



## Original Research



# Which evaluation criteria of the short-term efficacy can better reflect the long-term outcomes for patients with nasopharyngeal carcinoma?

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## ARTICLE INFO

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## ABSTRACT

**Purpose:** To compare the consistency of one-dimensional Response Evaluation Criteria in Solid Tumors (1D-RECIST), two-dimensional WHO criteria (2D-WHO), and three-dimensional (3D) measurement for therapeutic response assessment of nasopharyngeal carcinoma (NPC).

**Materials and methods:** Retrospective data of 288 newly diagnosed NPC patients were reviewed. Tumor size was assessed on magnetic resonance imaging (MRI) according to the 1D-RECIST, 2D-WHO, and 3D measurement criteria. Agreement between tumor responses was assessed using unweighted kappa statistics. The receiver operating characteristic (ROC) curve was used to determine the optimal cut-off point of the PTV. The Kaplan–Meier method and Cox regression were used for the survival analysis.

**Results:** The optimal cut-off point of the PTV for progression-free survival (PFS) was 29.6%. Agreement with PTV measurement was better for 1D measurement than for 2D and 3D measurements (kappa values of 0.646, 0.537, and 0.577 for 1D, 2D, and 3D measurements, respectively;  $P < 0.05$ ). The area under the curve of the 1D measurement (AUC=0.596) was similar to that of the PTV measurement (AUC=0.621). Compared with 2D and 3D measurements, 1D measurement is superior for predicting prognosis in NPC (C-index of 0.672, 0.663, and 0.646 were for 1D, 2D, and 3D measurements, respectively;  $P < 0.005$ ). Survival analysis showed that patients with non-responders had worse prognosis ( $P < 0.05$ ).

**Conclusions:** The 1D measurement more closely agreed with the PTV measurement than the 2D and 3D measurements for predicting therapeutic responses in NPC. Therefore, we recommend using the less time-consuming 1D-RECIST criteria in routine clinical practice.

## Introduction

Nasopharyngeal carcinoma (NPC) is a malignant tumor that is prevalent in southern China, where approximately 50–80 cases per 100,000 people are diagnosed each year [1]. Currently, the mainstay treatment for patients with NPC is radiotherapy, with or without chemotherapy [2]. However, tumor heterogeneity leads to variability in the tumor cells regarding their sensitivity to the same treatment

regimen, and approximately 20% to 30% of patients with NPC develop distant metastasis and/or recurrence after receiving the standard regimen [3]. Therefore, early monitoring of tumor response to therapy may help optimize treatment strategies and improve prognosis.

In recent years, induction chemotherapy (IC) has played a remarkable role in comprehensive treatment, owing to its ability to decrease tumor burden and improve survival [4]. Tumor volume changes during IC are closely related to the NPC prognosis, as patients who respond

**Abbreviations:** 1D-RECIST, one-dimensional Response Evaluation Criteria in Solid Tumors; 2D-WHO, two-dimensional WHO criteria; 3D, three-dimensional; NPC, nasopharyngeal carcinoma; IC, induction chemotherapy; CCRT, concurrent chemoradiotherapy; MRI, magnetic resonance imaging; PTV, primary tumor volume; ROC, receiver operating characteristic; PFS, progression-free survival; AJCC, American Joint Committee on Cancer; RR, relative reduction rate; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; C-index, concordance index.

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poorly to IC have a greater risk of tumor recurrence and metastasis than those who respond well [3–5].

The best means for accurately measuring the tumor burden changes and tumor size has not been determined, and the topic remains a matter of controversy [6–11]. Currently, 1D-RECIST criteria and 2D-WHO measurement guidelines are usually applied to evaluate treatment response. These methods are considered reliable for observing tumor burden changes for spherical masses, but most NPCs grow and shrink asymmetrically. To this end, some studies have proposed a three-dimensional (3D) measurement method suitable for use with irregularly shaped tumors [12,13]. However, to the best of our knowledge, there are no reports on 3D measurements for evaluating treatment response in NPC patients.

Therefore, the aim of the study was to compare the agreement of 1D, 2D, and 3D measurements in evaluating the therapeutic response of NPC with the standard of reference. In addition, we evaluated the prognostic value of early treatment response, aiming to guide clinicians in adjusting treatment plans.

## Method and materials

### Patients

We retrospectively analyzed patients with newly diagnosed NPC treated at the Fujian Cancer Hospital in mainland China between January 2015 and September 2016. The main inclusion criteria were as follows: patients (1) were pathologically confirmed as having NPC; (2) had no evidence of distant metastasis at initial diagnosis; (3) had recorded with complete clinical, laboratory, and follow-up data; (4) had undergone treatment with at least two cycles of IC, followed by intensity-modulated radiation therapy (IMRT) and concurrent chemotherapy; and (5) all underwent MRIs before and after two cycles of IC. Patients were reclassified according to the staging system described in the eighth edition of the American Joint Committee on Cancer (AJCC).

This study was conducted under the ethical guidelines of the Helsinki Declaration and was approved by the Fujian Cancer Hospital's Ethics Committee (K2021-074-01). The committee waived the requirement for individual informed consent because the patient medical data and follow-up data were extracted retrospectively.

### Measuring method

All patients had undergone MRI scans in a 3.0-T MultiTransmit Whole Body scanner (Achieva TX, Philips Healthcare, Best, The Netherlands) before and after IC. Based on the axial and coronal pre-contrast T1-weighted, postcontrast T1-weighted, and T2-weighted images of nasopharyngeal MRI, the boundary of the primary nasopharynx was identified. In the case of enhancement gradient, a point is selected to start the measurement, where there is a clear transition from non-enhancement to enhancement. In the case of non-enhanced cysts around the enhanced area, we used the same criteria to measure the longest diameter of the enhanced tumor regardless of the location of the cysts. The primary nasopharynx lesion was delineated and measured by an experienced radiation oncologist. When there were disputes about the measurements (such as the boundary between the nasopharyngeal lesion and the retropharyngeal lymph node was unclear), the other two doctors who had been engaged in clinical diagnosis of head and neck tumors for at least 15 years evaluated the MRI and resolved differences through consensus. 1D, 2D, and 3D measurements were defined as follows (unmeasurable lesions should not be included in the measurements):

1D: The longest diameter of the nasopharynx lesion measured in the axial plane.

2D: The product of the largest diameter and greatest perpendicular diameter in axial planes.

3D: The product of the largest diameter and greatest perpendicular diameter in axial planes and the greatest perpendicular diameter in coronal planes.

As a reference standard, primary tumor volume (PTV) was obtained using the Oncentra MasterPlan® v3.3 SP1. The whole tumor, including any portion invading the bony skull base, was included in the measurement.

The relative reduction rate (RR) in tumor size after two cycles of IC was determined according to the following formula:  $RR = (\text{pre-treatment value} - \text{post-treatment value}) / \text{pre-treatment value}$ . Tumor response was assessed as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD), as listed in Table 1, according to 1D-RECIST, 2D-WHO, and 3D criterion for therapeutic response thresholds [10,14,15]. Responders were defined as patients with CR or PR; non-responders were defined as patients with SD or PD.

### Treatment methods

All patients enrolled in this study had received at least two cycles of platinum-based neoadjuvant chemotherapy. The regimens included gemcitabine (1000 mg/m<sup>2</sup>, on days 1 and 8) plus platinum (80 mg/m<sup>2</sup>, on day 2), or paclitaxel (135 mg/m<sup>2</sup>, day 1) plus cisplatin (80 mg/m<sup>2</sup>, day 2). Concurrent chemotherapy had been administered to all the patients repeatedly (every three weeks).

Each patient had also received IMRT, with a prescribed dose of 70 Gy at 2.0–2.25 Gy/fraction in 31–35 fractions. The target volume and radiotherapy dose were implemented according to the institutional treatment protocol previously defined by our center [16]. Clinical target volume 1 (CTV-1) was defined as the high-risk region that included gross tumor volume (GTV) and nasopharyngeal mucosa plus 5 mm submucosal volume. Clinical target volume 2 (CTV-2) was designed for potentially involved regions, such as the nasopharyngeal cavity, maxillary sinus, pterygopalatine fossa, skull base, inferior sphenoid sinus, cavernous sinus, the anterior third of the clivus, and the cervical region.

### Follow-up and statistical analysis

All patients were assessed every three months during the first two years after completing CCRT, every six months in the next three to five years, and annually thereafter. The primary clinical endpoint was progression-free survival (PFS), defined as the time from diagnosis to the time of disease progression or death from any cause.

The receiver operating characteristic (ROC) curve was used to determine the optimal cut-off point of the PTV, and patients were divided into responders and non-responders. Bland-Altman plots were used to compare the bias between the 1D, 2D, and 3D measurements and the PTV measurement. Agreement between responders and non-responders was assessed using the concordance rate and k statistics.

**Table 1**

Definition of response categories for different measurement methods.

Response Category	1D criteria <sup>a</sup>	2D criteria <sup>b</sup>	3D criteria <sup>c</sup>
Non-responders			
PD	RR% ≤ -20	RR% ≤ -25	RR% ≤ -40
SD	-20 < RR% < 30	-25 < RR% < 50	-40 < RR% < 65
Responders			
PR	30 ≤ RR% < 100	50 ≤ RR% < 100	65 ≤ RR% < 100
CR	RR% = 100	RR% = 100	RR% = 100

Note: RR% = percentage of relative reduction of tumor size.

<sup>a</sup> Based on RECIST 1.1 guidelines.

<sup>b</sup> Based on WHO guidelines.

<sup>c</sup> According to correlation of alteration in surficial area to alteration in volume. Abbreviations: CR: complete response; PR: partial response; SD: stable disease; PD: disease progression.

The prognostic value of these four assessment methods was compared using the concordance index (C-index). The Kaplan–Meier method was used for survival analysis, and the difference between survival curves was evaluated using a log-rank test, and multivariate survival analysis was performed using the Cox proportional hazards model. All data analyses were performed using the SPSS v.26 and R version 4.0.3. The violin plots, Kaplan–Meier curve and correlation plots were performed by using Hiplot (<https://hiplot.com.cn>). Statistical significance was defined as a two-sided  $P$ -value  $< 0.05$ .

## Results

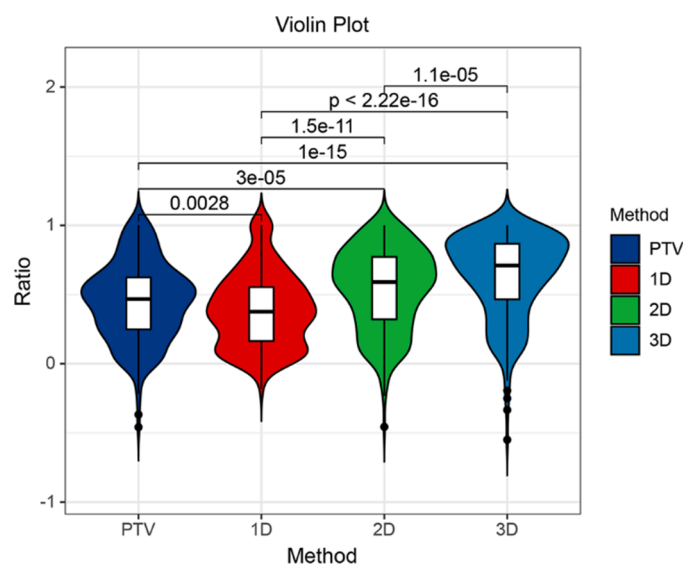
### Patient characteristics

A total of 288 eligible patients were enrolled in this study (Supplementary Fig. 1). The median age of this sample was 48 years (range, 15–68 years). Approximately 92.36% (266/288) of the patients were diagnosed with advanced-stage NPC (stages III to IV). The patient characteristics are summarized in supplementary Table 1. The median follow-up time was 55 months (range, 15–70 months). Of the 288 patients with NPC, 37 (12.8%) experienced recurrence, 41 (14.2%) had metastasis, and 12 patients (4.2%) had both recurrence and metastasis during the follow-up period. The three-year OS and PFS rates were 93.8% and 79.2%, respectively.

### Agreement between percentage reduction measurements

Before the start of treatment, the median maximum diameter of the NPC lesion was 4.02 cm (range, 1.15–8.63 cm) with 1D-RECIST measurement; the median cross-sectional area was 9.37 cm<sup>2</sup> (range, 0.81–36.97 cm<sup>2</sup>) with 2D-WHO measurement and the median cubic volume, based on 3D measurement, was 28.24 cm<sup>3</sup> (range, 0.75–249.56 cm<sup>3</sup>). The median tumor volume based on volume rendering was 23.89 cm<sup>3</sup> (range, 1.82–170.10 cm<sup>3</sup>). After two cycles of IC, the median maximum tumor diameter was 2.40 cm (range, 0.0–6.83 cm), the median cross-sectional tumor area was 3.60 cm<sup>2</sup> (range, 0.0–28.96 cm<sup>2</sup>), and the median tumor cubic volume was 7.34 cm<sup>3</sup> (range, 0.0–160.72 cm<sup>3</sup>). The median tumor volume was 12.91 cm<sup>3</sup> (range, 0.0–121.69 cm<sup>3</sup>).

The distribution of the relative reduction in the tumor burden is



**Fig. 1.** Violin plots of percentage changes in tumor size across patients for the four methods. Violin plots show median (black bars), quartiles (upper and lower borders in the white box), and density estimation (the fatter the image, the more concentrated the data) for each distribution.

shown in Fig. 1. The median of PTV, 1D, 2D, and 3D measurements was 46.70% (-45.86% – +100%), 37.60% (-18.34% – +100%), 59.02% (-45.65% – +100%), 70.99% (-54.97% – +100%), respectively. The Bland–Altman plot demonstrates that the mean differences between 1D and PTV measurements were the smallest (bias: 0.06) and closest to the zero line. The mean (lower and upper limits) for 1D, 2D, and 3D Bland–Altman plots were -0.06(0.30 to -0.42), 0.09(0.45 to -0.26), and 0.19 (0.54 to -0.17), respectively ( $P < 0.001$ ). Therefore, the 1D measurement had a significantly higher agreement with the PTV measurement than the 2D measurement ( $P < 0.05$ ), and the 2D measurement had higher agreement than the 3D measurement ( $P < 0.05$ ), as shown in Fig. 2.

### Agreement between methods for response assessment

The optimal cut-off point of PTV for PFS was at 29.6% (AUC = 0.621,  $P < 0.05$ ). The cut-off value was used to distinguish responders from non-responders with changes in PTV of  $> 29.6\%$  and  $\leq 29.6\%$ , respectively. We defined responders (CR, PR) and non-responders (SD, PD) based on changes in the relative reduction in tumor burden according to 1D-RECIST, 2D-WHO, and 3D measurement therapeutic response thresholds. When PTV was used as the reference standard, the concordance rate for 1D response evaluation was 83.33% (240 of 288), 78.13% (225 of 288) for 2D measurement, and 79.51% (229 of 288) for 3D measurement (Supplementary Table 2). The agreement was excellent for PTV measurement and 1D measurement, with a  $k$  value of 0.646; agreement was moderate for 2D measurement and 3D measurement, with  $k$  values of 0.537 and 0.577, respectively (Supplementary Table 3). A total of 89 patients (30.90%) were classified as non-responders with PTV measurement, 107 (37.15%) with the 1D-RECIST, 112 (38.89%) with the 2D-WHO, and 120 (41.67%) with the 3D measurement (Supplementary Fig. 2). When using volume measurement as the standard of reference, higher dimensions underestimated the tumor response to IC. Therefore, the 1D measurement had significantly better agreement with the PTV measurement compared to the 2D and 3D measurements.

### The comparison of the prognostic value

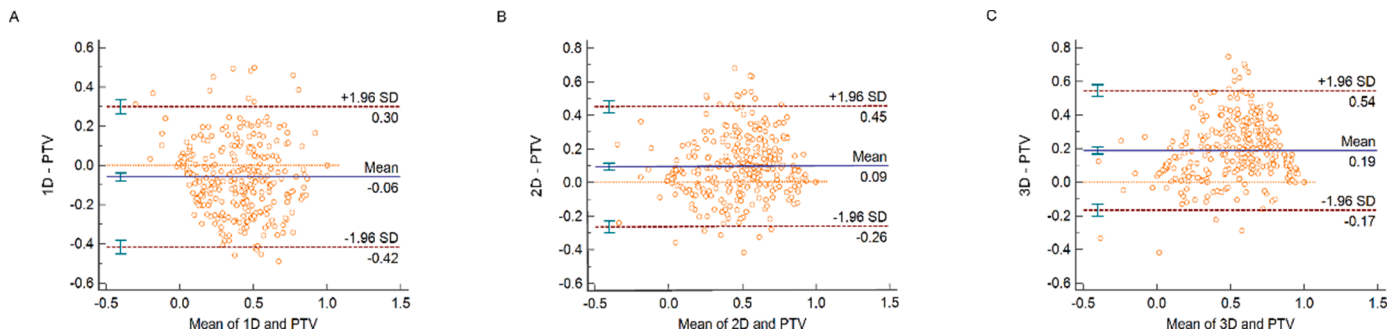
As indicated in Fig. 3, the ROC curves were generated to compare the prognostic value of PTV, 1D, 2D, and 3D measurements for PFS. Our study results show that AUC values of the tumor response based on PTV, 1D, 2D, and 3D measurements were very similar (AUC values were 0.621, 0.596, 0.593, and 0.583, respectively). However, 1D measurements were higher than 2D and 3D measurements, indicating that 1D measurement is superior to 2D and 3D measurements for predicting prognosis in NPC after IC. Moreover, similar results were obtained with C-index analysis (C-index of 0.723, 0.672, 0.663, and 0.646 for PTV, 1D, 2D, and 3D measurements, respectively ( $P < 0.005$ ), as shown in Table 2.

### Univariate and multivariate analyses

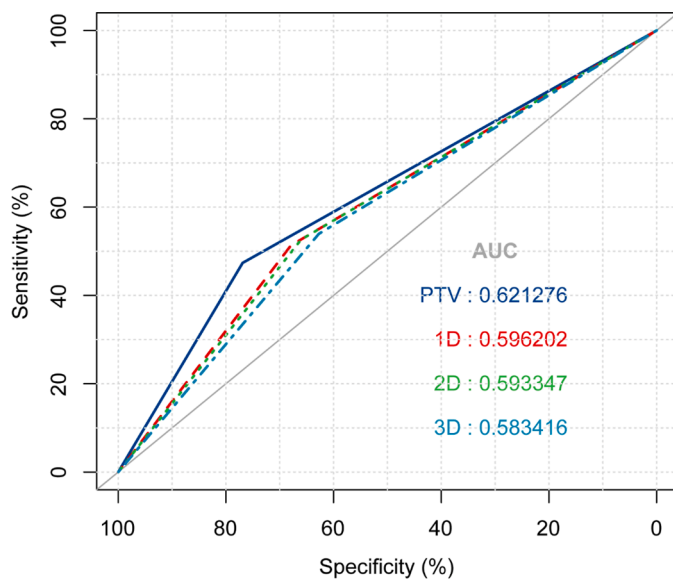
Univariate analysis showed that the four measurement criteria were significantly correlated with the PFS. The 3-year PFS between responders and non-responders defined by PTV, 1D, 2D, and 3D measurements were 84.2% vs. 67.1%, 83.4% vs. 72.0%, 83.5% vs. 72.3%, and 82.7% vs. 74.2%, respectively (Fig. 4, all  $P < 0.01$ ). The following six factors, which were considered to significantly affect prognosis, were included in further multivariate analysis: sex, age, T-stage, N-stage, clinical, and EBV DNA level after IC. Multivariate Cox analysis indicated that the four measurement methods were independent prognostic factors for PFS (Table 3).

## Discussion

Response assessments must be highly sensitive to provide early



**Fig. 2.** Bland-Altman plots. Comparison of the percentage change of tumor size on the basis of 1D-RECIST, 2D-WHO, and 3D measurements with volume-based tumor size percentage reduction. Solid line shows bias and broken line show 95% levels of agreement (mean  $\pm$  1.96 standard deviation of the differences): (A) PTV-1D measurement; (B) PTV-2D measurement; (C) PTV-3D measurement.



**Fig. 3.** Receiver operating characteristic (ROC) curve analysis for comparing the prognostic value of PTV, 1D, 2D, and 3D measurement in progression-free survival. Abbreviations: AUC, area under ROC curve.

**Table 2**

The Harrell's concordance index (C-index) of the comparison of the predictive accuracies of PTV, 1D, 2D, and 3D measurement.

Method	Harrell's C-Index (95%CI)	P-Value
PTV	0.723(0.631–0.816)	<0.001
1D	0.672(0.571–0.773)	<0.001
2D	0.663(0.561–0.765)	0.002
3D	0.646(0.541–0.750)	0.006

Abbreviation: 1D, one-dimensional response evaluation criteria in solid tumors; 2D, two-dimensional WHO criteria; 3D, three-dimensional; PTV, primary tumor volume; CI, confidence interval.

identification of non-responders during a period when other interventions can still affect prognosis. Patients with unfavorable clinical responses can be managed with more intensive systemic therapies such as adjuvant chemotherapy [17], targeted therapy, and immunotherapy [18,19] to improve prognosis as much as possible. Currently, measuring changes in tumor volume is considered the most effective method for evaluating the therapeutic response [6]. However, volumetric tumor measurements require downloading images and manually delineating tumor boundaries, which is not practical for clinical applications. Based on what is known about the use and validation of simple methods and suggestions that 3D measurement may be more effective for evaluating

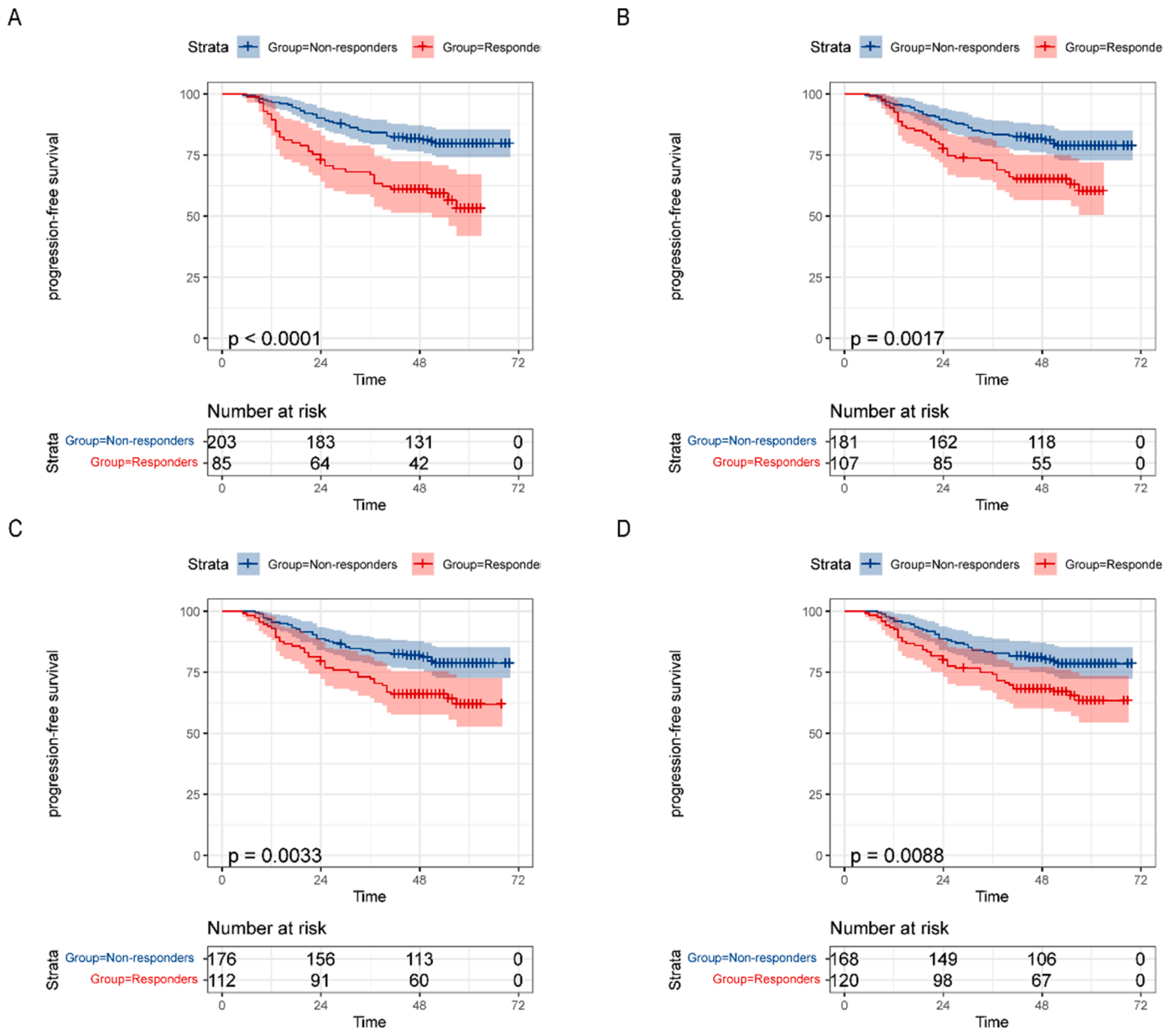
treatment response in patients with certain cancers [12], we investigated the agreement between 1D, 2D, and 3D measurements with PTV measurement and further compared their prognostic value.

In comparing various measurements of tumor size before and after IC in patients with NPC, our results showed that 1D, 2D, and 3D measurements were all significantly correlated with PTV measurement, but the 1D measurements more closely agree with PTV measurements than the others. Specifically, the AUC values of 1D measurements were higher than those of 2D and 3D measurements, indicating that 1D measurement is superior for predicting prognosis in NPC after IC. Similar results were obtained with the C-index analysis. Moreover, there were significant differences in PFS between responders and non-responders, as defined by the four measurement criteria. The results further showed that each measurement was an independent prognostic factor for PFS in the multivariate cox analysis. These results indicated that 1D measurement, a more widely used and quicker method than PTV, is sufficient for assessing tumor response.

It is well known that NPCs are prone to invade the bone, such as the skull base, clivus, petrous apex, or pterygoid process. In our study, PTV measurements included the area of bone infiltration; this area was excluded in the 1D-RECIST, 2D-WHO, and 3D criteria. Our results were consistent with previous studies that showed that PTV measurement was more sensitive than other measurements for detecting tumor non-response in NPC [6,20]. Although bone lesions are considered unmeasurable lesions using 1D, 2D, and 3D measurement criteria, there is still a significant correlation between linear measurements and PTV measurement. Compared with 2D and 3D measurements, 1D measurements showed better agreement with the PTV measurements. As the irregularity of the tumors increases the error in measuring each of the dimensions, and the calculation formula of high dimension measurement compounded the errors, these complications due to the nature of tumor type may explain why 2D and 3D measurements have limited sensitivity to tumor response. Conversely, the 1D tumor response assessment was better for identifying patients who did not respond to therapy and had a poor prognosis. Therefore, considering the high degree of agreement between PTV and 1D measurements, the latter are preferred because they are relatively easy to perform and readily available in a clinical context. In these regards, our results are consistent with those of previous studies that indicate 1D measurements might be suitable for assessing clinical response in NPC.

In a study by Liang et al. [8], the maximum primary tumor diameter was determined to be an important prognostic factor. Likewise, Liu et al. [3] found that poor IC response was associated with poor prognoses when 1D measurement was used to assess tumor response. Furthermore, Liu et al. [21] confirmed that early radiological responses assessed by 1D-RECIST criteria can be used to predict OS and PFS in patients with metastatic NPC. However, these conclusions contradict those of the recent studies. For example, Zeng et al. [6] found that early responses measured with 1D measurements have no prognostic value for NPC. In





**Fig. 4.** Survival curves of 288 patients with different treatment response based on PTV, 1D, 2D, and 3D criteria (responder and non-responder) in progression-free survival: (A) PTV measurement; (B) 1D measurement; (C) 2D measurement; (D) 3D measurement.

addition, King et al. [10] and Chang et al. [9] found that the 2D-WHO criterion had a better agreement than the 1D-RECIST criterion in evaluating the treatment response. One reason for the ambiguity between our results and these is the different measurement ranges. Also, some authors have included lymph nodes in their analyses; however, the positive lymph nodes with a short axis ( $\leq 15$  mm) but with central necrosis or extracapsular invasion were considered non-target lesions according to the RECIST 1.1 criteria, limiting the applicability of the 1D-RECIST criteria for reflecting the changes in lymph nodes [22,23]. Second, compared with CT imaging, MRI can enhance soft-tissue contrast resolution and provide a more accurate assessment of the parapharyngeal space, paranasal sinus, cranial invasion, and skull base. Therefore, previous studies on tumor response assessment based on CT techniques have had some limitations. Finally, an insufficient sample size may result in insufficient statistical power.

Compared with volume measurements, there are fewer responders based on 1D measurements. The reasons for 1D measurements' underestimation of tumor response to IC are as follows: 1D measurement

excludes the area of bony invasion, but PTV measurement includes areas of bony invasion; thus, 1D assessment may lead to significant information loss. In addition, as the tumor shrinks, the depth of the tumor perpendicular to the pharyngeal cavity may decrease, whereas the extent along the length of the pharyngeal wall may remain the same [10]; therefore, 1D measurements may underestimate the true tumor response.

We recognize several limitations of our research. First, this was a retrospective study performed at a single institution, and selection bias was inevitable. Therefore, further prospective multicenter and large-scale studies are needed to validate our findings. Second, tumor necrosis is an indicator of prognosis in various cancers, including NPC [24], but MRI has limited resolution capacity restricting its ability to distinguish between tumors and necrosis, cystic regions, and edema in the early stages of treatment. In this respect, the metabolic tumor response on positron emission tomographic (PET)/computed tomography (CT) images can provide an advantage [25]. The development of PET/MR technologies may provide more comprehensive information about the

**Table 3**  
Cox regression model of multivariable analysis for progression-free survival.

Variable		Hazard Ratio (95%CI)	P
Test for PTV			
sex	Female vs. Male	0.677(0.408–1.121)	0.130
age	≤50 vs. >50	1.745(1.092–2.787)	0.020
T stage	T1-T2 vs. T3-T4	0.854(0.504–1.449)	0.558
N stage	N0-N1 vs. N2-N3	1.205(0.735–1.975)	0.460
TNM stage	II–III vs. IV	1.479(0.925–2.364)	0.102
EBV DNA	Undetectable vs. Detectable	1.674(1.049–2.671)	0.031
PTV	Non-responder vs. Responder	2.516(1.570–4.030)	<0.001
Test for 1D			
sex	Female vs. Male	0.725(0.442–1.191)	0.204
age	≤50 vs. >50	1.703(1.070–2.713)	0.025
T stage	T1-T2 vs. T3-T4	0.859(0.504–1.464)	0.575
N stage	N0-N1 vs. N2-N3	1.084(0.663–1.775)	0.747
TNM stage	II–III vs. IV	1.442(0.900–2.312)	0.128
EBV DNA	Undetectable vs. Detectable	1.699(1.059–2.727)	0.028
1D	Non-responder vs. Responder	1.853(1.154–2.976)	0.011
Test for 2D			
sex	Female vs. Male	0.689(0.417–1.138)	0.146
age	≤50 vs. >50	1.721(1.080–2.745)	0.023
T stage	T1-T2 vs. T3-T4	0.873(0.513–1.485)	0.616
N stage	N0-N1 vs. N2-N3	1.107(0.676–1.815)	0.686
TNM stage	II–III vs. IV	1.460(0.912–2.337)	0.115
EBV DNA	Undetectable vs. Detectable	1.747(1.094–2.790)	0.019
2D	Non-responder vs. Responder	1.846(1.150–2.962)	0.011
Test for 3D			
sex	Female vs. Male	0.702(0.426–1.159)	0.167
age	≤50 vs. >50	1.748(1.096–2.787)	0.019
T stage	T1-T2 vs. T3-T4	0.866(0.506–1.480)	0.598
N stage	N0-N1 vs. N2-N3	1.114(0.679–1.827)	0.669
TNM stage	II–III vs. IV	1.470(0.917–2.356)	0.109
EBV DNA	Undetectable vs. Detectable	1.776(1.113–2.834)	0.016
3D	Non-responder vs. Responder	1.740(1.085–2.791)	0.022

Abbreviation: 1D, one-dimensional response evaluation criteria in solid tumors; 2D, two-dimensional WHO criteria; 3D, three-dimensional; PTV, primary tumor volume; EBV, Epstein–Barr virus; CI, confidence interval.

lesion than routine MR techniques, thereby improving the overall sensitivity of 1D assessment. In addition, the combined application of computer-assisted technology may be able to solve this problem well, and it deserves to be explored in future studies. Lastly, we did not evaluate the tumor response threshold that best correlated with the outcomes. In this study, we followed the respective therapeutic response thresholds using the RECIST, WHO, and 3D criteria. Whether the cut-off values need to be redefined requires further research in the context of this type of tumor and treatment.

## Conclusion

In conclusion, all four measurement methods for evaluating early tumor response were proven to be important in prognostic factors for patients with NPC. However, the 1D measurement more closely agreed with the PTV measurement than the 2D and 3D measurements in predicting the therapeutic response in NPC. Therefore, we recommend using the less time-consuming 1D-RECIST criteria in routine clinical practice, as their application could drive changes to therapeutic strategy choices for patients identified as non-responders.

## Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Ethics approval and consent to participate

This study was approved by the ethics committee of Fujian Medical University Cancer Hospital, Fuzhou, China (K2021-074-01).

## CRediT authorship contribution statement

**Li-qin Ma:** Methodology, Formal analysis, Writing – original draft, Data curation, Writing – review & editing. **Hai-xia Wu:** Methodology, Formal analysis, Writing – original draft. **Xiang-quan Kong:** Writing – review & editing, Formal analysis. **Zhao-dong Fei:** Formal analysis, Writing – review & editing, Methodology, Formal analysis, Writing – original draft. **Wei-ning Fang:** Writing – review & editing. **Kai-xin Du:** Writing – review & editing. **Fei Chen:** Data curation, Writing – review & editing. **Dan Zhao:** Writing – review & editing. **Zhu-peng Wu:** Writing – review & editing.

## Declaration of Competing Interest

The authors report no conflicts of interest in this work.

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## Supplementary materials

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