Original Article

The potential advantages of ^{18}F sodium fluoride positron emission tomography-computed tomography for clinical staging and management planning in patients with nasopharyngeal carcinoma

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Background: The staging and treatment planning of nasopharyngeal carcinoma (NPC) face challenges due to limited sensitivity of conventional imaging. ^{18}F-sodium fluoride (^{18}F-NaF) positron emission tomography-computed tomography (PET/CT) offers potential advantages in detecting early bone involvement. This retrospective cohort study aimed to assess the potential advantage of ^{18}F-NaF PET/CT for clinical staging and management planning in patients with NPC and to compare ^{18}F-NaF PET/CT findings with those of conventional imaging modalities.

Methods: We enrolled a cohort of patients with NPC who underwent ^{18}F-NaF PET/CT at our PET/CT center between July 1, 2017, and June 30, 2021, and analyzed the findings of ^{18}F-NaF PET/CT and conventional imaging modalities. Data from multidisciplinary team discussions on clinical staging and management planning both before and after ^{18}F-NaF PET/CT were recorded. Additionally, any changes in clinical staging and management planning following ^{18}F-NaF PET/CT were documented.

Results: A total of 58 patients were included in this study. After ^{18}F-NaF PET/CT imaging, clinical tumor-node-metastasis (TNM) staging was observed to have changed in seven cases (12.1%). Among these, four cases had changes in T stage and three cases in the M stage. Additionally, changes in clinical management plans were observed in eight patients (13.8%). Changes due the results of ^{18}F-NaF PET/CT included three cases with major modification (two cases switched from curative treatment to palliative treatment, and one case switched from palliative treatment to curative treatment) and five cases with minor changes. The minor changes involved alteration to the radiotherapy target volume (three cases with an increased target volume and one case with a reduced target area). Furthermore, one case required an alteration to the radiotherapy strategy for local bone involvement.

Conclusions: The use of ^{18}F-NaF PET/CT in patients newly diagnosed with NPC may offer potential advantages for clinical staging and treatment planning, enabling physicians to select a more individualized treatment approach.

Keywords: Nasopharyngeal carcinoma (NPC); ^{18}F-sodium fluoride positron emission tomography-computed tomography (^{18}F-NaF PET/CT); clinical staging; management plan

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Introduction

Nasopharyngeal carcinoma (NPC) is a malignant tumor derived from the nasopharyngeal epithelial tissue. According to cancer statistics in 2020, there were 133,354 new cases of NPC reported worldwide, leading to 80,008 deaths (1). The distribution of NPC is uneven, with it being relatively rare in many regions; however, it remains a significant public health concern in East and Southeast Asian countries (2,3). In the early stages of NPC, radiotherapy can result in a high survival rate. For instance, the 5-year survival rate of patients with stage I NPC can reach up to 90%. However, approximately 70% of patients with NPC are diagnosed at an advanced stage of T3–4, and 30–65% of these patients may develop distant metastasis, leading to a variable 5-year survival rate ranging from 40% to 70% (4). The primary causes of death among these patients are uncontrolled local growth, recurrence, and distant metastasis. Accurate clinical staging of NPC plays a crucial role in treatment selection and prognosis assessment (2). The presence of bone metastasis or skull base bone invasion (SBBI) in NPC can affect its clinical staging. Therefore, accurate diagnosis of bone metastasis and SBBI in NPC is essential for precise clinical staging, as it can inform subsequent treatment decisions. Multiple imaging modalities are used for the clinical staging of NPC, including magnetic resonance imaging (MRI), computed tomography (CT), ^{99m}Tc-methylene diphosphonate (MDP) bone scintigraphy, ^{18}F-flurodeoxyglucose (FDG) positron emission tomography-computed tomography (PET/CT), and ^{18}F-sodium fluoride (^{18}F-NaF) PET/CT. ^{99m}Tc-MDP bone scintigraphy is a noninvasive, conventional imaging modality that is commonly applied for the detection of bone metastases. It has been widely recommended as a grade I examination technique for NPC in China (5). The European Society for Medical Oncology (ESMO) guidelines recognize ^{99m}Tc-MDP bone imaging as a critical diagnostic tool for evaluating bone metastases in patients with NPC, especially among at advanced stages of the disease (6). However, when compared to advanced imaging methods, such as MRI and ^{18}F-NaF PET/CT, this method exhibits lower spatial resolution (7). Our previous research established the diagnostic value of ^{18}F-NaF PET/CT in detecting bone metastasis and SBBI in NPC (8-10). In comparison to ^{99m}Tc-MDP bone scintigraphy, ^{18}F-NaF PET/CT demonstrates significantly higher diagnostic accuracy in the detection of bone metastasis in NPC (11). Furthermore, a study conducted by Le *et al.* demonstrated the superior diagnostic accuracy of ^{18}F-NaF PET/CT compared to MRI in diagnosing SBBI (12). However, the value of ^{18}F-NaF PET/CT in the tumor-node-metastasis (TNM) staging of NPC, particularly in terms of its effect on changes in the management plan, remains to be determined.

Therefore, the objective of this study was to assess the potential advantages of ^{18}F-NaF PET/CT for TNM staging and treatment planning in patients with NPC. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-1671/rc).

Methods

Patients

The enrollment process for this retrospective cohort study was as follows: all patients with pathologically confirmed NPC who had undergone ^{18}F-NaF PET/CT examinations at the Department of Nuclear Medicine (PET-CT center) of the Affiliated Hospital of Guangdong Medical University between July 1, 2017, and June 30, 2021, were included. The exclusion criteria were as follows: (I) previous administration of antitumor treatments such as chemotherapy or radiation therapy; (II) history of other malignancies; (III) unclear final diagnosis of bone lesions; (IV) no ^{99m}Tc-MDP bone scintigraphy; and (V) an interval between ^{18}F-NaF PET/CT and other conventional examinations of more than 14 days. A total of 58 patients were ultimately enrolled in this retrospective study. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of the Affiliated Hospital of Guangdong Medical University (No. PJXJS2022-003). Written informed consent was obtained from all the patients. A flowchart summarizing the patient inclusion process is provided in *Figure 1*.

^{18}F-NaF PET/CT examination

^{18}F-NaF PET/CT imaging was performed following the guidelines provided by the Society of Nuclear Medicine and Molecular Imaging and the European Association of Nuclear Medicine. The patients received an intravenous injection of approximately 200 MBq of ^{18}F-NaF. The PET data were acquired using a Discovery Elite 690 PET/CT scanner (GE HealthCare, Chicago, IL, USA) at a mean ± standard deviation (SD) time of 64±6 minutes after tracer

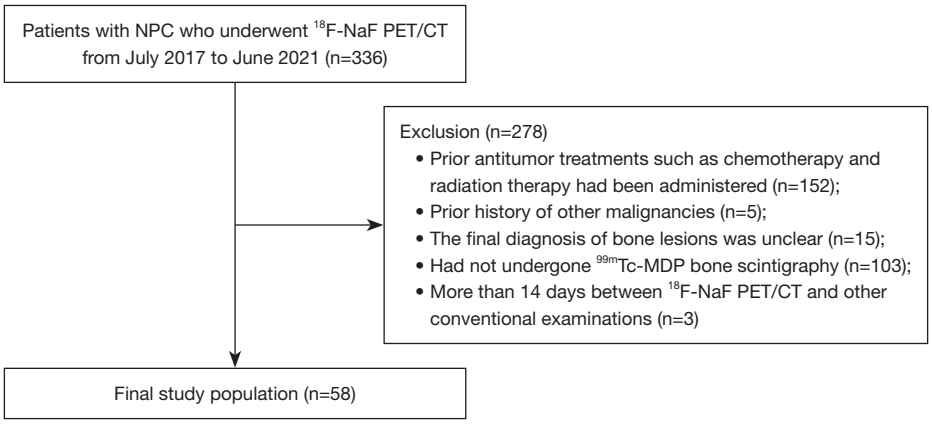

Figure 1 Patient selection and exclusion criteria flowchart for the initial study. NPC, nasopharyngeal carcinoma; ^{18}F-NaF PET/CT, ^{18}F-sodium fluoride positron emission tomography-computed tomography; ^{99m}Tc-MDP, ^{99m}Tc-methylene diphosphonate.

injection. A low-dose helical CT transmission scan was conducted under the following parameters: pitch, 0.984; current, 120–230 mAs; voltage, 120 kV; display field of view (FOV), 50.0 cm; slice thickness, 3.75 mm; and reconstructed slice thickness, 1.25 mm. The static emission scan spanned the entire body, with an acquisition time of 2 minutes per bed position with the Discovery-690 PET/CT scanner. The sinogram data from the CT scans were corrected for dead time, decay, and photon attenuation and then reconstructed into a 128×128 matrix. Image reconstruction was achieved using a fully three-dimensional (3D) maximum likelihood ordered subset expectation–maximization algorithm.

^{99m}Tc-MDP bone scintigraphy and MRI image acquisition

A ^{99m}Tc-MDP bone scintigraphy scan was conducted approximately 2–4 hours following the intravenous injection of 925 MBq (25 mCi) of ^{99m}Tc-MDP. The scan was obtained in both the anterior and posterior projections using a dual-head gamma camera (Symbia E, Siemens Healthineers, Erlangen, Germany) equipped with a low-energy, high-resolution collimator. The scan speed was set at 20 cm/min, with the photopeak centered at 140 keV and a 20% window. During the bone imaging procedure, six patients underwent single photon emission computed tomography (SPECT) to facilitate the precise localization of lesions.

MRI protocols

A 3 Tesla MRI scanner, equipped with an eight-channel head and neck coil (MR750, GE HealthCare), was used for MRI scans. The protocol included axial (parallel to the cranial base), sagittal, and coronal (parallel to the C3 vertebra) imaging orientations. The scanning series encompassed a comprehensive range of sequences: sagittal T1-weighted imaging (SAG-T1WI), axial T1WI (AX-T1WI), axial T2-weighted imaging (AX-T2WI), coronal short tau inversion recovery (COR-STIR), axial T1WI with contrast (AX-T1WIC+), coronal T1WI with contrast (COR-T1WIC+), and sagittal T1WI with contrast (SAG-T1WIC+).

Image interpretation and reference standard

Each patient's ^{18}F-NaF PET/CT and ^{99m}Tc-MDP bone scintigraphy images were independently interpreted by two board-certified nuclear medicine physicians who had extensive experience (evaluated over 3000 ^{18}F-NaF PET/CT scans as of the start of the study). Additionally, the MRI images of each patient were interpreted by a board-certified senior radiologist with 12 years of imaging experience. SBBI in NPC refers to the spread of cancer cells from the nasopharyngeal mucosa to the adjacent bones of the skull base (13). Distant bone metastasis in NPC refers to the dissemination of cancer cells to bones located away from the primary tumor site (2,14). The final diagnosis of SBBI and bone metastasis in the patients was established through a comprehensive evaluation of the imaging results (PET/CT, MRI, and CT) and clinical follow-up for at least 6 months.

Target delineation

The targets were delineated on the MRI and CT fused

Table 1 Clinical characteristics of patients with NPC

Characteristic	Values
No. of patients	58
Age (years), mean [range]	50.4 [28–67]
Stage, n (%)	
I	0
II	3 (5.2)
III	20 (34.5)
IVa	14 (24.1)
IVb	21 (36.2)

Clinical staging (stage I–IVb) was performed according to the eighth edition of the TNM classification of NPC for malignant tumors. NPC, nasopharyngeal carcinoma; TNM, tumor-node-metastasis.

images, with ^{18}F-NaF PET/CT images being used as a reference, whenever available. The gross target volume (GTV) of the primary tumor of the nasopharynx was manually outlined according to the images of CT and MRI by board-certified senior clinicians from the Department of Oncology. The GTV was calculated using the Pinnacle treatment planning system (Philips, Amsterdam, the Netherlands) with the summation-of-area technique.

Definition of changes in intended management

In the management of NPC, treatment approaches can be categorized into curative and palliative treatment strategies. Curative treatment typically involves administration of radiotherapy, often combined with neoadjuvant chemotherapy, with the aim of achieving a cure. Palliative treatment, on the other hand, focuses on symptom control and improving quality of life and may include systemic chemotherapy, immunotherapy, and targeted therapy. Treatment options can be further subclassified into major and minor adjustments based on the degree of change in the treatment plan. Major adjustments involve a significant shift in treatment strategy, such as transitioning from curative to palliative or vice versa. Minor adjustments, on the other hand, involve more nuanced changes, such as modifying the radiotherapy target volume of the primary nasopharyngeal tumor or the addition or omission of radiotherapy to bone metastases.

Impact of ^{18}F-NaF PET/CT on clinical stage and management planning

Clinical staging was performed according to the eighth edition of the TNM classification of NPC for malignant tumors (2,15). The institutional database was reviewed for all patients to determine the TNM staging and management plan after the first multidisciplinary conference. Subsequently, the management plan was determined after the second multidisciplinary conference, following the initial ^{18}F-NaF PET/CT scan. Prior to the initial ^{18}F-NaF PET/CT scan, the TNM staging and management plans relied on conventional imaging techniques, including CT or MRI, ^{99m}Tc-MDP bone scintigraphy, and ^{18}F-FDG PET/CT. A comparison of TNM staging and management plans before and after ^{18}F-NaF PET/CT was performed to evaluate its impact on the TNM staging and management planning.

Statistical analysis

All data are described as the mean (with range) and SD for continuous variables and numerical values (percentages) for categorical variables.

Results

Patients' clinical characteristics

A total of 58 patients were included in the analysis. Among these patients, 19 (32.8%) individuals were diagnosed with bone metastases. Based on the final results of ^{18}F-NaF PET/CT and clinical evaluation, patients' clinical characteristics are summarized in *Table 1*. Prior to treatment, all patients underwent routine MRI and ^{99m}Tc-MDP bone scans. Other staging images, including chest CT and ultrasound, are detailed in *Table 2*. These imaging modalities were used to evaluate the extent of the disease and aid in treatment planning.

Impact of ^{18}F-NaF PET/CT on TNM staging

Among the 58 patients with newly diagnosed NPC, 10.3% (6/58) showed changes in the number or location of lesions indicating SBBI when results from ^{18}F-NaF PET/CT combined with MRI were compared to diagnosis with MRI alone.

Table 2 Imaging modality preceding ^{18}F-NaF PET/CT

Imaging modality	Patients, n (%)
Head and neck MRI	58 (100)
^{99m}Tc-MDP bone scintigraphy	58 (100)
Chest CT	55 (94.8)
MRI (abdomen, spine, pelvis, etc.)	33 (56.9)
Abdominal ultrasound	35 (60.3)
^{18}F-FDG PET/CT	1 (1.7)
Others (X-ray etc.)	3 (5.2)

^{18}F-NaF PET/CT, ^{18}F-sodium fluoride positron emission tomography-computed tomography; MRI, magnetic resonance imaging; ^{99m}Tc-MDP, ^{99m}Tc-methylene diphosphonate; CT, computed tomography; ^{18}F-FDG, ^{18}F-flurodeoxyglucose.

Table 3 Impact of ^{18}F-NaF PET/CT on the staging of NPC

Staging	Patients, n	
	Before ^{18}F-NaF PET/CT	After ^{18}F-NaF PET/CT
T1	0	0
T2	12	10
T3	33	35
T4	13	13
M1	20	21
M0	38	37

^{18}F-NaF PET/CT, ^{18}F-sodium fluoride positron emission tomography-computed tomography; NPC, nasopharyngeal carcinoma.

Table 4 Impact of ^{18}F-NaF PET/CT on the management planning

Group	Pre-PET/CT		Post- PET/CT		PET/CT impact	
	Treatment goal	No. of patients	Treatment goal	No. of patients	Change in management	No. of patients (%)
1	Curative	38	Curative	36	Minor change[a]	4 (6.9)
			Palliative	2	Major change[b]	2 (3.4)
2	Palliative	20	Curative	1	Major change[b]	1 (1.7)
			Palliative	19	Minor change[a]	1 (1.7)

Minor change[a] therapies (including change in radiotherapy target volume). Major change[b] in therapy goal ("curative" *vs.* "palliative treatment"). ^{18}F-NaF PET/CT, ^{18}F-sodium fluoride positron emission tomography-computed tomography.

Five cases of NPC were additionally diagnosed with increased SBBI due to the detection of more lesions with ^{18}F-NaF PET/CT as compared to with MRI alone. The degree of SBBI was considered less severe in one case after ^{18}F-NaF PET/CT combined with MRI was performed; this was mainly because MRI indicated NPC invasion of the clivus, while ^{18}F-NaF PET/CT showed irregular increased density of the clivus with no NaF uptake, which was suggestive of a benign bone lesion. A follow-up MRI performed 6 months after treatment included no change in the signal of the clivus lesion, confirming the diagnosis as a benign bone lesion. In terms of T stage, 4 patients (6.9%) experienced alterations, with three cases upstaged from T2 to T3 and one case downstaged from T3 to T2. Additionally, 3 patients (5.2%) had changes in M stage, with one case adjusted from M1 to M0 and two cases adjusted from M0 to M1. Overall, adjustments in clinical TNM stage occurred in 7 patients (12.1%). The impact of ^{18}F-NaF PET/CT on the staging of NPC is summarized in *Table 3*.

Impact of ^{18}F-NaF PET/CT on management planning

Of the 58 patients with NPC, 8 (13.8%) had modifications in their treatment regimens. Among these, three patients underwent major changes, with one patient shifting from palliative to curative treatment and two transitioning from curative to palliative treatment. Five patients required minor adjustments in their treatment schedules. Among them, four patients had modifications in the radiotherapy target zones for nasopharyngeal primary lesions, and one patient needed adjustments in radiotherapy for local bone metastases. Among these cases, the radiotherapy target volume of the nasopharyngeal primary lesion was increased in three patients. In contrast, the radiotherapy target volume of the primary lesion was reduced in one patient. Additionally, radiotherapy for local bone metastases was cancelled in one patient. The impact of ^{18}F-NaF PET/CT on the management planning of NPC is summarized in *Table 4*.

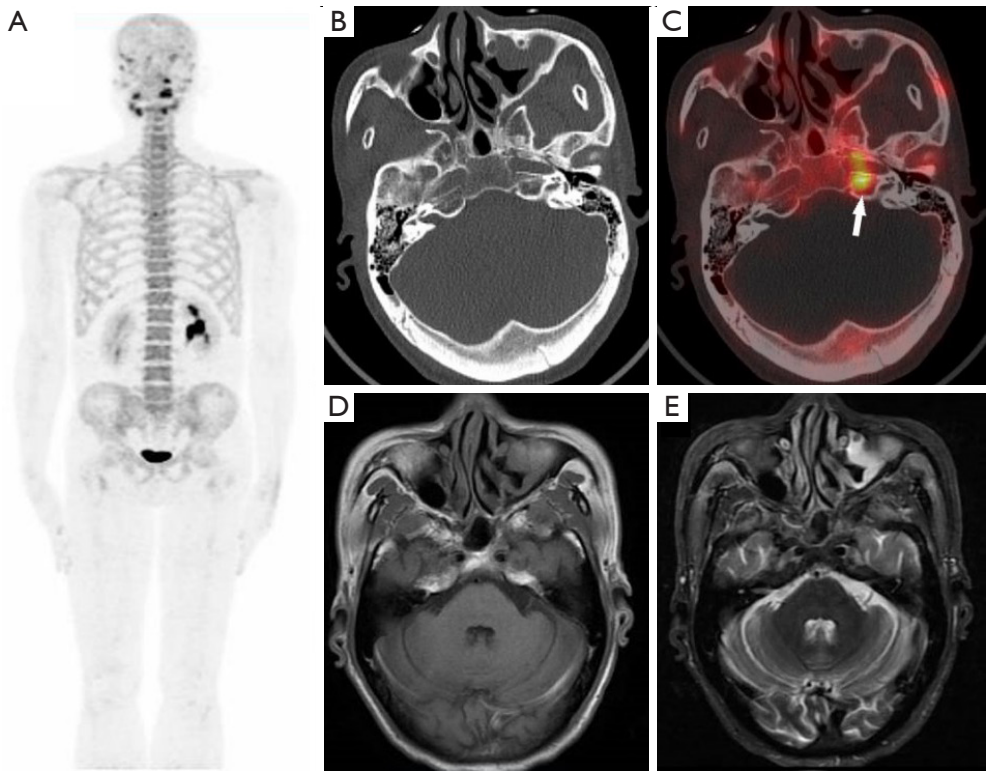

Figure 2 A 46-year-old male patient with NPC who underwent staging evaluation. Initial ^{18}F-NaF PET MIP imaging (A) did not reveal any evidence of bone metastasis. CT imaging (B) and subsequent ^{18}F-NaF PET/CT fusion imaging (C, arrow) demonstrated abnormal accumulation in the petrous part of the left temporal bone suggestive of SBBI by NPC. MRI with T1-weighted imaging (D) and T2-weighted imaging (E) did not reveal any abnormal signals in the skull base bone. Based on the MRI findings, the patient was initially classified as T2 stage NPC. However, upon the integration of the ^{18}F-NaF PET/CT and MRI data, the tumor staging was revised to T3. NPC, nasopharyngeal carcinoma; ^{18}F-NaF PET/CT, ^{18}F-sodium fluoride positron emission tomography-computed tomography; MIP, maximum intensity projection; CT, computed tomography; SBBI, skull base bone invasion; MRI, magnetic resonance imaging; ^{99m}Tc-MDP, ^{99m}Tc-methylene diphosphonate.

Discussion

Head and neck MRI is a commonly used modality for visualizing peripheral tissue involvement and determining the T stage in patients with NPC. It is the preferred imaging technique in clinical practice due to its excellent soft tissue contrast resolution and ability to assess the extent of tumor invasion (16). ^{18}F-NaF PET/CT exhibits high sensitivity in detecting bone lesions, and when combined with MRI images, its diagnostic performance for detecting SBBI is significantly superior to MRI alone. In this study, the combined used of ^{18}F-NaF PET/CT and MRI resulted in a modification of T staging from the original MRI only-based diagnosis in four cases of NPC, accounting for 6.9% of the cohort (*Figure 2*).

The superior sensitivity of ^{18}F-NaF PET/CT in diagnosing SBBI can be attributed to its ability to detect bone lesions with high accuracy. Meanwhile, MRI exhibits high specificity in visualizing soft tissue involvement. These modalities complement one an another, forming a synergy that offers several advantages and ultimately improves the accuracy SBBI diagnosis.

The accurate detection of bone metastases in NPC is of utmost importance. Bone scintigraphy with ^{99m}Tc-MDP as the imaging agent serves as a crucial diagnostic tool for the identification of bone metastases in various malignancies, including NPC (17-19). However, its sensitivity and specificity are significantly lower than those of ^{18}F-NaF PET/CT (20,21). Combining ^{99m}Tc MDP bone scintigraphy with CT observation may enhance diagnostic efficacy (11). In this study, chest CT imaging was performed on 55 patients (94.8%) and demonstrated accurate identification of subtle bone lesions,

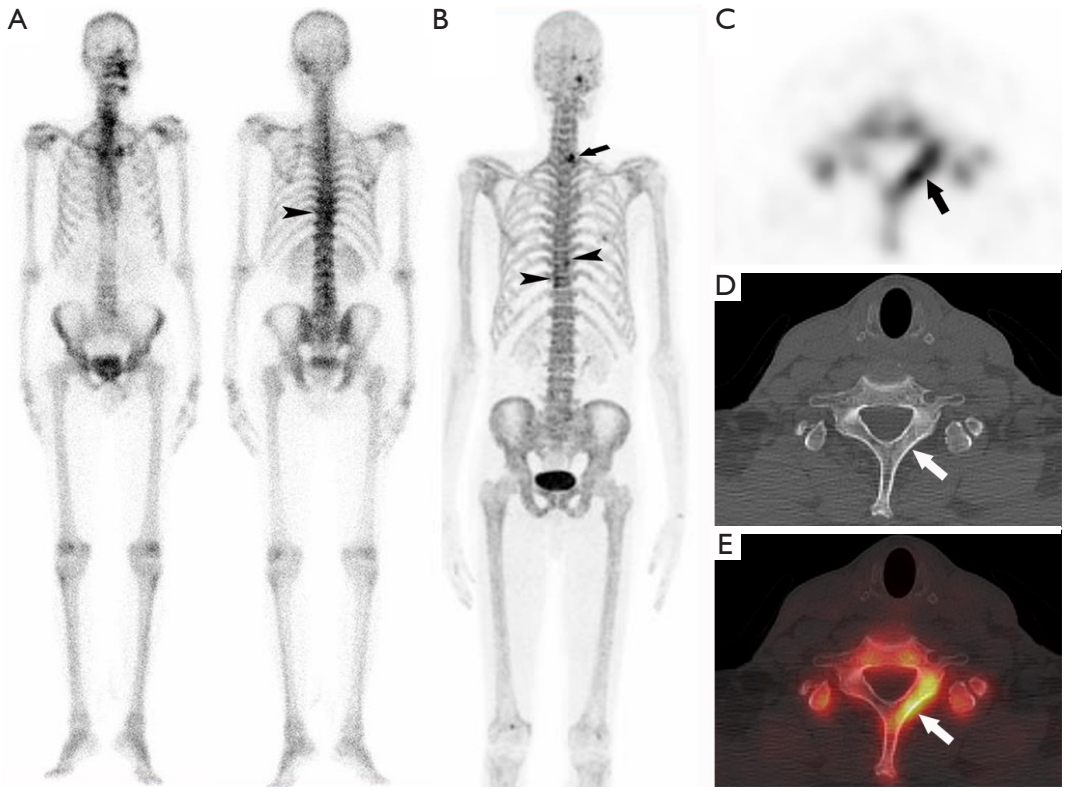

Figure 3 A 64-year-old male patient with NPC underwent initial staging evaluation. ^{99m}Tc-MDP bone scintigraphy in the posterior view (A) revealed a mild radiological abnormality with increased uptake in the T9–10 vertebrae (arrowhead) suggestive of degeneration. Subsequent ^{18}F-NaF PET MIP imaging (B) demonstrated mild abnormal NaF uptake in the T9–10 vertebrae (arrowheads), consistent with degenerative changes lesions. Additionally, the PET MIP image (B) revealed a localized abnormal NaF uptake in the left vertebral lamina of the C7 vertebra. Cross-sectional PET (C, arrow) and fusion PET/CT (E, arrow) images further confirmed abnormal NaF uptake at the corresponding location, with increased density observed on CT (D, arrow) suggestive of bone metastasis. Based on these findings, the staging of this patient was changed from M0 to M1. Consequently, the treatment plan was modified from initial radiotherapy to a comprehensive approach that included chemotherapy. NPC, nasopharyngeal carcinoma; ^{99m}Tc-MDP, ^{99m}Tc-methylene diphosphonate; ^{18}F-NaF PET, ^{18}F-sodium fluoride positron emission tomography; MIP, maximum intensity projection; CT, computed tomography.

including the internal dense foci of the ribs, sclerotic rings at the margins, and benign bone lesions. The combination of ^{99m}Tc-MDP bone scintigraphy and chest CT improved the diagnostic specificity and corrected the majority of false-positive lesions identified by ^{99m}Tc-MDP bone scintigraphy in patients with increased lesion uptake in the ribs or vertebral bodies of the chest. However, one patient showed a false-positive result on ^{99m}Tc-MDP bone scintigraphy in the lumbar spine and pelvis, but a true-negative result was obtained with ^{18}F-NaF PET/CT. This led to a downstaging in the M-stage from M1 to M0. We also found that ^{99m}Tc-MDP bone scintigraphy had low sensitivity in detecting bone metastases, as it failed to identify bone metastases in several patients. In contrast, ^{18}F-NaF PET/CT successfully identified early bone metastases, leading to accurate changes in the clinical stage of two patients from M0 to M1 (*Figure 3*).

Previous studies on malignancies, including prostate, breast, and lung cancer, have consistently demonstrated the significant impact of ^{18}F-NaF PET or PET/CT in modifying clinical management plans. The percentage of cases in which management plans were modified ranges from 8% to 68% (22,23). In this study, the impact of ^{18}F-NaF PET/CT on clinical management plans was evaluated, with 8 patients (13.8%) undergoing changes in their treatment regimens as a result of the imaging findings. Among these cases, three patients required major adjustments to their treatment plans, while five cases required minor adjustments. These findings are consistent

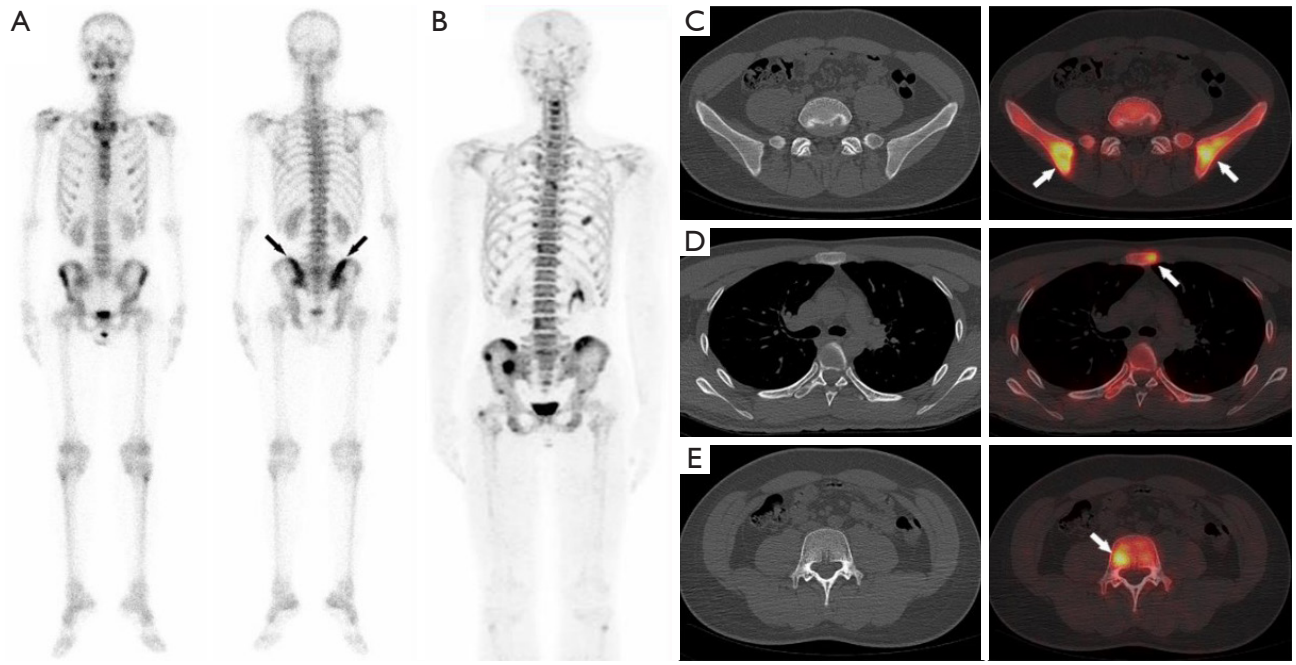

Figure 4 A male patient with NPC presented for staging evaluation. ^{99m}Tc-MDP bone scintigraphy (A) displayed symmetrical radiological abnormalities in the bilateral ilia suggestive of bone metastases. Subsequent ^{18}F-NaF PET MIP imaging (B) exhibited multiple abnormal increased uptakes in the bilateral ilia, vertebral bodies, ribs, and the right femur, consistent with widespread bone metastases. Additionally, cross-sectional CT and fusion PET/CT images convincingly revealed multiple metabolic changes in the bilateral ilia (C, arrows), sternum (D, arrow), and the fourth lumbar vertebra (E, arrow), among other locations, further supporting the diagnosis of multiple bone metastases. Notably, the ^{18}F-NaF PET/CT detected a significantly higher number of bone metastatic lesions compared to ^{99m}Tc-MDP bone scintigraphy. Consequently, the treatment decision was altered based on the findings of the ^{18}F-NaF PET/CT. The initially planned local iliac radiation therapy was cancelled in favor of a more comprehensive approach that considered chemotherapy and palliative care. NPC, nasopharyngeal carcinoma; ^{99m}Tc-MDP, ^{99m}Tc-methylene diphosphonate; ^{18}F-NaF PET, ^{18}F-sodium fluoride positron emission tomography; MIP, maximum intensity projection; CT, computed tomography.

with previous research (23).

Additionally, three patients in our study experienced significant changes in their treatment plans. Two of these patients initially showed no bone metastatic lesions on conventional imaging but were subsequently diagnosed with bone metastases using the highly sensitive ^{18}F-NaF PET/CT. This led to a clinical staging adjustment from M0 to M1 and a shift in treatment approach from radiotherapy-based curative treatment to chemotherapy-based palliative treatment (*Figure 3*). Additionally, one patient's initial diagnosis based on ^{99m}Tc-MDP bone scintigraphy falsely indicated the presence of bone metastases. However, further evaluation with ^{18}F-NaF PET/CT confirmed the absence of bone metastases, thereby preventing unnecessary systemic chemotherapy. Another patient initially showed bilateral iliac metastatic lesions on ^{99m}Tc-MDP bone scintigraphy, but ^{18}F-NaF PET/CT imaging indicated these were absent. However, ^{18}F-NaF PET/CT identified extensive bone metastases involving multiple locations, including the ribs, thoracolumbar spine, and ilium. This finding averted the need for radiotherapy planning for bilateral iliac metastases as initially suggested by ^{99m}Tc-MDP bone scintigraphy (*Figure 4*). It is essential to note that when patients have multiple or extensive bone metastatic lesions (more than five lesions), despite the superior detection capabilities of ^{18}F-NaF PET/CT, their staging and treatment plans were not altered or adjusted in line with NPC guidelines. Radiotherapy serves as the primary treatment for NPC. The target region for intensity-modulated radiotherapy (IMRT) is determined based on the local progression pattern of NPC and primarily encompasses the clinical target volume (CTV) of the primary tumor. Expert consensus holds that the boundaries of the radiotherapy target zone should be established based on imaging evidence (24,25). The precise

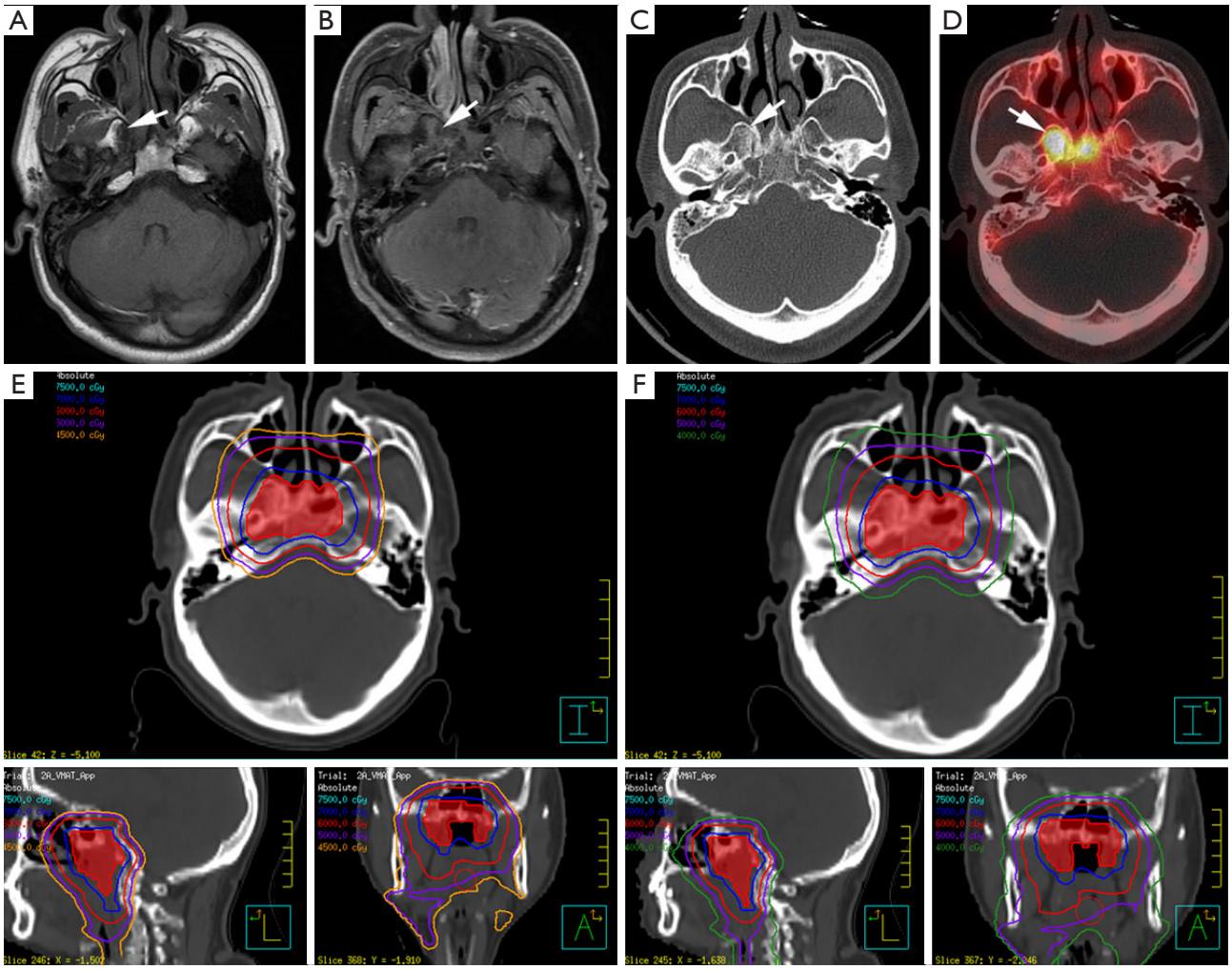

Figure 5 A 49-year-old male patient with NPC underwent diagnostic imaging evaluation. MRI T1WI (A) revealed a hypointense lesion (arrow) in the right sphenoid wing suggestive of tumor invasion. T1WI contrast enhancement (B) further confirmed abnormal enhancement (arrow) in the corresponding area. CT imaging (C) demonstrated a slight increase in density in the right sphenoid wing. Subsequent ^{18}F-NaF PET/CT fusion imaging (D) identified an abnormal increased uptake focus (arrow) in the greater wing of the right sphenoid, indicating a more extensive lesion than that observed on MRI. The GTV from the MRI scan of the target region was 37.4 cm³ (E). When combined with the ^{18}F-NaF PET/CT results, the GTV volume outlined by MRI was 38.7 cm³ (F). Thus, the radiotherapy target volume was larger with ^{18}F-NaF PET/CT combined with MRI than with MRI alone. NPC, nasopharyngeal carcinoma; MRI, magnetic resonance imaging; T1WI, T1-weighted imaging; CT, computed tomography; ^{18}F-NaF PET/CT, ^{18}F-sodium fluoride positron emission tomography-computed tomography; GTV, gross tumor volume.

delineation of the tumor target is pivotal for the success of IMRT. An undersized target volume can lead to tumor recurrence, while an over-sized target volume elevates the risk of radiation-induced damage to normal tissue organs (24,26,27). Consequently, accurate determination of the target region in NPC is imperative to achieving the desired clinical outcomes with IMRT.

In six patients with NPC in this study, there were discrepancies in the number of lesions detected by SBBI and the diagnostic results between ^{18}F-NaF PET/CT imaging and MRI. The oncology radiation therapists subsequently redefined the therapeutic target regions for these six patients using both ^{18}F-NaF PET/CT and MRI scans. The outcomes revealed modifications in the GTV in four cases, with an expanded target range in three cases (*Figure 5*) and a narrowed target range in one case. Wu *et al.*

reported that in the context of IMRT for early-stage NPC, ^{18}F-FDG PET/CT plays a pivotal role in radiotherapy planning for preventing inadequate dosing of the GTV. It is recommended that PET images be integrated into the treatment planning for patients with NPC (28). ^{18}F-NaF PET/CT holds potential advantages in the diagnosis of SBBI and radiotherapy target delineation in NPC, as it outperforms ^{99m}Tc MDP bone imaging in several respects. These include a shorter imaging time, higher bone resorption rate, faster plasma clearance, and superior image quality (29,30). These advantages of ^{18}F-NaF PET/CT imaging are of utmost importance for precise target area delineation in radiotherapy and primary tumor staging.

Staging with ^{18}F-NaF PET/CT may occasionally be inaccurate. In this study, one patient exhibited a mild increase in NaF uptake in the inferior wall of the sphenoid sinus, which was initially interpreted as tumor invasion of NPC. However, a follow-up ^{18}F-NaF PET/CT scan conducted a year later revealed that the NaF uptake of the lesion remained unchanged, indicating that the initial increase was likely due to long-term chronic inflammation within the sphenoid sinus. As a result, the GTV of this patient was erroneously enlarged, potentially leading to negative impacts on patient management and prognosis.

The study has certain limitations. First, selection bias might have been present due to the relatively small number of patient cases included. Second, the changes in clinical management plans were based on retrospective analysis and may not fully reflect real-world clinical decision-making. In actual clinical settings, effective management decisions often depend not only on ^{18}F-NaF PET/CT results but also on various other factors, such as patient compliance, physical tolerance, and other comorbidities. Therefore, this study primarily reflects a hypothetical scenario where clinical management plans are influenced by ^{18}F-NaF PET/CT results. The study design and methodologies employed are similar to those of previous studies that have examined how ^{18}F-FDG PET/CT impacts clinical management decisions in patients with cholangiocarcinoma, vaginal cancer, and lung cancer (31-33).

Conclusions

The potential advantages of ^{18}F-NaF PET/CT for clinical staging and management planning in patients with newly diagnosed NPC are promising. However, further large-scale, prospective studies are necessary to assess its practical impact on clinical management plans of NPC.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of the Affiliated Hospital of Guangdong Medical University (No. PJXJS2022-003). Written informed consent was obtained from all the patients.

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