# Value of PET scan compared with MRI scan in detecting occult primary with cervical lymph node metastasis

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**Abstract**

**Introduction:** Patients with metastatic carcinoma from an unknown primary site represent up to 15% of all patients with cancer who present to medical centres. The overall incidence of unknown primary tumours in the head and neck region ranges from 3% to 7% of all head and neck cancers. The low rate of primary detection has several causes, among which two are most important. First as the primary lesion is usually small, conventional imaging techniques may be difficult to read; this is especially true within the abdomen, pelvis, and head and neck, which are anatomically difficult areas. **Objective:** To study the value of PET scan compared with MRI scan in detecting occult primary with cervical lymph node metastasis. **Materials and Method:** The present study was conducted in the Army Hospital (Research and Referral), Delhi Cantt. The patients attending Head and Neck Oncology clinic with metastatic cervical lymph node(s) without evidence of primary by clinical evaluation were enrolled in the present study. Total 27 patients were selected and were analysed. All the selected patients underwent review of their medical history and thorough medical examination. The patients in whom a primary tumour was not detected were accrued into the study and classified as patients with Carcinoma of Unknown Primary Site (CUPS), and they formed the cohort of our study. All the study patients were subjected to ultrasonography of the abdomen, CT scan of the neck and chest and panendoscopy under general anaesthesia, to look for any evidence of a primary tumour. Along with PET CT all the patients were also evaluated by MRI also. MRI and PET findings were assessed separately and recorded as "positive" or "negative", and then correlated with the histological result. Depending on the histological results, the results of the imaging procedures were evaluated as "true-positive", "false negative", "true-negative" and "false-negative". **Results:** Out of the twenty seven patients, 23(85.19%) had unilateral and rest of the four bilateral cervical lymphadenopathy. FDG-PET-CT was negative in 14 (51.85%) patients and was positive in 13 (48.15%) patients. The sensitivity of PET CT was 87.5% whereas specificity was 89.5%. On MRI total 9 vases were positive for Carcinoma of unknown primary site (CUPS). Out of these 6 cases were also confirmed positive on Histopathological examination. The sensitivity of MRI in diagnosing Carcinoma of unknown primary site (CUPS) was 75% with specificity of 84.21%. The sensitivity of diagnosing the carcinoma of unknown primary site of PET CT was 87.5% whereas that of MRI was 75%. The specificity of PET CT was 89.5% whereas that of MRI was 84.21%. The difference observed in the diagnostic value of PETCT and MRI was statistically not significant. **Conclusion:** The sensitivity of diagnosing the carcinoma of unknown primary site of PET CT was 87.5% whereas that of MRI was 75%. The difference observed in the diagnostic value of PETCT and MRI was statistically not significant. Thus PET and MRI are characterized by a high sensitivity and specificity and represent important tools in current diagnosis of head and neck tumors.
**Key Words:** Carcinoma of unknown primary site, PET scan, MRI scan.

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Patients with metastatic carcinoma from an unknown primary site represent up to 15% of all patients with cancer who present to medical centres[1]. The overall incidence of unknown primary tumours in the head and neck region ranges from 3% to 7% of all head and neck cancers[2]. A metastasis of an unknown primary was defined by Abbruzzese and Raber in 1995 as a biopsy confirmed malignancy for which the site of origin is not identified by routine clinical work-up which consists of careful clinical examination, including, fibreoptic laryngoscopy/nasopharyngoscopy, detailed imaging in the

form of Computed Tomography (CT) and/or Magnetic Resonance Imaging (MRI) and panendoscopy with tonsillectomy and directed biopsies of at-risk sites like the tonsillo-lingual sulcus, base of tongue and nasopharynx.[3] The low rate of primary detection has several causes, among which two are most important. First as the primary lesion is usually small, conventional imaging techniques (such as CT or gastrointestinal contrast radiographic studies) may be difficult to read; this is especially true within the abdomen, pelvis, and head and neck, which are anatomically difficult areas. The second main cause relates to the biological features of the primary tumour: it is hypothesized that a primary tumour may disappear after seeding the metastasis because its angiogenetic incompetence leads to marked apoptosis and cell turnover and no diagnostic procedures can detect a primary lesion which has disappeared due to marked apoptosis.[4] PET scans are increasingly read alongside CT scans or MRI scans, the combination ("co-registration") giving both anatomic and metabolic information (i.e., what the structure is, and what it is doing biochemically). Because PET imaging is most useful in combination with anatomical imaging, such as CT, modern PET scanners are now available with integrated high-end multi-detector-row CT scanners. Because the two scans can be performed in immediate sequence during the same session, with the patient not changing position between the two types of scans, the two sets of images are more-precisely registered, so that areas of abnormality on the PET imaging can be more perfectly correlated with anatomy on the CT images. This is very useful in showing detailed views of moving organs or structures with higher amounts of anatomical variation, such as are more likely to occur outside the brain.[5] Modern diagnostic methods for head and neck tumors should allow for complete tumor assessment and the determination of tumor identity. The routinely performed imaging procedures such as magnetic resonance imaging (MRI), computed tomograhy (CT), positron-emission tomography (PET), and ultrasound, however, only partly meet these requirements. The objective of the present study was to assess the value of morphological MRI compared to functional PET with regard to the detection and determination of head and neck tumors.

## OBJECTIVE

To study the value of PET scan compared with MRI scan in detecting occult primary with cervical lymph node metastasis.

## MATERIALS AND METHOD

The present study was conducted in the Army Hospital (Research and Referral), Delhi Cantt. Following inclusion and exclusion criteria was used to select the study subjects.

**Inclusion Criteria**

1. The patients attending Head and Neck Oncology clinic with metastatic cervical lymph node(s) without evidence of primary by clinical evaluation
2. Those patients referred from oncology clinics from other service hospitals as CUPS.
3. Patients who had no prior history of cancer.
4. Those patients, who had not received treatment if the form of surgery, chemotherapy and/or radiation therapy, for malignancy.
5. The patients who are entitled, for undergoing PET scan at our centre, i.e. Personnel serving in the Armed Forces, their dependants, ex-service personnel and their dependants.

**Exclusion Criteria**

1. Primary tumour detected during work up prior to undergoing PET-CT scan.
2. Those patients who are not willing for regular follow-up.
3. The patients who has active infection or inflammatory disease at presentation.
4. Patients who were found to be hyperglycaemic.

Total 33 patients were enrolled in the present study. Out of which four patients were detected to have primary and in two patients cervical lymph nodes were not positive for metastases, hence were excluded from the study. Thus the total 27 patients were accrued into the study and were analysed. All the selected patients underwent review of their medical history and thorough medical examination. They underwent relevant clinical tests, including complete blood counts, LFT, RFT, urine analysis, and chest radiography. Further they were subjected to fibreoptic nasopharyngoscopy and laryngoscopy, followed by fibreoptic bronchoscopy and oesophagoscopy to look for any evidence of primary lesion. Those patients, who were found to have suspicious lesions, underwent biopsy of the suspected site. Thus the patients in whom a primary tumour was not detected were accrued into the study and classified as patients with Carcinoma of Unknown Primary Site (CUPS), and they formed the cohort of our study. All the study patients were subjected to ultrasonography of the abdomen, CT scan of the neck and chest and panendoscopy under general anaesthesia, to look for any evidence of a primary tumour. Then all the patients were subjected to whole body PET-CT scan. Written informed consent for PET-CT scan was taken and latest blood sugar level investigation was done. Patients were kept fasting for 12 hrs before the scan. The outcome of tests have been tabulated and analysed to ascertain the sensitivity,

specificity, positive and negative predictive values of whole body PET-CT scan in detecting the primary in CUPS with cervical lymph node metastasis. Along with PET CT all the patients were also evaluated by MRI also. MRI and PET findings were assessed separately and recorded as "positive" or "negative", and then correlated with the histological result. Depending on the histological results, the results of the imaging procedures were evaluated as "true-positive", "false negative", "true-negative" and "false-negative". The collected data was entered in the Microsoft excel and was analysed. The result of the study was presented with appropriate tables and graphs.

## RESULTS

**Table 1:** Distribution according to age, sex and Predisposing factors

| | | No of patients | Percentage |
|---|---|---|---|
| Age | ≤50 | 2 | 7.41 |
| | 51-60 | 10 | 37.04 |
| | 61-70 | 11 | 40.74 |
| | 71-80 | 3 | 11.11 |
| | >80 | 1 | 3.70 |
| Sex | Male | 23 | 85.19 |
| | Female | 4 | 14.81 |
| Predisposing factors | Tobacco chewer/smoker | 17 | 62.96 |
| | Tobacco and alcohol | 6 | 22.22 |
| | Teetotaler | 4 | 14.81 |

It was observed that age profile of the patients varied from 48 to 86 yrs with mean age as 62. Majority of the patients were in the age group of 51to 70 years of age (77.78%). Out of the total 27 patients, twenty three (85.19%) were male and four were female patients. Mean duration of symptoms before reporting was about three months, minimum being one month and maximum being seven months. Out of these twenty seven patients, 17 (62.96%) were tobacco chewers and/or smokers while 6 (22.22%) were habituated to tobacco as well as social drinking.

**Table 2:** Distribution of Cervical Lymphadenopathy

| Lymphadenopathy | | No of patients | Percentage |
|---|---|---|---|
| Lymphadenopathy | Unilateral | 23 | 85.19 |
| | Bilateral | 4 | 14.81 |
| Level of Lymphadenopathy | Level II and III | 3 | 11.11 |
| | Level IV | 5 | 18.52 |
| | Multiple | 19 | 70.37 |
| FNAC | Sq cell ca | 11 | 40.74 |
| | Adenocarcinoma | 7 | 25.93 |
| | Poorly | 6 | 22.22 |
| | differentiated | | |
| | Undifferentiated | 3 | 11.11 |

Out of the twenty seven patients, 23 (85.19%) had unilateral and rest of the four bilateral cervical lymphadenopathy. In 19 patients the lymphadenopathy was limited to the level above cricoid while 5 patients had level IV and rest had conglomerate of multiple lymph nodes. Eleven of these patients had squamous cell carcinoma, seven had adenocarcinoma, six had poorly differentiated carcinoma, and remaining three had undifferentiated carcinoma metastases.

**Table 3:** Efficacy of FDG-PET-CT as a diagnostic tool

| | Histopathological examination | |
|---|---|---|
| | Positive | Negative |
| PET-CT Positive | 7 (True +ve) | 2 (False +ve) |
| PET-CT Negative | 1 (False −ve) | 17 (True −ve) |

| Sensitivity | 87.5 % |
|---|---|
| Specificity | 89.5 % |
| Positive Predictive value | 77.8 % |
| Negative Predictive value | 94.4 % |

FDG-PET-CT was negative in 14 (51.85%) patients and was positive in 13 (48.15%) patients. Out of these thirteen patients, nine had primary tumour, while four patients had evidence of distant metastasis. These 9 cases were evaluated further and it was observed that 7 cases were also positive on Histopathological examination whereas 2 cases were false negative. Thus the sensitivity of PET CT was 87.5% whereas specificity was 89.5%.

**Table 4:** Efficacy of MRI as a diagnostic tool

| MRI | Histopathological examination | |
|---|---|---|
| | Positive | Negative |
| Positive | 6 (True +ve) | 3 (False +ve) |
| Negative | 2 (False −ve) | 16 (True −ve) |

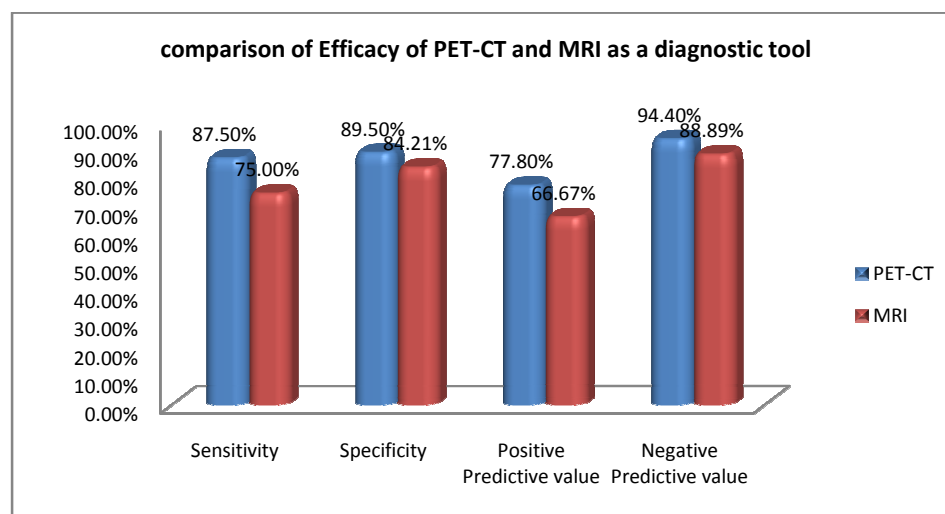| Sensitivity | 75.00% |
|---|---|
| Specificity | 84.21 % |
| Positive Predictive value | 66.67% |
| Negative Predictive value | 88.89 % |

All the cases were also evaluated by MRI and it was seen that on MRI total 9 vases were positive for Carcinoma of

unknown primary site (CUPS). Out of these 6 cases were also confirmed positive on Histopathological examination. Remaining three cases positive on MRI were diagnosed negative on Histopathological examination. Thus the sensitivity of MRI in diagnosing Carcinoma of unknown primary site (CUPS) was 75% with specificity of 84.21%.

**Table 5:** comparison of Efficacy of PET-CT and MRI as a diagnostic tool

| | Diagnostic value | |
|---|---|---|
| | PET- | MRI |

|  | CT | |
|---|---|---|
| Sensitivity | 87.5% | 75.00% |
| Specificity | 89.5% | 84.21% |
| Positive Predictive value | 77.8% | 66.67% |
| Negative Predictive value | 94.4% | 88.89% |



comparison of Efficacy of PET-CT and MRI as a diagnostic tool

It was seen that the sensitivity of diagnosing the carcinoma of unknown primary site of PET CT was 87.5% whereas that of MRI was 75%. The specificity of PET CT was 89.5% whereas that of MRI was 84.21%. The difference observed in the diagnostic value of PETCT and MRI was statistically not significant.

## DISCUSSION

The present study was conducted with objective to evaluate the value of PET scan in detecting occult primary with cervical lymph node metastasis compared with MRI scan. The study was conducted in the Army Hospital (Research and Referral). Patients with unknown primary tumours often undergo various extensive investigations, which will result in prolonged hospitalization and discomfort, often with no benefit for the patient. Total number of patients accrued into the study was thirty three from the entitled patients, out of which four patients were detected to have primary and in two patients cervical lymph nodes were not positive for metastases, hence not taken into the study. This left us with twenty seven patients, fulfilling the inclusion criteria and were accrued into the study. It was seen that majority of the patients were in the age group of 51to 70 years of age (77.78%). The age of patients in the study was in the range from 48 to 86 yrs with mean age as 62. Out of the total 27 patients, twenty three (85.19%) were male and four were female patients. Similar findings were also reported by Myriam Wartski *et al*[1].The male predominance corresponds to the higher prevalence of the common risk factors associated with cancers of head and neck region; tobacco smoking and chewing, one of the major risk factors, is seen more amongst the male population[7]. The mean duration of symptoms before presentation tends to be high because of the illiteracy and ignorance among the patients hailing from far flung villages. Due to sheer lack of awareness and non-availability of specialised health care centres patients tend to neglect their symptoms. Habituation to tobacco in the form of smoking and/or chewing is high among the rural Indian population[8], which is a major risk factor in the cancers of head and neck region. Out of the twenty seven patients, 23(85.19%) had unilateral and rest of the four bilateral cervical lymphadenopathy. In 19 patients the lymphadenopathy was limited to the level above cricoid while 5 patients had level IV and rest had conglomerate of multiple lymph nodes. Eleven of these patients had squamous cell carcinoma, seven had adenocarcinoma, six

had poorly differentiated carcinoma, and remaining three had undifferentiated carcinoma metastases. According to a study by Stefan AM Paul *et al*[9], the patients with primaries in the head and neck region had metastasis to lymph nodes above the level of cricoid, while those from lungs below the level of cricoids. FDG-PET-CT report was negative in 14 (51.85%) patients and was positive in 13 (48.15%) patients. Out of these thirteen patients, nine had primary tumour, while four patients had evidence of distant metastasis. It was seen that among the total 9 primary cases, two patients were PET-CT positive for primary in the base of tongue, two in the pyriform fossa and one each in the tonsil, parotid gland, and palate and two were outside head and neck region (lungs). Out of the four patients with distant metastasis, one had metastases in the thoracic vertebrae and lungs, while one patient showed skeletal, pulmonary, and adrenal metastases and the remaining two had FDG avid lesions suggestive of skeletal metastases. The rate of primary tumour detection by FDG-PET-CT was 33.33% in the present study and it was in agreement with most studies in the literature, with site detection rates of between 21% and 47%[6,10-14]. Only one study has indicated that PET-CT does not improve the detection of occult primary tumours in head and neck. These authors reported only 8% rate of primary tumour detection (1 out of 13) and also a high false positive rate[15]. Sensitivity of any diagnostic tool depicts the ability to bring out true positive and thereby correctly diagnose the presence of disease factor being studied; thus lesser the false negative, higher the sensitivity. Sensitivity of PET-CT in our study was 87.5%, while review of other studies revealed sensitivity ranging from 67 to 100%.[6,10-14] All the cases were also evaluated by MRI and it was seen that on MRI total 9 vases were positive for Carcinoma of unknown primary site (CUPS). Out of these 6 cases were also confirmed positive on Histopathological examination. Remaining three cases positive on MRI were diagnosed negative on Histopathological examination. Thus the sensitivity of MRI in diagnosing Carcinoma of unknown primary site (CUPS) was 75% with specificity of 84.21%. It was seen that the sensitivity of diagnosing the carcinoma of unknown primary site of PET CT was 87.5% whereas that of MRI was 75%. The specificity of PET CT was 89.5% whereas that of MRI was 84.21%. The difference observed in the diagnostic value of PETCT and MRI was statistically not significant. MRI as a morphological procedure allows for identification of a tumor due to its morphological and anatomical characteristics. However, this type of disease presents some problems with regard to identification. PET as functional procedure allows for the assessment and a possible definition of the identity of neoplasms based on their functional characteristics. In the context of primary diagnosis, the results of PET were better than the results of MRI. The superiority of PET was shown regarding the sensitivity as well as the specificity. However, the difference was not statistically significant. These findings correspond to data in the literature by other authers such as Bruschini P[16], Dammann F [17], Di Martino E[18], Dresel S[19] and Hannah A[20]. Regelink *et al*[21] conducted a study on 50 patients (37 men and 13 women) with cervical metastasis of an unknown primary, to compare the value of FDG-PET and conventional diagnostic modalities (CT and/or MRI) in detecting unknown primary tumours and distant metastases in patients suffering from cervical metastasis. All these patients underwent FDG-PET, in addition CT and/or MRI was obtained and panendoscopy was performed. The primary tumour could be detected in 16 patients (four detected exclusively by PET). The sensitivity and specificity of FDG-PET for detection of unknown primary tumours were 100 % and 94% respectively. For conventional diagnostic modalities these values were 92% and 76%.

## CONCLUSION

The sensitivity of diagnosing the carcinoma of unknown primary site of PET CT was 87.5% whereas that of MRI was 75%. The difference observed in the diagnostic value of PETCT and MRI was statistically not significant. Thus PET and MRI are characterized by a high sensitivity and specificity and represent important tools in current diagnosis of head and neck tumors.

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