Dual-Energy CT Iodine Map in Predicting the Efficacy of Neoadjuvant Chemotherapy for Hypopharyngeal Carcinoma: A Preliminary Study

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Article

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Abstract

Background: Induction chemotherapy has become one of the important means for advanced hypopharyngeal carcinoma. So far, there is no effective index to predict the curative effect. To investigate the value of normalized iodine map of dual-energy computed tomography (CT) in predicting the efficacy of neoadjuvant chemotherapy for hypopharyngeal carcinoma.

Methods: A total of 54 hypopharyngeal carcinoma patients who underwent two courses of TPF induction chemotherapy were recruited in this study. 3 cases had a complete response (CR), 36 cases had a partial response (PR), 11 cases had stable disease (SD), and 4 cases had a progressive disease (PD) after the chemotherapy. All patients underwent a dual-source CT scan before chemotherapy and rescanned after chemotherapy. The normalized iodine-related attenuation (NIRA) of the mean of maximum slice and most enhanced region of lesion at arterial and parenchymal phase were measured: $NIRA_{\text{mean-A}}$, $NIRA_{\text{max-A}}$, $NIRA_{\text{mean-P}}$, and $NIRA_{\text{max-P}}$, respectively. Correlation analysis was conducted between different metrics of NIRA and the diameter change rate of lesions, and the curative effect was evaluated based on the receiver operating characteristic (ROC) curve.

Results: There were a significant correlation between $NIRA_{\text{mean-A}}$, $NIRA_{\text{max-A}}$, $NIRA_{\text{mean-P}}$, $NIRA_{\text{max-P}}$ and the change rate of lesion's maximum diameter ($\Delta D$%) (all $P<0.01$). The $NIRA_{\text{max-A}}$, $NIRA_{\text{mean-P}}$, $NIRA_{\text{max-P}}$ had significant differences between CR, PR, SD, PD groups, but $NIRA_{\text{mean-A}}$ did not reach a significant difference. All $NIRA_{\text{mean-A}}$, $NIRA_{\text{max-A}}$, $NIRA_{\text{mean-P}}$, $NIRA_{\text{max-P}}$ had significant differences between effective (CR+PR) and ineffective (SD+PD) groups. The ROC analysis revealed that $NIRA_{\text{mean-P}}$ had the largest AUC and prediction efficacy (AUC=0.809).

Conclusion: Dual-energy CT normalized iodine map could predict the efficacy of neoadjuvant chemotherapy and provides imaging evidence to assist in treatment decisions for hypopharyngeal carcinoma patients.

Introduction

The hypopharyngeal carcinoma is relatively rare and accounts for about 3% of all head and neck cancers (HNCs). But it has a poor prognosis among all the HNCs with a 30–35% 5-year overall survival (OS) rate[1]. Around 80% of the patients were already at stage III and IV of the disease at the time of admission; only a few cases were detected at an early stage due to its concealed site and the infiltrating growth. In recent years, a comprehensive treatment model of induction chemotherapy, followed by concurrent radiotherapy and chemotherapy or surgery significantly improved the larynx preservation rate of locally advanced patients and improved the life quality of patients. Thus, predict the efficacy of chemotherapy is crucial for the optimization of the treatment and to avoid unnecessary system toxicity, cost, and treatment delay. The evaluation of the efficacy of chemotherapy relies mainly on medical imaging. Dual-source dual-energy CT (DECT) could not only obtain single-energy images at different kVs, but also could calculate iodine maps through data processing from different kV images, and which might
explicate the tissue characteristics of local hypopharyngeal carcinoma quantificationally[2]. And it was already reported that the enhanced CT iodine map could evaluate histopathological invasiveness of lung cancer[3].

This study aimed to explore the predicting value of dual-source DECT in the evaluation of the efficacy of neoadjuvant chemotherapy for hypopharyngeal carcinoma.

**Material And Methods**

**Patients**

A total of 54 patients (50 males and 4 females, age range: 42 ~ 81 years old) were recruited in this study in our Hospital from September 2014 to July 2019. All patients were pathologically confirmed presented hypopharyngeal squamous cell carcinomas, including 48 cases at piriform fossa (88.9%), 5 cases (9.2%) at posterior pharyngeal wall, and 1 case (1.9%) at postcricoid region. All patients were given induction chemotherapy with two courses of the modified TPF regimen (Docetaxel + Nedaplatin + Flurouracil). The study was conducted according to the principles expressed in the Declaration of Helsinki. All patients provided a written informed consent to participate in the study approved by the Ethics Committee of Tianjin First Central Hospital.

Inclusion criteria: (1) admitted to hospital due to hypopharyngeal neoplasms; (2) pathologically confirmed as hypopharyngeal carcinoma; (3) without any systematic treatment at the first diagnosis; (4) had no contraindications to chemotherapy and agreed to receive neoadjuvant chemotherapy; (5) underwent the dual-source DECT plain and enhanced scan prior to neoadjuvant chemotherapy, and rescanned within one week after the end of the second chemotherapy course.

Exclusion criteria: (1) poor image quality due to artifacts or other factors; (2) neoadjuvant chemotherapy was not performed on time because of complication, contraindication or adverse reaction of chemotherapy; (3) less than two courses of neoadjuvant chemotherapy due to other reasons.

**Scan settings**

The SOMATOM Definition Dual-source CT (DSCT; Siemens, Forchheim, Germany) was used to perform a routine plain and dual-energy enhanced scan. Patients lay in a prone position, breathed calmly, and were asked not to cough or swallow during CT scan. The plain scan was performed firstly, followed by an enhanced scan in dual-energy mode. A mechanical high-pressure syringe was used to inject the iodine contrast agent (350 mgI/ml) through the elbow vein with a flow of 3ml/s, dose 1 ~ 1.5 ml/kg and followed by 35 ml physiological saline. The dual-phase enhanced scan was performed at 30 ~ 45s (arterial phase) and 80 ~ 90s (parenchymal phase) after injection in energy mode.

**Image post-processing**
The image data was transmitted to a Siemens workstation (Syngo MMwP 70971) for post-processing. The fusion image of anatomy and iodine map was obtained after loading to the Dual-Energy software. The maximum diameter of the tumor before and after chemotherapy was measured for three times. The averaged diameter was recorded as \( D_{\text{Pre}} \) and \( D_{\text{Post}} \), and the change rate of maximum diameter was denoted as \( \Delta D\% \).

On the iodine map of the maximum slice of lesion, the iodine-related attenuation (IRA) of the mean of the lesion and most enhanced region were measured for three times. The averaged IRA of the whole lesion in this slice and most enhanced region in the arterial phase and parenchymal phase were recorded as \( \text{IRA}_{\text{mean-A}}, \text{IRA}_{\text{max-A}}, \text{IRA}_{\text{mean-P}} \) and \( \text{IRA}_{\text{max-P}} \). Moreover, these metrics were normalized by the IRA value of the common carotid artery on the same side of the lesion and denoted as \( \text{NIRA}_{\text{mean-A}}, \text{NIRA}_{\text{max-A}}, \text{NIRA}_{\text{mean-P}} \), and \( \text{NIRA}_{\text{max-P}} \) in percentage, respectively. The region of interests (ROIs) of most enhanced region were about 8mm\(^2\) in general and should include ten voxels at least for the minimum lesions, avoiding the gas, blood vessels, bones, cysts, and necrosis.

**Evaluating Metrics**

1. Change rate of lesion's maximum diameter (\( \Delta D\%) \) = (the tumor's maximum diameter before chemotherapy (\( D_{\text{Pre}} \)) - the tumor's maximum diameter after chemotherapy (\( D_{\text{Post}} \)) ) / the tumor's maximum diameter before chemotherapy (\( D_{\text{Pre}} \)) \times 100\%

2. Normalized iodine-related attenuation (NIRA) = iodine value of each period / iodine value of common carotid artery in the same period \times 100\%

3. According to Response Evaluation Criteria in Solid Tumors (RECIST), 1) complete response (CR): all lesions disappeared without any new lesion; 2) partial response (PR): the sum of the longest diameter of the measurable lesions is reduced by \( \geq 30\% \), and no new lesions appear; 3) stable disease (SD): lesion decline is less than PR or lesion increase is less than that of the progressive disease; 4) progressive disease (PD): the longest diameter of the measurable lesions is increased by \( \geq 20\% \), or new lesion appears. The CR + PR were considered effective while SD + PD were ineffective.

**Statistical analysis**

Data analyses were conducted using SPSS25.0 software, and the correlation analysis used the Spearman correlation method. Independent-sample Kruskal-Wallis test and independent-sample Mann-Whitney U test were used for enumeration data, and \( P < 0.05 \) indicated a statistically significant difference. The receiver operating characteristics curve (ROC) was plotted for curative effect evaluation, and the sensitivity, specificity, the area under the curve (AUC), and the optimal cutoff value were calculated. A combination of AUC > 0.5 and \( P < 0.05 \) in the ROC curve indicated a significant difference.

**Results**

**General information of patients**
All 54 patients, including 3 cases of CR, 36 cases of PR, 11 cases of SD, and 4 cases of PD, completed neoadjuvant chemotherapy and underwent CT scans as required. These patients were classified into effective and ineffective groups (n = 39 and 15, respectively). The information about the patients and diameter changes of the lesions were summarized in Table 1. Figure 1 showed a 66-year-old male patient with left piriform fossa carcinoma who had a partial response after chemotherapy. Figure 2 showed a 70-year-old male patient with right piriform fossa progressive carcinoma.

Table 1. Information of patients and diameter changes of the lesions

<table>
<thead>
<tr>
<th></th>
<th>Effective</th>
<th></th>
<th>Ineffective</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CR</td>
<td>PR</td>
<td>SD</td>
<td>PD</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>64.67 ± 15.57</td>
<td>60.89 ± 9.16</td>
<td>66.27 ± 9.57</td>
<td>67.50 ± 5.80</td>
<td>62.69 ± 9.52</td>
</tr>
<tr>
<td>Male/Female</td>
<td>3/0</td>
<td>34/2</td>
<td>10/1</td>
<td>3/1</td>
<td>50/4</td>
</tr>
<tr>
<td>D&lt;sub&gt;Pre&lt;/sub&gt;</td>
<td>2.50 ± 0.94</td>
<td>3.11 ± 0.97</td>
<td>3.07 ± 1.36</td>
<td>2.59 ± 0.48</td>
<td>3.03 ± 1.02</td>
</tr>
<tr>
<td>D&lt;sub&gt;Post&lt;/sub&gt;</td>
<td>0.00 ± 0.00</td>
<td>1.11 ± 0.63</td>
<td>2.49 ± 1.06</td>
<td>3.65 ± 0.72</td>
<td>1.52 ± 1.13</td>
</tr>
<tr>
<td>ΔD%</td>
<td>1.00 ± 0.00</td>
<td>0.63 ± 0.17</td>
<td>0.19 ± 0.12</td>
<td>-0.42 ± 0.27</td>
<td>0.48 ± 0.37</td>
</tr>
</tbody>
</table>

Note: CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; D<sub>pre</sub>: the diameter of the tumor before chemotherapy; D<sub>post</sub>: the diameter of the tumor after chemotherapy.

Normalized iodine-related attenuation (NIRA) and response evaluation (RECIST)

Spearman analysis revealed there were a significant correlation between NIRA<sub>mean−A</sub>, NIRA<sub>max−A</sub>, NIRA<sub>mean−P</sub>, NIRA<sub>max−P</sub> and the change rate of lesion's maximum diameter (ΔD%) (all P < 0.01, Fig. 3).

Further Kruskal-Wallis test on the NIRA<sub>mean−A</sub>, NIRA<sub>max−A</sub>, NIRA<sub>mean−P</sub>, NIRA<sub>max−P</sub> between different postchemotherapy response groups showed that NIRA<sub>max−A</sub>, NIRA<sub>mean−P</sub>, NIRA<sub>max−P</sub> had significant differences between CR, PR, SD, PD groups (all P < 0.01), but NIRA<sub>mean−A</sub> did not reach a significant difference (P = 0.05) (Fig. 4 and Table 2).
To evaluate the efficacy of neoadjuvant chemotherapy, all the cases were divided into effective group (CR + PR) and ineffective group (SD + PD). And Mann-Whitney U test revealed that all NIRA<sub>mean−A</sub>, NIRA<sub>max−A</sub>, NIRA<sub>mean−P</sub>, NIRA<sub>max−P</sub> had significant differences between effective and ineffective groups (Table 3).

### Table 3

Comparison of NIRAs between effective and ineffective groups.

<table>
<thead>
<tr>
<th>groups</th>
<th>NIRA&lt;sub&gt;mean−A&lt;/sub&gt;</th>
<th>NIRA&lt;sub&gt;max−A&lt;/sub&gt;</th>
<th>NIRA&lt;sub&gt;mean−P&lt;/sub&gt;</th>
<th>NIRA&lt;sub&gt;max−P&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>ineffective</td>
<td>0.153 ± 0.055</td>
<td>0.189 ± 0.060</td>
<td>0.330 ± 0.129</td>
<td>0.438 ± 0.180</td>
</tr>
<tr>
<td>effective</td>
<td>0.198 ± 0.084</td>
<td>0.257 ± 0.127</td>
<td>0.496 ± 0.157</td>
<td>0.609 ± 0.190</td>
</tr>
<tr>
<td>P value</td>
<td>0.022</td>
<td>0.030</td>
<td>&lt; 0.001</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Note: NIRA, Normalized iodine-related attenuation; NIRA<sub>mean−A</sub>, the mean NIRA of maximum slice of lesion at arterial phase; NIRA<sub>max−A</sub>, the NIRA of most enhanced region of lesion at arterial phase; NIRA<sub>mean−P</sub>, the mean NIRA of maximum slice of lesion at parenchymal phase; NIRA<sub>max−P</sub>, the NIRA of most enhanced region of lesion at parenchymal phase.

**ROC analysis and predicting the efficacy of neoadjuvant chemotherapy**

The ROC analysis revealed that all NIRA<sub>mean−A</sub>, NIRA<sub>max−A</sub>, NIRA<sub>mean−P</sub>, NIRA<sub>max−P</sub> could be used to predicting the efficacy of neoadjuvant chemotherapy (AUC > 0.5, P < 0.05). The NIRA<sub>mean−P</sub> had the largest AUC and prediction efficacy (AUC = 0.809) (Fig. 5 and Table 4). This indicated that Dual-energy CT
iodine enhancement could be valuable to predict the efficacy of neoadjuvant chemotherapy for hypopharyngeal carcinomas.

Table 4
The ability of different NIRA parameters in predicting the efficacy of neoadjuvant chemotherapy

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>P</th>
<th>Cut-off value</th>
<th>sensitivity</th>
<th>specificity</th>
<th>Youden index</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIRA\textsubscript{mean−A}</td>
<td>0.703</td>
<td>0.022</td>
<td>0.148</td>
<td>0.821</td>
<td>0.600</td>
<td>0.421</td>
</tr>
<tr>
<td>NIRA\textsubscript{max−A}</td>
<td>0.692</td>
<td>0.030</td>
<td>0.236</td>
<td>0.538</td>
<td>0.800</td>
<td>0.338</td>
</tr>
<tr>
<td>NIRA\textsubscript{mean−P}</td>
<td>0.809</td>
<td>&lt;0.001</td>
<td>0.375</td>
<td>0.769</td>
<td>0.800</td>
<td>0.569</td>
</tr>
<tr>
<td>NIRA\textsubscript{max−P}</td>
<td>0.757</td>
<td>0.004</td>
<td>0.494</td>
<td>0.744</td>
<td>0.800</td>
<td>0.544</td>
</tr>
</tbody>
</table>

Note: AUC, area under the curve; NIRA, Normalized iodine-related attenuation; NIRA\textsubscript{mean−A}, the mean NIRA of maximum slice of lesion at arterial phase; NIRA\textsubscript{max−A}, the NIRA of most enhanced region of lesion at arterial phase; NIRA\textsubscript{mean−P}, the mean NIRA of maximum slice of lesion at parenchymal phase; NIRA\textsubscript{max−P}, the NIRA of most enhanced region of lesion at parenchymal phase.

For the different parametrics of NIRA, the mean NIRA of maximum slice showed larger AUC and Youden index than the most enhanced region of lesion at the same time phase. The NIRA at parenchymal phase had a larger area under the ROC curve and predicting specificity than the arterial phase, but the NIRA\textsubscript{mean−A} had a higher sensitivity. The best cutoff values of NIRA\textsubscript{mean−A}, NIRA\textsubscript{max−A}, NIRA\textsubscript{mean−P}, NIRA\textsubscript{max−P} were 0.148, 0.236, 0.375, and 0.494, respectively (Table 4).

Discussion

Hypopharyngeal cancer is a severe malignancy with a poor prognosis and mortality rate. Neoadjuvant chemotherapy is one of the major methods of comprehensive treatment of head and neck squamous cell carcinoma and has been advocated in recent years with satisfactory results[4]. The evaluation of the efficacy of chemotherapy as early as possible has an important significance for the treatment and prognosis of patients. Various functional techniques, including positron emission tomography (PET)[5–9] or magnetic resonance imaging (MRI) diffusion-weighted imaging[10, 11] or dynamic contrast-enhanced MRI[9, 10], and CT perfusion[12, 13] were employed to evaluate the metabolism, hypoxia, cellularity, and perfusion of tumor. Nonetheless, some drawbacks, such as high cost, long scanning time, and poor resolution of small lesions, limit the clinical application of these methods. As new technology emerged in recent years, dual-source DECT imaging assesses the degree of tumor vascularization[14]. The applications of DECT in head and neck carcinoma (HNC) has increased, and several studies have shown the benefit of iodine characterization and virtual monoenergetic images for the detection and delineation
of HNC[15, 16], differentiation between metastatic, inflammatory, and benign cervical lymph nodes[17–19], or assessment of cartilage invasion[20–22]. However, the role of DECT-derived quantitative imaging to predict oncological outcomes in hypopharyngeal squamous cell carcinoma has not yet been investigated.

The images obtained in this study were used to evaluate the efficacy based on the morphological changes of RECIST[23]; however, the internal tumor variation, such as liquefaction necrosis, is unable to make an effective assessment due to these limitations[24, 25]. The RECIST standard assesses the curative effect based on the change in the maximum tumor diameter, which might include tumor and necrotic areas, while the modified RECIST (mRECIST) standard uses “surviving tumors” as the evaluation criteria, excluding the affect of necrotics, recommended by 2010 EASL(European Association for the Study of the Liver) guidelines[26]. Dual-energy CT can obtain a series of derivative images, including iodine map, virtual non-enhanced image, single energy spectrum image, and nonlinear fusion image. Among these, the iodine-related attenuation measured in the iodine map quantificationally reflects the distribution and uptake of iodine in the lesion to reveal its blood supply condition. Moreover, the iodine-related attenuation is more reliable than the density value if the lesion is enhanced, for example the iodine-related attenuation is not affected by intratumoral hemorrhage. The content of iodine in the tissue can reflect its blood supply, and our results showed it might be a promising biological marker for evaluating the efficacy of chemotherapy. In this study, the patients with hypopharyngeal carcinoma with higher iodine-related attenuation were sensitive to induction chemotherapy. Zima et al.[27] reported that HNC with high perfusion were sensitive to radiotherapy and chemotherapy, which is consistent with the current conclusion. Thus, it could be postulated that the high perfusion state of tumor tissue can concentrate the local drug than the low perfusion state, thereby promoting the cell killing effect. The hypoperfusion state of tumor tissue might be considered as tumor ischemia and hypoxia, inducing the insensitivity to radiotherapy and chemotherapy.

Induction chemotherapy is one of the comprehensive treatment measures for advanced hypopharyngeal cancer. In 1991, the Laryngeal Cancer Group of American Veterans discovered the laryngeal function-sparing effects of chemotherapy and radiotherapy[28]. In 2003, the US RTOG 91–11 study confirmed that the laryngeal function-sparing rates of concurrent radiotherapy and chemotherapy (CRC), radiotherapy (RT), and induction chemotherapy + radiotherapy (IC + RT) were 84%, 66%, and 71%, respectively[29]. Currently, non-surgical treatments, including CRC, IC + RT, and RT combined with EGFR[30] are applied to preserve function in laryngeal and hypopharyngeal cancer patients. However, some patients not sensitive to chemotherapy should need surgery. So that evaluate the effectiveness of the chemotherapy and adjust the treatment plan in time are critical to the survival and prognosis of the patient. Currently, there is no effective method to predict the curative effect before induction chemotherapy. This study revealed that Dual-energy CT iodine map could be used to screen out the cases might have favorable effects before chemotherapy and avoid the inappropriate treatment plan for ineffective cases.
The RECIST morphological standard was as the reference to evaluate the tumor curative effect objectively. In order to eliminate the influence of the injection rate and dose of contrast agent among different individuals, a normalized iodine-related attenuation (NIRA) was applied in this study, which is the ratio of the iodine-related attenuation (IRA) in the ROI to the IRA in the carotid artery of the same layer. The present study showed that the NIRAs before chemotherapy was significantly related to the change of tumor diameter, including NIRA$_{\text{mean} - A}$, NIRA$_{\text{max} - A}$, NIRA$_{\text{mean} - P}$, and NIRA$_{\text{max} - P}$. For the different parametrics of NIRA, the NIRA at parenchymal phase had a larger area under the ROC curve and predicting specificity than the arterial phase, but the NIRA$_{\text{mean} - A}$ had a higher sensitivity. In addition to measuring the mean NIRA of maximum slice of lesion (NIRA$_{\text{mean}}$), we also measured the NIRA of most enhanced region of lesion (NIRA$_{\text{max}}$) at the arterial and parenchymal phases which might avoid the influence of necrosis within the tumor. But the results showed that NIRA$_{\text{mean}}$ had a better predicting effect than NIRA$_{\text{max}}$, implied that NIRA$_{\text{mean}}$ might be better to reflect the global characteristic of tumor. The ROC curve reflects the correlation between the sensitivity and specificity of different NIRA parametrics, thereby rendering it as a comprehensive indicator of the test’s accuracy[31]. Other researches also confirmed that vascular iodine concentration reflects the efficacy of chemotherapy drugs within the tissue[32–36]. Yang et al.[37] revealed that patients with higher $\lambda\text{HU}$ values had a significantly low risk of progression and local recurrence, and DECT could easily identify CR patients and aid in choosing the appropriate treatment regimen for advanced laryngeal and hypopharyngeal squamous cell carcinoma (LHSCC). Bahig et al.[38] reported that maximum iodine concentration of the primary tumor and the high volume and iodine concentration standard deviation of involved lymph nodes predict the local regional recurrence in LHSCC. Therefore, DECT provides valuable information to evaluate the response of hypopharyngeal carcinoma which might be important for the clinical implementation of individualized treatment. In addition, Ge et al.[39] compared the radiation dose of DECT and conventional CT scan mode and did not find any significant difference in the mean radiation dose between DECT and the conventional CT scan, indicating that DECT did not cause additional radiation damage and was safe and suitable for efficacy evaluation.

Nevertheless, the present study has several limitations. The evaluation was only for short-term efficacy, and the reliability of the results for the long-term prognosis requires further verification with large sample data. Using dual-source CT iodine-related measurement to predict the effect of chemotherapy is a universal law based on correlation, and its accuracy and feasibility need to be assessed for individual cases. Moreover, the accuracy of iodine-related attenuation measurement is hindered by several factors.

**Conclusions**

In summary, our study showed that DECT iodine-related quantitative parameters might be useful in clinical practice as a tool to stratify patients into appropriate treatment of neoadjuvant chemotherapy.

**Declarations**
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Author contributions:

Xianfeng Wei: the conception and design of the study, drafting the article.

Rui Cao: dual-source CT measurement, data statistical analysis.

Han Li: normalized iodine-related attenuation measurement.

Miaomiao Long: data statistical analysis.

Peipei Sun: collection of patients data.

Yongzhe Zheng: revising the article.

Li Li: design of the study and analysis and interpretation of data.

Jianzhong Yin: revising the article critically for important intellectual content, final approval of the version to be submitted.

Data availability statement: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Additional Information (including a Competing Interests Statement): The authors declare no competing interests. This study was funded by Tianjin Key Medical Discipline Construction Project.

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Figures

**Figure 1**

A representative hypopharyngeal cancer patient showed partial remission after neoadjuvant chemotherapy. (A) Axial CT image of arterial phase before chemotherapy showed an obviously enhanced...
tumor at left piriform fossa extending to the posterior pharynx wall and postcricoid region. (B) The iodine map of arterial phase before chemotherapy, the red color showed obvious iodine-related attenuation in the tumor. (C) Follow-up CT image after chemotherapy, the lesion at the left piriform fossa was significantly smaller.

Figure 2

A representative patient with progressive hypopharyngeal cancer. (A) Axial CT image of arterial phase before chemotherapy, showed a tumor at the right piriform fossa but no obvious enhancement. (B) The iodine map of arterial phase before chemotherapy, there was no obvious color in the lesion which implied a low iodine-related attenuation. (C) Follow-up CT image after chemotherapy, showed that the tumor at right piriform fossa was significantly enlarged.

Figure 3
Scatter plot to illustrate the correlation between normalized iodine-related attenuation (NIRA) and the change rate of lesion's maximum diameter (ΔD%) (Spearman analysis, all P<0.01).

**Figure 4**

Histogram of the NIRAmean-A, NIRAmax-A, NIRAmean-P, NIRAmax-P between CR, PR, SD, PD groups. NIRAmax-A, NIRAmean-P, NIRAmax-P had significant differences but NIRAmean-A did not reach a significant difference between different postchemotherapy response groups.

**Figure 5**

ROC analysis NIRAmean-A, NIRAmax-A, NIRAmean-P, NIRAmax-P to predict the efficacy of neoadjuvant chemotherapy. The area under the ROC curve of NIRAmean-P was the largest and the effect of efficacy evaluation was the best. The area under the curve of NIRAmax-P was slightly lower than NIRAmean-P followed by NIRAmean-A, and NIRAmax-A has the worst evaluation effect.