

Role of Ultrasound and Computed Tomography in the Evaluation of Gallbladder Malignancy

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ABSTRACT

Background & objective: Ultrasonogram (USG) and computed tomography (CT) are often used in the evaluation of gall-bladder carcinoma. The present study was conducted to determine the usefulness of USG and CT scan in diagnosing gallbladder carcinoma.

Materials & Methods: This cross-sectional observational study was conducted at Department of Radiology and Imaging, BIRDEM in collaboration with the Departments of Hepato-biliary Surgery, and Histopathology of the same institute over a period of 3 years from July 2004 to June 2006. A total of 42 patients (ranging from 40-80 years) were initially included on the basis of signs and symptoms of gallbladder carcinoma and underwent USG and CT scan for preoperative radiological diagnosis, its extension and operability. Following operation all the resected specimens were sent for histopathological evaluation. The diagnostic accuracies of USG and CT scan were then compared against histopathological diagnoses by using Kappa statistics.

Result: In the present study, the mean age of the patients was 60 (range: 40-80) years with female preponderance. About 40% of the gall-bladder were contracted and reduced in size and 32.5% large and distended on USG examination, while 45% of the gall-bladder were contracted and reduced in size and 25% distended and large on CT examination. Approximately 40% had irregularly thickened wall and 21.2% diffusely thickened wall on USG and 30% of gallbladder wall were diffusely thickened and 45% irregularly thickened on CT scan. The present study showed hepatic parenchymal invasion to be 22.5% on USG and 42.5% on CT scan. The sensitivity and specificity of USG in diagnosing GB carcinoma were 93.9 and 71.4% respectively. Similarly, the sensitivity and specificity of CT scan in detecting GB carcinoma were 97.1 and 83.3% respectively. The test of agreement (Kappa test) revealed an almost 90% agreement between the two procedures meaning that the two diagnostic modalities are almost comparable in diagnosing gall bladder carcinoma ($p < 0.001$).

Conclusion: The study findings indicate that both USG and CT scan are ideal, non-invasive, safe imaging modalities for diagnosis of gallbladder carcinoma. CT scan has an additional advantage in defining the extension of the disease and involvement of surrounding structures including lymph nodes and hepato-duodenal ligament.

Key Word: Ultrasound (USG), Computed Tomography (CT), gallbladder carcinoma, diagnostic accuracy etc.

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Date of submission: 05.01.2017, Date of acceptance: 22.03.2017

Introduction

Carcinoma of gallbladder is the most common malignant tumor of the biliary tree. It is also the 5th most common gastrointestinal malignancy and comprises about 1-3% of all malignancies. Its peak occurrence is in the 5th decade or older and there is a female predilection of 3-4:1. It is a highly lethal disease and runs a fatal prognosis¹. The aetiology of carcinoma of the gallbladder remains unknown and the incidence varies greatly in different areas of the world. The patients may be asymptomatic or may present with symptoms and signs (upper quadrant pain, jaundice and weight loss with nausea, vomiting, loss of appetite, fatty food intolerance, dark urine etc.) mimicking cholecystitis or cholelithiasis². So early diagnosis of carcinoma gallbladder is difficult and rare as there are no specific signs and symptoms. Conventionally, carcinoma gallbladder is diagnosed on the basis of medical history; abdominal examination and using modern imaging techniques like transabdominal ultrasonography and computed tomography of upper abdomen. These are subsequently confirmed by postoperative histopathology of surgical specimen removed. Because the clinical presentation is confusing, the radiologist is often the first to suggest the correct diagnosis.

Transabdominal sonography and computed tomography have been found to be useful in suggesting the preoperative diagnosis of carcinoma gallbladder. Abdominal ultrasound is the examination of choice in the diagnosis of gallbladder and biliary duct lesion, but several diagnostic problems may arise in the differentiation from the polyps and acute inflammatory disease. CT scan better demonstrates gastrointestinal tract invasion and lymphadenopathy which can be a valuable finding for staging and treatment planning. Although the overall prognosis for this tumor remains poor, ultrasonography may facilitate early treatment of curable carcinomas by the fortuitous detection of tumor in patients who are asymptomatic and who have symptoms attributable to coexistent stones³. The typical CT scan findings of gallbladder carcinoma include three patterns - a mass replacing the gallbladder fossa, intraluminal mass and

gallbladder wall thickening. The mass replacing the gallbladder fossa is the most common appearance. CT scan can differentiate between complicated cholecystitis and advanced gallbladder carcinoma by few specific findings³.

In this country, gallbladder carcinoma is not uncommon. Ultrasonography and CT scan are two important diagnostic tools available in our country to evaluate the hepatobiliary system. By utilization of these advanced imaging modalities, carcinoma gallbladder can be detected early when these tumors are still localized. Thus survival time of the patients can be increased by early removal of tumors. To the best of our knowledge, no published data are available in this country in the field of radiologic evaluation (USG and CT scan) of carcinoma gallbladder in correlation with histopathological report and the superiority of one modality over the other. The present study is an attempt to fulfil this gap.

Materials and Methods

This cross-sectional observational study was conducted at Department of Radiology and Imaging, BIRDEM in collaboration with the Departments of Hepato-biliary Surgery, and Histopathology of the same institute over a period of 3 years from July 2004 to June 2006. A total of 42 patients (ranging from 40 - 80 years) were initially included on the basis of signs and symptoms of gallbladder carcinoma (such as upper abdominal pain, jaundice, itching, weight loss and upper abdominal mass) and underwent USG and CT scan for preoperative radiological diagnosis, its extension and operability. The USG diagnosis revealed 35 with carcinoma of gall bladder and the rest 7 with inflammatory lesion, while the CT scan diagnosed 36 as gallbladder carcinoma and 6 as cholecystitis. Of the carcinoma cases, 2 were found inoperable and hence were excluded leaving 40 for final evaluation. Following operation all the resected specimens were sent for histopathological evaluation. The statistical analyses were performed using computer software SPSS (Statistical Package for Social Sciences), version 11.5 and the test statistics used to analyse the data were descriptive statistics and kappa statistics. Kappa analysis was used to assess the strength of agreement between the two

diagnostic modalities used in this study to diagnose carcinoma of gall-bladder. While a kappa value of '1.0' indicates perfect agreement, a value of '0.0' indicates no agreement between the two diagnostic modalities. In between 0-1, the strength of agreement will be categorized as <0.2 = poor, $0.21 - 0.40$ = fair, $0.41-0.60$ = moderate, $0.61 - 0.80$ = good and $0.81-1.0$ = very good agreement. The level of significance was set at 5% and $p < 0.05$ was considered significant.

Results

Demographic, clinical and biochemical characteristics:

About two-thirds (65%) of the patients were in 5th to 6th decades of life (35% from 50 - 60 and 30% from 60 - 70 years) with mean age of the patients being 60 years. The study subjects were predominantly female (66.7%) with female to male ratio being roughly 2:1 (Table I). Upper abdominal pain (85%) was the cardinal complaints followed by nausea/vomiting (52.5%), jaundice (47.5%), itching (42.5%) and weight loss (37.5%). Over 22% of the patients had upper abdominal lump (Table II). The mean serum bilirubin and mean alkaline phosphates of the study subjects were $128.9 \pm 123.4 \mu\text{mol/L}$ and $391.2 \pm 290.7 \text{ U/L}$ respectively, while mean serum aspartate aminotransferase (AST) and mean alanine aminotransferase (ALT) were $75.9 \pm 49.7 \text{ U/L}$ and $80.2 \pm 69.7 \text{ U/L}$ respectively. All these biochemical parameters were found raised in majority of the cases (Table III).

Table I: Distribution of patients by their demographic characteristics (n = 40)

Demographic characteristics	Frequency	Percentage
<i>Age (years)*</i>		
40 - 50	10	25.0
50 - 60	14	35.0
60 - 70	12	30.0
≥ 70	4	10.0
<i>Sex</i>		
Male	14	35.0
Female	26	65.0

*Mean age = (60.1 ± 1.7) years; range = (40 - 80) years

Table II: Distribution of respondents by their clinical features (n = 40*)

Clinical features	Frequency	Percentage
Upper abdominal pain	34	85.0
Nausea /Vomiting	21	52.5
Jaundice	19	47.5
Itching	14	42.5
Weight loss	15	37.5
Upper abdominal mass	9	22.5

*Total will not correspond to 100%, for multiple response.

Table III: Distribution of respondents by their biochemical parameters (n = 40)

Biochemical parameters	Raised n(%)	Mean \pm SD	Range	Normal range
Serum bilirubin ($\mu\text{mol/L}$)	28(70.0)	128.9 ± 123.4	8-350	2-17
Alkaline phosphates (U/L)	33(82.5)	391.2 ± 290.7	95-1107	40-125
Serum AST (U/L)	32(80.0)	75.9 ± 49.7	18-272	10-35
Serum ALT (U/L)	29(72.5)	80.2 ± 69.7	20-345	10-40

Assessment of hepato-biliary system at USG and CT scan:

Ultrasonographic evaluation shows that about 40% of the gall-bladder were contracted and reduced in size and 32.5% large and distended. Approximately 40% had irregularly thickened wall and 21.2% diffusely thickened wall. The direct invasion of hepatic parenchyma was observed in 22.5% of cases and metastases in 12.5% cases. Enlarged lymph nodes were found in few cases. CT examination revealed 45% of the gall-bladder to be contracted and reduced in size and 25% distended and large. Thirty percent of gallbladder wall were diffusely thickened and 45% irregularly thickened. Direct invasion of hepatic parenchyma was observed in 42.5% and metastasis in 12.5%. Over half (55%) of the biliary tree was found dilated by both USG and CT scan. Gall stone was detected in 65% of the cases on USG and in 45% of the cases on CT examination. CT scan detected lymph node enlargement in 27.5% of the cases and the common site of enlarged lymph nodes were the portahepatic, peripancreatic, superior pancreaticoduodenal nodes and coeliac axis region nodes. Carcinoma margin of gallbladder was only found at CT scan. The gallbladder margin was well delineated in 35% and poorly delineated in 52.5%

cases. Hepatoduodenal ligament was not seen at USG examination, but was seen at CT scan (Table IV).

Table IV: Comparative findings of Gall-bladder at USG and CT scan (n = 40)

Radiological profile of Gall-bladder	USG	CT scan
Gallbladder size		
Normal	11(27.5)	12(30.0)
Contracted	16(40.0)	18(45.0)
Large (distended)	13(32.5)	10(25.0)
Gallbladder wall thickness		
Normal	15(37.5)	10(25.0)
Diffusely thickened	9(22.5)	12(30.0)
Irregularly thickened	16(40.0)	18(45.0)
Mass filling gallbladderlumen	24(60.0)	28(70.0)
Bile ducts		
Dilated	22(55.0)	22(55.0)
Not dilated	18(45.0)	18(45.0)
Involvement of hepatic parenchyma		
Direct invasion	9(22.5)	17(42.5)
Not involved	24(60.0)	15(37.5)
Metastasis	7(17.5)	4(12.5)
Presence of gall stones	26(65.0)	18(45.0)
Presence of enlarged Lymph nodes	5(12.5)	11(27.5)
Carcinoma Margin of gallbladder		
Well delineated	-	14(35.0)
Poorly delineated	-	21(52.5)
Not delineated	-	5(12.5)

Accuracy of USG and CT scan in the diagnosis of carcinoma gall-bladder:

The sensitivity of USG in differentiating GB carcinoma from inflammatory lesion was $31/33 \times 100 = 93.9\%$, while the specificity of the test in correctly differentiating those who did not have the disease was $5/7 \times 100 = 71.4\%$. The positive and negative predictive values of the test were 93.9% and 71.4% respectively, while the percentages of false positive and false negatives were 6.1% and 28.5% respectively. The diagnostic accuracy of the test was calculated to be $(31 + 5)/40 \times 100 = 90\%$ (Table V). Similarly, the sensitivity of CT scan in differentiating GB carcinoma from inflammatory lesion was 97.1%, while the specificity of the test in correctly ruling out those who did not have the disease was 83.3%. The positive and negative predictive values of the test were 97.1% and 83.3% respectively, while the percentages of false positive and false negatives were 2.9% and 16.7%

respectively. The diagnostic accuracy of the test was calculated to be $(33 + 5)/40 \times 100 = 95\%$ (Table VI). The Kappa test revealed an excellent agreement (89.7%) between the two procedures suggesting that the two diagnostic modalities are almost comparable in diagnosing gall bladder carcinoma ($p < 0.001$) (Table VII).

Table V: Accuracy of abdominal USG in diagnosing carcinoma gall-bladder (n=40)

USG diagnosis	Histopathological diagnosis	
	Carcinoma	Inflammatory lesion
Carcinoma	31	2
Inflammatory lesion	2	5

Table VI: Accuracy of abdominal CT scan in diagnosing carcinoma gall-bladder (n=40)

CT diagnosis	Histopathological diagnosis	
	Carcinoma	Inflammatory lesion
Carcinoma	33	1
Inflammatory lesion	1	5

Table VII: Strength of agreement between USG and CT scan in detecting gall bladder carcinoma

Disease studied	Diagnostic modalities	k-value	Strength of agreement
Gall-bladder carcinoma	USG CT	0.897	Excellent

Discussion

At one time gallbladder carcinoma was regarded as an uncommon disease. However, reports within the last few decades showed that it is not so rare as was previously supposed. Rather it is the most common malignant tumor of the biliary tract. But early diagnosis of carcinoma gallbladder is difficult as there are no specific signs and symptoms. Recent improvement in the hepatobiliary imaging techniques has been increasingly promising with respect to accurate preoperative diagnosis and assessment of the extent of gallbladder carcinoma. As the clinical presentation is confusing, these modern imaging modalities can play an important role in the diagnosis of the disease. However, the imaging appearance of gallbladder carcinoma in USG and in CT scan and their sensitivity, specificity

and accuracy in the correct diagnosis are not yet evaluated in our country.

In the present study, the mean age of the patients was 60 (range: 40-80) years⁵. In their series showed a higher mean age (70.6 years) of the patients having gallbladder carcinoma. Similarly, Paraskevopulos et al⁶ and Yeh⁷ reported similar mean age of patients with carcinoma of gallbladder (67.3, 64.8 and 62.3 years respectively). In terms of sex distribution of gallbladder carcinoma, a female preponderance was observed in our series, which compares well with the findings of Paraskevopulos et al⁶, Levy et al⁸, Chianakwana et al⁹, Yeh⁷ and Singh et al¹⁰.

The most common presenting symptoms of the patients in the present study were upper abdominal pain (85%) followed by nausea/vomiting (52.5%), jaundice (47.5%), itching (42.5%) and weight loss (37.5%). Rukmanappa et al² and Jeffery et al¹¹ observed similar presentations with upper abdominal pain being the commonest symptom, jaundice and weight loss were the next common symptoms. Similar findings were also observed by Levy et al⁸, Momen et al⁵, Pandey et al¹² and Sahin et al¹³.

About 40% of the gall-bladder were contracted and reduced in size and 32.5% large and distended on USG examination, while 45% of the gall-bladder were contracted and reduced in size and 25% distended and large on CT examination. Approximately 40% had irregularly thickened wall and 21.2% diffusely thickened wall at USG and 30% of gallbladder wall were diffusely thickened and 45% irregularly thickened on CT scan. Several studies¹³⁻¹⁵ demonstrated that focal or diffuse wall thickening of gallbladder is one of the imaging findings on CT and USG in patients having gallbladder carcinoma. Gallbladder carcinoma may appear as a mass lesion on imaging study. Mass may protrude into the lumen or large enough to occupy whole of the gallbladder, which is the most common appearance. In this study a mass was present in 24(60%) patients on USG and 28(70%) patients on CT scan. These findings in the present study are strengthened by similar observation made by several studies¹⁵⁻¹⁸.

In terms of echotexture of gallbladder mass, Levy et al⁸ heterogeneous echotexture of gallbladder mass reflecting varying degrees of tumor necrosis was observed. Echogenic foci and acoustic shadowing associated with the tumor may be related to coexisting gallstones. Yeh⁷ also observed that when gallbladder was filled with mass and associated with stones or necrotic center, it appeared like a "bull's eye" with diffuse low level echoes and highly echogenic center. Cholelithiasis is a well-established risk factor for the development of gallbladder carcinoma. Gall stones cause chronic irritation and inflammation of gallbladder leading to mucosal dysplasia and subsequent carcinoma. In the present study gallstones were found in 65% of patients on USG examination. This finding was quite lower on CT evaluation (45%). Probably this is due to presence of gallbladder cholesterol stone in those patients, because cholesterol stone shows almost similar density of gallbladder content at CT.

The present study showed hepatic parenchymal invasion to be 22.5% on USG and 42.5% on CT scan. This is in close agreement with the study of Ohtaniet al¹⁹ where hepatic parenchymal involvement was found in 65% patients. Bach et al²⁰ described that ultrasonography is reliable in the detection of primary gallbladder mass. However, sonographic findings do not accurately reflect the full extent of disease and sonography is particularly limited in the diagnosis of invasion to the liver, lymph nodes, peritoneum etc. CT scan more readily depicts subtle extension of tumor beyond the wall of the gallbladder and into the surrounding structures and lymph nodes.

In the present study, the sensitivity and specificity of USG in diagnosing GB carcinoma were 93.9 and 71.4% respectively. The positive and negative predictive values of the test were 93.9 and 71.4% respectively. The diagnostic accuracy of the test was 90%. Similarly, the sensitivity and specificity of CT scan in detecting GB carcinoma were 97.1, and 83.3% respectively. The positive and negative predictive values of the test were 97.1 and 83.3% respectively. The diagnostic accuracy of the test was 95%. The test for strength of agreement (Kappa test) revealed an almost 90% agreement between the two procedures meaning that the two diagnostic

modalities are almost comparable in diagnosing gall bladder carcinoma ($p < 0.001$). Yeh⁷ reported 84.6% accuracy of USG in the diagnosis of the gallbladder carcinoma. Courtney & Townsend²¹ described that sensitivity of ultrasound in the detection of gallbladder carcinoma ranges from 70-100%. In terms of CT as diagnostic modality in the evaluation of gallbladder carcinoma, the diagnostic accuracy was found to be 95% which compares well with that of Kumran et al²². who observed the accuracy of CT in the diagnosis of gallbladder carcinoma to be 93.3%. However, previous studies^{6,23} reported a low sensitivity of CT scan (from 69 - 80%) in the diagnosis of gallbladder carcinoma which might be that the previous CT technologies were low sensitive to diagnose gallbladder carcinoma compared to the present ones. From the result of the present findings as well as findings obtained from a number of other investigators, it is conceivable that both Ultrasonography and CT scan are ideal and accurate diagnostic imaging modalities for diagnosis of gallbladder carcinoma. However, CT scan is of greater value in the evaluation of extent of involvement to surrounding structures and thus determining its resectability.

Conclusion

As the histopathological diagnosis of the present study correlated well with USG and CT scan findings in the diagnosis of gallbladder carcinoma; It can be concluded that both USG and CT scan are useful imaging modalities for diagnosing this disease. However, CT scan has some distinct advantages over USG in detecting extension of tumor and involvement of surrounding structures including lymph nodes and hepatoduodenal ligament thus determining its resectability. However, as the sample size was small further large-scale study is recommended to validate the findings of the present study.

Conflict of interest: none

References

1. Smathers RL, Lee JKT, Heiken JP. Differentiation of complicated cholecystitis from gallbladder carcinoma by computed tomography. *Amer J Rongen* 1984; 143: 255-59.
2. Rukmanappa M, Tanga, Ewing JB. Primary malignant tumors of the gallbladder: report of 43 cases. *Surg* 1970; 6(3): 418--26
3. Haaga JR, Lanzieri CF, Gilkeson RC. CT and MRI imaging of the whole body, 4th ed, Mosby: Missouri; 2003. p1318-41.
4. Mondy MM, Chang MC, Bowton DL, Kilgo PD, Meredith JW, Miller PR. Prospective comparison of bronchoalveolar lavage and quantitative deep tracheal aspirate in the diagnosis of ventilator-associated pneumonia. *J Trauma* 2005; 59: 891-6.
5. Memon MA, Anwar S, Shiwani MH, Memon B. Gallbladder carcinoma: a retrospective analysis of twenty-two years experience of a single teaching hospital. *International Seminars in Surg Onco* 2005; 6(2): 79-81.
6. Paraskevopoulos JA, Baer H, Uttigea F, Dennison AR. The role of imaging techniques in the diagnosis of primary carcinoma of the gallbladder. *Br J Surg* 1994; 81(1):15.
7. Yeh H, Ultrasonography and computed tomography of carcinoma of the gallbladder. *Radio* 1979; 133: 167-73.
8. Levy AD, Murakata LA, Rohrmann CA. Gallbladder carcinoma: radiologic-pathologic correlation. *Radiographics* 2001; 21(2): 295-314.
9. Chianakwana GU, Okafor PIS, Anyanwu SNC. Carcinoma of the gallbladder at the Nnamdi Azikiwe University teaching hospital; a 5-year retrospective study. *Nigerian J Clinical Pract* 2005; 8(1): 10-13.
10. Singh A, Bagga SPS, Jindal VP, Singh K, Ratio SS, Gall bladder disease: An Analytical report of 250 cases. *J Indian Med Assoc* 1989; 87: 253-56.

11. Jeffrey M, Piehler, Jeffery W, Crichlow RW. Primary carcinoma of the gallbladder. *Surgery* 1978; 147(8): 929-42.
12. Pandey M, Pathak AK, Gautam A, Aryya NC, Shukla VK. Carcinoma of the gallbladder: a retrospective review of 99 cases. *Dig Dis Sci* 2001; 46(6):1145-51.
13. Sahin M, Aydin A, Sahin M. Carcinoma of the gallbladder. *J Turgut Ozal Med Cent* 1997; 4(1): 129-33.
14. Kumar A, Aggarwal S. Carcinoma of the gallbladder: CT findings in 50 cases. *Abdo Imaging* 1994; 19(4):304-08.
15. Weiner SN, Koenigsberg M, Morehouse H, Hoffman J. Sonography and computed tomography in the diagnosis of carcinoma of the gallbladder. *Amer J Rongen* 1984; 142:735-39.
16. Franquet T, Montes M, Ruiz de Azua Y, Jimenez FJ, Cozocolluela R. Primary gallbladder carcinoma: imaging findings in 50 patients with pathologic correlation. *Gastrointest Radial* 1991; 16(2):143-8.
17. Bates J, Irving HC. Gallbladder and Biliary tree. In: Meire H, Bates and Irving O, Dewbury K, Farrant P editors. *Clinical ultrasound a comprehensive text, Abdominal and General ultrasound*. 2nd ed. Churchill Livingstone: Edinburgh. 2001; p297-348.
18. Lee JKT, Sagel SS, Stanley RJ, Heiken JP editors. *Computed body tomography and MRI correlation*. 3rd ed. Lippincott: New York. 1998; p779-844.
19. Ohtani T, Shirai Y, Tsukada K, Muto T, Hatakeyama K. Spread of gallbladder carcinoma: CT evaluation with pathologic correlation. *Abdo Imaging* 1996; 21(3):195-201.
20. Bach AM, Loring LA, Hann LE, Illescas FF, Fong Y, Blumgart LH. Gallbladder cancer: can ultrasonography evaluate extent of disease? *J Ultrasound Med* 1998; 17(5):303-9.
21. Courtney M. Townsend Jr. *Sabiston Textbook of Surgery: The biological basis of modern surgical practice (textbook of surgery)*, 17th ed, WB Saunders 2004.
22. Kumaran V, Gulati S, Paul B, Pande K, Sahni P, Chattopadhyay K. The role of dual-phase helical CT in assessing resectability of carcinoma of the gallbladder. *Eur Radial* 2002; 12(8):1993-9.
23. Yoshimitsu K, Honda H, Shinozaki K, Aibe H, Kuroiwa T, Irie H, Chijiwa K, Asayama Y, Masuda K. Helical CT of the local spread of carcinoma of the gallbladder. *Amer J Rongen* 2002; 179:423-28.