

Significance of Morphological and Functional Imaging in Assessment of Residual and Recurrent Disease in Head and Neck Carcinomas

Abhishek Purkayastha*

Department of Radiation Oncology, Command Hospital, Pune, India

*Corresponding author: Abhishek Purkayastha, Department of Radiation Oncology, Command Hospital (Southern Command), Pune, India 411040, Tel: +9650901736; E-mail: abhi5296@gmail.com

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Abstract

Recent advances in therapeutic procedures and targeted agents in the treatment of Head and Neck Carcinoma (HNC) has resulted in increase in overall survival and disease-free survival. However, 15-50% of patients will still develop recurrent disease. Not only on-treatment patients but cancer survivors are also at high risk of developing second malignancies, of which one third occurring in the head and neck region. Increase in survival of these patients has in turn enhanced the detection chances of HNC recurrence which were normally not reported due to early mortality. For routine work-up, investigations like chest X-ray, Contrast Enhanced Computed Tomography (CECT) scan or Magnetic Resonance Imaging (MRI) is done while Positron Emission Tomography (PET) scan is recommended only in locally advanced disease. However, recent studies suggest that combining functional and morphological imaging with positron emission and computed tomography scan to be advantageous than individual imaging in detecting residual or recurrent lesion.

Keywords: Imaging; Morphological; Functional; Head and neck carcinoma; Residue; Recurrence

Introduction

Imaging modalities such as contrast enhanced computed tomography (CECT), magnetic resonance imaging (MRI), and ultrasonography (USG) have well-documented strengths and limitations [1,2] of their own. But none of these techniques has emerged as the test of choice for patients. They are insensitive in depicting small metastases or early post treatment recurrence because they rely on morphological changes that can be slow to progress. Functional imaging modalities such as positron emission tomography (PET) scan address this issue satisfactorily by interrogating the physiological properties of the tissues. The sensitivity and specificity of PET were comparatively higher and better compared to other techniques, and most studies [3,4] found PET to be superior. The technique of 18-fluoro-deoxy-glucose (FDG) with combined PET-CT is probably superior to both PET and conventional CECT imaging in assessing the presence of recurrence and helps in diagnosing other co-morbid conditions and distant metastasis in these patients that may affect the clinical treatment [5,6].

Discussion

Recurrence of HNC may develop in approximately 15-50% of patients [7,8]. Post treatment tissue changes formed due to Radiotherapy (RT) should not be misinterpreted as evidence of persistent or recurrent disease. Tissue necrosis after RT may be difficult to differentiate from recurrent tumor and in such circumstances patient management primarily depends on the combination of imaging and clinical findings. PET/CT can detect early recurrences as well as distant metastasis. For better results it is important to detect head and neck carcinoma (HNC) in early stages and early recurrence after treatment, as it will improve overall survival. Knowledge of sensitivity,

specificity, positive predictive value (PPV), negative predictive value (NPV) of CECT and PET-CT further aid in choosing an imaging modality for optimal results.

Differentiating and detecting residual/ recurrent tumor from post radiotherapy inflammation or scar is not easy using CECT scan. The contrast enhancement effect with CT is known to depend on vascularity, size of extra vascular space and vascular permeability of the tissues. These factors appear to be elevated in both inflammation and tumor. CT changes often show structural deformity, soft tissue swelling, and thickening of mucosal surface having no recurrent / residual tumor. Such soft tissue swelling, thickening of mucosal surface demonstrated on CT images does contain a small focus of recurrence, but a recurrent tumor cannot be diagnosed with certainty. More over if a small mass is detected, anatomical imaging cannot always be used to differentiate a recurrent tumor from granuloma, hematoma or post-RT inflammation. The larynx, base of tongue and oropharynx are particularly difficult to assess by CT because soft tissue swelling mimic or mask a recurrent tumor.

Finding out the optimal time to do a post-therapy imaging is an important and debated clinical issue. Performing CT or PET-CT as early as post-therapy seems logical as salvage treatment can be initiated early. However, imaging performed too early may lead to false-positive or false-negative result which decreases the specificity. Waiting too long might result in loss of therapeutic window and more morbid salvage procedures. Greven et al. [9] evaluated FDG-PET scans of 45 patients with head and neck cancer at 1, 4, 12, and 24 months after treatment. Specificity for detection of residual or recurrent tumor at 1 month was 95% and sensitivity 59%. At 4 months, specificity remained high at 90% but sensitivity increased to 100%. Therefore, they postulated the optimum time for post-treatment assessment between 2 to 4 months. Kim et al. [10] studied FDG-PET-CT scans of 143 patients at 3-6 and 12 months after primary treatment in HNCs and observed that sensitivities of 3-6 month and 12-month PET/CT scans at patient level were 96% and 93%, respectively. Also, 18FDG-

PET/CT scanning at 3–6 months and at 12 months after treatment is beneficial for the early detection of recurrence.

False negative results are generally less significant problem because of avid accumulation of FDG in tumor deposit [11]. False negative result may occur when a scan is performed soon after radiotherapy. False negative findings may also occur when tumor deposit is very small. When tumor is largely necrotic there are few viable cells to accumulate tracer or either the presence of microscopic metastasis not detected by 18FDG-PET/CT or by the proximity of nodal metastasis to the primary tumor which might obscure their detection. Early detection of HNC recurrence is critical because the disease-free survival after salvage surgery is highly dependent on the stage of the recurrent tumor. Diagnosis of recurrence is difficult with conventional imaging with CECT because of loss of symmetry and inflammation associated with healing. Routine biopsy is also not recommended. Metabolic imaging with FDG PET is more sensitive than CECT [11].

Conclusion

When the clinical suspicion of recurrent/ residue is high, FDG PET/CT may be performed first to identify patients who need to undergo further treatment. Patient with positive PET findings should be evaluated if there is reasonable salvage or palliative treatment option available. PET may help in tissue diagnosis and earlier treatment with potentially improved outcome. In addition, PET may detect distant metastasis which might spare some of patients from aggressive loco-regional treatment from which they might not benefit [12]. This is particularly important in newer paradigms of combined radiotherapy and concurrent chemotherapy, where close surveillance and early surgical treatment of tumor recurrence are essential to ensure optimal survival rates. Larger prospective studies are warranted to stabilize the definitive role in the management protocols and cost effectiveness of FDG PET/CT in the management of head and neck cancers.

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