# Small Artery Compliance in Cirrhotic Patients During Total Paracentesis

Jacob Kogan MD, Svetlana Turkot MD, Boris Golzman MD and Shmuel Oren MD

Department of Internal Medicine A, Barzilai Medical Center, Ashkelon, Israel

**Key words:** liver cirrhosis, paracentesis, pulse contour analysis, arterial compliance

## Abstract

**Background:** Hemodynamic changes, including systemic vascular resistance, in cirrhotic patients during massive paracentesis have been reported, but large and small artery compliance has not yet been investigated.

**Objective:** To investigate hemodynamic variables, including small and large artery compliance, in cirrhotic patients during total paracentesis.

**Methods:** The study included 15 cirrhotic patients admitted for an episode of tense diuretic-resistant ascites. Hemodynamic variables including vascular compliance were measured using an HDI pulse wave cardiovascular profiling instrument CR-2000. The variables were measured in these patients before, immediately after, and 24 hours following large volume (mean 5.6 L) paracentesis.

**Results:** Cardiac output increased immediately after paracentesis due to increment in stroke volume, with no change in heart rate. However, 24 hours later the cardiac output decreased to below the basal level. The fluctuation was statistically significant ($P < 0.05$). There was no change in large artery compliance, but small artery compliance increased after paracentesis ($P < 0.05$) and partially returned to the basal level after 24 hours. Systemic vascular resistance measurement showed the same pattern of change: vasodilatation occurred during paracentesis and was attenuated 24 hours later.

**Conclusions:** Large volume paracentesis with albumin replacement caused an accentuation of the vasodilatation (small but not large artery) already present in these patients. This may be the first sign of enhanced vasodilatation due to large volume paracentesis before the clinical expression of impaired hemodynamics and deterioration of renal function.

*IMAJ 2005;7:233–236*

Hypotension, low systemic vascular resistance, and reduced sensitivity to vasoconstrictors are features of hyperdynamic syndrome in portal hypertension and are pathogenetic factors triggering most serious clinical complications of liver cirrhosis. The hyperdynamic circulation begins in the portal venous bed as a consequence of portal hypertension due to the increased resistance to flow from the altered hepatic vascular morphology of chronic liver disease. Dilatation of the portal vein is associated with increased blood flow and leads to subclinical sodium retention, resulting in expansion of all body fluid compartments, including the systemic and central blood volumes. This blood volume expansion is associated with vasorelaxation and increased cardiac output [1–3]. Arterio-venous anastomoses open under the influence of vasodilator substances, body oxygen consumption is decreased, and tissue oxidation is abnormal [4]. The effective arterial blood volume falls, causing activation of the sympathetic and renin-angiotensin-aldosterone system, sodium and water retention and ascites formation. Profound systemic vasodilation is associated with marked neurohumoral activation, very low urinary excretion of sodium, renal vasoconstriction, and hepatorenal syndrome. Vasodilators such as nitric oxide, calcitonin gene-related peptide, endotoxin and cytokines could cause vasodilatation and increased arterial compliance [5–7]. Inhibition of nitric oxide secretion may reverse peripheral vasodilation and the vascular hyporesponsiveness to vasoconstrictors [8,9]. Arterial compliance was found to be significantly higher in cirrhotic patients than in controls and directly related to the severity of the disease [10,11].

Adaptations in arterial vasculature play a critical pathogenetic role in hemodynamic changes in cirrhosis. The altered static and dynamic functions of the arterial wall in cirrhosis may have implications for the circulatory and homoeostatic derangement, and potentially for therapy with vasoactive drugs [12].

Arterial compliance is usually investigated by measuring stroke volume and blood pressure, and determined as the stroke volume relative to pulse pressure. However, in cirrhotic patients, differentiation between small artery compliance and large artery compliance has not yet been performed. The increased demand from clinicians and researchers for the assessment of arterial compliance has led to the development and commercial availability of several non-invasive methods. One of them, pulse wave analysis, is used extensively in clinical studies for patients with atherosclerotic disease, arterial hypertension, diabetes mellitus and various other disorders and medical conditions. The effectiveness of this method has already been proven for the early detection of vascular disease [13], for assessing endothelial function [14], and for assessing the influence of vasoactive drugs on arterial compliance [15–17].

Pulse contour analysis provides measurements that capture both capacitive and cushioning (oscillatory) arterial functions. It uses the arterial pulse contour to provide an assessment of large artery (capacitance) behavior and the behavior of smaller arteries that represent the primary source of reflected waves or oscillations in the arterial system. Pulse contour analysis of diastolic pressure decay utilizes a modified Windkessel model, a well-established electrical system analogue [13] [Figure 1]. Components of the diastolic wave form are mapped to the modified Windkessel model equation, comprising components matched to the arterial circulation – namely, cardiac output,

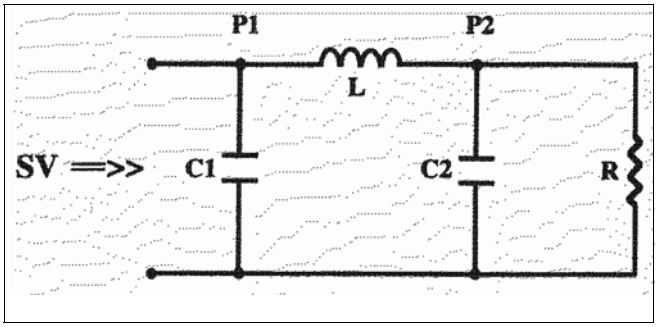


**Figure 1.** Modified Windkessel model used for analysis of vascular properties. SV = stroke volume, C1 = capacitive compliance, C2 = oscillatory compliance, R = systemic vascular resistance, L = inertia of the blood, P1 = proximal pressure, P2 = distal pressure [17].

capacitive and oscillatory compliance, systemic vascular resistance and impedence, distal and proximal blood pressure, and blood inertia. C1 is derived from the slope of the exponential diastolic decay and reflects large artery compliance, while C2 is derived from the oscillatory component of the diastolic decay and reflects small artery compliance.

Observing the pulse wave using the HDI-Pulse Wave CR 200 instrument enables evaluation of hemodynamic performance and compliance of large and small blood vessels in a non-invasive manner [13,18]. This instrument has recently come into use and is a means to evaluate blood vessel performance in epidemiologic studies. Using this technique we examined hemodynamic changes including small and large artery compliance in cirrhotic patients during total paracentesis.

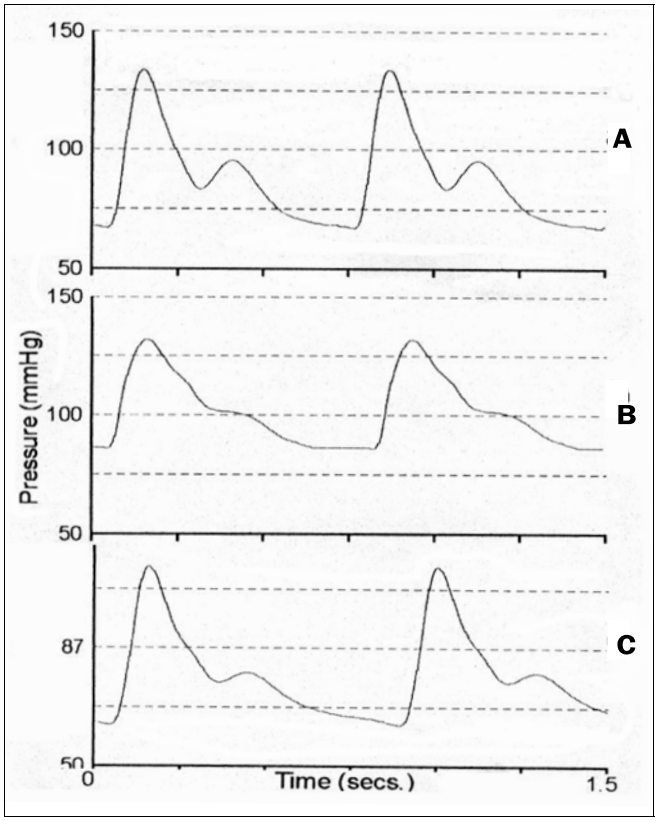


**Figure 2.** Typical waveforms in cirrhotic patient before **[A]**, after **[B]**, and 24 hours after **[C]** paracentesis

## Patients and Methods

### Patients

The study included 15 cirrhotic patients (2 women and 13 men; mean age 60.5 years, range 42–77) admitted to our department between May 2002 and March 2003 due to an episode of tense diuretic-resistant ascites. Cirrhosis was alcohol-related in 5 cases and post-hepatic in 10 (8 positive for hepatitis C virus and 2 for hepatitis B). Excluded were patients with concomitant disease – such as vascular disease, arterial hypertension, heart failure, diabetes mellitus, bacterial peritonitis, sepsis, hepatocellular carcinoma, and renal failure.

All the patients signed an informed consent and the study protocol conformed to the ethical guidelines of the Declaration of Helsinki.

### Paracentesis

On admission, patients were put on a low sodium diet (2 g/day) with unrestricted fluid intake and a bed-rest regimen. Diuretic administration and beta-blockers were discontinued at least 5 days before paracentesis. No vasoactive drugs were allowed before or during the study. Paracentesis was performed under sterile conditions with a cannula 1.4 x 45 mm in the left lower abdominal quadrant. Ascitic fluid was drained by gravity into a sterile container on the floor. The patients were given 8 g of albumin/L of ascites removed during the procedure.

### Arterial compliance method

Hemodynamic variables including vascular compliance were measured using an HDI pulse wave cardiovascular profiling instrument CR-2000 (Hypertension Diagnostics Inc/Pulse Wave$^{TM}$ CR-2000 Research Cardiovascular Profiling System, Minneapolis, USA). Radial artery waveforms were recorded with an arterial tonometer sensor array. The tonometry unit contained an array of piezo-resistive pressure transducers, each 0.2 mm apart, capable of measuring the relative intra-arterial pulse amplitude with high accuracy in arteries as small as 1.0 mm in diameter. Upon location of a strong pulse, a good quality radial artery waveform is normally obtained within a few minutes even by an untrained individual. Waveforms are recorded for 30 seconds on the right arm of the subject with an arterial tonometer sensor array for maintaining the sensor in position. The waveform is calibrated by the oscillometric method with a cuff on the opposite arm and an internal calibration. Figure 2 shows a typical waveform in cirrhotic patients. The variables were measured in these patients before, immediately after, and 24 hours following large volume (mean 5.6 L) paracentesis.

### Statistics

Statistical differences were calculated by using the descriptive analysis and paired samples *t*-test. Statistical significance was set at $P \leqslant 0.05$.

C1 = capacitive compliance
C2 = oscillatory compliance

**Table 1.** Hemodynamic changes and vascular compliance in cirrhotic patients during total paracentesis

| | Before paracentesis | After paracentesis | 24 hr after paracentesis |
|---|---|---|---|
| Systolic BP (mmHg) | 118.4 | 114.1 | 116.9 |
| Diastolic BP (mmHg) | 67.9 | 66.9 | 67.9 |
| Mean arterial BP (mmHg) | 87.1 | 83.3 | 85.4 |
| Pulse pressure (mmHg) | 50.5 | 47.2 | 49 |
| Pulse rate (beats/min) | 76.9 | 75.6 | 75.3 |
| Estimated cardiac ejection time (msec) | 289.2 | 313.7 | 289.1 |
| Estimated stroke volume (ml/beat) | 60.2 | 67.4 | 60.6 |
| Estimated stroke volume index (ml/beat/$m^2$) | 33.3 | 37 | 33.1 |
| Estimated cardiac output (L/min) | 4.5 | 5 | 4.4* |
| Estimated cardiac index (L/min/$m^2$) | 2.5 | 2.7 | 2.4* |
| Large artery elasticity index (ml/mmHg x 100) | 17.9 | 17.8 | 15.1 |
| Small artery elasticity index (ml/mmHg x 100) | 3.7* | 5.6 | 5 |
| Systemic vascular resistance (dyne.sec.$cm^{-5}$) | 1523.2 | 1400.5 | 1508 |
| Total vascular impedance (dyne.sec.$cm^{-5}$) | 125.4 | 116.9 | 135.1 |

* $P < 0.05$ compared to after paracentesis

## Results

No local complications related to the procedure were observed. There were no significant changes in serum urea and creatinine concentration before and 24 hours after paracentesis. The results of the study are summarized in Table 1.

Large volume paracentesis was accompanied by a non-significant fall in mean arterial pressure, which returned to basal level 24 hours later. Cardiac output increased immediately after paracentesis due to increment in stroke volume with no change in heart rate. However, 24 hours later the cardiac output decreased to below basal level. The fluctuation was statistically significant ($P < 0.05$). Pulse rate, pulse pressure, cardiac ejection time, stroke volume and total vascular impedance did not show any significant change during paracentesis.

There was no change in large artery compliance; however, small artery compliance increased after paracentesis ($P < 0.05$) and partially returned to basal level after 24 hours. Systemic vascular resistance measurement showed the same pattern of change: vasodilatation occurred during paracentesis and was attenuated 24 hours later.

## Discussion

The short-term hemodynamic effects of large volume paracentesis are well investigated, and the safety of this approach in cirrhotic patients with tense ascites has been proven in randomized controlled trials [19–21]. Large volume paracentesis ameliorates shortness of breath and early satiety experienced by these patients. It may also be associated with collateral advantages, such as reductions in the hepatic venous pressure gradient [22], intravariceal pressure, and variceal wall tension [22–24]. These parameters are considered important predictors of variceal bleeding and the improvement after paracentesis may decrease the risk of bleeding. Various hemodynamic parameters were investigated during paracentesis in cirrhotic patients. Several randomized controlled studies showed an increase in effective arterial blood volume, cardiac output and concentration of the plasma atrial natriuretic peptide, and a decrease in plasma renin activity, plasma aldosterone and plasma norepinephrin concentration. This early phase may be rapidly followed by a post-paracentesis circulatory dysfunction syndrome, characterized by an irreversible reduction in effective arterial blood volume and impaired renal function. An increase in plasma renin activity after paracentesis has been considered evidence of effective hypovolemia and is labeled post-paracentesis circulatory dysfunction [21]. Albumin administration may prevent this effect in cirrhotic patients in whom at least 5 L of ascitic fluid was removed.

Our study showed no significant changes in arterial pressure, heart rate, cardiac ejection time, stroke volume and systemic vascular resistance during paracentesis. Cardiac output increased immediately after paracentesis and decreased to below the basal level 24 hours later, as previously shown [25]. In our study, for the first time, we were able to differentiate between small and large artery compliance during paracentesis. Large artery compliance remained without significant change, but small artery compliance increased significantly immediately after paracentesis and decreased 24 hours later but not to the basal level. This parameter may be the first sign of enhanced vasodilatation due to large volume paracentesis before the appearance of any clinical expression of impaired hemodynamics and deterioration of renal function, and therefore may be a subclinical marker of post-paracentesis circulatory dysfunction.

In our study group there were no cases of serious circulatory dysfunction or impaired renal function. Such cases are associated with deterioration in mean arterial pressure despite the intense renal vasoconstriction. Renal blood flow decreases, causing a reduction in glomerular filtration rate and sodium excretion. Intensive peripheral vasodilatation is an important pathogenetic component in the development of hepatorenal syndrome. Our study did not yield data that would enable us to predict which patients could possibly develop renal failure during recurrent paracentesis. A possible future study with a larger number of patients might enable us to assess the degree of small artery compliance as a predictor of the development of renal failure after recurrent paracentesis.

## References


1. Rodriguez-Martinez D, Menon KV, Kamath PS. Regional and systemic hemodynamic disturbances in cirrhosis. *Clin Liver Dis* 20015(3):617–27.
2. Blendis L, Wong F. The hyperdynamic circulation in cirrhosis: an overview. *Pharmacol Ther* 2001;89(3):221–31.
3. Sherlock S. Vasodilatation associated with hepatocellular disease: relation to functional organ failure. *Gut* 1990;31(4):365–7.
4. Fernandez-Rodriguez CM, Prieto J, Zozaya JM, et al. Arteriovenous shunting, hemodynamic changes, and renal sodium retention in liver cirrhosis. *Gastroenterology* 1993;104(4):1139–45.

5. Lopez-Talavera JC, Merrill WW, Groszmann RJ. Tumor necrosis factor alpha: a major contributor to the hyperdynamic circulation in prehepatic portal-hypertensive rats. *Gastroenterology* 1995;108(3):761–7.
6. Stark ME, Szurszewski JH. Role of nitric oxide in gastrointestinal and hepatic function and disease. *Gastroenterology* 1992;103(6):1928–49.
7. Fernandez-Rodriguez CM, Prieto J, Quiroga J, et al. Plasma levels of substance P in liver cirrhosis: relationship to the activation of vasopressor systems and urinary sodium excretion. *Hepatology* 1995;21(1):35–40.
8. Spahr L, Martin PY, Giostra E, et al. Acute effects of nitric oxide synthase inhibition on systemic, hepatic, and renal hemodynamics in patients with cirrhosis and ascites. *J Investig Med* 2002;50(2):116–24.
9. Lee FY, Colombato LA, Albillos A, et al. Administration of N omega-nitro-L-arginine ameliorates portal-systemic shunting in portal-hypertensive rats. *Gastroenterology* 1993;105(5):1464–70.
10. Hadengue A, Moreau R, Gaudin C, et al. Total effective vascular compliance in patients with cirrhosis: a study of the response to acute blood volume expansion. *Hepatology* 1992;15(5):809–15.
11. Henriksen JH, Moller S, Schifter S, et al. Increased arterial compliance in decompensated cirrhosis. *J Hepatol* 1999;31(4):712–18.
12. Moreau R, Lebrec D. Endogenous factors involved in the control of arterial tone in cirrhosis. *J Hepatol* 1995;22(3):370–6.
13. Cohn J, Finkelstein S, McVeigh G, et al. Noninvasive pulse wave analysis for the early detection of vascular disease. *Hypertension* 1995;26:503–8.
14. Wilkinson IB, Hall IR, MacCallum H, et al. Pulse-wave analysis. Clinical evaluation of a noninvasive, widely applicable method for assessing endothelial function. *Arterioscler Thromb Vasc Biol* 2002;22:147–52.
15. Leibovitz E, Hazanov N, Zimlichman R, et al. Treatment with atorvastatin improves small artery compliance in patients with severe hypercholesterolemia. *Am J Hypertens* 2001;14(11 Pt 1):1096–8.
16. Shargorodsky M, Wainstein J, Gavish D, et al. Treatment with rosiglitazone reduces hyperinsulinemia and improves arterial elasticity in patients with type 2 diabetes mellitus. *Am J Hypertens* 2003;16(8):617–22.
17. Glasser SP, Arnett DK, McVeigh GE, et al. The importance of arterial compliance in cardiovascular drug therapy. *J Clin Pharmacol* 1998;38:202–12.
18. Resnick L, Militianu D, Cummings AJ, et al. Pulse waveform analysis of Presbyterian Hospital/Cornell University Med Center Arterial Compliance. *Am J Hypertens* 2000;13:1243–9.
19. Gines P, Arroyo V, Quintero E, et al. Comparison of paracentesis and diuretics in the treatment of cirrhotics with tense ascites: results of a randomized study. *Gastroenterology* 1987;93:234–41.
20. Gines P, Tito L, Arroyo V, et al. Randomized study of therapeutic paracentesis with and without intravenous albumin in cirrhosis. *Gastroenterology* 1988;94:1493–502.
21. Gines A, Fernandez Esparrach G, Monescillo A, et al. Randomized trial comparing albumin, dextran 70, and polygeline in cirrhotic patients with ascites treated by paracentesis. *Gastroenterology* 1996;111:1002–10.
22. Luca A, Feu F, Garcia-Pagan JC, et al. Favorable effects of total paracentesis on splanchnic hemodynamics in cirrhotic patients with tense ascites. *Hepatology* 1994;20:30–3.
23. Nevens F, Bustami R, Scheys I, et al. Variceal pressure is a factor predicting the risk of a first variceal bleeding: a prospective cohort study in cirrhotic patients. *Hepatology* 1998;27:15–19.
24. Kravetz D, Romero G, Argonz J, et al. Total volume paracentesis decreases variceal pressure, size, and variceal wall tension in cirrhotic patients. *Hepatology* 1997;25:59–62.
25. Paros MZ, Moore K, Vlavianos P, et al. Single, total paracentesis for tense ascites; sequential hemodynamic changes and right atrial size. *Hepatology* 1990;11:662–7.

**Correspondence:** Dr. J. Kogan, Dept. of Internal Medicine A, Barzilai Medical Center, Ashkelon 78306, Israel.
Phone: (972-8) 674-5685
Fax: (972-8) 674-5689
email: oranim@barzi.health.gov.il