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The potential of radionuclide diagnostic imaging in diffuse liver disease and portal hypertension

E.V. Migunova*, M.Sh. Khubutiya, N.E. Kudryashova, O.G. Sinyakova, G.A. Berdnikov, S.I. Rey, M.S. Novruzbekov, O.D. Olisov

[1]*N.V. Sklifosovsky Research Institute for Emergency Medicine, 3 Bolshaya Sukharevskaya Sq., Moscow 129090 Russia*

[2]*Department of Transplantology and Artificial Organs, A.I. Yevdokimov Moscow State University of Medicine and Dentistry, 1 Bldg. 20 Delegatskaya St., Moscow 127473 Russia*

*Correspondence to: Ekaterina V. Migunova, Cand. Med. Sci., Senior Researcher of the Radiology Department, N.V. Sklifosovsky Research Institute for Emergency Medicine, e-mail: emigunovasklif@mail.ru

Objective. *The study objective was to assess the scintigraphy potential in the evaluation of portal hypertension and the severity of liver damage in diffuse diseases and after liver transplantation.*

Material and methods. *The study enrolled 325 patients suffering from hepatitis and liver cirrhosis of various etiology and severity, including those after liver transplantation, namely, the patients with hepatitis (n=96), patients with liver cirrhosis of Child–Pugh class A (n=24), class B (n=87), and class C (n=118); 11 more healthy volunteers without clinical and laboratory signs of diffuse liver disease were enrolled as controls. The assessment of liver reticuloendothelial system was performed by scintigraphy with (99m)Tc-phytate colloid in a static planar mode and "whole body" mode by SPECT (Infinia II, GE).*

Results. *In contrast to the control group, significant radionuclide signs of hepatosplenomegaly were revealed with the predominant functional activity of the left lobe; the liver function was found impaired that correlated with the cirrhosis severity evaluated according to the Child–Pugh Classification. The analysis of scintigraphy quantitative parameters showed that the most informative of them were the intensity of radiopharmaceutical accumulation in the spleen (S%) and in bone marrow (Bm%), and the radiopharmaceutical uptake by the reticuloendothelial cells of the liver and spleen in percentage from the administered activity (L_{wb}%, S_{wb}%). Depending on the cirrhosis severity assessed by the Child–Pugh Score, the changes in quantitative parameters were accompanied by a progressive enlargement of the spleen, liver left lobe, the increase of (99m)Tc-phytate uptake by the bone marrow with a decreased radiopharmaceutical uptake by the liver. The study results showed that among the Child–Pugh class C patients, the impairment of liver reticuloendothelial function was more pronounced in the patients with cirrhosis of viral and mixed etiology, when compared to those with alcoholic cirrhosis.*

Conclusion. *The paper has identified the most informative parameters characterizing portal hypertension and the reticuloendothelial function for all Child–Pugh defined classes of cirrhosis. These parameters include the increase of (99m)Tc-phytate accumulation in the spleen (S%) and bone marrow (Bm%); the liver and spleen uptake of the radiopharmaceutical in percentage from the administered activity (L_{wb}%, S_{wb}%). The calculation of the remaining parameters is necessary for a detailed description of the organ function and for the assessment of the portal hypertension severity in repeated studies.*

Summary. *Criteria for the objective assessment of reticuloendothelial function and portal hypertension in diffuse liver diseases, including after liver transplantation, have been developed.*

Contrary to the control group, in patients with diffuse liver diseases, the radionuclide signs of hepatosplenomegaly (or a decreased liver size) with a predominant functional activity of the left lobe were identified, as were the changes in the quantitative parameters of the radiopharmaceutical uptake by the liver (L_{wb}%), including the radiopharmaceutical accumulation in the liver left lobe (Ll%), spleen (S_{wb}%), bone marrow (Bm%), and the liver-to-spleen area ratio (L_{ar}/S_{ar}).

The informative and reliable ($p<0.05$) parameters of the function L_{wb}%, S%, S_{wb}% and Bm% correlating with the cirrhosis classes assessed by Child–Pugh were identified.

The radionuclide method, being highly reproducible one, can be recommended for an objective assessment of liver function and the detection of portal hypertension in hepatitis and cirrhosis, as well as for post-transplant monitoring of the liver function to prevent complications in the early and late postoperative periods.

Keywords: colloid liver scintigraphy, hepatitis, liver cirrhosis, portal hypertension, liver transplantation

Conflict of interests Authors declare no conflict of interest

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CT, computed tomography

MRI, Magnetic Resonance Imaging

OLT, orthotopic liver transplantation

RPH, radiopharmaceutical

RES, reticuloendothelial system

US, ultrasound

Introduction

Diagnosis of liver cirrhosis at initial stage by using one of the radiology imaging techniques is difficult, and none of them can serve as universal [1–8]. The clinical and laboratory data obtained are not always reliable to assess the liver function [9–12].

The experience of the Radioisotope Diagnostic Department of N.V. Sklifosovsky Research Institute for Emergency Medicine based on studying more than 1,300 patients with liver cirrhosis and hepatitis of various etiologies, including the patients from the “waiting list” and after liver transplantation, showed that colloid scintigraphy was the most effective radiological method for diagnosing diffuse liver diseases and portal hypertension, being superior over many existing diagnostic imaging techniques such as ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) [13–16]. With repeated studies it can demonstrate the progression of hepatitis, cirrhosis, and the increasing portal hypertension even in the absence of cytolysis, i.e. with a stable biochemical status of the patient [9, 10, 14].

The radionuclide method is characterized by a moderate radiation load on the patient, absent adverse reactions (including allergic ones), highly

reproducible results, and a simple examination procedure. The possibility to obtain quantitative parameters of the function is an undoubted advantage of the radionuclide method [17–20]. Reticuloendothelial (Kupffer) cells of the liver, and extrahepatic macrophages of the spleen and bone marrow, which phagocytize ^{99m}Tc-phytate colloid radiopharmaceutical (RPH) are the most sensitive to disturbing factors, so scintigraphy with repeated examinations in patients with liver diseases, including pre- and post-transplant patients, can detect the portal hypertension signs and a decreased function of a transplanted organ even before the appearance of structural changes at ultrasound, CT, and MRI [14, 21–23].

The purpose of the study was to assess the potential of scintigraphy in identifying portal hypertension and assessing the liver damage severity in diffuse diseases and after organ transplantation.

Material and methods

Aimed at identifying the most informative scintigraphy parameters characterizing the liver function and the presence of portal hypertension, we analyzed in detail the data of 325 patients, 198 men (61%) and 127 women (39%) (mean age 52.2 ± 14.9) with hepatitis and liver cirrhosis of various etiology and severity, including those after liver transplantation: 96 patients with hepatitis, 24 with Child–Pugh class A cirrhosis, 87 with class B, and 118 with class C cirrhosis, and also the data of 11 healthy volunteers (control group, mean age 31.5 ± 3.2 years) without clinical and laboratory signs of diffuse liver disease. Liver scintigraphy was performed with the intravenous administration of 100–150 MBq of ^{99m}Tc-phytate colloid (Diamed, Russia), with the radiation load on a patient being 0.94–1.41 mSv.

The investigations were made on an Infinia II Gamma Camera (single-photon emission computed tomography system) (GE, USA) in a static planar mode in the anterior, posterior, and two lateral views (300 s/frame in 128×128 matrix) and in the “whole body” mode in anterior and posterior views with the table being moved at a speed of 30 cm/min.

The verification of the baseline data normal distribution was made using Shapiro–Wilk criterion, and the difference significance between mean values of the parameters in the compared groups was assessed by the unpaired Student's test. To assess the correlation dependence between the parameters, the Pierce correlation coefficient (r) was calculated.

The investigators of N.V.Sklifosovsky Institute for Emergency Care defined a number of new semi-quantitative parameters, besides those traditionally used, to assess the liver function and the portal hypertension severity. A total of 6 parameters characterizing the liver function were used: 1) S%, the RPH accumulation in the spleen (% from the summed amount of impulses in the liver and spleen); 2) Bm%, the RPH accumulation in the bone marrow (% of the ratio of the average impulse count in the three lumbar vertebrae to the average count in the liver); 3) L_{wb}% in the "whole body" mode (equivalent to the administered activity), the RPH capture by the liver averaged over the two (anterior and posterior) views in % of the total body impulse count; 4) S_{wb}%, in the “whole body” mode (equivalent to the administered activity), the RPH capture by the spleen averaged over two views in % of the total body impulse count; 5) Ll%, the contribution of the liver left lobe to the total function (the ratio of the count in 1–4 liver segments to the count of the entire liver in the anterior views; 6) L_{ar}/S_{ar}, the liver-to-spleen area ratio in two views.

Results

Table 1 presents the above defined parameters with their values for the normal liver function in the patients of the control group (n=11). (Fig.1) In this group, the RPH accumulation did not exceed 15% in the spleen (S%), 8% in the bone marrow (Bm%), the RPH capture by the liver parenchyma was not lower than 49% of the administered activity (L_{wb}%), etc.

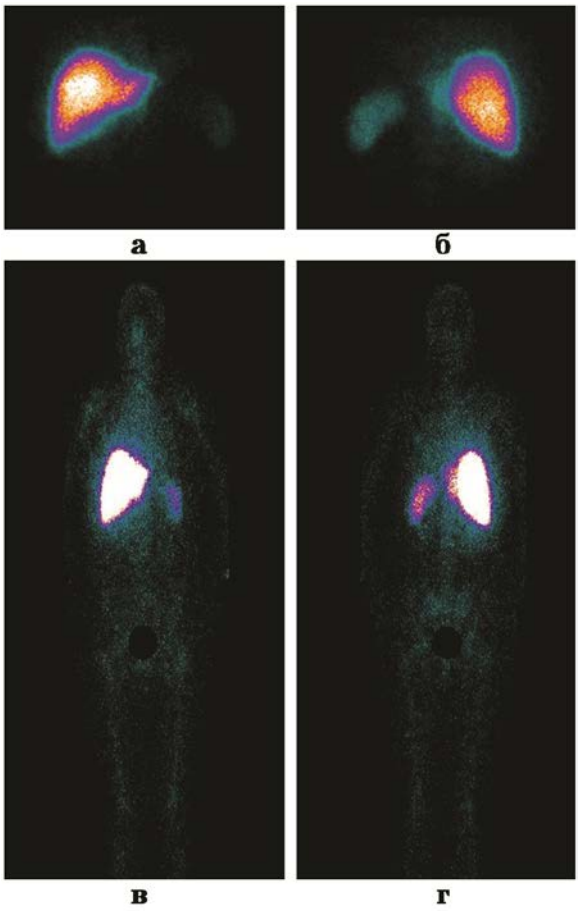

Fig. 1. The scintigrams of the normal liver and spleen in the anterior (a) and posterior (b) views in examined Patient B. of 33 years old; scintigrams in the anterior (c) and posterior (d) views taken in the "whole body" mode

Patient's name	S%	Bm%	L_{wb} %	S_{wb} %	Ll%	L_{ar}/S_{ar}
B., 33 y.o.	9.8	5.2	46.4	3.0	25.2	2.9

Table 1. Distribution of scintigraphy parameters in the control group and in diffuse liver diseases

Patient Group	n	S%	Bm%	L_{wb} %	S_{wb} %	Ll%	L_{ar}/S_{ar}
Control group	11	11.9 ± 4.1	6.9 ± 1.1	47.5 ± 1.5	3.9 ± 0.5	31.0 ± 3.5	3.1 ± 0.2
Hepatitis	96	19.4 ± 1.0	10.9 ± 1.0	49.7 ± 0.8	5.9 ± 0.3	33.9 ± 0.7	2.7 ± 0.1
Cirrhosis A	24	34.5 ± 2.4	16.0 ± 1.2	37.7 ± 1.7	11.3 ± 1.0	42.8 ± 2.2	1.9 ± 0.1
Cirrhosis B	87	50.2 ± 1.7	27.2 ± 1.9	28.5 ± 1.1	17.5 ± 0.9	46.9 ± 1.5	1.6 ± 0.1
Cirrhosis C	118	61.9 ± 1.5	46.3 ± 3.2	21.2 ± 0.9	20.5 ± 0.7	46.7 ± 1.1	1.5 ± 0.1

Note: the Table shows the mean values of the parameters with the standard error of mean **M ± m**

The portal hypertension signs in scintigraphy were displayed by the increased RPH accumulation in the spleen tissue and/or bone marrow, by the enlarged spleen. It should be noted that in some cases of hepatitis confirmed by clinical and biochemical data, scintigraphy could reveal barely distinguishable signs of portal hypertension (Fig. 2), which had an important prognostic value (transformation into liver cirrhosis). When comparing all parameters of liver function between the patients with hepatitis and cirrhosis graded from Child-Pugh class A and further, statistically significant differences were found ($p<0.005$), which also evidenced a high sensitivity of the radionuclide method. (Table 1, 2). For example, a clear significant difference was seen between the “hepatitis” and “cirrhosis A” groups in the parameters of RPH accumulation in the spleen, bone marrow, and liver parenchyma: S% (19.4 ± 1.0% in hepatitis and 34.5 ± 2.4 % in cirrhosis A); Bm% (10.9 ± 1.0% in hepatitis and 16.0 ± 1.2% in cirrhosis A), and L_{wb}% (49.7 ± 0.8% in hepatitis and 37.7 ± 1.7% in cirrhosis A).

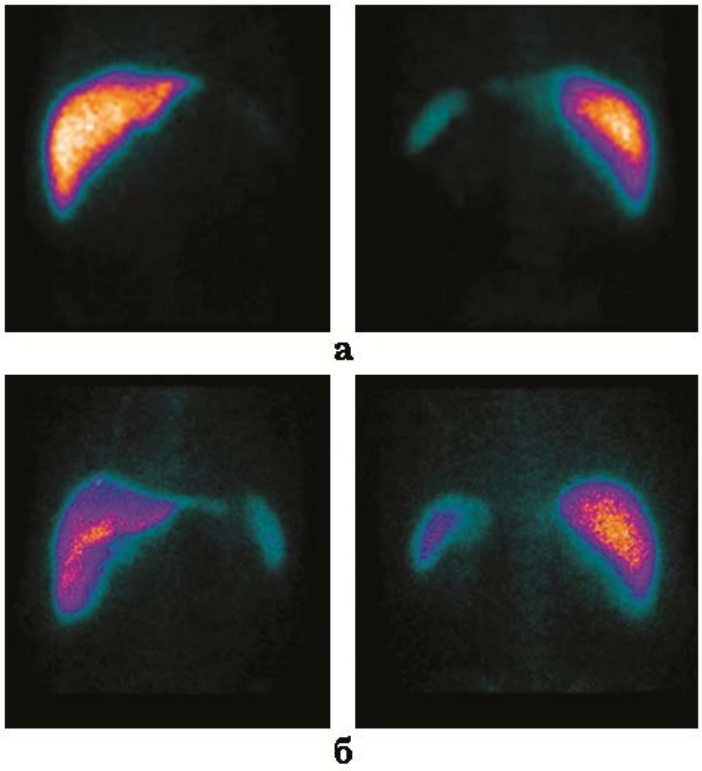

Fig. 2. Scintigrams of the liver and spleen in anterior and posterior views obtained in Patient N., 63 years old, having hepatitis without signs of portal hypertension (a)

Patient's name	S%	Bm%	L_{wb}%	S_{wb}%	Ll%	L_{ar}/S_{ar}
N., 63 y.o.	7.1	7.9	56.7	2.4	26,6	5.1

Scintigrams of the liver and spleen in anterior and posterior views obtained in Patient Sh., 63 years old, having hepatitis with the signs of portal hypertension (b)

Patient's name	S%	Bm%	L_{wb}%	S_{wb}%	Ll%	L_{ar}/S_{ar}
Sh., 63 y. o.	19.4	12.8	33.9	5.6	35.3	3.3

Table 2. The significant differences (p) in parameters between the patient groups as analyzed using the unpaired Student's t-test

Patient Groups	S%	Bm%	L_{wb}%	S_{wb}%	Ll%	L_{ar}/S_{ar}
Hepatitis vs. cirrhosis A, B, C	<0.0001	<0.001	<0.0001	<0.0001	<0.001	<0.0001
Cirrhosis A vs. B	0.0001	0.0001	0.0001	0.0001	> 0.05	> 0.05
Cirrhosis A vs. C	0.0001	0.0001	0.0001	0.0001	> 0.05	0.01
Cirrhosis B vs. C	0.0001	0.0001	0.0001	0.01	> 0.05	> 0.05

In liver cirrhosis, regardless of etiology, scintigraphy with radiocolloid revealed signs of impaired RES function, the liver deformity that aggravated in Child-Pugh class C cirrhosis, and abnormal organ size: the liver was significantly enlarged in 208 patients (64%) at all stages of the disease, the organ was of normal size, regardless of the cirrhosis class in 55 patients (17%); and a decreased liver size was observed in 62 patients (19%) of class C. All patients showed the spleen enlargement as the disease progressed (the length from 13 to 22 cm and over). The nature of the RPH distribution in the liver was diffusely heterogeneous in 228 patients (70%), diffusely focal in 81 (25%) and the foci of the reduced radiocolloid accumulation were increasing in size with the cirrhosis progression due to their merging. In a number of patients, the accumulation of radiopharmaceuticals in the liver was practically absent and was comparable to the background, meanwhile, we observed the smoothness of typical cuts, blurred contours of the image, an intensified extraorgan background, increased radiocolloid capture by the left lobe and bone marrow.

When analyzing the results of radionuclide studies in 24 patients with Child-Pugh class A cirrhosis (Fig. 3), the liver enlargement with a diffuse-

inhomogeneous RPH distribution was observed (S%=34.5±2.4% and S_{wb}%=11.3 ± 1.0), as well as a increased RPH capture by the bone marrow (Bm%=16.0 ± 1.2%), a decreased RPH capture by the liver against the administered activity (L_{wb}%=37.7 ± 1.7%) with RPH predominant accumulation in the left lobe (Ll%=42.8 ± 2.2%), and also a decrease in the liver-to-spleen area ratio (L_{ar}/S_{ar}=1.9 ± 0.1). We should note that the values of scintigraphy parameters for class A cirrhosis highly significantly differed from those in the control group and the hepatitis group (See Table 1).

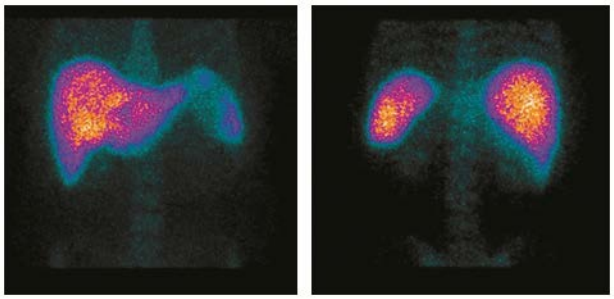

Fig. 3. Scintigrams of the liver and spleen in anterior and posterior views obtained in Patient Ch., 53 years old, having Child-Pugh class A cirrhosis

Patient's name	S%	Bm%	L_{wb}%	S_{wb}%	Ll%	L_{ar}/S_{ar}
Ch., 53 y.o.	37.9	14.5	36.0	11.2	37.4	2.0

The patients with Child-Pugh class B cirrhosis (Fig. 4) showed a progressive increase in the RPH capture by the enlarged spleen (S%=50.2 ± 1.7% and S_{wb}%=17.5 ± 0.9%) and bone marrow (Bm% 27.2 ± 1.9%) with a significantly predominant RPH accumulation in the liver left lobe (Ll% 46.9 ± 1.5%), a decreased RPH capture by the liver (L_{wb}%=28.5 ± 1.1%) and a decrease in the liver-to-spleen area ratio (L_{ar}/S_{ar}=1.6 ± 0.1). Significant differences were found ($p < 0.0001$) between cirrhosis classes A and B in S%, Bm%, L_{wb}%, and S_{wb}% (See Table 2).

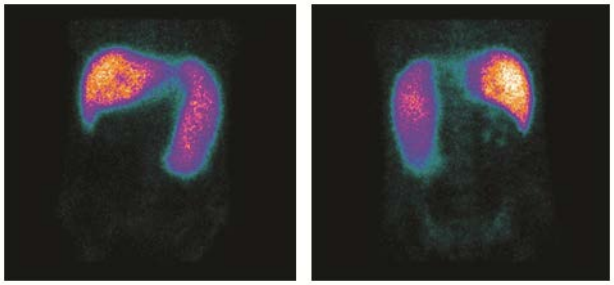

Fig. 4. Scintigrams of the liver and spleen in anterior and posterior views obtained in Patient N., 21 years old, having Child-Pugh class B cirrhosis

Patient's name	S%	Bm%	L_{wb}%	S_{wb}%	Ll%	L_{ar}/S_{ar}
N., 21 y.o.	44.1	12.8	30.9	25.9	44.3	1.1

The signs of portal hypertension (splenomegaly and bone marrow hyperplasia) in Child-Pugh class C cirrhosis reached maximum values in cases of RPH capture by the spleen (S%=61.9 ± 1.5% and Swb%=20.5 ± 0.7%) and the bone marrow (Bm%=46.3% ± 3.2%) (Fig. 5), which came along with an abrupt decrease of RPH accumulation in the liver parenchyma (Lwb%=21.2% ± 0.9%). A deformed liver was visualized in patients due to its left lobe hypertrophy (Ll% = 46.7 ± 1.1%). There was a direct correlation between the increase in the RPH accumulation in the spleen and the increase in the RPH accumulation in the bone marrow (r = 0.64); however, in some patients, the spleen took the main reticuloendothelial function, and the bone marrow was poorly visualized. There differences in the parameters S%, Bm%, L_{wb}%, and S_{wb}% were significant ($p < 0.05$) both between the cirrhosis classes A and B, and between the cirrhosis classes B and C (See Table 2) .

We should note that in repeated studies of the patients within the same Child-Pugh class, the scintigraphy data helped detecting the signs of liver cirrhosis progression in the presence of small fluctuations in biochemical

parameters sometimes only slightly deviating from the norm. That was manifested by a decreased RPH accumulation by the liver parenchyma against the administered activity (L_{wb}%) and an increased RPH accumulation by the spleen and bone marrow.

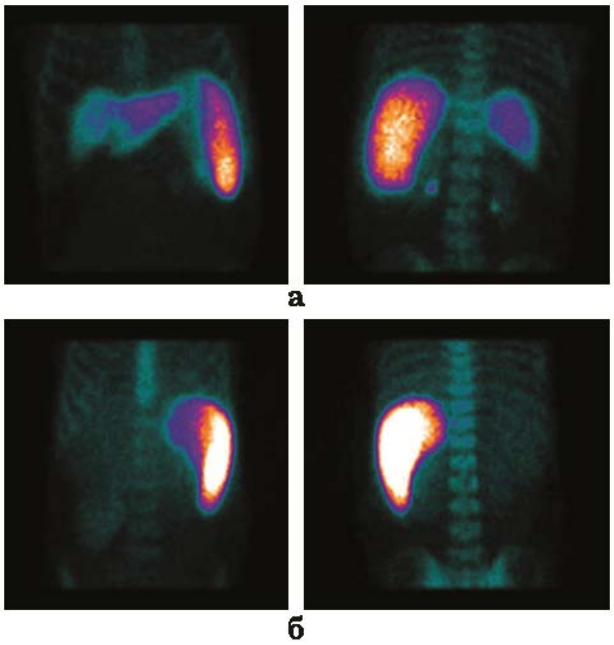

Fig. 5. Scintigrams of the liver and spleen in anterior and posterior views obtained in Patient K., 68 years old, having Child-Pugh class C cirrhosis with severe liver deformity (a)

Patient's name	S%	Bm%	L_{wb}%	S_{wb}%	Ll%	L_{ar}/S_{ar}
K., 68 y.o.	80.5	44.7	12.2	28.8	64.0	1.0

Scintigrams of the liver and spleen in anterior and posterior views obtained in Patient S., 35 years old, having Child-Pugh class C cirrhosis with no radiopharmaceutical accumulation in the liver (b)

Patient's name	S%	Bm%	L_{wb}%	S_{wb}%	Ll%	L_{ar}/S_{ar}
S., 35 y.o.	92.5	176.2	5.3	38,8	35.4	1.6

When comparing the scintigraphy data considering the levels of protein, blood protein fractions, and liver enzymes (aspartate

aminotransferase, alanine aminotransferase, gamma-glutamyl peptidase, lactotdehydrogenase, creatine phosphokinase, alkaline phosphatase), we noted a weak inverse correlation between the increase in RPH capture by the spleen and bone marrow and the increased levels of the these enzymes (r=–0.2–0.3). It could be explained by the fact that with the decreased number of viable liver cells and the decreased levels of liver enzymes characterizing the damage to the organ parenchyma, the functional activity of RES cells in the spleen and bone marrow increased.

The spleen size in portal hypertension demonstrated by scintigraphy and ultrasound was not decisive for assessing the liver damage severity. For example, in 53 examined patients (16.3%), the scintigraphy performed prior to liver transplantation showed a marked portal hypertension and an enlarged spleen (16.9 ± 0.7 cm long, 8.6 ± 0.5 cm wide), an intense RPH accumulation in the RES cells of the spleen and bone marrow (S%=54.4 ± 2.8%, Bm%=21.0 ± 1.4%). The majority of patients (49 of 53) showed an evident regression of portal hypertension at 2–4 weeks after transplantation that was statistically significant ($p<0.0001$), being manifested in the form of a decreased S% (to 30.0 ± 1.7%) and Bm% (up to 9.1 ± 0.6%), i.e. a decreased RPH capture by the spleen by 45% and by the bone marrow by 57%. Meanwhile, the spleen dimensions, according to ultrasound and scintigraphy results, decreased only slightly (the length to 15.4 ± 0.7 cm, the width to 7.9 ± 0.3) , the difference being non-significant ($p=0.11$). Studies have shown that in the early posttransplant period (2–4 weeks), the radionuclide method can identify the portal hypertension regression in persisting splenomegaly. (Fig. 5).

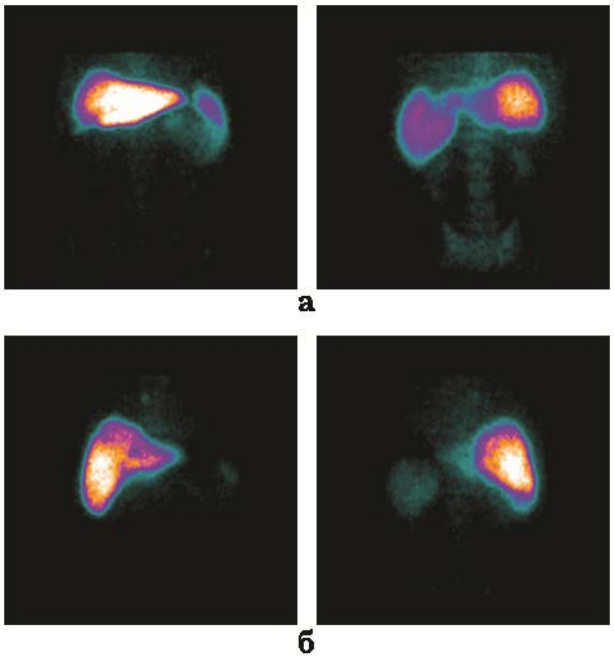

Fig. 6. Scintigrams of the liver and spleen in anterior and posterior views obtained in Patient O., 60 years old, before (a) and 21 days after (b) orthotopic liver transplantation

Patient's name	S%	Bm%	L_{wb}%	S_{wb}%	Ll%	L_{ar}/S_{ar}
O., 60 years before OLT	41.4	17.4	35.1	11.4	61,8	1.0
21 days after OLT	9.3	6.5	49.9	2.8	34.5	2.1

Note: OLT, orthotopic liver transplantation

Having analyzed a large amount of clinical data (more than 1000 patients with diffuse liver diseases), we identified a correlation between the scintigraphy parameters and defined the most informative of them characterizing the portal hypertension severity and RES function impairments in hepatitis and cirrhosis of Child–Pugh classes A, B, C (See Table 1, 2).

The scintigraphy data of 47 patients with Child-Pugh class C cirrhosis of various etiologies: alcoholic, viral, and mixed are worth consideration. In recent years, the number of patients with cirrhosis of mixed etiology has increased; the specific feature of such cirrhosis clinical course is the rapid

development of hepatocellular failure [24-26]. Differences were identified between the selected groups in the following parameters S%, Bm%, L_{wb}% and S_{wb}% (Table 3). More pronounced portal hypertension and impaired liver function in class C were noted in cirrhosis of viral and mixed etiology compared to alcoholic cirrhosis: the RPH capture by the spleen (S%) was 61.2 ± 2.9% and 48.0 ± 5.8%, respectively; the RPH capture by the spleen against the administered activity (S_{wb}%) made 18.9 ± 1.7% and 16.4 ± 4.2%; the RPH capture by the liver parenchyma against the administered activity (L_{wb}%) made 19.0 ± 1.4% and 20.4 ± 2.1%. The RPH capture by the bone marrow was the greatest in mixed liver cirrhosis (Bm%=40.0 ± 5.1%; $p<0.05$). The difference was significant in RPH accumulation in the spleen (S%) between cirrhosis of viral etiology and other cirrhosis types: $p<0.001$ vs. alcoholic etiology, $p<0.05$ vs. mixed cirrhosis. The reticuloendotelial liver function (L_{wb}%) and the RPH capture by the spleen against the administered activity (S_{wb}%) were less abnormal in alcoholic cirrhosis versus other cirrhosis types ($p<0.05$ and $p<0.001$). Analysis of the radionuclide study results of 47 patients showed that, within class C, the patients with cirrhosis of viral and mixed etiology had more severe portal hypertension and decreased liver reticuloendothelial function compared to those with alcoholic cirrhosis (Table 3).

Table 3. Liver function parameters in cirrhosis of alcoholic, viral, and mixed etiology

Etiology of cirrhosis	**n**	**S%**	**Bm%**	**L_{wb}%**	**S_{wb}%**
Alcoholic	14	37, 9 ± 5.4	26.4 ± 4.1	25.8 ± 2.7	8.2 ± 1.5
Viral	23	61.2 ± 2.9	26.6 ± 2.7	19.0 ± 1.4	18.9 ± 1.7
Mixed	10	48.0 ± 5.8	40.0 ± 5.1	20.4 ± 2.1	16.4 ± 4.2

Note: the Table shows the mean values of the parameters with the standard error of the mean **M ± m**

Discussion

Liver scintigraphy with ^{99m}Tc-phytate colloid capable of being accumulated in reticuloendothelial liver cells is an objective test for assessing liver function in diffuse diseases such as hepatitis and cirrhosis. The radionuclide method provides the detection of portal hypertension signs at early stages of the disease, including the stage of hepatitis passing into cirrhosis. The quantitative parameters of liver function in scintigraphy correlate with the cirrhosis classes according to the Child-Pugh Classification and can be used as additional criteria for grading cirrhosis stages. The radionuclide method is highly reproducible that makes it an indispensable tool for the repeated studies recording the slightest changes in the liver function even within the same class of cirrhosis, and also in stable blood biochemical status. Liver scintigraphy with ^{99m}Tc-phytate colloid can be successfully used in patients before and after transplantation, both for evaluating the initial function of the transplanted organ and for follow-up in the early and late period after liver transplantation. Early identification of disorders, including minimal ones, may assist the clinician in optimizing the treatment tactics and selecting the patients who require a closer attention.

The paper highlights the most informative parameters characterizing the degree of portal hypertension and the function of the reticuloendothelial system in liver cirrhosis of any Child-Pugh class; they include the RPH accumulation in the spleen (S%) and bone marrow (Bm%), the RPH capture by the liver and the spleen as a percentage of the administered activity (L_{wb}% and S_{wb}%). The calculation of the remaining parameters is necessary for a detailed description of the liver function and for the assessment of the portal hypertension severity in repeated studies.

Conclusions

1. Criteria for objective assessment of reticuloendothelial function and portal hypertension in patients with diffuse liver diseases, including after organ transplantation, have been developed.

2. Radionuclide signs of hepatosplenomegaly (or a decreased liver size) with a predominant functional activity of its left lobe in diffuse liver diseases were identified in comparison with the control group, and the changes in quantitative parameters in terms of the RPH capture by the liver (L_{wb}%), including the RPH accumulation in its left lobe (Ll%), spleen (S% and S_{wb}%), bone marrow (Bm%), and the liver-to-spleen area ratio (L_{ar}/S_{ar}) were studied.

3. The informative and reliable ($p<0.05$) parameters of the function: L_{wb}%, S%, S_{wb}%, and Bm% correlating with cirrhosis Child-Pugh classes have been defined.

4. The radionuclide method, being a highly reproducible, can be recommended for an objective assessment of liver function and the detection of portal hypertension in hepatitis and cirrhosis, as well as for dynamic monitoring of the liver functional status after liver transplantation for the timely prevention of complications in the early and late postoperative periods.

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Information about authors

Ekaterina V. Migunova, Cand. Med. Sci., Senior Researcher of the Radiology Department, N.V. Sklifosovsky Research Institute for Emergency Medicine, https://orcid.org/0000-0001-7521-487x

Mogeli Sh. Khubutiya, Acad. of RAS, Prof., Dr. Med. Sci., President of N.V. Sklifosovsky Research Institute for Emergency Medicine, Head of the Department of Transplantology and Artificial Organs A.I. Yevdokimov Moscow State University of Medicine and Dentistry, https://orcid.org/0000-0002-0746-1884

Natalya E. Kudryashova, Dr. Med. Sci., Chief Researcher of the Radiology Department, N.V. Sklifosovsky Research Institute for Emergency Medicine, https://orcid.org/0000-0003-1647-1635

Olga G. Sinyakova, Cand. Techn. Sci., Scientific Consultant of the Radiology Department, N.V. Sklifosovsky Research Institute for Emergency Medicine, https://orcid.org/0000-0003-1686-6952

Gennadiy A. Berdnikov, Cand. Med. Sci., Senior Researcher of the Department of Urgent Surgery, Endoscopy, and Intensive Care, N.V. Sklifosovsky Research Institute for Emergency Medicine, https://orcid.org/0000-0002-3726-3256

Sergey I. Rey, Cand. Med. Sci., Senior Researcher of the Department of Urgent Surgery, Endoscopy, and Intensive Care, N.V. Sklifosovsky Research Institute for Emergency Medicine, https://orcid.org/0000-0001-7802-2283

Murad S. Novruzbekov, Dr. Med. Sci., Head of the Scientific Liver Transplantation Department, N.V. Sklifosovsky Research Institute for Emergency Medicine, https://orcid.org/0000-0002-6362-7914

Oleg D. Olisov, Cand. Med. Sci., Senior Researcher of the Liver Transplantation Department, N.V. Sklifosovsky Research Institute for Emergency Medicine, https://orcid.org/0000-0002-0691-5581

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