



UTILITY OF MDCT IN STAGING AND RESECTABILITY OF GALLBLADDER CARCINOMA WITH POSTOPERATIVE CORRELATION OF IMAGING FEATURES

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ABSTRACT

Aims & objective: The main aim of our study was to review the imaging features of gallbladder carcinoma (GBC) and assess the utility of MDCT in staging & resectability of GBC with postoperative histopathological correlation.

Methods and Material: The present study was a prospective observational study with internal validation by operative and histopathological correlation. Time period of study was 2 years (August 2014 to July 2016). The patients (n=110) were referred from Department of Surgery with clinical suspicion of GBC. All patients were subjected to preliminary ultrasonography. After taking informed consent, the above patient group was subjected to CT examination of abdomen and pelvis using 64-slice computerized tomography examination as per international protocol. Out of 110 patients, 30 patients were surgically explored & postoperative findings noted.

Results: Majority of cases presented in 5th-6th decade with female preponderance. Most common morphological type was gallbladder wall thickening (44.5%). Loco regional spread was more common than distant metastasis with adjacent hepatic parenchymal infiltration as most common site. Lymphatic spread show predilection towards N2 station of nodes. Most common site of distant metastasis was liver. Other features included skeletal, pulmonary, adrenal metastasis, cholecystoduodenal fistula and vascular invasion. Osteolytic lesions were most common type of bony metastasis. Adenocarcinoma was most common histological type (86.6%).

Conclusions: In our study, there was corresponding change in morphologic pattern of the disease from wall thickening to mass replacing gallbladder fossa with progression in the disease stage. Gallbladder fossa mass with hepatic infiltration was the commonest pointer for resectable carcinoma gallbladder. MDCT was found to be quite effective in resectability of the tumour as well as disease staging.

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INTRODUCTION

Biliary tract cancers are adenocarcinomas that arise from the epithelial lining of the gallbladder, intrahepatic and extrahepatic bile ducts. Although anatomically these malignancies are related and have similar metastatic patterns, each has a distinct clinical presentation, molecular pathology, and prognosis¹. Gallbladder cancer is the most common malignancy of the biliary tract, representing 80-95% of biliary tract cancers worldwide². Carcinoma gallbladder is the seventh most common malignancy of the alimentary tract³. Incidence of carcinoma gallbladder shows a lot of variations based on geographical region and ethnicity. Gallbladder cancer has a particularly high incidence in Chile, Japan, and northern India⁴. The basis for this variance likely resides in differences in environmental exposure and intrinsic genetic predisposition to carcinogenesis. For gallbladder cancer, several conditions associated with chronic inflammation are considered risk factors, which include gallstone disease, porcelain gallbladder, gallbladder polyps, chronic Salmonella infection, congenital

biliary cysts, and abnormal pancreaticobiliary duct junction^{1,4}. Most of the times asymptomatic nature of the disease poses challenges in the early diagnosis and treatment. As symptoms like abdominal pain, abdominal lump, anorexia, jaundice, nausea and vomiting are common to other gastrointestinal tract conditions, the gallbladder cancer is commonly confused with other gastrointestinal diseases. Unfortunately, in a study area like eastern Uttar Pradesh and Bihar, most often patients visit hospital only when the disease is in its advanced stage and thus, have a poor prognosis. Roentgenology too is non-specific, however, with the advent of newer imaging techniques some carcinomas may be detected early, but the overall outcome for the patient is still bleak. Thus, urgent ultrasonography followed by cytological investigations is needed to diagnose the gall bladder disease. Ultrasonography and computed tomography have revolutionized the diagnosis and management of carcinoma gallbladder. Computed tomography scan has the ability to detect local invasion of the liver, lymph nodes, and the presence of hepatic and peritoneal metastasis⁵. Computed Tomography has been shown to

diagnose carcinoma gallbladder correctly in 60-70% of cases⁶. Most gallbladder carcinomas present when the disease is at advanced stage. As a result, the prognosis for gallbladder carcinoma remains poor. Gallbladder carcinoma is highly lethal, as anatomic factors promote early local spread. The ease by which this tumour invades the liver and surrounding structures including the biliary tree contributes to its high mortality. As surgery is the only definitive cure, it is important to diagnose this disease at an early stage and also determine its extent accurately. Early diagnosis and identification of high-risk cases and providing prophylactic cholecystectomy could offer a potential cure for patients.

Table 1 Morphological appearance of carcinoma gall bladder (n=110)

Morphology	No. of cases	Percentage
Wall thickening	52	47.3
Focal	28	25.5
Diffuse	24	21.8
Mass replacing gall bladder fossa	16	14.5
Focal gall bladder mass	42	38.1

Table 2 Locoregional spread of carcinoma gall bladder (n=110)

Locoregional spread	NO. of cases	Percentage
Bile duct dilatation		
Present	71	64.5
Mild	37	33.6
Moderate	28	25.4
Gross	6	5.5
Absent	39	35.5
Hepatic parenchymal invasion		
Left Lobe	60	54.5
Right Lobe	75	68.2
Bilateral Lobes	43	39.1
Antropyloric region involvement		
Present	16	14.5
Abutting	9	8.2
infiltrating	7	6.3
Absent	94	85.5
Duodenal involvement		
Present	44	40.0
Abutting	18	16.4
infiltrating	26	23.6
Absent	66	60.0
Hepatic Flexure involvement		
Present	36	32.7
Abutting	19	17.3
infiltrating	17	15.4
Absent	74	67.3

Table 3 Distant spread of carcinoma gall bladder (n=110)

	No. of cases	Percentage
Hepatic metastasis		
Right lobe	36	32.7
Left lobe	27	24.5
Bilateral lobes	25	22.8
Peritoneal Deposits		
Present	17	15.4
Absent	93	84.6
Omental deposits		
Present	28	25.4
Absent	82	74.6
Adrenal metastasis		
Present	4	3.6
absent	106	96.4
Pulmonary metastasis		
Present	20	18.2
absent	90	81.8
Skeletal metastasis		
Present	6	5.4
Absent	104	94.6
Extrahepatic solid organ metastasis		
Present	2	1.8
absent	108	98.2

Table 4 Distribution of pathology in patients with carcinoma gallbladder

Findings	Tumor stage				Total
	T1	T2	T3	T4	
Wall thickening (focal/diffuse)	0	12	32	8	52
Mass replacing gallbladder fossa	0	0	3	13	16
Focal GB mass	0	7	22	13	42
Overall	0	19	57	34	110
Overall percentage	0	17.2	51.8	31.0	100.0

Table 5 Cholecystoduodenal fistula in relation to carcinoma gallbladder

Morphology of GB carcinoma	Cholecystoduodenal fistula			
	Present	%	Absent	%
Thickening of gallbladder wall	0	0	52	100
Mass replacing GB fossa	2	12.5	14	87.5
Focal GB mass	1	2.4	41	97.6
Overall	3	2.7	107	97.3

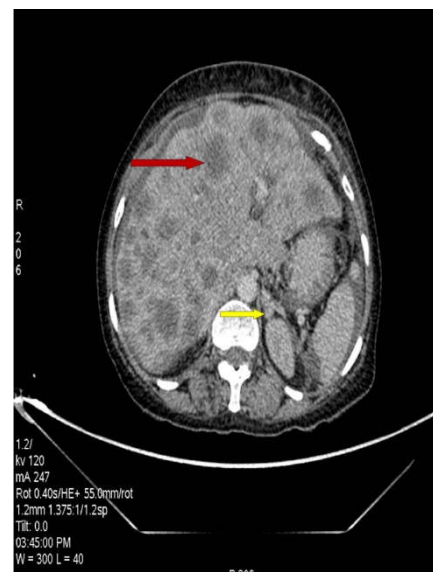
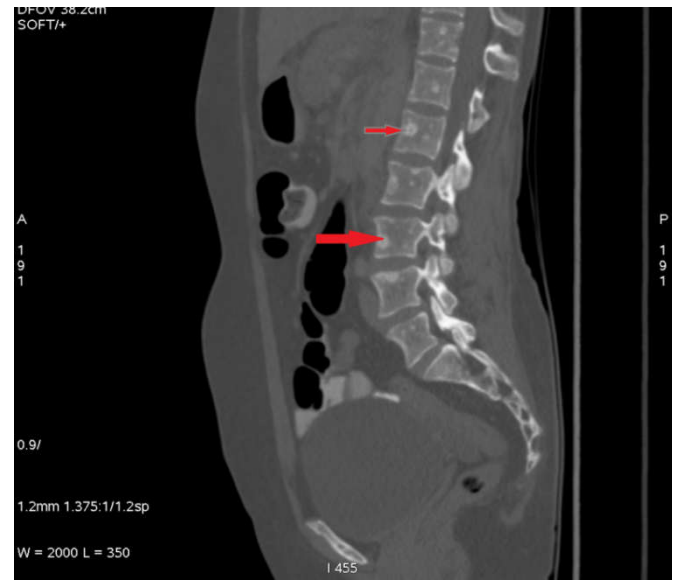
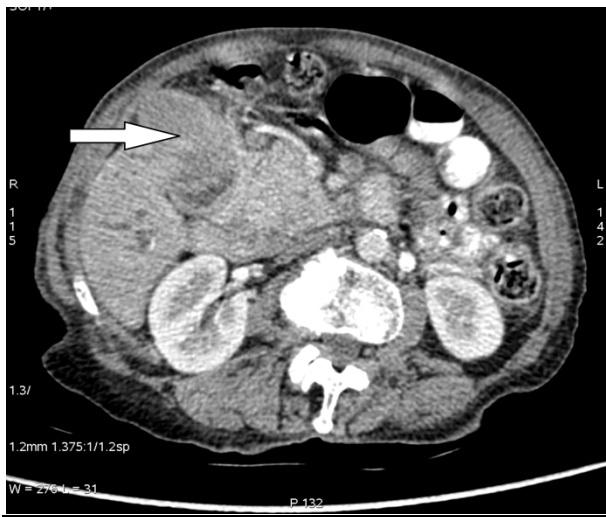
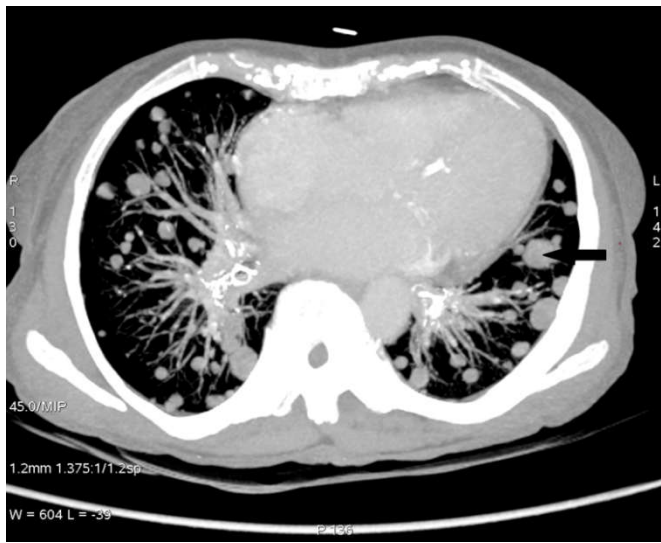


Figure 1: Carcinoma gallbladder with adrenal & hepatic metastases. A. Sagittal CECT section of abdomen shows heterogeneous mass lesion at neck of gallbladder (white arrow) with associated cholelithiasis (black arrow). B. Axial CECT section of abdomen in same patient shows multiple hepatic metastases (red arrow) and bulky medial limb of left adrenal showing enhancing eccentric nodule (yellow arrow) indicating adrenal metastasis.



B

Figure3: Gallbladder carcinoma with osteoblastic metastases A. Axial CECT abdominal section shows diffuse asymmetrical gallbladder wall thickening (black arrow). B. sagittal section in bone window show multiple sclerotic lesions in visualized dorsolumbar vertebral column (red arrow).



B

Figure2: Carcinoma gallbladder with pulmonary metastasis A. Axial CECT section of abdomen shows focal intraluminal gallbladder mass in fundal region (White arrow). B. MIP axial CT image of same patient shows multiple soft tissue density nodules (black arrow) diffusely involving bilateral lung fields indicating pulmonary metastasis.

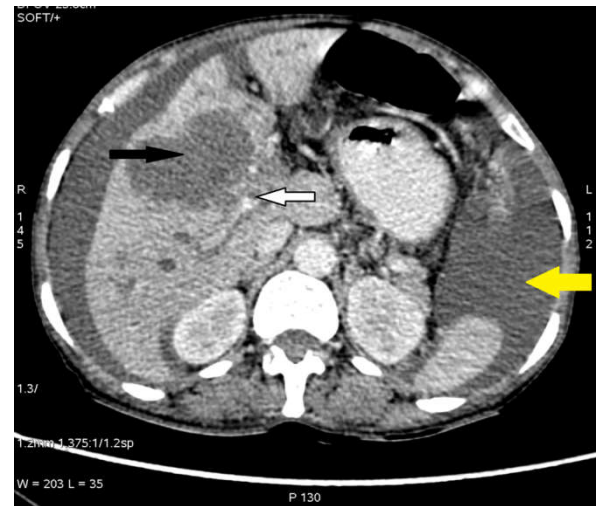


Figure-4: Axial CECT section of abdomen shows hypodense mass replacing gallbladder fossa (black arrow) with hypodense filling defect in portal vein lumen just proximal to its bifurcation (white arrow) indicating portal vein thrombosis. Yellow arrow indicates ascites.

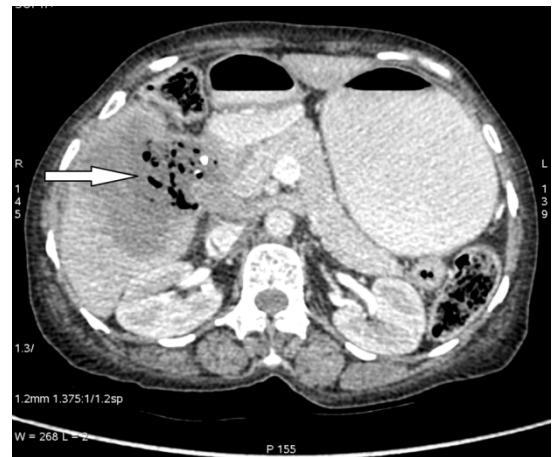
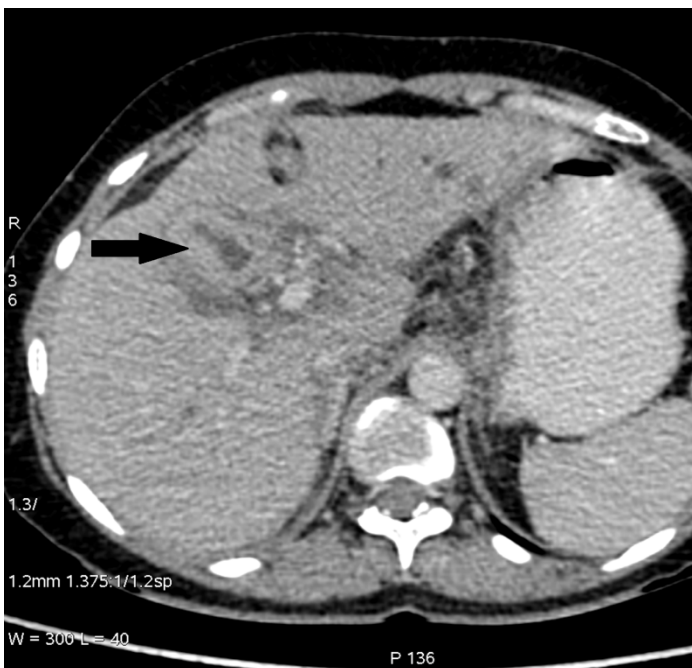


Figure 5. Axial CECT abdominal section showing predominantly hypodense mass replacing gallbladder fossa (white arrow) infiltrating D2 segment of duodenum with multiple air loculi visible inside gallbladder mass lesion indicating cholecystoduodenal fistula.

Subjects and Methods

All the patients with clinical suspicion of carcinoma gallbladder were subjected to preliminary ultrasonography. Ultrasonography was done on Philips IU 22. Informed consent for CT examination was taken. All contrast helical CT scans were performed using multidetector 64 slice CT scanner (General Electric Medical Systems, Milwaukee, WI). The patients did not eat or drink for 4-6hr prior to CT scan. Initial 5mm contiguous, noncontrast axial sections of the upper abdomen were obtained a single helical acquisition starting from the mid portion of the xiphisternum to umbilicus. One hundred milliliters of nonionic iodinated contrast (300 mg I/mL) was then injected at a rate of 2 mL/sec through a 18-gauge IV cannula using a pressure injector. The 5-mm-thick slices (at 120kv, 350mAs, with an increment of 5mm, pitch 1.0) were obtained in a single helical acquisition starting from the mid portion of the xiphisternum to the pubic symphysis. The total scan time was 5-7sec during one breath-hold. Reconstructed slices at 1.25mm intervals are secondarily obtained with a field of view of 45 cm focused on the umbilical region. This procedure (lasting ~5 min) yielded 400 reconstructed images, which were then transferred to a workstation (Advantage Windows; General Electric Medical Systems) for post-processing and analysis.

RESULTS

The mean age in the gallbladder cancer group was 55.13±13.58 ranging from 30-98 years. Most of the patient in our study were females. The study comprised of 76(69.1%) females and 34(30.9%) males in carcinoma gallbladder group with Female to male ratio of 2.23:1. Most common observed morphological pattern in our study was wall thickening, seen in 52 cases (44.5%). Focal intraluminal gallbladder mass which was the another presentation was seen in 42 cases (38.1%). Third pattern mass replacing gallbladder fossa was seen in 16 cases (14.5%) (Table 1). Cholelithiasis was more common association in females with carcinoma with female: male ratio of 4.5:1.

Among the locoregional spread of carcinoma (Table 2), intrahepatic biliary radical dilatation was seen in 71 patients (64.5% cases), which was either due to contiguous spread of mass compressing/invading CBD or extrinsic compression by lymph nodes.

Contiguous involvement of adjacent liver parenchyma was seen involving right lobe more commonly (68.2%) as compared to left lobe (54.5%). Antropyloric region was involved in 14.5% cases. Duodenal involvement by contiguous spread was seen in 40% cases. Hepatic flexure was involved in 33% cases.

Out of distant metastasis (Table 3), hepatic metastasis was seen in both the lobes (22.8% cases) (Figure 1a). Peritoneal deposits were seen in 15.4% cases. Omental metastasis was seen in 25.4% cases. Metastasis to adrenal gland was seen in 3.6% cases (Figure 1b). Metastasis to Lungs was seen in 18.2% cases (Figure 2). Skeletal metastasis was seen in 5.4% cases (Figure 3). Extrahepatic solid organ metastasis was seen in 1.8% cases. Vascular thrombosis was seen in 20.0% cases (Figure 4).

Findings were stratified using the TNM system⁷ following the contrast enhanced CT study. Most of the cases in our study were in T3 stage (51.8%) at the time of presentation (Table 4).

Overall incidence of cholecystoduodenal fistula was 2.7% in our study with maximum incidence in mass replacing GB fossa type morphology (12.5%) (Table 5) (Figure 5).

In our study, 30 cases were followed for histopathology out of which adenocarcinoma was seen in 86.6% patients (n=26). Among the various subtypes of histopathologically proven adenocarcinoma, poorly differentiated adenocarcinoma was most common subtype.

DISCUSSION

Primary carcinoma of the gallbladder is uncommon; however it is the most common malignancy of the biliary tract⁸. The mean age of presentation in the gallbladder cancer group was 55.13±13.58 year compared to the median age 67 years in a Memorial Sloan-Kettering report of 435 gallbladder cancer patients⁹. It was seen commonly affecting the persons in fifth to sixth decade. Mean age of presentation was comparatively less than reported age in western literature. Most of the patient in our study were females (69.1%). The exact aetiology of carcinoma gallbladder is unknown, however, several associated risk factors have been identified. The closest association is with cholelithiasis, which is seen in 65-95% of patients as reported in different series^{10,11,12}. In our study, association of cholelithiasis with carcinoma gallbladder was seen in 44 cases (40%).

Weiner *et al* observed mass replacing gall bladder fossa was the most common presentation of GBC¹³. However asymmetric gall bladder wall thickening was most common presentation in our study.

Adjacent hepatic parenchymal infiltration was seen affecting right lobe more commonly (68.2%) as compared to left lobe (54.5%). Spread to bilateral lobes was seen in 39.1% cases. It was due to contiguous spread by gallbladder mass. In the right lobe most common involved segment was segment V. Segment IVb was most commonly involved in left lobe. Fong Y *et al* explained the propensity of carcinoma gallbladder to invade the liver segments IVb and V adjacent to the gallbladder fossa by the anatomical characteristic of the gallbladder wall having a narrow lamina propria and only a single muscle layer¹¹.

Distant metastasis is less common in carcinoma gallbladder than locoregional spread. According to Arminski metastases occur to every organ including liver, lymph nodes, adrenal, kidney, spleen, brain, breast, thyroid, heart and uterus, those to the skeletal system are least frequent¹⁴. Metastasis in carcinoma gall bladder is uncommon and occurs late in the course of the disease. Adrenal metastases and venous occlusion due to tumour thrombus are unusual in newly diagnosed gallbladder carcinoma patients¹⁵. Metastases to lung¹⁶, bone¹⁷, Scalp¹⁸ have been previously reported in the literature. All previous mentioned sites of metastasis were seen in our study.

Bilateral adrenal masses were seen in our patient. Though bilateral metastatic involvement of adrenals is well known but carcinoma of gallbladder is an unusual primary site. Metastasis to adrenal gland was seen in 3.6% cases. On imaging alone it was difficult to ascertain whether it was primary malignancy of liver or of gallbladder or whether the adrenal masses were metastatic in nature or not. Ultrasound guided fine needle aspiration cytology of adrenal masses was suggestive of

metastatic adenocarcinoma that was similar to the cytology of primary mass-an adenocarcinoma of gallbladder.

The incidence of skeletal metastasis was seen in 5.4% cases. The metastasis to the skeletal system is generally osteolytic with osteoblastic lesions being rare. In case of lumbar vertebral and iliac wing involvement the lesions were hyperdense suggesting osteoblastic metastasis (Figure-4). Osteolytic lesion was noted involving dorsal vertebra. Ala of sacrum showed mixed type of metastasis. In cases of skeletal metastasis of carcinoma gallbladder, 66.7% were purely osteolytic, 16.7% were osteoblastic and 16.6% were mixed type.

In our study, heterogeneous enhancement and diameter more than 1.0 cm were taken as two major radiological criteria to diagnose lymph nodal metastasis at CT imaging. These diagnostic criteria were based on two characteristics of metastatic lymph nodes: cancerous necrosis for heterogeneous enhancement, and nodal enlargement for increase in diameter¹⁹. In our study, N1 group were involved in 19.1% cases while N2 were seen in 63.6% cases. Lymphadenopathy was absent in 17.3% cases. Distant lymph nodal metastasis was more common probably due to late stage of presentation of patients in our hospital.

Chandar *et al* described cholecystocolonic fistula as an uncommon but pertinent complication of gallbladder disease, occurring in 0.06 to 0.14% of patients with biliary disease²⁰. Among the different types of cholecystoenteric fistulas, the cholecystoduodenal is the most common with cholecystocolonic fistulas being the second most common²¹. In our study 2.7% cases were diagnosed as having cholecystoduodenal fistula (Figure-5).

The criteria for nonresectability were as follows²²: involvement of main portal vein or hepatic artery; involvement of the portal vein or hepatic artery branches of both lobes of the liver; simultaneous involvement of the ipsilateral hepatic artery and contralateral portal vein; simultaneous invasion in both lobes of the liver at the level of confluence of segmental bile ducts to form the hepatic ducts; contiguous involvement of more than two segments each in both lobes of the liver; contiguous extensive infiltration of the colon, duodenum, or pancreas; the presence of hepatic metastases; and the presence of peritoneal metastases.

Most of the time, the disease is diagnosed in advanced stage, making the prognosis poor. Bulk of patients presented in T3 stage according to TNM system (51.8%).

In this study a changing epidemiological pattern in the gender distribution as well as a shift of the mean age at diagnosis into the sixth decade of life was observed. There is a corresponding change in morphologic pattern of the disease with progression in the disease stage from wall thickening to mass lesion replacing entire gallbladder. Focal or diffuse mass lesions in the gallbladder fossa with infiltration of liver was the commonest pointer for resectable carcinoma gallbladder. MDCT was quite effective in identifying the criteria for resectability of the tumour and in disease staging. The overall prognosis is significantly determined by metastatic spread to the lymph nodes²³. Median survival rate in patients of carcinoma gallbladder with distant metastases is only 3 to 4 months and these patients may not be offered any intervention¹⁷. So in this endemic zone of eastern Uttar Pradesh & Bihar, MDCT can obviate surgical exploration in

appropriately selected cases. Significant improvement in survival rate can be achieved by early stage of detection of malignancy.

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