The Role of ^{18}F-FDG PET/CT in staging of gallbladder carcinomas

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ABSTRACT

Background/Aims: Gallbladder Carcinoma (GBC) is the most common and aggressive tumor of the biliary tract. Patients are typically diagnosed during advanced stages, and the mean overall survival is short. In our study, we aimed to demonstrate the uptake patterns of ^{18}F-FDG PET/CT in GBC, as well as its association with survival and diagnostic value during the initial stage.

Materials and Methods: Overall, 17 patients with GBC were retrospectively included in the study. ^{18}F-FDG PET/CT study was performed for pretreatment staging. Two different standardized uptake values (SUVmax and SUVmean), metabolic tumor volume 40% (MTV40), and tumor lesion glycolysis (TLG) of the primary tumors were compared between the clinical and histopathological groups.

Results: Of the 17 patients, 11 were women (64.7%), and 6 (35.3%) were men. The mean age of the patients was 69.7±8.8 years. ^{18}F-FDG uptake was detected in all lesions. Mean SUVmax was calculated to be 15.4±13.7 (median=10.6, range=3.4-46.8). All distant metastases (52.9%) were detected in the liver. Semiquantitative metabolic parameters (SUVmax and SUVmean, MTV40, and TLG) obtained from patients with distant metastasis were not significantly higher than those without distant metastasis. Similar results were obtained in patients with and without nodal metastasis. No statistically significant intergroup difference was observed regarding metabolic parameters. However, a statistically significant negative correlation was observed between the patient's age and the SUVmax of the primary lesion and metastatic lymph nodes (r=−0.564, p=0.018). During 10.7±10.4 months of mean follow-up, the mean survival of patients with distant metastases (6.1±11.0 months) was significantly shorter than that of patients with no organ metastases (15.8±7.1 months).

Conclusion: In our study, distant metastases and age were observed to be crucial prognostic factors in patients with gallbladder carcinoma (GBC). In addition, we believe that ^{18}F-FDG PET/CT imaging will help to stage the GBC, detect nodal and distant metastasis, and evaluate the metabolic state of gallbladder lesions.

Keywords: Gallbladder carcinoma, ^{18}F-fluorodeoxyglucose positron emission tomography/computerized tomography (^{18}F-FDG PET/CT), adenocarcinoma, staging

INTRODUCTION

Gallbladder carcinoma (GBC) is a rare form of cancer with a worldwide prevalence of less than 2 in 100,000. This rate varies according to the geographic, ethnic, and cultural characteristics of societies. As such, GBC is more frequently reported in developing countries (1). The various risk factors for GBC are advanced age, female sex, gallstones, obesity, inflammation, smoking, and infection (2).

Adenocarcinoma is the most common histopathologic subtype of gallbladder tumors with a 98% rate. Gallbladder carcinoma (GBC) may remain asymptomatic until advanced stages or may produce nonspecific symptoms. They have an aggressive nature and tend to show rapid progression (3). A crucial factor directly affecting the prognosis is the tumor's anatomical origin. Because of the absence of a serosal layer separating the gallbladder from the liver, direct and local hepatic metastases occur rapidly, followed by lymphatic dissemination and hematogenous spread (4).

Patients with GBC are reported to have dramatically low rates of survival, with the 5-year survival rates being <5% and the mean survival rate being as low as 6 weeks (4), primarily because of the insidious onset and progression of adenocarcinomas, resulting in late diagnosis (4, 5). Invasion to surrounding tissues, cholelithiasis, calcification, wall thickening, and increased vascularity are indicators of malignant gallbladder lesions (4). However, conventional imaging techniques remain inefficient in the early

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diagnosis of gallbladder cancers. Curative surgical resection is potentially achievable with early diagnosis, yet this is only possible in less than 10% of the patients (6).

Recently, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computerized tomography (PET/CT), which is an imaging modality that relies on in-vivo glucose hypermetabolism, has been increasingly used for pretreatment and postoperative staging, as well as to detect nodal and distant metastases (7). In our study, we aimed to demonstrate the association of clinical characteristics of patients with their survival and ^{18}F-FDG uptake patterns, as well as the predictive and diagnostic value of PET/CT imaging in disease staging.

MATERIALS AND METHODS

Patients

Overall, 17 patients with GBC were retrospectively included in the study. Histopathologic diagnosis and ^{18}F-FDG PET/CT imaging were obtained before surgical resection and chemotherapy-radiation therapy. The study was approved by the Istanbul Training and Research Hospital's Ethical Committee (No:1227, Date: 04.20.2018). Written and verbal informed consent was obtained from all subjects.

The diagnosis and histopathologic analysis of primary GBC was verified using materials obtained through surgery or from the biopsy of liver metastases. The staging was performed according to the Tumor Node Metastasis (TNM) staging system for GBC in concordance with the American Joint Committee on Cancer Guidelines (8).

^{18}F-FDG PET/CT Imaging

In our study, primary gallbladder lesions were assessed using PET/CT according to the size or wall thickness, location, ^{18}F-FDG uptake of the tumor, and the presence of lymph node and distant metastases. Patients whose blood glucose levels were below 150 mg/dl after 6 hours of fasting were suitable for the procedure. Sixty minutes after the intravenous injection of 3.7-5.2 MBq/kg^{18}F-FDG, the PET/CT imaging was obtained from the vertex to the upper femur (in 4 patients with Biograph 6 HD LSO, and 13 patients with Biograph mCT ultra HD LSO PET/CT; Siemens Molecular Imaging; Hoffman Estates, IL, USA). Combined image acquisition began approximately 60 min after 18F-FDG injection. CT was performed from vertex to the mid-thigh at 140 kV, 80 mA, and 2 mm slice thickness. PET scan was performed in the same position. The emission scan time was 1.5 min/bed position, and 8-10 bed positions covered the scanning range. CT-based scatter and attenuation correction PET images were reconstructed on 512×512 matrices, two iterations, and 16 subsets. The PET data were reconstructed using the standard iterative algorithm (time of flight + true X algorithm), and ultra HD images were obtained. Transaxial, sagittal, and coronal images and fused images were analyzed on the workstation (Syngo.via, Siemens Molecular Imaging).

The tumor contours were semi-automatically delineated, and maximum activity (SUVmax) was calculated as the highest ^{18}F-FDG uptake on the tumoral lesion. SUVmax was calculated automatically by using the software and the following formula: maximum activity within a voxel of interest (VOI) (MBq/mL) divided by the injected ^{18}F-FDG dose (MBq/kg). Using the same VOI, the mean activity (SUVmean) was calculated as the average ^{18}F-FDG uptake in the tumoral lesion. In addition, a 40% threshold of SUVmax in the lesion was used to calculate the metabolic tumor volume (MTV40). MTV values and SUVmean multiplication were used to calculate the tumor lesion glycolysis (TLG) within the VOI. Diameters of the primary tumors and the long axis of the metastatic lymph nodes were measured using the CT of the PET/CT imaging.

Statistical analysis

All data were analyzed using the Statistical Package for Social Sciences (SPSS) software for Windows v21.0 (IBM Corp.; Armonk, NY, USA). Data were expressed as mean and standard deviation, median (min-max), distribution frequencies, and percentages, as appropriate. The normalization of data distribution was evaluated using the Kolmogorov–Smirnov test. For variables that were not normally distributed, a comparison was performed using the Mann–Whitney and Kruskal–Wallis tests, whereas correlation was performed using Pearson's test. Categorical variables were evaluated using the chi-squared test. The overall survival rates were analyzed using the Kaplan–Meier analysis. A $p<0.05$ was considered statistically significant.

RESULTS

Of the 17 patients with a histopathologic diagnosis of GBC, 11 were women (64.7%), and 6 were men (35.3%). The mean age was 69.7±8.8 years (range: 50-84 years). The mean age of male patients was 65.7±10.5 years, whereas that of the female patients was 71.9±7.4 years. No statistically significant difference was observed between the mean ages of male and female patients ($p=0.365$).

Table 1. Clinical characteristics and PET/CT findings of patients.

No	Age	Gender	Follow-up (Month)	Localization	Primary tumor size (cm)	NodalMet.	Metastatic lymph node (long axis, cm)	Distant Organ Met.	Distant Metastatic Lesion SUVmax	Metastatic Lymph Node SUVmax	Primary tumor SUVmax	Primary tumor SUVmean	Primary tumor MTV40	Primary tumor TLG
1	66	Female	0.7	Diffuse	3.0	+	2.1	Liver	17.7	33.3	32.5	18.6	3.8	71.4
2	69	Female	18.8	Fundus	1.2	+	4.0	-	-	15.1	15.4	8.7	10.8	94.0
3	71	Female	2.3	Diffuse	6.0	-	-	Liver	3.7	-	6.4	3.7	41.7	154.9
4	72	Female	1.2	Diffuse	2.1	+	2.0	Liver	7.8	11.9	6.3	3.7	10.5	38.6
5	84	Female	0.4	Diffuse	1.9	-	-	Liver	10.2	-	4.5	2.4	9.8	23.6
6	77	Female	8.8	Diffuse	18.3	-	-	-	-	-	10.6	5.9	8.0	47.3
7	69	Female	34.3	Diffuse	1.7	-	-	Liver	12.2	-	7.9	4.8	9.3	44.9
8	81	Female	1.7	Fundus	1.5	-	-	Liver	8.6	-	7.8	4.5	6.9	30.9
9	78	Female	13.5	Fundus	1.5	-	-	-	-	-	9.2	5.2	3.6	18.8
10	61	Female	16.2	Diffuse	2.3	-	-	-	-	-	25.8	14.2	5.3	75.6
11	63	Female	7.1	Diffuse	3.0	-	-	-	-	-	16.2	8.8	17.9	156.7
12	70	Male	20.7	Diffuse	2.7	-	-	-	-	-	5.3	NA	NA	NA
13	50	Male	12.4	Diffuse	3.6	+	2.9	-	17.7	34.1	46.2	26.2	5.9	155.3
14	76	Male	29.4	Fundus	2.0	-	-	-	-	-	46.8	29.9	3.0	89.3
15	71	Male	1.0	Diffuse	3.0	+	3.2	Liver	23.1	12.5	10.5	6.5	6.1	39.6
16	72	Male	11.2	Diffuse	0.9	+	2.0	Liver	13.8	2.2	4.6	2.6	9.4	24.5
17	55	Male	2.3	Diffuse	5.7	+	1.7	Liver	31.0	12.4	31.5	19.2	4.5	86.1
Mean±SD											16.9±13.8	10.3±8.4	9.8±9.0	72.0±46.5
Median											10.5	6.2	7.4	59.3
Range											4.6-46.8	2.6-29.9	3.0-41.7	23.6-156.7

Met: Metastasis; SUVmax: Standart Uptake Value maximum; MTV: Metabolic Tumor Volume; TLG: Total Lesion Glycolysis; SD: Standart Deviation; PET/CT: Positron Emission Tomography/Computed Tomography

The clinical characteristics of all patients are presented in Table 1. All lesions (N=17) had ^{18}F-FDG uptake and the mean SUVmax was 16.9±13.8 (median=10.5, range=4.5-46.8). The mean±SD, median, and range values obtained for the SUVmean, MTV40, and TLG are given in Table 1. The size of the primary tumor obtained from the CT slices of PET/CT imaging (N=17) revealed the mean total tumor size to be 3.6±3.9 cm (range=0.9-18.3 cm). The relationship between metabolic parameters obtained using the PET/CT and the clinical and histopathological features of patients are presented in Table 2. No significant correlation was observed between the primary tumor size and primary lesion SUVmax (r=0.047, p=0.879). However, a significant negative correlation was noted between primary lesion SUVmax and patient age (r=−0.564, p=0.018) (Table 3). Regarding the tumor location, 76.5% of lesions (n=13) were evaluated as having diffuse involvement, whereas 23.5% (n=4) were localized to the fundus of the gallbladder (Figure 1). Even though wide ranges of metabolic parameters, such as SUVmax of primary tumors, were calculated in our study group, these wide ranges were not observed to be associated with the clinical and histopathological characteristics of the tumor (Table 2).

Seven patients (41.2%) had nodal metastasis detected on ^{18}F-FDG PET/CT imaging, of which three (17.6%) were locoregional, and four (23.5%)

were both locoregional and distant nodal metastasis. The mean SUVmax of the primary lesion was 19.5±14.9 in patients with nodal metastasis, whereas it was 12.6±12.8 in patients without nodal metastasis (p=0.283) (Table 2). Mean SUVmax of patients with metastatic lymph nodes (n=7) was estimated to be 17.4±11.9. A statistically significant positive correlation was noted between the mean SUVmax of metastatic lymph nodes and the SUVmax of the primary lesion (r=0.786, p=0.036) (Table 3). Considering the patients whose lymph node size data was obtained using the CT slices of ^{18}F-FDG PET/CT imaging (n=7), the mean lymph node size was 2.6±0.8 cm (range=1.7-4.0 cm). No significant correlation was observed between lymph node size and the SUVmax of

Table 2. The association among metabolic parameters and clinical, histopathologic features of patients.

	Clinical Variables	n (%)	SUVmax (Mean±SD)	p	SUVmean (Mean±SD)	p	MTV40 (Mean±SD)	p	TLG (Mean±SD)	p
Tumor Localization	Diffuse	13 (75.5%)	16.0±13.6	0.49	9.0±8.0	0.49	10.2±10.4	0.42	70.6±53.6	0.82
	Fundus	4 (23.5%)	19.8±18.3		12.1±12.0		6.1±3.6		58.2±38.9	
Gender	Female	11 (64.7%)	13.0±8.9	0.52	7.3±5.0	0.14	11.6±10.7	0.14	68.8±48.7	0.66
	Male	6 (35.3%)	24.2±19. 9		16.9±12.0		5.8±2.4		79.0±51.2	
Nodal Metastasis	Absent	10 (58.8%)	14.0±13.1	0.43	7.9±8.6	0.30	10.6±12.0	0.84	64.2±54.9	0.55
	Present	7 (41.2%)	21.0±15.8		12.2±9.1		7.3±2.9		72.8±44.8	
Distant Organ Metastasis	Absent	8 (47.1%)	21.9±16.3	0.83	12.4±10.5	0.14	6.8±5.5	0.24	79.6±57.4	0.29
	Present	9 (52.9%)	12.4±11.2		7.3±6.7		11.3±11.6		57.2±42.2	

*p<0.05 statistically significant.

Met: Metastasis; SUVmax: Standart Uptake Value maximum; MTV: Metabolic Tumor Volume; TLG: Total Lesion Glycolysis; SD: Standart Deviation

Table 3. Correlation analysis of primary lesion mean SUVmax.

	Primary tumor size		Metastatic Lymph Node SUVmax		Lymph Node Size		Metastatic Organ (Lesion) SUVmax		Age	
	R	p	R	p	R	p	R	p	R	p
Primary tumor SUVmax	0.047	0.879	0.786	0.036*	0.090	0.848	0.717	0.030*	-0.564	0.018*

*p<0.05 statistically significant.

SUVmax: Standart Uptake Value maximum; R: Correlation coefficient

Table 4. Comparison of patients' clinical/histopathological features and mean survival times.

	Clinical Variables	n (%)	Survival (month) (Mean±SD)	p
Tumor Localization	Diffuse	13 (75.5%)	9.12±10.0	0.21
	Fundus	4 (23.5%)	15.84±11.5	
Gender	Female	11 (64.7%)	9.54±10.5	0.48
	Male	6 (35.3%)	12.82±10.8	
Nodal involvement	Absent	10 (58.8%)	13.43±11.7	0.20
	Present	7 (41.2%)	6.80±7.2	
Distant Organ Metastasis	Absent	8 (47.1%)	15.8±7.1	0.01*
	Present	9 (52.9%)	6.11±11.0	

*p<0.05 statistically significant.

SD: Standart Deviation; n: number

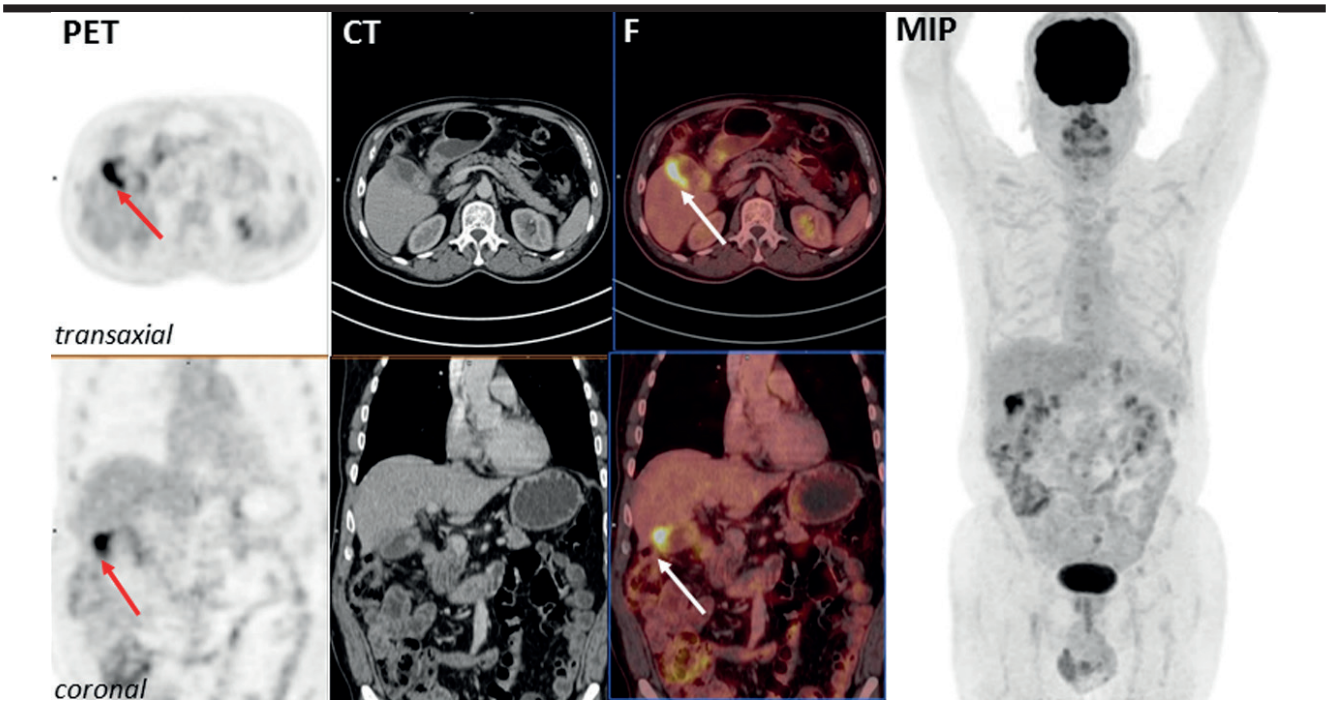

Figure 1. 61-year-old man with adenocarcinoma in the fundus of the gallbladder. Primary tumor axial diameter: 2.3 cm, Arrows show FDG uptake of the primary tumor, Primary tumor: SUV max:16.5 PET: positron emission tomography, CT: computed tomography, F: Fusion, MIP: maximum intensity projection.

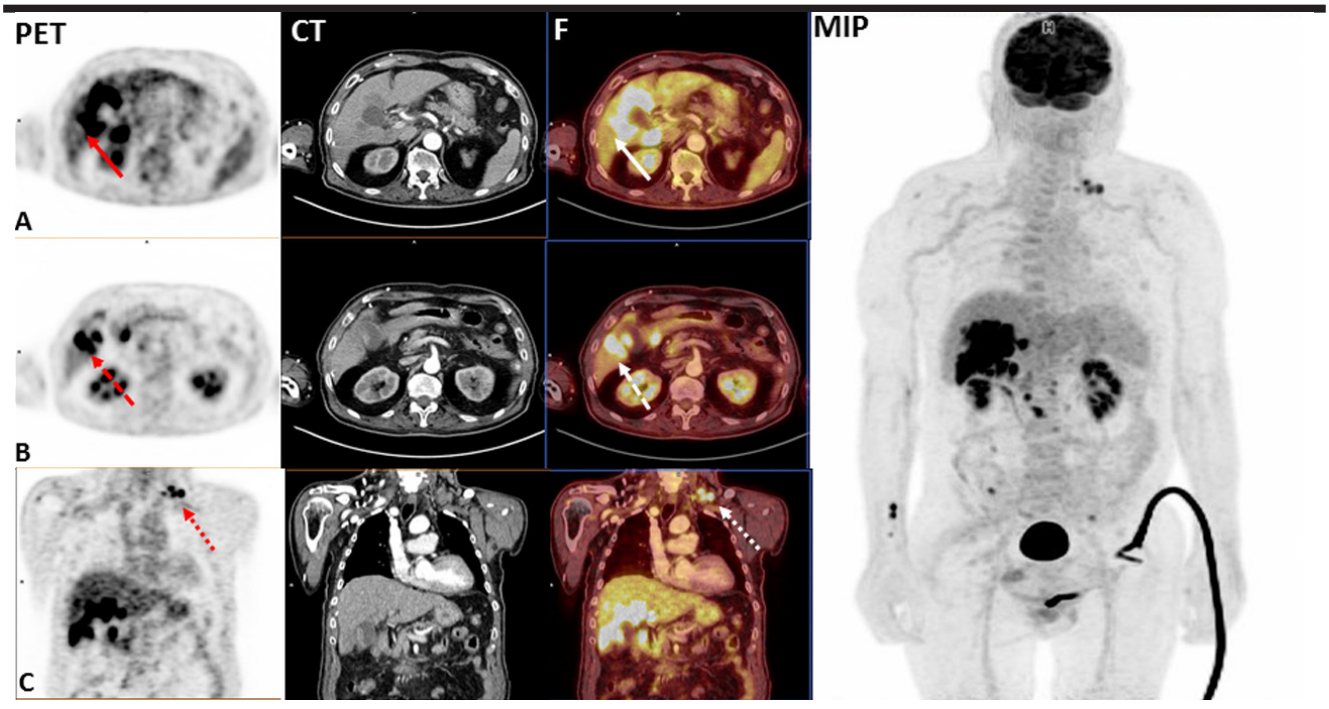

Figure 2. a-c. 71-year-old man with adenocarcinoma in a) Primary tumor SUV max:12.1 at the corpus of the gallbladder and the axial diameter: 3 cm b) liver and intraperitoneal involvement of tumor c) supraclavicular metastatic lymph nodes are shown with arrows in PET/CT images. PET: positron emission tomography, CT: computed tomography, F: Fusion, MIP: maximum intensity projection.

primary lesion (r=0.090, p=0.848) (Table 3). However, a statistically significant negative correlation between the mean SUVmax of metastatic lymph nodes and mean patient age was observed (r=−0.775, p=0.041).

Distant organ metastasis was observed in nine patients (52.9%). The mean SUVmax of the metastatic lesion in patients with distant metastasis was 14.2±8.5. The mean SUVmax of the primary lesion was not significantly different between patients with or without distant organ metastasis (p=0.083) (Table 2). The mean SUVmax of the metastatic lesion positively correlated with the mean SUVmax of the primary lesion (r=0.717, p=0.030) (Table 3). Eight patients (47.1%) received a histopathologic diagnosis through surgical resection. On the other hand, the remaining nine patients received a histopathologic diagnosis with a biopsy of hepatic metastasis (Figure 2).

The mean follow-up duration was 10.7±10.4 months (range=0.4–34.3 months). Comparison of clinical characteristics of patients against the mean survival is presented in Table 4. The mean survival of patients with distant metastasis (6.1±11.0 months) was significantly shorter than patients without distant metastasis (15.8±7.1 months) (p=0.012, Log Rank=0.023). Tumor localization, gender, and nodal involvement was observed to have no statistically significant effect on the mean survival (p=0.213, 0.482, and 0.205, respectively) (Log Rank=0.423, 0.766, and 0.056, respectively).

DISCUSSION

GBC is a disease characterized by high mortality rates, late diagnosis, and poor prognosis worldwide (2, 4). Its prevalence increases with age and is reported two to six times more frequently in women than men (6). Toba et al. (9) conducted a study on 61 patients with GBC and reported a mean age of 68.9 years (range, 44-92 years) and a 43:18 female-to-male ratio. Similarly, in our study, 64.7% of 17 patients with GBC were women, whereas 35.3% were men, with the mean age of 69.7±8.8 years. Furthermore, the mean patient age had a statistically significant negative correlation with the mean SUVmax of the primary lesion and the mean SUVmax of metastatic lymph nodes. Therefore, a higher SUVmax observed in younger patients would indicate a poor prognosis, thereby iterating the significance of staging and management in this population.

Recent studies have pointed out that ^{18}F-FDG PET/CT imaging plays a crucial role in the prognosis of GBC (5). In their study with 78 gallbladder-biliary tract patients, of which 14 were GBC, Park et al. (10) retrospectively analyzed the ^{18}F-FDG PET/CT imaging results of 64 patients and determined that increasing tumor size was significantly associated with higher mean SUVmax (p=0.001) . Koh et al. (11) assessed the lesion size with ^{18}F-FDG PET/CT scan in 16 patients with gallbladder lesions and concluded that FDG uptake lacks the required sensitivity in small lesions with high malignancy potential or increasing tumor size, and is thus inadequate in the differential diagnosis of benign and malignant lesions.

The most crucial prognostic factors in the progression of GBC are tumor stage, invasion to surrounding tissues, distant metastasis, and lymph node involvement (12). Moreover, studies have reported that GBC staging with ^{18}F-FDG PET/CT imaging can alter the treatment protocol in one-fourth of patients (4). In their study involving 49 GBC lesions, Ramos-Font et al. (13) achieved 95.5% diagnostic accuracy in primary lesions (SUVmax 7.92±6.25), 85.7% in lymph node involvement (SUVmax 4.33±65.97), and 95.9% in metastatic lesions (12 hepatic) (SUVmax 7.20±7.06) using ^{18}F-FDG PET/CT imaging. The researchers observed high ^{18}F-FDG uptake in 32% of patients, suggesting nodal involvement. Hu et al. (14). performed a meta-analysis involving 116 studies and concluded that ^{18}F-FDG PET/CT is a suitable technique for the assessment of primary tumor (for gallbladder; 95% CI: 1.97 to 84.80), lymph nodes (95% CI: 4.79 to 26.80), and distant metastasis (95% CI: 12.50 to 181.83) in patients with cholangiocarcinoma. Lee K. et al. (15) reported that FDG PET/CT achieved a significantly higher rate of PPV in regional nodal involvement (94.1 vs.77.5%, p=0.04) and higher sensitivity in distant metastasis (94.7 vs. 63.2%, p=0.02) than multidetector-row CT in patients with GBC. Similarly, in a prospective cohort study involving 42 patients with suspicious gallbladder malignancies, the diagnostic sensitivity of ^{18}F-FDG PET/CT was noted to be 83.3% for primary lesions, 88.9% for lymph node involvement, and 85.1% for distant metastasis. Detection of unexpected metastasis by using ^{18}F-FDG PET/CT technique could change the treatment protocol in 14.8% of patients (16). The study of Kim et al. (17) highlighted that ^{18}FDG PET/CT demonstrated more acceptable predictive value for the resectability of the tumor than CT, particularly in patients with unsuspected distant metastasis. In contrast, Petrowsky et al. (18) could only detect 2 of 17 regional lymph node metastases in 61 patients with gallbladder-biliary tract cancer, of which 14 were GBC, by using ^{18}F-FDG PET/CT. The same study reported higher ^{18}F-FDG uptake in all 12 patients with distant metastases. The researchers underlined that ^{18}F-FDG PET/CT technique

is quite superior to conventional techniques in terms of detecting distant metastasis but lacks sufficiency when it comes to detecting lymph node involvement. Kula et al. (19) reported limited efficiency of ^{18}F-FDG PET/CT imaging with lymph node involvement in 13 patients with GBC, yet highly recommended the technique for detecting distant metastases (six hepatic and five hepatic hilus metastases). In a meta-analysis by Annunziata et al. (20) that comprised 21 studies and 495 patients with GBC, ^{18}F-FDG PET/CT was noted to have 87% sensitivity and 78% specificity in detecting the primary tumor. The authors concluded that using ^{18}F-FDG PET/CT alone is convenient and efficient, but the probability of false-negative and false-positive results should always be kept in mind. Leung et al. (21) concluded that ^{18}F-FDG is not effective in patients with negative CT/MRI and should, therefore, be employed to complement the conventional methods, particularly on suspicious nodes. Similarly, in our study, all patients with distant metastases were observed to have hepatic metastases. The mean SUVmax of the primary lesion in patient groups that had nodal and distant metastases were not significantly different from the mean SUVmax in patients without nodal or distant metastases. However, the mean SUVmax of the primary lesion had a statistically significant positive correlation with the mean SUVmax of metastatic lymph node and the mean SUVmax of the distant metastatic organ. Our findings enabled the therapeutic management of patients in terms of referral to surgery or medical oncology. Distant metastasis in gallbladder malignant neoplasms is associated with short survival, limited to only a few weeks despite treatment (14). In their population-based study with data from 18 centers between 2001 and 2012, Jaruvongvanich et al. (2) observed that 81% (n=6295) of 7769 patients with GBC received a diagnosis of adenocarcinoma subtype. Overall, 40.5% of patients in the study (n=3150) had distant metastases, and distant nodal and organ metastasis was associated with high mortality risk. Similarly, Butte et al. (22) observed 46% metastasis in 49 patients with GBC and reported that the mean survival decreased significantly in patients with metastasis (p=0.001). Chun et al. (23) determined MTV useful in predicting metastatic lesions (p=0.031) and overall survival (p=0.006) in locally advanced and metastatic GBC. Yoo et al. (24) evaluated survival and associated prognostic factors with ^{18}F-FDG PET/CT imaging in 44 patients with GBC for a mean follow-up period of 22.2±10.4 months and achieved the statistically shortest survival of 6.0±1.1 months in patients with stage IV disease (p<0.001). Additionally, in a separate study conducted at three different centers in three different countries with 261 patients with GBC, Butte et al. (25) noted that the tumor size and nodal involvement did not affect the mean survival, yet metastatic stage decreased the mean survival significantly (p=0.03). Parikh et al. (26) concluded that ^{18}F-FDG PET/CT imaging is a convenient technique in staging and prognosis assessment in patients with cholangiocarcinoma and GBC. In concordance with the literature, our study, with a mean follow-up period of 10.70±10.43 months, revealed that mean survival was significantly shorter in patients with distant organ metastasis (6.11±11.0 months). In addition, increased tumor size and nodal involvement were noted to have no statistically significant effect on mean survival.

In conclusion, our study suggested that distant organ metastasis and younger age could be major prognostic factors in patients with GBC. Furthermore, we think that ^{18}F-FDG PET/CT would contribute to staging and detecting distant metastases when conventional imaging techniques become inefficient. However, SUVmax and other semiquantitative metabolic parameters obtained from the primary tumor did not correlate with localization or gender in this study. An unexpected result for us was the nonexistent relationship between metabolic parameters and nodal or distant tumoral involvements. Further studies with a larger sample size are warranted to clarify the contribution of PET/CT in GBC management.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Istanbul Training and Research Hospital (No:1227, Date: 04.20.2018).

Informed Consent: Written and verbal informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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