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# ROLE OF PET CT IN GALL BLADDER CANCER-A META ANALYSIS

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## Abstract

**Introduction:** Primary gall bladder carcinoma is a rare cancer, however it is one of the most prevalent bile system cancers. Cholelithiasis is the most frequent risk factor for the development of gallbladder carcinoma worldwide, with a varying incidence of gallbladder carcinoma across geographic areas due to cholelithiasis prevalence. Gallbladder cancer is one of the most common cancers in the Gangetic and Brahmaputra valleys of Northern and Eastern India. Gallbladder cancer is identified preoperatively in less than 20% of instances, while the remaining cases are diagnosed intraoperatively or after laparoscopic cholecystectomy in 74-92% of cases.

**Materials and Methods:** A search was conducted using the following terms: gallbladder cancer; gallbladder neoplasms; cholangiocarcinoma; bile duct cancer; PET; positron emission tomography. The search was conducted separately by two authors (SS, BM) using the PRISMA statement's verified techniques. There were no language restrictions. MEDLINE, the Cochrane Central Register of Controlled Trials, EMBASE, PubMed, Scopus, Doaj, Cochrane and Web of Science were the databases analysed. To identify further relevant studies, the reference lists of all included papers, as well as related review articles, were manually searched.

**Results:** Seven studies examined the role of PET-CT in gallbladder carcinoma though two studies did not report their results specifically. Butte et al investigated 32 patients with incidental gallbladder carcinoma following laparoscopic cholecystectomy. Thirteen patients had negative PET-CT results, 9 refused further resection with only one of the four patients resected having residual disease on operative exploration. PET-CT changed management in 12 out of 32 patients (38%) demonstrating unexpected disseminated disease in 10 patients and localised resectable disease in 2 patients.

**Conclusion:** 230 records were screened, 49 were assessed and 7 studies were included in the systematic review. PET-CT has a low sensitivity for regional lymph node metastases from cholangiocarcinoma and gallbladder cancer but a high specificity. In one study, PET-CT appears to be effective in assessing all nodal basins related to the liver, bile ducts and gallbladder. PET-

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CT has no role in the assessment of hepatic satellite lesions but is useful in defining extra-abdominal metastatic disease and recurrent disease and to assess specific areas of concern defined on CT scan and/or magnetic resonance scan.

**Key Words:** Primary gall bladder carcinoma, PET-CT, specificity, bile duct cancer.

## INTRODUCTION

Primary gall bladder carcinoma is a rare cancer, however it is one of the most prevalent bile system cancers. Cholelithiasis is the most frequent risk factor for the development of gallbladder carcinoma worldwide, with a varying incidence of gallbladder carcinoma across geographic areas due to cholelithiasis prevalence. Gallbladder cancer is one of the most common cancers in the Gangetic and Brahmaputra valleys of Northern and Eastern India.[1] Gallbladder cancer is identified preoperatively in less than 20% of instances, while the remaining cases are diagnosed intraoperatively or after laparoscopic cholecystectomy in 74-92% of cases.[2]

Gallbladder carcinoma is one of the most malignant tumours of the gastrointestinal tract, having a terrible prognosis. Early-stage gall bladder carcinaoma patients have a better prognosis.[2] They are frequently discovered incidentally following a cholecystectomy for a benign condition, such as gallstones or chronic cholecystitis, either during surgery or on the final histological report of the specimen. It is advised that all cholecystectomies be followed by a histological evaluation.[3]

Early diagnosis is challenging since it is clinically quiet in the early stages, and many gallbladder carcinomas go undetected before surgery. Gallbladder carcinoma is pathologically staged based on the depth of invasion into the gallbladder wall, tumour spread to the peritoneal or hepatic side of the gallbladder, and lymph node involvement.[4] According to the AJCC 8th edition, direct tumour spread into the liver and other surrounding organs such as the common bile duct, colon, stomach, duodenum, diaphragm, and abdominal wall is not considered distant metastasis.[5]

## MATERIALS AND METHODS

**Study design:** Meta analysis.

**Study location:** Department of Surgical Oncology, RIMS, Ranchi, Jharkhand, India.

A search was conducted using the following terms: gallbladder cancer; gallbladder neoplasms; cholangiocarcinoma; bile duct cancer; PET; positron emission tomography. The search was conducted separately by two authors (SS, BM) using the PRISMA statement's verified techniques. There were no language restrictions. MEDLINE, the Cochrane Central Register of Controlled Trials, EMBASE, PubMed, Scopus, Doaj, Cochrane and Web of Science were the databases analysed. To identify further relevant studies, the reference lists of all included papers, as well as related review articles, were manually searched.

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**Inclusion Criteria**: Published studies that evaluated the use of PET-CT in patients with primary or recurrent cholangiocarcinoma or gallbladder cancer were included.

**Exclusion criteria:** Studies published prior to 2008; review articles; case reports; articles not specific to PET-CT and cholangiocarcinoma/ gallbladder cancer. Papers were scrutinised for inclusion independently by two authors (SS, BM) with disagreement resolved by consultation with the senior author (JBK) if consensus could not be reached.

The characteristics of the study were noted, and the outcomes of interest were the detection of primary illness, satellite lesions, nodal disease, and metastases. As needed, recurrent disease was investigated. These outcomes were observed separately for gallbladder cancer and cholangiocarcinoma, with the latter further stratified by anatomic site. When more information was not available, the results were indicated for cholangiocarcinoma carcinoma or biliary cancer alone. Statistical measures of accuracy were recorded by reporting sensitivity and specificity, as well as the final proportion of patients whose care was altered as a result of the use of PET-CT.

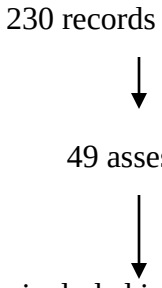


**Figure 1: PRISMA Statement of search results**

## RESULTS

The literature search yielded 7 papers for inclusion in the study. The study characteristics for all included papers are summarised in Table 1.

| Author, year | No of patients | Malignancy |
|---|---|---|
| Kumar et al (2012) | 49 | Gall bladder cancer |
| Lee et al (2011) | 50 | Gall bladder cancer |
| Kitajima et al (2009) | 50 | Gall bladder cancer |
| Shukla et al (2008) | 24 | Gall bladder cancer |
| Butte et al (2009) | 32 | Gall bladder cancer |
| Furukawa (2008) | 72 | Gall bladder cancer |
| Corvera (2008) | 126 | Gall bladder cancer |

**Table 1: Study characteristics**

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Seven studies examined the role of PET-CT in gallbladder carcinoma though two studies did not report their results specifically. Butte et al investigated 32 patients with incidental gallbladder carcinoma following laparoscopic cholecystectomy. Thirteen patients had negative PET-CT results, 9 refused further resection with only one of the four patients resected having residual disease on operative exploration. PET-CT changed management in 12 out of 32 patients (38%) demonstrating unexpected disseminated disease in 10 patients and localised resectable disease in 2 patients.

Corvera et al studied 126 patients with gallbladder cancer within their published series. They demonstrated a sensitivity of 86% and a specificity of 50% for detection of the primary tumour and a sensitivity of 87% and specificity of 89% for detection of nodal/ distant disease respectively. This resulted in a change in treatment for seven (23%) patients. Shukla et al evaluated the role of PET-CT in 24 patients with incidental gallbladder cancer prior to radical resection. They demonstrated that PET-CT predicted resectability with a sensitivity of 100% but was not significantly superior to conventional CT. PET-CT demonstrated residual disease with a sensitivity of 28.5% and with a specificity of 80.9%.

These results may have changed clinical management for two patients. Kumar et al evaluated the role of PET-CT in detecting recurrent gallbladder cancer in 49 patients. These investigators demonstrated a sensitivity and specificity of 97.6% and 90% respectively for detecting recurrent disease. PET/CT was shown to be more specific than conventional imaging (100% vs. 50%) and would have resulted in a change in management for 5 (20%) patients.

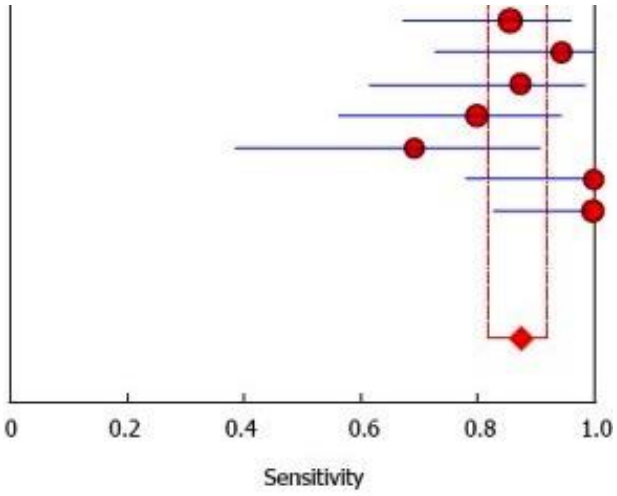


**Figure 2: Sensitivity values of PET CT in the studies (*n* = 7) included in the meta-analysis**

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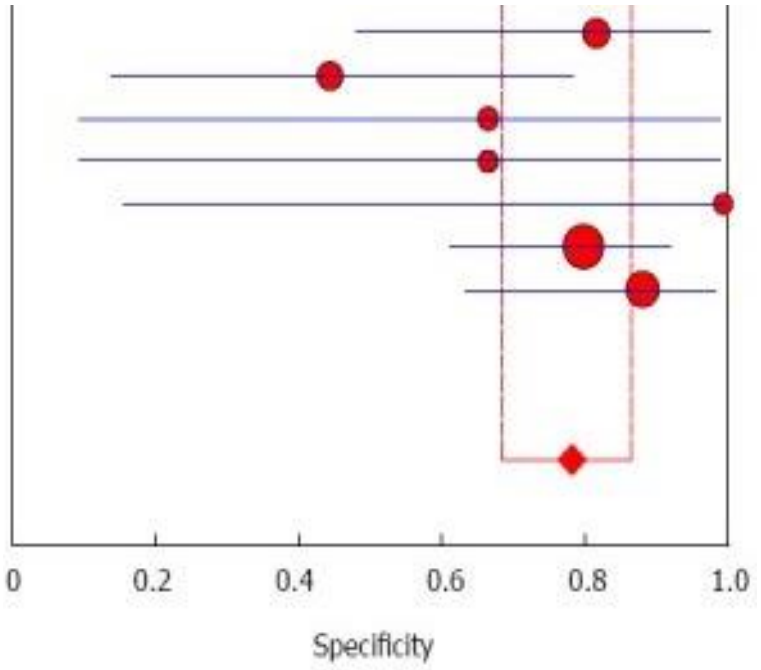


**Figure 3: Specificity values of PET CT in the studies (*n* = 7) included in the meta-analysis**

## DISCUSSION

PET-CT has a high specificity for regional lymph node metastases with most studies in cholangiocarcinoma reporting this between 89% and 100%. Ruys et al reported a lower specificity of 67% (12 of 18 positive nodes) respectively.[6] These investigators emphasize that their results may have underestimated the effectiveness of PET-CT since three patients with positive scans did not have nodes assessed histologically because of tumour unresectability. Kim et al have emphasized that small tumour size and the growth pattern of cholangiocarcinomas, with small nests of cells embedded in a fibrous stroma, may compromise the accuracy of PET-CT in low volume deposits seen in regional lymph nodes.[7]

However, the high specificity emphasizes that a positive scan is a useful and accurate means of determining lymph node status preoperatively while a negative scan is less reassuring. Only Shukla et al formally assessed the efficacy of PET-CT in defining nodal metastases in different lymph node basins with specificities reported between 90% and 100% in nodes in the porta, retropancreatic, pericholedochal and para-aortic basins. There is reason to believe that similar results would be obtained for regional lymph node metastases in gallbladder cancer although only Butte et al report limited results for the use of PET-CT in these patients. Minimal use of PET-CT has been made in the definition of satellite lesions in either cholancarcinoma or gallbladder cancer.[8]

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Butte et al reported the effectiveness of PET-CT in defining liver metastases in patients with carcinoma of the gallbladder. All reported studies rely on standard cross-sectional imaging with triple phase CT scan or MRI to formally assess the liver for metastatic deposits.[9]

The use of PET-CT in defining recurrent disease after treatment is an emerging indication as systemic therapies for patients with recurrent disease improve. Butte et al reported 10 of 32 patients with positive PET-CT scans with residual carcinoma in the gallbladder bed following initial treatment with laparoscopic cholecystectomy alone. Lee et al reported that PET-CT was useful in detecting lymph node metastases and hepatic recurrence following radical resection for gallbladder carcinoma. However Corvera et al emphasized that while PET-CT identified recurrent cancer in 76% of their patients, in all but three patients (9% of those evaluated) the recurrences were visible on standard cross-sectional imaging with CT or MRI.[10]

## CONCLUSION

230 records were screened, 49 were assessed and 7 studies were included in the systematic review. PET-CT has a low sensitivity for regional lymph node metastases from cholangiocarcinoma and gallbladder cancer but a high specificity. In one study, PET-CT appears to be effective in assessing all nodal basins related to the liver, bile ducts and gallbladder. PET-CT has no role in the assessment of hepatic satellite lesions but is useful in defining extra-abdominal metastatic disease and recurrent disease and to assess specific areas of concern defined on CT scan and/or magnetic resonance scan.

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