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Complex ultrasonography in the assessment of intrarenal hemodynamic impairments in patients with portal hypertension

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Abstract

Rationale. *Hepatorenal syndrome is a threatening complication in patients with liver cirrhosis and portal hypertension. The occurrence of renal dysfunction associated with hepatorenal syndrome manifestations significantly affects the condition severity, the disease duration, and the survival time during the waiting period for liver transplantation.*

The study purpose *was to investigate the potential of a complex ultrasonography examination in the assessment of intrarenal hemodynamic impairments in patients with various diffuse liver diseases.*

Material and methods. *The ultrasound examination results of 167 patients were analyzed. The 1st group included 28 patients with confirmed diffuse liver diseases of viral etiology who did not have signs of cirrhosis formation, the 2nd group included 139 patients with liver cirrhosis due to diffuse liver diseases of various etiologies, and the 3-rd group included 137 patients who had previously been in the 2nd group in whom orthotopic liver transplantation was performed.*

Results. *The study revealed a statistically significant increase in the incidence of secondary hemodynamic impairments in kidney function in patients with liver cirrhosis and no relationship of their severity and incidence to the disease etiology, and also to such markers of the portal hypertension severity as splenomegaly, ascites, and portal vein thrombosis.*

Conclusions. *The resistive index measured on the renal arterial branches by Doppler ultrasound, has a certain predictive value in relation to hepatorenal syndrome in patients with liver cirrhosis of various origins. This also makes it possible to timely identify a group of patients at a high risk of developing severe renal dysfunction and to assess the efficacy of the treatment that has been given*

Keywords: portal hypertension, hepatorenal syndrome, Doppler ultrasound/ultrasonography

Conflict of interests Authors declare no conflict of interest

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AIC, autoimmune cirrhosis

CGC, cryptogenic cirrhosis

HRS, hepatorenal syndrome

IHI, intrarenal hemodynamic impairment

KWD, Konovalov-Wilson disease

LC, liver cirrhosis

LT, liver transplantation

PBC, primary biliary cirrhosis

PSC, primary sclerosing cholangitis

RARI, renal arterial resistive index

SL, spleen length

SPL, separation of peritoneum layers

TLD, toxic liver damage

US, ultrasonography/ultrasound examination

VLD, viral liver damage

VOLL, veno-occlusive liver lesions

Introduction

Liver cirrhosis (LC) is the end stage of diffuse liver diseases of various etiologies. The progression of the primary disease, which is often asymptomatic, causes the development of fibrosis with the formation of false lobules, which inevitably leads to polymorphic functional disorders of portal and splanchnic blood flow. Portal hypertension, which occurs due to the increased vascular resistance to blood flow in marked structural changes in the liver, includes a number of pathological manifestations, such as ascites, the development of splenomegaly and hepatorenal syndrome (HRS) [1, 2].

The mechanism of HRS occurrence is associated with the phenomenon that an increased pressure in the portal vein system is accompanied by blood pooling in the splanchnic bed. As a result, intrarenal hypoperfusion develops, the renin-angiotensin-aldosterone system is activated, and a secondary spasm occurs in the renal arterial bed [3, 4].

The development of ascites due to the progression of portal hypertension at an early stage of the disease or with a primary episode of LC decompensation occurs in 20-75% of cases. Ultrasonography (US) is

a primary method to diagnose LC and detect the signs of developing portal hypertension [5, 6].

The renal dysfunction in liver cirrhosis caused by the HRS presence is diagnosed in 40% of cases and can significantly affect the survival time of patients waiting for liver transplantation (LT) [7, 8].

In most clinics, the diagnosis of HRS in LC is made based on the criteria developed by the International Ascites Club in San Francisco (USA) in 2005. These criteria include the indications of the absence of other causes for the manifestation of renal dysfunction, as well as the laboratory data recording the increase in blood plasma creatinine level making more than 135 mcmol/L (1.5 mg%) [9]. Meantime, investigators note that the laboratory assessment of the impaired renal function in developing HRS is not always informative since the muscle mass in patients of this group is reduced which makes it difficult to make conclusions about the renal function status by creatinine concentration [10, 11].

An increased pressure in the portal vein system of LC patients plays a leading role in the development of splanchnic hemodynamic impairments and significantly increases the risk of blood clots in the portal system. The assessment of portal vein patency and a timely diagnosis of portal thrombosis are especially important when examining the patients waiting for surgery and LT [12].

While searching for the literature on this topic, we found conflicting data on the use of Doppler ultrasonography techniques in assessing the timing and severity of secondary arterial angiospasm in LC patients.

Thus, A. Abdallah et al. (1999), at examination of 21 children with diagnosed LC, recorded increased resistive index values at the level of the renal artery branches as early as in the pre-ascitic period, and found no

correlation between the values of the renal arterial resistive index (RARI) and the severity of portal hypertension phenomena [13]. E.Z. Qu et al. (2014), based on the investigation of 50 LC patients, indicated significant differences in the degree of RARI increases recorded on the branches of the renal arteries between the patients with ascites and without it [14]. All these dictate the need for further gathering the experience in the use of complex ultrasonographic techniques in such patients.

The purpose of the study was to investigate the typical features of portal hypertension manifestations and the incidence of secondary renal hemodynamic impairments in patients with various diffuse liver diseases.

Material and methods

To achieve the study goal, we analyzed the results of complex ultrasonography examinations in 167 patients.

We identified three groups of patients, in whom, according to the medical history and a comprehensive examination results, primary kidney pathology was excluded. The first group consisted of 28 patients: 14 men and 14 women aged from 21 to 53 years (median age 41 years) with confirmed diffuse liver diseases of viral etiology, who had no signs of LC formation. The second group consisted of 139 patients aged from 17 to 69 years (median age 51 years) with LC in the outcome of diffuse liver diseases of various etiologies who had been included in the waiting list for LT.

Among the etiological factors of LC, viral liver damage (VLD), primary sclerosing cholangitis (PSC), and toxic liver damage (TLD) were the most common (Table 1).

Table 1. Patient distribution depending on LC etiology

LC etiology	VLD	PSC	TLD	PBC	CGC	AIC	KWD	VOLL
%	61	12.5	11.1	5.1	4.4	2.9	1.5	15

Notes: PBC, primary biliary cirrhosis; CGC, cryptogenic cirrhosis; AIC, autoimmune cirrhosis; KWD, Konovalov-Wilson disease; VOLL, veno-occlusive liver lesions.

The third group consisted of 137 patients previously included in the second group, who were examined at different times of the postoperative period after LT.

During the study, all patients underwent a comprehensive ultrasound assessment of the abdominal organs and portohepatic and renal hemodynamics. The severity of the portal hypertension markers such as splenomegaly and the ascites development was evaluated in a two-dimensional mode. Alongside, the maximum spleen length (SL) was determined, and when free fluid was detected in the abdominal cavity, the separation of peritoneum layers (SPL) was quantitated to obtain the values eligible for comparison.

Doppler techniques were used both to exclude or confirm the presence of portal vein thrombosis, and also to study the incidence and severity of secondary intrarenal hemodynamic impairments. For this purpose, color and pulse Doppler sonography modes were used to visualize interlobar renal arteries and determine the RARI values at their level, as the most reliable, angle-independent parameter reflecting the degree of the increased intrarenal vascular resistance to blood flow. The US examinations were performed on the ultrasound diagnostic systems LOGIQ (USA) and TOSHIBA Aplio XG (Japan).

Obtained results and their discussion

The conducted examinations revealed statistically significant differences between the patients of the first and second groups in mean values of SL and RARI suggesting the absence of identical abnormalities in portohepatic and renal hemodynamics in diffuse liver lesions before and after LC formation (Table 2).

Table 2. Comparison of the mean values of the spleen length and renal arterial resistive index in the patients with and without liver cirrhosis

Patient group	SL (mm)	RARI (M±SD)
1st	111.6±13	0.59±0.01
2nd	179±31	0.69±0.06

Note: $p<0.04$

In the patients of the first group, neither Doppler sonography signs of impaired renal hemodynamics were recorded in any case, nor was the development of severe splenomegaly and ascites detected, either.

In the patients of the second group, persistent or transient increases in RARI values due to secondary intrarenal hemodynamic impairments were diagnosed in 88.4% of cases (Fig. 1, 2).

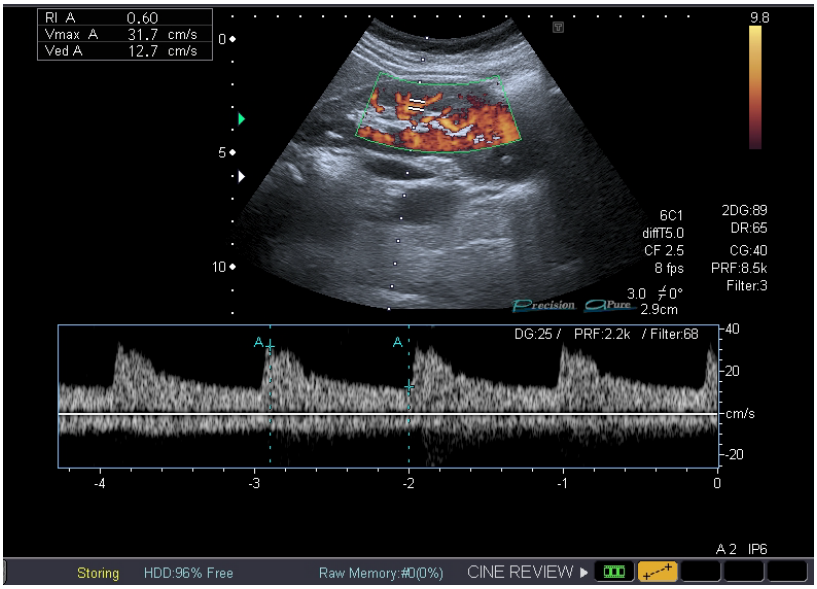

Fig. 1. Ultrasonorgaphy image of a patient from the 1st group. No signs of intrarenal hemodynamic impairment have been registered. Renal arterial resistive index is 0.6

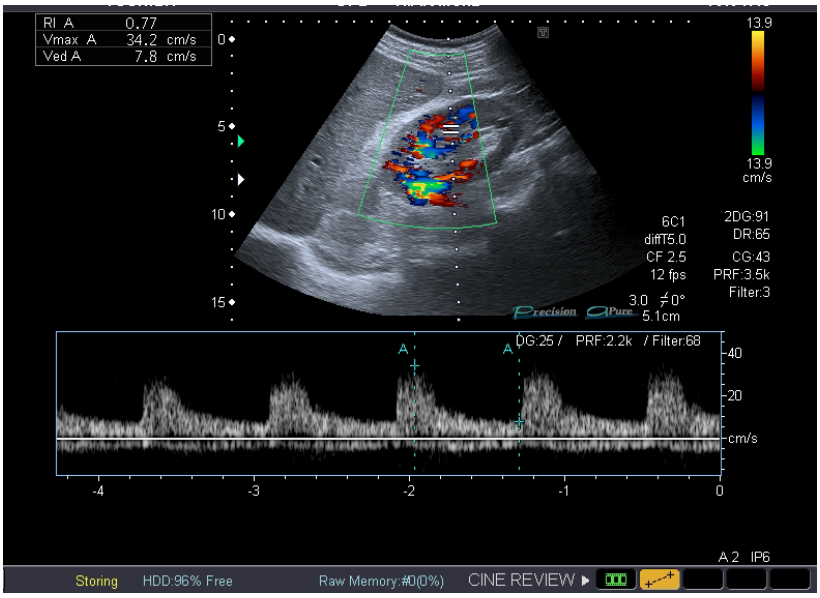

Fig. 2. Ultrasonography image of a patient from the 2nd group. The signs of the secondary angiospasm presence at the level of the renal artery branches have been revealed. Renal arterial resistive index is 0.78

We registered no statistically significant differences in the severity of splenomegaly and intrarenal hemodynamic impairments (IHI) between the subgroups of patients with different, most common etiological factors of LC development. (Table 3).

Table 3. Mean values of the renal arterial resistive index and the detection rates for renal hemodynamic impairments in liver cirrhosis of various etiology

	VLD	PSC	TLD	PBC
RARI (M±SD)	0.68±0.06	0.67±0.07	0.7±0.07	0.7±0.04
IHI (%)	91	76	93	100
SL (mm)	175 ±36	180±34.5	162±16	162±30

Note: p>0.09

There were no statistically significant differences in the incidence of the increase in RARI values between the patients of the second group with moderate (SL 120-140 mm) and severe splenomegaly (SL 140-210 mm) (Table 4).

Table 4. Mean values of the renal arterial resistive index in the patients with splenomegaly of various severity

	Moderate splenomegaly 9.5% (n=13)	Severe splenomegaly 90.5% (n=124)
RARI (M±SD)	0.68±0.06	0.68±0.06
IHI (%)	100%	90.5 %

Note: p>0.05

Among patients waiting for LT, the presence of ascites was diagnosed in 97 patients (70.8%). In 20 patients (14.4%), a significant amount of free fluid was detected in the abdominal cavity with a SPL of up to 60-114 mm. We recorded no statistically significant differences in the splenomegaly severity between the patients with pre-ascitic LC stage

and those with a significant amount of free fluid in the abdominal cavity. We also noted that IHI incidence was similar in the cases of no free abdominal fluid and in the cases of severe ascites. There were no statistically significant differences in the degree of RARI increase between the patients of these groups (Table 5). This is consistent to the data from A. Abdallah et al. [13] who recorded an increase in RARI values as early as at pre-ascitic stage, and indicated that secondary renal hemodynamic impairments may be the earliest marker of splanchnic blood flow impairments in portal hypertension and a predictor of the HRS development.

Table 5. The incidence of renal hemodynamic impairments in the patients with and without ascites

Ascites	Number of cases	RARI (M±SD)	Incidence of IHI (%)
Severe	20 (14.4 %)	0.66 ±0.05	80 %
Not identified	40 (29.2 %)	0.68±0.08	85%
		p>0.05	p>0.05

Signs of portal vein thrombosis of varying severity were diagnosed in 31 patients of the second group (22%) in a complex ultrasound examination in the preoperative period. At the same time, according to M. Yerdel et al. classification for portal vein thrombosis, 18 (58%) of them were found to have Grade I, 6 Grade II, and 7 Grade III portal vein thrombosis (Figs. 3, 4).

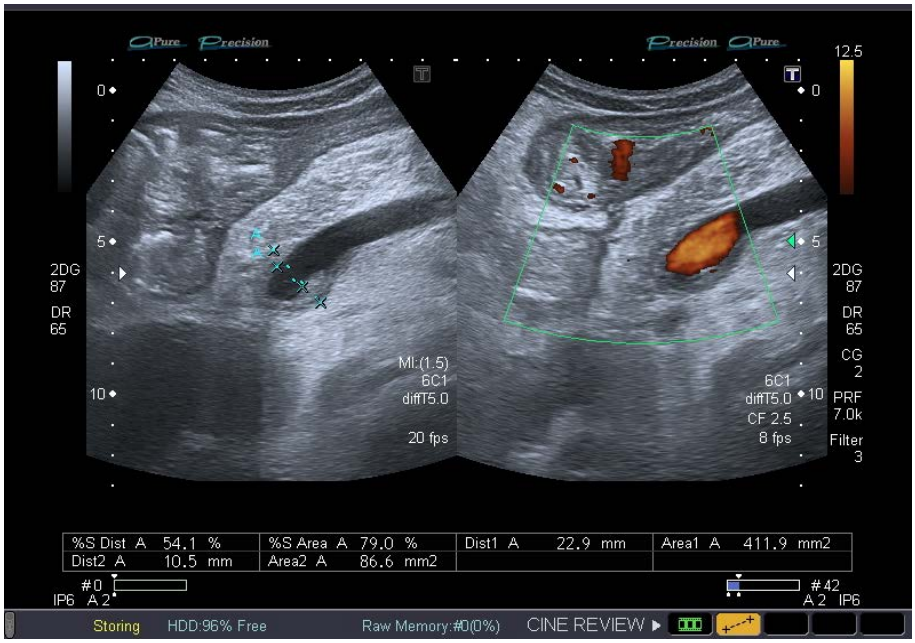

Fig. 3. Ultrasonography image of a patient from the 2nd group with the signs of Grade I portal vein thrombosis by Yerdel classification

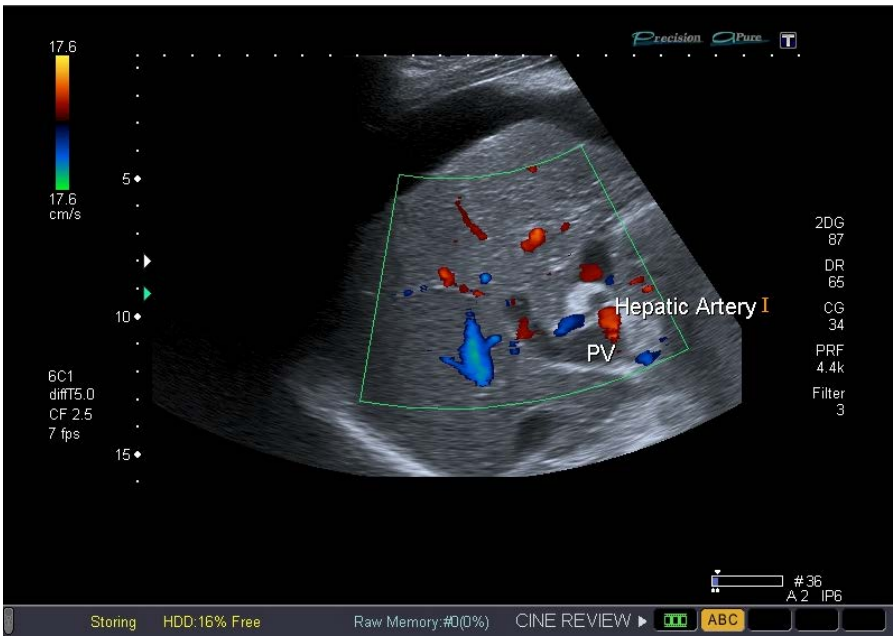

Fig. 4. Ultrasonography image of a patient from the 2nd group with the signs of Grade III portal vein thrombosis by Yerdel classification

We have found no statistically significant differences in the mean RARI values between the patients with unaffected blood flow in the

portal vein system and the patients with portal vein thrombosis, which suggests that this complication poses no impact on the increase in secondary angiospasm at the level of the intrarenal arterial bed in patients with LC. Meanwhile, the splenomegaly severity in patients with Grade III thrombosis was statistically significantly higher than in patients without signs of thrombotic masses in the lumen of the portal system veins (Table 6).

Table 6. The impact of the portal vein thrombosis on the incidence of intrarenal hemodynamic impairments and the severity of splenomegaly

The presence of thrombosis	Number of cases	RARI (M±SD)	Incidence of IHI (%)	SL mean, mm
Not identified	107 (78 %)	0.68±0.06	88%	172±30
Identified	31 (22.2 %)	0.7 ±0.05	93.5%	180±23
		p>0.05	p>0.05	p>0.05

The data obtained indicate that there is no direct relationship between the occurrence of IHI and such markers of portal hypertension severity as splenomegaly, ascites, and portal vein thrombosis. This indicates a complex nature of the mechanisms giving rise to renal hemodynamic disorders in LC. Should RARI values not monitored, this complication is not diagnosed in a timely manner.

Two female patients of the first group died within two months from the start of the follow-up before they were placed on the waiting list for LT. In both cases, the cause of death was type 1 HRS with progressing renal and multiple organ failure. Ultrasonography monitoring in dynamics showed signs of aggravating portal hypertension and persistent intrarenal hemodynamic impairments with increased RARI values to 0.78 in both cases.

LT was performed in 137 recipients. In the early postoperative period, 6 of them having Doppler ultrasonographic signs of previous IHI and an increase in RARI values in the range of 0.68–0.82 developed an acute renal failure, which required renal replacement therapy that produced a positive effect and renal function recovery in 5 of them. In the nearest following months, one patient with persistent signs of renal hemodynamic impairments, showed the progression of structural and functional abnormalities in the kidneys, which resulted in the chronic renal failure development. Subsequently, he underwent successful kidney transplantation. No patients with preoperative normal RARI values experienced any acute renal failure events after LT.

When assessing renal hemodynamics in 136 patients of the third group in the late postoperative period, we found that the mean values of SL, RARI, and the IHI incidence were statistically significantly lower than were those observed in these patients during the waiting period for LT. This indicates not only a regression of portal hypertension phenomena, but also an improvement in splanchnic and intrarenal blood flow after LT (Table 7).

Table 7. Detection rates for renal hemodynamic impairments. Mean values of the renal arterial resistive index and spleen length in the patients before and after liver transplantation

Patient groups	RARI (*M*±SD)	Incidence of IHI, (%)	SL mean, mm
2nd	0.68	81.6	176±31
3rd	0.61	44.7	138.8±27.6
	$p < 0.05$	$p < 0.05$	$p < 0.05$

Thus, the data we have obtained indicate a high incidence of secondary intrarenal hemodynamic impairments in patients with liver

cirrhosis of various origins and a positive LT effect on this pathological process.

Conclusions

1. The increase in the resistive index on the branches of the renal arteries is observed in 88.4% of patients with liver cirrhosis and portal hypertension syndrome; however, the correlation between the etiology of cirrhosis and the presence of thrombosis in the portal vein system is statistically insignificant.

2. Intrarenal hemodynamic impairments after liver transplantation resolve almost in half of the recipients, which can be used to assess the efficacy of the given treatment.

3. The resistive index on the branches of the renal artery measured by Doppler ultrasonography has a certain predictive value for the development of hepatorenal syndrome in patients with liver cirrhosis of various origins.

References

1. Huber M, Schwars W, Vogl T, Zeuzem S. Clinical aspects of liver cirrhoses and its complications and diagnostic problems. *Radiologe.* 2001;41(10):840–851. PMID: 11715575 https://doi.org/10.1007/s001170170055

2. Blaker H, Theuer D, Otto HF. Patho-logy of liver cirrhosis and portal hypertension. *Radiologe.* 2001;41(10):833–839. PMID: 11715574 https://doi.org/10.1007/s001170170054

3. Garcia-Tsao G, Parikh CR, Viola A. Acute kidney injury in cirrhosis. *Hepatology.* 2008;48(6):2064–2077. PMID: 19003880 https://doi.org/10.1002/hep.22605

4. Erly B, Carey WD, Kapoor B, McKinney JM, Tam M, Wang W. Hepatorenal syndrome: a review of pathophysiology and current treatment options. *Semin Intervent Radiol.* 2015;32(4):445–454. PMID: 26622108 https://doi.org/10.1055/s-0035-1564794

5. Lim JK, Groszmann RJ. Vasoconstrictor therapy for the hepatorenal syndrome. *Gastroenterology.* 2008;134(5):1608–1611. PMID: 18471529 https://doi.org/10.1053/j.gastro.2008.03.034

6. Sahmeddini MA, Amini A, Naderi N. The effect of octreotide on urine output during orthotopic liver transplantation and early postoperative renal function; a randomized, double-blind, placebo-controlled trial. *Hepat Mon.* 2013;13(9):e12787. PMID: 24282425 https://doi.org/10.5812/hepatmon.12787

7. Sansoè G, Silvano S, Mengozzi G, Smedile A, Touscoz G, Rosina F, et al. Loss of tubuloglomerular feedback in decompensated liver cirrhosis: physiopathological implications. *Dig Dis Sci.* 2005;50(5):955–963. PMID: 15906775 https://doi.org/10.1007/s10620-005-2671-0

8. Gonzalez SA, Trotter JF. Renal Function and MELD: Being direct is better. *J Hepatol.* 2010;52(5):622–623. PMID: 20347171 https://doi.org/10.1016/j.jhep.2010.01.002

9. Salerno F, Gerbes A, Gines P, Wong F, Arroyo V. Diagnosis, prevention and treatment of hepatorenal syndrome in cirrhosis. *Postgrad Med J.* 2007;56(9):1310–1318. PMID: 17389705 https://doi.org/10.1136/gut.2006.107789

10. Arroyo V, Fernandes J, Ginès P. Pathogenesis and treatment of hepatorenal syndrom. *Semin Liver Dis.* 2008;28(1):81–95. PMID: 18293279 https://doi.org/10.1055/s-2008-1040323

11. Vasilchenko MI, Lesovik VS, Dibirov MD, Gaydukova EV, Sosnin PV. Diagnostic features of multispiral computer and magnetic

resonance imaging in patients with portal hypertension. *Eksperimental'naia i klinicheskaia gastroenterologiia = Experimental & clinical gastroenterology.* 2012;(10):22–25. (In Russ.)

12. Procopet B, Berzigotti A. Diagnosis of cirrhosis and portal hypertension: imaging, non-invasive markers of fibrosis and liver biopsy. *Gastroenterol Rep (Oxf).* 2017;5(2):79–89. PMID: 28533906 https://doi.org/10.1093/gastro/gox012

13. Abdallah AF, Bakr AM, El-Haggar M, Amer T. Renal hemodynamic changes in children with cirrhosis. *Pediatr Nephrol.* 1999;13(9):854–858. PMID: 10603136 https://doi.org/10.1007/s004670050715

14. Qu EZ, Zhang YC, Li ZY, Liu Y, Wang JR. Contrast-enhanced sonography for quantitative assessment of portal hypertension in patients with liver cirrhosis. *J Ultrasound Med.* 2014 Nov;33(11)1971–7. PMID: 25336484 https://doi.org/10.7863/ultra.33.11.1971

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