



Pathophysiology and Prevention of Paracentesis-induced Circulatory Dysfunction: A Concise Review

Anand V Kulkarni*¹, Pramod Kumar¹, Mithun Sharma¹, T R Sowmya¹, Rupjyoti Talukdar², Padaki Nagaraj Rao¹ and D Nageshwar Reddy²

¹Department of Hepatology, Asian Institute of Gastroenterology, Hyderabad, India; ²Department of Gastroenterology, Asian Institute of Gastroenterology, Hyderabad, India

Abstract

Annually, 10% of cirrhotic patients with ascites develop refractory ascites for which large-volume paracentesis (LVP) is a frequently used therapeutic procedure. LVP, although a safe method, is associated with circulatory dysfunction in a significant percentage of patients, which is termed paracentesis-induced circulatory dysfunction (PICD). PICD results in faster reaccumulation of ascites, hyponatremia, renal impairment, and shorter survival. PICD is diagnosed through laboratory results, with increases of >50% of baseline plasma renin activity to a value ≥ 4 ng/mL/h on the fifth to sixth day after paracentesis. In this review, we discuss the pathophysiology and prevention of PICD.

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Introduction

Ascites is a major complication of liver cirrhosis, with an annual incidence of 5–10% in compensated cirrhosis.¹ Dietary sodium restriction and oral diuretics are the first treatment choices for uncomplicated ascites.^{2,3} Annually, 10% of cirrhotic patients with ascites develop refractory ascites, which is associated with a poor prognosis that reduces transplant-free survival to 50% per year.⁴ In refractory ascites, transjugular intrahepatic portosystemic shunt (TIPS), increased doses of diuretics, or large-volume paracentesis (LVP) are the few effective measures apart from liver transplant in routine practice. Of these, LVP is the preferred treatment of choice as it is faster, more effective, and associated with fewer side effects.⁵ TIPS,⁴ although effective in a selected group of patients, may be associated with ascites recurrence and hepatic encephalopathy. In addition, its high cost and lack of availability at some places

Keywords: Refractory ascites; Plasma renin activity; Large-volume paracentesis; Cirrhosis; Portal hypertension.

Abbreviations: LVP, large-volume paracentesis; MAP, mean arterial pressure; PICD, paracentesis-induced circulatory dysfunction; PRA, plasma renin activity; TIPS, transjugular intrahepatic portosystemic shunt.

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*Correspondence to: Anand V Kulkarni, Department of Hepatology, Asian Institute of Gastroenterology, Hyderabad, India. E-mail: anandvk90@gmail.com, dranand.v@aighospitals.com

make it a less desirable option. Therapeutic paracentesis in patients with cirrhosis and tense ascites leads to circulatory dysfunction, which is termed paracentesis-induced circulatory dysfunction or post paracentesis circulatory dysfunction.^{6,7} PICD usually occurs following LVP (>5–6 L) and results in faster reaccumulation of ascites, hyponatremia, renal impairment, and shorter survival.⁷

Epidemiology

The incidence of PICD is estimated to be 80% among patients not receiving any plasma volume expander, 33% to 38% in patients receiving polygeline/saline solution/dextran 70, and 11% to 20% among patients receiving albumin.^{8,9}

The definition of PICD

Gines *et al.*⁸ first defined PICD as an increase in plasma renin activity (PRA) on the sixth day after paracentesis of more than 50% of the pretreatment value to a level > 4 ng/ml/h. The value of 4 ng/mL/h was determined based on 36 healthy volunteers who were on a 50 mmol/day sodium diet for 7 days. The mean value in healthy volunteers was 1.35 ± 0.94 ng/mL/h (range, 0.1–4.0). Whether this value of 4 ng/mL/h holds for patients with cirrhosis and refractory ascites who have a hyperactive renin-angiotensin-aldosterone system is still unclear. In the same study, 280 cirrhotic patients with ascites had documented PRA value at baseline. The baseline value in those who developed PICD ($n = 85$) was 8.0 ± 7.3 ng/ml/h, which was similar to those who did not ($n = 195$), i.e., 9.3 ± 11.5 ng/ml/h. The landmark study by Wilkinson *et al.*¹⁰ showed that cirrhosis with refractory ascites would invariably have high PRA due to reduced renal blood flow with the highest value being 21.77 nmol/L/h and mean value of 9.5 nmol/L/h, while those with ascites would have a value double that of the healthy controls (3.99 nmol/L/h and 1.82 nmol/L/h, respectively). This indicates that the PRA needs to rise by >50% on day 6 in patients with cirrhosis and refractory ascites to be called PICD. The diagnosis of PICD is primarily based on the laboratory value of PRA and can be diagnosed only after 5 to 6 days of paracentesis. Although it is a valid objective measure, the difficulties of measuring PRA due to the technical requirements (blood sample should be taken after overnight fasting and at least 1 h of bed rest), cost, and questionable benefit in patients with refractory ascites who undergo repeated paracentesis, makes it a less favored option for clinicians. The PRA is dependent on age^{11,12} (PRA and plasma aldosterone levels

are highest in newborns and lowest in the elderly population), gender (more in men),¹² race (more in whites),¹² sodium intake (increased sodium intake suppresses renin activity),¹³ diurnal variation (sleep inhibits renin activity),¹⁴ posture (upright posture for 120 m increases renin activity),¹⁵ drugs such as diuretics (chronic treatment with diuretics increases the PRA),^{16,17} and beta-blockers (beta-blockers profoundly suppress renin activity).¹⁷ Measuring aldosterone concentration has no significant role in diagnosing PICD.

Pathophysiology of PICD

LVP causes mechanical decompression of the splanchnic vascular bed leading to splanchnic vasodilation, a further decrease in the arterial filling, and activation of neurohormonal systems. This results in free water and sodium retention. As a consequence, patients develop rapid reaccumulation of ascites, hyponatremia, renal injury, and encephalopathy (Fig. 1). Maintaining the intraabdominal pressure by pneumatic girdle prevents the circulatory disturbance occurring after paracentesis.¹⁸ This was the argument of peritoneovenous shunt proponents that ascites will have unidirectional flow from the abdomen into the systemic circulation leading to the expansion of effective arterial blood

volume, increase in cardiac output, renal blood flow, right atrial pressure, and atrial natriuretic peptide concentration and decrease in renin and aldosterone concentrations.^{19,20} This procedure has not been widely accepted due to several complications, including sepsis, coagulopathies, and pulmonary edema, and is currently extinct.²¹

The degree of activation of the renin-angiotensin-aldosterone system and sympathetic nervous system 6 days after paracentesis correlates inversely with changes in systemic vascular resistance (SVR).²² Within 60 m of paracentesis (<5 L), a significant increase in cardiac output, together with a reduction in mean arterial pressure (MAP), and consequently, calculated SVR experiences a significant decrease.²³ The flow rate of ascites has no relationship to the development of PICD.²⁴ There is increased cardiac output and PRA and decreased central venous and wedge pressure 24 h after LVP.²⁵ Whether edematous or not, all patients undergoing LVP have reduced creatinine clearance from 77 to 60 mL/m after 48 h.¹⁶

Prevention of PICD

Albumin^{8,26-28} Albumin is an essential plasma protein produced by hepatocytes. It accounts for 75% of the plasma

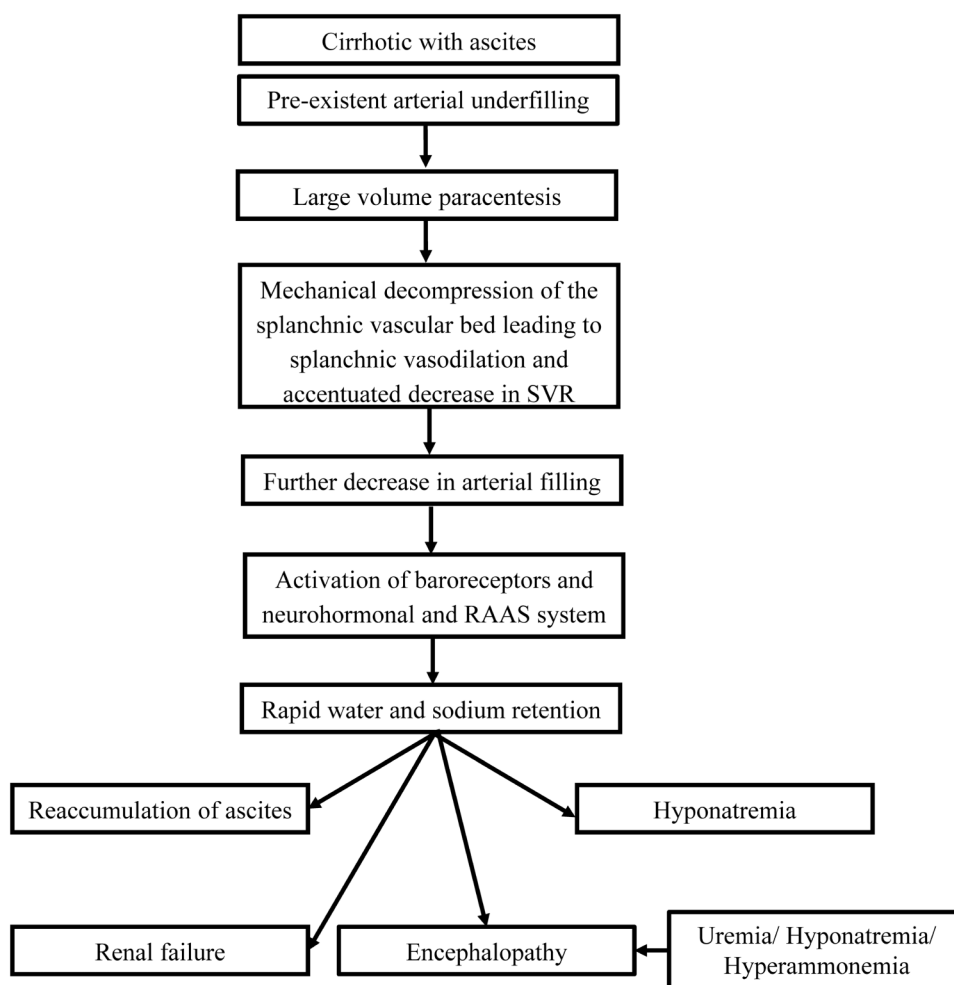


Fig. 1. Mechanism of PICD and complications.

colloid oncotic pressure and has a half-life of 15–21 days. With a molecular weight of 67 kDa and 607 amino acids, albumin is an asset for physicians. The free cysteine (Cys-34) residue accounts for the single free redox-active thiol (-SH) moiety, which accounts for ~80% of extracellular antioxidant properties through nitrosylation, oxidation, and thiolation. Patients with ascites usually have hypoalbuminemia. The causes of hypoalbuminemia are i) reduced hepatic synthesis and secretion, ii) dilution by increased intravascular and interstitial volume, and iii) loss in the ascitic fluid. The combination of hypoalbuminemia and impaired albumin function leads to marked disturbance in the transport, metabolism, and excretion of many endogenous and exogenous substances. Infusion of exogenous albumin in ascites patients may serve the dual purpose of replenishing the levels of circulating albumin and the functional activity of the albumin pool. These are effects specific to albumin not shared by other plasma volume expanders and may contribute to superior effectiveness. Albumin is available in preparations of 5%, 20%, and 25% solutions, with a sodium content equivalent to that of serum. The studies on PICD have involved only 20% albumin in either 8 g/L of ascitic fluid tapped or 4 g/L of ascitic fluid removed.

The first study was conducted by Pere Gines,²⁹ who evaluated 105 patients with daily paracentesis of 4–6 L until the disappearance of ascites. Fifty-two patients received albumin (40 g with each tap), and the other group received no volume expander. The number of complications (acute kidney injury [AKI] and hyponatremia) was significantly higher in patients who had no albumin infusion. However, the authors reported no mortality benefit with albumin infusion. This landmark study paved the path for further studies on albumin.

In 1996, Gines *et al.* compared albumin with dextran 70 and polygeline for the prevention of PICD.⁸ A total of 289 patients undergoing paracentesis were enrolled, and it was reported that albumin decreased the incidence of PICD to 18.5% compared to 34.4% in the dextran 70 group and 37.8% in the polygeline group. The mean PRA was 9.2 ± 10.3 ng/ml/h in the albumin arm, 9.5 ± 11.7 in dextran 70, and 8.6 ± 9.8 in the polygeline group, indicating that the upper limit (i.e., two standard deviations) was about 30 ng/ml/h in some patients. PICD was associated with a shorter time to readmission and shorter survival. This was the first randomized study to demonstrate the superiority of albumin.

A randomized study comparing saline versus albumin in 2003 also showed significant benefits with albumin.³⁰ Seventy-two patients were enrolled (35 in the saline group and 37 in the albumin group). The baseline heart rate and MAP in the saline group were 83.1 ± 8.6 m and 81.5 ± 12.2 mmHg and 82.4 ± 10.6 m and 83.1 ± 11.7 mmHg in the albumin group, respectively. The serum albumin was also comparable with 2.67 ± 0.48 g/dL in the saline group and 2.56 ± 0.65 g/dL in the albumin group. The baseline PRA value in the saline group was 5.4 ± 5.4 , and in the albumin group was 5.2 ± 4.5 ng/mL/h. The volume of ascites removed was comparable in both groups (>6 L) over a mean duration of ~90 min. The amount of albumin given was 260 ± 115.1 mL (20% albumin at 8 g/L ascites), and saline was 1075 ± 365 mL (170 mL of 3.5% saline solution per L ascites removed at 999 mL/h). There were 10 patients with complications in the saline group compared to only 6 in the albumin group. The incidence of PICD (based on PRA rise) was 33.3% in the saline group and only 11.4% in the

albumin group ($p = 0.03$). When <6 L was tapped, the incidence of PICD was similar in both groups (6.7% in saline vs. 5.6% in the albumin group; $p = 0.9$). MAP, hemoglobin, and potassium levels at baseline were predictors of PICD. The type of plasma expander was found to have a significant preventive effect on PICD by both univariate and multivariate analysis. Albumin was a better alternative when >6 L was tapped.

A pilot study by Richard Moreau *et al.*,³¹ conducted in 2000 (published in 2006) comparing synthetic colloid (3.5% polygeline) with albumin, concluded that albumin was more effective in preventing liver-related complications. The study was prematurely discontinued because of safety concerns about bovine-derived products. A total of 68 patients were enrolled: 30 in the albumin group and 38 in the polygeline group. One unit of the study colloid (blinded) provided either 20 g albumin or 17.5 g polygeline. The amount transfused was fixed as 1 U if below 4 L, 2U if between 4 L and below 6 L, 3U if between 6 L and below 8 L, and 4 U if 8 L or more. The patients were followed up for 6 months, and the number of taps and complications due to liver disease was assessed. The polygeline group had a 1.6-fold higher risk of developing liver-related complications than the albumin group.

An open-label randomized study comparing half the dose of albumin (4 g/L of ascites tapped) with the conventional dose (8 g/L ascites) concluded that half the dose was effective and economical for preventing the complications (PICD) of LVP.³²

Terlipressin³³ Terlipressin (*N*- α -triglycyl-8-L-lysine-vasopressin) (formula: $C_{52}H_{74}N_{16}O_{15}S_2$) is a vasopressin 1 (V1) receptor agonist with a molecular weight of 1227.4. It is a cyclic dodecapeptide that exists as a white freeze-dried fluffy powder, with a distribution half-life of ~8 m. Terlipressin plasma concentrations decline exponentially following intravenous IV administration, with an elimination half-life of approximately 1 h and plasma clearance of approximately 9 ml/kg/min. Terlipressin, a prodrug, is cleaved by endopeptidases, resulting in slow release of lysine vasopressin, the active metabolite. Measurable concentrations of vasopressin appear in the plasma from about 20–30 m post-dose, peaking at 1–2 h post-dose. Although terlipressin is used in PICD, its short half-life requires it to be given for prolonged periods to achieve a sustained MAP rise. Terlipressin increases systemic vascular resistance, reduces the portal pressure, and has been used for variceal bleed,³⁴ hepatorenal syndrome (HRS),³⁵ septic shock,^{36,37} and prevention of PICD.³⁸

A pilot study comparing the efficacy of terlipressin versus albumin showed that terlipressin is as effective as albumin in maintaining the arterial volume post paracentesis.³⁸ The authors randomly allotted 11 patients to terlipressin and 13 to the albumin arm. A total of 3 mg terlipressin was given, 1 mg at the onset of paracentesis, and then 1 mg at 8 h and 16 h. Albumin was given at a dose of 8 g/L ascites removed. Fifty percent within 2 h and 50% after 6 h of paracentesis. After completion, only 10 in each arm were included for analysis. The volume of ascites removed was similar in both groups. They measured the plasma renin concentrations (not the PRA). The number of patients (three in each arm) who had decreased arterial blood volume (based on >50% decrease in plasma renin concentrations on day 6) did not differ between the two groups. Only one patient in each group developed hyponatremia. There were no adverse

events noted in either group. The authors concluded that terlipressin is as efficacious in maintaining the arterial blood volume post paracentesis by splanchnic vasoconstriction.

Another pilot study of 40 patients comparing terlipressin with albumin showed that terlipressin is as efficacious as albumin in the prevention of PICD.³⁹ The baseline PRA was similar in both the treatment group with 19.15 ± 12.17 ng/mL/h in the albumin group vs. 20.11 ± 10.60 ng/mL/h in the terlipressin group. There were no side effects reported in the study; neither there was any difference in the occurrence of PICD. There was an insignificant decline in sodium levels 6 days after paracentesis, which was also similar in both groups. The authors concluded that terlipressin is equivalent to albumin.

Midodrine⁴⁰ Midodrine is an α 1-agonist whose active metabolite is desglymidodrine. It acts on the alpha-adrenergic receptors of the arteriolar and venous vasculature, producing an increase in vascular tone and elevation of blood pressure. It is rapidly absorbed orally. The bioavailability of midodrine is similar, whether given intravenously or orally. Plasma levels of the prodrug peak after about 0.5 h and decline with a half-life of approximately 25 m. Blood concentrations of desglymidodrine peak at 1 to 2 h after a dose of midodrine and has a half-life of about 3 to 4 h. The absolute oral bioavailability is 93% and is unaffected by food. Neither midodrine nor desglymidodrine is bound significantly to plasma proteins, and 80% of the drug is eliminated via the renal route by active secretion. An increase in PRA after short-term noradrenaline infusion (also an alpha-adrenergic agonist) has been demonstrated in patients with hepatorenal syndrome, suggesting a vasoconstrictive effect on the renal artery.⁴¹ It is unknown whether midodrine also exerts similar effects. Midodrine has been used for refractory ascites,⁴² HRS,³⁵ and prevention of PICD.⁴³

Two small pilot studies done on midodrine had conflicting results. One pilot study with 40 patients concluded that midodrine is as effective as albumin.⁴³ Midodrine was administered at a dose of 5–10 mg (mean 8.62 ± 1.51 mg) three times per day to maintain a MAP at 10mmhg higher than baseline. Albumin was given at a dose of 8 g/L ascitic fluid removed (mean 48.4 ± 12.1 g). PRA at baseline and 6 days post paracentesis did not differ among the two groups. Alcohol was the most common etiology of liver disease in both groups. Other causes of liver disease were hepatitis B virus, hepatitis C virus, autoimmune, and idiopathic. Most interestingly, even with such a high Child's score (~10), patients had preserved serum albumin levels of 3.2 ± 0.54 g/dL in the albumin group and 3.17 ± 0.49 g/dL in the midodrine group. Two patients had an increase in PRA by >50% from baseline in the albumin group, but none in the midodrine group had significant PRA elevation. None developed AKI or hyponatremia, although there was a significant decrease in serum sodium levels on day 6 in both groups. A significant increase in 24-h urine volume and urine sodium excretion was observed in the midodrine group. One patient in the albumin group developed a febrile reaction, and one patient in the midodrine group developed headaches and pruritis. Only three patients (two in the albumin group and one in the midodrine group) required repeat paracentesis within 3 months of the treatment. This was a randomized trial with a follow-up of 3 months and also reported adverse events.

A pilot study by Appenrodt *et al.*⁴⁴ evaluating the role of midodrine in prevention PICD after LVP⁴² concluded that

midodrine in a fixed short-term dose is ineffective compared to albumin. A total of 24 patients with 13 in the albumin arm and 11 in the midodrine arm were included. Midodrine was given at a dose of 12.5 mg three times a day for 2 days post paracentesis and albumin at a dose of 8 g per L ascites removed. The causes of liver cirrhosis in the study were alcohol, hepatitis (the cause of hepatitis was not mentioned in the article), and idiopathic. The median volume of ascites removed was 6.3 L. A total of 4 patients (2 in each arm) recruited were in Child's class B, and 20 were Child C cirrhotic (11 in the albumin and 9 in the midodrine groups). PICD developed in six patients in the midodrine group (60%) and four patients (31%) in the albumin group. None of the patients in the albumin group developed AKI compared to two in the midodrine arm. Hyponatremia was noted in seven patients in the albumin group compared to four in the midodrine group. Plasma renin concentration increased from 677.5 to 1337.5 μ U/mL in the midodrine arm, whereas in the albumin arm, it increased from 385 to 402 μ U/mL on day 6. There were no side effects, even with 37.5 mg midodrine/day.

Noradrenaline⁴⁵ Noradrenaline is the principal neurotransmitter of the sympathetic nervous system produced by the adrenal medulla. Noradrenaline is preferred over adrenaline in shock as it causes global vasoconstriction, while adrenaline leads to venoconstriction and promotes venous return to the heart. Noradrenaline is a potent alpha agonist. Although noradrenaline is an economical choice, its benefits in the prevention of PICD are not well known. As the duration of action is only 1–2 m, it needs to be given by slow infusion. Noradrenaline infusion can cause severe peripheral and visceral vasoconstriction leading to a decrease in renal blood flow by 20% and cerebral blood flow by 10% without affecting the skeletal muscle and liver blood flow.⁴⁶ Post paracentesis, cirrhotics develop hypovolemia, and the systemic effects can be worsened by noradrenaline infusion. Moreover, cirrhotics with ascites have higher levels of norepinephrine, but the receptors are desensitized; hence, norepinephrine infusion is less effective in cirrhotics.⁴⁷ Norepinephrine has been used in shock,³⁷ HRS,⁴⁸ and PICD.⁴⁹

A small pilot study comparing noradrenaline with albumin reported that noradrenaline is an economical and efficacious choice over albumin.⁴⁹ Noradrenaline was started in a continuous infusion at an initial dose of 0.5 mg/h with a maximum dose given up to 3 mg/h. The infusion rate was titrated in steps of 0.125 mg/h to maintain the MAP at 10 mmHg above the baseline. The MAP was maintained at that level for the next 72 h with close monitoring. Effective arterial blood volume, as indicated by PRA before and 6 days after paracentesis, did not differ in the two groups (mean ~20 ng/mL/h). All patients underwent LVP. Two patients in the noradrenaline group and one in the albumin group had a rise in PRA by >50% on the sixth day. None of the patients developed renal impairment or hyponatremia. Only one patient receiving noradrenaline complained of restlessness. Further, one patient in each arm developed spontaneous bacterial peritonitis (SBP) on follow-up.

Contraindications to LVP: LVP leads to an accentuation of the arteriolar vasodilation, which is already present in cirrhotic patients with ascites. Therefore, LVP should be deferred in patients with spontaneous bacterial peritonitis (SBP), hepatorenal syndrome, and variceal bleed.

Combination therapies

A large trial of 150 patients (presented as an abstract at a major conference) on combination therapy of vasoconstrictor and albumin showed a significant decrease in the number of complications in patients receiving midodrine with albumin.⁵⁰ The benefit was lacking when terlipressin was used with albumin. However, terlipressin was given for only 1 day, whereas midodrine was given for 3 days. Complications such as pain abdomen, headache, and bradycardia were common in the terlipressin arm and whereas patients receiving midodrine experienced urinary retention, headache, hypertension, and anxiety. The combination therapy should be further explored for the prevention and treatment of PICD.

Meta-analysis

A meta-analysis by Bernardi *et al.* in 2012, which compared albumin with other therapies such as colloids or vasoconstrictors, showed that albumin remains the best choice for patients undergoing LVP.⁹ Seventeen randomized controlled trials, reported from 1988 to 2010 with a total of 1,225 patients, met all selection criteria and were included (Table 1). The mean age of the study population ranged from 46.9 to 61.4 years. Seventy-four percent were males (range, 60.0-90.0%) with mean baseline serum albumin ranging from 26 to 29 g/L, and the mean Child-Pugh score ranged from 8.8 to 11.0. The mean volume of ascitic fluid removed ranged from 5.5 to 15.9 L. The dose of albumin varied from 5–10 g/L of fluid tapped. The vasoconstrictors were terlipressin, midodrine, and noradrenaline. Compared

to no treatment, albumin reduced the odds of PICD by 93%, 61% when compared to another volume expander, and 30% when compared to a vasoconstrictor. Compared to untreated control patients in whom 16.5% developed hyponatremia, only ~4% developed hyponatremia in the albumin group. In total, albumin reduced the odds of developing PICD by 66%, hyponatremia by 42%, and death by 36%.

Another meta-analysis⁵¹ that included 16 trials on albumin concluded that albumin use significantly reduced the risk of paracentesis-induced circulatory dysfunction, but there was a nonsignificant difference in complications and mortality. The authors also noted that there was a significant reduction in mortality and renal impairment when albumin was used in cirrhosis with infection.

A recent Cochrane review,⁵² which included 27 randomized trials, concluded that there was neither any benefit nor any adverse effect in using any plasma expander, including albumin, polygeline, dextrans, hydroxyethyl starch, intravenous infusion of ascitic fluid, and crystalloids in patients undergoing paracentesis. The data on albumin/volume expanders originated from a few, small, short-term trials that were at high risk of systemic errors, selection bias, and random errors. They also suggested that more extensive trials with adherence to CONSORT and SPIRIT guidelines are required to assess the role of plasma expanders, including albumin, in paracentesis. The review did not consider trials comparing vasoconstrictors with volume expanders. The advantages and disadvantages of the drugs that have been used for PICD prevention are shown in Table 2.

Table 1. Meta-analysis on the role of albumin in patients undergoing paracentesis

Author	No. of trials included	Characteristics of trials included	Conclusions
Bernardi <i>et al.</i> ⁹ , 2012	17 (<i>n</i> = 225 participants)	Nine trials comparing albumin with other volume expanders formed the leading category, i.e. 74% (903 of 1,225) of all patients in the meta-analysis, compared with 13% each for trials with no treatment or vasoconstrictor as the control regimen.	Albumin remains superior to other treatment modalities, and further added that the combination of vasoconstrictor with albumin would further decrease the incidence of PICD, which has not been investigated to date.
Kwok <i>et al.</i> ⁵¹ , 2013	16 (<i>n</i> = 1518 participants)	Four studies with no active comparator, and eight studies comparing plasma expander to albumin, and four other studies of cirrhotic patients with infection compared the use of antibiotics with and without albumin	Albumin use significantly reduced risk of paracentesis-induced circulatory dysfunction, but there was a nonsignificant difference in complications and mortality.
Simonetti <i>et al.</i> ⁵² , 2019	27 (<i>n</i> = 1592 participants)	Five of the trials assessed plasma expanders (albumin in four trials and ascitic fluid in one trial) versus no plasma expander. The remaining 22 trials assessed one type of plasma expander, i.e. dextran, hydroxyethyl starch, polygeline, intravenous infusion of ascitic fluid, crystalloids, or mannitol versus another type of plasma expander, i.e. albumin in 20 of these trials and polygeline in one trial.	There was neither any benefit nor any adverse effect in using any plasma expanders including albumin, polygeline, dextrans, hydroxyethyl starch, intravenous infusion of ascitic fluid, and crystalloids in patients undergoing paracentesis.

Table 2. Drugs used in the prevention of PICD

Drug	Advantages	Disadvantages
Albumin	Evidence from a higher number of trials	Cost Need for IV infusion
Terlipressin	Efficacy similar to albumin	Evidence from small pilot studies
Noradrenaline	Efficacy similar to albumin Economical	Adverse events are common Need for IV infusion/ admission
Midodrine	Good oral bioavailability Maintains MAP effectively Can be given in daycare/outpatient	Small pilot studies Less studied Efficacy still controversial

Abbreviations: IV, intravenous; MAP, mean arterial pressure.

Table 3. Differential diagnosis of PICD complication

Complication of PICD	Common differentials in practice
Hyponatremia	Diuretic induced/dilutional
Encephalopathy	Type B/C encephalopathy Dyselectrolytemia Uremia
Acute kidney injury	Diuretic-induced

Differential diagnosis

The complications of PICD are usually attributed to cirrhosis of the liver and are thought to be a complication of the disease (cirrhosis). The usual differentials, which are considered in practice while missing the history of LVP, are shown in Table 3.

Treatment of PICD

Volume expansion with albumin infusion is the mainstay of treatment. The use of vasoconstrictors can also help in treatment but needs to be evaluated. However, avoiding paracentesis and withholding diuretics/beta-blockers during PICD prevents the worsening of hemodynamics and encephalopathy.

Conclusions

PICD is a dreaded complication of paracentesis and is associated with a high incidence of morbidity and mortality. It is often overlooked and is a commonly missed diagnosis. The differentials in any patient presenting with worsening of complications of cirrhosis should include PICD. The diagnosis is clinical, and the measurement of PRA may or may not aid in diagnosis. PICD should be redefined as any complication (kidney injury, hyponatremia, encephalopathy, variceal bleed) developing after paracentesis with or without a concurrent rise in PRA.

Way forward

More extensive randomized trials involving a larger sample size on the prevention of PICD with vasoconstrictors (with or without volume expanders) with clinical endpoints other than laboratory-based are suggested.

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Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Study concept and design (AVK, MS, STR), compilation and critical revision (AVK, MS, RT, PK, PNR, and DNR). All members approved the final draft.

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