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Delayed Enhancement of Ascites After IV Contrast Material Administration at CT: Time Course and Clinical Correlation

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Abstract

OBJECTIVE—The objective of our study was to determine the prevalence and clinical predictors of delayed contrast enhancement of ascites.

MATERIALS AND METHODS—In this retrospective study, 132 consecutive patients with ascites who underwent repeated abdominopelvic CT examinations performed within 7 days of each other were identified. These patients included 112 patients who received and 20 who did not receive IV contrast material at the initial CT examination. For each examination, we recorded the CT attenuation of the ascites. For the follow-up scan, the presence of delayed enhancement of ascites was defined as an increase in CT attenuation > 10 HU over baseline. The Fisher's exact test, unpaired Student's *t* test, and logistic regression were used to determine predictors of delayed enhancement of ascites.

RESULTS—A threshold increase in the attenuation of ascites by > 10 HU or more between the initial and follow-up CT examinations occurred only when IV contrast material was given with the initial examination. The increased attenuation was due to delayed contrast enhancement of ascites and occurred in 15 of the 112 patients (13%). Of the 16 patients scanned less than 1 day apart, 10 (63%) showed delayed enhancement of ascites. Delayed enhancement was not observed 3 or more days after IV contrast material administration. For each 1 mg/dL increase in serum creatinine level, the likelihood of delayed enhancement of ascites increased (odds ratio, 2.02; 95% CI, 1.11–3.69). Multivariate logistic regression showed that a short time interval between examinations ($p < 0.001$), increased serum creatinine level ($p < 0.001$), and presence of loculated ascites ($p = < 0.01$) were independent predictors of the magnitude of delayed enhancement of ascites.

CONCLUSION—Delayed contrast enhancement of ascites occurs commonly after recent prior IV contrast material administration and should not be mistaken for hemoperitoneum or proteinaceous fluid such as pus.

Keywords

abdomen; ascites; contrast media; CT; delayed enhancement

At CT, simple ascites typically measures between –20 and 20 HU and is commonly seen with a wide range of processes, including simple fluid overload, congestive heart disease, cirrhosis, intraperitoneal inflammation, neoplasm, trauma, or recent surgery [1]. In contrast, the finding of high-attenuation ascites raises concern for an acutely life-threatening process such as hemoperitoneum, visceral perforation with intraperitoneal extravasation of contrast material from the gastrointestinal or urinary tract [2,3], or peritonitis [4]. A previously described caveat to this useful rule is the phenomenon of benign delayed contrast enhancement of ascites.

Published case reports and small case series have shown that the CT attenuation of ascites increases on delayed scans obtained 10 minutes–7.5 hours after an initial IV contrast-enhanced examination [5–8]. A large patient study has not been previously performed, to our knowledge, to define how often delayed enhancement of ascites occurs, how long it lasts, what patient factors may contribute to its appearance, or whether apparent enhancement occurs without IV contrast material. With the increasing reliance on CT to diagnose and monitor intra-abdominal processes, it has become commonplace to perform repeated short-interval CT examinations, often within days of each other, so the importance of understanding the phenomenon of benign delayed contrast enhancement of ascites is growing. Therefore, the purpose of our study was to retrospectively determine the prevalence, magnitude, and clinical predictors of delayed contrast enhancement of ascites.

Materials and Methods

Patient Selection

This retrospective study was approved by our institutional review board and did not require informed consent. We performed a computerized search of our radiology information system (IDXrad, software version 9.7.1, IDX Systems Corporation) for the period January 1, 2005, through December 31, 2007, and identified all patients imaged at our institution who had homogeneous-appearing ascites and two or more abdominopelvic CT examinations performed within 7 days of each other. Eleven patients with proven hemoperitoneum were excluded. Additionally, three patients who underwent a recent nonabdominopelvic contrast-enhanced CT examination were excluded because the baseline CT attenuation of ascites was not available.

The final study population of 132 patients was sorted into two groups: The case group consisted of 112 consecutive patients who received IV contrast material at the initial CT examination and the control group consisted of 20 consecutive patients who did not receive IV contrast material at the initial CT examination. Patient demographics are summarized in Table 1. The average age of the study population was 54 years (range, 1–94 years) and there were 70 males (53%) and 62 females (47%). The indications for the initial CT examinations were to evaluate for abscess or infection ($n = 35$), surgical complication ($n = 17$), or possible neoplasm ($n = 14$); identify a cause for abdominal pain ($n = 25$); or miscellaneous ($n = 41$). The indications for the short-interval follow-up CT scans were to evaluate for abscess or infection ($n = 28$) or possible neoplasm ($n = 13$); imaging guidance for a procedure ($n = 20$); identify a cause for abdominal pain ($n = 12$); or miscellaneous ($n = 59$).

CT Technique

CT examinations were performed using MDCT scanners (LightSpeed, GE Healthcare). All 112 patients in the case group received IV contrast material at the initial CT examination (150 mL of iohexol [Omnipaque 350, GE Healthcare]), and none of the 20 control patients received IV contrast material at the initial CT examination. Additionally, 54 patients in the case group (48%) and six patients in the control group (30%) received oral contrast material (800 mL of meglumine diatrizoate [Hypaque, Sanofi-Aventis]) at the initial CT examination.

Image Interpretation

One attending abdominal radiologist with 6 years of subspecialty experience reading abdominopelvic CT scans and one trainee, both without any knowledge of the clinical data, reviewed all 269 CT scans by consensus on a PACS workstation (Impax, Agfa). Three randomly chosen and non-overlapping attenuation measurements were recorded in an area of uniform density using manually drawn oval (mean $\pm$ SD, $1 \pm 0.05 \text{ cm}^2$) regions of interest (ROIs) at similar locations on pairs of CT scans. The readers also recorded the size of the ascites

as small, moderate, or large and recorded whether the ascites was visibly loculated. Collections were considered to be loculated if findings of mass effect with rounded convex borders with the adjacent structures were identified. The size of the ascites was determined by the following criteria: small, less than 3 cm in shortest dimension; moderate, 3–6 cm in shortest dimension; and large, greater than 6 cm in shortest dimension.

Clinical Data

The clinical medical records were reviewed to record the following: serum creatinine level and albumin value within 1 day of the initial and second CT examinations, history of abdominal surgery within 14 days before the initial CT examination, a pathologic (tissue) diagnosis of cancer, presence of peritoneal carcinomatosis, and presence of cirrhosis. The mean of the serum creatinine and albumin values from the initial and second scan dates were calculated and used for all analyses. Serum creatinine measurements were unavailable in seven patients and albumin values were unavailable in 54 patients. Among the patients with significant delayed enhancement of ascites, which is defined later in this article, all medical records were reviewed to determine potential explanations for the increased attenuation of ascites.

Data and Statistical Analysis

The mean attenuation of ascites on each examination and the SD of CT attenuation measurements were calculated from the three ROI measurements, and the difference in average attenuation between scans was calculated by subtracting the mean attenuation of ascites from the initial examination from that of the subsequent examination. Delayed enhancement of ascites was considered to be present when the CT attenuation of ascites increased by at least > 10 HU and also by at least two times the SD of the three attenuation measurements calculated for each scan [5].

Fisher's exact test and the unpaired Student's t test were used to compare the demographic, clinical, and imaging characteristics of patients with and those without significant delayed enhancement of ascites. Among patients with evidence of delayed enhancement of ascites (change in attenuation > 10 HU and > 2 times the largest SD), five patients had a third examination performed within 7 days of the initial examination and the attenuation of ascites was plotted over the three time points for those five patients.

Multivariate linear and logistic regression models were obtained with the change in attenuation or presence of delayed enhancement of ascites, respectively, between pairs of CT scans in the case group as the outcome variable and days between scans, serum creatinine level, and loculated ascites as the predictors. The predictors were selected for use in the multivariate analysis if their univariate p value was less than 0.1. All statistics were calculated using a Stata software package (version 8.0, Stata Corporation). A p value of less than 0.05 was considered to be significant.

Results

Descriptive Statistics and Univariate Analysis

The threshold increase in ascites attenuation of > 10 HU between the initial and follow-up CT examinations occurred only when IV contrast material was given at the initial CT examination and was due to delayed contrast enhancement of ascites. Among those who received IV contrast material at the initial CT scan, 15 showed delayed enhancement of ascites. Among the patients with delayed enhancement, the change in attenuation of ascites ranged from 10 to 25 HU with a mean of 16 HU (Table 1 and Fig. 1), and the time between CT scans ranged from 2.9 hours to 2.6 days with a mean of 22 hours; the change in attenuation of ascites was not observed more than 3 days after the initial scan. Among patients without delayed enhancement of ascites, the

change in attenuation of ascites ranged from -8 to 9 HU with a mean of 1 HU, and the time between scans ranged from 3.6 hours to 7.5 days with a mean of 3.9 days. Among the 16 patients with follow-up scans that were obtained less than 1 day after the initial IV contrast-enhanced CT scan, 10 (63%) had delayed enhancement of ascites. Among the 22 patients with scans 1–2 days after the initial IV contrast-enhanced CT, four (18%) showed delayed enhancement of ascites (Fig. 2).

The Student's *t* test showed that patients with delayed enhancement of ascites were imaged with a shorter mean time interval between the initial IV contrast-enhanced CT examination and the subsequent examination (0.9 vs 3.9 days, respectively, $p < 0.001$), had a higher mean serum creatinine level (2.4 vs 1.2 mg/dL, respectively, $p = 0.006$), had a higher frequency of peritoneal carcinomatosis (75% [3/4] vs 19% [9/47], respectively, $p = 0.041$), and had a higher frequency of loculated ascites (33% [5/15] vs 1% [1/97], respectively, $p < 0.001$). Age, sex, size of ascites, albumin value, cirrhosis, recent surgery, cancer, and administration of oral contrast material at the initial examination were not associated with delayed enhancement.

Of the five patients with three CT examinations performed within 7 days, all showed an increase in the attenuation of their ascites within 1 day followed by a return to baseline values within 7 days for the patients who did not receive IV contrast material with the second CT scan (Fig. 3). One of the two patients who received IV contrast material with the second scan had persistent delayed enhancement of ascites at the third follow-up scan.

Multivariate Analysis

A multivariate linear regression model showed that independent predictors of increased CT attenuation of ascites after an initial IV contrast-enhanced scan were a short time interval between the initial and subsequent CT examinations ($p < 0.001$), higher serum creatinine levels ($p < 0.001$), and presence of loculated ascites ($p < 0.01$). Peritoneal carcinomatosis was not an independent predictor of increased CT attenuation of ascites in this model ($p = 0.190$).

A separate multivariate logistic regression model showed that there was an 83% decrease in the likelihood of finding delayed enhancement for each additional day between the initial IV contrast-enhanced examination and subsequent CT examination (odds ratio, 0.17; 95% CI, 0.06–0.52; $p < 0.005$) and that there was a 200% increase in the likelihood of finding delayed enhancement of ascites for each 1 mg/dL increase in serum creatinine level (odds ratio, 2.02; 95% CI, 1.11–3.69; $p < 0.05$).

Chart Review

Review of the medical records showed that none of the 15 patients with delayed enhancement of ascites had clinical or laboratory evidence of or underwent subsequent treatment for an acute intraabdominal hemorrhage, bowel perforation, or peritonitis. In contrast, clinical radiology reports for two of these 15 patients (13%) raised concern for an acute abdominal catastrophe: One of the reports suggested bowel perforation with extravasation of oral contrast material and the other suggested proteinaceous fluid, such as pus, as an explanation for the delayed enhancement of ascites (Fig. 4). None of the 15 radiology reports mentioned benign delayed enhancement of ascites as a possible explanation for the increased attenuation of the ascites.

Discussion

Our results show that delayed enhancement of ascites can be seen up to 3 days after initial administration of IV contrast material. The magnitude of delayed enhancement is greater when the prior IV contrast administration is more recent and when the serum creatinine level is higher. The likelihood of observing delayed enhancement drops by 83% for each additional

day beyond the time of the initial IV contrast material administration. Furthermore, the likelihood of finding delayed contrast enhancement of ascites is greater with the finding of loculated ascites. Nonrecognition of the phenomenon of benign delayed enhancement of ascites resulted in misdiagnosis of abdominal catastrophe in 13% of the cases in our series.

Delayed enhancement of ascites was misdiagnosed as hemoperitoneum and bowel perforation in two patients. Furthermore, none of the radiology reports mentioned delayed enhancement as a possible explanation for the increased attenuation of ascites. In some cases, high-attenuation ascites caused by hemoperitoneum may be easily distinguished from delayed contrast enhancement. With delayed contrast enhancement of ascites, the abdominal fluid is homogeneously high attenuation (Fig. 4B). A new intraperitoneal hemorrhage may be similar in attenuation to the surrounding abdominal fluid, but within hours, the intraperitoneal blood will clot, showing focal areas of increased attenuation compared with the surrounding abdominal fluid. Another imaging finding in fresh intraperitoneal hemorrhage is the hematocrit effect with erythrocytes layering dependently in the abdomen or pelvis [9].

In prior reports, investigators have shown the phenomenon of delayed enhancement with increases in attenuation of 7 to 80 HU for time intervals of 10 minutes to 7.5 hours [5–8]. Ours is the first systematic study to address delayed enhancement of ascites beyond 7.5 hours and to evaluate for predictors of this benign process. For CT scans obtained less than 1 day apart, our study found that 63% of patients showed delayed enhancement of the ascites. This finding is consistent with that of a previous study that showed delayed enhancement of ascites in 54% of patients with a 10-minute to 1.7-hour time delay between IV contrast material injection and follow-up CT [5]. The same prior study found that the size of ascites was inversely proportional to the degree of enhancement [5]. We did not find this correlation, possibly related to the longer time interval between the examinations in our study compared with this prior study. Another difference is that we found serum creatinine level to be a predictor of both a higher magnitude and a greater likelihood of delayed enhancement of ascites, whereas the prior study did not find this result [5]. This difference in results can be explained simply on the basis of method: The prior study used a binary, and hence less sensitive, measure of renal failure versus normal renal function, whereas our study addressed serum creatinine level as a continuous variable.

The mechanism of delayed enhancement of ascites remains unknown, but our findings support prior speculation that it may be related to increased vascular–peritoneal permeability due to abdominal disease or injury [5]. Our finding that delayed enhancement is more common in patients with peritoneal carcinomatosis or loculated ascites supports this claim because both processes are associated with increased vascular permeability. Additionally, loculation of fluid may prolong the dwell time of contrast material by restricting diffusion of contrast material out of this contained fluid. However, most of the patients with delayed enhancement of ascites did not have peritoneal disease, and we found that a strong predictor for delayed enhancement of ascites was poor renal function. Poor renal excretion of IV contrast material results in a prolonged dwell time of radiodense material in the body. In particular, water-soluble iodinated contrast materials are all of small molecular size, less than 2 kDa, and are known to readily diffuse through the pores of vasculature into the extravascular extracellular space [6,8,10]—including into third-space fluid collections such as ascites. Given the direct correlation between the magnitude of delayed enhancement and serum creatinine level, another possible cause is retained contrast material in the body due to decreased renal excretion. Another new finding in our study is the occurrence of delayed contrast enhancement in loculated ascites, suggesting that the inflammatory process leading to loculation also increases the permeability of the blood–peritoneum barrier.

Our study has a number of limitations. First, it is a retrospective study. Patients had various times between studies and had only 2–3 CT examinations performed within a 7-day period.

Although our study addressed delayed enhancement of the ascites beyond 7.5 hours, a previous study has shown that it may be present as early as 10 minutes [5]. An ideal study design would be to image patients multiple times at set time intervals to fully understand the time to peak and the time to return to baseline for the attenuation of ascites. However, a study of this design would be unethical given the risks of unnecessary radiation exposure. A benefit of our study design is that patients who underwent repeated CT examinations for clinical reasons were evaluated, so our study group probably resembles the type of patient in whom delayed enhancement of ascites is likely to be seen.

A second limitation is that we did not investigate whether IV contrast material administered for the follow-up examination may potentially cause an increased attenuation of the ascites so as to mimic delayed enhancement. However, all the CT scans were obtained within 80 seconds of administration of IV contrast material; therefore, significant enhancement of ascites at that time on the follow-up scans is unlikely.

A third limitation is that renal function was not optimally assessed because serum creatinine level is a rough estimate of overall renal capacity. In this analysis, we judged estimated glomerular filtration rates (GFR) as a suboptimal alternative because the most accepted estimated GFR calculations are known to be inaccurate for patients with normal or only mildly impaired renal function [11], which comprise most of the patients in our study.

A fourth limitation is that the researchers were not blinded to the time interval between studies or the use of IV contrast material, but we believe that the objective measurement of CT attenuation is unlikely to be subject to bias.

Last, our study did not contain a control group of patients with documented hemoperitoneum or extravasation of contrast material from the bowel or urinary tract. Future study will be needed to determine CT findings, such as a marbled appearance of fluid or fluid–debris levels, that may be useful for distinguishing true abdominal catastrophe from benign delayed enhancement of ascites.

In conclusion, our study showed that delayed contrast enhancement of ascites occurs commonly after recent prior IV contrast material administration and should not be mistaken for intraperitoneal catastrophe. The likelihood of finding delayed enhancement of ascites increases with a shorter time interval between the initial IV contrast-enhanced examination and subsequent CT examination and with higher serum creatinine levels.

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Fig. 1.

Scatterplot of time interval between initial and follow-up CT examinations versus change in CT attenuation of ascites. At time of initial CT examination, 112 patients received IV contrast material. Fifteen of those 112 patients showed delayed enhancement of ascites. None of 20 patients who had undergone unenhanced CT or CT with oral contrast material for initial CT examination had delayed ascites enhancement on follow-up scan (data not shown). Changes > 10 HU (*dashed line*) were considered to represent delayed contrast enhancement of ascites.

Fig. 2.

Histogram shows percentage of patients with delayed enhancement of ascites on follow-up CT versus number of days after initial IV contrast-enhanced CT examination that follow-up CT was performed.

Fig. 3.

CT attenuation of ascites for five patients with more than two consecutive CT examinations performed less than 1 week apart. Initial CT examination for all five patients was obtained with IV contrast material. For patients 1 and 2, second examination was also performed with IV contrast material.

Fig. 4.

68-year-old woman with abdominal pain who underwent imaging to be evaluated for small-bowel obstruction. Avg = average attenuation within the region of interest.

A and B, Initial CT scan (**A**) obtained with IV contrast material shows ascites and follow-up CT scan (**B**) obtained 26 hours after **A** shows high-attenuation ascites. High-attenuation ascites was misdiagnosed as extravasation of oral contrast material from perforated bowel. Clinically, patient did not have evidence of bowel perforation, and her symptoms resolved spontaneously.

TABLE 1

Characteristics of Patients With and Those Without Delayed Enhancement of Ascites on After an Initial CT Examination With or Without IV Contrast Material

Parameter	Initial CT Performed With IV Contrast Material (n = 112)			Initial CT Performed Without IV Contrast Material (n = 20)
	Delayed Ascites Enhancement (n = 15)	No Delayed Ascites Enhancement (n = 97)	p	
Demographics				
Age (y)				
Mean $\pm$ SD (range)	54 $\pm$ 24 (1–85)	54 $\pm$ 17 (15–94)	0.9902	62 $\pm$ 14 (38–95)
Sex				
No. (%) of males	5 (33)	53 (55)	0.104	12 (60)
CT parameters				
Time between initial and follow-up CT, mean $\pm$ SD (d)	0.9 $\pm$ 0.7	3.9 $\pm$ 2.1	< 0.001	3.0 $\pm$ 2.5
No. (%) of patients who received oral contrast material at initial CT	10 (67)	44 (45)	0.104	6 (30)
Clinical data				
Serum creatinine level ^a , mean $\pm$ SD (mg/dL)	2.4 $\pm$ 2.7	1.2 $\pm$ 1.3	0.006	2.7 $\pm$ 2.2
Albumin value ^b , mean $\pm$ SD (U/L)	1.9 $\pm$ 0.6	2.2 $\pm$ 0.7	0.220	1.9 $\pm$ 0.5
Surgery performed < 14 d before initial CT, no. (%) of patients	2 (13)	28 (29)	0.347	4 (20)
Cancer, no. (%) of patients	4 (27)	47 (48)	0.164	8 (40)
Peritoneal carcinomatosis, no. (%) of patients	3 (75)	9 (9)	0.041	0 (0)
Cirrhosis, no. (%) of patients	1 (7)	15 (15)	0.691	1 (5)
Imaging findings				
Change in ascites CT attenuation (HU)				
Mean $\pm$ SD (range)	16 $\pm$ 4.1 (10–25)	1 $\pm$ 4.2 (–8 to 9)	NA	0 $\pm$ 4.2 (–6 to 7)
Size ^c of ascites, no. (%) of patients			0.341	
Small	4 (27)	43 (44)		8 (40)
Medium	6 (40)	25 (26)		7 (35)
Large	5 (33)	29 (30)		5 (25)
Loculated ascites, no. (%) of patients	5 (33)	1 (1)	< 0.001	0 (0)
Attenuation of ascites (HU)				
Mean at initial scan $\pm$ SD (range)	13 $\pm$ 6.3 (2–28)	13 $\pm$ 4.9 (5–30)	0.986	14 $\pm$ 6.8 (4–31)
Mean at follow-up scan $\pm$ SD (range)	30 $\pm$ 6.0 (6–40)	15 $\pm$ 5.4 (2–30)	< 0.001	14 $\pm$ 6.9 (5–35)

Note—Fisher's exact test and unpaired Student's *t* test were used for univariate significance levels comparing those with and those without delayed contrast enhancement of ascites. **Boldface** indicates *p* < 0.05 and was considered to be statistically significant. NA = not applicable.

^aUnavailable in seven patients.

^bUnavailable in 54 patients.

^cThe size of the ascites was determined by the following criteria: small, < 3 cm in shortest dimension; moderate, 3–6 cm in shortest dimension; and large, > 6 cm in shortest dimension.