The role of ultrasound in portal hypertension

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Key words: portal vascular system; Doppler measurements; types of portal hypertension; elastography

Received: 12. 5. 2017
Accepted: 25. 1. 2019

Abstract

Portal hypertension is the result of various organ and vascular conditions that are involved in portal circulation. Different diseases have similar complications. In the era of new investigative methods for early detection of the presence of portal hypertension, the question arises of the position that ultrasound examination should have in this diagnostic area. The article tries to elucidate the advantages and usability of the ultrasound investigation in the field of portal hypertension, as well as to draw attention to areas where this diagnostic investigation is no longer useful.

Cite as: Hari A, Tepeš K, Štabuc B. [The role of ultrasound in portal hypertension]. Zdrav Vestn. 2019;88(3–4):161–7.

DOI: 10.6016/ZdravVestn.2680

1 Introduction

Portal hypertension (PH) is pressure difference (pressure gradient) at both extreme ends of the portal vascular system (hepatic vein end and portal end). It occurs as a result of resistance to blood flow through the hepatic tissue (difference in pressure (Δp) = resistance (R) × flow (V)). In physiological conditions, the difference in pressure does not exceed 2–4 mmHg, which can be precisely evaluated by invasive haemodynamic measurement, i.e. by measuring hepatic venous pressure gradient (HVPG). An increased HVPG value of more than 10 mmHg is indicative of the presence of clinically relevant PH. Increased pressure value is followed by a passive filling of the relatively well-adapting portal venous system (consisting of the portal, upper mesenteric and the lineal vein), clinical evidence of which is venous congestion of the GI tract. Pathophysiologcal response to the congestion is vasoconstriction of the visceral arterial vessels, which in a long run further aggravates venous congestion due to a strong regulatory release of vasodilatory substances. Thus the characteristic of advanced stages of PH is vasodilatation of the abdominal vessels (except for the renal system!). Simultaneously with early compensatory mechanisms as part of angiogenesis, a number of portocaval venous collaterals are created. Clinically relevant sequels of PH occurrence include hepatic encephalopathy, ascites, oedema of the intestinal mucosa, infections due to frequent translocations of intestinal bacteria, and the occurrence of GIT varices (esophagus, stomach, rectum). At the same time,

secondary splenomegaly is often present (1-3).

The physiologically and clinically most useful classification of PH types is the one that classifies PH according to the position in relation to liver sinusoid. Thus, we distinguish a pre-, post- and sinusoidal PH type. The causes for the onset of different types of PH are very diverse (see Table 1) (4).

In addition to the already mentioned invasive HVPG* measurement, various less invasive or non-invasive investigation methods are available as modern devices for assessing the presence of clinically relevant PH or its complications. The leading role in assessing the presence of clinically relevant sinusoidal PH associated with liver cirrhosis belongs to ultrasound elastography of the liver and spleen (5). The elastography is based on the principle of measuring liver stiffness by estimating the rate of wave propagation through the liver tissue (a result in kPa), the result of which is well correlated with the stage of liver fibrosis. In patients with a sufficiently large spleen in whom the measurement is feasible, elastographic measurement of the spleen parenchyma is also an important parameter (6). A detailed view of the patency and appearance of the portal vascular circulation is also facilitated by various radiological investigations with or without a contrast medium (CT, MRI). Often, the first random finding of PH complications is found during the upper GI endoscopy, showing the presence of varices or portal hypertensive gastropathy. Contrast enhanced ultrasound (CEUS) may play an important complementary role in the detection of pre- and

Table 1: Classification of portal hypertension (PH) (4).

Presinusoidal PH	Sinusoidal PH	Postsinusoidal PH
Lineal vein thrombosis	Cirrhosis	Hepatic vein thrombosis (Budd-Chiari syndrome)
Portal vein thrombosis	Porto-sinusoidal vascular disease	Congenital malformation and thrombosis of the inferior vena cava
External compression of the portal vein	Congenital liver fibrosis	Constrictive pericarditis
Congenital portal vein stenosis	Polycystic liver disease	Tricuspid valve disease
	Idiopathic PH	
	Granulomatous disorders (sarcoidosis, tuberculosis, PBC, schistosomiasis)	
	Amyloidosis	
	Liver infiltration from haematological diseases	
	Hepatic veno-occlusive disease	
	Hepatic cell carcinoma	
	Severe viral or alcoholic hepatitis	

posthepatic causes of PH. Studies on the role of CEUS for assessing the presence of sinusoidal PH and for a non-invasive evaluation of HVPG are still underway.

Considering all this, it seems reasonable to evaluate the role and usability of ultrasound examination as part of the PH diagnostics. The article further thus provides an overview of the possibilities, advantages and drawbacks of ultrasonography for evaluating PH.

2 Investigation method description

Before deciding to undertake an US examination, we must be aware of the main limitations that affect its results. The quality of the investigation performed depends significantly on the type of US device, the quality of the probe and, above all, the investigator's knowledge and skill. Significant negative factors affecting the quality of the examination in the abdominal cavity also include overweight or underweight of the subject, the presence of intestinal gases and peristalsis, and in the case of PH diagnosis, the position of the liver and spleen in relation to the chest - abdominal cavity ratio and the breathing phase. Thus, every US finding suspicious for PH should also include the description of visibility and the type of ultrasound device. All morphological examinations should preferably be performed in several projections in order to avoid the most common error of an US examination (2D-examination of a 3D-space).

3 Morphological examination

Investigation is started with a morphological examination of the liver and spleen. The size of the organ, echogenicity and homogeneity of the parenchyma, and any morphological evidence of the presence of advanced liver fibrosis are described and measured (7). The presence of free fluid (ascites) in the abdominal cavity is assessed by examination of typical sites.

This is then followed by the examination of the vena cava inferior (VCI) with the description of its diameter and respiratory variability. We examine the inflows of all three hepatic veins (right, middle and left) and follow their course within the hepatic parenchyma. We measure their diameter at a distance of 1 cm from the inflow into the VCI to assess excessive dilation and describe possible reduction in the diameter or uneven course of the wall. In the caval venous system, attention should be paid to signs indicating the presence of thrombotic masses or obstruction in any of the hepatic veins, these being the most common causes of postsinusoidal PH.

This is followed by an examination of the portal venous system. We examine both main intrahepatic portal branches (occasionally, an additional median anatomical variant is present), the portal vein, the confluence, the lineal vein and the superior mesenteric vein. In the appropriate sites, we determine the diameters of all three main veins. Again, we are looking for signs of excessive dilation, thrombotic masses and signs of obstruction or blockage of any of the veins. A detailed morphological examination of this part of the venous system may detect the majority of most common causes of presinusoidal PH and allows an indirect conclusion about the presence of sinusoidal PH in many cases. The examination is complemented by searching for the presence of portosystemic collaterals, which are characteristic for PH. The most common sites of collaterals are: the left gastric vein (esophageal varices), short gastric veins (gastric varices),

splenorenal shunts, coronary collateral circulation and the paraumbilical vein. In the presence of signs of thrombosis, attention is paid to the echogenicity of the thrombus, which is indirectly indicative of the duration of thrombosis (an acute thrombus is generally hypoechogenic, while a chronic one is hyperechogenic and structurally organised) and of the presence of a so-called cavernous transformation of the portal vein, indicating a chronic thrombosis in this region (Table 2).

4 Colour Doppler US

The next step in the investigation is colour Doppler US imaging, where the presence of the colour signal as well as the direction and the intensity of the flow via the colour scale are checked in all the above-described vascular systems. In principle, any thrombosis or blocked vein is first defined morphologically and only then additionally by colour Doppler US imaging. The assumed absence of flow due to a very slow flow in the advanced PH phase is the most common cause of an incorrect diagnosis of venous thrombosis. Therefore, the so-called slow-flow colour option or renal colour Dopper US is used. The flow direction is described as "in the direction of the liver" or "in the direction away from the liver". Namely, the very frequently used terms of "hepatopetal" and "hepatofugal" flow are not among the standard medical terms and should therefore be used only exceptionally (8).

5 Doppler measurements

The investigation is completed with Doppler measurements performed in accordance with the principles applicable to the measurements in the venous and arterial systems. TAMV* (time estimate of the mean velocity of the flow

Table 2: Values of the most frequently used indexes with cut off values indicative of portal hypertension.

Morphological measurement	Diameter (mm)	Comment (measurement site)
Hepatic vein (right)	>10	1 cm from the inflow into VCI
Portal vein	>12	at the crossing point with the hepatic artery
Lienal vein	>9	1 cm before the confluence
Superior mesenteric vein	>9	1 cm before the confluence
Doppler measurement	**Value**	**Comment (measurement site)**
TAMV	<15 cm/s	Portal vein
CI	<0.08 cm*s	Portal vein
PI	<0.5	Portal vein
RI	>0.60	Lineal artery

HVPG – hepatic venous pressure gradient TAMV – time averaged mean blood velocity, CI – congestion index, PI – pulsatility index, RI – resistive index, VCI – Lat. vena cava inferior.

in the portal vein), CI* (congestion index, which includes the indirectly estimated portal vein volume in addition to the calculated velocity), PI * (pulsatility index) and indicators of arterial circulation are preferred as the most useful when evaluating PH presence. Among the latter, a special place belongs to RI*, i.e. the resistive index of the lineal artery. Its higher values are typically indicative of the sinusoidal form of PH. There are, of course, several other indicators that an experienced investigator of this field should be familiar with. Each Doppler imaging also includes a description of the recorded Doppler signal (phasicity, sinusoidality, direction, intensity), which is of particular importance in the description of hepatic vein signal. Advanced stage of PH is characterised by the presence of a damped, slow and poorly variable monophasic signal that occasionally passes even in the direction away from the liver. The resistance against the arterial flow is increased.

6 Specific situations

Doppler imaging can be more or less easily also used for assessing the treatment success in patients with clinically relevant PH that required therapy. Thus, ultrasound examination in the same steps and with specific features is used to assess the patency of inserted interventional or surgical stents (stents in the caval system, transjugular intrahepatic portosystemic shunt (TIPS), bypass surgeries). When assessing the patency of TIPS, in the event of an uncertainty, the investigation can be supplemented with ultrasonography with a contrast medium (9,10).

7 The use of ultrasonography in daily practice

Before the introduction of elastographic investigation techniques, US served as a complementary method to assess the presence of PH as a result of the sinusoidal PH. Ever since this type of PH is diagnosed according to the principles applicable to elastographic measurements of the liver and spleen, clearly, ultrasonography does not provide accurate findings in the early phase of sinusoidal PH. Thus US findings do not influence the decision for endoscopic screening of the presence of upper gastrointestinal varices. In the hands of an experienced investigator, however, it may accurately detect the presence of the most common collaterals between the portal and caval venous systems, which are not accessible to examination by endoscopy or would require the use of some other radiological methods (CT, MRI). US is also the fastest and the least invasive method for quick evidence of the presence of ascites or splenomegaly. In these cases, it is the investigation method of choice. Together with a detailed examination of liver surface (linear probe assessment) it is also an excellent complement to confirm a significant stage of liver fibrosis and thereby a presence of sinusoidal PH when elastographic measurements provide doubtful results (inclusion or rule-in value). The negative predictive (exclusion or rule-out) value of investigation, however, is much greater and thus can be reliably used to exclude indirect signs of the presence of PH.

Morphological and colour Doppler US examinations are the methods of choice for the evaluation and diagnosis of the cause of pre- and post-sinusoidal PH. In the hands of an experienced investigator, the diagnosis is reliable and in emergency cases (suspicion of acute thrombosis) also accurate enough so that there is no need for complemental CT or MRI scan prior to the initiation of therapy. Advantages in these cases include low cost, bedside investigation, repeatability, absence of contrast medium (common concomitant renal impairment in these patients) and of irradiation. US can also be a method that - in the case of an unclear clinical picture – allows for a suspicion and afterwards a rapid confirmation of diagnosis by CT, followed by a subsequent treatment of PH in these cases. Due to a narrow therapeutic window in acute venous thrombosis, it facilitates quick and accurate diagnosis and thus, in the case of successful treatment, prevents the onset of neoangiogenesis (varices). Furthermore, by means of ultrasonography, it is possible to distinguish reliably between the acute and chronic phase of thrombosis via the aforementioned indirect signs.

Doppler scan with index and velocity measurements is probably the most interesting field for the investigator, but we must be aware that it only provides a rough assessment of the condition. When estimating the velocity in the portal venous system, the results are highly dependent on the patient's compliance (fasting status, inspiration/exhalation phase) and the quality of measurements. As a rule, the result is improved by at least three consecutive measurements. Moreover, indicative results are only present in the advanced or late phase of PH, when clinical signs of the disease are clearly evident too. Thus, the investigation is not useful for PH screening purpose, but only for evaluating an already established PH (early or late phase of the disease). Currently, there is no solid evidence to link Doppler indices to distinguish between responders and non-responders to therapy with beta blockers (1).

Ultrasonography combined with Doppler US imaging is a method of choice for monitoring the patency and functionality of inserted TIPS in accordance with the principles set for post-intervention follow up. According to the latest studies, the rationale of regular US monitoring of TIPS patency due to the use of a new generation of covered stents is considered questionable. However, there have been no amendments to the guidelines in this area as yet. The method is reliable for detecting TIPS thrombosis as well as for evaluating stent dysfunction (a relative stenosis in the early or late phase, which requires balloon dilatation). When in doubt regarding the obstruction, CEUS can be used, which perfectly shows the passage of contrast particles from the portal into the caval venous system. US scan is also a theoretical method of choice for follow up of the patency of surgical bypasses, although in practice the investigation is often difficult to perform and accurate only in patients with lean body structure. Otherwise, another radio-morphological examination is used for follow up (9,10).

8 Conclusion

In the era of modern elastographic investigation methods, the classic US examination has a limited usability for the early detection of clinically relevant sinusoidal PH. The latter is the most frequent cause of PH due to liver cirrhosis. In these cases, the presence of indirect signs that may indicate the presence of PH are entered in the report findings. A

much higher predictive value is attributed to the absence of aforementioned signs, which in principle enables the centres without access to elastography of the liver and spleen to follow up their patients by excluding the presence of US evidence of PH. The latter can be considered in patients with liver cirrhosis, who have problems tolerating gastroscopy or refuse it. At the same time, we must be aware that a clinically relevant PH cannot be diagnosed by ultrasonography alone, while the confirmation of the latter phase of the disease represents the foundation of the up-to-date pharmacological and non-pharmacological treatment.

But, nevertheless, ultrasonography still remains the method of choice for quick detection of certain complications of PH (ascites, portosystemic collaterals outside the upper GI area). It is also crucial for the identification of the presence of pre- or post-sinusoidal PH and the detection of the cause of either form of PH. In the hands of an experienced investigator, it is indispensable for evaluating the treatment success and follow up of interventional therapy for PH (TIPS). As a supplemental investigation it is conditionally useful for assessing the PH-related complications.

In the current treatment of patients with vascular liver disease, ultrasonography in combination with Doppler US imaging is a supplemental investigation method, and often the hepatologist's expertise in the correct treatment of a patient with portal hypertension is of key importance.

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