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REVIEW

Liver cirrhosis and arterial hypertension

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Abstract

Characteristic findings in patients with cirrhosis are vasodilatation with low overall systemic vascular resistance, high arterial compliance, increased cardiac output, secondary activation of counter-regulatory systems (renin-angiotensin-aldosterone system, sympathetic nervous system, release of vasopressin), and resistance to vasopressors. The vasodilatory state is mediated through adrenomedullin, calcitonin gene-related peptide, nitric oxide, and other vasodilators, and is most pronounced in the splanchnic area. This constitutes an effective (although relative) counterbalance to increased arterial blood pressure. This review considers the alterations in systemic hemodynamics in patients with cirrhosis in relation to essential hypertension and arterial hypertension of the renal origin. Subjects with arterial hypertension (essential, secondary) may become normotensive during the development of cirrhosis, and arterial hypertension is rarely manifested in patients with cirrhosis, even in cases with renovascular disease and high circulating renin activity. There is much dispute as to the understanding of homoeostatic regulation in cirrhotic patients with manifest arterial hypertension. This most likely includes the combination of vasodilatation and vasoconstriction in parallel.

Keywords: Arterial compliance; Central vascular filling; Chyperdynamic circulation; Kidney function, Nitric oxide; Blood pressure regulation; Renin–angiotensin–aldosterone system; Sympathetic nervous system; Vasodilatation; Vasoconstriction

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INTRODUCTION

Arterial hypertension is seldom found in patients with liver disease, but patients with alcoholic fatty liver quite often present with raised arterial blood pressure. Renal involvement is seen in hepatitis B and in certain cases this may be accompanied by arterial hypertension. Otherwise, the clinical course of most liver diseases is characterized by low arterial blood pressure. This paper focuses on the circulatory dysfunction in cirrhosis, which is the most common characteristic of the chronic liver diseases.

Abnormalities in the splanchnic circulation are well described in patients with cirrhosis[5-7]. These include increased inflow to the splanchnic system and portal venous hypertension. Moreover, such patients are often hyperkinetic with increased heart rate and cardiac output. The hyperkinetic systemic circulation is related to the severity of cirrhosis, sodium-water retention, and presence of ascites[8]. The overall systemic vascular resistance is decreased, the blood volume is abnormally distributed with relative and absolute central hypovolemia, and cardiovascular, renal, and other organ dysfunction is common, including abnormal neurohormonal regulation[8-10]. Essential hypertension is frequently reported in both developed and developing countries, and the prevalence of essential hypertension in patients with cirrhosis would be expected to be around 15%[11,12]. However, most reports put the coexistence of cirrhosis and arterial hypertension much lower. As in patients with essential hypertension, most circulatory changes in cirrhosis are dysfunctional, rather than structural.

This review considers the cardiovascular system, neurohormonal regulatory systems, kidney function, and sodium-water retention with respect to arterial blood pressure and its regulation in patients with cirrhosis with the purpose of analyzing the background of the profound circulatory changes, their development, and complications. These elements are considered with respect to essential hypertension and arterial hypertension of renal origin.

HEPATOSPLANCHNIC CIRCULATION

The mechanisms behind the circulatory changes in the hepatosplanchnic system are both functional and structural[13]. Thus, a reduced hepatic vascular cross-sectional area, owing to the formation of fibrosis and noduli, is well known[13]. Swelling of hepatocytes and contraction of myofibrillary cells also contribute to hinder the hepatic outflow. Low content in endothelial cells of the vasodilator, nitric oxide (NO), may contribute to

Table 1 Haemodynamics in central and peripheral vascular beds in patients with cirrhosis

Heart
Heart rate ↑
Cardiac output ↑
Left atrial volume ↑
Left ventricular volume → (↑)
Left ventricular end-diastolic pressure →
Right atrial volume →↑↓
Right atrial pressure →↑
Right ventricular volume →↑↓
Right ventricular end-diastolic pressure →
Systemic circulation
Plasma volume ↑
Total blood volume ↑
Central and arterial blood volume ↓ (→)
Noncentral blood volume ↑
Arterial blood pressure ↓ (→)
Systemic vascular resistance ↓
Arterial compliance ↑
Total vascular compliance ↑
Pulmonary circulation
Pulmonary blood flow ↑
Pulmonary artery pressure →↑
Pulmonary vascular resistance ↓ (↑)
Skeletal and cutaneous muscle circulation
Skeletal muscular blood flow ↑ → ↓
Cutaneous blood flow ↑ → ↓
Hepatic and splanchnic circulation
Hepatic blood flow ↑ → (↑)
Hepatic venous pressure gradient ↑
Renal circulation
Renal blood flow ↓
Glomerular filtration rate ↓ →

↑, increase; →, no change; ↓, decrease. Parentheses denote minor changes.

hepatic vasoconstriction[14]. In addition, vasodilators are produced in excess and escape degradation by the diseased liver, which may play a role in splanchnic and systemic vasodilatation in concert with local factors, especially shear stress[6,15,16]. The result is an increased splanchnic inflow that aggravates and prolongs the portal hypertension, which is an essential element in cirrhosis[7]. The formation of portosystemic collaterals with a highly increased flow through the azygos venous system contributes to the decreased overall vascular resistance[5,7].

SYSTEMIC CIRCULATION

Overall systemic vascular resistance

Overall systemic vascular resistance is decreased in most patients with cirrhosis. Recent studies have shown that the circulation in most vascular territories is disturbed. A close look at the individual organs and tissues reveals vascular beds with decreased perfusion, normal perfusion, and increased perfusion. This indicates areas with high resistance (such as the kidneys), normal resistance (such as the brain), and low resistance (such as the splanchnic system)[6,7] (Table 1). The pathogenesis of hyporeactivity of the vascular system in cirrhosis is multifactorial[17]. Clinical and experimental observations favor the presence of a surplus of circulating vasodilators. Combined with a decreased sensitivity to pressor substances, this leads to vasodilatation and reduced vascular resistance[7,17]. Vasodilatation and the resulting activation of counter-regulatory mechanisms are closely related to the circulatory dysfunction in chronic liver disease[18,19]. The reduced vascular responsiveness may be generated by a decrease in the number of receptors, a change in receptor affinity, and several postreceptor defects[20]. Recent evidence suggests that all of these mechanisms are working in concert in cirrhosis[20].

The coexistence of decreased splanchnic resistance (as in cirrhosis) and increased peripheral resistance (as in essential arterial hypertension) is likely and may depend on the altered circulating vasoactive substances, reactivity of vasomotor and regulatory systems, etc[21,22] The result may be increased, normal, or decreased systemic vascular resistance. However, most evidence indicates that a decreased overall systemic vascular resistance with a low arterial blood pressure is most often the outcome, even in patients with primary essential hypertension[23-25]. Research on vascular hyporeactivity has primarily focused on calcitonin gene-related peptide (CGRP), NO, tumor necrosis factor-α (TNF-α), adrenomedullin, and endocannabinoids[17,18]. In addition, there is substantial evidence of autonomic defects in patients with cirrhosis. Thus, the sympathetic nervous system is both dysfunctional and overactivated The reason for vasoconstriction in some vascular areas is mainly overwhelming activity of pressor systems, but dysfunctional elements are also present[5,19,26].

Arterial blood pressure

The arterial blood pressure depends on the cardiac output and the systemic vascular resistance. The former is primarily determined by heart rate, venous return, and myocardial contractility. The latter is determined by the tone of smooth muscle cells in the small arteries and arterioles, which is governed by complex local and central neurohumoral factors. Arterial blood pressure has a circadian rhythm, but is kept within its habitual range by negative feedback baroreceptor reflexes, volume regulation, and other regulatory systems[12].

According to standardized recommendations, arterial blood pressure in patients with cirrhosis is often measured in the morning. However, 24-h determinations of blood pressure show that, during the day, the arterial blood pressure is substantially reduced compared with that of the controls, but at night it is normal[27]. The shifted and flat blood pressure-heart rate relation in patients with cirrhosis suggests that the regulation of their blood pressure is abnormal[27]. Moreover, the hemodynamic dysregulation is more pronounced with increasing severity of the liver disease[9]. The abnormal diurnal variation of the arterial blood pressure and the drastic activation of the neurohormonal systems probably contribute to the sodium-water retention.

Studies of patients with cirrhosis and arterial hypertension show that the prevalence is substantially reduced with raised arterial blood pressure in only 3-7% of such patients[21,24,28,29]. In addition, a few longitudinal studies have indicated that in patients with essential arterial hypertension, the raised arterial blood pressure is

Table 2 Haemodynamics and neuroendocrine mechanisms in patients with cirrhosis and different types of arterial hypertension

	Cirrhosis	Cirrhosis with hypertension	Essential hypertension	Renovascular hypertension
Plasma and blood volume	↑	↑	→	→
Central blood volume	→↓	→↓	→(↑)	→(↑)
Systemic vascular resistance	↓	→	↑	↑
Arterial compliance	↑	→	↓	↓
Renal blood flow	↓	↓→	↓	↓
Sodium retention	↑	↑	→↑	↑
Sympathetic nervous activity	↑↑	↑	→	→↑
Renin–angiotensin–aldosterone system	↑↑	↑→	→↓	↑
Vasopressin	↑		→	→

→ ↑ ↓, denote normal, increased, and decreased values, respectively; parentheses denote minor changes.

reduced to normal values after the onset of cirrhosis[23]. Thus, patients with essential hypertension may become normotensive during the development of chronic liver disease. In patients with cirrhosis, the liver disease may protect against the development of arterial hypertension, and in patients with advanced cirrhosis raised arterial pressure is very uncommon[24,30].

Gentilini *et al.* have investigated patients with early non-alcoholic cirrhosis and arterial hypertension[21]. They found that the arterial hypertensive cirrhotic patients were normodynamic with a normal heart rate and cardiac output. By contrast, their normotensive cirrhotic counterparts were hyperdynamic in the supine position and normodynamic in the upright position. They concluded that hypertensive cirrhotic patients had an impaired cardiovascular response to postural changes, but a lesser degree of renal dysfunction while standing than that of their normotensive counterparts[21]. No difference in the plasma renin activity of the normotensive and hypertensive cirrhotics was present[21]. By contrast, Veglio *et al* had previously found that hypertensive cirrhotic patients had a lower plasma renin activity, both supine and upright[29]. They concluded that the peripheral pressor effect of vasoactive hormones was increased and the effective blood volume was enhanced in arterial hypertensive cirrhotic patients[29]. The authors of the present review have been unable to confirm Gentilini *et al's* result of a normodynamic circulation in early hypertensive cirrhotic patients and Veglio *et al's* hypothesis of an enhanced effective blood volume in these patients[31]. However, Henriksen *et al's* study showed that hypertensive cirrhotic patients are less vasodilated than their normotensive counterparts[31], (Figure 1).Essential differences in arterial hypertension and cirrhosis are summarized in Table 2.

Arterial compliance

Arterial compliance (i.e., an increase in intra-arterial volume relative to an increase in transmural arterial blood pressure) is raised in patients with decompensated cirrhosis[9,21]. Recent investigations have shown that the altered static and dynamic characteristics of the wall of large arteries in patients with cirrhosis are closely associated with the circulatory and homoeostatic derangement[9,21,32-35]. The changes in arterial mechanics are, at least in part, reversible[32]. Arterial compliance is an important determinant of the coupling between the heart and the arterial system and of the dynamics of intravascular volume relocation[36]. Reduced arterial blood volume and blood pressure are the most likely elements in the elevated arterial compliance in advanced cirrhosis[9,13]. The increased arterial compliance in patients with cirrhosis is directly related to the severity of the liver disease and the circulating level of the vasodilator CGRP[32]. It is inversely related to circulating adrenaline, but is not significantly related to the indicators of the potent vasoconstrictor systems (sympathetic nervous system (SNS) and endothelin-1)[32-35]. In addition, the abnormal arterial compliance is related to blood volume abnormalities, hypoxia, and to the abnormalities in the C-type natriuretic peptide (CNP), but not to the atrial natriuretic peptide (ANP)[33,35]. Arterial compliance is not affected by beta-adrenergic blockade, but infusion of the vasopressin analog terlipressin almost normalizes it[37]. Both types of drugs are used in the treatment of portal hypertension[38]. In arterial hypertensive cirrhotic patients, arterial compliance is normal or almost normal[31].

Blood volume distribution

Patients with cirrhosis have increased blood and plasma volumes[8,10]. Distribution of blood to the different vascular beds is abnormal and more so in severe liver disease[39-42]. Moreover, dynamic, as well as static, methods have revealed that the central (thoracic) blood volume is most often decreased, (Figure 1c), whereas the non-central (especially splanchnic) blood volume is increased in patients with cirrhosis[10,39]. The effective arterial blood volume is decreased, and the abnormal volume distribution contributes to the systemic circulatory derangement[42]. Thus, the central circulation time (that is, central blood volume relative to the cardiac output) in cirrhosis has a significant relation to the survival and is substantially reduced also in cirrhotic patients with arterial hypertension[31]. During volume expansion (either by blood transfusion, or infusion of albumin or osmotic material) most cirrhotic patients respond with a further reduction in systemic vascular resistance rather than an increase in arterial blood pressure[33,42]. Future studies may disclose whether raised arterial blood pressure is indicative of normal arterial filling or the result of arterioconstrictive adaptation to a low arterial blood volume . Moreover, the balance between vascular areas with vasodilatation and vasoconstriction may be substantially altered in arterial hypertensive patients with cirrhosis[31].

Cardiac dysfunction

In patients with advanced cirrhosis increased heart rate and stroke volume led to a high cardiac output[18,36]. A left ventricular failure may be latent, because of the decreased afterload (as reflected by reduced systemic vascular resistance and increased arterial compliance)[20,36]. Cardiac dysfunction may become manifest under stran or treatment with vasoconstrictors. Cirrhotic cardiomyopathy includes

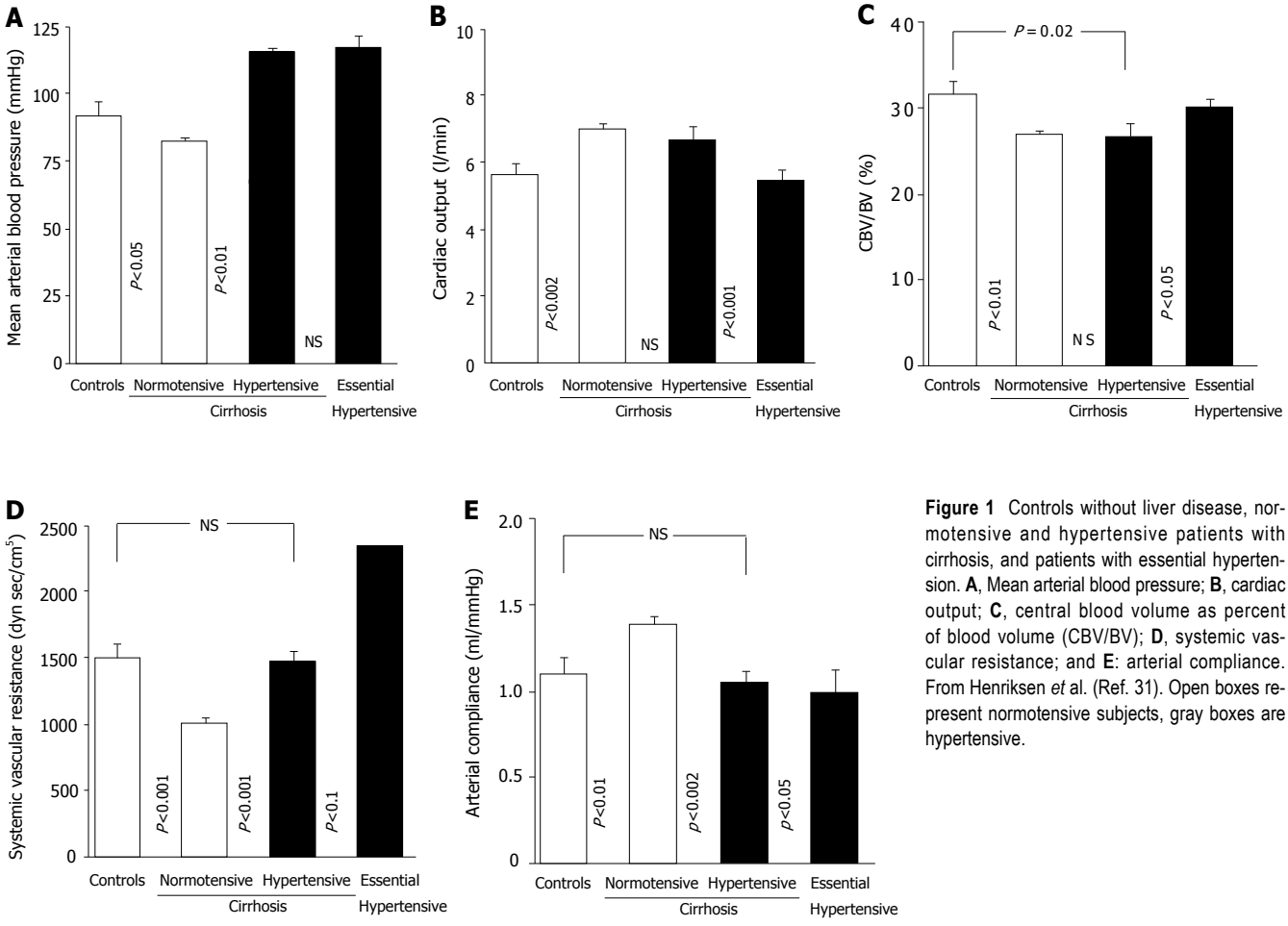

Figure 1 Controls without liver disease, normotensive and hypertensive patients with cirrhosis, and patients with essential hypertension. **A**, Mean arterial blood pressure; **B**, cardiac output; **C**, central blood volume as percent of blood volume (CBV/BV); **D**, systemic vascular resistance; and **E**: arterial compliance. From Henriksen *et* al. (Ref. 31). Open boxes represent normotensive subjects, gray boxes are hypertensive.

impaired cardiac contractility (systolic dysfunction), diastolic dysfunction, prolonged *Q-T* interval, reduced beta-adrenoceptor density, postreceptor signal defects, abnormal excitation-contraction coupling, and molecular abnormalities[20,36,43]. Recently, it has been substantiated that the elevated levels of circulating pro-brain natriuretic peptide (pro-BNP) and brain natriuretic peptide (BNP) found in patients with cirrhosis are not related to the decreased disposal of these peptides, but to the increased production in the cirrhotic heart, thus indicating cardiac dysfunction in cirrhosis[44]. In cirrhotic patients with arterial hypertension signs of myocardial involvement may be especially pronounced[21,30].

Cirrhotic cardiomyopathy must be differentiated from alcoholic heart muscle disease, which is caused by impaired contractile protein synthesis and formation of immunogenic cardiac protein-acetaldehyde adducts. The presence of antibodies to these adducts may be a marker for alcoholic heart muscle disease and possibly for its pathogenesis[36].

NEUROHUMORAL REGULATION OF ARTERIAL BLOOD PRESSURE AND VOLUME DISTRIBUTION IN CIRRHOSIS

Splanchnic arteriolar vasodilatation may lead to abnormal distribution of the circulating medium with a decrease in the effective blood volume and low arterial blood volume and pressure, and to an expansion of the non-central blood volume, including the splanchnic bed[14,26,42]. Most patients with advanced decompensated cirrhosis have a highly increased activity of vasopressor systems with a highly elevated plasma renin activity, circulating noradrenaline, and plasma vasopressin[5,6,26]. In most cases there is a progressive increase from normal values to moderately increased values in preportal hypertensive patients to a further increase in portal hypertensive patients to highly increased values in ascitic patients, especially in those with functional renal failure[5,45]. Recent studies indicate that infusion of albumin may suppress the renin–angiotensin–aldosterone system (RAAS), especially in patients with advanced cirrhosis, and this may prevent further circulatory dysfunction and even reduce it[33].

In addition to the activation of the SNS, RAAS, and vasopressin, several studies have shown increased circulating endothelin-1, which indicates that endothelin systems are also activated in advanced cirrhosis[46]. Systemic vasodilatation is a key feature in the activation of vasoconstrictive and sodium-water retaining systems[5,16,22]. Systemic hemodynamic alterations are also important for the low renal blood flow and renal dysfunction in cirrhosis. The pressor systems most often counter-regulate the otherwise low arterial blood pressure in cirrhosis to a level almost within the normal range. Whereas a significant negative correlation of endothelin-1 to arterial blood pressure has been described, most studies have focused on the very low arterial blood pressure after the blockade

of the SNS (for instance, by clonidine, prazosin), RAAS (for instance by ACE-inhibitors, A II blockers), and the vasopressin effect (V_1 antagonists)[16,45-48]. The activity in the pressor systems in advanced cirrhosis is among the most extreme known to pathophysiology. The presence of autonomic defects in patients with cirrhosis is evident from various studies on hemodynamic response to standardized cardiovascular reflex tests, such as heart rate variability, the Valsalva ratio, and isometric exercise[17]. Most studies on these issues have found a high prevalence of autonomic dysfunction in cirrhosis directly associated with liver dysfunction and survival. The results point to receptor and postreceptor defects as important elements of the hyporeactive response in cirrhosis. Other studies suggest that the autonomic dysfunction secondary to liver dysfunction is temporary, and potentially reversible after liver transplantation[48]. Arterial hypertensive cirrhotic patients may have less impaired blood pressure regulation and cardiovascular reflexes[21], but this topic needs further investigation. In cirrhosis the plasma concentration of CGRP, a powerful vasodilating neurotransmitter, is increased[18,32]. Circulating CGRP relates to cardiac output, systemic vascular resistance, arterial compliance, and liver dysfunction. In experimental studies, specific antagonists of CGRP partly reverse the vasodilatation and hyperdynamic circulation. Vallance and Moncada have proposed that NO could be implicated in the vasodilatation in cirrhosis[49]. Several human and animal studies have supported this concept, whereas others have been unable to do so. To support the hypothesis, blockade of NO formation significantly improves the systemic hyperdynamic circulation, and infusion of the NO donor, L-arginine, aggravates the systemic vasodilatation and hyperdynamic circulation. Other vasodilating substances, such as adrenomedullin, the natriuretic peptides, and cannabinoids, may also be involved[18]. Adrenomedullin, a polypeptide similar to CGRP, is increased in patients with decompensated cirrhosis. From the family of natriuretic peptides, ANP, BNP, CNP, urodilatin, the two cardiac peptides, ANP and BNP, may be raised in patients with cirrhosis[35,45]. ANP is often increased in patients with ascites, owing to an enlarged left atrium and atrial stretching caused by a change in anatomical location of the heart. Circulating BNP (and pro-BNP) is especially increased in patients with cirrhotic cardiomyopathy[36,44]. Urodilatin is often normal and CNP may be reduced in advanced cirrhosis[35]. The increased natriuretic peptides and other vasodilators in cirrhosis may contribute to vasodilatation, and thereby counteract any increased arterial blood pressure from the coexistence of essential or secondary arterial hypertension.

According to the peripheral arterial vasodilatation theory of Schrier and co-workers, peripheral and splanchnic vasodilatation leads to a reduction in systemic vascular resistance and arterial blood volume and pressure, which are primary events in the retention of sodium and water[6]. Over the past few years several vasodilators have been candidates, and those mentioned above are involved in the cirrhotic vasodilatation, but further research is needed in order to answer a number of unsolved questions, especially in relation to the vascular beds which are dilated and constricted.

KIDNEY FUNCTION AND FLUID RETENTION

Functional renal failure in cirrhosis (hepatorenal syndrome) is characterized by renal insufficiency consequent on hepatic failure[5,16,45,47]. No clinical or patho-anatomical signs of other known causes of renal failure are present. In general, the hepatorenal syndrome is characterized by a decrease in the renal blood flow and glomerular filtration rate, avid sodium-water retention, azotemia, and later oliguria. The condition may be considered as a progressive functional nephropathy, consequent on dyscirculatory and dysregulatory collapse[5,16]. The renal perfusion pressure is decreased, not only because of the low arterial blood pressure, but also because of the elevated renal venous pressure, especially in patients with tense ascites[16]. The enhanced sympathetic nervous activity may alter the autoregulation curve of the kidney with a shift to the right[50]. Patients with hepatorenal syndrome have the highest plasma levels of circulating catecholamines, and there are several indicators that enhanced renal SNS activity plays an important role in the renal vasoconstriction. The highly significant inverse relation between renal noradrenaline overflow on the one hand and renal blood flow on the other may illustrate this[16].

Activation of the RAAS may contribute to decreased renal perfusion, but the RAAS may also have more complex regulatory effects inside the kidney[16,18,26]. It has been shown that vasopressin does not substantially change renal perfusion[26]. Noradrenaline, adrenaline, and endothelin-1 are important elements in the renal hypoperfusion and sodium-water retention in advanced cirrhosis[16,46,47]. Local vasodilators, such as prostaglandins and NO, most likely compensate for, at least in part, the progressive renal vasoconstriction seen in advanced cirrhosis[5]. In decompensated patients, normalization of or an increase in arterial blood pressure may increase renal perfusion and improve renal function[50]. Accordingly, a combination of prolonged administration of ornipressin or terlipressin and albumin has recently been reported to improve functional renal failure in cirrhosis[45]. Treatment with alpha-adrenergic blockers and potentially with endothelin-1 blockers may reverse renal vasoconstriction, but their lowering effect on arterial blood pressure may overrule beneficial local effects on the kidney[16]. Improvement of the cardiac dysfunction in cirrhosis may also improve the renal dysfunction[51].

Loyke found that renal and neurogenic mechanisms able to elevate the blood pressure remained intact in patients with cirrhosis[25,28]. This conclusion was based on several patients with coexistent cirrhosis and glomerular nephritis. However, today this is a rather uncommon combination, at least in patients with alcoholic liver disease. Later, Loyke reported examples of renal hypertension, which returned to normotension when the patients developed cirrhosis[23].

The hemodynamic changes in cirrhosis point towards renal hypoperfusion as being, at least initially, a physiological response to the changes in the systemic circulation. Increased SNS activity is a pathogenic factor, but other systems, such as the RAAS and endothelins, may also play a role. Angiotensin II mainly acts on the efferent arteriole and a low dose of an ACE-inhibitor

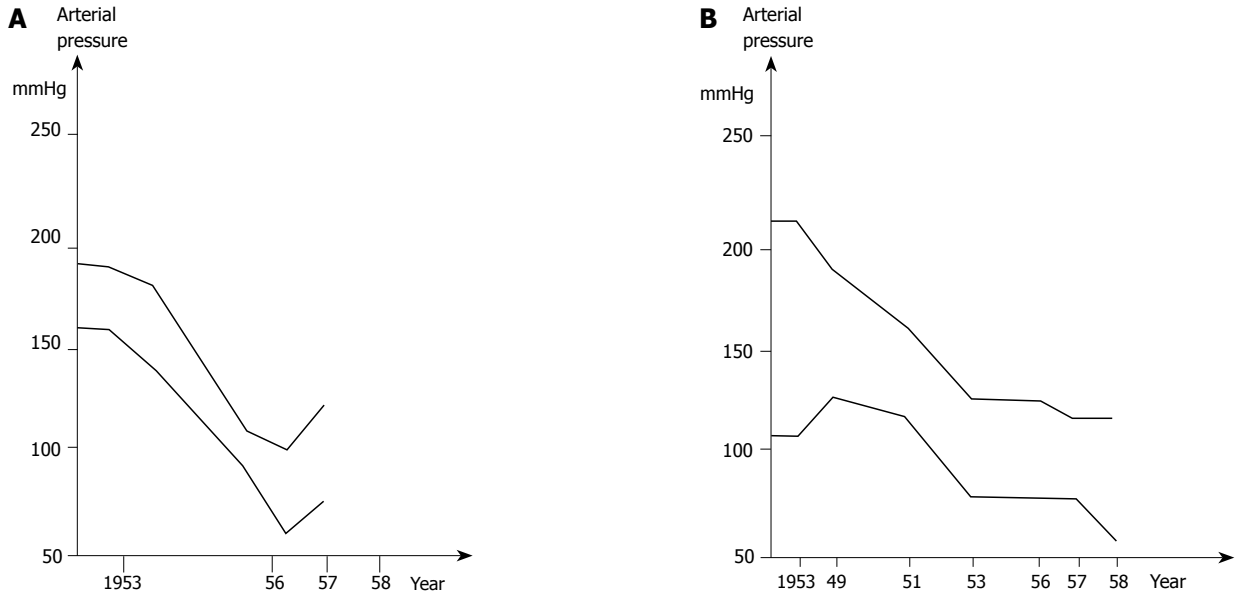

Figure 2 Change in arterial blood pressure in two patients with arterial hypertension. (**A**, 39-year-old woman with essential hypertension; **B**, 59-year-old woman with hypertension of renal origin.) A decrease in the arterial blood pressure is seen when the patients develop cirrhosis. From Loyke 1962 (reproduced with the permission of Archives of Internal Medicine, Ref. 23).

may induce a significant reduction in glomerular filtration and a further reduction in sodium excretion, even in the absence of a change in arterial blood pressure. This suggests that the integrity of the RAAS is important for the maintenance of renal function in cirrhotic patients, and that RAAS overactivity does not solely contribute to the adverse renal vasoconstriction. Infusion of terlipressin or ornipressin has, along with a rise in arterial blood pressure, demonstrate beneficial effects with increased GFR in patients with hepatorenal syndrome.

A few cases have been reported where patients with cirrhosis with renal involvement may develop arterial hypertension, especially in patients with early cirrhosis[52]. After the onset of severe cirrhosis most patients with renal hypertension become normotensive, like patients with essential hypertension (Figure 2). However, nephropathy in cirrhosis most often leads to low arterial blood pressure, in spite of the highly increased activity in the RAAS system. In most types of bilateral organic renal failure with vascular involvement and sodium retention, hypertension will be the outcome, but not in patients with cirrhosis, where the mechanisms are quite the reverse. Alterations in hemodynamic and homoeostatic mechanisms in renal hypertension and cirrhosis are summarized in Table 1.

ARTERIAL HYPERTENSION IN CIRRHOSIS

The prevalence of arterial hypertension in cirrhotic patients is substantially reduced, especially in advanced cirrhosis. Characteristic findings in patients with cirrhosis are vasodilatation with low overall systemic vascular resistance, high arterial compliance, increased cardiac output, secondary activation of counter-regulatory systems (RAAS, sympathetic nervous system, release of vasopressin), and resistance to vasopressors. The vasodilatory state is mediated through adrenomedullin, CGRP, NO, and other vasodilators, and is most pronounced in the splanchnic area. This constitutes an effective (although relative) counterbalance to raised arterial blood pressure. Subjects with arterial hypertension may become normotensive during the development of chronic liver disease, and arterial hypertension is rarely manifested in patients with cirrhosis, even in cases with renovascular disease and high circulating renin activity. There is much dispute as to the understanding of homoeostatic regulation in cirrhotic patients with manifest arterial hypertension. This condition most likely includes the combination of vasodilatation and vasoconstriction in parallel. As hypertensive patients are often effectively treated with diuretics, calcium channel antagonists, beta-blockers, ACE-inhibitors, etc., and some of these drugs are also applied in the treatment of cirrhosis and portal hypertension (Table 3), the natural history and prevalence of cirrhosis in patients with arterial hypertension, arterial hypertension in patients with cirrhosis, and the inter-relationship of these two diseases may be difficult to study today in prospective and untreated cases. Nevertheless, such studies are relevant, since there are many unsolved questions.

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Table 3 Effects of propranolol, diuretics, terlipressin, and albumin on pressures, vascular resistance, vascular compliance, blood flow, blood volume distribution, portal pressure, and sodium excretion in patients with cirrhosis

	Non-selective beta-blocker	Diuretics	Terlipressin	Albumin
Arterial blood pressure	(↓)	(↓)	↑	→
Systemic vascular resistance	↑↑		↑↑	↓
Arterial compliance	→	→	↓	↑→
Total effective vascular compliance		↓→		
Cardiac output	↓↓	↓	↓	↑
Central and arterial blood volume	→	(↓)	↑	↑→
Plasma volume	→	↓	↓	↑
Hepatic venous pressure gradient	↓→	↓	↓	→
Urinary sodium excretion	→	↑	↑	↑

→ ↑ ↓, denote normal, increased, and decreased values, respectively. Parentheses denote minor changes.

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