

Body Imaging

Factors influencing incidental ^{18}F -FDG uptake in the gallbladder in a large cohort of patients: A retrospective study



Karl Asmar^a, Mohammad Ali El Amine^b, Antoine Bejjani^c, Maha Makki^d, Hani Tamim^e,
Alain S. Abi-Ghanem^{b,*}

^a Department of Radiology, American University of Beirut Medical Center, Riad El-Solh 1107 2020, PO Box 11-0236, Beirut, Lebanon

^b Department of Radiology, American University of Beirut Medical Center, Riad El-Solh 1107 2020, PO Box 11-0236, Beirut, Lebanon

^c American University of Beirut Medical Center, Riad El-Solh 1107 2020, PO Box 11-0236, Beirut, Lebanon

^d Department of Emergency Medicine, American University of Beirut Medical Center, Riad El-Solh 1107 2020, PO Box 11-0236, Beirut, Lebanon

^e Department of Internal Medicine, American University of Beirut Medical Center, Riad El-Solh 1107 2020, PO Box 11-0236, Beirut, Lebanon

ARTICLE INFO

Keywords:

FDG PET/CT

Gallbladder

Incidental uptake

ABSTRACT

Objectives: This study aims to assess the incidence of incidental activity in the gallbladder and the factors that may contribute to it in a large cohort of patients undergoing ^{18}F -fluorodeoxyglucose-PET/CT for cancer evaluation.

Methods: 8096 PET/CTs were retrospectively reviewed. Data pertaining to patient demographics and PET/CT parameters were collected. Patients' records were reviewed for gallbladder disorders for up to 3 years after the exam. The presence/absence of gallbladder uptake was visually assessed. Findings were classified as focal, diffuse increased and diffuse increased wall uptake, or no uptake. Volumetric measurements of the gallbladder and SUVmax of the gallbladder, liver and blood pool were measured. Chi-square and Student's *t*-test were used for statistical analysis.

Results: 54 cases (0.67%) of incidental gallbladder uptake were detected (uptake group). 162 exams without uptake were selected as control (no uptake group). The injection-to-scan interval, SUVmax of the liver and blood pool, and the gallbladder volume did not differ significantly between both groups. Higher blood glucose levels were observed in the uptake (109.9 ± 32.5) vs. no uptake group (97.4 ± 18) ($p = 0.01$), with levels > 150 mg/dL more common in the uptake group ($p = 0.004$). The incidence of gallbladder disease within 3 years after imaging was higher for the uptake group (12/36) compared to the no uptake group (15/115) ($p = 0.02$). Diffuse increased wall uptake was more likely in the group who later developed a pathology (4/12) ($p = 0.03$).
Conclusion: Incidental gallbladder uptake in patients is independent of the injected FDG dose, injection-to-scan interval or gallbladder volume, but may be related to blood glucose level. There's a higher incidence of gallbladder pathology three years after the exam particularly in cases of diffuse increased wall uptake.

1. Introduction

The use of PET/CT for cancer staging has become the standard of care in several malignancies, mainly cancers of the head and neck, esophagus, stomach, lung, thyroid, bone and lymphoid tissue [1]. Over 2 million exams in total were performed in the US in 2018 [2].

^{18}F -fluorodeoxyglucose (FDG) is the most commonly used radiopharmaceutical. It localizes to metabolically active cells such as cells with high rates of mitoses [3]. However, false positives commonly occur in areas of infection and inflammation, decreasing the specificity of the exam for tumor detection and delineation [4,5]. This task is

further challenged by variable physiological uptake in the bowels and myocardium or by incidental uptake in certain parts of the body, such as the pituitary gland, the thyroid gland and the gallbladder [4,6].

The decision to investigate FDG uptake in these locations should always be considered in the presence of clinical symptoms or laboratory abnormalities [7]. But in the absence of these, should we engage in costly investigations, follow-up examinations or invasive procedures to clarify these "abnormalities"? In fact, studies examining thyroid incidentalomas on FDG PET/CT in 16,000 [8] and 46,000 exams [9] found an incidence of 1–2% with 50% of these FDG-avid lesions representing malignant thyroid neoplasms. However, both studies could

* Corresponding author.

E-mail addresses: kra04@aub.edu.lb (K. Asmar), me128@aub.edu.lb (M.A. El Amine), aeb08@mail.aub.edu (A. Bejjani), mm209@aub.edu.lb (M. Makki), htamim@aub.edu.lb (H. Tamim), aa277@aub.edu.lb (A.S. Abi-Ghanem).

<https://doi.org/10.1016/j.clinimag.2020.01.003>

Received 3 September 2019; Received in revised form 8 December 2019; Accepted 3 January 2020

0899-7071/© 2020 Elsevier Inc. All rights reserved.

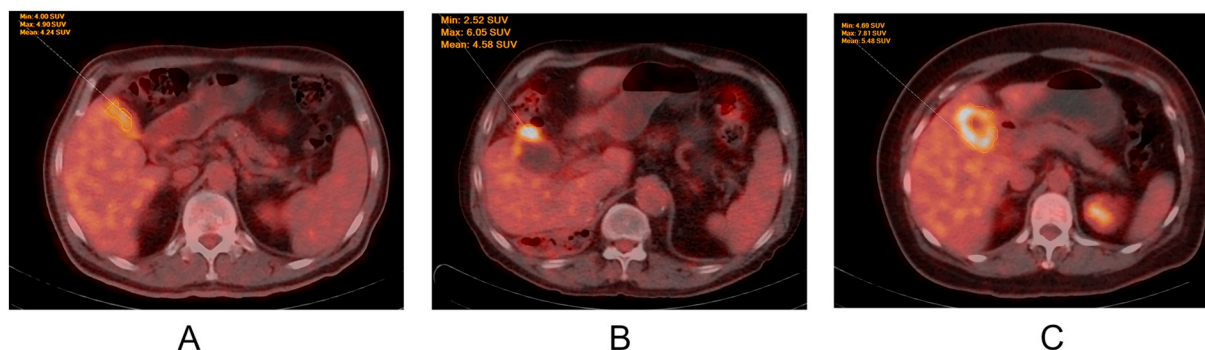


Fig. 1. Axial fused PET and CT images with ^{18}F -FDG at the level of the upper abdomen showing incidental gallbladder uptake and adaptive threshold SUV measurements with the three patterns encountered: diffuse increased uptake in the entire gallbladder (pattern 1, A), focal uptake in the gallbladder wall (pattern 2, B) and diffuse increased uptake in the gallbladder wall only (pattern 3, C).

not confidently suggest investigating thyroid incidentalomas in light of the short life expectancy due to the primary malignancy [8,9]. Another study investigating pituitary incidentaloma found a 0.2% incidence in a sample of 8400 PET/CTs and 50% of these cases were also found to be malignant [10].

Similarly, the gallbladder is not usually FDG-avid unless a pathological process is occurring such as adenomyomatosis, cholecystitis or malignancy [11,12]. Nevertheless, incidental uptake has been reported in the literature, albeit scarcely, and very few studies have investigated the significance or the circumstances that might lead to such an uptake [13,14].

Therefore, we conducted a study to assess the incidence of incidental gallbladder uptake and the factors which may contribute to it in a large cohort of patients undergoing FDG PET/CT for cancer evaluation.

2. Materials and methods

2.1. Study design

This study has been approved by the Institutional Review Board and the need for written informed consent was waived.

10,020 consecutive PET/CT cases performed between January 2014 and August 2018 at a single institution for the purpose of diagnosis, staging or follow-up of malignancy were retrospectively reviewed. Cases that did not cover the gallbladder region or use FDG as radiotracer were excluded. All CT scans of the PET/CT exams were reviewed for the presence of the gallbladder and a total of 8096 PET/CTs were finally selected for analysis.

A review of all the images was conducted to detect any gallbladder uptake in the PET/CT exams, and the medical charts of each of these patients were reviewed for data pertaining to age, sex, body mass index (BMI), injected activity of FDG, blood glucose level at the time of scan, indication for PET/CT and injection-to-scan time interval. Every medical condition related to the gallbladder was followed up for up to 3 years after the PET/CT exam that showed gallbladder uptake.

Any pathology of the gallbladder within that time period was recorded including cholecystectomy, wall calcification, polyps or non-specific findings that were seen on follow-up examinations.

Finally, 3 PET/CT exams without FDG uptake in the gallbladder were selected chronologically, starting with the oldest available cases to serve as “no uptake” control group for every case with gallbladder uptake. These exams were matched for age, sex, BMI and injected activity of FDG. The same data were collected from the medical records of these subjects.

2.2. Image acquisition

Patients were imaged on a Philips Gemini Time of Flight PET/CT

(Philips Healthcare, Amsterdam, Netherlands) combining a 16-slice multidetector CT scanner with a dedicated, full-ring PET scanner with bismuth germanate crystals. The CT scan protocol was acquired using a weight-based low-dose protocol (120 kVp < 60 kg or 140 kVp \geq 60 kg and 35 mA < 60 kg or 50 mA if 60–80 kg or 65 mA if 80–100 kg or 100 mA if > 100 kg). Total imaging time was approximately 20 min. Attenuation-corrected PET images were reconstructed with an iterative reconstruction (ordered-subset expectation maximization algorithm). Orthogonal CT, PET and fused PET/CT images were displayed simultaneously on a Philips IntelliSpace Portal Workstation (Amsterdam, Netherlands). The PET data were also displayed in a rotating maximum-intensity projection.

2.3. Image analysis

Visual assessment was performed by consensus agreement by 3 experienced radiologists for the presence or absence of gallbladder uptake. The findings were classified as 1) diffuse increased uptake in cases of increased uptake in the gallbladder wall and lumen, 2) focal uptake in cases of increased focal uptake in the gallbladder wall only, 3) diffuse increased wall uptake in cases of increased uptake in the gallbladder wall only, or 4) no increased uptake (controls). In cases of diffuse increased uptake, SUVmax of the gallbladder was measured using a circular ROI that fits the largest gallbladder lumen; in cases of increased focal uptake, SUVmax was measured using a seed ROI based on adaptive threshold (Fig. 1). In negative cases, gallbladder SUVmax was measured by a circular ROI that fits the largest gallbladder lumen. For hepatic and blood pool uptake, the same methods were used for both positive and negative cases: in the liver, SUVmax was measured using a circular ROI of 3 cm diameter in the most homogeneous part of the parenchyma (mostly in the right hepatic lobe); the blood pool activity was measured in the ascending aorta and aortic arch using a circular ROI that fits the lumen. Three dimensional volumetric measurements of the gallbladder were performed using the tumor tracking function of Philips IntelliSpace on low-dose body CT for both uptake and no uptake groups.

2.4. Statistical analysis

The Statistical Package for Social Sciences (SPSS), version 24.0 was used for data cleaning, management and analyses. Data were described as number and percent for categorical variables, whereas the mean and standard deviation (\pm SD) was calculated for continuous variables. The comparison between the uptake group, no uptake group and other categorical variables was assessed using the Chi-square test, whereas Student's *t*-test was used for the association with continuous variables. $p < 0.05$ was considered statistically significant.

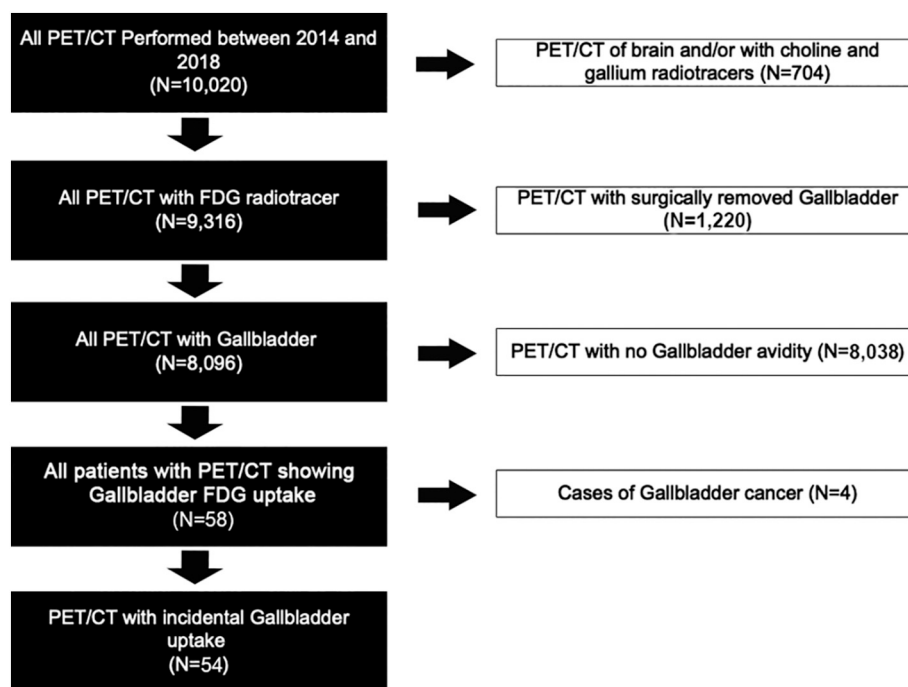


Fig. 2. Consort flow diagram representing the identification and selection of the study population.

3. Results

After screening all 10,020 PET/CT exams performed between January 2014 and August 2018, 8096 cases met the eligibility criteria for analysis. 54 exams (0.67%) were found to have incidental gallbladder uptake (Fig. 2). No gallbladder pathology was seen in any of these cases at the time of exam. A total of 162 “no uptake” controls matched for age, gender, BMI and injected activity of FDG were selected. Our sample of 216 exams consisted of more men (51.9%) than women (48.1%) with an average age of 50.5 ± 17.9 years and a BMI mostly between normal ($20\text{--}24.9 \text{ kg/m}^2$), overweight ($25\text{--}29.9 \text{ kg/m}^2$) and obese ($30\text{--}34.9 \text{ kg/m}^2$). The mean injected FDG activity was $252.7 \pm 43.3 \text{ MBq}$.

Table 1 summarizes the differences between our uptake and no uptake groups. There was no significant difference for the matched variables. The indication for PET/CT, i.e. the primary malignancy, was similar for both groups ($p\text{-value} = 0.07$) with most of our patients presenting with lymphoma, breast cancer, lung cancer, genitourinary and gastrointestinal (excluding gallbladder) malignancies. Additionally, the injection-to-scan time did not differ significantly ($p\text{-value} = 0.17$) with $70.1 \pm 18 \text{ min}$ for the uptake group and $66.6 \pm 15.9 \text{ min}$ for the no uptake group.

The gallbladder showed $\text{SUV}_{\text{max}} 4.4 \pm 1.7$ in the uptake group compared to 1.5 ± 0.5 in the no uptake group ($p\text{-value} < 0.0001$). The pattern of gallbladder uptake in our uptake group was predominantly diffuse (pattern 1: 44.4%), then focal (pattern 2: 42.6%) then wall uptake (pattern 3: 13.0%).

SUV_{max} of the liver and SUV_{max} of the blood pool were not significantly different between the 2 groups. Both $\text{SUV}_{\text{max}_{\text{Gallbladder}}}/\text{SUV}_{\text{max}_{\text{Liver}}}$ and $\text{SUV}_{\text{max}_{\text{Gallbladder}}}/\text{SUV}_{\text{max}_{\text{Blood Pool}}}$ ratios were significantly higher for the uptake group ($p\text{-value} < 0.001$). While the gallbladder volume (mL) did not vary between the uptake group and the no uptake group (30.9 ± 26.1 vs. 34.8 ± 21.5 , $p\text{-value} = 0.28$), the $\text{SUV}_{\text{max}_{\text{Gallbladder}}}/\text{Vol}_{\text{Gallbladder}}$ ratio was significantly higher for the uptake group ($p\text{-value} < 0.0001$).

Our results show a significantly higher blood glucose level (mg/dL) in the uptake group (109.9 ± 32.5) vs. the no uptake group (97.4 ± 18) with a $p\text{-value}$ of 0.01. When pooled in ranges (< 100 ,

$100\text{--}150$ and $> 150 \text{ mg/dL}$), 55.6% of the uptake group had a $\text{BGL} < 100 \text{ mg/dL}$ vs. 71% of the no uptake group ($p\text{-value} = 0.004$). The most significant difference was observed in patients with a $\text{BGL} > 150 \text{ mg/dL}$ (13% of the uptake group vs. 1.9% of the no uptake group, $p\text{-value} = 0.004$). However, the pattern of gallbladder uptake in the uptake group was not affected by the blood glucose level (Table 2).

Within 3 years after the PET/CT exam, both groups had an equal percentage of patients who had no information on follow-up (18/54 in the uptake group—33.3% and 47/162 in the no uptake group—29.0%) (Table 1). From those who had follow-up, the incidence of gallbladder disease was significantly higher for the uptake group (12/36, 33.3%) compared to the no uptake group (15/115, 13.0%) with a $p\text{-value}$ of 0.02. The average number of days between the date of scan and the date of presentation with a gallbladder pathology for the no uptake group was 351 ± 171 days with a median of 334 days and a range of 115–639 days, while for the uptake group it was 337 ± 215 days with a median of 257 days and a range of 90–721 days. Cholelithiasis was the most common pathology encountered in the uptake group on follow-up (5/12 cases, 42%), followed by diffuse wall calcifications (2/12 cases, 17%) and diffuse wall thickening (2 case, 17%), gallbladder polyps (1 case, 8%), focal wall calcifications (1 case, 8%) and cholangiocarcinoma (1 case, 8%). The no uptake group however only exhibited cholelithiasis (9/15 cases, 60%), gallbladder polyps (4/15 cases, 27%) and metastatic deposit (2/15 cases, 13%) (Fig. 3). Within the uptake group cases that had a follow-up within 3 years, a pattern of diffuse increased wall uptake (pattern 3) was significantly more likely in those who developed a pathology (4/12, 33.3%) compared to those who did not (2/24, 8.3%) ($p = 0.03$). On the other hand, a pattern of diffuse increased uptake (pattern 1) was significantly less likely in those who developed a pathology (1/12, 8.3%) compared to those who did not (11/24, 45.8%) ($p = 0.03$) (Table 3). Of the 4 cases in the uptake group with diffuse increased wall uptake (pattern 3) who developed pathology within 3 years, 2/4 (50%) had diffuse wall calcifications, 1/4 (25%) had diffuse wall thickening and 1/4 (25%) had cholelithiasis.

4. Discussion

The incidence of incidental gallbladder uptake in our sample of

Table 1
Comparison of collected data between uptake and no uptake groups.

		Uptake group (%) N = 54	No uptake group (%) N = 162	p-Value
Gender	Male	28 (51.9)	84 (51.9)	1.00
	Female	26 (48.1)	78 (48.1)	
Age (years)	Mean (± SD)	50.4 ± 18	50.5 ± 18	0.97
BMI (kg/m ²)	Mean (± SD)	25.6 ± 4.6	25.6 ± 4.4	0.91
	Under weight	4 (7.4)	8 (4.9)	0.66
	Normal	22 (40.7)	69 (42.6)	
	Overweight	17 (31.5)	50 (30.9)	
	Obese	9 (16.7)	33 (20.4)	
	Extremely obese	2 (3.7)	2 (1.2)	
Injected FDG dose (MBq)	Mean (± SD)	252.3 ± 44	253.1 ± 42.9	0.94
Follow-up at three years	No pathology	24 (44.4)	100 (61.7)	0.02
	Pathology	12 (22.2)	15 (9.3)	
	No follow up	18 (33.3)	47 (29.0)	
SUVmax _{Gallbladder}	Mean (± SD)	4.4 ± 1.7	1.5 ± 0.5	< 0.0001
SUVmax _{Liver}	Mean (± SD)	3.1 ± 0.7	3.3 ± 0.8	0.09
SUVmax _{Blood Pool}	Mean (± SD)	2.1 ± 0.5	2.2 ± 0.5	0.62
Ratio SUVmax _{Gallbladder} /SUVmax _{Liver}	Mean (± SD)	1.5 ± 0.6	0.5 ± 0.2	< 0.0001
Ratio SUVmax _{Gallbladder} /SUVmax _{Blood Pool}	Mean (± SD)	2.2 ± 0.9	0.7 ± 0.2	< 0.0001
Ratio SUVmax _{Gallbladder} /Vol _{Gallbladder}	Mean (± SD)	0.2 ± 0.2	0.06 ± 0.05	< 0.0001
Blood glucose level (mg/dL)	Mean (± SD)	109.9 ± 32.5	97.4 ± 18.0	0.01
	< 100	30 (55.6)	115 (71.0)	0.004
	100–150	17 (31.5)	44 (27.2)	
	> 150	7 (13.0)	3 (1.9)	
Injection-to-scan interval (min)	Mean (± SD)	70.1 ± 18	66.6 ± 15.9	0.17
Vol _{Gallbladder} (mL)	Mean (± SD)	30.9 ± 26.1	34.8 ± 21.5	0.28
Primary malignancy	Breast cancer	9 (16.7)	38 (23.5)	0.07
	GI	10 (18.5)	21 (13.0)	
	GU	6 (11.1)	14 (8.6)	
	Head and neck cancer	1 (1.9)	8 (4.9)	
	Lung cancer	5 (9.3)	23 (14.2)	
	Lymphoma/blood	23 (42.6)	43 (26.5)	
	MSK and Skin	0 (0.0)	15 (9.2)	
Gallbladder uptake in positive cases	Pattern 1 — diffuse increased uptake	24 (44.4)		
	Pattern 2 — focal increased uptake	23 (42.6)		
	Pattern 3 — diffuse increased wall uptake	7 (13.0)		

Bold data indicates significant at p < 0.05

8096 PET/CTs was 0.67% or 1 case for every 150 PET/CT performed. Incidental findings on ¹⁸F-FDG PET/CT should not be overlooked. Agress et al. [15] investigated 1750 PET/CTs and found 42 incidental foci of uptake at various locations in the body (incidence: 2.4%). A total of 30 (71%) foci were identified as malignant or pre-malignant on biopsy. One of these 30 foci was in the gallbladder and was revealed to be a gallbladder carcinoma on histology. Taking into consideration the massive burden of gallbladder disease which was reported to be 6.5 billion USD for the year 2000 in the USA [16], the need to investigate even a rarely occurring incidental finding in the gallbladder should be assessed.

SUVmax is a semi-quantitative tool for assessing metabolic uptake in a region of interest. This is highly dependent on BMI, age, sex and injected FDG activity [17]. However, in an effort to eliminate this variability, all the patients were scanned on the same camera. In addition, we were able to match our uptake group cases with no uptake controls for the aforementioned variables. Our uptake and no uptake groups were comparable since SUVmax measurements in the blood pool (2.1 ± 0.5 vs. 2.2 ± 0.5, p = 0.62) and liver (3.1 ± 0.7 vs. 3.3 ± 0.8, p = 0.09) were not significantly different. As a result, the detected incidental uptake in the gallbladder is not a relative finding. In fact, SUVmax_{Gallbladder}/SUVmax_{Blood Pool} as well as SUVmax_{Gallbladder}/

SUVmax_{Liver} ratios were both significantly higher for the uptake group indicating a real and isolated gallbladder uptake independent of blood pool and liver activity.

One of the methodological factors that might affect gallbladder uptake is injection-to-scan time interval. Our results did not show a correlation between incidental uptake and the injection-to-scan interval. This is in contradiction with the literature. In fact, Murata et al. reported a higher SUV uptake in the gallbladder when the injection-to-scan interval increased [13]. However, the population of that study consisted of patients without visible gallbladder uptake. They also compared the SUV activity of the gallbladder in a group of patients undergoing delayed abdominal PET/CT. In their study, they found a higher SUV activity in the delayed phase (143 min) compared to the early phase (73 min) [13]. Although uptake did increase with a longer injection-to-scan time interval, this increase was not sufficient to be visually detectable since neither of their scan resulted in incidental uptake. In fact, their findings are more suggestive of FDG excretion in bile because of simultaneous significant decrease in Liver SUV and increase in gallbladder SUV, particularly within the gallbladder lumen rather than the gallbladder wall. Incidental gallbladder uptake in our study was not limited to diffuse uptake and is less likely to be explained by a simple accumulation within the lumen.

Table 2
Comparison of gallbladder uptake pattern and blood glucose levels within the uptake group.

Blood glucose (mg/dL)	Pattern 1 — diffuse increased uptake	Pattern 2 — focal increased uptake	Pattern 3 — diffuse increased wall uptake	p-Value
< 100	12 (50.0)	14 (60.9)	4 (57.1)	0.81
≥ 100	12 (50.0)	9 (39.1)	3 (42.9)	

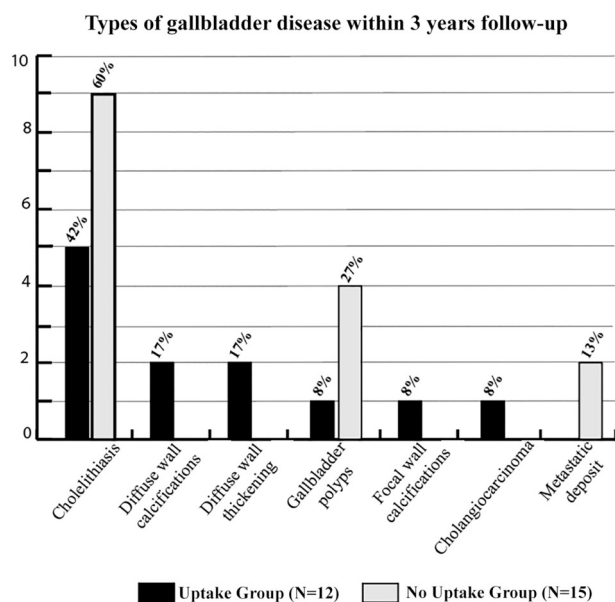


Fig. 3. Bar graph representing the types of gallbladder disease within 3 years of follow-up.

The effect of gallbladder volume on incidental gallbladder uptake was evaluated. A larger gallbladder could in theory result in a higher accumulation of FDG which would be perceived as uptake. Alternatively, a smaller gallbladder could result in a more concentrated FDG accumulation and also be perceived as avid. We found similar gallbladder volumes between our uptake and no uptake groups, therefore negating the correlation between volume and uptake. Our findings are not concordant with those of Murata et al. who reported a higher SUV value with smaller gallbladder volumes. Their study however, included gallbladder without visual FDG uptake rather than clear visual activity with the patterns we encountered in our series [13].

The relationship between FDG uptake and blood glucose levels was addressed. In our study, blood glucose level at the time of scanning, specifically BGL > 150 mg/dL, was the only factor to correlate with incidental gallbladder uptake regardless of the pattern of uptake. The uptake of FDG at the cellular level is mediated by the glucose transporters (GLUT) family and the expression of GLUT subtypes varies between tissues [18]. Because these transporters carry both FDG and unlabeled glucose, there is a possibility that competitive binding between FDG and endogenous glucose would result in lower FDG binding and subsequent accumulation in the blood which eventually end up in the gallbladder [19]. In tissues such as the brain and skeletal muscles, competitive binding will result in decrease FDG uptake in cases of chronic hyperglycemia or diabetes. In a non-diabetic patient however, skeletal muscles react differently in episodes of acute hyperglycemia. The insulin peak activates GLUT4 (an insulin-dependent transporter) resulting in increased FDG uptake [20,21]. This competitive binding

results in more FDG in the circulation and a higher likelihood of FDG uptake by normal organs. In a similar fashion, during acute hyperglycemia, FDG activity is increased in the blood pool via upregulation of GLUT1 in red blood cells. In patients with dysfunctional glucose homeostasis such as pre-diabetic or diabetic patients, FDG uptake may be accentuated in more receptive organs such as the gallbladder [19]. Unfortunately, in addition to our small sample size, our data lack enough information on the pathophysiology of our patients' hyperglycemia to allow us to confidently study the correlation between blood glucose levels and incidental gallbladder uptake.

It is more likely that an early inflammatory response or an insidious pathological process is underway resulting in incidental uptake in the gallbladder. In fact, the incidence of pathology within 3 years is significantly higher when the patient was found to have incidental gallbladder uptake (Table 1, Fig. 3), particularly when the uptake pattern was diffuse and increased in the gallbladder wall (Table 3). Our results show that a small number of our no uptake cases presented with a gallbladder pathology and the vast majority only had cholelithiasis. Although the most occurring pathology in our uptake group was cholelithiasis, three of twelve cases developed a more serious pathology including cholangiocarcinoma and diffuse calcifications — porcelain gallbladder, an entity known to have a high association with gallbladder adenocarcinoma [22]. Our results also showed that the more serious pathologies such as porcelain gallbladder were more likely when pattern 3 was encountered. Therefore, further investigation of the incidental gallbladder uptake may be warranted when it follows pattern 3 and the primary malignancy for which the PET/CT is being done has a favorable prognosis. This is in line with a similar study assessing incidental thyroid uptake [9].

The major strength of this study is the use of all PET/CTs performed at our institution, which significantly reduced sampling issues and selection bias, particularly in the uptake group. The detected incidence of incidental gallbladder uptake, although low, reflects the true incidence in our population. Its significance however is unclear, given that a large portion of these patients were lost to follow up, which is the major weakness of our study. The decision to investigate and provide early intervention is better assessed with a multicentric prospective study, which could collect a large enough sample to draw more significant and validated conclusions.

5. Conclusion

In summary, we found that incidental gallbladder uptake in a patient with no specific symptoms is independent of the injected FDG dose, injection-to-scan interval or gallbladder volume, but may be related to the blood glucose level at the time of scanning. More dedicated studies should be performed to better understand this correlation. We also found a higher incidence of subsequent clinically relevant gallbladder pathology within three years of an exam showing incidental uptake, particularly when this uptake showed a pattern of diffuse increased wall uptake. A larger sample size study with a prospective

Table 3 Comparison of incidental uptake pattern in the gallbladder between groups with pathology and no pathology within 3 years of follow-up.

		No pathology within 3 years of follow-up N = 24	Pathology within 3 years of follow-up N = 12	p-Value
Uptake pattern	1) Diffuse increased uptake	11 (45.8%)	1 (8.3%)	0.03
	2) Focal fundal uptake	11 (45.8%)	7 (58.3%)	
			Cholelithiasis	
			3 cholelithiasis	
			1 gallbladder polyp	
			1 adenomyomatosis	
			1 cholangiocarcinoma	
			1 focal wall calcification	
			2 diffuse wall calcification	
			1 diffuse wall thickening	
			1 cholelithiasis	
	3) Diffuse increased wall uptake	2 (8.3%)	4 (33.3%)	

design should be considered to validate the benefit of further investigation or follow-up imaging.

Funding

No funding was provided for this article.

IRB approval

This study is approved by the Institutional Review Board at the American University of Beirut.

Declaration of competing interest

None by all authors.

References

- [1] Anderson T, Elman S, Matesan M, Carnell J, Mitra E, Behnia F. Pictorial review of NCCN guidelines for use of FDG PET in oncology. *J Nucl Med* 2017;58(supplement 1):974.
- [2] IMV PET Census Database. PET imaging market summary report. <https://imvinfo.com/product/pet-imaging-market-summary-report-2019>; 2019.
- [3] Paans AM, van Waarde A, Elsinga PH, Willemsen AT, Vaalburg W. Positron emission tomography: the conceptual idea using a multidisciplinary approach. *Methods* 2002;27(3):195–207.
- [4] Culverwell AD, Scarsbrook AF, Chowdhury FU. False-positive uptake on 2-[(1)(8) F]-fluoro-2-deoxy-D-glucose (FDG) positron-emission tomography/computed tomography (PET/CT) in oncological imaging. *Clin Radiol* 2011;66(4):366–82.
- [5] Shreve PD, Anzai Y, Wahl RL. Pitfalls in oncologic diagnosis with FDG PET imaging: physiologic and benign variants. *Radiographics* 1999;19(1):61–77.
- [6] Zincirkeser S, Sahin E, Halac M, Sager S. Standardized uptake values of normal organs on ¹⁸F-fluorodeoxyglucose positron emission tomography and computed tomography imaging. *J Int Med Res* 2007;35(2):231–6.
- [7] Wang G, Lau EW, Shakher R, Rischin D, Ware RE, Hong E, et al. How do oncologists deal with incidental abnormalities on whole-body fluorine-18 fluorodeoxyglucose PET/CT? *Cancer* 2007;109(1):117–24.
- [8] Are C, Hsu JF, Schoder H, Shah JP, Larson SM, Shaha AR. FDG-PET detected thyroid incidentalomas: need for further investigation? *Ann Surg Oncol* 2007;14(1):239–47.
- [9] Pattison DA, Bozin M, Gorelik A, Hofman MS, Hicks RJ, Skandarajah A. ¹⁸F-FDG-avid thyroid incidentalomas: the importance of contextual interpretation. *J Nucl Med* 2018;59(5):749–55.
- [10] Abdelmalik A, Sarajlic L, Muzaffar R, Osman M. Pituitary adenoma: incidentaloma identified by F18-FDG PET/CT. *J Nucl Med* 2012;53(supplement 1):101.
- [11] Kostakoglu L, Hardoff R, Mirtcheva R, Goldsmith SJ. PET-CT fusion imaging in differentiating physiologic from pathologic FDG uptake. *Radiographics* 2004;24(5):1411–31.
- [12] Oe A, Kawabe J, Torii K, Kawamura E, Higashiyama S, Kotani J, et al. Distinguishing benign from malignant gallbladder wall thickening using FDG-PET. *Ann Nucl Med* 2006;20(10):699–703.
- [13] Murata Y, Watanabe H, Kubota K, Toda K, Nakamura S, Okouchi K, et al. PET/CT evaluation of the physiologic accumulation of ¹⁸F-FDG within the gallbladder vesicle. *Nucl Med Biol* 2007;34(8):961–6.
- [14] Bai X, Wang X, Zhuang H. FDG accumulation in the lumen of the gallbladder without related pathology. *Clin Nucl Med* 2018;43(5):383–5.
- [15] Agress Jr. H, Cooper BZ. Detection of clinically unexpected malignant and pre-malignant tumors with whole-body FDG PET: histopathologic comparison. *Radiology* 2004;230(2):417–22.
- [16] Sandler RS, Everhart JE, Donowitz M, Adams E, Cronin K, Goodman C, et al. The burden of selected digestive diseases in the United States. *Gastroenterology* 2002;122(5):1500–11.
- [17] Batalles SM, Villavicencio RL, Quaranta A, Burgos L, Trezzo S, Staffieri R, et al. Variations of the hepatic SUV in relation to the body mass index in whole body PET-CT studies. *Rev Esp Med Nucl Imagen Mol* 2013;32(1):26–32.
- [18] Wood IS, Trayhurn P. Glucose transporters (GLUT and SGLT): expanded families of sugar transport proteins. *Br J Nutr* 2003;89(1):3–9.
- [19] Eskian M, Alavi A, Khorasanizadeh M, Vigiante BL, Jacobsson H, Barwick TD, et al. Effect of blood glucose level on standardized uptake value (SUV) in ¹⁸F-FDG PET-scan: a systematic review and meta-analysis of 20,807 individual SUV measurements. *Eur J Nucl Med Mol Imaging* 2019;46(1):224–37.
- [20] Kelley DE, Mintun MA, Watkins SC, Simoneau JA, Jadal F, Fredrickson A, et al. The effect of non-insulin-dependent diabetes mellitus and obesity on glucose transport and phosphorylation in skeletal muscle. *J Clin Invest* 1996;97(12):2705–13.
- [21] Williams KV, Bertoldo A, Mattioni B, Price JC, Cobelli C, Kelley DE. Glucose transport and phosphorylation in skeletal muscle in obesity: insight from a muscle-specific positron emission tomography model. *J Clin Endocrinol Metab* 2003;88(3):1271–9.
- [22] Grand D, Horton KM, Fishman EK. CT of the gallbladder: spectrum of disease. *AJR Am J Roentgenol* 2004;183(1):163–70.