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When do heterogeneous splenic enhancement patterns occur in contrast-enhanced CT studies of the abdomen?

Reinhard Groell[1], Rainer Rienmüller[1], Martin M. Uggowitzer[1], Christian Kugler[1], Rudolf E. Stauber[2], Peter Fickert[2]

[1] *Department of Radiology, University Hospital Graz, Austria*
[2] *Department of Internal Medicine, University Hospital Graz, Austria*

Background. *This study determines when heterogeneous splenic enhancement patterns occur in contrast-enhanced CT in patients with and without liver cirrhosis.*

Patients and methods. *Electron-beam CT of the abdomen was performed in 195 patients following intravenous injection of contrast agent according to one of three injection protocols (protocol 1: n=132, 120 ml, 2 ml/sec, scan delay: 50 sec; protocol 2: n=30, 90 ml, 3 ml/sec, scan delay:10 sec; protocol 3: n=33, 50 ml, 5 ml/sec, scan delay: 10 sec). Thirty-four of these patients had liver cirrhosis.*

Results. *A heterogeneous splenic enhancement pattern was observed in 77% (protocol 2) and 65% (protocol 3) of the patients without liver disease and in 23% (protocol 2) and 20% (protocol 3) of the patients with liver cirrhosis. A heterogeneous enhancement pattern was visible between 14 and 58 sec after the administration of contrast agent. In all patient groups and protocols it never occurred later than 58 sec following the contrast agent application. Three patients had a splenic lesion (hemangioma, lymphoma, metastasis), these lesions were also visible after 58 sec following the injection.*

Conclusions. *These results indicate that heterogeneous splenic enhancement patterns do not occur later than 58 sec after the contrast agent injection, even when the contrast agent is still being injected at that time.*

Key words: tomography, X-ray computed, electron-beam, enhancement; splenomegaly, liver cirrhosis

Introduction

With the advent of fast imaging methods providing high temporal and spatial resolution (fast magnetic resonance imaging, helical- and electron-beam computed tomography) a heterogeneous splenic enhancement pattern is frequently observed after the administration of iodinated or gadolinium-based contrast agents.[1-3] These heterogeneous enhancement patterns are regarded as reflecting the pathways of splenic microcirculation.[3] The interpretation of these heterogeneous patterns may be a matter of concern, as they may mimic focal or diffuse splenic lesions such as metastases, hemangiomas, lymphatic infiltration, or infarction.

The objectives of this study were to deter-

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Correspondence to: Reinhard Groell, MD, Department of Radiology, University Hospital Graz, Austria, Auenbruggerplatz 9, A - 8036 Graz, Austria; Phone: +43 316 385 2411; Fax: + 43 316 385 3231; E-mail: reinhard.groell@kfunigraz.ac.at

mine how long heterogeneous splenic enhancement patterns normally persists, and beyond which time the radiologist should worry about focal or infiltrative splenic diseases.

Methods

The study group consisted of 195 patients who were referred for electron-beam CT (Evolution, Siemens, Erlangen, Germany) of the abdomen. The patients were examined according to one of 3 different contrast agent injection protocols using the same non-ionic contrast agent (iopromide 300mgI/ml, Ultravist, Schering, Berlin, Germany) which was applied by power injector (Angiomat 6000, Liebel-Flarsheim, Cincinnati, Ohio) (Table 1). The non-dynamic CT-protocol 1 represented the routine protocol for patients referred to our department for CT studies of the abdomen. This protocols mimics that in use for spiral CT of the abdomen. The dynamic CT-protocols 2 and 3 were used in patients with suspected focal or diffuse liver lesions to evaluate hepatic perfusion.

Protocol 1

The study group consisted of 121 patients (66 male, 45 female, mean age: 56±15 years) without and 11 patients (7 male, 4 female, mean age 60±10 years) with clinical and biochemical signs of liver cirrhosis. In 4 patients the diagnosis of cirrhosis was also confirmed by biopsy. The electron-beam CT images were acquired in mid-inspiration using an incremental „single-slice mode" in the cranio-caudal direction (exposure time: 500 msec, interscan delay: 1.3 sec, slice thickness: 6 mm). The scans were taken after intravenous application of 120 ml of contrast agent at a flow rate of 2 ml/sec. The scan was taken with a delay of 50 sec after the contrast agent injection had been started. The exact time of image administration was documented automatically on each CT image.

Protocol 2

Dynamic electron-beam CT of the abdomen was performed in 30 patients of whom 13 patients (8 male, 5 female, mean age: 61±10 years) had biopsy proven liver cirrhosis. Seventeen patients (4 male, 13 female, mean age = 42±14 years) without liver cirrhosis were examined because of suspected liver lesions (later proven by biopsy as: focal nodular hyperplasia n=12, hepatic adenoma n=1, hepatic hemangioma n=2). All 30 patients were studied using a „multi-slice mode" for „flow studies" with 6 levels covering a volume of 5.6 cm in the z-axis without table movement (exposure time 50 msec, slice thickness 8 mm, 6 levels). Ninty ml of non-ionic contrast agent was injected into an antecubital vein with a flow of 3ml/sec. Scans were taken 10, 12, 14, 16, 20, 24, 28, 38, 48, 58, 88, 118, 148 sec after the injection had been started. The scans were performed in inspiration, therefore the patients were asked to hold their breath for the first 18 sec and were instructed to breathe between the subsequent scans.

Table 1. Protocols of contrast agent injection

	Amount of CA (ml)	Injection rate (ml/sec)	Bolus duration (sec)	Scan delay (sec)	Scan mode
Protocol 1	120	2	60	50	SSM
Protocol 2	90	3	30	10	MSM
Protocol 3	50	5	10	10	MSM

SSM=single-slice mode. MSM=multi-slice mode. CA=contrast agent

Protocol 3:

Thirty-three patients with suspected liver lesions were examined using identical electron-beam CT image acquisition parameters as described in protocol 2. However, contrary to protocol 2, a contrast agent flow of 5ml/sec and a volume of 50ml were used. Ten patients (8 male, 2 female, mean age: 54±5 years) had clinical and biochemical signs of liver cirrhosis, in 6 of these patients cirrhosis was also confirmed by biopsy. In 23 patients (13 male, 10 female, mean age: 53±12 years) neither clinical signs nor CT-evidence of liver cirrhosis were found. Six of these 23 patients revealed a liver lesion (focal nodular hyperplasia: n=2, hemangioma: n=1, metastasis: n=3).

Image analysis

Each study was qualitatively analyzed on a digital image workstation (DRC104, Siemens, Erlangen, Germany) independently by consensus of two radiologists. In addition to the standard window settings (window center: 30 HU, window width: 300 HU) the readers changed the center and width of the windows as they felt necessary. Any visible irregular or non-homogenous enhancement of the spleen visualized on any image level was defined as a heterogeneous enhancement pattern. Additionally, in the dynamic CT studies using protocol 2 and 3 the times were documented when a heterogeneous enhancement pattern became visible and when it disappeared.

A Wilcoxon rank sum test (p=0.05) was used to compare the aortic enhancement and the time frames of splenic enhancement patterns of protocol 2 and 3 in cirrhotic and in non-cirrhotic patients.

Results

In 3 patients examined with protocol 1, splenic cysts were seen with a diameter of 1-3 cm which were later confirmed by sonography. In three of the patients examined with protocol 2, one patient had splenic hemangioma, one patient had biopsy proven splenic lymphoma and a third patient had splenic metastasis of a breast carcinoma. The hemangioma was confirmed by sonography and by prior conventional CT studies. The metastasis was confirmed by follow-up examinations.

Table 2. Times of the occurrence of heterogeneous splenic enhancement patterns on electron-beam CT of the abdomen

				Visualization of heterogeneous splenic enhancement patterns		
	n		n	Start [sec]	End [sec]	Duration [sec]
Protocol 2	30	non-cirrhotic	17	22.5±2.5 (20-28)	33.1±6.7 (24-58)	10.6±7.6 (4-34)
		Cirrhotic	13	25.3±4.3 (24-28)	41.3±4.7 (38-48)	16.0±5.9 (14-24)
Protocol 3	33	non-cirrhotic	23	21.7±3.5 (14-28)	29.9±5.1 (24-38)	8.1±5.6 (4-24)
		Cirrhotic	10	19.0±1.0 (18-20)	33.0±5.0 (28-38)	14.0±4.0 (10-18)
p-value*		cirrhotic vs. non-cirrhotic		0.65	0.04	0.08

The times are calculated in seconds from the start of injection. The numbers indicate the mean times and their standard deviation (mean±SD), the time range (minimum-maximum) is listed in the parentheses below.
*Wilcoxon rank test.

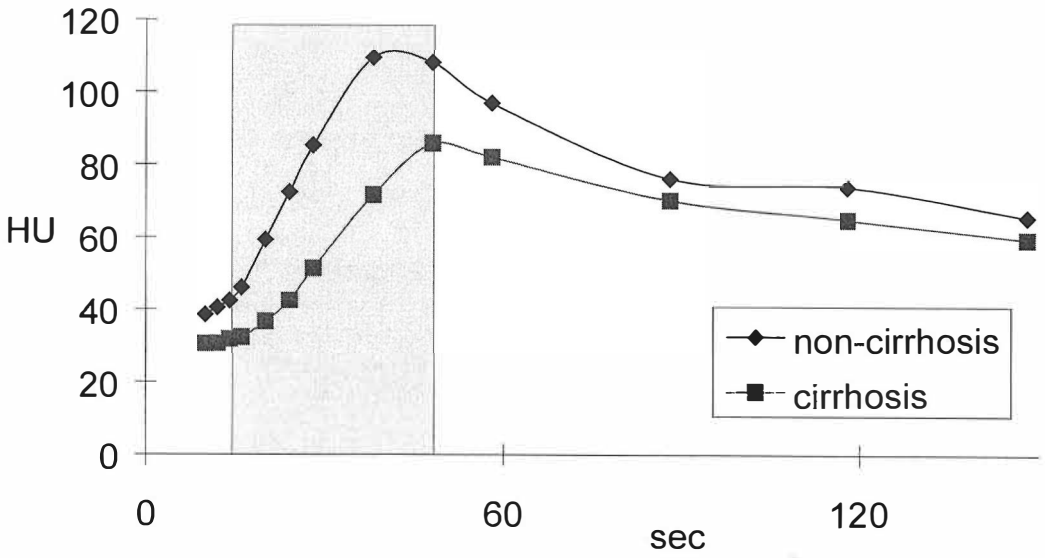

Figure 1a. Mean time-density-curves of the spleen for the patients studied according to protocol 2. In none of the patients did a heterogeneous enhancement pattern (marked area) occur later than 60 sec after the contrast agent injection had been started.

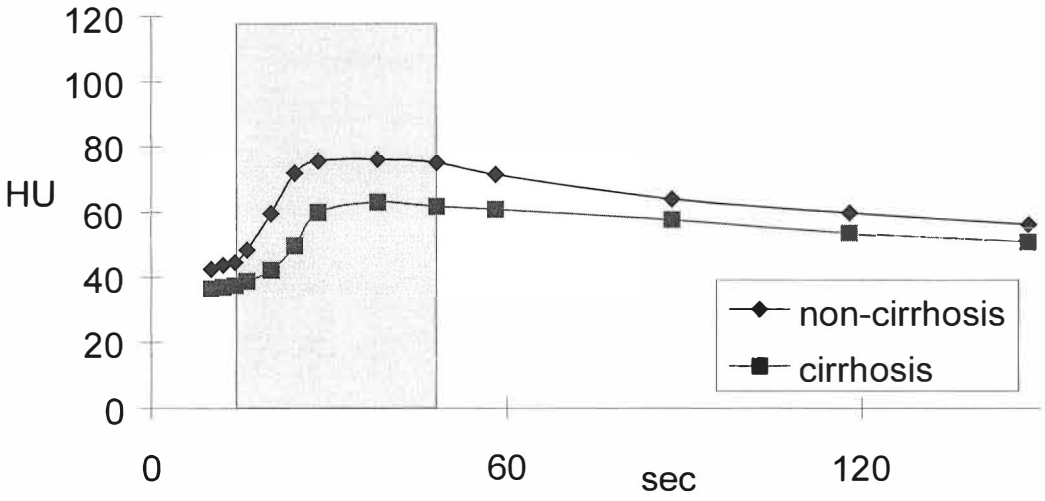

Figure 1b. Mean time-density-curves of the spleen for the patients studied according to protocol 3. In none of the patients did a heterogeneous enhancement pattern (marked area) occur later than 60 sec after the contrast agent injection had been started.

In all 132 patients examined according to protocol 1, the spleen appeared homogeneously enhanced on all CT-levels regardless of the presence or absence of liver cirrhosis.

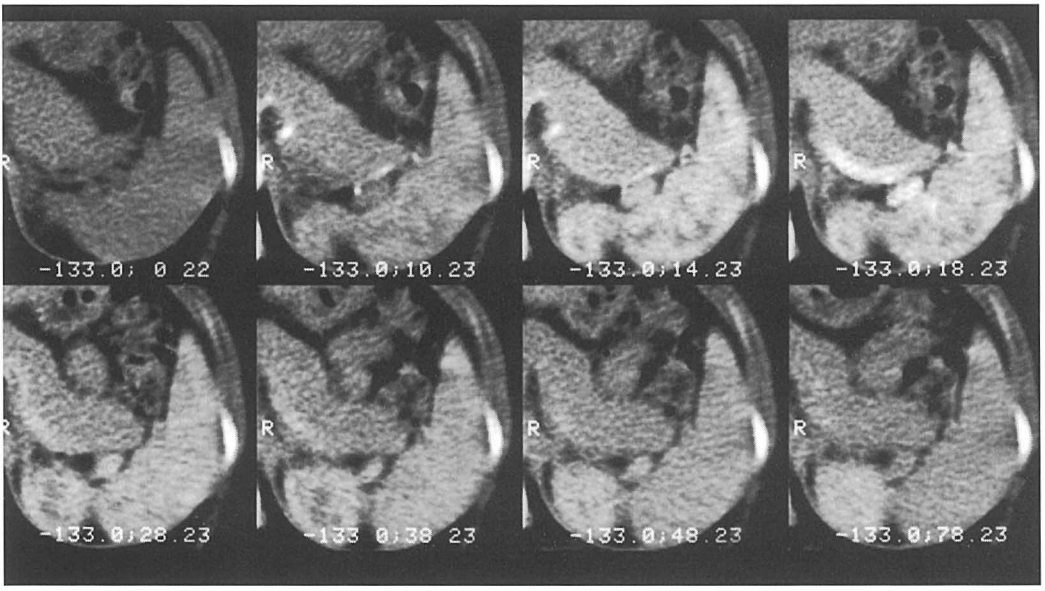

Figure 2. One level scanned over 90 sec after the injection of contrast agent. A heterogeneous enhancement pattern occurs in the early arterial phase.

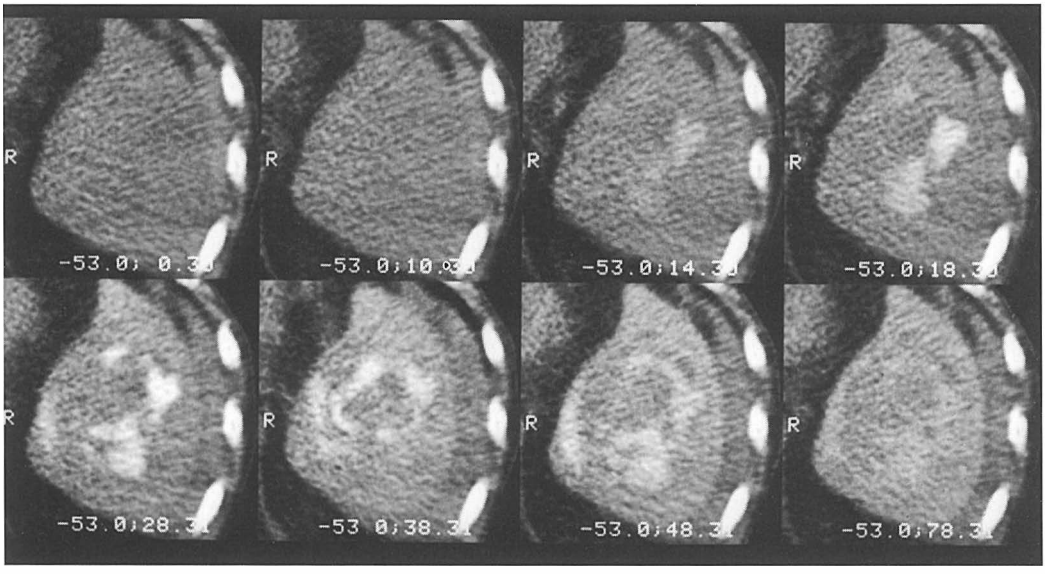

Figure 3. Splenic lymphoma also visible in the later bolus phase.

The time frames of heterogeneous enhancement patterns could be determined in the dynamic studies (protocols 2 and 3). Figure 1 shows the mean time-density-curves of the spleen of all patients studied according to protocol 2 (Figure 1a) and 3 (Figure 1b). The time-density-curve of the spleen examined according to protocol 2 showed a later maximum and a higher value of peak enhancement when compared to protocol 3.

The times when heterogeneous enhancement patterns occurred are listed in Table 2. A heterogeneous enhancement patterns appeared between 14 and 28 sec and disappeared between 24 and 58 sec after the contrast application had been started (Figure 2). In all patients studied by protocol 1, 2 and 3 (n=195), the splenic parenchyma became homogeneous beyond 58 sec after the of bolus injection had been started, except for the 3 above mentioned patients with splenic cysts and for the 3 patients with splenic hemangioma, metastasis and lymphoma (Figure 3), respectively.

Heterogeneous enhancement patterns were visible more frequently in non-cirrhotic than in cirrhotic patients ($p<0.01$). During the dynamic CT studies of the patients without liver cirrhosis (n=40) using protocol 2 and 3, a heterogeneous enhancement pattern was observed in 76.5% (13/17) and 65.2% (15/23), respectively. A heterogeneous splenic enhancement pattern was only observed in 23.1% (3/13) and 20% (2/10) of the patients with cirrhotic liver disease as examined by protocol 2 and 3, respectively.

Discussion

Heterogeneous enhancement patterns of the spleen as observed on contrast-enhanced CT and in gadolinium-enhanced MRI examinations were assumed to reflect the mechanism of slow and fast blood flow in the pathways of splenic microcirculation.[1-5] However, heterogeneous enhancement patterns may also simulate pathoanatomical changes of the spleen.[1-3,4] It is therefore important to define the possible variations in normal splenic appearance.

Histologically the spleen comprises the white and red pulp. The white pulp consists of lymphatic tissue encasing the splenic arteries. It also forms the lymphoid follicles. The red pulp is a reticular meshwork where red blood cells are conditioned before their destruction. The fast splenic pathway bypasses the reticular meshwork of the red pulp. It takes its route via direct capillary-venous connection inside the lymphoid follicles of the white pulp. This pathway accounts for 80-90% of total splenic blood flow. The slow pathway constitutes 10-20% of total splenic perfusion. After having passed the white pulp, the blood is filtrated into the splenic chords of the red pulp where abnormal blood cells are labeled for their destruction.

In a recent study using „functional CT" imaging, Miles *et al*[3] showed that splenic regions with early enhancement revealed higher arterial perfusion values than those with delayed contrast enhancement. These early enhancing areas of the spleen are thought to reflect the regions in which the fast pathway is predominant and vice versa.[3]

With the advent of fast imaging techniques the spleen is often scanned within this early phase of enhancement showing a heterogeneous pattern.[1-3] To our knowledge no exact time frames have been reported when these patterns occur and whether they vary with different contrast agent injection protocols or different pathophysiologies as may happen in patients with liver cirrhosis.

Advanced cirrhosis may increase portal venous pressure, consecutive chronic splenic venous hypertension and an elevated splenic sinus pressure. Miles et al. showed that splenic arterial blood flow is slower in patients with liver cirrhosis compared to those without cirrhosis.[3]

This study, using 3 different injection protocols with the same contrast agent, showed that the heterogeneous enhancement patterns were never seen later than 58 sec after the bolus injection had been started, even if the contrast agent was still being injected as in protocol 1, regardless of the presence or absence of liver cirrhosis. Using the two dynamic protocols with different amounts (50 vs. 90 ml) and flow rates (3 vs. 5 ml/sec) of

contrast agent, the time frames of heterogeneous enhancement patterns did not change significantly. The injection protocol 1 is similar to that used for spiral CT of the abdomen. Therefor, we suppose that the results of our study (heterogeneity should not be visible beyond 58 sec after the contrast injection had been started) may also be relevant for the interpretation of spiral CT studies of the abdomen.

In conclusion, the results of our study show that heterogeneous splenic enhancement patterns are visible more frequently in patients without than in patients with liver cirrhosis, probably due to decreased splenic blood flow in patients with liver cirrhosis. Regardless of the presence of liver cirrhosis, heterogeneous splenic enhancement patterns appear between 14 and 58sec after the contrast agent administration had been started. After 58 sec, the spleen is homogeneously enhanced, even when the contrast agent is still being injected at that time.

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