Systemic and pulmonary hemodynamics in patients with extrahepatic portal vein obstruction is similar to compensated cirrhotic patients

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Abstract

Background Patients with cirrhosis and portal hypertension exhibit a hyperdynamic circulation manifesting as increased cardiac output, heart rate and plasma volume; and decreased arterial blood pressure, systemic vascular resistance, and pulmonary vascular resistance. It is believed that these changes are related to both hepatocellular dysfunction and portal hypertension. However, the role of portal hypertension per se in producing these changes in circulation has not been clear. Extrahepatic portal vein obstruction (EHPVO), a vascular disorder of the liver characterized by cavernomatous transformation of the main portal vein, is an excellent model to study the role of portal hypertension per se in producing these changes because there is no hepatic dysfunction in EHPVO. The main aim of our study was, therefore, to evaluate alterations of systemic and pulmonary vascular systems in patients with EHPVO and compare them with patients with compensated cirrhosis.

Patients and methods Consecutive patients of EHPVO, 15 years or older, and past variceal bleeders were studied. For comparison, consecutive patients with compensated cirrhosis and history of variceal bleed, matched for variceal status, and body surface area were included. The hemodynamic studies included the measurements of cardiac

index (by Fick's oxygen method), and systemic and pulmonary vascular resistance indices.

Results Fifteen patients of EHPVO and same number of controls (compensated cirrhotics) were included in the study. The baseline parameters in the two groups were comparable. Both EHPVO patients and cirrhotics had similar values in all the measured systemic and pulmonary hemodynamic parameters. The median (range) cardiac index in EHPVO was 3.8 (2.3–7.7) $\text{l min}^{-1} \text{m}^{-2}$, whereas it was 4.4 (2.8–8.9) $\text{l min}^{-1} \text{m}^{-2}$ in cirrhosis ($P = 0.468$). The median (range) systemic vascular resistance index in EHPVO was 1,835 (806–3400) $\text{dyne s cm}^{-5} \text{m}^{-2}$, which was similar to that in cirrhotic patients (1,800 [668–3022], $P = 0.520$). Similarly, the values of median (range) pulmonary vascular resistance index were comparable in the two groups (71 [42–332] vs. 79 [18–428], $P = 0.885$). A subgroup analysis was done for 8 patients of EHPVO and 8 age-matched compensated cirrhotic patients, which also revealed similar values of cardiac index, cardiac output, systemic vascular resistance index, systemic vascular resistance, pulmonary vascular resistance index, and pulmonary vascular resistance in the two groups.

Conclusions EHPVO patients have hyperdynamic circulation manifested by high cardiac index and low systemic and pulmonary vascular resistance indices. These hemodynamic changes are comparable with compensated cirrhotic patients who have similar grade of portal hypertension. This suggests a predominant role of portal hypertension per se in the genesis of systemic and pulmonary hemodynamic alterations.

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Introduction

Extrahepatic portal vein obstruction (EHPVO) is a vascular disorder of the liver defined by the obstruction and cavernomatous transformation of the main portal vein with or without involvement of the intrahepatic portal vein, splenic vein, or superior mesenteric vein [1]. It is characterized by noncirrhotic, presinusoidal, and prehepatic portal hypertension [2]. It is an important cause of portal hypertension, especially in children in the developing countries [3]. Portal vein obstruction associated with chronic liver disease or neoplasia is a separate entity and does not constitute EHPVO.

EHPVO entails a high, early, and prolonged risk of gastrointestinal bleeding mainly from esophageal and/or gastric varices, and less often a risk of cholangiopathy or protein-losing enteropathy [2]. Patients with EHPVO are generally children and young adults who most commonly present with repeated attacks of well-tolerated variceal bleeding, splenomegaly, and preserved hepatic functions. It accounts for up to 30% of all variceal bleeds and is only second to cirrhosis [1]. EHPVO is generally considered as a benign disease, but hepatic dysfunction in the form of ascites and deranged liver functions occasionally occurs especially in patients with prolonged portal hypertension [4].

Patients with compensated cirrhosis mimic EHPVO patients, but liver function tests, viral serology, and liver histology can easily distinguish the two. Moreover, portal cavernoma detected by Doppler ultrasound is characteristic of EHPVO. Patients with cirrhosis and portal hypertension exhibit a hyperdynamic circulation manifesting as increased cardiac output, heart rate and plasma volume; and decreased arterial blood pressure, systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR). These changes are brought about by peripheral and splanchnic arterial vasodilatation with abnormal distribution of blood, leading to reduced central or effective blood volume and hyperactive renin–angiotensin–aldosterone system [5]. It is believed that these changes are related to both hepatocellular dysfunction and portal hypertension. In cirrhotic patients, the severity of hemodynamic abnormalities correlates with the Child–Pugh status of these patients and hepatic parenchymal dysfunction is considered to play a major role in the progressive hemodynamic abnormalities. However, the role of portal hypertension per se in producing these changes in circulation has not been clear. EHPVO is an excellent model to study the role of portal hypertension alone in producing these changes because there is no hepatic dysfunction in EHPVO.

Only a few studies have been done on hemodynamic alterations in patients with noncirrhotic portal hypertension [5–9], especially EHPVO, in contrast to many reports on hemodynamics in cirrhotic patients. Moreover, the effect of

portal vein obstruction on systemic and pulmonary hemodynamics and collateral formation has not been clear. The main aim of our study was, therefore, to evaluate alterations of systemic and pulmonary vascular system in patients with EHPVO and compare them with patients with compensated cirrhosis. The rationale for this investigation was to study the role of portal hypertension per se on systemic and pulmonary hemodynamics in EHPVO as compared with the hemodynamic changes produced by hepatic dysfunction *plus* portal hypertension in cirrhotic patients.

Patients and methods

Study population

This was a prospective study conducted in the Department of Gastroenterology, G B Pant Hospital, New Delhi, India, between September 2005 and June 2006. The study population consisted of consecutive EHPVO patients, 15 years or older, who attended the department during this period. All patients were past variceal bleeders. The diagnosis of EHPVO was based on normal liver histology finding and imaging techniques such as Doppler ultrasound, which demonstrated the presence of portal vein obstruction (an intraluminal thrombus in the portal vein and/or portal vein cavernoma) in a patient presenting with (a) history of variceal bleed, (b) well-preserved hepatic functions as assessed clinically and biochemically, (c) splenomegaly, and (d) normal hepatic venous pressure gradient (HVPG). *Exclusion criteria* were (a) other causes of portal vein obstruction such as hepatocellular carcinoma or cirrhosis, (b) evidence of viral, autoimmune, metabolic, or inherited liver disease, (c) presence of cirrhosis on the liver biopsy, and (d) patients on β -blockers or antiviral therapy. For comparison, consecutive patients with compensated cirrhosis and history of variceal bleed, matched for variceal status (to ensure that they had same degree of portal hypertension) and body surface area, attending our department during the same period, were included. Hemodynamic studies were done at least 4 weeks after the last bleeding episode. All patients gave informed consent to participate in the study. The study was approved by the institutional ethics committee.

Hemodynamic studies

The hemodynamic studies included the measurements of HVPG, right atrial pressure (RAP), pulmonary arterial pressure (PAP), pulmonary capillary wedge pressure (PCWP), and mean arterial pressure (MAP). The hemodynamic studies were done after an overnight fast. Under

aseptic conditions, the patients received local anaesthesia in the femoral region and a venous introducer was placed in the right femoral vein by the Seldinger technique. For measuring HVPg, a 7F balloon-tipped Swan-Ganz catheter was introduced into the main right hepatic vein under fluoroscopic guidance. Free hepatic venous pressure (FHVP) and wedged hepatic venous pressure (WHVP) were measured using pressure transducers and Nihon Kohden (Tokyo, Japan) hemodynamic monitor. Measurements were performed in triplicate, and a mean was taken. HVPg was obtained as the difference between WHVP and FHVP. The normal HVPg in our laboratory is up to 5 mmHg. The Swan-Ganz catheter was then advanced into the right atrium, pulmonary artery, and then pulmonary capillaries for measurement of the RAP, PAP, and PCWP, respectively. MAP was measured simultaneously by introducing the catheter through the femoral artery.

Blood samples were taken from both the pulmonary artery and the femoral artery for estimating oxygen saturation. Heart rate was derived from continuous electrocardiogram monitoring. Cardiac output was calculated by Fick's oxygen method [10] as follows: Oxygen consumption (ml min^{-1}) $\div$ Arteriovenous oxygen difference (ml l^{-1}). The systemic vascular resistance (SVR, in dyne s cm^{-5}) was calculated as: $(\text{MAP in mmHg} - \text{RAP in mmHg}) \times 80 \div \text{cardiac output (in l min}^{-1})$. The pulmonary vascular resistance (PVR in dyne s cm^{-5}) was calculated as: $(\text{PAP in mmHg} - \text{PCWP in mmHg}) \times 80 \div \text{cardiac output (in l min}^{-1})$. Cardiac output was indexed by body surface area and expressed as cardiac index ($\text{l min}^{-1} \text{m}^{-2}$).

Statistical analyses

Statistical analysis was performed using the SPSS, Version 15.0, statistical package (SPSS Inc., Chicago, IL). All results were expressed as the median (range) or as frequencies (%). Comparisons within each group were performed using the Mann–Whitney *U* test or Fisher's exact test. A *P* value below 0.05 was considered significant.

Results

Fifteen EHPVO patients and the same number of controls (compensated cirrhotic patients) were included in the study. The controls were matched by variceal status and body surface area. Both cases and controls had history of variceal bleed. The baseline parameters in the two groups were comparable (Table 1). Moderate splenomegaly was present in all EHPVO patients. One EHPVO patient had ascites, another had history of jaundice, and none of them had developed hepatic encephalopathy. Of the 15 patients with cirrhosis, the etiology was alcoholic in 6, hepatitis B in 3, hepatitis C in 3, and cryptogenic in remaining 3. All of them had compensated cirrhosis with a median Child–Pugh score of 6. They did not have history of pedal edema, ascites, jaundice, or hepatic encephalopathy.

The median (range) HVPg in EHPVO patients was 3 (2–10) mmHg. All the patients had HVPg level 6 mmHg or less, except one patient who had HVPg value of 10 mmHg. On the other hand, the median (range) HVPg levels in patients with compensated cirrhosis was

Table 1 Baseline characteristics of included patients

Parameter	EHPVO (<i>n</i> = 15)	Cirrhosis (<i>n</i> = 15)	<i>P</i>
Median age (range), years	20 (15–40)	42 (20–65)	<0.01
Sex ratio (male:female), <i>n</i>	10:5	13:2	0.390
Median body surface area (range), m^2	1.5 (1.3–1.7)	1.5 (1.3–1.9)	0.384
Median hemoglobin (range), g dl^{-1}	10 (6–14)	10 (8–13)	0.867
Median serum creatinine (range), mg dl^{-1}	0.9 (0.5–1.2)	0.8 (0.3–2.1)	0.900
Median serum bilirubin (range), mg dl^{-1}	1.2 (0.5–2.0)	1.5 (0.6–2.9)	0.723
Median serum albumin (range), g dl^{-1}	4.0 (3.3–4.8)	3.5 (2.8–4.5)	0.001
Median PT prolongation (range), s	2 (0–6)	3 (1–14)	0.128
Median grade of esophageal varices (range)	3 (1–4)	3 (2–4)	0.837
Patients with gastric varices, <i>n</i> (%)	6 (40)	6 (40)	1.000
Patients with PHG, <i>n</i> (%)	7 (47)	9 (60)	0.715
Median HVPg (range), mmHg	3 (2–10)	14 (9–26)	<0.01
Etiology of cirrhosis, <i>n</i> (%)			
Alcohol		6 (40)	
Hepatitis B		3 (20)	
Hepatitis C		3 (20)	
Cryptogenic		3 (20)	
Median Child–Pugh score (range)	–	6 (5–7)	–

EHPVO extrahepatic portal vein obstruction, SD standard deviation, PT prothrombin time, PHG portal hypertensive gastropathy, HVPg hepatic venous pressure gradient

significantly higher (14 [9–26] mmHg; $P < 0.01$) than the EHPVO patients. None of the cirrhotic patients had HVPG less than 9 mmHg.

Hemodynamic studies

The results of hemodynamic studies are given in Table 2. Both EHPVO patients and cirrhotic patients had similar values in all the measured hemodynamic parameters. The median (range) cardiac index in EHPVO was $3.8 (2.3\text{--}7.7) \text{ l min}^{-1} \text{ m}^{-2}$, whereas it was $4.4 (2.8\text{--}8.9) \text{ l min}^{-1} \text{ m}^{-2}$ in cirrhosis ($P = 0.468$) (Fig. 1). The median (range) systemic vascular resistance index (SVRI) in EHPVO was $1,835 (806\text{--}3400) \text{ dyne s cm}^{-5} \text{ m}^{-2}$, which was similar to that in cirrhotic patients ($1,800 [668\text{--}3022]$, $P = 0.520$) (Fig. 2). Similarly, the values of median (range) PVR index (PVRI) were comparable in the two groups ($71 [42\text{--}332]$ vs. $79 [18\text{--}428]$, $P = 0.885$) (Fig. 3).

A subgroup analysis was done for 8 EHPVO patients and 8 age-matched compensated cirrhotic patients, which also revealed similar values of cardiac index, cardiac output, SVRI, SVR, PVRI, and PVR in the two groups (Table 3).

Discussion

Our study showed that EHPVO patients have hyperdynamic circulation manifested by high cardiac index and low systemic and PVR indices. These hemodynamic changes are comparable with compensated cirrhotic patients who have similar grade of portal hypertension. Furthermore, as EHPVO and cirrhotic patients in our study were not age matched, we did a separate subgroup analysis

Fig. 1 Median cardiac index in EHPVO and cirrhosis

of age-matched patients of both the groups and found similar results.

EHPVO patients have a normal liver functions and hepatic parenchyma but raised portal pressure quite comparable with that seen in cirrhotic portal hypertension. HVPG is within normal limits, but intrasplenic pressure is significantly elevated, indicating the presinusoidal nature of the block [6]. Thus, these patients allow a unique opportunity to study the development of portal hypertension and associated hemodynamic changes in the absence of hepatic parenchymal disease.

There are only a few studies on the hemodynamic alterations in patients with noncirrhotic portal hypertension [5–9] in contrast to several studies on the hemodynamic

Table 2 Systemic and pulmonary hemodynamics of included patients^a

Parameter	EHPVO ($n = 15$)	Cirrhosis ($n = 15$)	P
Median MAP (range), mmHg	89 (80–116)	91 (74–128)	0.771
Median RAP (range), mmHg	3 (0–8)	4 (0–10)	0.346
Median PAP (range), mmHg	12 (8–21)	13 (4–25)	0.466
Median PCWP (range), mmHg	8 (0–14)	8 (0–14)	0.787
Median cardiac index (range), $\text{l min}^{-1} \text{ m}^{-2}$	3.8 (2.3–7.7)	4.4 (2.8–8.9)	0.468
Median cardiac output (range), l min^{-1}	5.7 (3.5–13.1)	7.1 (4.5–14.9)	0.254
Median SVRI (range), $\text{dyne s cm}^{-5} \text{ m}^{-2}$	1835 (806–3400)	1800 (668–3022)	0.520
Median SVR (range), dyne s cm^{-5}	1207 (496–2213)	967 (448–1738)	0.191
Median PVRI (range), $\text{dyne s cm}^{-5} \text{ m}^{-2}$	71 (42–332)	79 (18–428)	0.885
Median PVR (range), dyne s cm^{-5}	46 (26–257)	48 (12–246)	0.694

EHPVO extrahepatic portal vein obstruction, SD standard deviation, MAP mean arterial pressure, RAP right atrial pressure, PAP pulmonary arterial pressure, PCWP pulmonary capillary wedge pressure, SVRI systemic vascular resistance index, SVR systemic vascular resistance, PVRI pulmonary vascular resistance index, PVR pulmonary vascular resistance

^a Normal values: cardiac index, $2.5\text{--}4.2 \text{ l min}^{-1} \text{ m}^{-2}$; SVRI, $1970\text{--}2390 \text{ dyne s cm}^{-5} \text{ m}^{-2}$; PVRI, $255\text{--}285 \text{ dyne s cm}^{-5} \text{ m}^{-2}$ (from Ref. [23]). Values of cardiac output, SVR, and PVR depend on the body surface area

Fig. 2 Median systemic vascular resistance index in EHPVO and cirrhosis

Fig. 3 Median pulmonary vascular resistance index in EHPVO and cirrhosis

alterations in cirrhotic patients. To the best of our knowledge, this is the first study in the literature that has compared the pulmonary and systemic hemodynamic alterations of EHPVO with those of cirrhotic patients.

Lebrec et al. [7] in their small study on 5 adult patients with portal vein obstruction showed that cardiac index averaged $3.8 \pm 0.6 \text{ l min}^{-1} \text{ m}^{-2}$, not significantly

different from that measured in cirrhotic patients but significantly higher than in patients of the control group. In our study, we had similar findings, and, in addition, we documented the alterations in systemic and PVR and pressures, which were not studied by Lebrec et al.

Harada et al. [8] studied systemic hemodynamics in 19 noncirrhotic patients with prominent esophageal varices. They found an increase in the cardiac index and a decrease in the total peripheral resistance in these patients when compared with 12 healthy controls. There was a significant correlation between the cardiac index and plasma volume in the 14 noncirrhotic patients with portal hypertension ($r = 0.537$, $P < 0.05$), but no significant relationships were identified between the cardiac index and liver function values. They suggested that the expanded plasma volume, secondary to the enlargement of the portal bed, might be closely related to the mechanism of hyperdynamic systemic circulation in noncirrhotic portal hypertension. Furthering to findings of Harada et al., our study actually documents the similar hemodynamics of EHPVO and cirrhosis, since we took compensated cirrhotic patients as controls, unlike normal subjects taken as control by Harada et al. [8].

The disparity between clinical manifestations of porto-systemic collateralization and the normal HVP is a key finding in EHPVO patients. The hyperdynamic changes in cirrhotic patients are primarily due to increased plasma volume, peripheral arteriovenous shunting, increased vasodilators mainly nitric oxide, enhanced sympathetic nervous activity, and activation of renin-angiotensin system leading to peripheral and splanchnic arterial vasodilatation. EHPVO patients predominantly have preserved liver functions compared with cirrhotic patients and thus there may be considerably lower quantity of the abnormal humoral factors causing these systemic abnormalities. Studies of experimental portal hypertension have demonstrated that splanchnic vascular endothelial cell is primarily responsible for mediating splanchnic vasodilatation through generation of nitric oxide. Cytokines such as $\text{TNF-}\alpha$ and possibly endothelins may play important roles in generating hyperdynamic circulation [11].

Portal pressure is an important factor that regulates vasodilatation in the splanchnic arterial circulation through endothelial nitric oxide synthase (eNOS) activation with different mechanisms of induction of this enzyme [12]. Severity of portal hypertension has been shown to influence eNOS activation in the splanchnic circulation [13]. Using a surgical model of portal hypertension, partial ligation of portal vein, the relation between portal pressure and the development of the hyperdynamic circulatory state was studied. The degree of portal pressure generated by partial ligation of portal vein was significantly related to the severity of the hyperdynamic circulatory state in rats.

Table 3 Systemic and pulmonary hemodynamics of a subgroup of EHPVO patients and age-matched compensated cirrhotic patients^a

Parameter	EHPVO (<i>n</i> = 8)	Cirrhosis (<i>n</i> = 8)	<i>P</i>
Median age (range), years	27 (20–40)	36 (20–42)	0.105
Median cardiac index (range), l min ⁻¹ m ⁻²	3.9 (2.3–7.7)	5.6 (3.5–8.9)	0.115
Median cardiac output (range), l min ⁻¹	6.1 (3.5–13.1)	8.6 (5.1–14.9)	0.172
Median SVRI (range), dyne s cm ⁻⁵ m ⁻²	1728 (806–3400)	1309 (668–1993)	0.401
Median SVR (range), dyne s cm ⁻⁵	1099 (496–2213)	870 (448–1358)	0.345
Median PVRI (range), dyne s cm ⁻⁵ m ⁻²	79 (44–119)	72 (18–101)	0.294
Median PVR (range), dyne s cm ⁻⁵	51 (26–73)	47 (12–56)	0.208

EHPVO extrahepatic portal vein obstruction, SD standard deviation, SVRI systemic vascular resistance index, SVR systemic vascular resistance, PVRI pulmonary vascular resistance index, PVR pulmonary vascular resistance

^a Normal values: cardiac index, 2.5–4.2 l min⁻¹ m⁻²; SVRI, 1970–2390 dyne s cm⁻⁵ m⁻²; PVRI, 255–285 dyne s cm⁻⁵ m⁻² (from Ref. [23]). Values of cardiac output, SVR, and PVR depend on the body surface area

Furthermore, different degrees of portal pressure initiated physical stimuli to induce eNOS activation in the different parts of the splanchnic arterial circulation and with different molecular mechanisms [13]. For instance, an acute and higher portal pressure induced vasoconstriction first in large arteries of the splanchnic circulation owing to a myogenic reflex caused by a sudden increase in portal pressure, which then caused phosphorylation and activation of eNOS through Akt/PKB activation, ultimately leading to increased NO production and vasodilatation [14, 15]. Activation of Akt might be due to an increase in shear stress induced by this myogenic reflex and vasoconstriction. In contrast, when milder portal hypertension was surgically generated, eNOS in the intestinal microcirculation, not in the large- or medium-size arteries of the splanchnic circulation, was upregulated. Interestingly, this eNOS activation seems to be induced by increased production of vascular endothelial growth factor (VEGF) [13].

VEGF and platelet-derived growth factor (PDGF) pathways are crucial to angiogenesis, a process that contributes significantly to the pathogenesis of portal hypertension. Maintenance of increased portal pressure, hyperkinetic circulation, splanchnic neovascularization, and portosystemic collateralization is regulated by VEGF and PDGF in portal hypertensive rats [16]. A recent study determined the effects of inhibition of VEGF and/or PDGF signaling on hyperdynamic splanchnic circulation and portosystemic collateralization in rats with completely established portal hypertension. Portal vein-ligated rats were treated with rapamycin (VEGF signaling inhibitor), imatinib mesylate (Gleevec; PDGF signaling inhibitor), or both simultaneously, when portal hypertension was already fully developed. Combined inhibition of VEGF and PDGF signaling significantly reduced splanchnic neovascularization and pericyte coverage of neovessels, which translated into hemodynamic effects of a 40% decrease in portal pressure, a 30% decrease in superior mesenteric artery blood flow, and a

63% increase in superior mesenteric artery resistance, yielding a significant reversal of the hemodynamic changes provoked by portal hypertension in rats. Portosystemic collateralization was reduced as well [16].

The development of portosystemic venous collateral circulation in patients with portal venous obstruction contributes to the hyperkinetic circulatory state. In cirrhotic patients, in whom liver function is restored after transplantation, these hyperdynamic changes persist, possibly because of persistent collateral circulation, which may keep portal tributary blood flow elevated [17]. Development of collateral circulation, an essential factor in the natural history of portal hypertension, may lead to further aggravation of the portal hypertensive syndrome. This vicious cycle leading to hyperdynamic circulation may be related to soluble vascular cell adhesion molecule-1 (sVCAM-1). Lo Iacono et al. [18] found sVCAM-1 to be inversely related to SVR ($r = -0.37$; $P = 0.005$). The development of collateral circulation in cirrhosis is not only a passive process of opening of preexisting vascular channels but also a neoangiogenetic process, driven, at least in part, by VEGF.

The hyperkinetic circulatory syndrome observed in patients with presinusoidal portal hypertension may also be related to an increase in β -adrenergic activity as shown by Brailon et al. [9]. They studied systemic and splanchnic hemodynamics and the effect of propranolol in 15 patients with presinusoidal portal hypertension. These patients exhibited a hyperkinetic circulatory syndrome characterized by high cardiac index and low SVR despite normal liver function and sinusoidal pressure. These authors showed that intravenous propranolol administration reduced the hyperkinetic circulatory syndrome, with a significant decrease in heart rate, cardiac index, and azygos blood flow, and a significant increase in SVR [9].

Another significant finding in our study was that we found pulmonary vascular abnormalities in EHPVO comparable with cirrhotics. Both the groups of patients had low

PVR. Our group had previously shown that patients of noncirrhotic portal fibrosis have low PVR comparable with Child's A cirrhotic patients [19]. However, there were no studies till now that have examined pulmonary vascular complications in EHPVO. The cause of decreased PVR may be microvascular dilatation within pulmonary arterial circulation resulting from decreased precapillary arteriolar tone or additional mechanisms, such as angiogenesis, remodeling, and vasculogenesis. Further aggravation of these changes may lead to hepatopulmonary syndrome. Indeed, it has been shown previously that hepatopulmonary syndrome may occur in patients with EHPVO [20, 21]. Thus, portal hypertension per se is responsible for pulmonary complications of liver disease as well.

Many EHPVO patients decompensate after a bleeding episode in the form of ascites, jaundice, or encephalopathy. It is important to see whether changes in humoral factors have an important role in the development of decompensation. It has been shown in experimental EHPVO that although the liver functions temporarily deteriorate by portal vein obstruction, such as portal vein thrombosis, hepatic blood flow and the liver functions improve with the formation of collateral veins to liver [22].

Our study had several limitations, one of them being its small sample size. To adequately support the conclusions derived, at least 150 patients in each limb would be required for the equivalence trial, assuming α of 0.05 and β of 0.20 (power of 80%). EHPVO being a relatively rare disease, this sample size is almost impossible to achieve. So our results, at best, show a trend that hemodynamic alterations in EHPVO may be similar to compensated cirrhotic patients. The other limitation is a lack of healthy control group. Subjecting healthy subjects to the invasive interventions of cardiac catheterization is not justified; hence, again, having a healthy control group was not possible.

In summary, our results demonstrate that EHPVO has features of hyperdynamic circulation with increased cardiac index and decreased systemic and PVRI. These changes are similar to those seen in patients with cirrhosis. This suggests a predominant role of portal hypertension per se in the genesis of systemic and pulmonary hemodynamic alterations.

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