

SHORT COMMUNICATION

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Impact of fasting on ^{18}F -fluorocholine gastrointestinal uptake and detection of lymph node metastases in patients with prostate cancer

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Abstract

Background: ^{18}F -fluorocholine PET/CT is used to detect lymph node metastases in prostate cancer patients. Physiological ^{18}F -fluorocholine in the gastrointestinal tract, especially in the intestines, may interfere with the detection of malignant lymph nodes. Fasting is frequently proposed in literature; however, scientific support is lacking. This study aims to determine the impact of fasting on ^{18}F -fluorocholine uptake in the gastrointestinal tract.

Methods: Eighty patients were studied, 40 fasted for at least 6 h prior to ^{18}F -fluorocholine administration while the other 40 did not fast. ^{18}F -fluorocholine uptake pattern and intensity were evaluated in the intestine near the abdominal aorta and four regions near the iliac arteries. ^{18}F -fluorocholine intensity was also measured in the liver, pancreas, stomach and spleen.

Findings: No statistically significant differences were found in ^{18}F -fluorocholine uptake in the gastrointestinal tract between the fasting and non-fasting group.

Conclusions: Fasting for 6 h has no effect on ^{18}F -fluorocholine uptake in the gastrointestinal tract. Therefore, no effects on the detection of malignant lymph nodes are expected, and fasting is not recommended in our opinion.

Keywords: ^{18}F -fluorocholine, PET/CT, Prostate cancer, Urology, Patient preparations

Introduction

Choline-PET/CT is widely used in patients with prostate cancer. Clinically, the imaging technique is used mainly for restaging of patients with a biochemical relapse and less frequently for initial staging. One of the strengths of choline-PET/CT is the detection and localisation of prostate cancer metastases in patients with slightly elevated PSA. Lymph node metastases can be detected in lymph nodes, which do not show malignant characteristics on conventional imaging such as CT and MRI. Patients with limited lymph node metastases may be selected for procedures with curative intent, while patients with more

extensive disease can be protected from the morbidity of senseless aggressive therapies.

Detection of lymph node metastases may be hampered by high physiological choline uptake in the gastrointestinal tract commonly seen on choline-PET/CT. In the literature, fasting is frequently proposed before ^{18}F -fluorocholine PET/CT, as can be found in a summary of literature by Chondrogiannis et al. [1]. Four hours of fasting before administration of ^{11}C -choline is suggested in a document of the Society of Nuclear Medicine and Molecular Imaging [2]; however, both the Society of Nuclear Medicine and Molecular Imaging and the European Association of Nuclear Medicine have no specific guidelines for ^{18}F - or ^{11}C -choline PET/CT. To the best of our knowledge, there is no evidence that supports fasting prior to choline-PET/CT in order to suppress physiological choline uptake in the gastrointestinal tract. In a small animal study, fasting was not found to affect tracer

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uptake in the liver for both ^{11}C -choline and ^{18}F -fluorocho-
line [3]. This study aims to determine the impact of
fasting, for at least 6 h, on ^{18}F -fluorocho-
line uptake in the
gastrointestinal tract.

Methods

From May 2013 data of all ^{18}F -fluorocho-
line-PET/CTs at our department were prospectively entered in a data-
base. All patients gave written consent for the use of
their anonymous data. Initially, all patients were scanned
without prior fasting. Due to the observed high physio-
logical ^{18}F -fluorocho-
line uptake in the intestine, the
patient preparation protocol for prostate cancer patients
was changed after the first 40 patients had been scanned.
In the revised patient preparation protocol, patients were
asked to fast for at least 6 h prior to administration of
 ^{18}F -fluorocho-
line. All scans were evaluated after a sec-
ond cohort of 40 patients was scanned that had properly
followed the revised patient preparation protocol.

LIST-mode data of the prostatic region were acquired
for 10 min directly after ^{18}F -fluorocho-
line administration (190 MBq, mean), followed by late images from the
inguinal region to the base of the skull approximately
45 min later (Siemens Biograph-16 TruePoint PET/CT,
Siemens Healthcare, Knoxville, USA).

For each patient, the LIST-mode data was used to
determine the choline time-activity pattern in the in-
testine during the first 10 min after ^{18}F -fluorocho-
line administration (software: Siemens syngo.via, Siemens
Healthcare, Knoxville, USA). The Kolmogorov-Smirnov
test was used to check for a normal distribution in the
data. A *T* test or the Mann-Whitney *U* test was used
to check for the differences between the groups at each
time point after injection. A *T* test was used when the
data in both groups showed a normal distribution; other-
wise, the Mann-Whitney *U* test was used.

Late data was used to determine the ^{18}F -fluorocho-
line uptake in the liver, spleen, stomach, pancreas and in-
testine. In five different regions: 1 cm or less in the
proximity of the aorta, both the left and right common
iliac arteries, and both the left and right external iliac
arteries, intestinal activity were measured. A *T* test or
the Mann-Whitney *U* test was used to check for the
differences between the groups in measured SUV_{max}
and SUV_{peak} , for each evalu-
ated organ/region.

Findings

Patient population

In both the fasting and non-fasting group, 40 patients
were included. Mean age was 71.9 years (range 59–83)
and 69.1 (range 51–83) for the fasting and non-fasting

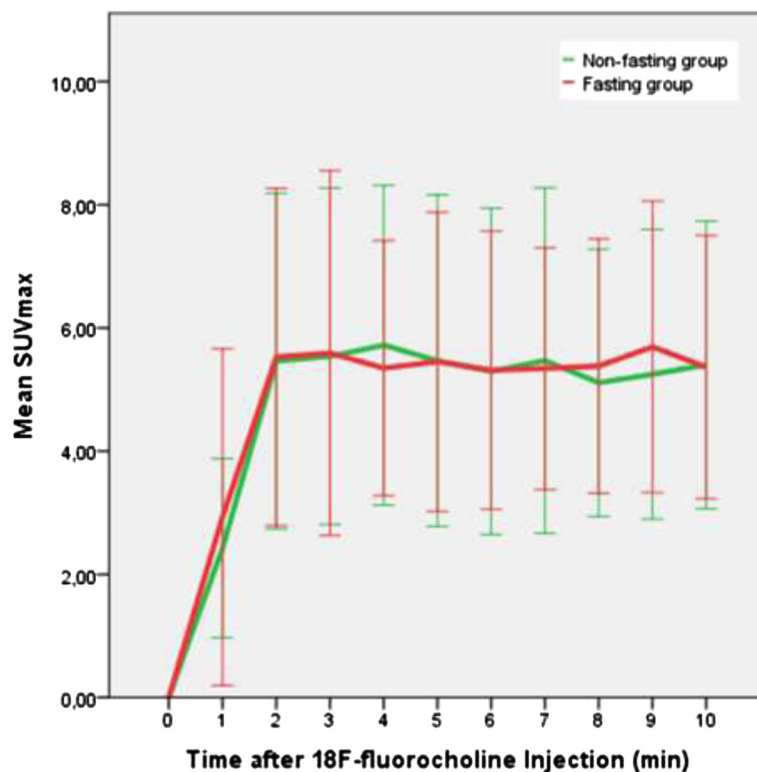


Fig. 1 Mean intensity and uptake pattern of ^{18}F -fluorochole in intestine in the pelvis in the first 10 min after intravenous ^{18}F -fluorochole administration in both the fasting and non-fasting group. Error bars showing the standard deviation

Table 1 Intensity of ¹⁸F-fluorocholine uptake in the intestine in five perivascular regions in pelvis and abdomen for fasting and non-fasting group

| | Fasting | Number | Mean | σ | p |
|--|---------|--------|------|----------|--------|
| SUV _{max} intestine in region near | | | | | |
| Abdominal aorta | No | 40 | 5.69 | 1.43 | 0.421* |
| | Yes | 40 | 5.25 | 1.69 | |
| Right common iliac artery | No | 26 | 3.27 | 1.79 | 0.876# |
| | Yes | 32 | 3.25 | 1.56 | |
| Left common iliac artery | No | 15 | 4.66 | 2.48 | 0.075* |
| | Yes | 18 | 3.64 | 1.59 | |
| Right external iliac artery | No | 37 | 3.65 | 1.50 | 0.954# |
| | Yes | 39 | 3.58 | 1.21 | |
| Left external iliac artery | No | 27 | 3.88 | 2.05 | 0.909# |
| | Yes | 32 | 3.50 | 1.41 | |
| SUV _{peak} intestine in region near | | | | | |
| Abdominal aorta | No | 40 | 4.91 | 1.24 | 0.226* |
| | Yes | 40 | 4.44 | 1.37 | |
| Right common iliac artery | No | 26 | 2.78 | 1.55 | 0.784# |
| | Yes | 32 | 2.77 | 1.33 | |
| Left common iliac artery | No | 15 | 3.98 | 2.03 | 0.115* |
| | Yes | 18 | 3.11 | 1.39 | |
| Right external iliac artery | No | 37 | 2.93 | 1.08 | 0.909# |
| | Yes | 39 | 2.99 | 1.05 | |
| Left external iliac artery | No | 27 | 3.14 | 1.63 | 0.982# |
| | Yes | 32 | 2.88 | 1.05 | |

Statistical analysis with *T test and #Mann-Whitney U test

group, respectively. Median PSA was 5.6 (0.3–194) and 4.3 (1.0–43.6), respectively. Indication for ¹⁸F-fluorocholine PET/CT was primary staging in six patients and three patients, biochemical relapse in 33 and 37 patients and other in one patient and zero patients for the fasting and non-fasting group, respectively.

Early dynamic phase

¹⁸F-fluorocholine PET/CT shows a rapid uptake of the ¹⁸F-fluorocholine in the intestine in the first 2 min followed by a more or less stable concentration. No statistical differences were found between the fasting and non-fasting groups at any time-point (Fig. 1).

Late phase

In all patients’ intestinal activity, which possibly interfered with lymph node metastases detection, was found near the aorta, especially in the duodenum. Possible interfering activity was found near the right common iliac artery in 65 and 80 % of the patients for the non-fasting and fasting group, respectively, right external iliac artery (93 and 98 %) and left external iliac artery (68 and 80 %). Activity near the left common iliac artery was found less frequently (37 and 45 %). The intensity of ¹⁸F-fluorocholine uptake in these regions was not significantly different between the fasting and non-fasting groups (Table 1, Fig. 2). In general, the intestinal activity near the aorta is higher than in the other regions, $0.003 \geq p \geq 0.000$ for SUV_{max} and $0.002 \geq p \geq 0.000$ for SUV_{mean} (ANOVA with post hoc Scheffe’s test). No significant differences were found between the activities in the other regions.

No significant differences were found in the ¹⁸F-fluorocholine activity uptake in the liver, spleen, stomach and pancreas between the fasting and the non-fasting groups (Table 2).

Discussion

The data of our study shows that physiological intestine activity in the vicinity of the abdominal aorta and iliac arteries, regions in which lymph node metastases of prostate cancer are frequently found, is present in all prostate cancer patients receiving ¹⁸F-fluorocholine PET/CT, especially near the abdominal aorta. In earlier

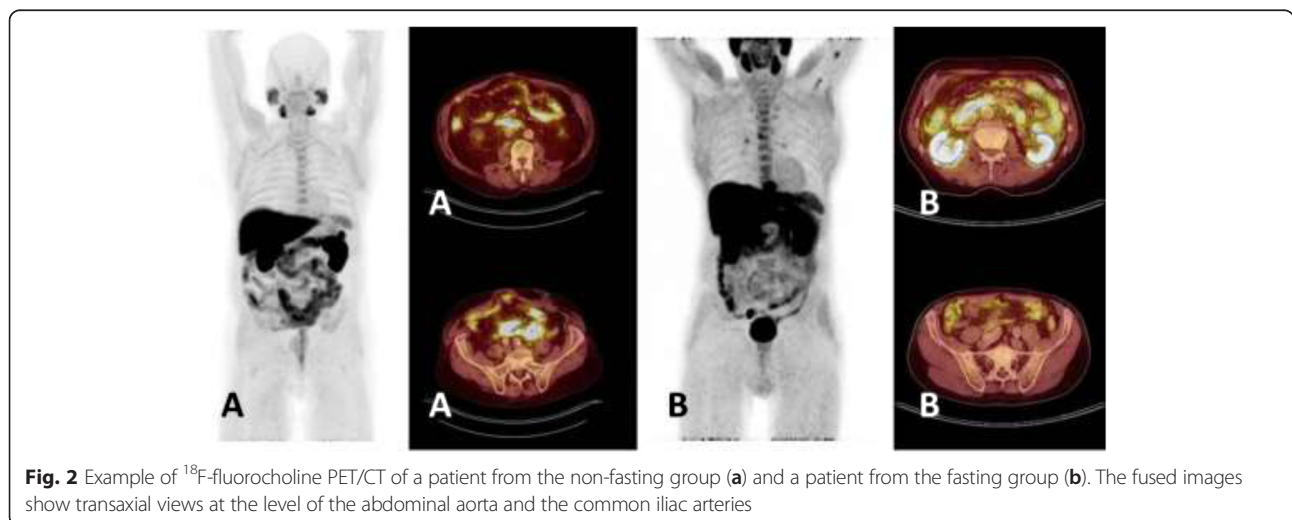


Fig. 2 Example of ¹⁸F-fluorocholine PET/CT of a patient from the non-fasting group (a) and a patient from the fasting group (b). The fused images show transaxial views at the level of the abdominal aorta and the common iliac arteries

Table 2 Intensity of ¹⁸F-fluorocholine uptake in pancreas, liver, spleen and stomach for fasting and non-fasting group

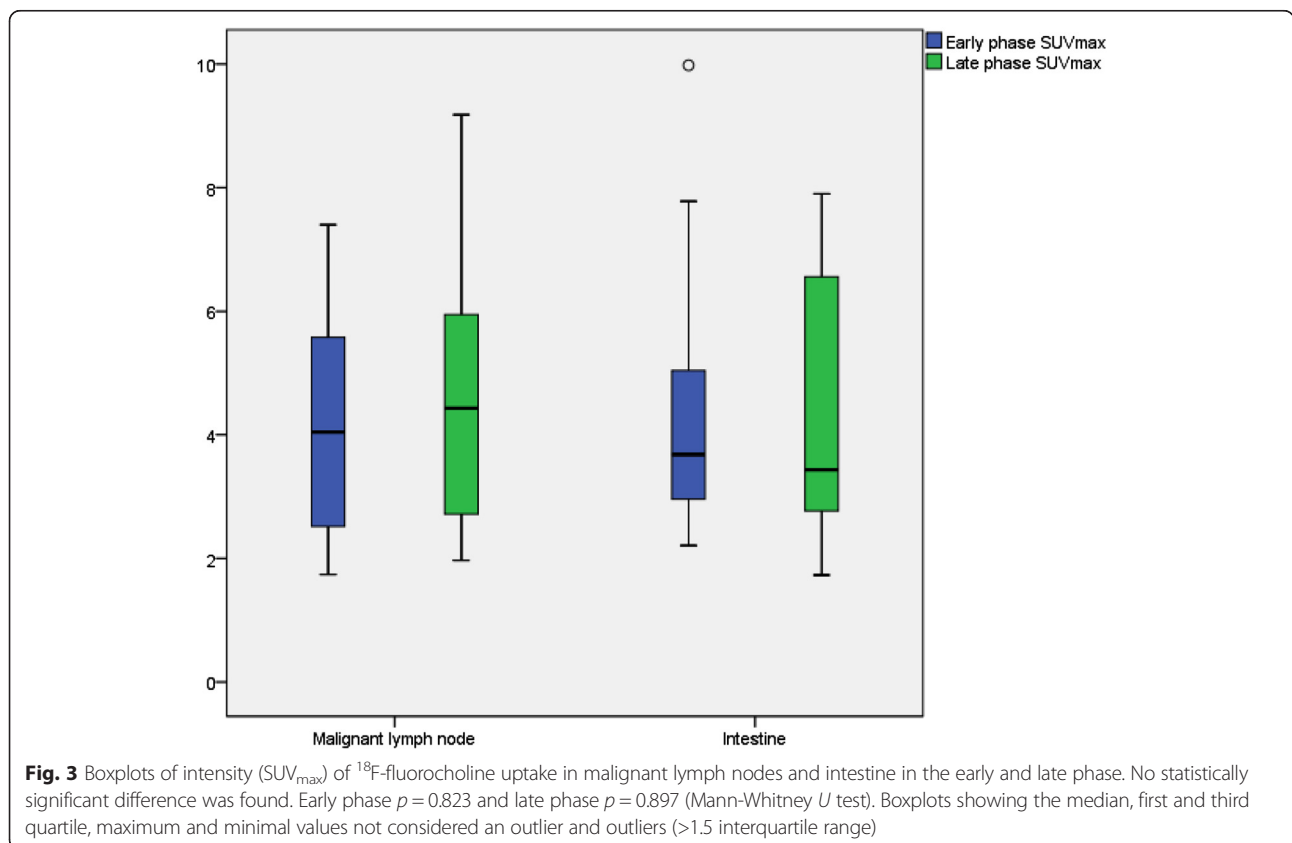
| | Fasting | Number | Mean | σ | p |
|---------------------------|---------|--------|-------|----------|--------|
| SUV_{max} | | | | | |
| Pancreas | No | 40 | 9.39 | 2.10 | 0.661* |
| | Yes | 40 | 9.14 | 2.83 | |
| Liver | No | 40 | 11.04 | 2.34 | 0.165* |
| | Yes | 40 | 11.78 | 2.39 | |
| Spleen | No | 40 | 4.72 | 0.65 | 0.326* |
| | Yes | 40 | 4.91 | 1.01 | |
| Stomach | No | 40 | 7.15 | 1.79 | 0.952* |
| | Yes | 40 | 7.12 | 1.78 | |
| SUV_{peak} | | | | | |
| Pancreas | No | 40 | 8.41 | 1.81 | 0.526* |
| | Yes | 40 | 8.10 | 2.51 | |
| Liver | No | 40 | 10.21 | 2.27 | 0.128# |
| | Yes | 40 | 10.87 | 2.19 | |
| Spleen | No | 40 | 4.25 | 0.54 | 0.620# |
| | Yes | 40 | 4.45 | 0.95 | |
| Stomach | No | 40 | 6.34 | 1.74 | 0.860* |
| | Yes | 40 | 6.27 | 1.62 | |

Statistical analysis with *T test and #Mann-Whitney U test

data from our group, we found in 100 patients that the activity (SUV_{max}) in malignant lymph nodes and physiological intestine activity does not significantly differ at both early and late data acquisition time points (Fig. 3, unpublished). Therefore, interference of physiological activity in the intestine with detection of lymph node metastases is realistic.

Most papers on acquisition protocols of ¹⁸F-fluorocholine deal with the time-point of acquisition and with the effects of voiding and hydration on detection of lesions in the prostate. Fasting is regularly proposed in acquisition protocols without scientific support [1]. Our data show that the nutritional status has no impact on the uptake of ¹⁸F-fluorocholine in the gastrointestinal tract and, more specifically, in regions in the gastrointestinal tract that may interfere with the detection of lymph node metastases.

The CT part of the PET/CT is important to detect lymph nodes in areas with high intestinal activity. To distinguish lymph nodes in these areas, acquisition of CT images of diagnostic quality with administration of intravenous iodinated contrast is necessary. Once lymph nodes are detected on CT, the combination of PET and CT may distinguish malignant lymph nodes from physiological lymph nodes, however, especially in small lymph nodes, characterisation may remain difficult.



The statistical power may be a shortcoming of the study. In all regions, the observed differences in the mean SUV_{max} and SUV_{peak} are relatively small in comparison to the observed standard deviation. One could suggest that the large study populations would be needed to exclude the presence of statistically significant differences. However, in our opinion, the clinical value of such findings would still be irrelevant. Regarding the overlap of found ^{18}F -fluorocholine intensity in all intestine regions in both groups with the intensity in malignant lymph nodes, no effects on the detection of lymph node metastases are expected.

Conclusion

Intestinal activity that possibly interferes with the detection of lymph node metastases is encountered in all prostate cancer patients receiving ^{18}F -fluorocholine PET/CT. Fasting for at least 6 h before administration of ^{18}F -fluorocholine does not influence the uptake of ^{18}F -fluorocholine in the gastrointestinal tract in these patients. Therefore, fasting is not recommended in our opinion.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Competing interest

All authors declare that he/she has no competing interest.

Authors' contributions

MW participated in the design of the study, carried out the data acquisition and statistical analysis and drafted the manuscript. FvdZ and RK participated in the design of the study and helped to draft the manuscript. JP and IJdJ participated in the design of the study, statistical analysis and helped to draft the manuscript. All authors read and approved the final manuscript.

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