

To Find Out Differential CT Scan Diagnosis for Cirrhotic and Malignant Ascites

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ABSTRACT

Aim: To assess different CT signs for differentiating between malignant and cirrhotic ascites.

Methods: We accomplished study of 102 CT scans in adults, distributed into 2 groups based on the cirrhotic or malignant etiology of ascites. The CT signs studied were ascites volume and relative distribution between the greater peritoneal cavity (GPC) and the omental bursa (OB), the density of the ascites, the thickness of the gallbladder wall and the thickness of the parietal peritoneum and its degree of enhancement, and tethered-bowel sign.

Results: The CTScan signs associated with malignant ascites were: presence of fluid in the omentabursa ($P=0.003$), thickening of the peritoneum its degree of enhancement ($P=0.005$), increased density of the ascites ($P=0.01$), and loss of mobility of bowel loops in the ascites ($P=0.001$). There in gallbladder wall thickness between the two groups doesn't show any difference.

Conclusion: The CT scan can play a role in diagnosing malignant ascites and confirm the usefulness of the indirect signs composed of distribution of ascites fluid, thickening and enhancement of the parietal peritoneum, and loss of mobility of the bowel loops in the ascites.

Keywords: CT scan, ascites, cirrhosis and malignancy.

INTRODUCTION

Cirrhosis is by far the most common etiology of ascites, alone responsible for more than 3/4 of cases¹. The main differential diagnosis is malignant ascites, which represents 10% of cases of ascites. Furthermore, 5% of cases are so-called "mixed" ascites, since they combine several causes². The discovery of ascites in an oncologic contest is always difficult, the problem being to differentiate between cirrhotic and malignant ascites. The currently recommended workup when ascites is discovered is a combination of history-taking, physical examination, blood and urine tests, abdominal ultrasound, and paracentesis^{3,4}. In its current state, imaging alone is not in a position to be a reliable tool for characterizing malignant ascites. The objective of our analysis was to confirm the main indirect signs in the literature for differentiating between ascites of malignant and cirrhotic etiology.

MATERIALS AND METHODS

We used radiology information system (RIS) as a database. A keyword search allowed us to form two groups of 51 adults who had a computed tomography (CT) scan between March 2011 and February 2014. Subjects were assigned to a group based on ascites etiology, either cirrhosis confirmed by liver biopsy

(Group 1) or peritoneal carcinomatosis confirmed by ascites fluid cytology performed before or prescribed during the CT scan (Group 2). The types of cancer varied greatly: pancreatic ($n=13$), ovarian ($n=9$), colon ($n=9$), gastric ($n=5$), renal ($n=4$), breast ($n=4$), other ($n=7$).

The standardized protocol included an abdominopelvic volume acquisition 90 seconds after intravenous iodinated contrast injection). The images were read by a senior radiologist specializing in abdominal imaging, blind to the patient's clinical picture. The reconstruction slice thickness was 3 mm and the windowing was adjusted for abdominal analysis (width 350 HU, center 50 HU).

The study criteria were ascites volume and relative distribution between the greater peritoneal cavity (GPC) and the omental bursa (OB); density of the ascites; thickness of the gallbladder wall; thickness and degree of enhancement of the parietal peritoneum and tethered-bowel sign. The statistical analysis (Fisher's exact test and Student's *t* test) was performed with STATA 8.0 software (Stat Corp., TX, USA). For all comparison and correlation tests, the significance threshold was set at $P < 0.05$.

RESULTS

Group 1 (cirrhotic ascites) was composed of 33 men and 18 women (sex ratio 1.8, mean age 62 years, minimum age 32 years, maximum age 92 years). Group 2 (malignant ascites) was composed of 22 men and 29 women (sex ratio: 0.8, mean age: 63 years, minimum age: 31 years, maximum age: 81 years).

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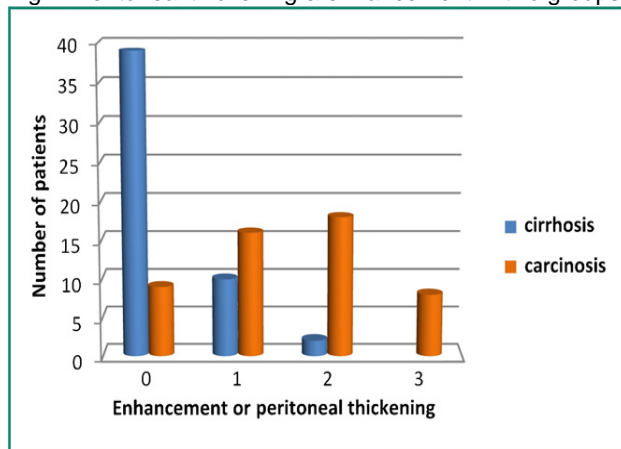
In Group 1, there was no fluid in the OB in 41% of cases. The OB was empty whenever the amount of ascites was low or moderate in the GPC (12 of 51 cases, i.e., 23% of cirrhotic ascites cases), in other words, fluid was found in the OB only when ascites was abundant in the GPC. Even in that situation, the OB was still empty in nine of 39 cases (23%).

In Group 2, the OB was rarely empty (four of 51 subjects, i.e., 8% of cases), while on average the ascites was less abundant in the GPC (low and moderate in 19 subjects, i.e., 37% of cases). The presence of fluid in the OB correlated with malignancy of the ascites ($P = 0.003$).

The mean density was lower in cirrhotic ascites cases (mean density 6.7 ± 5 HU, minimum 0 HU, maximum 20 HU) compared with malignant ascites (mean density 11.5 ± 5 HU, minimum 0 HU, maximum 20 HU). There was a significant difference between the two groups ($P = 0.01$). The mean thickness of the gallbladder wall was 3.6 mm in Group 1 and 3.1 mm in Group 2. This difference was not significant ($P = 0.42$). This sign could not be analyzed for 22 patients due to a cholecystectomy ($n = 18$) or a scleroatrophic gallbladder ($n = 4$). Thickening of the parietal peritoneum was statistically more common and extensive in malignant ascites ($P = 0.005$) (Fig. 1). Tethered-bowel sign could be analyzed in 71 of 102 patients (69.6%). These were patients with very abundant ascites in the GPC (grade 3). The etiology of the ascites was cirrhotic in 39 cases and malignant in the other 32. In the malignant ascites group, this sign was positive in 28 (87.5%) of the 32 patients in whom this could be tested.

It was never positive in the 39 patients with ascites of cirrhotic etiology. There were four false negatives (12.5%) in the malignant ascites group. Tethered-bowel sign correlated with malignancy of the ascites ($P = 0.005$).

Fig 1: Peritoneal thickening & enhancement in two groups.



DISCUSSION

After observing a different ascites distribution based on etiology, several studies have hypothesized that the presence of fluid in the OB was not a typical manifestation of generalized ascites and that it should lead to testing for involvement of adjacent organs or peritoneal carcinomatosis^{6,7}. The results of our series tally with those findings, showing a different ascites distribution in the two groups. In our study, the presence of fluid in the OB appears to be a differentiating factor between the two types of ascites ($P = 0.003$). We found it in practically all cases of malignant ascites (92%). On the contrary, in cirrhotic ascites, which depends on a portal hypertension mechanism, there was predominantly an accumulation of fluid in the GPC. Other than in cases where ascites was very abundant in the GPC, no ascites was ever found in the OB. We are in agreement with Gore et al⁷ on the hypothesis that fluid transfer between these two spaces is not totally free, despite their theoretical connection through the epiploic foramen.

Protein concentration respectively greater than or equal to 25 g/L or less than 25 g/L has long been a basis for categorizing ascites as exudative (including malignant ascites) or transudative (including cirrhotic ascites). The significant difference in density between our two types of ascites ($P = 0.01$) could reflect a lower protein concentration in cirrhotic ascites. However, this sign appears to be unusable due to significant overlaps in density values. In addition, it is currently acknowledged that the relationship between protein concentration and etiology of ascites has long been overestimated and a source of error. For example, hemodynamic-related cardiac ascites has long been wrongly considered to have a low protein concentration^{8,9}. The same applies to cirrhotic ascites cases, 15% of which have a protein concentration greater or equal to 25 g/L and to malignant ascites cases, 20% of which have a low protein concentration¹⁰. This explains why this indicator has been abandoned and now replaced with calculation of the serum ascites albumin gradient, which is much more sensitive and specific for differentiating ascites associated with portal hypertension (> 11 g/dL) from ascites dependent on other physio-pathologic mechanisms, such as peritoneal inflammation or carcinomatosis (< 11 g/dL). The latter makes it possible to identify the causal mechanism in 97% of cases versus only 55% with protein concentration².

Delayed enhancement of peritoneal fluid has been reported in the literature in situations other than vascular, urinary, or digestive extravasation of contrast. It was shown that this is a nonspecific

phenomenon, exceeding 10 HU in 54% of ascitic patients, regardless of the time to measurement (10—104 minutes), inversely proportional to the amount of fluid, and whose magnitude is independent of the type of contrast injected, serum creatinine levels, and etiology of the ascites (malignant or otherwise) [11]. Later enhancement was observed in a more recent study of 112 subjects. The enhancement could persist for up to 2 days and was present in a smaller number of patients (13%)¹². Contrary to the initial study, this showed a significant relationship between elevated serum creatinine values and the presence of this enhancement (odds ratio 2.2, $P < 0.05$). However, the results of that study should be interpreted cautiously due to the small sample size of patients with cirrhosis ($n=16$) and peritoneal carcinomatosis ($n=12$). The time to enhancement of the ascites is not known. Enhancement was not an analyzable factor in our retrospective study, which focused on CT scans with immediate contrast injection. Its impact on the measurement of density, however, seems limited, since all of our studies were performed with the same delay, the same injection rate, and comparable contrast doses.

Several prior studies report that thickening of the gallbladder wall greater than 3 mm on the ultrasound is a commonly found sign in cirrhotic ascites (82% of cases) and that, conversely, the wall is thin in 95% of cases of malignant ascites¹³. When ascites is present, they suggest that the respective sensitivities and specificities are 83.3% and 87.5% for malignant ascites when this sign is normal, and 84.6% and 91.9% for cirrhotic ascites when there is thickening¹⁴. The results of our study, which find no significant difference in gallbladder wall thickness between the two groups, do not concur. First and foremost, it is possible to think that this discrepancy is related to the fact that our study uses a different procedure, given that ultrasound has proven superior for analyzing the gallbladder wall¹⁵. In fact, our results report frequent thickening of the gallbladder wall in the two groups. If we take into account the fact that the main criticism of CT is that it underestimates the thickness of the gallbladder wall¹⁶ these results prove that the lack of difference is actually not attributable to a lack of sensitivity of the CT scan. After ascites, thickening and enhancement of the parietal peritoneum are the most CT signs most commonly found in cases of peritoneal carcinomatosis (62% of patients).

These signs are, however, absent in cases of cirrhotic ascites⁶. In our series, the frequency of thickening and strong enhancement of the peritoneum was significant in the malignant ascites group (82%). In more than one out of every two cases, the peritoneum was strongly enhanced or showed nodular thickening. Although less frequently, these signs were also found in 23% of cirrhotic ascites

cases, but more weakly in 10 out of 12 cases. In two patients only, the enhancement was deemed moderate. In keeping with the earlier study, no peritoneal nodule was found in the cirrhotic ascites group. In short, thickening and enhancement of the parietal peritoneum appear to be statistically more common and extensive in malignant ascites ($P=0.005$). The likelihood of detecting thickening is increased by the presence of ascites, which makes it easier to locate the parietal peritoneum by emphasizing its contours. One hypothesis is that this thickening may simply be related to the chronicity of the effusion, which would be consistent with the endoscopic and postmortem findings of two studies that confirmed significant remodeling of the peritoneum in decompensated cirrhosis, not found in the control group^{17,18}.

It was initially noticed on the ultrasounds that the way the intestinal loops floated in the peritoneal fluid could predict the etiology of the ascites¹⁹. Similar CT findings established the correlation between peritoneal carcinomatosis and visualization of matted bowel loops that could no longer come in contact with anterior parietal peritoneum (tethered-bowel sign)²⁰.

That study in 40 patients (22 with malignant ascites and 18 with cirrhotic ascites) reported 85% sensitivity and 96% specificity, with only one false positive due to chronic inflammatory bowel disease²⁰. In our study, tethered-bowel sign was the sign with the greatest diagnostic power, when it could be analyzed. It was never found in cases of cirrhotic ascites, but was present in 87% of cases of malignant ascites. Our results turned out to be similar to the study by Seltzer²⁰ with 87.5% sensitivity & 100% specificity.

Our study clearly has several biases, the first being patient selection to form two groups with the same sample size, while the proportions of cirrhotic and malignant ascites cases are very different in the general population. We are also open to criticism for having consciously excluded several cases of ascites with common scenographic signs of peritoneal carcinomatosis. These included cases of tuberculous ascites, effusion in peritoneal dialysis patients, gelatinous ascites, and primary malignant tumors of the peritoneum. It is in fact unusual for these conditions to occur in isolation in our routine practice. In addition, in view of their rarity, it would seem difficult to represent them significantly in a prospective series with a small sample size. Although the specific cases constitute a diagnostic challenge for the radiologist, he/she has only prima facie evidence and can but rarely make the diagnosis when blinded to the clinical and laboratory picture. Finally, as in the cases of malignant ascites, the final proof is most often supplied by the histology or bacteriology, the added value of the CT scan being to point us toward those tests.

Secondly, our study has the handicap of a single observer, which precludes any reproducibility study. A third limitation concerns its retrospective recruitment method. It seems obvious that the positivity of the studied signs correlated with the stage of the carcinomatosis at the time when the examination was performed. In our study, we were not able to distinguish the patients in Group 2 with known peritoneal carcinomatosis at the time of the examination from those with a diagnosis that was confirmed after ascites was discovered on the CT scan. For that reason, the mean stage of disease progression should be more advanced in our series, due to the share of patients with a prior diagnosis of peritoneal carcinomatosis.

Another legitimate comment is the relatively high prevalence in our series of cases of peritoneal carcinomatosis of gastrointestinal origin, and pancreatic in particular (25%), which were greater in number than cases of ovarian cancer (17%), which is the most common etiology in most series in the literature (30—54%). This selection bias, related to our local recruitment, could be responsible for an over estimation of the diagnostic value of localization of fluid in the OB in suspecting peritoneal carcinomatosis, which is anatomically promoted in cases of pancreatic cancer. However, the analysis results in these two subgroups does not lead us in that direction, since ascites is present in the OB with the same frequency in the two main types of cancer. The quantity of fluid in the GPC was also on the same order and abundant in 50% of pancreatic cancer and 55% of ovarian cancer cases. Finally, the association of fluid in the OB with a small or moderate amount of fluid in the GPC was found with the same frequency which was precisely the configuration in which this sign was most important, since it never existed in cases of cirrhotic ascites. Finally, one last reservation is related to the fact that certain signs were not evaluable for all patients. For example, it was possible to analyze tethered-bowel sign only in cases of very abundant ascites in the GPC, which excluded 31% of patients in our study.

CONCLUSION

Although a CT scan is not one of the procedures usually done as part of an ascites workup, we think it can sometimes help refine the etiologic diagnosis when it is done. In our study, tethered-bowel sign was one of two signs with the greatest diagnostic reliability for malignant ascites. Its main limitation is that it was not usable in cases where the amount of ascites was low or moderate, which represent edone-third of all patients. The second was ascites distribution, since predominant localization in the OB was mainly found in malignant ascites. Finally,

thickening and enhancement of the parietal peritoneum was found in both types of ascites, but was most often mild with hemodynamic causes, whereas severe or nodular thickening strongly correlated with the existence of peritoneal carcinomatosis.

REFERENCES

1. Reynolds TB. Ascites. *Clin Liver Dis* 2000;4:151—68 [vii].
2. Runyon BA, Montano AA, Akriviadis EA, Antillon MR. The serum-ascites albumin gradient is superior to the exudate-transudate concept in the differential diagnosis of ascites. *Ann Intern Med* 1992;117:215—20.
3. European Association for the Study of the Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. *J Hepatol* 2010;53:397—417.
4. Moore KP, Wong F, Gines P et al. The management of ascites in cirrhosis: report on the consensus conference of the International Ascites Club. *Hepatology* 2003;38:258—66.
5. Jolles H, Coulam CM. CT of ascites: differential diagnosis. *AJR Am J Roentgenol* 1980;135:315—22.
6. Walkey MM, Friedman AC. CT manifestations of peritoneal carcinomatosis. *AJR Am J Roentgenol* 1988;150:1035—41.
7. Gore RM, Callen PW, Filly RA. Lesser sac fluid in predicting the etiology of ascites: CT findings. *AJR Am J Roentgenol* 1982;139:71—4.
8. Christou L, Economou M. Characteristics of ascitic fluid in cardiac ascites. *Scand J Gastroenterol* 2007; 42: 1102—5.
9. Runyon BA. Cardiac ascites: a characterization. *J Clin Gastroenterol* 1988;10:410—2.
10. Alexandrakis MG, Moschandrea JA, Koulocheri SA. Discrimination between malignant and nonmalignant ascites using serum and ascitic fluid proteins in a multivariate analysis model. *Dig Dis Sci* 2000;45:500—8.
11. Cooper C, Silverman PM, Davros WJ. Delayed contrast enhancement of ascitic fluid on CT: frequency and significance. *AJR Am J Roentgenol* 1993;161:787—90.
12. Benedetti N, Aslam R, Wang ZJ, Joe BN, Fu Y, Yee J, et al. Delayed enhancement of ascites after i.v. contrast material administration at CT: time course and clinical correlation. *AJR Am J Roentgenol* 2009; 193:732—7.
13. Tsujimoto F, Miyamoto Y, Tada S. Differentiation of benign from malignant ascites by sonographic evaluation of gallbladder wall. *Radiology* 1985;157:503—4.
14. Sari R, Yildirim B, Sevinc A, Bahceci F, Hilmioğlu F. Gallbladder contractility in patients with cirrhotic versus malignant ascites. *J Clin Ultrasound* 2002;30:477—80.
15. Noone TC, Semelka RC, Chaney DM, Reinhold C. Abdominal imaging studies: comparison of diagnostic accuracies resulting from ultrasound, computed tomography, and magnetic resonance imaging in the same individual. *Magn Reson Imaging* 2004;22:19—24.
16. Brook OR, Kane RA, Tyagi G, Siewert B, Kruskal JB. Lessons learned from quality assurance: errors in the diagnosis of acute cholecystitis on ultrasound and CT. *AJR Am J Roentgenol* 2011;196:597—604.
17. Buhac I, Jarmolych J. Histology of the intestinal peritoneum in patients with cirrhosis of the liver and ascites. *Am J Dig Dis* 1978;23:417—22.
18. Buhac I. Biopsy of the peritoneum in decompensated cirrhosis of the liver. *Am J Gastroenterol* 1981;76:32—4.
19. Yeh HC, Wolf BS. Ultrasonography in ascites. *Radiology* 1977;124:783—90.
20. Seltzer SE. Analysis of the tethered-bowel sign on abdominal CT as a predictor of malignant ascites. *Gastrointest Radiol* 1987;12:245—9.

