Diagn Interv Radiol 2022; 28:179–184



NUCLEAR MEDICINE AND MOLECULAR IMAGING

ORIGINAL ARTICLE

# Association between prostatic $^{18}$F-FDG uptake and lower urinary tract symptoms assessed by International Prostate Symptom Score

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**PURPOSE**
Inflammation is known to induce prostatic growth and lower urinary tract symptoms (LUTS) progression in patients with benign prostatic hyperplasia (BPH), but clinical indicators for intraprostatic inflammation other than biopsy have not yet been established. While 2-deoxy-2-[18F]fluoro-D-glucose (FDG) positron emission tomography/computed tomography (PET/CT) is a useful tool for investigating inflammatory conditions, prostatic FDG uptake in patients with BPH has not been elucidated. Therefore, we evaluated the association between prostatic FDG uptake and LUTS.

**METHODS**
A total of 391 men in their 50s who underwent FDG PET/CT during health examinations were included. Mean and maximal prostatic standard uptake values (SUVs) on FDG PET/CT were measured. Prostatic volume, focal FDG uptake, and calcification were also evaluated. The International Prostate Symptom Score (IPSS) for LUTS was collected at baseline and follow-ups. The correlation between IPSS and other variables was analyzed.

**RESULTS**
The mean age of the study participants was 51.7 years, and the mean follow-up interval was 39.7 months. The average of the mean and maximal SUV for prostatic FDG uptake was 1.8 and 2.6, respectively. The prostate volume was 18.5 $cm^3$. The mean IPSS was 4.82 at baseline and 5.46 at follow-ups. Neither the mean SUV nor the maximal SUV of prostatic FDG uptake was correlated with IPSS at baseline or follow-ups. Conversely, prostate volume was associated with baseline IPSS and follow-up IPSS.

**CONCLUSION**
Prostatic FDG uptake did not show a significant association with IPSS on FDG PET/CT as well as at follow-ups. FDG uptake may not reflect prostatic growth in nonmalignant cases.

Benign prostatic hyperplasia (BPH) is the most common urologic disease in elderly men with a prevalence that increases with age.[1] BPH is histologically associated with smooth muscle and epithelial cell proliferation within the prostate transition zone.[2] Lower urinary tract symptoms (LUTS) due to BPH affect individuals' quality of life (QOL) and are determining factors for the management of BPH.[3] The International Prostate Symptom Score (IPSS) is a well-established tool for the systematic evaluation of LUTS.[4] The IPSS questionnaire comprises four questions about voiding symptoms, three questions about storage symptoms, and additionally one question about the overall impact of LUTS on the patient's QOL.

Not all men with BPH experience LUTS, although LUTS are often clinically regarded as synonymous with BPH.[5] Prostate volume is the major factor that causes LUTS. Patients with increasing prostate volumes have a higher risk of symptomatic deterioration.[6] Inflammation is one of the significant components of prostatic growth and LUTS progression.[7,8] Several studies have evaluated the association between high-sensitivity C-reactive protein level, a marker of systemic inflammation, and LUTS.[9–11] However, most previous studies on prostatic inflammation have been conducted using surgical or prostatic biopsy specimens, and to the best of our knowledge, no other objective indicator for the clinical evaluation of inflammation within the prostate has been established to date.[12]

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Received 20 August 2020; revision requested 16 September 2020; last revision received 19 November 2020; accepted 1 December 2020.

Published online 11 February 2022.

DOI: 10.5152/dir.2022.20677

You may cite this article as: Kim SJ, Chang H, Youn I, Joo KJ, Ryu S, Kim YH. Association between prostatic 18F-FDG uptake and lower urinary tract symptoms assessed by International Prostate Symptom Score. *Diagn Interv Radiol*. 2022;28(2):179-184.

2-deoxy-2-[$^{18}$F]fluoro-D-glucose (FDG) positron emission tomography/computed tomography (PET/CT) is a noninvasive imaging tool used for investigating oncologic diseases including genitourinary systems.[13] Meanwhile, FDG PET/CT is also useful for evaluation of inflammatory conditions as well as oncologic diseases.[14] Incidental prostatic FDG uptake has been reported to be associated with bacterial isolation from expressed prostatic secretions.[15] Prostatic FDG uptake has been frequently observed in patients with bladder cancer and Bacillus Calmette-Guérin (BCG) instillation therapy, thus, BCG-induced granulomatous prostatitis has been reported as a potential cause of incidental prostatic FDG uptake.[16] Meijer et al.[17] analyzed 43 patients with incidental prostatic FDG uptake, of whom, 15 (35%) were diagnosed with histopathologically benign prostatic diseases, including BPH, prostatitis, and prostatic intraepithelial neoplasia. Another study by Jakse et al.[18] reported that the FDG uptake in histologically confirmed BPH and prostate cancer shows a significant overlap with one another. However, factors associated with FDG uptake in BPH remain inadequately understood. Moreover, to the best our knowledge, no previous study has evaluated the association between FDG uptake and the clinical symptoms of BPH.

We hypothesized that increased prostatic FDG uptake is associated with high IPSS on FDG PET/CT, thus aiming to investigate the association between baseline prostatic FDG uptake variables and IPSS.

**Main points**

- Inflammation is known to facilitate prostatic growth and progression of LUTS in patients with BPH.
- While clinical indicators for intraprostatic inflammation other than biopsy remain unestablished, FDG PET/CT is a useful tool for investigating inflammatory conditions.
- In our study, prostatic FDG uptake did not show a significant association with LUTS, measured by IPSS, at baseline nor did it predict the follow-up LUTS.
- Prostate volume correlated with IPSS both at baseline and follow-ups and showed a significant association with the voiding component but not with the storage component of IPSS.

# Methods

## Study participants

The study population comprised 415 men in their 50s who underwent FDG PET/CT for health examinations at the Total Healthcare Screening Center of our institute from January 2014 to December 2014 and who were followed up at least once after FDG PET/CT before December 2018. We excluded two participants because their imaging data were lost. One participant who reported a history of prostate surgery and another participant who reported a history of medication for relieving BPH at the day of FDG PET/CT were excluded. All eligible participants denied a history of prostate cancer on the day of FDG PET/CT. A total of 18 participants who did not respond completely to the IPSS questionnaires at baseline or follow-ups were also excluded. In addition, we excluded two participants because of their high blood glucose levels (≥200 mg/dL) on the day of FDG PET/CT. Finally, 391 participants were included in this study.

This retrospective observational study was approved by our institutional review board, and the requirement for written informed consent from the study participants was waived (KBSMC 2019-09-013).

## FDG PET/CT

Participants fasted for at least 8 h prior to undergoing FDG PET/CT, and their blood glucose levels were less than 200 mg/dL at the time of FDG injection. At 60 min after injecting 3.7 MBq/kg of FDG, imaging was performed using a Discovery 600 system (GE Healthcare) without intravenous or oral contrast. Whole-body CT was performed using a continuous spiral technique with a 16-slice helical CT scanner (120 kVp; 40-120 mA; section thickness, 3.75 mm). After CT, an emission PET scan was obtained from the skull base to the thigh. Scanning was performed at 2-4 min per bed position in 3D mode. PET images were reconstructed using an ordered-subset expectation maximization algorithm (16 subsets and two iterations) with attenuation-corrected images. Standardized uptake values (SUVs) were calculated using body weight of subjects. Uniformity phantom test and well counter correction were performed in our institution to ensure that SUV values of the PET studies are accurate and reproducible.

## Image analyses

FDG PET/CT images were reviewed by a nuclear medicine physician at a dedicated workstation (AW; GE Healthcare). A spherical volume-of-interest (VOI) was drawn on the PET images, encompassing an area as large as possible but remaining confined to the prostate gland and not including FDG activity in the urinary bladder or rectum. The mean and maximal prostatic standard uptake values ($SUV_{mean}$ and $SUV_{max}$, respectively) were measured in each VOI. Meanwhile, the maximal right to left distance, maximal anterior to posterior distance, and maximal cranial to caudal distance of the prostate gland were measured on the CT images of each participant to estimate prostate volumes using the following ellipsoid formula.[19]

Prostate volume = $\pi/6$ [maximal right to left distance (cm) × maximal anterior to posterior distance (cm) × maximal cranial to caudal distance (cm)]

The findings of prostatic focal FDG uptake on PET images and/or prostatic calcification on CT images were also evaluated, and the location of focal FDG uptake was classified as central or peripheral if observed.

## Clinical data collection

Clinical data such as demographic characteristics, medical history, and medication use were collected from standardized self-administered questionnaires at baseline and follow-ups. The Korean version of the IPSS was adopted in the questionnaire.[20] We also collected data regarding height, weight, and serum prostate specific antigen (PSA) levels from the healthcare screening results of the study participants at each time point.

## Statistical analyses

The mean and standard deviation (SD) of each variable are presented. The severity of LUTS was graded according to IPSS as mild LUTS (0–7), moderate LUTS (8-19), or severe LUTS(20-35). [4] Body mass index (BMI) was calculated from height and weight information. We used Student t test, chi-square test, or Fisher exact test for comparison. Baseline and follow-up IPSS were compared using a Wilcoxon signed rank test. Bivariate correlations between baseline IPSS and age; baseline serum PSA level; baseline BMI; baseline FDG PET/CT characteristics such as prostatic $SUV_{mean}$, $SUV_{max}$, volume, focal FDG uptake, or calcification

were evaluated, and Spearman rho ($\rho$) values were presented. Similarly, bivariate correlation analyses between follow-up IPSS and other variables were performed. Meanwhile, correlation between follow-up IPSS and baseline FDG PET/CT characteristics was additionally analyzed and partial correlation coefficients adjusted by follow-up interval ($r$) were presented. Statistical analysis was performed using the Statistical Package for the Social Sciences version 24.0 for Windows software program (IBM Corp.), and a $P$ of less than .05 was considered statistically significant.

## Results

The mean age of the study participants was 51.7 years (range, 50.01-59.97 years), and the mean follow-up interval was 39.7 months (Table 1). Among 391 participants, 308 (78.8%) had mild LUTS, whereas the remaining 83 (21.2%) participants had moderate to severe LUTS at baseline. There were no significant differences in age and follow-up interval between these two groups according to the baseline LUTS status. Among the 391 participants, 7 (1.8%) initiated medication for relieving the symptoms of BPH during the follow-up period. More participants with moderate to severe LUTS at baseline initiated medication for relieving the symptoms of BPH than those with mild LUTS at baseline (6.0% vs. 0.6%; $P$ = .006). None of the study participants were diagnosed with prostate cancer at follow-ups. The mean serum PSA level and BMI were not significantly different between participants with mild LUTS and those with moderate to severe LUTS either at baseline or follow-ups.

The prostatic $SUV_{mean}$ of FDG uptake in the study participants was 1.8 ± 0.2 (range, 1.2-2.6), whereas the prostatic $SUV_{max}$ of FDG uptake was 2.6 ± 0.3 (range, 1.7-3.9) (Figure 1). The mean prostate volume, which was calculated from the CT images of FDG PET/CT, was 18.5 ± 6.3 $cm^3$ (range, 6.0-44.7 $cm^3$). The prostate volume and $SUV_{mean}$ showed a weak negative correlation ($\rho$ = − 0.137; $P$ = .007) (Figure 2). Prostatic focal FDG uptake was observed in 25 of 391 participants (6.4%), and 7 of them were observed in the central portion of the prostate glands (Table 1). The mean prostatic $SUV_{max}$ of 25 participants with prostatic focal FDG uptake was higher than the remaining 366 participants (3.2 ± 0.4 vs. 2.5 ± 0.3; $P$ < .001). The mean prostatic $SUV_{mean}$ of the participants with prostatic focal FDG uptake was also slightly higher than the remaining participants (1.9 ± 0.2 vs. 1.8 ± 0.2; $P$ = .004). Meanwhile, mean $SUV_{max}$ of focal FDG uptakes was not significantly different between central and peripheral locations (3.2 ± 0.3 vs. 3.1 ± 0.4; $P$ = .596). It was also true for mean $SUV_{mean}$ (1.8 ± 0.1 vs. 1.9 ± 0.2; $P$ = .312).

Prostatic calcification was observed in 109 of the 391 (27.9%) participants. The prostate volume was higher in participants with moderate to severe LUTS at baseline than in those with mild LUTS at baseline (19.7 ± 6.2 $cm^3$ vs 18.1 ± 6.3 $cm^3$; $P$ = .036), whereas the prostatic $SUV_{mean}$, $SUV_{max}$, focal FDG uptake, and calcification showed no significant differences between participants with mild LUTS and those with moderate to severe LUTS at baseline.

The mean IPSS of the 391 study participants was 4.82 and 5.46 at baseline and follow-ups, respectively ($P$ = .001) (Table 2). The adjusted mean difference in IPSS according to the follow-up interval was 0.22/year. Both the questionnaire components about voiding and storage symptoms showed significant increases at follow-up. Individual components about IPSS questions, including those about intermittency, weak stream, straining to void, urgency, and nocturia increased at follow-ups compared with those at baseline. Conversely, IPSS components about incomplete emptying, frequency, and QOL did not change significantly.

**Table 1.** Characteristics of 391 participants and their baseline FDG PET/CT characteristics

| | | | | |
|---|---|---|---|---|
| n (%) | 391 | 308 (78.8) | 83 (21.2) | |
| Age (mean ± SD; (years), mean ± SD | 51.7 ± 2.3 | 51.6 ± 2.2 | 52.1 ± 2.6 | .064[a] |
| Follow-up interval (months), mean ± SD | 39.7 ± 13.4 | 39.4 ± 13.5 | 40.7 ± 13.2 | .417[a] |
| Initiation of medication for BPH during follow-ups, n (%) | 7 (1.8) | 2 (0.6) | 5 (6.0) | .006[b] |
| Diagnosis of prostate cancer during follow-ups, n | 0 | 0 | 0 | |
| Baseline serum PSA (ng/mL), mean ± SD | 1.03 ± 0.75 | 1.00 ± 0.73 | 1.11 ± 0.83 | .252[a] |
| Follow-up serum PSA (ng/mL), mean ± SD | 1.07 ± 0.80 | 1.03 ± 0.73 | 1.20 ± 1.03 | .181[a] |
| Baseline BMI ($kg/m^2$), mean ± SD | 24.4 ± 2.9 | 24.4 ± 2.9 | 24.4 ± 2.9 | 1.000[a] |
| Follow-up BMI ($kg/m^2$), mean ± SD | 24.5 ± 2.7 | 24.5 ± 2.7 | 24.4 ± 2.8 | .776[a] |
| Baseline prostatic FDG PET/CT characteristics | | | | |
| Whole-prostate $SUV_{mean}$ | 1.8 ± 0.2 | 1.8 ± 0.2 | 1.8 ± 0.2 | .856[a] |
| Whole-prostate $SUV_{max}$ | 2.6 ± 0.3 | 2.6 ± 0.3 | 2.6 ± 0.3 | .696[a] |
| Volume ($cm^3$) | 18.5 ± 6.3 | 18.1 ± 6.3 | 19.7 ± 6.2 | .036[a] |
| Focal FDG uptake, n (%) | 25 (6.4) | 19 (6.2) | 6 (7.2) | .726[c] |
| Central | 7 (1.8) | 5 (1.6) | 2 (2.4) | .643[b] |
| Peripheral | 18 (4.6) | 14 (4.5) | 4 (4.8) | 1.000[b] |
| Calcification, n (%) | 109 (27.9) | 79 (25.6) | 30 (36.1) | .058[c] |

LUTS, lower urinary tract symptom; mild, IPSS 0-7; moderate to severe, IPSS 8-35; SD, standard deviation; BPH, benign prostatic hyperplasia; PSA, prostate specific antigen; BMI, body mass index.
[a]Student t test; [b]Fisher exact test; [c]chi-square test.

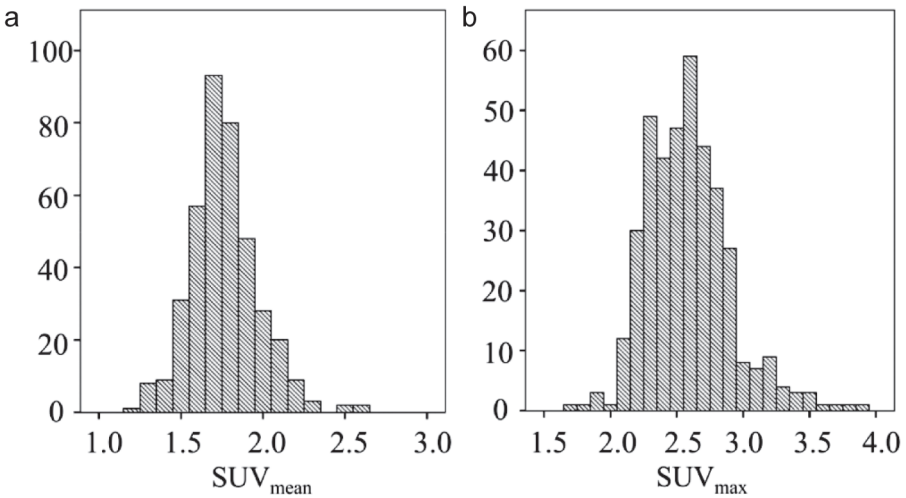


**Figure 1. a, b.** Histograms of $SUV_{mean}$ and $SUV_{max}$ for prostatic FDG uptake in 391 participants; (**a**) $SUV_{mean}$ ranged from 1.2 to 2.6 (median: 1.7, mean: 1.8, SD: 0.2); (**b**) $SUV_{max}$ ranged from 1.7 to 3.9 (median: 2.6, mean: 2.6, SD: 0.3).

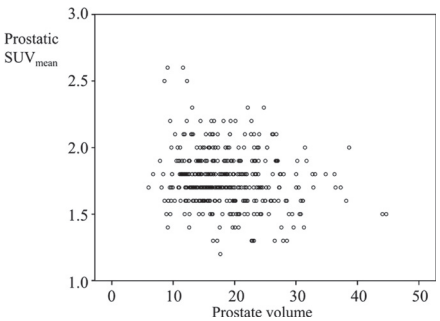


**Figure 2.** A scatterplot of prostate volume and $SUV_{mean}$ for prostatic FDG uptake. A negative relationship ($\rho = -0.137$; $P = .007$) was observed.

Baseline IPSS was associated with prostate volume on FDG PET/CT at baseline ($\rho = 0.154$; $P = .002$) (Table 3 and Figure 3). Age, baseline serum PSA level, baseline BMI, and other baseline FDG PET/CT characteristics such as prostatic $SUV_{mean}$, $SUV_{max}$, focal FDG uptake, and calcification showed no significant correlation with baseline IPSS. Follow-up IPSS was also associated with baseline prostate volume ($\rho = 0.164$; $P = .001$) as well as age at follow-ups ($\rho = 0.127$; $P = .012$). Baseline prostate volume also showed significant correlation with follow-up IPSS when the correlation was adjusted by follow-up interval ($r = 0.201$; $P < .001$). Follow-up serum PSA levels, follow-up BMI, and other baseline FDG PET/CT characteristics such as prostatic $SUV_{mean}$, $SUV_{max}$, focal FDG uptake, and calcification did not correlate with follow-up IPSS. It was also true when the correlation between follow-up IPSS and baseline prostatic $SUV_{mean}$, $SUV_{max}$ or focal FDG uptake was adjusted by follow-up interval. But baseline prostatic calcification showed weak association with follow-up IPSS after follow-up interval adjustment ($r = 0.103$, $P = .043$).

Baseline prostate volume correlated with the voiding component of IPSS at both baseline and follow-ups ($\rho = 0.186$ and 0.197, respectively; $P < .001$ for both) but showed no association with the storage component of the questionnaire either at baseline or follow-ups. Furthermore, age at follow-ups was not associated with the voiding component of IPSS but was associated with the storage component at follow-up ($\rho = 0.168$; $P = .001$). In addition, weak associations were noted between age and baseline QOL ($\rho = 0.108$; $P = .032$), and between baseline prostate volume and follow-up QOL ($\rho = 0.107$; $P = .034$).

## Discussion

In the present study, we analyzed FDG PET/CT characteristics and clinical variables of LUTS in 391 men in their fifties without prostatic malignancy. Prostatic FDG uptake did not show a significant association with IPSS at baseline nor did it predict the follow-up IPSS. All the variables derived from prostatic FDG uptake, including $SUV_{mean}$, $SUV_{max}$, and focal FDG uptake, showed no association with IPSS. Conversely, prostate volume correlated with IPSS both at baseline and follow-ups and showed a significant association with the voiding component but not with the storage component of IPSS.

Several studies have supported the significant role of inflammation in BPH. Di Silverio et al.[21] observed inflammation in 43.1% (1700/3942) of histologically diagnosed BPH cases. The reported incidence of inflammation in surgically resected hyperplastic prostates was up to 98.1% according to Kohnen et al.[22] In addition, the degree of prostatic inflammation has been

**Table 2.** Baseline and follow-up IPSS of study participants

| | | | |
|---|---|---|---|
| IPSS | 4.82 ± 4.36 (4, 0-24) | 5.46 ± 5.00 (4, 0-31) | .001[a] |
| Severity, n (%) | | | |
| Mild (0-7) | 308 (78.8%) | 284 (72.6%) | .045[b] |
| Moderate (8-19) | 81 (20.7%) | 100 (25.6%) | .107[b] |
| Severe (20-35) | 2 (0.5%) | 7 (1.8%) | .177[c] |
| IPSS_V | 3.00 ± 3.20 (2, 0-15) | 3.40 ± 3.68 (2, 0-20) | .002[a] |
| Incomplete empty | 0.80 ± 1.11 (0, 0-5) | 0.86 ± 1.15 (0, 0-5) | .200[a] |
| Intermittency | 0.74 ± 1.00 (0, 0-5) | 0.87 ± 1.15 (0, 0-5) | .007[a] |
| Weak stream | 1.16 ± 1.32 (1, 0-5) | 1.27 ± 1.41 (1, 0-5) | .010[a] |
| Straining to void | 0.30 ± 0.62 (0, 0-4) | 0.40 ± 0.76 (0, 0-5) | .010[a] |
| IPSS_S | 1.82 ± 1.71 (2, 0-10) | 2.06 ± 1.84 (2, 0-11) | .002[a] |
| Frequency | 0.85 ± 0.94 (1, 0-5) | 0.92 ± 0.98 (1, 0-5) | .135[a] |
| Urgency | 0.46 ± 0.73 (0, 0-4) | 0.57 ± 0.79 (0, 0-5) | .002[a] |
| Nocturia | 0.51 ± 0.59 (0, 0-3) | 0.58 ± 0.65 (1, 0-4) | .035[a] |
| IPSS_QOL | 2.09 ± 1.15 (2, 0-5) | 2.09 ± 1.27 (2, 0-5) | .941[a] |

Data are presented as mean ± standard deviation (median, min-max) unless indicated otherwise.
IPSS, International Prostate Symptom Score; V, voiding symptoms; S, storage symptoms; QOL, quality of life.
[a]Wilcoxon signed rank test; [b]chi-square test; [c]Fisher exact test.

| Table 3. Correlation analyses between IPSS and other variables | | | |
|---|---|---|---|
| Baseline IPSS | | | |
| | Age | 0.096 | .059 |
| | Baseline serum PSA level | 0.061 | .228 |
| | Baseline BMI | −0.018 | .715 |
| | Baseline prostate volume | 0.154 | .002 |
| | Baseline prostatic $SUV_{mean}$ | 0.014 | .786 |
| | Baseline prostatic $SUV_{max}$ | 0.045 | .375 |
| | Baseline prostatic focal FDG uptake | 0.030 | .560 |
| | Baseline prostatic calcification | 0.062 | .220 |
| Follow-up IPSS | | | |
| | Age at follow-ups | 0.127 | .012 |
| | Follow-up serum PSA level | 0.080 | .114 |
| | Follow-up BMI | −0.036 | .478 |
| | Baseline prostate volume | 0.164 | .001 |
| | Baseline prostatic $SUV_{mean}$ | 0.008 | .867 |
| | Baseline prostatic $SUV_{max}$ | 0.079 | .117 |
| | Baseline prostatic focal FDG uptake | −0.017 | .737 |
| | Baseline prostatic calcification | 0.074 | .142 |

IPSS, International Prostate Symptom Score; PSA, prostate specific antigen; BMI, body mass index.

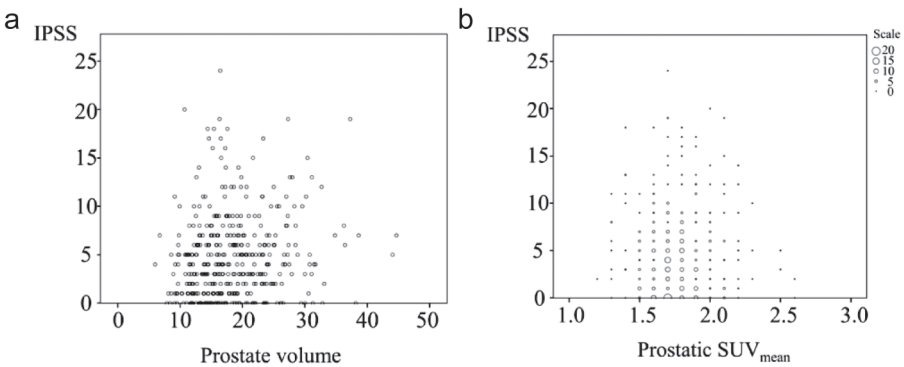


**Figure 3. a, b.** Baseline IPSS plotted according to prostate volume and $SUV_{mean}$ for prostatic FDG uptake; (**a**) a linear relationship was noted between prostate volume and IPSS ($\rho = 0.154$; $P = .002$); (**b**) $SUV_{mean}$ showed no significant association with IPSS ($\rho = 0.014$; $P = .786$). The plot for $SUV_{mean}$ and IPSS is presented using scale binning.

associated with the degree of LUTS due to BPH.[23] FDG uptake at the site of inflammation is known to increase through both acute and chronic phases via increased tissue perfusion and enhanced glycolysis of inflammatory cells.[14] The infiltration of T lymphocytes, B lymphocytes, and activated macrophages, and the upregulation of proinflammatory cytokines in BPH tissues have been reported.[24] However, prostatic FDG uptake did not present a significant association with the severity of LUTS in the present study.

Jadvar et al.[25] reported that the population averages of $SUV_{mean}$ and $SUV_{max}$ for prostatic FDG uptake were 1.3 and 1.6, respectively, in 145 men without prostatic pathology; these SUVs are lower than those reported in the present study; however, the accuracy of the comparison is restricted because of differences in the measurement methods and study populations between these studies. Interestingly, the $SUV_{mean}$ for prostatic FDG uptake in the study by Jadvar et al.[25] showed a tendency to decrease as the prostate size increased ($r = -0.16$; $P = .058$), similar to that observed in the present study.

Normal prostate glands in healthy individuals are approximately 20-30 g.[1] Berges and Oelke[26] reported age-stratified normal values for prostate volume determined by transrectal ultrasound in a German male population. The mean prostate volume was 24 $cm^3$ for men aged of 50-54 years, and it increased with age in their study. Bosch et al.[6] demonstrated that the real increase in prostate volume, defined as a relative increase of ≥26% or an absolute increase of ≥10 $cm^3$, is associated with a greater risk of symptomatic deterioration of BPH. In the present study, the mean prostate volume calculated from the CT images of FDG PET/CT was 18.5 $cm^3$, which is lower than those reported by previous studies using transrectal ultrasound. The difference might attribute limited quality of CT images of FDG PET/CT, obtained without contrast enhancement and breath hold (while patients breathing freely), had lower resolution than US. It is difficult to apply the categorization system established according to absolute values of prostate volumes in previous studies to the present study, and this could be one of our study limitations. However, prostate volume calculated from CT images using the abovementioned ellipsoid formula showed strong agreement with prostate volume derived from transrectal ultrasound or 3D reconstruction of CT images.[19] Furthermore, the outcomes of correlation analysis among continuous variables such as prostate volume and IPSS were not influenced by absolute cutoff values in the present study.

In the present study, IPSS of the study participants was 4.82 at baseline and it increased to 5.46 at follow-ups with an annual change of 0.22. Fukuta et al.[27] observed the natural history of LUTS during a 15-year longitudinal community-based study and reported that the mean IPSS of participants aged 50-59 years was 5.6 at baseline, but it increased significantly at follow-ups with an annual change of 0.10. Meanwhile, there are reports detailing varying LUTS prevalence rates according to IPSS in various regions.[28] The prevalence of moderate-to-severe LUTS, defined as an IPSS ≥ 8, in the present study was 21.2% at baseline, which is comparable with the 16%–17.7% reported in men aged 50-59 years in a community-based study.[29]

There are various clinical definitions of BPH established on the basis of different combinations of parameters such as symptoms, prostate volume, and bladder outflow obstruction. The lack of consensus regarding the clinical definition of BPH leads to the wide range of BPH prevalence rates reported in the literature.[29,30] In this context, the occurrence of need for a workup and treatment for BPH during follow-ups has been emphasized as a meaningful outcome. In the present study, 7 of the 391 (1.8%) participants initiated medication for BPH during follow-ups. The mean $SUV_{mean}$ and $SUV_{max}$ for prostatic FDG uptake of the seven participants according to baseline FDG PET/CT were 1.7 and 2.7, respectively, which were not significantly different from those of the remaining participants (1.8 and 2.6; $P$ = .234 and .403, respectively). The presence of prostatic focal FDG uptake was not associated with the initiation of medication for BPH ($P$ = .373, Fisher exact test). However, the mean prostate volume calculated from baseline FDG PET/CT was higher in the seven participants who eventually initiated medication for BPH than in the remaining participants (25.9 vs. 18.3 $cm^3$; $P$ = .002). This result also supports the association between prostate volume and the symptoms of BPH.

The present retrospective observational study has several limitations. First, it was not a community-based study and it only included participants who underwent healthcare screenings more than once; therefore, men with serious healthcare problems might not be included. Second, prostate volume was derived from the CT images of FDG PET/CT, rather than from transrectal ultrasound, which is more widely used. Third, it cannot be excluded that the possibility of intra-prostatic urethra activity was observed as central focal FDG uptake of prostate gland. Nevertheless, mean $SUV_{mean}$ and $SUV_{max}$ of focal FDG uptakes were not significantly different between central and peripheral locations. Finally, liver SUV measurements which serves as an internal control were not performed.

In conclusion, prostatic FDG uptake did not show a significant association with IPSS at baseline FDG PET/CT as well as at follow-ups. Conversely, the prostate volume derived from the CT images of FDG PET/CT was associated with IPSS both at baseline and follow-ups. Taken together, FDG uptake may not reflect prostatic growth in nonmalignant cases.

### Conflict of interest disclosure

The authors declared no conflicts of interest.

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