 10 mm in short axis; partial response [PR]: >30% reduction in the sum of the diameters or >65% reduction in the sum of the volumes of the target lesions; stable disease [SD]: neither adequate shrinkage nor progression to qualify for PR or PD; disease progression [PD]: >20% increase in the sum of the diameters or 40% increase in sum of the volumes of the target lesions). The unidimensional and volumetric criteria are listed in Table 1. Although CR was defined as target lymph nodes with short-axis size of < 10 mm, there were still measurable entities in volumetric criteria. In clinical practice, the

purpose of the response criteria is to identify the response and nonresponse groups relative to anticancer treatment. Thus, in the present study, CR and PR were integrated as overall response (OR). Hence, the response criterion was classified into 3 categories: OR, SD, and PD.

Statistical Analysis

All data were analyzed using SPSS 17.0statistical software (SPSS Inc, Chicago, IL). Student's *t* test or nonparametric Mann–Whitney *U* test was used to compare the continuous quantitative variables. The parameters were expressed as mean

TABLE 1. The Category of RECIST 1.1 and Volumetric Criteria

Category	Unidimensional Criteria[*]	Volumetric Criteria[†]
Complete response	Any pathologic lymph nodes must have reduction in the short axis to < 10 mm	Tumor disappearance
Partial response	>30% reduction in size	>65% reduction in size
Stable disease	Neither sufficient shrinkage to qualify for PR or PD	Neither sufficient shrinkage to qualify for PR or PD
Disease progression	>20% increase in size	>40% increase in size

PD = disease progression, PR = partial response, RECIST = response evaluation criteria in solid tumors.
[*] According to RECIST 1.1 guidelines.
[†] Based on relationship of change in surficial area to change in volume.

and standard deviation or median and interquartile range (IQR) according to the distribution of variables. The general linear model with univariate analysis was used to assess whether Ax-short, Ax-long, Cor-short, and Cor-long were associated with VM. The intraclass correlation coefficient (ICC) was used to measure inter-observer reliability. The percentage change or absolute change was used in the calculation of tumor response in each group. The tumor response was categorized into OR, SD, or PD according to the aforementioned criteria. The κ statistic and McNemar's test were used to evaluate the degree of agreement and discordance in response categorization among different measurements. All statistical analyses were performed using 2-tailed tests and a *P* value <0.05 was considered statistically significant.

RESULTS

Patient Characteristics

A total of 37 patients (29 men, 8 women) were enrolled in this study. The median age was 41 years (range: 23–61 years). The patients with NPC were further categorized based on lymph node involvement, which was as follows: N1 (n = 12), N2 (n = 17), and N3 (n = 8). Patients' characteristics were displayed in Table 2. There were a total of 48 target lesions in 37 patients: 27 with 1 target lesion, 9 with 2 target lesions, and 1 with 4 target lesions.

Measurement of Tumor Size at Diagnosis

Tumor volumes at initial diagnosis ranged from 1.0 to 112.0 cm^3 with a mean of 21.96 cm^3 and IQR of 17.55 cm^3. The mean or median sizes of measurement parameters are summarized in Table 3. It was found that there were no significant differences between Ax-short and Cor-short at diagnosis (*P* = 0.143). Long-axis diameters on coronal planes were significantly larger than those on axial planes (*P* < 0.001). The relation of VM with Ax-short, Ax-long, Cor-short, and Cor-long is shown in Table 4. All 4 diameter lines were significantly related to VM at diagnosis, in the context of absolute change and percentage change in VM. The intra-rater reliability for VM, Ax-long, Ax-short, Cor-long, Cor-short is displayed in Table 3. The ICCs for VM were markedly high, whereas ICCs for short-axis in axial or coronal axis were slightly higher than those for long-axis.

Assessment of Tumor Response

First, the percentage changes of target lymph nodes in 4 directions were investigated. As shown in Table 3, it was found

that the shrinkage of target lesions appeared to be in an inconsistent way. The percentage changes of Ax-short were significantly higher than those of Ax-long, Cor-short, and Cor-long (*P* = 0.002, 0.006, and 0.039, respectively). However, there was no statistical difference in percentage changes of diameters among Ax-long, Cor-short, and Cor-long (*P* = 0.148, 0.726, and 0.421, respectively). Next, with regard to tumor response according to VM, there were 24 OR and 24 SD, with no PD. With regard to tumor response according to Ax-short (RECIST 1.1), there were 30 OR and 18 SD, with a κ value of 0.583. According to the VM criterion, Ax-short misclassified 2 OR cases as SD and misclassified 8 SD cases as OR (*P* = 0.109, McNemar's test). With regard to tumor response according to Ax-long, there were 25 OR and 23 SD, with a κ value of 0.625. According to the VM criterion, Ax-long misclassified 4 OR cases as SD and misclassified 5 SD cases as OR (*P* = 1.0, McNemar's test). With regard to tumor response according to Cor-short, there were 27 OR and 21 SD, with a κ value of 0.792.

TABLE 2. Patients' Characteristics

Characteristic	Number of Patients	%
Gender		
Male	29	78.4
Female	8	21.6
Age (median 41 y, range from 23 to 61 y)		
<41	17	45.9
≥41	20	54.1
Histopathology (WHO type)		
Type II	3	8.1
Type III	34	91.9
N-classification		
N1	12	32.4
N2	17	45.9
N3	8	21.6
AJCC stage		
III	17	45.9
IVa–IVb	20	54.1
NACT regimen		
PTX + DDP	10	27.0
GEM + DDP	27	73.0

AJCC = American Joint Committee on Cancer, DDP = cisplatin, GEM = gemcitabine, NACT = neoadjuvant chemotherapy, PTX = paclitaxel.

TABLE 3. Summaries of Mean or Median Sizes and Intraclass Correlation Coefficients of Parameters

	Mean (SD)*/Median (IQR)†	Range	ICC (95%CI)
Ax-short[pre]	1.85 (0.69cm)*	1.50−3.68cm	0.976 (0.960−0.987)
Ax-long[pre]	2.69 (1.10cm)*	1.66−7.56cm	0.943 (0.838−0.981)
Cor-short[pre]	1.89 (0.60cm)*	1.30−3.78cm	0.981 (0.960−0.991)
Cor-long[pre]	4.02 (1.58cm)†	2.07−9.71cm	0.961 (0.919−0.984)
VM[pre]	13.50 (17.55cm3)*	1.00−112cm3	0.999 (0.997−1.000)
Percentage change of Ax-short	37.04% (19.89%)†	−4.00 to 70.10%	−
Percentage change of Ax-long	31.30% (21.71%)†	−16.90 to 81.90%	−
Percentage change of Cor-short	33.83% (18.62%)†	−5.00 to 70.50%	−
Percentage change of Cor-long	32.13% (19.91%)†	−2.3 to 73.00%	−
Percentage change of VM	67.31% (37.80%)*	6.40 to 95.50%	−

Ax-long = long axial axis, Ax-short = short axial axis, CI = confidence interval, Cor-long = long coronal axis, Cor-short = short coronal axis, ICC = intraclass correlation coefficient, IQR = interquartile range, SD = standard deviation, VM = volume.
* According to the normal distribution of variables, the data is described by mean and standard variation.
† According to the non-normal distribution of variables, the data is described by median and interquartile range.

According to the VM criterion, Cor-short misclassified 1 OR as SD and misclassified 4 SD as OR ($P = 0.375$, McNemar's test). With regard to tumor response, according to Cor-long, there were 25 OR and 23 SD, with a κ value of 0.625. According to the VM criterion, Cor-long misclassified 4 OR as SD and 5 SD as OR ($P = 1.0$, McNemar's test). The kappa values of 4 diameters are summarized in Table 5. Using VM as a reference standard, Ax-short, Ax-long, Cor-short, and Cor-long misclassified the response in 10 of 48 cases (21%), 9 of 48 cases (19%), 5 of 48 cases (10%), and 9 of 48 cases (19%), respectively.

Measuring the Single Largest Lesion and 2 Lesions Per Organ to Assess Tumor Response

According to RECIST 1.1, the selection of 2 representative lesions per organ was arbitrary. In the current analysis, the maximum and the second largest lymph nodes (labeled as 1st + 2nd) were chosen as the representative lesions.

In terms of tumor response and according to the volumes of all target lesions, there were 5 OR and 5 SD, with no PD. Meanwhile, with regard to tumor response according to Ax-short (1st + 2nd), there were 7 OR and 3 SD, with a κ value of 0.600. Using VM results as the reference criterion, Ax-short (1st + 2nd) misclassified 2 SD cases as OR ($P = 0.500$, McNemar's test). With regard to tumor response according to Maximum Ax-short, there were 7 OR and 3 SD, with a

κ value of 0.600. Using VM results as the reference criterion, the maximum Ax-short misclassified 2 SD cases as OR ($P = 0.500$, McNemar's test). The objective response rates of cisplatin-based chemotherapy were not statistically different between 2 criteria (70% vs 70%, $P = 1.0$).

DISCUSSION

Volume methods that manually outlined each cross-sectional image using 3D treatment-planning software may most accurately reflect the tumor size, with high reproducibility and they are not confined to the shape of the tumor.[9,11] However, this technique requires more time and mastery of expertise and manpower which are unavailable for daily clinical practice. New semiautomated techniques for measuring tumors are being evaluated in order to replace the manual tracing method; however, they remain require relatively intensive in labor and are not of widespread availability.[14,15] Hence, at present, the simple unidimensional measurement approach is prevalent. However, little attention has been given to assess the validity of RECIST 1.1 in evaluating regional lymph nodes in patients with NPC. Moreover, there is a pressing need to use a feasible method of taking an alternative plane for unidimensional measurement in the 3-dimensional MRI era. In the present study, it was found that Ax-short (RECIST 1.1) was significantly associated with VM at diagnosis, absolute change, and percentage change in a single target lesion. The assessment of tumor response revealed good agreement between RECIST 1.1 and the volumetric criteria. However, inconsistent lymph nodal shrinkage in 4 directions was observed. The percentage changes of Ax-short were significantly higher than those of Ax-long, Cor-short, and Cor-long. Interestingly, when utilizing the alternative plane for unidimensional measurement to assess tumor response, the coronal short-axis showed the best concordance to the volume. In addition, in the analysis of 10 patients who had at least 2 target lesions, it was found that the same κ value and OR rates were achieved by measuring the single largest lesion and 2 lesions per organ.

The first part of the present study showed that the 4 diameter lines for measuring tumor size were all correlated with VM at diagnosis. The short-axis diameters at diagnosis were not significantly different on the axial and coronal planes; however, the long-axis diameters on the coronal planes were

TABLE 4. Probability (*P*) Values for Association of 4 Diameters With VM

	VM at Diagnosis	Absolute Change in VM After NACT	Percentage Change in VM After NACT
Ax-short	<0.001	<0.001	<0.001
Ax-long	<0.001	<0.001	<0.001
Cor-short	<0.001	<0.001	<0.001
Cor-long	<0.001	<0.001	<0.001

Ax-long = long axial axis, Ax-short = short axial axis, Cor-long = long coronal axis, Cor-short = short coronal axis, NACT = neoadjuvant chemotherapy, VM = volume.

TABLE 5. The Summaries of the kappa Values of Different Response Criteria

| | kappa Value | 95%CI | | Misclassify SD as OR | Misclassify OR as SD | *P* Value |
		Upper Limit	Lower Limit			
Ax-short	0.583	0.347	0.792	8	2	0.109
Ax-long	0.625	0.379	0.833	5	4	1.0
Cor-short	0.792	0.598	0.958	4	1	0.375
Cor-long	0.625	0.379	0.826	5	4	1.0

Ax-long = long axial axis, Ax-short = short axial axis, Cor-long = long coronal axis, Cor-short = short coronal axis, OR = odds ratio, SD = stan-standard deviation.

significantly larger than those on the axial planes ($P < 0.001$). However, the ratio of Cor-long to Ax-long was <2 in 97.9% of the target lesions. This is consistent with the study of Steinkamp et al who also observed that lymph nodes with L/T (the ratio of maximal longitudinal to maximal axial diameter) <2 provided an accurate assessment of malignant nodes.[16] Aforementioned results supported our clinical experiments that the pretreatment metastatic lymph node was an approximately round or elliptical conformation.

In the second part, with regard to the percentage change in 4 diameters, inconsistent shrinkage of target lesions in 4 directions was observed. Despite 4 diameters were all associated with VM at percentage change in size, the percentage changes of Ax-short were significantly higher than those of Ax-long, Cor-short, and Cor-long, whereas there was no significant difference in percentage changes of diameters among Ax-long, Cor-short, and Cor-long. These results indicated that the shrinkage of Ax-short axis was more rapid than the other 3 diameters. To our knowledge, it is the first study to evaluate the shrinking way of target lymph nodes after induction chemotherapy. However, which diameter is the optimal index to assess the treatment response needs further evaluation.

In the third part, with regard to tumor response according to the VM criterion, the results showed that the kappa values of Ax-short and Ax-long were both >0.46, indicating a good agreement. However, Ax-short has been confirmed to be more reproducible and less sensitive to spatial orientation of the lymph node when compared with Ax-long.[8,17] Moreover, many investigators have confirmed the role of short axis in axial images in diagnosing the malignant metastatic lymph nodes.[18–20] Thus, it was reasonable and accurate to take Ax-short instead of Ax-long in RECIST1.1 criteria. However, it should be noted that Ax-short may misclassify more nonresponders into response groups, which may amplify the therapeutic effect of anticancer drugs.

Interestingly, Cor-short showed the highest kappa value of 0.792, which corresponded to almost perfect agreement with VM. To the best of our knowledge, cervical lymph nodes have a caudal–cranial orientation that follows lymphatic drainage, and coronal images may be better aligned with this orientation.[21] Hence, it may be extrapolated from our findings that Cor-short is closer to the real short-axis in 3D model based on the caudal–cranial orientation, which resulted in perfect agreement of tumor response by volumetric criteria. Furthermore, there is an increasing amount of investigations confirming the role of coronal images in improving the diagnostic value of metastatic lymph nodes.[22,23] The incorporation of coronal images with current axial criteria into the assessment of tumor response may

have bright prospects, especially in caudal–cranial oriented head and neck lymph nodes.

Although the revised RECIST 1.1 has established uniform criteria concerning the number of target lesions and the size of lymph nodes to be measured, the standard of 2 target lesions per organ is a random and arbitrary selection and it has not been confirmed by any objective evidence. Hence, further study is still needed to investigate the optimal number of target lesions per organ to exactly assess the tumor response. Recently, a pooled analysis of data of advanced nonsmall cell lung cancer, gastric cancer, and colorectal cancer was performed to investigate the feasibility of measuring the single largest lesion per organ (mRECIST 1.1) to assess the tumor response. In the analysis, high concordance and the same OR rate of chemotherapy were found between the mRECIST and RECIST 1.1.[24] Analogous to this pooled analysis, the present study data also showed that mRECIST and RECIST criteria had good agreement with volumetric assessment criteria. However, mRECIST criteria needed to be further validated due to the small sample size.

To the best of our knowledge, it is the first study to validate the accuracy of RECIST 1.1 in assessing lymph nodal response. The present study results showed that Ax-short may be appropriate to be used to evaluate target lymph nodes after induction chemotherapy in patients with NPC. In addition, incorporation of the coronal diameters into the tumor assessment system was also studied. However, the present study has several limitations. First, the sample size of the present study remained small. Hence, further investigations involving larger sample sizes are needed to improve the statistical power and to achieve more meaningful results. In addition, although several studies have been conducted to validate the feasibility of sagittal plane in diagnosis,[25] the effect of using sagittal plane to assess tumor response remains unknown. Although the present study did prove that RECIST 1.1 was appropriate for evaluating the target lesions, it could be noteworthy to assess nontarget lesions and OR with RECIST 1.1 in subsequent studies. Finally, whether RECIST 1.1 can be applicable to the assessment of retropharyngeal lymph node (RLN) remains unknown. Given that RLNs frequently conglomerate with primary nasopharyngeal tumor, RLNs were excluded in this study. Conglomerated RLNs are difficult to measure objectively and reproducibly, such that many investigations are prone to contour RLNs with the primary tumor. Nevertheless, whether the shrinkage of RLNs is closer to the primary tumor or cervical lymph nodes has not been supported by any reliable evidence.

In conclusion, for patients with NPC, Ax-short may effectively reflect target lymph nodal burden or change in size, and

RECIST 1.1 may be applicable to assess the target lymph nodal response after induction chemotherapy. However, it should be noted that Ax-short may amplify the therapeutic response. In addition, Cor-short is an easy and quick measurement, but its role in the assessment of tumor response needs further evaluation.

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