Section: Radiodiagnosis & Interventional Radiology

Original Research Article

EVALUATION OF CERVICAL LYMPH NODE METASTASIS IN HEAD AND NECK MALIGNANCIES USING CT PERFUSION

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ABSTRACT

Background: Cervical lymph node metastasis is a crucial prognostic factor in head and neck malignancies and significantly influences staging and treatment decisions. Conventional imaging modalities rely primarily on morphological criteria, which have limited sensitivity in detecting early or micrometastatic nodal disease. CT perfusion imaging provides functional assessment of tissue microvascular characteristics and may improve differentiation between metastatic and benign cervical lymph nodes.

Materials and Methods: This prospective observational study included 57 patients with newly diagnosed, untreated head and neck malignancies. All patients underwent contrast-enhanced CT and CT perfusion imaging of the neck. Quantitative perfusion parameters—blood flow, blood volume, mean transit time, and permeability surface—were assessed in cervical lymph nodes. Histopathology served as the reference standard. Conventional CT features and CT perfusion parameters were compared between metastatic and benign lymph nodes. Diagnostic performance was evaluated using receiver operating characteristic curve analysis.

Results: Histopathological analysis revealed metastatic involvement in 34 (59.6%) cervical lymph nodes. Conventional CT features such as nodal size, round shape, central necrosis, and extranodal extension showed significant association with metastatic nodes ($p < 0.05$). CT perfusion demonstrated significantly higher blood flow, blood volume, and permeability surface, along with lower mean transit time, in metastatic lymph nodes compared to benign nodes ($p < 0.001$). Receiver operating characteristic analysis showed excellent diagnostic performance, with permeability surface (AUC 0.91) and blood volume (AUC 0.90) yielding the highest accuracy. CT perfusion achieved higher sensitivity (88.2%), specificity (86.9%), and overall accuracy (87.7%) compared to conventional CT.

Conclusion: CT perfusion imaging significantly improves the detection and characterization of metastatic cervical lymph nodes in head and neck malignancies by providing functional information beyond conventional morphological assessment. Its integration into routine imaging protocols can enhance nodal staging accuracy and support improved clinical decision-making.

Keywords: CT perfusion; cervical lymph nodes; head and neck malignancies; metastasis; angiogenesis; computed tomography.

INTRODUCTION

Head and neck malignancies represent a significant global health burden, accounting for approximately 650,000 new cases and over 330,000 deaths annually worldwide.[1] Squamous cell carcinoma constitutes nearly 90% of these tumors, commonly arising from the oral cavity, oropharynx, hypopharynx, and larynx.[2] Cervical lymph node metastasis is one of the most critical prognostic determinants in head and neck cancers, reducing overall survival by nearly 50% when present and significantly increasing the risk of locoregional recurrence and distant metastasis.[3] Accurate detection and characterization of metastatic cervical lymph nodes are therefore essential for appropriate staging, treatment planning, and prognostication.

Conventional imaging modalities such as ultrasonography, contrast-enhanced computed tomography (CECT), and magnetic resonance imaging (MRI) primarily rely on morphologic criteria including nodal size, shape, internal necrosis, and extranodal extension to differentiate benign from malignant lymph nodes.[4] However, these size-based and structural parameters have limited sensitivity, as micrometastases may be present in morphologically normal-sized nodes, while reactive inflammatory nodes may be enlarged and mimic malignancy.[5] Positron emission tomography–computed tomography (PET-CT) provides functional information and improves staging accuracy, but its routine use is limited by high cost, limited availability, radiation burden, and reduced spatial resolution for small lymph nodes.[6]

CT perfusion (CTP) imaging has emerged as a promising functional imaging technique that evaluates tissue microvascular characteristics by analyzing dynamic contrast enhancement patterns. CTP allows quantitative assessment of perfusion parameters such as blood flow (BF), blood volume (BV), mean transit time (MTT), and permeability surface area product (PS).[7] Tumor angiogenesis, a hallmark of malignant transformation and metastatic spread, leads to increased neovascularity, abnormal vessel permeability, and altered hemodynamics, which can be objectively quantified using perfusion imaging.[8] Metastatic lymph nodes demonstrate higher blood flow and blood volume with increased capillary permeability compared to benign or reactive nodes due to tumor-induced angiogenesis.[9]

Several studies have demonstrated the utility of CT perfusion in primary head and neck tumors for assessing tumor aggressiveness, predicting treatment response, and differentiating recurrent disease from post-therapeutic changes.[10] However, the application of CT perfusion specifically for the evaluation of cervical lymph node metastasis remains relatively underexplored, with limited and heterogeneous data available. Early evidence suggests that perfusion parameters may improve diagnostic accuracy in differentiating metastatic from non-metastatic lymph nodes beyond conventional size criteria, particularly in borderline or subcentimeter nodes.[11]

Given the pivotal role of nodal staging in treatment decision-making—especially in determining surgical approach, extent of neck dissection, and the need for adjuvant radiotherapy or chemoradiotherapy—there is a growing need for imaging techniques that provide both anatomical and functional insights.[12] Incorporating CT perfusion into routine imaging protocols may enhance the detection of metastatic cervical lymph nodes, facilitate early and accurate staging, and ultimately contribute to improved patient outcomes.

In this context, the present study aimed to evaluate the role of CT perfusion imaging in the assessment of cervical lymph node metastasis in patients with head and neck malignancies, with particular emphasis on its ability to distinguish metastatic from benign lymph nodes using quantitative perfusion parameters.

MATERIALS AND METHODS

Study Design and Study Population

This prospective observational study was conducted in the Department of Radiodiagnosis of a tertiary care teaching hospital over a defined study period after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrollment. Patients with clinically or histopathologically suspected head and neck malignancies who were referred for contrast-enhanced computed tomography (CECT) of the neck were consecutively recruited for the study. Adult patients aged 18 years and above with newly diagnosed, untreated primary head and neck cancers and clinically palpable or radiologically detectable cervical lymph nodes were included. Patients who had received prior surgery, radiotherapy, or chemotherapy to the head and neck region, those with known allergy to iodinated contrast media, impaired renal function, pregnancy, or inability to cooperate during scanning were excluded from the study.

Reference Standard for Nodal Status

Histopathological examination of lymph nodes obtained either by fine-needle aspiration cytology (FNAC), core needle biopsy, or surgical neck dissection was considered the reference standard for determining metastatic involvement. In cases where multiple lymph nodes were present, the largest or most suspicious node on imaging was selected for correlation. Lymph nodes were classified as metastatic or benign based on histopathological findings, and imaging results were correlated accordingly (Figure 1).

CT Acquisition Protocol

All patients underwent imaging on a multidetector CT scanner using a standardized protocol. Initial non-contrast CT of the neck was performed followed by contrast-enhanced CT and CT perfusion imaging. Patients were positioned supine with the neck slightly extended to minimize motion artifacts. Conventional CECT images were acquired from the skull base to the thoracic inlet using standard parameters including tube voltage of 120 kVp, automatic tube current modulation, slice thickness of 0.625–1.25 mm, and a pitch appropriate for neck imaging. Nonionic iodinated contrast medium was administered intravenously at a dose of approximately 1.5 mL/kg body weight using a power injector at a flow rate of 4–5 mL/s, followed by a saline flush.

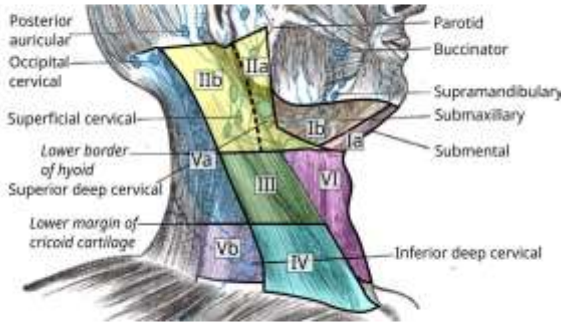

Figure 1: Anatomical Diagram of Cervical Lymph Node Levels (Levels I–VI). Schematic illustration of the standardized cervical lymph node levels used for nodal staging in head and neck malignancies (based on the American Joint Committee on Cancer / Union for International Cancer Control classification). Level Ia (submental), Ib (submandibular), II (upper jugular), III (middle jugular), IV (lower jugular), V (posterior triangle), and VI (anterior compartment) are labelled

CT Perfusion Technique

CT perfusion imaging was performed targeting the cervical lymph node of interest identified on prior conventional CT images. A limited z-axis coverage was selected to reduce radiation exposure while ensuring adequate coverage of the node. Dynamic acquisition was initiated simultaneously with intravenous injection of contrast medium, typically using 40–50 mL of nonionic contrast at a flow rate of 5 mL/s, followed by a saline chaser. Sequential images were acquired at short temporal intervals over a duration sufficient to capture the arterial inflow and venous outflow phases. Patients were instructed to breathe gently and avoid swallowing during image acquisition to minimize motion artifacts.

Image Post-Processing and Perfusion Analysis

CT perfusion data were transferred to a dedicated workstation (IntelliSpace Portal, Philips Healthcare, Best, The Netherlands) equipped with CT perfusion analysis software. Motion correction algorithms were applied prior to analysis. An arterial input function was obtained by placing a region of interest (ROI) over a major cervical artery, usually the common or internal carotid artery. Another ROI was placed over a venous structure to generate the venous output function. Freehand or circular ROIs were carefully drawn within the solid enhancing portion of the lymph node, avoiding areas of necrosis, calcification, or adjacent vessels. Quantitative perfusion parameters including blood flow (BF), blood volume (BV), mean transit time (MTT), and permeability surface area product (PS) were automatically calculated by the software using deconvolution algorithms. The average values from multiple ROIs within the node were recorded for analysis.

Image Interpretation

All images were independently reviewed by two experienced radiologists who were blinded to the histopathological results. Conventional CT criteria such as nodal size, shape, presence of central necrosis, margin irregularity, and extranodal extension were assessed. CT perfusion parameters were recorded separately and compared between metastatic and benign lymph nodes. In cases of disagreement, a consensus reading was obtained.

Radiation Dose Considerations

Radiation dose parameters including volume CT dose index (CTDIvol) and dose-length product (DLP) were recorded for each examination. Efforts were made to minimize radiation exposure by restricting the perfusion scan length, optimizing tube current settings, and adhering to the ALARA (As Low As Reasonably Achievable) principle.

Statistical Analysis

Statistical analysis was performed using SPSS 20.0 statistical software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Perfusion parameters between metastatic and non-metastatic lymph nodes were compared using appropriate parametric or non-parametric tests based on data distribution. Receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic performance of CT perfusion parameters and to identify optimal cut-off values for differentiating metastatic from benign lymph nodes. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 57 patients with head and neck malignancies were included in the study. The mean age of the study population was 54.8 ± 11.2 years, with a male predominance (73.7%). The most common primary tumor site was the oral cavity (45.6%), followed by the oropharynx (19.3%), hypopharynx (15.8%), and larynx (14.0%). Squamous cell carcinoma was the predominant histological subtype, accounting for 91.2% of cases. Clinically palpable cervical lymph nodes were present in 68.4% of patients at presentation. [Table 1]

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population

Variable	Frequency (%)/Mean ± SD
Age (years)	54.8 ± 11.2
Age range (years)	32–78
Gender	

• Male	42 (73.7%)
• Female	15 (26.3%)
Primary tumor site	
• Oral cavity	26 (45.6%)
• Oropharynx	11 (19.3%)
• Hypopharynx	9 (15.8%)
• Larynx	8 (14.0%)
• Others	3 (5.3%)
Histology	
• Squamous cell carcinoma	52 (91.2%)
• Others	5 (8.8%)
Clinical nodal status	
• Palpable nodes	39 (68.4%)
• Non-palpable nodes	18 (31.6%)

SCC: squamous cell carcinoma.

Histopathological evaluation revealed metastatic involvement in 34 (59.6%) cervical lymph nodes, while 23 (40.4%) lymph nodes were benign or reactive in nature. Histopathology served as the reference standard for comparison with imaging findings in all cases. [Table 2]

Table 2: Histopathological Status of Cervical Lymph Nodes

Nodal status	Number (%)
Metastatic lymph nodes	34 (59.6%)
Benign/reactive lymph nodes	23 (40.4%)
Total	57 (100%)

Metastatic lymph nodes demonstrated significantly larger short-axis diameters compared to benign nodes (13.6 ± 3.1 mm vs 8.9 ± 2.4 mm; $p < 0.001$). Morphological features such as round nodal shape, central necrosis, irregular margins, and extranodal extension were significantly more frequent in metastatic lymph nodes. Central necrosis was observed in 61.8% of metastatic nodes compared to 8.7% of benign nodes ($p < 0.001$). Extranodal extension was exclusively seen in metastatic lymph nodes (26.5%), showing a statistically significant association with malignancy ($p = 0.006$). These conventional features showed significant association with metastatic involvement ($p < 0.001$ for size, round shape, and necrosis), though with lower overall diagnostic accuracy compared to CT perfusion (Table 3 and Figure 2).

Table 3: Association Between Conventional CT Morphological Features and Histopathological Nodal Status

CT Feature	Metastatic (n=34)	Benign (n=23)	p value
	Frequency (%)/Mean ± SD		
Mean short-axis diameter (mm)	13.6 ± 3.1	8.9 ± 2.4	<0.001
Round shape	26 (76.5%)	6 (26.1%)	<0.001
Central necrosis	21 (61.8%)	2 (8.7%)	<0.001
Irregular margins	18 (52.9%)	4 (17.4%)	0.009
Extranodal extension	9 (26.5%)	0 (0%)	0.006

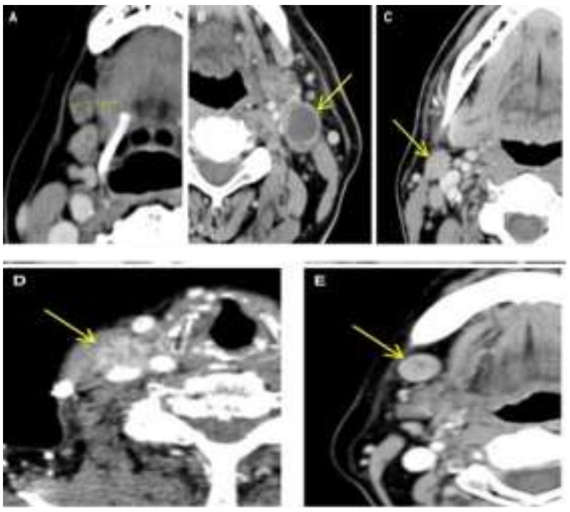

Figure 2: (A) Enlarged round lymph node with short-axis diameter >10 mm and central necrosis (arrow), highly suggestive of metastasis. (B) Lymph node demonstrating irregular margins with peripheral enhancing rim and central necrosis (C) Smaller, oval-shaped reactive/benign node without necrosis or irregular margins. (D)Node with clear extranodal extension and surrounding fat stranding (arrowheads), exclusively observed in metastatic cases. (E) Node with heterogenous enhancement with few interspersed necrotic foci within its core.

CT perfusion analysis demonstrated significantly higher blood flow, blood volume, and permeability surface values in metastatic lymph nodes compared to benign nodes ($p < 0.001$ for all). Mean blood flow was 78.4 ± 18.6 mL/100 g/min in metastatic nodes versus 42.7 ± 12.3 mL/100 g/min in benign nodes. Blood volume and permeability surface were also significantly elevated in metastatic nodes. Conversely, mean transit time was significantly lower in metastatic lymph nodes (5.8 ± 1.2 seconds) compared to benign nodes (7.9 ± 1.5 seconds; $p < 0.001$). These patterns match the significantly higher BF, BV, PS and lower MTT in metastatic versus benign nodes ($p < 0.001$), providing functional evidence beyond morphological criteria. (Table 4 and Figure 3).

Table 4: Comparison of CT Perfusion Parameters Between Metastatic and Benign Cervical Lymph Nodes

Parameter	Metastatic (n=34)	Benign (n=23)	p value
	Mean ± SD		
Blood Flow (BF) (mL/100 g/min)	78.4 ± 18.6	42.7 ± 12.3	<0.001
Blood Volume (BV) (mL/100 g)	6.2 ± 1.4	3.1 ± 0.9	<0.001
Mean Transit Time (MTT) (sec)	5.8 ± 1.2	7.9 ± 1.5	<0.001
Permeability Surface (PS) (mL/100 g/min)	18.6 ± 5.1	9.4 ± 3.2	<0.001

BF: blood flow; BV: blood volume; MTT: mean transit time; PS: permeability surface.

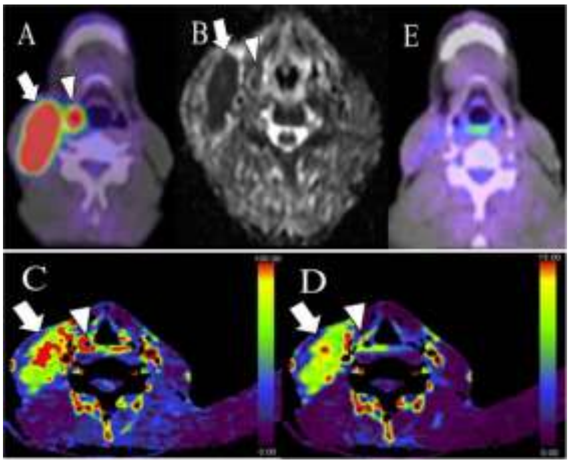

Figure 3: Axial CT perfusion images from representative cases of metastatic cervical lymph nodes in head and neck squamous cell carcinoma. (A) Blood flow (BF) map showing markedly elevated perfusion in the solid component of the metastatic node (red/orange high-flow regions, ~70–90 mL/100 g/min range). (B) Reference anatomical contrast-enhanced CT slice for correlation (enlarged, heterogeneously enhancing node with arrows indicating suspicious region). (C) Blood volume (BV) map demonstrating increased vascular volume (warm colors/yellow-red for high BV >5–6 mL/100 g). (D) Permeability surface (PS) map highlighting high capillary permeability due to angiogenesis (red/yellow high-PS areas >15–18 mL/100 g/min). (E) Mean transit time (MTT) map with shortened transit time in the metastatic node (cooler/blue regions <6 seconds, reflecting high-flow, low-resistance vasculature)

Receiver operating characteristic analysis revealed excellent diagnostic performance of CT perfusion parameters. Permeability surface demonstrated the highest diagnostic accuracy with an AUC of 0.91, followed by blood volume (AUC = 0.90) and blood flow (AUC = 0.88). Mean transit time showed comparatively lower but statistically significant diagnostic performance (AUC = 0.83). All perfusion parameters showed statistically significant discrimination between metastatic and benign lymph nodes (p < 0.001) (Table 5 and Figure 4).

Table 5: Diagnostic Performance of CT Perfusion Parameters in Detecting Metastatic Cervical Lymph Nodes

Parameter	Cut-off value	Sensitivity (%)	Specificity (%)	AUC (95% CI)	p value
Blood Flow (BF)	**>60 mL/100 g/min**	85.3	82.6	0.88 (0.78–0.96)	<0.001
Blood Volume (BV)	**>4.5 mL/100 g**	82.4	86.9	0.90 (0.81–0.97)	<0.001
Mean Transit Time (MTT)	**<6.5 sec**	79.4	78.3	0.83 (0.72–0.93)	<0.001
Permeability Surface (PS)	**>13 mL/100 g/min**	88.2	84.7	0.91 (0.83–0.98)	<0.001

AUC: area under the curve; ROC: receiver operating characteristic.

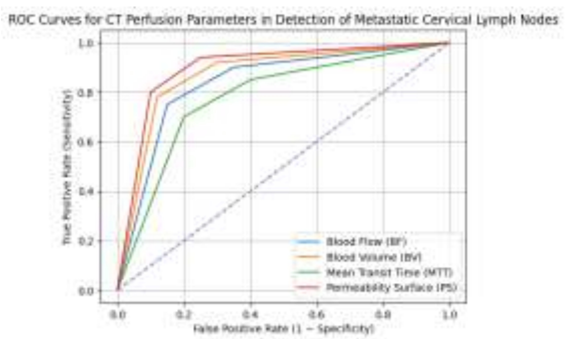

Figure 4: Receiver operating characteristic (ROC) curves of CT perfusion parameters for differentiation of metastatic and benign cervical lymph nodes

CT perfusion imaging demonstrated superior diagnostic performance compared to conventional CT. CT perfusion achieved higher sensitivity (88.2%), specificity (86.9%), and overall diagnostic accuracy (87.7%) compared to conventional CT, which showed sensitivity of 70.6%, specificity of 73.9%, and accuracy of 71.9%. [Table 6]

Table 6: Comparison of Diagnostic Accuracy Between Conventional CT and CT Perfusion

Modality	Sensitivity (%)	Specificity (%)	Accuracy (%)
Conventional CT	70.6	73.9	71.9
CT Perfusion	88.2	86.9	87.7

DISCUSSION

Accurate assessment of cervical lymph node metastasis is pivotal in the staging and management of head and neck malignancies, as nodal involvement significantly influences treatment decisions and prognosis. In the present study, CT perfusion imaging demonstrated superior diagnostic performance over conventional CT by providing functional insights into tumor angiogenesis, thereby enabling improved differentiation between metastatic and benign cervical lymph nodes.

The demographic profile of the study population reflects the epidemiological pattern of head and neck cancers in Indian studies by Chauhan et al., and Lakhera et al., with a clear male predominance and oral cavity being the most common primary site.[13,14] This distribution is consistent with previously published Indian studies by Yadav et al., and Gupta et al., where tobacco chewing and smoking are established etiological factors.[15,16] Squamous cell carcinoma constituted over 90% of cases, reinforcing the relevance of perfusion-based imaging techniques in evaluating this angiogenesis-driven malignancy.

Histopathological analysis revealed metastatic involvement in nearly 60% of cervical lymph nodes, highlighting the high burden of nodal disease at presentation in Indian patients.[17] This underscores the limitations of clinical examination alone and the need for reliable imaging biomarkers.[18] Conventional CT morphological criteria such as nodal size, round shape, central necrosis, and extranodal extension showed significant association with metastatic nodes in the present study. However, despite statistically significant correlations, these features are known to suffer from limited sensitivity, particularly in subcentimeter nodes and early metastatic disease. Similar observations have been reported in prior studies by Garg et al., Henson et al., and Pisani et al., where size-based criteria failed to detect micrometastases and reactive nodes mimicked malignancy.[18,19,20]

CT perfusion parameters demonstrated a marked ability to distinguish metastatic from benign lymph nodes. Metastatic nodes showed significantly higher blood flow, blood volume, and permeability surface values, along with reduced mean transit time, compared to benign nodes ($p < 0.001$ for all parameters). These findings can be explained by tumor-induced angiogenesis, characterized by increased microvascular density, dilated and tortuous vessels, and increased endothelial permeability.[21,22] Elevated blood flow and blood volume reflect increased neovascular supply, while higher permeability surface values indicate leaky tumor capillaries facilitating contrast extravasation. The reduction in mean transit time in metastatic nodes further supports the presence of high-flow, low-resistance vascular channels.[23,24]

These results are in agreement with previous CT perfusion studies by Suryavanshi et al., and Chaukar et al., conducted on primary head and neck tumors and metastatic lymph nodes, which have consistently reported higher perfusion parameters in malignant tissue compared to benign or inflammatory nodes.[25,26] Suryavanshi et al., and Chaukar et al., have demonstrated blood volume and permeability surface to be the most reliable indicators of malignancy, as they directly reflect angiogenic activity.[25,26] The present study corroborates these findings and extends their applicability to cervical lymph node evaluation.[25,26]

Receiver operating characteristic analysis further reinforced the diagnostic value of CT perfusion imaging. Permeability surface and blood volume demonstrated excellent diagnostic performance with AUC values exceeding 0.90, followed closely by blood flow. Mean transit time, although slightly inferior, still showed good discriminatory ability. These AUC values are comparable to or marginally better than those reported in prior studies by Mittal et al., and Bisdas et al., suggesting robust performance even within a modest sample size.[27,28] Importantly, the statistically significant p-values (<0.001) across all perfusion parameters indicate strong and consistent separation between metastatic and benign nodes.

When compared with conventional CT, CT perfusion imaging showed substantially higher sensitivity, specificity, and overall diagnostic accuracy. While conventional CT relies predominantly on morphological changes that may appear late in the disease course, CT perfusion captures early microvascular alterations associated with metastatic infiltration [28,29]. This functional advantage is particularly relevant in cases with equivocal nodal morphology, borderline nodal size, or absence of necrosis.

From a clinical standpoint, incorporation of CT perfusion into routine neck imaging protocols has the potential to improve nodal staging accuracy, reduce false-negative interpretations, and guide optimal treatment planning.[27] Improved identification of metastatic nodes may influence decisions regarding elective neck dissection, radiation field planning, and the need for adjuvant therapy.[30] Additionally, CT perfusion offers a practical alternative to PET-CT in resource-limited settings, providing functional information at lower cost and with wider availability.[30]

Limitations

Despite these strengths, the findings should be interpreted in the context of certain limitations, including limited z-axis coverage and radiation exposure inherent to perfusion imaging. Nevertheless, adherence to optimized protocols and ALARA principles can mitigate these concerns. Overall, the present study supports the growing body of evidence that CT perfusion is a valuable adjunct to conventional CT in the evaluation of cervical lymph node metastasis in head and neck malignancies.

CONCLUSION

CT perfusion imaging demonstrates significant diagnostic value in the evaluation of cervical lymph node metastasis in patients with head and neck malignancies. By providing quantitative functional parameters reflecting tumor angiogenesis, CT perfusion offers superior sensitivity, specificity, and overall diagnostic accuracy compared to conventional CT morphology alone. Elevated blood flow, blood volume, and permeability surface, along with reduced mean transit time, were reliable indicators of metastatic nodal involvement. Incorporation of CT perfusion into routine imaging protocols can enhance nodal staging accuracy, aid in early detection of metastatic disease, and facilitate optimal treatment planning. CT perfusion thus represents a valuable adjunct to conventional CT in the comprehensive evaluation of cervical lymph nodes in head and neck cancers.

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