EVALUATION OF NEOADJUVANT CHEMOTHERAPY RESPONSE AMONG BREAST CANCER PATIENTS VIA 18 FLUORINE-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY IMAGING

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Abstract

Background: Breast carcinoma is the most frequently diagnosed life-threatening cancer in women and leading cause of cancer death among women. In Western Europe and the United States, the incidence is highest in the 40 - 55 age range, and its prevalence is still on rise. It accounts for 40,000 and 14,000 deaths yearly in the US and UK, respectively, and that makes it the second cause of cancer death in women in those countries. Positron emission tomography (PET) with 18 fluorine (18f) flurodeoxy glucose (FDG) has an important role in oncology. Its role in management of breast cancer is evolving. These past years, combined PET and computed tomography (CT)(PET\CT) systems have replaced PET alone in most nuclear medicine departments. The CT portion of PET\CT provides anatomic information useful for accurate interpretation of PET signal. It also provides a map used for attenuation correction of PET images. To best of our knowledge, we conducted this review to identify the prevalence rate and probable risk factors of gestational diabetes among the pregnant women attending the Qena university hospital.

Conclusion: PET/CT is a reliable whole body single imaging which can be used in monitoring and evaluation of NAC response in breast cancer patients showing response, high sensitivity, and accuracy compared to CT alone or other modalities.

Key words: PET/CT; fluorine; fluorodeoxyglucose; Chemotherapy; Breast.

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Introduction:

Breast carcinoma is the most frequently diagnosed life-threatening cancer in women and leading cause of cancer death among women. In Western Europe and the United States, the incidence is highest in the 40 - 55 age range, and its prevalence is still on rise. It accounts for 40,000 and 14,000 deaths yearly in the US and UK, respectively, and that makes it the second cause of cancer death in women in those countries (1).

Positron emission tomography (PET) with 18 fluorine (18f) flurodeoxy glucose (FDG) has an important role in oncology. Its role in management of breast cancer is evolving. These past years, combined PET and computed tomography (CT)(PET\CT) systems have replaced PET alone in most nuclear medicine departments. The CT portion of PET\CT provides anatomic information useful for accurate interpretation of PET signal. It also provides a map used for attenuation correction of PET images (2).

The usefulness of neo-adjuvant chemotherapy (NAC) in breast cancer (BC) has been well-established and NAC is now routinely used especially in patients with inoperable tumors or to permit breast conservative surgery in young patients. Yet, this treatment is not devoid of toxicity. It is thus important to define which patients will benefit from NAC as breast cancer patients who achieve complete pathological response (pCR) on the surgical specimen have a better prognosis. FDG PET/CT with SUVmax changes during NAC has shown good results to predict pCR (3).

Aim of work:

To assess 18 fluorine-fluorodeoxyglucose positron emission tomography/computed tomography imaging role in evaluation of neoadjuvant chemotherapy response among breast cancer patients.

Histological classification of breast cancer:

Microscopic Types Breast carcinoma is usually classified primarily by its histological appearance, originating from the inner lining epithelium of the ducts or the lobules that supply the ducts with milk. For the morphological study of breast carcinoma, two main questions should be answered: is the tumor limited to the epithelial component of the breast (in situ carcinoma) or has invaded the stroma to become invasive carcinoma and does the tumor arise from the duct (ductal carcinoma) or from the lobule (lobular carcinoma)? (4).

Both tumor types arise from the same segment of the mammary gland. For diagnostic purposes, in daily histopathological practice, the cytoarchitectural features should be used to determine the tumor to be ductal or lobular, rather than its precise location within the breast tissue (4).

Fundamentals of PET/CT imaging:

While 18F-FDG uptake is not specific to cancer, it is well known that there is increased transport of glucose into malignant cells and up-regulation of enzymatic activity resulting in increased tracer uptake. Combined PET/CT facilitates the separation of normal physiologic uptake from pathologic uptake, provides accurate localization of functional abnormalities, and reduces the incidence of false-positive and false-negative imaging results (5).

The CT serves three functions: (1) provides the anatomical correlation for the functional information, (2) the means for CT-based attenuation correction of the PET data and (3) provide clinical diagnostic-quality CT images. The PET scanner is located behind the CT scanner and housed in the same extended-length gantry. CT images are acquired first and are used to generate attenuation-correction factors (ACFs) to be applied to the PET data to correct for the effect of photon attenuation (5).

PET is performed following the CT study without moving the patient for the same axial extent. Approximately six to seven bed positions are planned in the three-dimensional acquisition mode for scanning the entire patient with 5-7-minute acquisition at each bed position (6). The volume of data generated is enormous. Hundreds of trans-axial PET and CT images are first reconstructed. These are then reformatted into coronal and sagittal images to facilitate image interpretation. For each of these sets of PET and CT images, corresponding "fusion" images, combining the two types of data, also are generated (7).

How molecular imaging detect cancer?

Malignant cells have increased glucose utilization due to up regulation of hexokinase activity. Glucose is taken up by tumor cells by facilitated transport (via glucose transporters [GLUT]) and then undergoes glycolysis with the formation of pyruvate under aerobic conditions. However, under hypoxic conditions (in a necrotic tumor), glucose is metabolized under anaerobic conditions with resultant increased tumor lactate levels (8). 18F-FDG is taken up by metabolically active tumor cells using facilitated transport similar to that used by glucose. The rate of uptake of 18F-FDG by the tumor cells is proportional to their metabolic activity. Like glucose, it undergoes phosphorylation to form 18F-FDG-6-phosphate; however, unlike glucose, it does not undergo further metabolism, thereby becoming trapped in metabolically active cells (8).

The metabolic differences between normal tissue and cancer:

Cancer tissue generally has increased glycolysis, protein synthesis, more anoxic and hypoxic cells, increased or decreased receptors and increased DNA synthesis, increased blood flow and increased amino acid transport. The disproportionately higher metabolic rate in malignant cells combined with 18F-FDG's resemblance to glucose is the basis behind tumor imaging with 18F-FDG-PET (9).

Mechanisms of increased uptake of 18F-FDG in cancer cells include the following: increased glucose transport because of an increased density of plasma membrane GLUT molecules, increase in vascularity with endothelial cell uptake of 18F-FDG and increased enzyme activity in the glycolytic pathway (10).

General Principles of 18F-FDG Production:

Bombarding 18O-enriched water with protons in the cyclotron results in a mixture of H2 (F-18) and 18O-enriched water. Synthesis of 18F-FDG from this mixture is an automated computer-controlled radiochemical process that takes approximately 50 minutes to complete. The 18F-FDG thus produced is a sterile, non-pyrogenic, colorless, and clear liquid, with residual solvent of less than 0.04%. The radioactive purity is greater than 95%, and the residual activity is approximately one-third to one-half of the original activity (which may vary depending on the synthesis process) (8).

Factors degrading PET imaging:

The images generated by PET scanners are accurate representations of the objects being analyzed, but there are several factors that can degrade image quality. Absorption and scatter are two such factors. Attenuation refers to the decrease in intensity of a photon signal as it passes through matter either by absorption or by scatter (11-13). Attenuation effects are directly proportional to the density and thickness of the various tissues through which photons travel. If the matter through which a photon is traveling stops the photon completely, it is

called absorption. Scatter refers to the alteration in the direction of a photon's path due to its interaction with matter (e.g. tissues) along that path. These effects are related, and both give rise to image reconstruction errors that can adversely affect the accuracy of a PET scan (9).

Practical Points in the Interpretation of PET/CT Scans:

There are different methods for assessment of radiotracer uptake by normal and pathologic tissues, such as visual inspection, the standardized uptake value (SUV), and the glucose metabolic rate. Visual inspection is frequently used in analysis of PET/CT results by viewing fused PET/CT images (8). The standardized uptake value of a lesion is calculated to determine if the lesion is more likely to be benign or malignant. The SUV is dependent on many variables, including body mass and the region of interest, and is higher in obese patients and with smaller regions of interest (12).

The SUV (Standardized Uptake Value) is a unit-less ratio that can be understood as the concentration of 18F-FDG within a lesion divided by the concentration of radiotracer distributed throughout the body. Mathematically, it can be expressed as follows:

SUV=C (T)/(dose injected/body weight) where C is the tissue concentration of 18F-FDG at time T. An SUV is a simplified index of 18F-FDG uptake and provides a relative indication of the degree of metabolism within the lesion being evaluated. The SUV measurement is directly proportional to metabolic activity. SUV can be notated as the maximum value within a lesion (SUVmax), or the average value within a region of interest drawn around a lesion (SUVavg). The SUVmax is more robust because it is more reproducible, being less affected by the size and placement in the region of interest. The SUV should be used with caution as it is affected by multiple factors, and it is subjected to error (9).

Conclusion and recommendations:

We concluded that PET/CT is a reliable whole body single imaging which can be used in monitoring and evaluation of NAC response in breast cancer patients showing response, high sensitivity, and accuracy compared to CT alone or other modalities.

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