Dual phase $^{18}$F-fluorodeoxyglucose positron emission tomography/computed tomography in diagnostic imaging evaluation of bladder cancer

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ABSTRACT

Introduction: $^{18}$F-FDG PET has been regarded as a limited value in urooncology due to urinary excretion of the tracer. The purpose of this retrospective study was to investigate the clinical value of dual-phase FDG PET/CT with forced diuresis protocol (iv furosemide-voiding and oral hydration) in invasive or high grade bladder cancer.

Methods: Fifty-one patients were included in this study. All patients underwent standard staging procedures and dual-phase FDG PET/CT before planned therapy. PET/CT findings before and after furosemide were compared with each other for pelvic region. Dual phase PET/CT findings were also compared with the results of prior imaging studies and all findings were correlated with final diagnosis (histopathology or clinical follow-up for at least 12 months).

Results: Intravesical FDG activity significantly decreased in 90% of the patients with forced diuresis protocol. Eighty eight percent of the bladder findings and 20% of the local lymph node metastases, and other pelvic findings (local invasion and second primary malignancy of prostate) were detected only by the additional pelvic PET/CT images. As a result, dual phase PET/CT changed the staging and/or the therapy strategy in 16 patients (31%).

Conclusion: Dual phase FDG PET/CT contributes staging and decision of therapy strategy by detecting local disease and pelvic metastases with high accuracy when combined with forced diuresis protocol. Thus, we recommend dual phase imaging method with forced diuresis protocol in FDG PET/CT for bladder cancer and all other urogenital system malignities.

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Tomografía por emisión de positrones/tomografía computarizada de doble fase con $^{18}$F-fluorodeoxiglucosa y diuresis forzada en el diagnóstico por imagen del cáncer de vejiga

RESUMEN

Introducción: Se considera que la $^{18}$F-FDG PET tiene un valor limitado en oncología urológica debido a la excreción urinaria del trazador. El propósito de este estudio retrospectivo fue investigar el valor clínico de FDG PET/TC de doble fase con protocolo de diuresis forzada (furosemida i.v. e hidratación oral) en el cáncer de vejiga invasivo o de alto grado.

Métodos: El estudio incluyó a 51 pacientes con cáncer de vejiga. Todos ellos tuvieron un procedimiento estándar de estadificación y una FDG PET/TC antes de planificar el tratamiento. Los hallazgos de la PET/TC antes y después de la administración de furosemida i.v. se compararon para determinar la detección de patología pélvica en cada estudio. Los hallazgos de imagen se correlacionaron con el diagnóstico final (histología o seguimiento clínico durante al menos 12 meses).

Resultados: La actividad intravesical de FDG se redujo significativamente en el 90% de los pacientes con el protocolo de diuresis forzada. El 88% de los hallazgos en vejiga, el 20% de las metástasis linfáticas regionales y otros hallazgos en los órganos pélvicos (invasión local y tumor síncope de próstata) se detectaron solo en las imágenes de PET/TC adicionales de pelvis. La PET/TC de doble fase cambió la estadificación y/o la estrategia terapéutica en 16 pacientes (31%).

Conclusión: La FDG PET/TC de doble fase contribuyó a la estadificación y a la toma de decisiones terapéuticas detectando enfermedad local y metástasis pélvicas con gran precisión cuando se combinó con el protocolo de diuresis forzada. Por consiguiente, recomendamos la técnica de doble fase en la PET/TC con protocolo de diuresis forzada para el estudio del cáncer vesical y otras neoplasias del aparato urogenital.

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Introduction

The most common tumor found in urinary tract is bladder carcinoma; and the most frequent histological type is transitional cell carcinoma (TCC). Approximately 25% of patients with TCC present with high grade or invasive cancer which is characterized by progressive local invasion, extension to pelvic organs and the development of regional and distant metastases.\(^1,2\)

The occult metastatic disease may be present at the initial diagnosis in more than half of the high grade tumors and common sites of metastases are pelvic and retroperitoneal lymph nodes, lungs, liver and bones.\(^3\)

The standard therapy of nonmetastatic TCC is radical cystectomy with lymphadenectomy.\(^4,5\) Since the patients with regional lymph node metastases have higher risk of recurrence and distant metastases, the extent of primary tumor invasion and the local lymph node metastases effects the outcome of the local therapy. This patient group shows a 5-year survival of only 20–25%.\(^5,9\) Therefore, accurate staging of bladder cancer is of vital importance when selecting the appropriate treatment strategy.

Noninvasive imaging plays a crucial role in the staging of invasive or high grade bladder cancer where chest radiograph and the computerized tomography (CT) scan of the abdomen and pelvis are mostly used. Since metastases of bladder cancer is not necessarily reflected by changes in the shape or size of an affected lymph node, anatomical imaging techniques such as CT and magnetic resonance imaging (MRI) have some limitations in evaluating the extent of local or regional disease. The accuracy range for lymph node staging is 70–90% for CT with false-negative rates of 25–40% and approximately 75% for MRI.\(^7,10\)

Recently, PET with 2-deoxy, 2-(18-F) fluoro-d-glucose (FDG) in combination of CT (FDG-PET/CT) has become an important noninvasive imaging modality for staging of several malignancies.\(^11\) \(^18\)F-FDG uptake by bladder cancer was first demonstrated by Harney et al. in rats, with an estimated high uptake ratio of tumor to normal bladder.\(^12\) However, the use of \(^18\)F-FDG PET has been limited in urooncology due to urinary excretion of \(^18\)F-FDG PET.\(^13\)–\(^16\)

Some investigators have tried to increase the sensitivity of PET by washing out the excreted \(^18\)F-FDG bladder catheterisation or retrograde irrigation of bladder with saline solution or with furosemid injection before image acquisition; but their results have not been of much success.\(^17\)–\(^20\) Furthermore, continuous bladder irrigation technique may result in considerable morbidity to the patient, in addition to unwanted radiation dose to the PET personnel.\(^21\)

As the urinary FDG activity is reduced with standard PET/CT scanning combined with additional pelvic imaging after forced diuresis protocol (iv furosemide-voiding and oral hydration), it is easier to evaluate the pathological findings in pelvic region.\(^22\)–\(^25\) Furthermore, refilling the bladder with oral hydration dilutes the urine and makes it easier to detect the bladder wall pathologies.\(^22\)–\(^26\)

The confounding effect of excreted FDG on the visualisation of the primary tumor may also be overcome by radiopharmaceuticals such as \(^11\)C methionine, \(^11\)C choline or \(^11\)C acetate, without or only limited renal excretion, but these agents have still limited availability.\(^27\)–\(^30\)

The purpose of this retrospective study was to evaluate the usefulness of \(^18\)F-FDG PET/CT scan with additional pelvic images after diuretic and oral hydration (dual phase imaging) in the staging and selecting the appropriate treatment strategy in patients with invasive or high grade bladder cancer.

Table 1

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Abbreviations: Tis: carcinoma in situ, bx: biopsy, TUR: transurethral resection and BCG: Bacillus Calmette–Guerin.

Materials and methods

Patient population

78 patients with bladder carcinoma who underwent FDG PET/CT scan in our clinic between May 2009 and June 2011 were evaluated. Nineteen cystectomized patients and 2 patients with chronic renal failure were excluded from the study.

The standard staging procedures, including history, physical examination, laboratory tests, cystoscopy with biopsy and CT of the abdominopelvic region were applied to all of the patients who were diagnosed with histopathologically confirmed invasive (>T2) or high grade (G3) TCC. In some patients, other techniques such as bone scan, chest CT or pelvic MRI were also performed in terms of signs and symptoms.

In 51 of 57 patients a final diagnosis was available; other 6 patients with bladder cancer without cystectomy were excluded from the study since we could not reach the follow-up information.

The detailed demographic and clinical characteristics of 51 patients are summarized in Table 1.

Written informed consent was obtained from all patients before PET/CT imaging.

Dual phase PET–CT protocol

Patients were directed to fast for at least 6 h before the intravenous injection of 0.15 mCi/kg of \(^18\)F-FDG. Blood glucose level was measured before injection of the tracer to ensure glucose levels below 140 mg/dL. Before and after injection, patients were kept lying comfortably in a quiet room and 200 mL saline infusion was given. Whole body PET/CT images were acquired 60 min after FDG injection using a dedicated full-ring PET/CT scanner (Biograph 2; Siemens Medical Systems, Erlangen, Germany). Nonenhanced CT images were acquired 130 kV and 90 mA (mean), with a section width of 5 mm. The PET emission scan was obtained immediately after CT scan. 5–7 bed positions were used, with an acquisition time of 4 min for each. CT-based attenuation corrections were performed for the PET images and reconstruction was carried out using an iterative reconstruction algorithm.
After the standard PET/CT scan, forced diuresis protocol was applied. In order to carry it out; the patients were injected with 0.5 mg/kg of furosemide intravenously, and were asked to void frequently and they also received oral hydration 500–750 mL of water. Additional pelvic images were acquired 30–45 min after the furosemide injection.

**Evaluation of PET/CT images**

Each PET/CT study was interpreted by two experienced nuclear medicine physicians who had full access to the patients' history and the results of prior imaging studies (USG, CT, MRI, bone scintigraphy) and after reaching a consensus, the final decision was made for the report. All PET/CT images were evaluated visually and quantitatively. After visual analysis, volumes of interest were drawn around the foci of pathologic 18F-FDG accumulation and quantification of metabolic activity of focus was obtained using the standardized uptake value (SUV) normalized to body weight, and the maximum SUV (SUVmax) for each of them was calculated.

PET/CT findings before and after furosemide were compared with each other for pelvic region (bladder and pelvic lymph nodes). All positive findings of bladder detected by PET/CT or pelvic CT were evaluated histopathologically. For negative results, patients were followed-up for at least 12 months (clinical examination and/or other imaging methods such as CT and MRI). Dual phase PET/CT findings were also compared to prior imaging (US, CT, MR and bone scintigraphy) results which mainly consisted of CT and all findings were correlated with final diagnosis. The final diagnosis was based on histopathology of materials obtained during primary surgery (n = 24), transurethral resection of bladder tumor (TUR-B) (n = 8), a positive histological confirmation of metastatic disease before chemotherapy (n = 4), or confirmation of a lesion by means of dedicated investigations (CT, MRI) within a 12-month period (n = 4) and a negative clinical and/or radiological follow-up of 12 months (n = 11). The additional value of dual phase PET/CT in evaluation of patients with bladder cancer was assessed by means of changing the stage of disease (upstaged or downstaged by dual phase PET/CT) or modification of the therapy strategy.

The sensitivity, specificity and accuracy of methods were calculated using the standard definition. The difference between the SUVmax value of the urine in the bladder was assessed using a paired t test. A p value less than 0.05 was taken to indicate a significant difference (SPSS 17.0 software).

**Results**

High urinary FDG activity in the bladder was seen after standard PET/CT scan in all patients, expectedly. The mean SUVmax values of intravesical urine on standard PET/CT scan were 28.1 (9.8–72). In additional pelvic images after forced diuresis protocol (iv furosemide-voiding and oral hydration), intravesical FDG activity was efficiently reduced to optimal level in 46 patients (90%) with SUVmax values <4. In 5 patients with intravesical SUVmax values between 4.5 and 8.9, a second delayed pelvic image was obtained after iv hydration, aiming at reducing the urinary activity to optimum level. The mean SUVmax values of intravesical urine on additional pelvic images were 3.7 (1.8–6.8) (p < 0.01) (Figs. 1 and 2).

**Bladder wall**

In 32 of 51 patients (62.7%), one or more hypermetabolical foci were detected in bladder wall with dual phase PET/CT. The SUVmax values of those bladder lesions were 4.2–21.3 (mean: 12.8). In 28 out of 32 patients with hypermetabolical foci on bladder wall (88%), lesions could only be seen in additional pelvic images after forced diuresis protocol. In remaining 4 patients, hypermetabolical bladder foci could already be distinguished with standard PET/CT scan (mean SUVmax: 17.2) The existence of tumor in bladder was verified histopathologically in 30 out of 32 patients who had the residue or recurrence detection with dual phase PET/CT. In 24 of 30 patients, pelvic CT had revealed bladder wall thickening. Therefore, in 6 patients, residue or recurrence that did
not cause significant changes in bladder wall anatomically could be detected by dual phase PET/CT (false negative CT). Nineteen patients who did not have any pathological metabolical activity in bladder wall had no sign of tumor existence in the follow up. But in 3 of those 19 patients, pelvic CT revealed bladder wall thickening. After histopathological evaluation, none of these 3 patients had positive cytology for tumor (false positive CT). Two patients had increase in metabolical activity due to inflammatory reactions (false positive PET). Hypermetabolical bladder lesion was the single positive finding in these patients who had TUR within 6 weeks and inflammatory changes were revealed with cystoscopic biopsy. The sensitivity, specificity, and accuracy of PET/CT and CT for residue or local recurrence are summarized respectively in Table 2.

**Pelvic lymph nodes**

In 20 patients, hypermetabolical pelvic lymph nodes were detected with dual phase PET/CT. In 4 of them, local hypermetabolical lymph nodes (in close contact with the bladder) could only be detected by additional pelvic images after forced diuresis protocol. All patients with pelvic lymph node metastases underwent surgery except for 3 patients who had also distant metastases. In 18 patients, lymph node metastases were verified with final diagnosis (histopathologically or radiologically follow-up) but inflammatory changes were revealed after lymphadenectomy in other 2 patients (false positive PET) although one of them had lymph node of pathological size. In 2 out of 18 patients, metastatic lymph nodes were <1 cm (false negative CT). Furthermore, lymph node metastases were ruled out with dual phase PET/CT in 5 patients whom had the pelvic lymphadenopathy (false positive CT). Only in 1 of the 26 patients who had no positive findings in pelvic lymph nodes by dual phase PET/CT or CT, metastasis was detected after the surgery (false negative PET/CT and CT). Sensitivity, specificity, and accuracy of PET/CT and CT for lymph node metastases respectively are summarized in Table 3.

After forced diuresis, additional pelvic images detected hypermetabolical lesions in distal ureter in 1 patient (Fig. 3) and in prostate in 3 patients. Local invasion to prostate in 2, second primary malignancies of prostate in 1 of them were confirmed histopathologically.

**Distant lymph node or distant organ metastases**

Increased metabolical activity was detected in distant lymph nodes in 12 patients (1 jugular, 1 axillary, 3 mediastinal and 7 abdominal). In 2 of these patients, lymph nodes (1 abdominal, 1 jugulary) were not in pathological size (false negative CT). All of the distant lymph node metastases were confirmed to be positive for metastases histopathologically or by radiological follow up.

With PET/CT scan, hypermetabolical foci in distant organs were detected in 10 patients (lung, liver, bone and adrenal). Metastatic diseases were already detected in all of those patients with staging procedures prior to PET/CT scan, but in 6 of them, additional metastatic foci in different organ and/or additional focus in the same organ were detected with PET/CT.

Five patients had one or more lesions with pathological metabolic activity in the lung. In 2 of them, the findings of CT and PET/CT suggested the existence of a second primary malign-

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**Table 2**

Residual/local recurrence with PET/CT and CT; correlation with gold standard.

<table>
<thead>
<tr>
<th></th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>PPV</th>
<th>NPV</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
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<td>2</td>
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<td>94%</td>
<td>100%</td>
<td>100%</td>
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<td>CT</td>
<td>24</td>
<td>18</td>
<td>3</td>
<td>6</td>
<td>89%</td>
<td>75%</td>
<td>80%</td>
<td>86%</td>
<td>82%</td>
</tr>
</tbody>
</table>

*Abbreviations: TP: true positive, TN: true negative, FP: false positive, FN: false negative, PPV: positive-predictive value, and NPV: negative-predictive value.*

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**Fig. 2.** A 65-year-old male patient with bladder cancer. The transaxial image of CT, standard PET/CT scan, and additional pelvic images (from left to right). CT slices show an irregular posterior wall of bladder but it is masked due to urinary activity (SUV_{max} = 17.2) in standard PET/CT scan. Forced diuresis protocol shows excellent FDG washout (intravesical SUV_{max} = 2.3) and recurrence is ruled out with no pathological FDG activity in posterior wall of bladder where thickening is reported by pelvic CT (a). In the same patient diffuse increased FDG activity is observed in prostate and second primary malignancy is confirmed with histopathology (b).
nancy in lung. Those were confirmed histopathologically and they underwent surgery for bladder and lung malignancy. There were another metastatic sites in 2 patients and they were treated with chemo-radiotherapy. On the other hand, one patient with active tuberculosis PET/CT revealed false positive results expectedly.

While only one patient could be detected with bone metastasis (vertebral) with CT, in all the other 4 patients bone metastases (vertebra, pelvic bones) were detected by only PET/CT. Radiotherapy protocol has been modified for those patients.

Patients with distant organ metastases had chemotherapy and radiotherapy to the related site. TUR was also applied to some patients for reducing symptoms.

Furthermore, distant organ metastases were ruled out with PET/CT in 3 patients, who had the distant lymphadenopathy and suspected metastatic lesions in lung, adrenal and liver by CT scan, so they could be treated with cystectomy or TUR-bladder (false positive CT). Sensitivity, specificity, and accuracy of PET/CT and CT for distant (lymph node or visceral organ) metastases respectively are summarized in Table 4.

As a result, dual phase PET/CT confirmed the findings of routine staging studies in 35 out of 51 patients, and it had the additional value in 16 (31%) patients by changing the stage of disease and/or treatment strategy. Four patients were upstaged, 9 patients were downstaged and the therapy strategy was modified in 3 patients with metastatic disease. The findings of studies in these 16 patients were summarized in Table 5.

Out of all the prostate and ureter findings, 20% of the local lymph node metastases, and 88% of the bladder findings could not be evaluated by the standard PET/CT scan. The stage of disease and/or treatment strategy changed in 16 (31%) patients by dual phase PET/CT. In 11 of the patients, CT and dual phase PET/CT findings of the bladder were discordant; however, the histopathological studies confirmed the PET/CT findings in 9 of them, while the remaining 2 patients with false positive PET/CT findings had the recent history of invasive procedures for bladder.

Anjos et al. also managed to reduce the intravascular FDG concentration closer to the background activity with force diuresis and additional pelvic imaging. In this study, similar to our results, in 6 out of 11 patients, hypermetabolical lesions could only be detected by additional pelvic imaging. Also, in 2 out of 8 patients with pelvic lymph node metastases, hypermetabolical foci could only be differentiated in additional pelvic images after forced diuresis and prostate invasion is reported in 1 patient after intravascular FDG density is diminished.

Harkirat et al. could manage to reduce the intravascular FDG density close to background activity in 95% of bladder cancer patients with dual phase PET by using the same protocol we used. Similar to our results, all hypermetabolical bladder lesions could only be detected in additional pelvic images with the sensitivity of 87%, and specificity of 100%. In their study, hypermetabolical foci were also visualized with additional pelvic images after forced diuresis protocol in 2 out of 6 patients with pelvic lymph node metastases, and these results changed the staging of those patients.

Recently, Yang et al. also investigated the utility of 18-F FDG PET/CT with additional pelvic images (voiding-refilling) in detection of recurrent bladder cancer and 45% of recurrent lesions were detected only after additional pelvic images. No diuretics were used in their study, and the sensitivity, specificity and accuracy were reported to be slightly lower than our results: 91.7%, 87% and 88.6% respectively.

Kamel et al. added iv hydration to the iv furosemide and oral hydration protocol and they were able to reduce the intravesical FDG activity close to the background activity in additional pelvic images in 97% of patients who underwent dual phase PET/CT scanning. Kamel et al. detected all hypermetabolical bladder lesions in additional pelvic images, and the recurrence is ruled out in 3 patients with post-therapeutic radiological changes. Thus, it is reported that in 40% of the patients, dual phase PET/CT effected the staging.

In our study, similar to the results in the literature, dual phase FDG PET/CT had 100% sensitivity, 90% specificity and 96% accuracy in detecting bladder lesions, and for lymph node metastases the sensitivity was 95%, specificity was 94% and accuracy was 94%.

It is obvious that PET/CT is crucial in distant metastases evaluation. In our study, one or more new metastatic foci were detected with PET/CT scan in more than half of the patients with metastatic disease. Four patients were upstaged with PET/CT scan by detection of distant metastases.

### Table 3
<table>
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<tr>
<th>TP</th>
<th>TN</th>
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Abbreviations: TP: true positive, TN: true negative, FP: false positive, FN: false negative, PPV: positive-predictive value, and NPV: negative-predictive value.

### Table 4
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Abbreviations: TP: true positive, TN: true negative, FP: false positive, FN: false negative, PPV: positive-predictive value, and NPV: negative-predictive value.

### Discussion

Appropriate staging affects therapy strategy and survival time in bladder cancer, as in all malignancies. 18-F-FDG PET/CT is used for diagnostic and prognostic evaluation in most malignancies, but the major limiting factor for use in bladder cancer is the renal excretion of FDG. In bladder cancer, although it is effective in determining the distant metastases, due to the intravesical FDG stasis, standard FDG PET/CT is insufficient in evaluating local recurrence and pelvic metastases. 14,15

Dual phase PET/CT with forced diuresis protocol without using the bladder catheterization is applied to patients with all types of pelvic malignancies in our clinic. By this method, the intravesical FDG activity could be reduced to an optimum level in additional pelvic images after iv furosemide-voiding and oral hydration in 90% of patients. Furthermore, we were able to evaluate the bladder wall pathologies better, when the bladder was full with urine with low concentration of FDG. For all the prostate and ureter findings, 20% of the local lymph node metastases, and 88% of the bladder findings could not be evaluated by the standard PET/CT scan. The stage of disease and/or treatment strategy changed in 16 (31%) patients by dual phase PET/CT. In 11 of the patients, CT and dual phase PET/CT findings of the bladder were discordant; however, the histopathological studies confirmed the PET/CT findings in 9 of them, while the remaining 2 patients with false positive PET/CT findings had the recent history of invasive procedures for bladder.
Fig. 3. A 50-year-old male patient with bladder cancer. The transaxial image of CT, and additional pelvic images (from left to right). CT slices show an irregular thickness in the right lateral wall of bladder which invades the right ureter (a), but it is masked due to urinary activity ($\text{SUV}_{\text{max}} = 17.2$) in standard PET/CT scan. Forced diuresis protocol shows excellent FDG washout (intravesical $\text{SUV}_{\text{max}} = 2.3$) and recurrence is ruled out with no pathological FDG activity in posterior wall of bladder where thickening is reported by pelvic CT. In the same patient diffuse increased FDG activity is observed in prostate and second primary malignity is confirmed with histopathology (b). In a 50-year-old-man PET/CT demonstrates primary tumor of bladder after forced diuresis protocol. (a) Coronal slices of PET/CT scan also reveal metastasis of liver, vertebrae, ribs, femur in addition to pelvic and abdominal lymph node metastasis. (b) The patient treated with chemo-radiotherapy. Because of additional metastatic foci in skeletal system; radiotherapy protocol has been modified after PET/CT scan.

There are many studies in the literature using different methods to accelerate FDG excretion.

Kosuda et al. applied retrograde bladder irrigation to reduce the intravesical FDG activity, but reported 40% false negative results in detecting the recurrent and residual bladder tumors.\textsuperscript{18} Lin et al., reported misinterpretations due to the intravesical concentrated urinary residue after bladder irrigation.\textsuperscript{23} Koyama et al. applied retrograde bladder irrigation for evaluating the
Table 5  
Findings of CT and dual phase PET/CT studies in patients whom had a change in the stage of disease and/or treatment strategy.

<table>
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gynecological malignancies, but they failed to reduce the intravesical FDG activity in 20% of the patients. García Vicente et al. used retrograde bladder irrigation to reduce the intravesical FDG activity, despite the presence of residual urine activity in some cases, they did not obtain any false negative or false positive results due to urine interference and the sensitivity, specificity were reported as 100%, 93% respectively in their study. This invasive method has the risk of infections with the need of continuous bladder irrigation, decreasing the comfort of the patient, and increasing the exposure of personnel to radiation. 

Another way to reduce the urinary FDG activity is to accelerate its excretion by diuretic effect. Driessens et al. investigated the contribution of PET/CT to CT in staging of advanced bladder cancer by the method of injecting iv furosemide after 10 min of FDG administration followed by standard PET/CT scanning. In their study, it was shown that in detecting the distant metastases and survival prediction, PET may have contribution to CT, but not in local staging. In a study by Kibel et al., false positive and false negative results were reported for local evaluation, by the method of diuretic administration 20 min after FDG injection and Foley catheter usage.

False positive results depending on the invasive procedures are commonly encountered problems for PET/CT, and to overcome this problem, there should be enough time between the procedure and the scanning. Yang et al. reported that three false positive results testified to be inflammatory tissues by cystoscope and they suggested that the interval between the cystoscope and the PET/CT scan should be at least 1 month. Anjos et al. had no false positive results when the PET/CT scans were done 3 months after the invasive procedure. As our study is retrospective, we had no chance to standardize the time interval between invasive procedure and PET/CT scan, but we observed no false positive results in patients with >6 weeks between invasive procedure and PET/CT scan.

As the lung cancer and the bladder cancer have common predisposing factors, they may be diagnosed synchronously, and PET/CT findings may point the diagnosis. In our patient group, 2 patients had findings of second primary malignancy in the lung, then they were histopathologically confirmed and could be treated surgically.

To increase the sensitivity of PET/CT in bladder cancers, tracers which have less renal excretion than FDG can be used. 11-C methionine is an example for those tracers, but its uptake is in direct proportion with the grade of the primary tumor. Another agent is 11-C choline. de Jong et al. could visualize all bladder tumors except for premalignant lesions in a study conducted with 11-C choline. Also Gofrit et al. detected 11-C choline uptake in all TCCs and lymph node metastases which are smaller than the pathological size. Picchio et al. reported that 11-C choline PET is successful in determining the residual tumor and is superior to CT in detecting the lymph node metastases. Although these results are promising, more studies and larger series for the usage of different pharmaceuticals are required. And as the availability of these pharmaceuticals is limited, it seems hard for them to replace FDG yet, and the methods aiming at reducing the urinary FDG activity keep their importance.

As this study is retrospective, it is done among a chosen patient population and all negative findings could not be correlated histopathologically, and those are the limitations for our study. And as a result of the time interval between PET/CT and invasive procedure could not be standardized, false positive results due to inflammatory processes could not be avoided.

Conclusion

FDG PET/CT scan detects distant metastases of bladder cancer with the advantages of evaluating the metabolic and anatomical changes concomitantly and has the advantage of whole body scanning at the same session. In addition to that, it contributes staging and decision of therapy strategy by detecting local disease and pelvic metastases with high accuracy when combined with forced diuresis protocol (iv furosemide-voiding and oral hydration) and dual phase imaging. Thus, we recommend dual phase imaging method with forced diuresis protocol in PET/CT for bladder cancer and all other urogenital system malignancies.

Conflict of interest

The authors declare no conflict of interest.

References


