Original Article

Does Intravenous Contrast Improve the Diagnostic Yield of Fluorodeoxyglucose Positron-emission Tomography/Computed Tomography in Patients with Head-and-neck Malignancy

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Abstract

Introduction: In the present time, iodinated contrast agents are increasingly being used in the computed tomography (CT) component of positron-emission tomography (PET) study with the assumption that contrast-enhanced CT (CECT) will provide better diagnostic yield, although the utility of this procedure is still being debated. The aim of the study was to evaluate the effect of contrast CT on the diagnostic yield of PET-CT scan in patients with head-and-neck malignancies. **Materials and Methods:** In a prospective study, 204 patients (140 males and 64 females) of head-and-neck malignancies underwent contrast-enhanced and nonenhanced fluorodeoxyglucose (FDG)-PET-CT for various clinical indications following informed consent. After a plain CT scan, CECT was done using iodinated contrast iopromide-370 at a dose of 1 ml/kg intravenously. After CECT acquisition, FDG-PET acquisition was done and images were reconstructed to obtain whole-body PET/CT and PET-CECT images. **Results:** Both the modalities could detect similar number of primary lesions (n = 127), lymph nodal lesions (n = 118), and metastatic involvement (n = 55) with no significant difference between SUVmax. However, conspicuity of primary tumors and lymph nodal architecture was significantly better delineated with CECT, leading to better interpreter confidence. **Conclusion:** CECT data as part of the combined PET-CT examination provide precise anatomic localization and delineation of the primary tumor in comparison to nonenhanced PET-CT. However, no significant diagnostic changes are noted in the nodal and metastatic staging.

Keywords: *Head-and-neck malignancy, iodinated contrast, positron-emission tomography*

Introduction

Proper management of a patient with malignancy includes evaluation of primary and metastatic sites. Anatomical imaging modalities remain the mainstay for disease evaluation. Since it is known that molecular changes precede anatomical changes, much emphasis is being placed on functional imaging which utilizes a tumor-seeking substance, distribution of which can be monitored by specific imaging device such as gamma camera or positron-emission tomography (PET) scanner.

Inherent limitation of functional imaging is low spatial resolution and lack of anatomical details. To overcome these limitations, combined anatomical and functional imaging is currently being used. Conventionally, combined modality was done using a low-resolution computed tomography (CT) scanner; however, iodinated contrast agents were not used routinely. It is well accepted that iodinated contrast agents provide additional informations.[1] In the present time, high-resolution diagnostic quality CT is universally acquired along with whole-body PET, and iodinated contrasts are also increasingly being used in the CT component of PET study with the assumption that contrast-enhanced CT (CECT) will provide better diagnostic yield, although the utility of this procedure is still being debated.[1,2] The aim of the study was to evaluate the effect of additional contrast CT on the diagnostic yield of PET-CT scan in patients with head-and-neck malignancies.

Materials and Methods

A prospective study of 204 patients (140 males and 64 females) of histologically proven head-and-neck malignancies was

How to cite this article: Barai S, Ora M, Gambhir S, Singh A. Does intravenous contrast improve the diagnostic yield of fluorodeoxyglucose positron-emission tomography/computed tomography in patients with head-and-neck malignancy. Indian J Nucl Med 2020;35:13-6.

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Received: 26-06-2019, **Revised:** 08-07-2019, **Accepted:** 30-08-2019, **Published:** 31-12-2019.

Access this article online
Website: www.ijnm.in
DOI: 10.4103/ijnm.IJNM_119_19
Quick Response Code:

done. Patients were referred for ^{18}F-PET-CT scan with clinical indications such as initial staging, restaging, and response evaluation. All patients gave informed consent for the study.

Inclusion criteria were histopathologically proven head-and-neck malignancy, age >18 years, nondiabetic/ or controlled diabetic (blood glucose <150 mg/dl), and adequate renal function (serum creatinine <1.5 mg %). Patients were recruited only after 8 weeks postsurgery or radiotherapy. Any patient not giving consent for the study, not fulfilling inclusion criteria, and all pregnant and lactating females were excluded.

Procedure of the positron-emission tomography–contrast-enhanced computed tomography scan

Patient preparation, image acquisition, reconstruction, and processing were done as per the recommendation laid down in the Society of Nuclear Medicine (SNM) Procedure Guideline for PET-CT.[3]

After the acquisition of scout image, whole-body (vertex to mid-thigh) plain CT scan was obtained using CT with field of view of 50 cm with 300 mA 140 kvP with 1.0 s rotation, 64 detector rows, 5.0 mm thickness Pitch 0.75: 1 at a speed 7.5 mm/rotation. After plain CT scan, CECT of the same region was done using the same parameter. Iodinated contrast (iopromide: 370 mg I/ml, osmolality: 607 mOsm/kg, and density 1.322 g/cm^3 at 37°C) was administered intravenously at a rate of 3 ml/s using Medrad® Intego PET Infusion System. A dose of iodinated contrast (1 ml/kg) was calculated according to the patients' body weight. CECT images were obtained after 30 s from the initiation of contrast administration to decrease contrast density in the major vessels and to allow a more uniform distribution of contrast. After CECT acquisition, PET acquisition was done using 2 min per bed position. After completion of PET acquisition, reconstruction was done and two set of images were obtained using whole-body PET-CT and PET-CECT.

Data analysis

Two experienced nuclear medicine physicians and one radiologist evaluated the images independently. Lesions were evaluated in accordance to the SNM General Guidance of Reporting of Findings.[4] Special attention was paid to evaluate if the CECT images are providing any incremented information over and above noncontrast plain CT regarding tumor margin, nodal architecture, or tissue characterization. Lesion conspicuity was measured in all the suspicious lesions on PET-CT and PET-CECT. It was predefined by its percentage circumferential delineation, and for the purpose of this study, it was categorized into four grades, that is, <25%, 25%–49%, 50%–75%, or >75% circumferential delineation. All contrast-enhanced images were evaluated for contrast-induced artifacts.

Statistical analysis

A statistically significant difference between modalities was defined as $P < 0.05$. All statistical tests were performed using the SPSS Statistics Software Package for Microsoft Windows (SPSS Version 21; IBM Corp., New York, Un ited states of America). The Wilcoxon signed-rank test was used for comparison of lesion conspicuity.

Results

In this prospective study, 204 patients (140 males and 64 females) with histologically proven head-and-neck cancer were enrolled. The mean age of patients was 51.8 ± 15.2 years. In the study, there were 55 cases of buccal mucosa, 40 cases of lymphoma, 32 cases of carcinoma tongue, 22 cases of carcinoma lip, 20 cases of carcinoma nasopharynx, 16 cases of alveolar carcinoma, 16 cases of oropharynx, 12 cases of carcinoma larynx, 7 cases of thyroid cancer, and 12 were others like salivary gland and sinus carcinomas, etc.

Evaluation of tumor size (T-stage)

One hundred and twenty-seven patients (62%) have local lesions in the form of primary lesion, residual tumor, or recurrent disease. No lesion was missed on the PET-CT which was detected on the PET-CECT. Regarding the conspicuity of primary tumors [Table 1], PET-CECT imaging was performed significantly better [Figure 1] for delineation of tumor margin and detecting infiltration and invasion of adjacent structures than PET-CT (Wilcoxon signed-rank test, $P < 0.001$). There was no significant difference between SUVmax measured by PET-CT to PET-CECT protocol ($P = 0.5$).

Nodal stage

Metastatic lymph nodes were noted in total 118 (57%) patients. Primary lesion/recurrence disease was also noted in 76 (37%) of them, while only lymphadenopathy was seen in 42 (20%) patients. The same number of involved lymph nodes was noted in the contrast-and noncontrast-enhanced PET-CT. No difference in SUVmax measurement was noted. Regarding the conspicuity of hypermetabolic lymph nodes, significant difference was found between

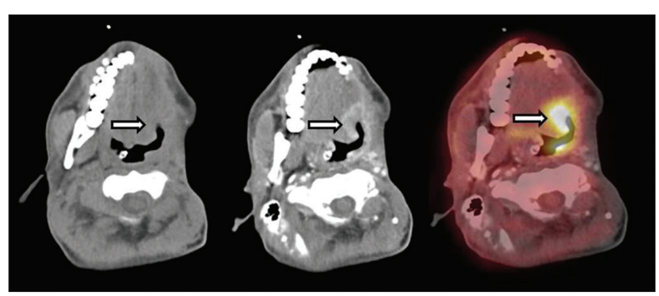

Figure 1: Comparative images of a noncontrast computed tomography, contrast-enhanced computed tomography, and fused FDG-positron-emission tomography image of a patient of buccal mucosal cancer showing excellent tumor margin delineation by intravenous contrast

PET-CECT and PET-CT imaging (Wilcoxon signed-rank test, $P < 0.01$). Nodal architecture such as shape, size, fatty hilum, and presence of necrosis was better appreciated in contrast study.

Distant metastasis

Distant metastasis was present in 55 patients of 268 cases. Distant metastases were seen in the lung (28 cases), skeletal (21 cases), adrenal (4 case), soft tissue (3 cases), and others (2 cases). Distant metastases were identified with both PET-CT and PET-CECT in all patients. No difference in SUVmax measurement was noted.

Contrast-induced artifacts

Contrast in subclavian vein artifact was noted in 6 patients of 204. None of it interfered with the interpretation of the regional soft tissue. The low incidence of subclavian artifact is likely to be due to the use of 30 ml of saline flush after injection of contrast and slower rate of contrast injection 2.5 ml/s by automated injector.

Discussion

There is no consensus regarding the best imaging approach for staging head-and-neck cancer. Lesion detection with CT is based on features such as attenuation differences between the lesion and adjacent structures and CT enhancement characteristics such as phase and pattern.[5] Most parenchymal organs and the lesions affecting them have similar attenuation values, which lie within a relatively narrow range, typically 30–80 HU, and a contrast material is used to increase the attenuation difference between normal and abnormal tissue.[6] This results in increased lesion conspicuity, which is of particular importance in lesions in which are not accumulating fluorodeoxyglucose (FDG). Furthermore, intravenous (IV) contrast enhancement can help differentiate benign from malignant lesions that have nonspecific FDG-PET uptake. In addition, IV contrast material may outline lesions within vascular structures and localize lesions that have increased FDG uptake but that would not be conspicuous on unenhanced CT images due to lack of a contour abnormality or would have similar attenuation values to the surrounding structures.

Previous studies have shown that the use of IV contrast agents for PET-CT yields considerable additional information.[7,8] The greatest benefit of diagnostic CT is the improved localization of FDG uptake and improved local tumor staging, which frequently results in alteration in treatment plan. Certain tumors and their metastatic lesions have relatively low glucose metabolism; the use of IV contrast material is of particular importance in identification and characterization of these tumors.[9] However, the use of IV contrast agents results in higher attenuation values, and when a concentrated contrast bolus passes within vascular structures, it can cause artifacts.[10] In the current study, subclavian artifact was noted in 6 (2.9%) patients. This apparently lower incidence of subclavian artifact could be the result of use of diluted contrast agent injected by automated injector system. The use of IV contrast material also adds to cost and introduces the risk of possible allergic reactions and nephrotoxicity, but these disadvantages are considered clinically acceptable as part of standard CT protocols for oncologic indications.

Regarding diagnostic accuracy, no advantage of contrast could be demonstrated in our study, and both noncontrast and contrast-enhanced PET-CT were performed similarly in identifying the site of primary tumor. This observation is in accordance with published literature. However, lesions were significantly more conspicuous on contrast-enhanced PET-CT study, leading to enhanced confidence while interpreting the images. The reason for upstaging is better delineation of tumor margin, leading accurate size measurement. Our findings are in accordance with the study of the existing literature.[11-14] In restaging scans, postoperative and postradiation inflammatory changes are seen frequently and show FDG uptake as well as contrast enhancement. This issue was not specifically addressed in our work. Any confirmation of viable tumor versus inflammatory tissue present at operative bed or radiation site would require histopathological verification, which was neither medically required nor ethically appropriate in all patients. However, 33 patients diagnosed to have recurrent disease underwent repeat surgery, and histopathology confirmed viable tumor in all the patients.

In our study, distant metastases were correctly identified with both PET-CT and PET-CECT in 55 cases. PET-CT remains an excellent investigation to upstage ~ 27% patient, thus excluding the possibility of localized treatment. Regarding detection of distant metastasis, addition of

Table 1: Mean lesion conspicuity in different lesions

Anatomical location	PET-CT Lesion	PET-CECT Lesion	PET-CT Lymph node	PET-CECT Lymph node
Buccal mucosa	2.3	3.1	2.4	3.2
Tongue	2.5	4.0	3.7	4.1
Lip	1.9	3.3	3.1	3.2
Nasopharynx	2.3	3.3	3.0	3.8
Lymphoma	2.0	3.0	2.6	3.6
Oropharynx	2.3	3.0	2.8	3.8

PET: Positron-emission tomography, CT: Computed tomography, CECT: Contrast-enhanced CT contrast was found to have minimal or no incremental value.

Conclusion

CECT data as part of the combined PET-CT examination provide precise anatomic localization and delineation of the primary tumor in comparison to nonenhanced PET-CT. However, no significant diagnostic changes are noted in the nodal and metastatic staging.

Routine use of IV contrast does not change the performance of PET-CT in metastatic workup; however, it may be added in those selective cases where surgical or radiotherapy intervention is anticipated.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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