The role of ultrasonography and computed tomography in determining the etiology of ascites

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ABSTRACT

Objective: To determine the role of ultrasonography (US) and computed tomography (CT) in the evaluation of ascites etiology.

Methods: From 2000-2006, patients admitted to the Radiology Department, Uludag University Medical School Hospital, Bursa, Turkey, were studied to determine the etiology of ascites, or those in whom ascites was determined during the course of other investigations were evaluated using US and CT. Existence of septa-debris, accompanying organ pathology, omental involvement, intestinal wall thickening, peritoneal implant, lymph node, diameter of portal vein, thickening of gall bladder wall, pleural effusion, collateral vascular structure, and cavernous transformation were also investigated.

Results: A total of 30 cases were included. Causes were determined to be malignant in 15 (50%) cases and 15 (50%) benign. The US was significantly superior to CT in the evaluation of gall bladder thickening. Omental thickening, thickening of intestinal wall, and peritoneal implant development were seen significantly more frequently in malignant compared to benign cases, while thickening of the gall bladder wall was seen more frequently in benign cases. Ascites density of malignant cases detected in slices without contrast was higher than in benign cases. The probability of malignancy was 98% when omental thickening, thickening of intestinal wall, and peritoneal implant were present together in the same case.

Conclusion: Although CT and US may help to evaluate ascites, however, the differential diagnosis of ascites etiology remains a challenge.

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Ascites is a common clinical problem.[1-3] It may be the first finding of a systemic disease or can develop due to a disease of abdominal origin. Determination of the ascites etiology is necessary for establishing an appropriate treatment plan. In most cases, investigation of the existence of, and reason for, the ascites starts with physical examination and laboratory tests. Ascitic fluid analysis performed following the abdominal paracentesis is an easy and economical method. Clinical diagnosis may be difficult in cases with limited ascites amount. Imaging plays a significant role in patients with ascites for assessing the amount of ascitic fluid, and for assisting sampling or draining of ascitic fluid.[1-5] Ultrasonography (US) and computed tomography (CT) are the primary imaging tools, and magnetic resonance (MR) imaging is used in selected cases such as demonstration of peritoneal or ascitic fluid enhancement, particularly in patients with compromised renal function.[5,6] However, the differential diagnosis of ascites etiology remains a challenge. This prospective and blind study aimed to determine the diagnostic role of CT and US in the evaluation of ascites and determination of its etiology.

Methods.

Patient selection. From 2000-2006, the patients (not in consecutive order) admitted to the Radiology Department, Uludag University Medical School Hospital, Bursa, Turkey, to determine the etiology of ascites, or those in whom ascites was determined during the course of other investigations were included in the study. Patients with impaired renal function were excluded from the study to avoid occurrence of a possible contrast material associated nephropathy. All cases were evaluated with abdominopelvic US and CT. Analyses of ascites material obtained with abdominal paracentesis were performed simultaneously.

All CT examinations were performed with spiral CT system (Somatom Plus, Siemens, Erlangen, Germany) with an evice following a fasting period of at least 4 hours. A CT slice through the umbilical level without contrast was obtained to measure the density of the ascites fluid. A sample of 150 ml non-ionic contrast material was injected intravenously. Assuming the start of contrast material injection as "0" time point, following a lag period of 60 seconds, the examination was performed in 2 separate stages, the upper abdomen first followed with the pelvis. In order to investigate the late-stage ascites staining, a single scan slice was obtained from the reference region through the umbilical level without contrast, 30 minutes after the contrast material injection. By using the region of interest, the density measurements of ascites fluid were performed on 1-2 cm^2 surface areas of images obtained without contrast material administration, at the bolus phase after the contrast material injection, and at 30 minutes. All US examinations were performed using SSA-250A (Toshiba, Tokyo, Japan), by the same radiologist with an evice following a fasting period of at least 4 hours. The US and CT scan examinations were evaluated by 2 radiologists who were blinded to the clinical findings and pathological results of the cases. The results of the evaluations were recorded on previously standardized forms. Existence of septa-debris, accompanying organ pathology, omental involvement, intestinal wall thickening, peritoneal implant, lymph node, diameter of portal vein, thickening of gall bladder wall, pleural effusion, collateral vascular structure, and cavernous transformation were investigated on US and CT examinations. Result of biopsy or surgical intervention was regarded as the gold standard for the pathological diagnosis in all cases. Informed consent was obtained from each patient.

Statistical analysis. Fisher's exact chi-square and Mann-Whitney U tests was carried out to evaluate the consistency of US and CT scan in determining the pathologies, and the pathological differences observed between malignant and benign cases. A p-value of <0.05 indicated a statistically significant difference.

Table 1 - Pathological diagnosis of cases included in the study (n=30).

Diagnosis	N
Hepatic cirrhosis	12
Peritonitis carcinomatosa	10
Metastatic adenocarsinoma of liver	3
Peritoneal mesothelioma	3
Tuberculous peritonitis	2

Table 2 - Pathologies determined with ultrasound (US) and computed tomography (CT).

Pathology	Benign		Malignant	
	US	CT	US	CT
Generalized ascites	11	11	12	13
Septa-debris	3	2	5	4
Organ pathology	13	13	13	13
Omental involvement	1	1	12	12
Thickening of intestinal wall	1	1	6	7
Peritoneal implant	0	1	7	9
Lymph node	4	4	4	4
Increase in portal vein diameter	2	1	1	0
Thickening of gall bladder wall	12	5	3	2
Pleural effusion	5	5	5	5
Collateral vascularization	2	2	0	0
Cavernous transformation	0	0	0	0

US - ultrasound, CT - computed tommography

Table 3 - Density values and staining amount of ascites fluid according to the etiology.

Etiology	Density measurement (Hounsfield unit)		
	Without contrast	Bolus phase	Balance phase
Benign	7.28±3.39	9.44±3.98	12.74±5.05
Malignant	12.41±4.25	15.92±4.21	26.62±7.32

Results. A total of 30 cases (16 male [53%], 14 female [47%]; age range 25 - 71 years, mean 53.9±10.9) were investigated in this study. Malignant and benign causes were determined in 15 (50%) cases each, the definite diagnosis was made in 9 cases (30%) with surgical intervention, and in 21 cases (70%) with biopsy. The diagnoses of cases are presented in **Table 1**. The US and CT pathologies of malignant and benign cases are presented in **Table 2**. The US was significantly superior to CT scan in the evaluation of gall bladder thickening (p<0.01). No significant differences between the 2 methods were observed in the evaluation of the remaining parameters (p>0.05). The density and enhancement of ascites of benign and malignant cases is presented in **Table 3.** The sensitivity, specificity, positive and negative predictive value, and validity rates of significant findings are summarized in **Table 4**. The probability of malignancy approached 98% if omental thickening, thickening of intestinal wall, and peritoneal implant were present in the same case.

Discussion. There are 2 questions that should be answered in cases with suspicion of ascites; first, whether or not ascites exists in the case, and the second

Table 4 - Percentages of ultrasound and computed tomography scan findings showing significant differences between malignant and benign ascites cases.

Findings	Sensitivity	Specificity	PPV	NPV	Validity
Omental thickening	76	91	93	71	82
Thickening of intestinal walls	62	86	93	42	68
Peritoneal implant	68	88	93	57	75
Thickening of gall bladder wall	80	88	86	77	81
Density of ascites	67	60	57	64	63

PPV - positive predictive value, NPV - negative predictive value

is the etiological factor. Our study, when compared to previous studies, covers more parameters regarding determining the etiology. Diagnosis is usually not possible with physical examination; when ascites fluid level is limited, radiological methods such as US and CT should be used.[4] The sensitivity and specificity of US in detection of free intraperitoneal fluid is over 90%.[7,8] However, its value is limited in the presence of overlying bowel gas.[9] Usually, a multiple, fine, complete or incomplete, and mobile strands of fibrin and debris are seen within the ascites. The CT, unlike US, is not limited by bowel gas, however, fails to demonstrate the internal septa.[9,10] According to our study, the US provides a simple, rapid, and highly sensitive approach for the detection of ascitic fluid and other imaging modalities such as the CT and MR are rarely needed. In CT and US studies of peritoneal masses, a group of investigators reported that with the exception of obese patients, and with the help of an appropriate gain adjustment, the US is superior to CT[11] whereas another study group reported that CT has a more prominent role.[12] Ha et al[13] reported that small-sized implants cannot be determined by a CT scan. However, they are easier to determine with CT if the peritoneal implants are calcified.[14] According to Vanhoenacker,[9] the US may demonstrate diffuse hypoechoic peritoneal thickening of 2-6 mm, or irregular nodular thickening with tiny nodules of less than 5 mm, only if a considerable amount of ascites is present. The CT demonstrates smooth, mild peritoneal thickening and pronounced enhancement. Although omental and small bowel mesentery involvement has been demonstrated with US as a hyperechogenic, heterogeneous mass anterior to the bowel CT is the modality of choice to examine the mesentery and omentum.[9] According to our results, the US appears superior to CT in evaluation of gall bladder wall thickness. Although the US is known as a subjective method, dependent on the technician, in our study, there was no significant difference between US and CT, in any of the parameters aside from gall bladder wall thickness. The US examinations were performed by a single radiologist, and this may have contributed in the decreased of chances for technician-dependent mistakes. Additionally, recording of the evaluated parameters on a standardized form for both methods may have prevented oversight of probable pathologies.[15] As the US is accepted as the gold standard for evaluating the biliary system, it is not surprising that it would be more useful in determining the wall thickness.[16-18] Many different mechanisms may have a role in the thickening of the gall bladder wall seen during the course of ascites, which can develop due to intrinsic factors such as cholecystitis, and to extrinsic factors such as hypoalbuminemia and portal hypertension. Hence, an increase in the thickness of the gall bladder wall is a finding more often seen in the course of ascites of benign origin.[19]

A diseased mesentery is characterized by mesenteric thickening, loss of the normal mesenteric configuration and nodular lesions, consisting of micro- (<5 mm) or macro nodules (>5 mm), lymph nodes, or abscesses. Bowel loops may be fixed by a radiating thickened mesentery, creating a "stellate appearance" both on the US and CT.[9] With peritoneal malignant mesothelioma, malignant ascites is a common presentation.[20] In a study investigating the US findings of peritoneal mesothelioma, it was found that in addition to the peritoneal thickening, fixation of intestinal loops, and thickening of the mesentery, ascites was minimal.[21] It has been reported that ascites accumulation in the course of mesothelioma, which is the primary malignant tumor of the peritoneum, is to a lesser degree and this finding may be helpful in the differential diagnosis of mesothelioma and carcinomatous peritonitis.[22] In mesothelioma cases in our study, we found diffuse ascites similar to carcinomatous peritonitis cases. In all cases with mesothelioma and carcinomatous peritonitis, diffuse ascites including mobile septa characterized by thickening of omentum and implants on peritoneum and organ surfaces were observed. Our findings show that those seen during the course of both, these

pathologies display common features and that there is no existing specific radiological method that can contribute to differentiating between them. In fact, all neoplasms with peritoneal dissemination are typically under staged by current radiologic tests (CT, MR), and the variable uptake of sugar by the small bowel limits the use of positron-emission tomography imaging for peritoneal malignant mesothelioma.[20]

Determining the correct diagnosis of abdominal tuberculosis still remains challenging, as the clinical and radiological features have a wide spectrum, mimicking numerous diseases.[9,23,24] According to the results of various studies investigating the US and CT findings, 3 types of tuberculous peritonitis are defined: wet ascetic type characterized by loculated fluid and thickened mesentery, dry plastic type accompanied by adhesion and enlarged lymph nodes with calcification necrosis, and fibrotic fixed type with thickened omentum. The most important cause for the diagnostic problem is that the US and CT scan vary according to the mentioned types. Thickened omentum and peritoneum sheets due to granulomatous infiltration, hypodense lymph nodes connected centrally to the necrosis, moving fibrin septa, radial accumulation of intestinal loops resulting in sliced bread appearance, granulomas on liver and spleen surface, and high density ascites are the findings seen during the course of tuberculous peritonitis, however, they are not specific.[9,13,22-29] These findings are similar to those seen during the course of ascites of malignant origin, and a differential diagnosis is not possible.[9,23,24] Extension of the inflammation through the peritoneum into the extraperitoneal compartment suggests tuberculosis and can be helpful in the differential diagnosis from peritoneal carcinomatosis.[9,30] In our study population, in the course of peritonitis in 2 cases, diffuse ascites characterized by thick and mobile septa was present. Solid organ pathology was not identified in the cases. In one of these cases, small nodular formations on the omentum were observed. According to our results and in accordance with the literature, tuberculous peritonitis is a pathology that displays nonspecific radiological findings, which do not permit differentiation from malignant cases. However, ascites due to tuberculous peritonitis was seen in only 2 cases of our study population, and the small number may preclude appropriate interpretation of the situation.

In cases with liver cirrhosis, which accounted for the majority of our cases of benign origin, diffuse ascites without septa and debris was found. An umbilical vein enlargement in one case, and collateral vascular formation development in the distal esophagus and gastric fundus in another, were determined, which were essentially portal hypertension findings and suggested that ascites was due to a benign cause. Additionally, detection of radiological findings of liver cirrhosis, such as accompanying nodular formations on hepatic boundaries, left lobe and caudal lobe hypertrophy, and right lobe atrophy, contributed to the diagnosis.[29] This fact shows that secondary findings seen during the course of the disease may assist in the diagnosis.

There is a continuous material exchange between the vascular bed and peritoneal space. The density of simple ascites varies between 0-30 Hounsfield unit. In the etiology of an ascites with a higher density, extravasation of proteins, leukocytes, blood content or contrast material into the peritoneal cavity should be considered.[31-33] In malignant cases, fragile neo vascularization, leakage of protein-like fluid or blood from the tumor implants and secretion of substances from tumor cells that increase the vascular permeability are mentioned as the cause of the ascites staining.[33,34] Cooper et al,[34] investigated the staining of ascites fluid in late images following contrast material administration and stated that in relation to the underlying pathology, vascular-peritoneal permeability of the peritoneum was increased and staining could be enhanced. These investigators suggested that the amount of staining was independent from the type of contrast material, latency period, and clinical diagnosis of the cases, and reported that the amount of the staining is mainly determined by the amount of ascites.[34] It is natural that in the course of an excess amount of ascites, the dilution of the contrast material leaking to the peritoneal cavity as the increased permeability will prevent enhanced staining of the ascites. In our study, density measurements and calculations of staining amount performed in the slices without contrast, following the contrast injection during bolus and balance phase showed that density measurements of malignant cases without contrast showed a statistically significant difference compared to benign cases. This result seems to be related, as malignant ascites is rich in protein and blood content. However, the low sensitivity (68%) of this finding limits its role in the differentiation of benign-malignant cause. We determined that the amount of ascites staining is not a subsidiary finding for differential diagnosis. This result supports the interpretation that the staining amount is related to the ascites amount.

It was not possible to show the surgical correlation of all the radiological findings in view of the invasiveness of procedures. Additionally, the limited case number in some issues prevented generalization of our conclusions. It is expected that MR, which is the best method given its soft tissue resolution potential, may give valuable information with regard to differential diagnosis.[6] However, the fact that MR was not applicable in all cases in our study is one of its drawbacks. According to our results in patients with ascites, the combination of the US and CT may help to obtain the correct etiological factor. A large study should be carried out

to obtain better results with MR examination, and the role of radiology in determining etiology may also be improved.

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