

Research Article

Impact of ¹⁸F-FDG Positron Emission Tomography - Computed Tomography (PET-CT) on Management of Gallbladder Carcinoma

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Abstract

Background: Reports concerning the clinical usefulness ¹⁸F-FDG PET-CT for patients with gallbladder cancer are relatively scarce. The purpose of this study was to assess the diagnostic value of ¹⁸F-FDG PET-CT in relation to a conventional imaging modality, multidetector row CT (MDCT), for patients with gallbladder cancer.

Materials and Methods: Seventy patients with suspected gallbladder cancer who underwent both PET-CT and MDCT for initial staging were included in our study. The results of these two imaging modalities for evaluating primary tumors, regional lymph nodes and distant metastases were compared with the final diagnoses based on histopathological examination. Change in management of patients with gallbladder cancer based on PET-CT was also evaluated.

Results: A maximum standardized uptake value (SUV_{max}) of 5.37 was taken as cutoff value for detecting a malignant tumor. PET-CT demonstrated no significant advantage over MDCT for the diagnosis of a primary tumor. PET-CT showed a significantly higher accuracy (90.8 vs. 80.0%, P = 0.04) than that found for MDCT in the diagnosis of regional lymph node metastasis. PET-CT showed higher sensitivity (92.3 vs. 61.5%, P = 0.04) than that found for MDCT in the diagnosis of distant metastasis. Addition of PET-CT in preoperative staging of the disease changed management in 10 patients (14.3%).

Conclusions: In patients with gallbladder carcinoma, the addition of ¹⁸F-FDG-PET-CT to standard staging CT may be helpful in detecting distant nodal metastasis and unsuspected metastatic disease that may preclude patients from surgical resection and result in a change of management in a significant number of patients.

Keywords: Gallbladder carcinoma; ¹⁸F-FDG-PET-CT

Abbreviations

AJCC: American Joint Committee on Cancer; AUC: Area under the Curve; CA19.9: Carbohydrate Antigen 19.9; CBD: Common Bile Duct; CC: Chronic Cholecystitis; CEA: Carcino Embryonic Antigen; CECT: Contrast Enhanced Computerized Tomography; ¹⁸F-FDG: ¹⁸F-Fluorodeoxyglucose; FN: False Negative; FNAC: Fine Needle Aspiration Cytology; FP: False Positive; GBC: Gallbladder Carcinoma; IAC: Inter Aortocaval Lymph Node; MDCT: Multidetector Computed Tomography; NPV: Negative Predictive Value; PET-CT: Positron Emission Tomography-Computed Tomography; PPV: Positive Predictive Value; SUV_{max}: Maximum Standardized Uptake Value; XGC: Xanthogranulomatous Cholecystitis

Introduction

The global incidence of gallbladder cancer varies significantly by geographic region and racial group [1]. Women are affected two to four times more often than men. The highest incidence of gallbladder cancer is found in Chilean Mapuche Indian women followed by women living in India [2].

Most patients have advanced or unresectable disease at diagnosis

[3,4]. Early stage cancer is often incidentally diagnosed after a cholecystectomy for presumed benign disease [5]. GBCs have a tendency to metastasize early and widely, spreading *via* lymphatics, hematogenously and intraperitoneally [6]. While the overall prognosis is poor, a good outcome after a complete resection is possible for early disease (T1/T2, N0) [7,8]. The role of surgery for locally advanced disease (T3/T4) and regional nodal disease (N1) is more controversial, but surgery remains the only chance for long-term survival for these patients [4,5,8-11]. Distant metastatic disease and nodal disease beyond the hepatoduodenal ligament (N2) are generally considered contraindications to surgery because of poor survival outcomes after resection.

Therefore, an extensive work-up is mandatory in order to accurately define the tumor stage, with a particular emphasis placed on detecting regional lymph nodes and distant metastases in order to identify those patients who may benefit from surgery. Even with recent improvements in diagnostic imaging, diagnosing gallbladder cancer remains a difficult task until the tumor has grown to an advanced stage [12-14]. A sensitive and specific imaging modality that could noninvasively detect gallbladder cancer would be an extremely useful

adjunct to existing modalities.

Positron Emission Tomography (PET) using ^{18}F -2-fluoro-2-deoxy-D-glucose (^{18}F -FDG) can show malignant tumors since cancer cells utilize more glucose than normal tissue cells. Thus, it can provide physiological or metabolic information about the tumors. However, non-anatomical visualization features have some limitations such as low-resolution images and poor anatomical localization. To overcome these drawbacks combination of a PET scanner with a multi-detector row helical CT-Integrated Positron Emission Tomography and Computed Tomography (PET-CT) was proposed [15]. The advantages of this new technique have been established for many solid cancers [16]. However, there are only a few reports on PET-CT for biliary tract tumours and most studies were done without differentiation between the gallbladder and other biliary tract tumors due to the relative low incidence of these diseases [17,18].

In northern India, gallbladder carcinoma is more common than other parts of world. Most of the patients present with advanced or metastatic disease, by adding preoperative PET-CT we can detect any additional nodal and metastatic disease which is not seen in primary imaging and thus avoid unnecessary radical surgery and associated morbidity. The aim of this study was to evaluate impact of PET-CT on the management of gall bladder carcinoma and its role in assessing primary tumor, regional lymph node metastasis and distant metastatic disease.

Materials and Methods

The study was a single institutional Prospective observational study conducted from September 2018 to August 2020, in a tertiary care center in northern India. The calculation of sample size was performed using the G*Power software, version 3.1.9.2, using the parameters of effect size (medium level 0.5), acceptable α error probability (0.05), power (1 - β error) probability (0.90) and 5 degrees of freedom. The sample size was calculated as 66 patients.

All patients with suspected gallbladder carcinoma fulfilling the inclusion criteria were evaluated and detailed history, examination and investigation findings were noted. Imaging was done by triphasic abdominal and pelvic CECT/MRI with IV contrast, chest CT + IV contrast. On CT a GB mass/irregular wall thickening, locoregional lymphadenopathy, liver infiltration, adjacent organ involvement, liver metastasis and extra abdominal metastasis were noted. With CT scan, lymph nodes more than 10mm in diameter, grouping of nodes, central necrosis, rounded/oval shape or pathological contrast material enhancement were usually considered as metastatic involvement of LN. All patients with GBC, underwent an ^{18}F -FDG-PET-CT and Standardized Uptake Values (SUV) were calculated. A cutoff of greater than 5.37 was calculated as cut off using ROC curve. Abnormal PET avidity was noted in the primary site (gallbladder or gallbladder resection bed), lymph nodes (regional or distant) and distant sites. Cancer classification and staging were based on the 7th edition of AJCC Staging Manual and wherever possible pathological T classifications were reported. For patients without pathological confirmation, accurate clinical T classifications were inherently difficult. However, evidence of gross invasion into the liver on imaging was taken as evidence of T3 disease. Resectability was determined on a case-by-case basis but contraindications to resection

included distant metastases, discontinuous liver metastases, nodal metastases beyond the hepatoduodenal ligament and unresectable T4 disease that invaded major vascular structures or multiple organs. CT/MRI and PET results were classified as positive, if evidences of malignancy were present and negative, if no evidence of metastatic disease was present. The utility of PET was defined by whether PET provided additional information to conventional imaging that influenced the management. PET was considered helpful if it avoided a non-therapeutic operation, or it led to a successful resection in patients deemed unresectable by CT/MRI. In cases, where PET led to unnecessary procedures, negative impact of PET was separately reported.

Disease resectability was confirmed at surgery, metastatic disease was confirmed by biopsy or FNAC. The sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) for PET to detect metastatic disease were calculated for metastases to any site, to the peritoneum, lymph nodes, liver and lung. For pathological confirmation of metastatic disease resected specimen, biopsy or FNAC were used. True positives included patients with disease confirmed by surgical exploration, biopsy or FNAC. True negatives were also confirmed by surgical exploration, biopsy or FNAC. All PET false positives were confirmed histologically by surgical excision or biopsies. False negatives were confirmed by surgical exploration or biopsy. During surgery, staging laparoscopy was done in all patients. Intra-operatively, if the lesion was found resectable a cholecystectomy and en bloc hepatic resection (at least 2cm liver wedge) + lymphadenectomy + excision of CBD (if malignant involvement found on frozen section) was done and if unresectable disease a biopsy was taken and sent for histopathological examination. On exploration, if disease apparently looked benign, simple cholecystectomy and frozen section analysis was done and if frozen section turned out positive for malignancy, procedure completed as standard. Intra-operative details, lymph node sampling, presence of metastatic disease, involvement of organ other than liver, vascular involvement, common bile duct involvement were noted. On histopathological reports for malignant lesion; site of tumor, pathological stage, histological grade, histological type, margins, lymph node involvement, liver involvement were recorded. If the final histopathological examination showed a benign disease it was also recorded as XGC, Acute or chronic cholecystitis. The study was approved by institutional ethical committee-IEC No.39/17.

Statistical analysis

Statistical analysis was done with statistical software (SPSS version 19.0 for Windows). Sensitivity, specificity, accuracy, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) for CT and PET-CT were calculated and compared by chi square test, Fisher's exact test, or McNemar test. Descriptive statistics will calculate frequency, percentage, mean, median and inter quartile range. Two-sided P values less than 0.05 were considered statistically significant.

Results

Patients Demographic, radiological and pathological characteristics are presented in Table 1. Total 70 patients included in the study and all of them underwent FDG-PET-CT and Contrast enhanced CT. Most of them were female (78.5%) and median age

Table 1: Patients demographic, radiological and pathological characteristics.

Total patients	70
Age years, median (interquartile range)	51
Male gender	15
Female	55
No prior cholecystectomy	64
Post-cholecystectomy,	6
Resectable on CT	62
Resectable on PET-CT	55
Found unresectable on exploration	5
Curative resection	50
Benign pathology	14
Carcinoma gallbladder R0 resection	36
T stage	
1a	5
1b	7
2	8
3	14
4	2
N1	13
Average lymph node resected	11.3
Average lymph node positive	1.17
Well differentiated	16
Moderately differentiated	14
Poorly differentiated	6
Lymphovascular invasion	15
Perinural invasion	5

was 51 years (Figure 1 and 2). Only 55 patients underwent surgery and 50 patients had curative resection with negative resection margin (Flow chart 1). On final histopathological examination 14 patients had benign disease and 36 patients had diagnosed as carcinoma gallbladder. 13 out of 36 have nodal metastasis and average resected lymph nodes were 11.3. 16 had well differentiated adenocarcinoma and 6 patients had poorly differentiated carcinoma.

Diagnosis of the primary tumor

The criteria for a correct detection by PET-CT are a positive FDG uptake as well as the correct anatomic localization of the tumor. Overall, 48 of 51 malignant tumors of gallbladder were correctly identified with PET-CT (sensitivity 94.1%) and 46 of 51 tumors by MDCT (sensitivity 90.2%). Median SUVmax for the primary tumor was 8.7.

Additionally, the specificity, PPV, NPV and accuracy of PET-CT in primary tumor detection were 60.00%, 85.70%, 85.70% and 85.70%, respectively, and demonstrated no statistically significant advantage over MDCT in the diagnosis of a primary tumor (Table 2). MDCT detected the primary tumor in 46 of 51 patients with gallbladder cancer (90.2%), and specificity, PPV, NPV and accuracy of MDCT in primary tumor detection were 60.0%, 85.2%, 75.0% and 82.8%, respectively.

Diagnosis of regional lymph node metastasis

Thirty out of 70 patients (42.8%) showed histology-proven metastases in regional lymph nodes. Regional lymph node metastases were detected by PET-CT in 27 of 30 patients (90.0%) and by MDCT in 21 of 30 patients (70.0%), (Table 3). Specificity, PPV, NPV and accuracy for detecting lymph node metastasis by PET-CT were 95.0%, 93.1%, 92.6% and 90.8% respectively.

PET-CT demonstrated a trend towards PET-CT for sensitivity of detecting lymph node metastasis but this did not reach statistical

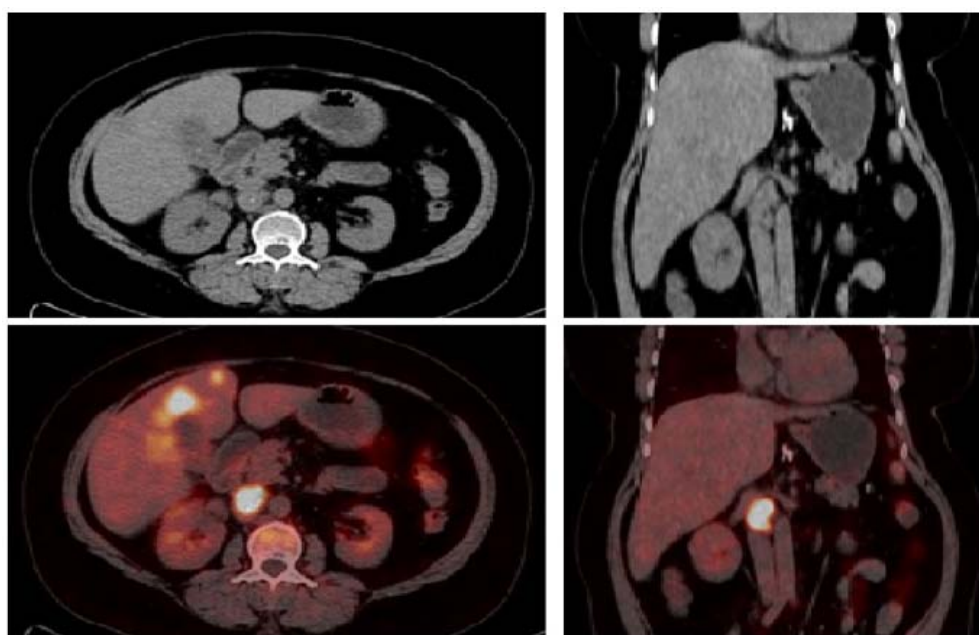


Figure 1: ¹⁸F-DG-PET avid Gallbladder mass and interaortocaval lymph node. CT guided FNAC from interaortocaval lymph node positive for malignancy.

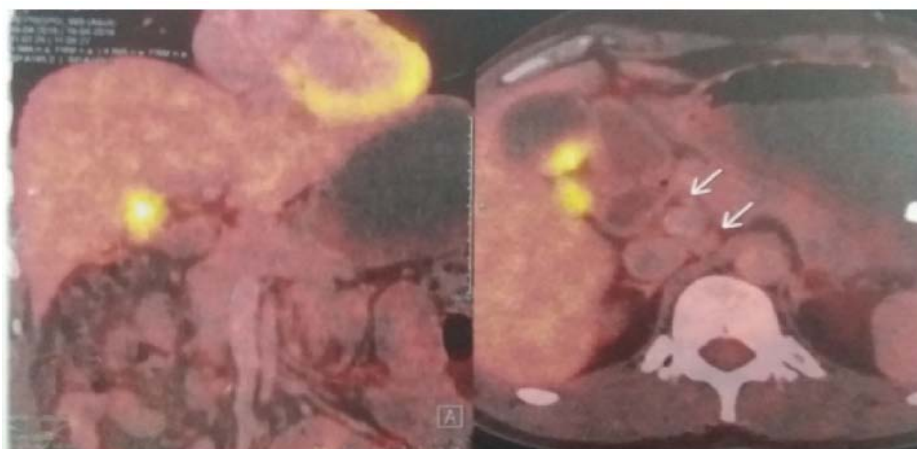
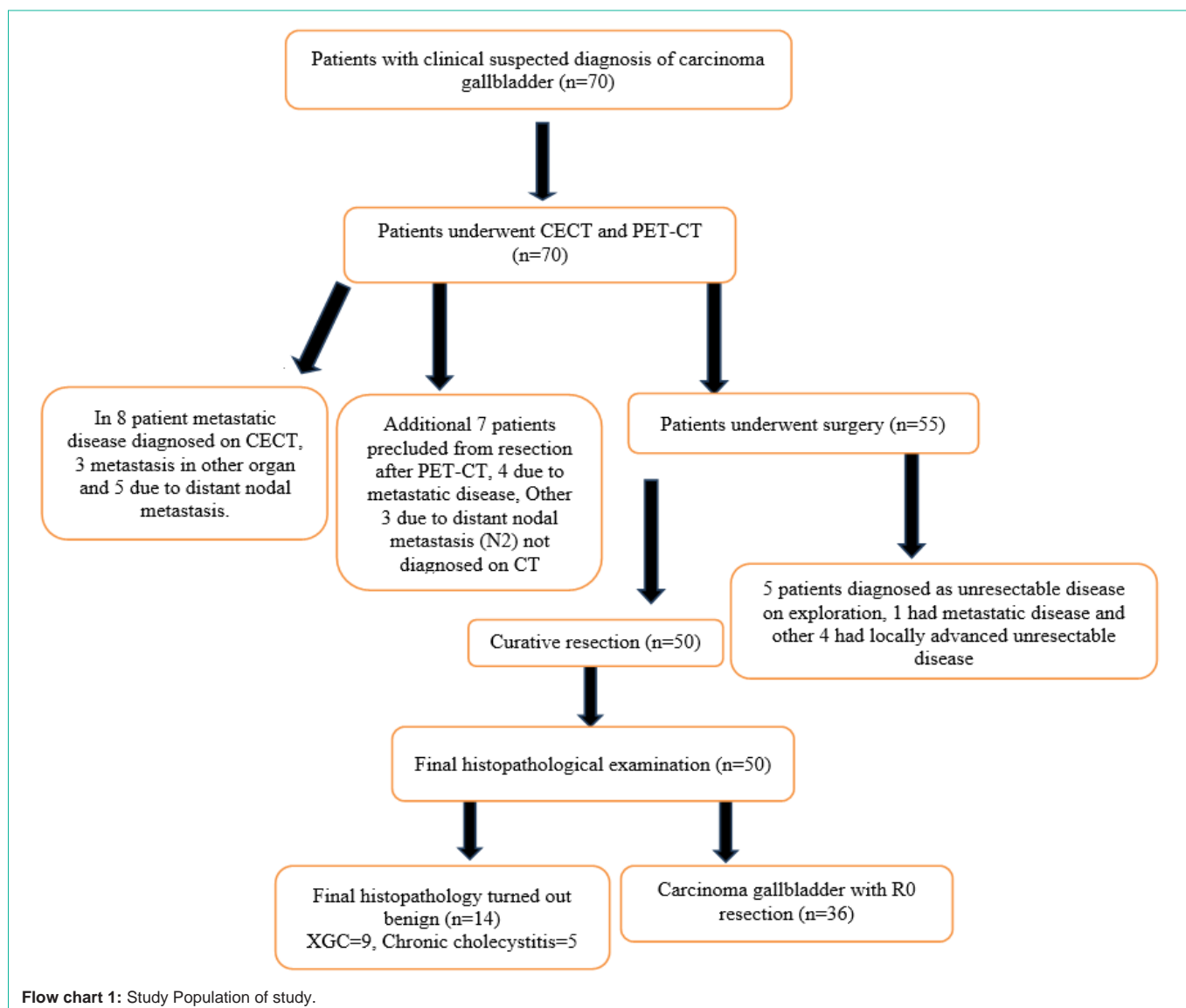


Figure 2: ¹⁸FDG-PET avid Gallbladder mass and non ¹⁸FDG avid interaortocaval lymph node. Interaortocaval lymph node sampling done and send for frozen-negative for malignancy.



Flow chart 1: Study Population of study.

significance. However PET-CT demonstrated significantly higher accuracy (90.8%) than MDCT (80.0%, $P = 0.04$).

Diagnosis of distant metastases

Distant metastases were present in 13 of 70 patients (21.42%). PET-CT showed a higher sensitivity in detecting distant metastases than MDCT (92.3% vs. 61.5%, $P = 0.08$, Table 4). Specificity, PPV, NPV and accuracy for detecting distant metastasis were 96.3%, 85.7%, 98.1% and 95.7% respectively. None of them showed significant difference from MDCT.

Impact of PET-CT on the management of patients with gallbladder

Local resectability and the presence of distant metastases determine the management of patients with gallbladder cancer. Additional findings by PET-CT might lead to changes in the management. Therefore, we evaluated the impact of PET-CT on the oncological management of patients with gallbladder cancer. Following standard staging evaluation, 62 of 70 patients were deemed to be resectable, while 8 patients were unresectable. When the resectable patients were analyzed, PET-CT had modified the treatment approach in ten patients (14.3%). In seven patients, radical resection was avoided due to presence of N2 lymph nodal disease or distant metastases not identified on CT scan. The remaining three patients who were deemed to be malignant on preoperative evaluation but PET did not show avidity at primary site, in these patients gallbladder was removed and sent for frozen section analysis; two of them were diagnosed as xanthogranulomatous cholecystitis and other one as chronic cholecystitis (Table 5).

In two patients, PET detected unrelated findings not seen on CT, including one secondary malignancy and one false positive lesion. One patient had a PET-avidity at multiple sites including mediastinum and bilateral axilla, after axillary lymph node biopsy this was diagnosed as diffuse large B-cell lymphoma, which was treated by medical management. In this case PET correctly identified the second malignancy. The second patient had PET avidity in iliac bone which led to a bone marrow biopsy and diagnosed as inflammatory condition. The gallbladder cancer was successfully resected in these patients.

Table 2: Diagnosis of primary tumor by MDCT and PET-CT.

	MDCT (%)	PET-CT (%)	MDCT versus PET-CT
Sensitivity	46/51(90.2)	48/51(94.1)	0.751
Specificity	12/20(60)	12/20(60)	1
Positive predictive value	46/54(85.2)	48/56(85.7)	0.937
Negative predictive value	12/16(75)	12/14(85.7)	0.657
Accuracy	58/70(82.8)	60/70(85.7)	0.816

Table 3: Diagnosis of lymph node metastasis by MDCT and PET-CT.

	MDCT (%)	PET-CT (%)	MDCT versus PET-CT
Sensitivity	21/30(76)	27/30(90)	0.245
Specificity	35/40(87.5)	38/40(95.0)	0.432
Positive predictive value	21/26(80.7)	27/29(93.1)	0.236
Negative predictive value	35/44(79.5)	38/41(92.6)	0.154
Accuracy	56/70(80)	65/70(90.8)	0.048 (Statistically Significant)

Discussion

This is a relatively large-scale, prospectively designed comparison study of PET-CT and MDCT for the evaluation of primary tumor, lymph node metastasis and distant metastases in gallbladder carcinoma. The development of the PET scan has offered a new diagnostic option through the visualization of tumor metabolic activity rather than the anatomic structures, and so PET-CT technology offers the advantage of improved anatomic localization. Several studies have evaluated the role of PET-CT in comparison with conventional imaging techniques, such as contrast enhanced CT or Magnetic Resonance Imaging (MRI), in patients with gallbladder cancer and cholangiocarcinoma [22-24]. They have shown that PET-CT provides comparable sensitivity, specificity, PPV, NPV, and accuracy for the diagnosis of the primary tumor in patients with cholangiocarcinoma and/or gallbladder cancer. Compared to contrast enhanced CT scan and MRI, PET-CT revealed significantly higher accuracies for diagnosing regional lymph node metastases and distant metastases in patients with cholangiocarcinoma [22]. A study by Petrowsky H, et al. showed a similar result; i.e., that PET-CT was superior to contrast-enhanced CT scan in the diagnosis of distant metastases in patients with gallbladder cancer and cholangiocarcinoma [24]. However, it gave disappointing results in terms of its ability to detect regional lymph node metastases of PET-CT (12%) compared to contrast-enhanced CT scan (24%) in these patients [24].

In our study, PET-CT exhibited no diagnostic advantage over MDCT in detecting a primary tumor (Table 2).

Several studies have reported the similar results; i.e., that PET-CT was not superior to contrast-enhanced CT and/or MRI in the diagnosis of a primary biliary tumor [22,24]. Therefore, PET-CT may not be the optimal primary tool, but it can play a complementary role to conventional imaging in the diagnosis of a primary tumor [25-28]. In our study we found the specificity was only 60% rather than previously reported 70.6% and 79.3% [18,22]. Reason for this may be high false positive rate of PET-CT in benign conditions like xanthogranulomatous cholecystitis and some cases of chronic cholecystitis [29-31]. The sensitivity of PET in distinguishing a benign from a malignant gallbladder mass has been reported as 75-80%, and specificity of 82-88% [13-15].

Accuracy of PET-CT for lymph node metastasis was 90.8% which was significantly higher compared to accuracy (80.0%) of MDCT ($p = 0.04$) in our study. Other studies reported similar results; one study reported 87% sensitivity and 89% specificity of PET-CT for detection of nodal disease and other showed sensitivity and specificity of 82.1% and 95.3% respectively with significantly higher positive predictive value for PET-CT compared to MDCT for detection of

Table 4: Diagnosis of distant metastasis by MDCT and PET-CT.

	MDCT (%)	PET-CT (%)	MDCT versus PET-CT
Sensitivity	8/13(61.5)	12/13 (92.3)	0.046 (Statistically Significant)
Specificity	54/57(94.7)	55/57 (96.3)	1
Positive predictive value	8/11(72.7)	12/14 (85.7)	1
Negative predictive value	54/59(91.5)	55/56 (98.1)	0.149
Accuracy	62/70(88.5)	67/70(95.7)	0.209

Table 5: Cases which showed discrepancies between CT, PET-CT and histopathological examination.

S. No	Results	CECT staging	PET-CT staging	Final staging	Description
1	FN on CT	T3N1	T3N1M1	ycTxNxM1	CT guided FNAC proved omental metastasis
2	FN on CT	T1/2N1	T1/2 N2	yT3N2	Open surgical biopsy proven LN metastasis in IAC nodes
3	FN on CT	T4N1	T4N1M1	yTxNxM1	CT guided biopsy proven omental deposits
4	FN on CT	T4N1	T4N2	yTxN2	CT guided biopsy of celiac axis positive for malignancy
5	FN on CT [#]	T1/2 N1	T1/2N2	yTxN2	CT guided biopsy of IAC LN positive for malignancy
6	FN on CT	T3N1	T3N2	yT3N2	Open surgical biopsy proven IAC positive for malignancy
7	FN on CT	T3N1M0	T3N1M1	yTxNxM1	Laparoscopic biopsy of liver surface nodule positive for malignancy
8	FP on CT	T1/2N0	No avidity on PET	XGC	Open cholecystectomy specimen sent for frozen section proved XGC
9	FP on CT	T1/2 N0	No avidity on PET	XGC	Open cholecystectomy specimen sent for frozen section proved XGC
10	FP on CT	T3N1	No avidity on PET	Chronic cholecystitis	Open cholecystectomy specimen sent for frozen section proved XGC
11	FP on PET	T3N1M0	T3N1M1	T3N1M0	Axillary biopsy proven large B-cell lymphoma
12	FP on CT [§]	T4N2M0	T4N0M0	T3N0M0	No evidence of LN metastasis in Final HPE
13	FN on CT	T3N0M0	T3N1M0	T3N1M0	LN metastasis on final HPE

Management changed in initial 10 cases with addition of Preoperative PET-CT. # as showed in Figure 1. § as showed in Figure 2.

lymph node metastasis in gall bladder carcinoma [18,25,27]. Other studies conducted on biliary tract malignancies demonstrated higher accuracy of PET-CT compared to MDCT for detection of lymph node metastasis [22,32]. However only 12% regional nodal metastasis detected by PET and CECT identified 24% nodal metastasis in similar study conducted on the patients of biliary tract malignancies [24].

A systematic review included 12 studies conducted on gallbladder and cholangiocarcinoma and demonstrated low sensitivity and high specificity of PET-CT for detection of lymph node metastasis. They recommended role of PET-CT scan to investigate abnormal appearing lymph nodes seen on standard cross-sectional imaging [28]. The resectability of patients with nodal disease is also controversial. In the study by D'Angelica et al. nodal positivity was associated with a much worse prognosis, with a median survival of 18 months and 5 years disease-specific survival of 17%, compared with 65 months and 51%, respectively, for node-negative patients [8]. Several studies have shown that regional nodal involvement, although still a poor prognostic factor, represents a better group than distant nodal disease [33-35]. In the 7th edition of AJCC Cancer Staging Manual (2009), nodal disease is now separated into N1 (regional nodes including portal and hepatoduodenal) and N2 (distant nodes including periaortic, pericaval, superior mesenteric artery and celiac), with the latter upstaging the patient from stage III in AJCC 6th edition to stage IVA [36]. On the contrary, there have been some Japanese studies that showed the number of positive nodes but not the location of the nodes independently predicted survival [37,38]. On the basis of these studies, in 8th edition of AJCC cancer staging manual, now staging of gallbladder carcinoma is based on number of positive lymph node rather than location [39]. There is probably no benefit in resecting extensive nodal disease, but these patients may benefit from a neoadjuvant approach and pre-operative PET may help identify these patients.

PET-CT was especially valuable compared to MDCT in the detection of unsuspected distant metastases in patients with carcinoma gallbladder. Distant metastases in biliary neoplasms are associated with poor survival (only a few months), regardless of the

therapy. Thus most patients with distant metastases do not qualify for curative resection. It is, therefore, of paramount importance to detect distant metastases in order to offer surgery only to those who may benefit from it. The current study demonstrated that PET-CT detected the distant metastatic focus in 14 of 15 patients (93.3%, Table 4). This is also confirmed by other studies in which PET-CT showed a higher sensitivity, PPV and accuracy than contrast enhanced CT, and it exhibited 100% sensitivity in detecting distant metastases in patients with gallbladder cancer and cholangiocarcinoma [22,24]. In a similar study PET-CT showed a significantly higher sensitivity (94.7 vs. 63.2%, $P = 0.02$) than that found for MDCT in the diagnosis of distant metastasis [18]. However in a systematic review conducted on 12 studies they found no role of PET-CT in the assessment of hepatic satellite lesions and they recommended the use of PET-CT to assess specific areas of concern defined on CT and/or MRI [28]. Leung et al. reported lower sensitivity (57%) for PET-CT for detecting metastatic disease and concluded that due to the high false negative rate for peritoneal disease (16%). Small tumour volume (<1cm) peritoneal disease may be difficult to diagnose on PET pre-operatively [27]. In our study, compared to MDCT, PET-CT detected unsuspected metastatic lesions in four additional patients, who otherwise may have been subjected to an unnecessary operation. These data imply that PET-CT is not only a useful tool for assessing the prognosis, but that it can also be used to select patients who should be precluded from surgical resection. Comparable data were reported by others for colorectal, pancreatic and lung cancer, where additional PET-CT staging led to a change in patient management in 15-21% [19-21].

In current study PET-CT had modified the treatment approach in ten patients (14.28%). In seven patients, radical resection was avoided due to presence of N2 lymph nodal disease or distant metastases not identified on CT scan. The remaining three patients who were deemed to be malignant on preoperative CECT but PET did not show avidity at primary site, in these patients gallbladder was removed and sent for frozen section analysis; two of them were diagnosed as xanthogranulomatous cholecystitis and other one as chronic cholecystitis. Comparable data were reported by different studies, where additional PET-CT staging led to a change in patients

management in 9.8%, 23% and 17% of patients [18,24,25].

There is relatively sparse data in the literature pertaining to the use of PET in GBC. Most published series of utility of PET in GBC have a small number of patients, often combined with cholangiocarcinoma and most of them were of retrospective in nature [18,24,33,40-42].

Current study was prospectively designed, exclusively including patients with suspected carcinoma of gallbladder and demonstrated that PET-CT is particularly valuable for detecting unsuspected lymph node and distant metastases that may preclude patients from surgical resection.

Conclusion

In gallbladder carcinoma, the addition of PET to standard staging CT may be helpful in detecting nodal metastasis and unsuspected metastatic disease and thus unnecessary surgical resection and associated morbidity can be avoided. Addition of preoperative PET-CT in staging of gallbladder carcinoma, also result in change of management in significant number of patients.

Limitations

There were certain lacunae which were identified during the course of the study, some of which are mentioned below. Most of the patients included in the study were potentially resectable carcinoma gallbladder and very few of them having a metastatic disease so sensitivity, specificity, PPV, NPV and accuracy for metastatic disease might not reflect the true values owing to selection bias. PET scans were not reviewed by a blinded radiologist. As the PET scans were often performed after the CT scans were reported, the interpretation of the PET may be biased. Lack of standardization of imaging; some of the CECT and PET-CT were performed at another institution, which may introduce some heterogeneity in the interpretation and reporting of metastatic lesions. Future studies attempting to circumvent these limitations may yield better results, and could be recommended for subsequent research work.

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