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The Effect of Hydration in 18F-FDG PET/CT Image Quality and External Radiation Exposure.

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ABSTRACT:

AIM: Measuring the effect of patient hydration on PET-CT image quality using qualitative and semi-quantitative analysis suggesting a method to decrease external radiation dose rate before patient discharge after PET/CT scan. **Materials and methods**: 60 Patients over the age of 18 who came to the nuclear medicine department, National Cancer Institute, Cairo university. to undergo 18F-FDG PET-CT for different indications and were willing to participate in our study were selected. Results 60 patients who came to undergo 18F-FDG PET-CT were randomly divided into 2 groups (30 patients each). Group A receives a hydration while group B did not receive any form of hydration External radiation dose rate at 1 m distance of group A and group B at different times were as follows: **Results:** post-injection measurement (measurement 1) was 28.8±5.8 µSv/h and 38.5±9.8 µSv/h, post-voiding 1 measurement (measurement 2) was 20.1±5.4 µSv/h and 24.8 ±7.1 µSv/h, post-scan measurement (measurement 3) was 16.8±4.5 µSv/h and 20.4±5.8 µSv/h, post-voiding 2 measurement (measurement 4) was 15.2±4.2 µSv/h and 18.6±5.6 µSv/h respectively (P value <0.05) The Qualitative analysis showed a total of 3 patients (5%) with poor image quality, of these 3 patients, 1 patient (3.3%) in group A and 2 (6.6%) were in group B. A total of 20 patients (33.3%) with fair image quality, of whom 3 patients (10%) were among group A and 17 (56.7%) among group B. A total of 37 patients (61.7%) with good image quality, 26 (86.7%) of whom were among group A and 11 (36.7%) among group B (P value < 0.001). **Conclusion**: The patient's hydration helps reduce the external radiation dose rate, enhances image quality by qualitative analysis, however, it does not affect other parameters of the semi-quantitative analysis.

Key Words: hydration , 18FDG PET/CT.

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INTRODUCTION:

The use of FDG PET-CT has been rapidly increased and with the extensive use of FDG a concern has been raised about the risk of radiation exposure of the patients, public and medical staff which might increase the potential for cancer risk(1).

The effective dose depends mainly on the injected dose of radiotracer and the CT protocol used. The effective doses from PET-CT investigations are reported to be 25 mSv, however, it can vary from 13.45 - 31.91 mSv for female patients and 13.65 – 32.18 mSv for male patients when using different PET/CT protocols (2,3)

In a recent study, some interventions were tried to reduce the radiation exposure rate of the patients before leaving the nuclear medicine department The study found that advising patients to wait for 30 minutes after the PET-CT scan then void significantly reduced the radiation exposure rate (4)

The detection of a pathologic finding (hot spot) on a PET-CT scan is related to the degree of metabolic activity in the lesion and, in particular, to the difference in 18F-FDG uptake between the tumor and surrounding normal tissues, or target-to-background ratio.

Qualitative analysis:

Visual analysis of the PET images, especially MIP and major organs (brain, heart, liver, spleen, urinary bladder and pelvic organs) is required to detect any increase in FDG uptake in an area where it does not belong. (5).

Semi-quantitative analysis:

Standardized Uptake Value (SUV): it is the measured activity normalized for body weight/surface area and injected dose. SUV = 1.0 if the injected dose is uniformly distributed all over the surveyed body. Achieving reproducible SUVs is difficult and require identical patient preparation, using the same dose of 18F-FDG and comparable times of uptake and clearance of the tracer between the baseline and follow up PET-CT. In the current practice liver (hepatic SUV max) _ and mediastinal blood pool in cases of lymphoma (BP SUV max) _ SUV max are used as references to determine the response to therapy between the baseline study and the post-therapy study (6,7)

PATEINTS AND METHODS:

Patient population:

60 Patients over the age of 18 who came to the nuclear medicine department, National Cancer Institute, Cairo university. to undergo 18F-FDG PET-CT for different indications and were willing to participate in our study were selected. Patients arrived at the nuclear medicine department early in the morning, medical history, vital and physical parameters, random blood glucose, patient's weight, height and age were taken. The patients had the following Inclusion criteria: age above 18 years and patients indicated for undergoing

18F-FDG PET-CT. the Exclusion criteria includes Patients with documented renal impairment, below the age of 18, with blood glucose level>200, with mediastinal, lung or chest wall lesions, received chemotherapy less than 3 weeks before, received radiotherapy less than 6 weeks before or with pathological FDG uptake at the areas where we measure the SUV max.

Patients randomization: 60 patients were randomly divided into 2 groups (30 patients each). Group A receives a hydration of 1000 ml of water starting 3 hours before, during and after the exam. Group B who did not receive any form of hydration 3 hours before, during or after the end of 18F-FDG PET-CT exam.

Patient preparation: Fasting for 4-6 hours prior to the study, avoid severe muscles exercise for 24 hours prior to the study and blood glucose level before the F18 FDG administration should not exceed 200 mg/dl.

Imaging procedure:

Dose: Patients received a weight calculated dose of F-18 FDG injected, approximately 0.11 mCi/kg body weight of 18-F FDG.

Image acquisition: FDG PET/CT study was done using a dedicated PET-CT scanner (GE Medical System,). Injection was followed by approximately 60 minutes of uptake. Immediately before entry to scan patients were instructed to void (pre-scan voiding). Acquisition time was approximately 13 minutes. After the scan patients were instructed to void again.

Initially, patients were examined in the supine position with arms elevated, and CT scanning was started with the following parameters: 140 keV, 80 mA, PITCH: 1.375, slice thickness: 3.75 mm. No CT contrast agents were administered. Both PET and CT scans were performed for patients under normal tidal breathing. The CT scans were acquired from skull vault reached caudally to the mid thighs. PET was performed immediately after acquisition of the CT images (6-8 bed positions; acquisition time, 2 min/bed position). From the raw emission data collected, the image was reconstructed by iterative reconstruction with CT-derived attenuation correction using the ordered subsets expectation maximization algorithm.

The external radiation dose rate was measured in 4 occasions for every patient, every occasion consisted of 3 consecutive measurements, 10 seconds each, using a GM tube ,placed at a distance of 1 m to the patient's mid-chest and the average of the three readings was taken and recorded in µSv/h. A dedicated isolated room was used for that purpose, away from the resting area of other patients and the hot lab with no other patients around. Measurement 1 was immediately after dose injection, measurement 2 after pre-scan voiding, measurement 3 immediately after the 18F-FDG PET-CT scan, measurement 4 after a second voiding immediately after the PET-CT scan.

The post-voiding 2 step is not implemented in the commonly used PET-CT imaging protocol, however, we wanted to investigate the effect of a second voiding in reducing the external radiation dose exposure before patient’s discharge.

Although the American Nuclear Regulatory Commission has well-established guidelines for the release of patients undergoing therapeutic procedures the guidelines for releasing patients after undergoing PET-CT scan are not clear. We used 20 µSv/h external radiation dose (the maximum accepted exposure of the public from a material source as a benchmark to examine the difference between the patients who received hydration and those who did not receive any hydration to determine the effect of hydration on external radiation dose. (8,9,10)

Image quality: PET-CT images were reviewed on the manufacturer's GE review station, which provides multiplane reformatted images and enables display of the PET images, CT images, and fused PET/CT. The 18F-FDG PET-CT of every patient of the 60 patients was reviewed blindly and separately on different days by two experienced nuclear medicine consultants for qualitative and semi-quantitative analysis.

Qualitative analysis is to be done by reviewing the maximum intensity projection (MIP) images and the tracer bio-distribution. Images were viewed and assessed blindly and separately by 2 expert nuclear medicine readers, a separate score is given to every scan by the two readers and the average score is calculated and reported collectively as (poor, fair and good image quality)

semi-quantitative analysis, the nuclear medicine physicians referred to PET scans fusion images to set a spherical volume of interest (VOI) over the regions of interest at fixed anatomical regions: background represented by muscle (gluteus Maximus bilaterally), adipose tissues (lumbar region and abdominal sub-dermal regions), Liver (right lobe), blood pool (aortic arch lumen) as a reference and bladder cavity to determine the effect of hydration on bladder activity. Subjects with inflammatory process, malignant disease or any pathological FDG uptake at these regions were excluded. The maximum standardized uptake value (SUV max) was recorded for every region and the mean value for every SUV max measured by the two expert physicians was taken.

Statistical analysis: Data management and analysis were performed using Statistical Package for Social Sciences (SPSS) vs. 28. Numerical data were summarized using means and standard deviations or medians and/or ranges, as appropriate. Categorical data were summarized as numbers and percentages. Estimates of the frequency were done using the numbers and percentages. Numerical data were explored for normality using Kolmogrov-Smirnov test and Shapiro-Wilk test. Chi square or Fisher's tests were used to compare between the independent groups with respect to categorical data, as appropriate. Comparisons between two groups for normally distributed numeric variables were done using the Student's t-test while for non-normally distributed numeric variables, comparisons were done by Mann-Whitney test. Comparison between multiple related groups of normally distributed numerical data was done using Repeated measures ANOVA. Comparison between multiple related groups of non-normally distributed numeric variables was done using Friedman test.

To measure the strength of association between the normally distributed measurements, Pearson's correlation coefficients was computed (r is the correlation coefficient & it ranges from -1 to +1), **Spearman's correlation** coefficients was calculated for non-normally distributed variables (r: fom 0 to 0.25 (-0.25) = little or no correlation; from 0.25 to 0.50 (-0.25 to 0.50) = fair degree of correlation; from 0.50 to 0.75 (-0.50 to -0.75) = moderate to good correlation; greater than 0.75 (or -0.75) = very good to excellent correlation). All tests were two tailed & Probability (p-value) ≤ 0.05 is considered significant [11].

RESULTS:

Of the 60 patients, 36 were females (60%) of whom 15 female patients (50%) in group A and 21 female patients (70%) in group B. 24 patients were males (40%) of whom 15 patients (50%) in group A and 9 patients (30%) in group B. The mean age for group A 40±11 years and 43±10 years for group B. A total of 40 patients (66.7%) had different types of lymphoma and 20 patients (33.3%) had other malignancies shown in **table 1**

Table (1): Clinical data of the 2 groups of the study.

Type of group	Hydration	No Hydration	
	Mean ± SD	Mean ± SD	P value
Weight	78.9 ±11.6	80.1±9.3	0.668
Height	165.1 ±8.3	162.7±8.4	0.365
Body mass index	29.2±5	30.4±4.6	0.301
Creatinine	0.8±0.1	0.8±0.1	0.337
Random blood sugars	102.8±11.1	108 ±24.8	0.991

External radiation dose at 1 m distance of group A and group B at different times were as follows: post-injection measurement (measurement 1) was 28.8±5.8 μSv/h and 38.5±9.8 μSv/h, post-voiding 1 measurement (measurement 2) was 20.1±5.4 μSv/h and 24.8

±7.1 µSv/h, post-scan measurement (measurement 3) was 16.8±4.5 µSv/h and 20.4±5.8 µSv/h, post-voiding 2 measurement (measurement 4) was 15.2±4.2 µSv/h and 18.6±5.6 µSv/h respectively (P value <0.05)

The post-scan measurement showed that a total of 18 patients (30%) showed an external radiation dose of >20 µSv/h while a total of 42 patients (70%) showed external radiation dose of ≤ 20 µSv/h. Of The 18 patients, 7 patients (23.3%) were in group A and 11 patients (36.7%) were in group B. The percentage change between the post-scan measurement and post-voiding 2 measurement were comparable: 8.4% for group A and 8.7% for group B with 4 patients (13.3%) of group A remaining >20 µSv/h and 10 patients (33.3%) of group B remaining >20 µSv/h shown in **table 2**.

Table (2): Comparison between time of measurements in the 2 groups.

Type of group	No hydration Mean ± SD	Hydration Mean ± SD	P value
post-injection time	2.8 ±1.3	2.9±1.2	0.876
post-voiding 1 time	49 ±23.6	50.7±24.4	0.933
Entry to the scan time	60.4 ±23.9	62 ±26.5	0.985
Post-scan time	72.5±23.9	74.2±26.5	0.956
Post-voiding 2 time	81.3 ±21.6	83.3 ±27.6	0.939

The Qualitative analysis done by the two expert nuclear medicine readers showed a total of 3 patients (5%) with poor image quality, of these 3 patients, 1 patient (3.3%) in group A and 2 (6.6%) were in group B. A total of 20 patients (33.3%) with fair image quality, of whom 3 patients (10%) were among group A and 17 (56.7%) among group B. A total of 37 patients (61.7%) with good image quality, 26 (86.7%) of whom were among group A and 11 (36.7%) among group B (P value < 0.001) as shown in **figure 1**.

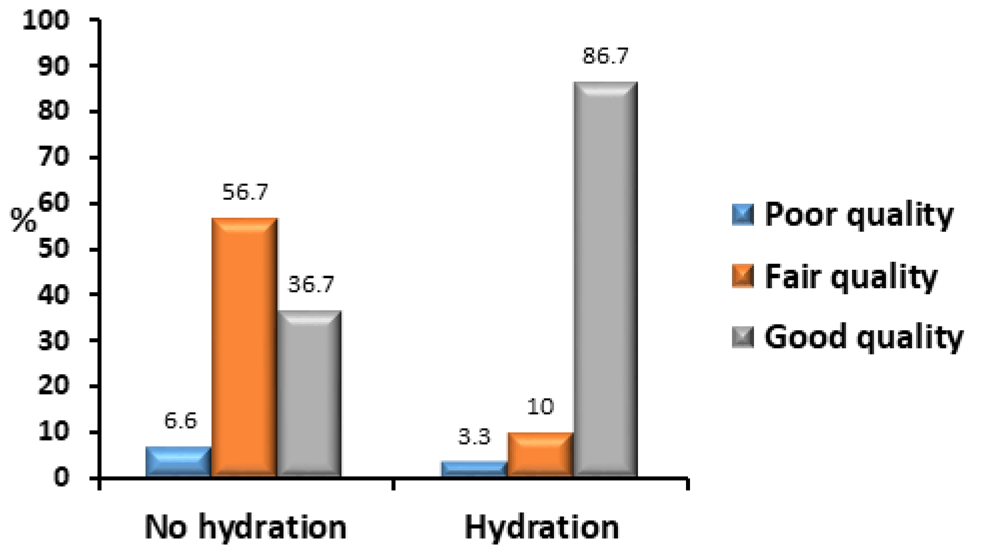

Fig (1): Bar graph representing qualitative analysis of the image quality among the 2 groups.

The semi-quantitative analysis showed significantly less activity in the bladder in group A than group B (P value = 0.003), however, no significant difference was found between the two groups regarding hepatic, blood pool, adipose tissue and muscle uptake between the 2 groups shown in **table 3.**

Table (3): Semi-quantitative analysis of the 2 groups.

Type of group	No Hydration Median (range)	Hydration Median (range)	P value
Hepatic SUV max	**4 (2.2-6.2)**	**3.9 (1.7-6.3)**	**0.921**
Blood pool SUV max	**2.7 (0.4-4.6)**	**2.7 (1.5-4)**	**0.944**
Urinary bladder SUV max	**40.6 (16.5-551.2)**	**52.8 (13.1-423.9)**	**0.003**
Adipose SUV max	**0.7(0.1-3.1)**	**0.6 (0.3-1.2)**	**0.122**
Muscle SUV max	**1.7(0.3-5.1)**	**1.7 (0.5-2.8)**	**0.544**

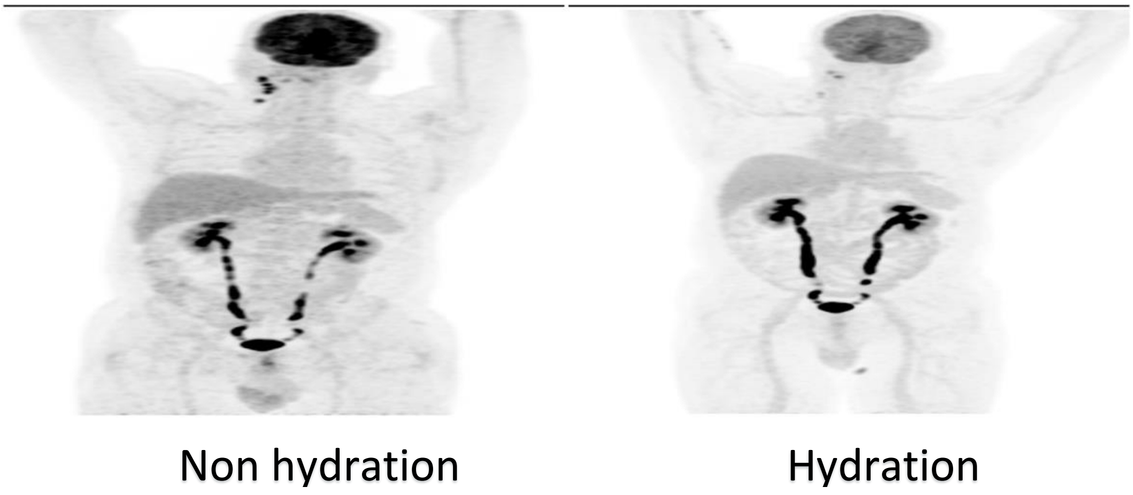

Fig (2): MIP images of both PET-CT scans of case no.1. Non-hydration PET-CT scan on the left and hydration PET-CT scan on the right.

Regarding the semi-quantitative analysis, there was no significant difference between the 2 scan regarding hepatic, blood pool, muscle and adipose tissue SUV max, with lower FDG activity detected at the bladder in the 2nd PET-CT scan.

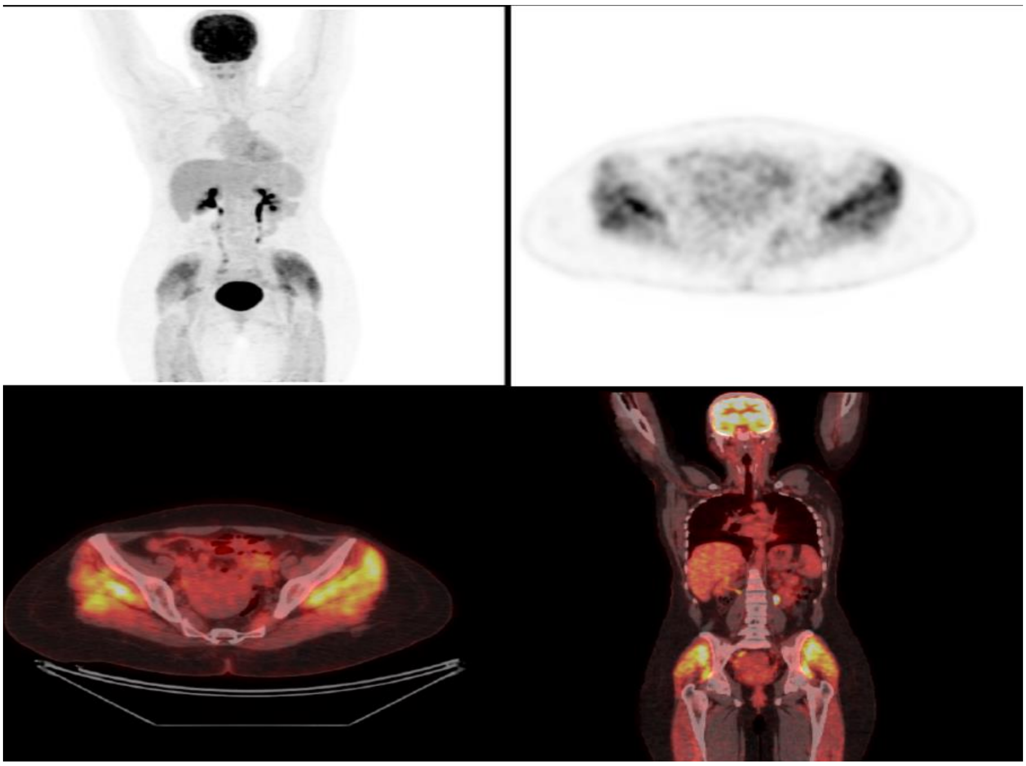

Fig (3): a 31-year-old female patient with HL, underwent end of therapy PET-CT evaluation, The patient received hydration of 1000 ml of water before and after the injection.

The Qualitative analysis showing Diffuse bilateral FDG uptake seen at the muscles of both lower limbs with overall poor image quality by qualitative analysis

Table (4): Semi-quantitative analysis of case no.1 showing increased muscle FDG uptake with SUVmax~13.1

	Hydration
Hepatic SUV max (g/ml)	5.2
Blood pool SUV max (g/ml)	3.8
Muscle SUV max (g/ml)	13.1
Adipose tissue SUV max (g/ml)	0.71
Urinary bladder SUV max (g/ml)	45.67

The PET-CT done under hydration condition shows generally lower external radiation dose rate than the PET-CT done under no hydration condition. Muscle effort might affect the PET-CT showing as diffuse intense FDG uptake, locally affecting image quality and hindering lesions at the affected area of the body. Post-voiding 2 step reduce the external radiation dose rate under 20 µSv/h.

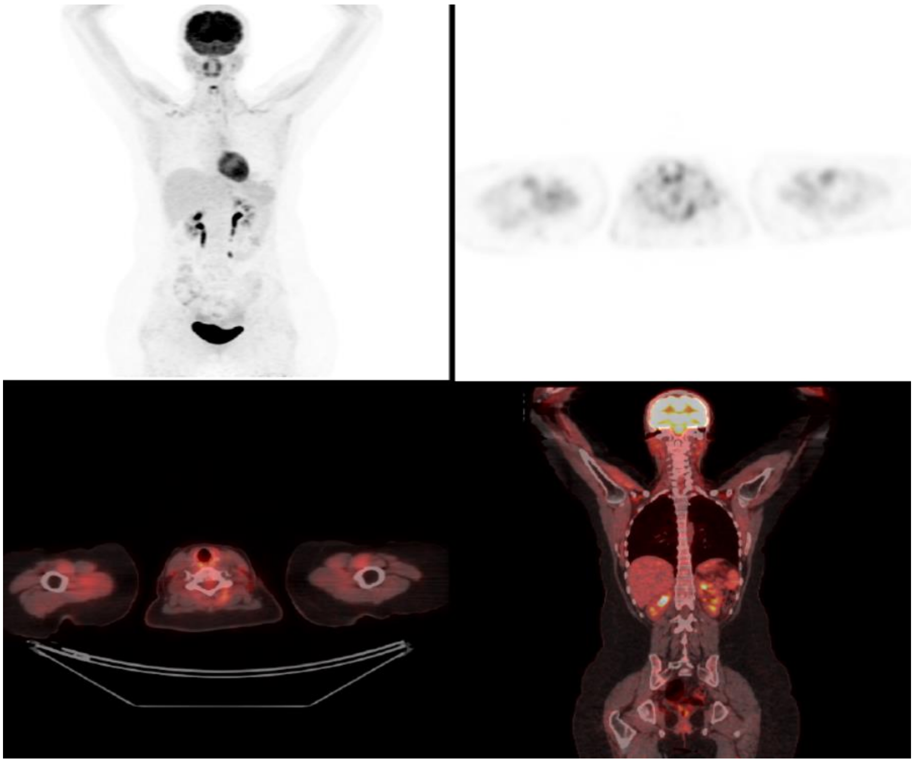

Fig (4): a 31-year-old female patient with HL, underwent interim PET-CT. The patient did not receive hydration.

The Qualitative analysis showed fair image quality with increased FDG uptake at upper limbs muscles that might be due to muscular effort done by the patient. Apart from increased uptake at both ureters, the rest of the body showed normal tracer bio distribution with low background activity.

Table (5): Semi-quantitative analysis of case No.2 with increased muscle uptake

	No hydration
Hepatic SUV max (g/ml)	4.1
Blood pool SUV max (g/ml)	2.7
Muscle SUV max (g/ml)	5.1
Adipose tissue SUV max (g/ml)	0.71
Urinary bladder SUV max (g/ml)	135.35

Although dose injected, creatinine level and RBS in case 2 were comparable to case 1, the external radiation dose rate emitted from case 2 was higher with the post-voiding 2 for case 2 > 20 µSv/h. Muscular effort might affect the PET-CT showing as diffuse intense FDG uptake, locally affecting image quality and hindering lesions at the affected area of the body.

DISCUSION:

With recent significant increase in the use of PET-CT, there were major concerns regarding radiation exposure and the risk it carries for the public and medical personnel in direct contact with the patient after the PET-CT exam [(1)].

Reports had shown that hydration with or without the use of diuretics might be of benefit in improving image quality and enhancing tumor detection especially in abdomino-pelvic neoplasms as a result of increase tracer excretion and elimination by kidneys and urinary bladder that might hinder a true lesion [(12,13,14)].

Hydration is also associated with solving another problem that nuclear medicine doctors face which is the increased background activity and the dilemma created by the low tumor/background ratio that might directly affect the ability of the nuclear medicine physicians to read and report the PET-CT scans.

In the current study we investigated the effect of hydration on both the external radiation dose rate and the images quality.

Our study showed that throughout the 4 measurements, patients who received hydration showed external radiation dose rate lower than patients who did not receive hydration (P value <0.05). IHN HO CHO et al, a cross sectional study published in 2012 investigating the factors affecting external radiation dose rate in patients undergoing PET-CT showed similar results with patients who received more hydration before tracer injection eliciting less external radiation exposure dose rate. The study also showed that patients who received hydration post-injection elicited lower external radiation dose rate than patients who did not receive hydration after the tracer injection. Hence, encouraging patients to drink more water before and after the tracer injection might be advised as a simple cheap method to reduce external radiation exposure dose rate [(15).]

In our study, we found that there is a strong correlation between body weight and external radiation dose rate (r=0.94 & P value < 0.001). Since the injected tracer dose was calculated based on body weight, patients with higher body weight received a higher dose which resulted in higher external radiation dose exposure rate especially in post-injection measurement (measurement 1) even with more tissue attenuation in patients with higher body weight. Hence it is advisable to use the minimum dose possible to reduce the external radiation dose rate, provided that it does not affect the image quality.

An 8.4% percentage decrease in radiation exposure dose rate of group A was found between the post-scan measurement and post-voiding 2 measurement with only 13.3% of patients remaining >20 μSv\h, therefore, post-scan voiding might be advised to reduce the external radiation dose rate although there was no significant difference between the percentage decrease in radiation exposure dose rate between the 2 groups after the post voiding 2 step (P value = 0.924).

Muzaffar et al, a randomized clinical trial study published in seeking to develop simple methods to reduce external radiation dose rate showed more significant decrease in external radiation dose rate after the post-scan voiding step: 20% with 33% of patients remaining >20 μSv\h, which might be due to incomplete urination and improper emptying of bladder by the subjects in our study [(16).]

Quantitative analysis categorizing patients into 3 categories according to the image quality: poor, fair and good image quality showed that patients who received hydration showed overall better image quality than patients who did not receive hydration with 26 patients (86.7%) in group A showing good image quality, 3 patients (10%) showing fair image quality and only 1 patient (3.3%) showing poor image quality. Group B consisted of 11 patients (36.7%) with good image quality, 17 patients (56.7%) with fair image quality and 2 patients (6.6%) showing poor image quality.

The semi-quantitative analysis of both groups using the maximum standardized uptake showed no significant difference between the 2 groups median hepatic, blood pool, adipose tissue and muscular SUV max, while the urinary bladder SUV max was significantly different between the 2 groups: These results might be because hydration increases the urine volume with increase in elimination of the tracer by the kidneys and bladder, which is of significant importance especially in patients with pelvic neoplasms.

Ceriani et al, a clinical trial study published in 2011 comparing different hydration protocols effect on semi-quantitative analysis of PET-

CT image quality showed that free oral hydration is worse than other hydration protocols with or without the use of furosemide regarding background activity (muscle and adipose tissue SUV max), however, there was no study comparing background activity between hydration and non-hydration patients to our knowledge. [17].

CONCLUSIONS:

Proper hydration significantly decreases the external radiation dose in patients who undergo PET-CT scans with a significant decrease in radiation exposure dose rate after voiding before their discharge. Hydration also affects the qualitative image showing good image quality than those images with no hydration.

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