Low cardiac output predicts development of hepatorenal syndrome and survival in patients with cirrhosis and ascites

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Low cardiac output predicts development of hepatorenal syndrome and survival in patients with cirrhosis and ascites

A Krag,1,2 F Bendtsen,1 J H Henriksen,2 S Møller2

ABSTRACT

Objectives: Recent studies suggest that cardiac dysfunction precedes development of the hepatorenal syndrome. In this follow-up study, we aimed to investigate the relation between cardiac and renal function in patients with cirrhosis and ascites and the impact of cardiac systolic function on survival.

Patients and design: Twenty-four patients with cirrhosis and ascites were included. Cardiac function was investigated by gated myocardial perfusion imaging (MPI) for assessment of cardiac index (CI) and cardiac volumes. The renal function was assessed by determination of glomerular filtration rate (GFR) and renal blood flow (RBF) and the patients were followed up for 12 months.

Results: In patients with a CI below 1.5 l/min/m2 on MPI, GFR was lower (39 (SD 24) vs 63 (SD 23) ml/min, p = 0.03), RBF was lower (352 (SD 232) vs 561 (SD 229) ml/min, p = 0.06), and serum creatinine was higher (130 (SD 46) vs 78 (SD 29) µmol/l, p < 0.01). The number of patients who developed hepatorenal syndrome type 1 within 3 months was higher in the group with low CI than in the high CI group (43% vs 5%, p = 0.04). Patients with the lowest CI (N = 8) had significantly poorer survival at 3, 9, and 12 months compared to those with a higher CI (N = 16), p < 0.05. In contrast, the Model for End-stage Liver Disease (MELD) score failed to predict mortality in these patients.

Conclusions: The development of renal failure and poor outcome in patients with advanced cirrhosis and ascites seem to be related to a cardiac systolic dysfunction. Other parameters may be more important than MELD score to predict prognosis.

Ascites occurs in about 50% of patients with cirrhosis within 10 years after diagnosis and is associated with a 50% mortality within 2 years.1 2 In many of these patients the renal function deteriorates with the development of the hepatorenal syndrome. According to the peripheral arterial vasodilation hypothesis, renal impairment and hepatorenal syndrome develop in the setting of a hyperdynamic circulation with severe arterial underfilling due to progressive splanchnic arterial vasodilation.1–4 However, it has recently been shown that a cardiac dysfunction with reduction of cardiac index (CI) precedes the hepatorenal syndrome and accordingly a modified peripheral arterial vasodilation hypothesis has been proposed.2 5 7 This hypothesis is mainly based on two studies. The first study showed a decreased CI in patients with spontaneous bacterial peritonitis who developed renal failure during treatment.5 The second study identified CI as an independent predictor of development of hepatorenal syndrome.5 7 The finding that a decreased cardiac output has a role in the development of hepatorenal syndrome has some therapeutic implications. Thus, improvement of the systolic cardiac function could be part of the treatment strategy to improve survival of the hepatorenal syndrome. Approximately 60–80% of patients hospitalised for heart failure have renal dysfunction, which is associated with a significantly increased morbidity and mortality.6 However, the presence of a cardio-renal relation, its pathophysiological background, and clinical importance in patients with cirrhosis and ascites needs to be further elucidated. The primary aim of this study was therefore in patients with advanced cirrhosis and ascites to assess the relation between cardiac and renal function and secondarily to assess the impact of cardiac systolic function on survival.

PATIENTS AND METHODS

Twenty-four patients with alcoholic cirrhosis and ascites without hepatorenal syndrome type 1 according to previous definitions of the International Ascites Club were included in the study.9 Nine patients, five of whom had serum creatinine above 133 µmol/l, had refractory ascites and 15 had non-refractory ascites according to these criteria.9 12 were classified as Child B and 11 as Child C. Patients were in a stable condition: none had gastrointestinal bleeding within the week before the study, spontaneous bacterial peritonitis, insulin-dependent diabetes, acute or chronic intrinsic renal or cardiovascular diseases, arterial hypertension, abnormal electrocardiogram or any acute medical conditions such as infections or acute heart or lung diseases. Furthermore, alcohol abstinence for 6 weeks was required. Pre-existing cardiac diseases were excluded by a negative history of arterial hypertension, cardiac or pulmonary diseases, a normal clinical examination and a normal electrocardiogram (ECG). All had normal baseline ECG, oxymetry and myocardial perfusion imaging (MPI) without signs of ischaemia. Diuretics and beta-blockers were discontinued 3 days before the investigations. None of the patients were receiving any other drugs that could interfere with cardiovascular system or nephrotoxic drugs. The patients were put on a sodium-restricted diet of 60 mmol/day the last 72 h before the investigations, and they were instructed orally and given written information on sodium restriction by a dietician. All patients recruited were hospitalised during the last 24 h prior to the study.

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Cirrhosis
and the nutrition unit prepared their food with a 60 mmol/day sodium diet. After the investigations the patients were followed for 12 months or until death by regular clinical controls.

Patients were studied at 9:00 am after a 9 h fast. At 10:00 pm the previous day, an oral dose of 300 mg of lithium carbonate was administered. An oral water load of 200 ml of tap water was given every half hour from 9:00 am to the end of the clearance periods and the patients were in the supine position throughout the investigation. A bladder catheter was placed before the clearance periods to ensure correct urine sampling. 51Cr-EDTA and 131I-hippuran were used to determine glomerular filtration rate (GFR) and effective renal plasma flow (ERPF).10–14 Renal blood flow = ERPF/(1 – Cx/GFR). Plasma and urinary lithium concentrations were measured by flame-emission photometry (Perkin Elmer, Wellesley, Massachusetts, USA). Sodium in atomic absorption spectrophotometry (Perkin Elmer 2380; Plasmatron, Tranum, Denmark). Blood sampling was immediately after the clearance periods and the patients were in the supine position throughout the investigation. A gated myocardial scintigraphy with single photon emission computed tomography (SPECT) was performed in all patients after an overnight fast. Gated SPECT is considered an accurate and reproducible method, which corresponds very well with findings of magnetic resonance imaging.10 19 Studies on serial reproducibility of gated SPECT-assessed ejection fraction in patients with ischaemic heart disease have shown a mean difference between two sequential measurements at rest of 0.09%, with a 95% limit of agreement (2 SDs) at 5.8%.20 The nature of this method as a non-invasive, observer-independent and reproducible method makes it an attractive investigational tool. The patients were placed in the supine position 1 h before the study. 99mTc-methoxy-allylisonitrile (99mTc-MIBI) (Cardiolite) was used as perfusion tracer and infused intravenously in a dose of 600 MBq 0.5 h before data acquisition. A low-energy, high-resolution collimator was used and the studies were acquired in a 64×64 matrix on a dual headed gamma camera (Millenium VG Nuclear Imaging System; GE).


dation during the steady state was calculated by the standard formula Cx = Ux×V/Px, where Cx = renal clearance of substance x, Ux = concentration in urine of substance x, V = urine flow rate, and Px = mean plasma concentration of substance x in the clearance period. Lithium clearance is used as a marker of proximal sodium reabsorption based on the assumption that lithium is filtered freely across the glomerulus, is reabsorbed in proportion to sodium and water in the proximal tubules and that no reabsorption or secretion takes place in the distal tubules.21–23 The excretion fraction of x is calculated as: Cx/GFR.

### Scintigraphic method

A gated myocardial scintigraphy with single photon emission computed tomography (SPECT) was performed in all patients after an overnight fast. Gated SPECT is considered an accurate and reproducible method, which corresponds very well with findings of magnetic resonance imaging.10 19 Studies on serial reproducibility of gated SPECT-assessed ejection fraction in patients with ischaemic heart disease have shown a mean difference between two sequential measurements at rest of 0.09%, with a 95% limit of agreement (2 SDs) at 5.8%.20 The nature of this method as a non-invasive, observer-independent and reproducible method makes it an attractive investigational tool. The patients were placed in the supine position 1 h before the study. 99mTc-methoxy-allylisonitrile (99mTc-MIBI) (Cardiolite) was used as perfusion tracer and infused intravenously in a dose of 600 MBq 0.5 h before data acquisition. A low-energy, high-resolution collimator was used and the studies were acquired in a 64×64 matrix on a dual headed gamma camera (Millenium VG Nuclear Imaging System; GE).

### Table 2: Demographic, clinical and biochemical data of 24 patients with alcoholic cirrhosis and ascites with cardiac index above or below 1.5 l/min/m²

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CI&lt;1.5 n = 8</th>
<th>CI&gt;1.5 n = 16</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57 (8)</td>
<td>58 (6)</td>
<td>56 (9)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>14/10</td>
<td>5/3</td>
<td>9/7</td>
</tr>
<tr>
<td>Child–Pugh score</td>
<td>8.6 (1.9)</td>
<td>8.5 (1.3)</td>
<td>8.6 (2.2)</td>
</tr>
<tr>
<td>MELD score</td>
<td>10.5 (6.0)</td>
<td>11.8 (6.6)</td>
<td>9.9 (5.8)</td>
</tr>
<tr>
<td>Ascites/refractory ascites/HRS-2</td>
<td>15/4/5</td>
<td>2/2/4</td>
<td>13/2/1</td>
</tr>
<tr>
<td>Serum creatinin, mmol/l</td>
<td>200 (400)</td>
<td>125 (400)</td>
<td>200 (375)</td>
</tr>
<tr>
<td>Serum sodium, mmol/l (136–146)</td>
<td>136 (5)</td>
<td>132 (10)</td>
<td>137 (3)</td>
</tr>
<tr>
<td>Serum creatinine, μmol/l (60–130)</td>
<td>95 (42)</td>
<td>130 (46)</td>
<td>78 (30)*</td>
</tr>
<tr>
<td>Plasma creatinine, μmol/l (540–800)</td>
<td>449 (96)</td>
<td>415 (82)</td>
<td>467 (102)</td>
</tr>
<tr>
<td>Serum albumin, μmol/l (4–22)</td>
<td>19 (73)</td>
<td>18 (26)</td>
<td>21 (69)</td>
</tr>
<tr>
<td>QTc, s</td>
<td>0.436 (0.029)</td>
<td>0.429 (0.029)</td>
<td>0.57</td>
</tr>
<tr>
<td>Serum proANP, pg/ml</td>
<td>1874 (2818)</td>
<td>1117 (2230)</td>
<td>0.03</td>
</tr>
<tr>
<td>Serum proBNP, pg/ml</td>
<td>717 (4185)</td>
<td>602 (3881)</td>
<td>0.72</td>
</tr>
<tr>
<td>RBF, ml/min</td>
<td>352 (232)</td>
<td>561 (229)</td>
<td>0.06</td>
</tr>
<tr>
<td>GFR, ml/min</td>
<td>39 (24)</td>
<td>63 (23)</td>
<td>0.03</td>
</tr>
<tr>
<td>Cx/mrn, ml/min</td>
<td>0.31 (0.30)</td>
<td>0.86 (0.80)</td>
<td>0.03</td>
</tr>
<tr>
<td>log serum aldosterone, pmol/l</td>
<td>3.21 (2.06)</td>
<td>2.66 (2.15)</td>
<td>0.08</td>
</tr>
<tr>
<td>Plasma renin, pg/ml</td>
<td>86 (3996)</td>
<td>20 (1207)</td>
<td>0.28</td>
</tr>
<tr>
<td>Serum creatinin, μmol/l</td>
<td>130 (46)</td>
<td>78 (29)</td>
<td>0.003</td>
</tr>
<tr>
<td>Dead &lt;3 months</td>
<td>4/8</td>
<td>1/6</td>
<td>0.01</td>
</tr>
<tr>
<td>Hepatorenal syndrome type 1 ≤3 months</td>
<td>3/7*</td>
<td>1/6</td>
<td>0.04</td>
</tr>
<tr>
<td>Dead ≥9 months</td>
<td>5/8</td>
<td>2/6</td>
<td>0.006</td>
</tr>
<tr>
<td>Dead &lt;12 months</td>
<td>5/8</td>
<td>4/6</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Results are given as mean (SD) or median (range).

*One patient died outside hospital.

AC, arterial compliance; Cx, lithium clearance; C Na, sodium clearance; Fe Na, fractional sodium excretion; GFR, glomerular filtration rate; HR, heart rate; MAP, mean arterial pressure; Pro ANP, pro atrial natriuretic peptide; Pro BNP, pro brain natriuretic peptide; QTc, QT interval corrected for heart rate; RBF, renal blood flow; SV, stroke volume; SVI, stroke volume index; SVR, systemic vascular resistance.
Healthcare, Milwaukee, Wisconsin, USA). The camera heads were positioned in a 90° angle and the studies were acquired with 30 projections in steps of 3° each of 25 s giving a total acquisition time of 25 min. The zoom factor was set at 1.28. All gates were reconstructed using filtered back-projection (Butterworth filter). Gated data were analysed on a Xeleris Functional Imaging Workstation (GE Healthcare, Milwaukee, Wisconsin, USA) by the QGS programme (Quantitative Gated SPECT, Cedar-Sinai Medical Center, Los Angeles, California, USA).

The cardiac cycle was divided into 16 intervals (frames) to obtain the highest temporal resolution and the gating was triggered by the ECG signal. This allows evaluation of left ventricular ejection fraction, end diastolic volume, end systolic volume, stroke volume and left ventricular regional wall motion and wall thickening.20 Furthermore, it improves the diagnostic accuracy of perfusion imaging and the functional gated SPECT data represent images of the left ventricular myocardium during acquisition and not at the time of tracer injection.20 Cardiac output was assessed as stroke volume x heart rate and cardiac index (CI) = cardiac output/body surface area (Dubois formula).21 Mean arterial pressure (MAP) was calculated MAP = systolic pressure + (diastolic pressure x 2)/3. Arterial compliance was assessed as stroke volume/pulse-pressure (systolic minus diastolic blood pressure) and the systemic vascular resistance as MAP*80/cardiac output.

ECG was recorded by a conventional non-computerised electrocardiogram (Siemens-Elema, Erlangen, Germany) to evaluate conductive and possible ischaemic changes. The Q-T interval was determined from the ECG (25–50 mm/s), as described elsewhere.22

Blood samples for analyses of vasoactive hormones were obtained from a cubital vein. The circulating plasma renin concentration was determined by commercially available two-site immunoradiometric assay (DGR International, Hamburg, Germany). Aldosterone was measured with a commercial kit, DSL-8600 (Diagnostic Systems Laboratories, Webster, Texas, USA). N-terminal pro ANP (1–30) was measured radioimmunologically with antiserum and calibrator material from Peninsula Laboratories (Los Angeles, California, USA) and tracer prepared in-house.

Statistics

Results are expressed as the mean with the SD or medians and total range if non-normal distribution. Statistical analyses were performed by the unpaired Student t test or the Mann–Whitney test as appropriate. Correlations were performed by the Pearson regression analysis. Survival is given in Kaplan–Meier survival curves and differences analysed by the logrank test. All reported p values are two-tailed, with values less than 0.05 considered significant. The SPSS 10.1 statistical package was applied throughout.

Patients were divided into two groups according to their CI to separate those with the lowest CI, and compared with respect to survival and cardiac and renal functions. The cut off to divide the patients based on CI was pragmatically chosen to be 1.5 l/min/m2, though supported by a study in heart failure that linked CI below 1.5 to liver function abnormalities.23 CI is used because cardiac output increases in proportion with body surface area and individual values indexed by body surface area are therefore more accurate in the comparison of individuals with different body texture.24

RESULTS

Patient’s characteristics are given in table 1, both as pooled data and according to CI group. Those with the lowest CI had higher serum creatinine (p = 0.01) and borderline lower serum sodium concentration (p = 0.06). Both the Model for End-stage Liver Disease (MELD) score and the Child–Pugh score failed to separate the two groups (table 1). Although there was a tendency towards lower values of cardiac output in the nine patients with refractory ascites this did not differ significantly from those without (1.7 (SD 0.8) vs 2.1 (SD 0.6) l/min/m2, p = 0.2).

Cardiac function

Low CI was due to chronotropic incompetence as reflected by a relatively low heart rate p<0.01 and inotropic incompetence reflected by a lower stroke volume, p = 0.02 (table 2). The group

![Figure 1](gut.bmj.com/ on February 18, 2010 - Published by group.bmj.com)
of patients with low CI had higher systemic vascular resistance (mean difference 0.01039 Newton s cm⁻⁵, confidence interval 0.00374 to 0.01704 Newton s cm⁻⁵, p = 0.004); however, arterial compliance and MAP did not differ between the groups (table 2). End diastolic volume (77 vs 51 ml, p = 0.06), end systolic volume (21 vs 13 ml p = 0.23) ejection fraction, myocardial wall motion, and wall thickening were not significantly different between the groups.

Renal function
In patients with low CI, GFR was lower (mean difference 23 ml/min, confidence interval 2 to 46 ml/min, p = 0.03), and renal blood flow lower (mean difference 209 ml/min, confidence interval −7 to 425 ml/min, p = 0.06) and serum creatinine higher (p < 0.01) than in patients with higher CI. Sodium clearance (mean difference 0.48 ml/min, confidence interval 0.06 to 0.89 ml/min, p = 0.05) and fractional sodium excretion (p = 0.05) was lower in patients with low than those with high CI. Lithium clearance was lower although this difference did not reach statistical significance (table 2, p = 0.058). GFR correlated with log serum aldosterone (r = −0.55, p = 0.006) (fig 1a). GFR correlated with MAP (r = 0.52, p = 0.01) (fig 1b). There was no linear correlation between CI and GFR. There were no significant differences in plasma noradrenaline or plasma renin between the two groups, however plasma proANP concentrations were significantly higher in the low CI group (p = 0.03) (table 2).

Survival
Patients with ascites and CI below 1.5 l/min/m² (N = 8, CI 1.3 (SD 0.2) l/min/m²) had a poorer survival at 3, 9, and 12 months, than those with a CI above 1.5 l/min/m² (N = 16, CI 2.3 (SD 0.6) l/min/m²), p < 0.05 (fig 2a). Furthermore, patients with a MAP below 80 mm Hg had a lower 12 months survival (fig 2b). The number of patients who died from hepatorenal syndrome type 1 within 8 months was significantly higher in the low CI group than in the high CI group (45% (5/7) vs 6% (1/16), p = 0.04). Patients with a cardiac output below the mean of 3.6 l/min had a borderline significant poorer 12 month survival than those with a cardiac output above the mean level (logrank test p = 0.059). The mean cardiac output (CO) did not separate those with the lowest GFR (51 (SD 23) vs 64 (SD 28) ml/min, p = 0.2; below vs above mean cardiac output). Among patients with normal serum creatinine at baseline 11% (2/19) developed hepatorenal syndrome type 1 and died within 3 months. Among patients with a serum creatinine above upper normal limit at baseline 80% (4/5) had a CI below 1.5 l/min/m².

In subsequent analyses, we compared cardiac and renal parameters in patients who died within 12 months (n = 9) with survivors (N = 15) (table 3). CI was significantly higher in survivors (mean difference 0.7 l/min/m², confidence interval 0.2 to 1.2, p = 0.007) and heart rate was 17% higher (p = 0.04). All renal function parameters were significantly impaired in non-survivors compared to survivors (table 3): renal blood flow was 36% lower (mean difference 208 ml/min, confidence interval 10 to 405, p = 0.05) and GFR was 57% lower (mean difference 23.1 ml/min, confidence interval 2.0 to 44.2, p = 0.05). Although there was a tendency towards a higher MELD score (15.1 vs 8.9, p = 0.10) and Child-Pugh score (9.3 vs 8.1, p = 0.14) in patients with low CI, this difference did not reach statistical difference.

**DISCUSSION**
This is the first study to describe the association between cardiac and renal dysfunction and survival in patients with advanced cirrhosis. Our data support the hypothesis that renal and cardiac dysfunctions are closely related in cirrhosis. A cardio-renal relation in cirrhosis is most likely the result of chronic circulatory stress combined with more acute events, such as bacterial translocation and systemic inflammatory response, which trigger a systemic response. This may lead to progression of a systolic failure with a decrease in CI, starting a vicious circle in which the decreased CI leads to accentuated arterial underfilling, decreased MAP and decreased renal perfusion and perfusion pressure, resulting in deterioration of the renal function, which further enhances cardiac and renal deterioration.

In these patients with ascites but a relatively low MELD score of 10.6 at mean (table 1), the MELD score failed to predict mortality in contrast to CI. This suggests that other parameters as CI may also be more important determinants and reflect secondary organ dysfunction in advanced cirrhosis. Similar...
Observations were reported in the studies by Ruiz-del-Árbol, in which the baseline MELD and Child-Pugh scores did not differ between the patients who developed hepato-renal syndrome and those who did not. A relatively low heart rate is a main factor responsible for the low CI. Treatment with beta-blockers further decreases heart rate and CI may therefore have deleterious effects on haemodynamics and renal function in this group of patients and thereby influence survival negatively. Future studies should therefore specifically look at this aspect and beta-blockers should in the meanwhile be administered cautiously in these patients.

This study has some limitations. Gated SPECT has not been validated in cirrhosis. To validate gated SPECT in patients with cirrhosis and due to the observation of rather low CI in all patients, we compared it with magnetic resonance imaging (MRI) in 20 other patients with cirrhosis. There was a close linear correlation between the two modalities (r = 0.74, p < 0.0001); however, gated SPECT systematically underestimated CI by on the average 1.1 l/min/m², 95% confidence interval 0.85 to 1.37 in cirrhotic patients compared to MRI. This is a problem regarding absolute values, but not in terms of relative values or in separating those with the lowest CI. We have no data on the variability relating to the size of the cardiac index but in our opinion it should be small as compared with the variability relating to the size of the cardiac volumes (ie, lower number of counts/s). Smaller values of EDV and ESV are associated with a higher variability but the variability of the SV depends on the size of the volumes (number of counts/s) of which the calculation of SV is based. Thus, the same SV based on acquisition of larger volumes are associated with a lower variability compared to a numerical identical SV based on acquisition of smaller volumes.

The failing heart in cirrhosis appears to be a general dysfunction comprising systolic and diastolic dysfunction and conductance abnormalities partly as a result of prolonged exposure to activated SNS, RAAS, endocannabinoids, inflammation and other systems that interact with cardiac energy metabolism and physiology. In patients with heart failure, a similar cardio-renal relation, with co-existence of cardiac and renal failure that amplifies the progression of failure of the individual organs have been described. Whether this condition is similar to the pathophysiology in cirrhosis is unknown, but primary heart failure and cardiomyopathy in cirrhosis share several characteristics. From a pathophysiological point of view the key physiological factor is effective arterial underfilling. It may induce or amplify disturbances in the cardio-renal homeostasis and neurohumoral integrity, which is a result of arterial vasodilation, relatively or absolutely decreased CI and ultimately both as described in this study. Albumin that expands central blood volume and increases CI and MAP and thereby ameliorates arterial underfilling can prevent hepato-renal syndrome and reduce mortality in spontaneous bacterial peritonitis and post paracentesis. The primary mechanisms responsible for deterioration of renal function are renal hypoperfusion and impaired filtration, and GFR in advanced cirrhosis is critically dependent on blood flow and perfusion pressure. In this study we observed that GFR was correlated to MAP and the activation of RAAS (fig 2). Whether renal impairment is a direct consequence of low CI cannot be ruled out in this paper, ie, we cannot exclude that both low CI and low GFR are results of hypovolaemia.

**Implications**

A low CI seems to develop in parallel with renal impairment in cirrhosis and ascites and may play an important role at this stage of the disease. Therefore future treatments of hepato-renal syndrome should aim not only at improving renal function but also at preserving a sufficient CI. Vasocostriction with terlipressin is an important treatment in hepato-renal syndrome which improves renal function, but this treatment decreases CI. Some patients with hepato-renal syndrome type 1 already have a decreased or relative low CI and a further decrease in

### Table 3 Haemodynamics and renal function in patients dead within 12 months compared to survivors

<table>
<thead>
<tr>
<th></th>
<th>Alive &gt;12 months</th>
<th>Dead &lt;12 months</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CO, l/min</strong></td>
<td>4.1 (1.5)</td>
<td>2.8 (0.8)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>CI, l/min/m²</strong></td>
<td>2.3 (0.7)</td>
<td>1.6 (0.4)</td>
<td>0.007</td>
</tr>
<tr>
<td><strong>SV, ml</strong></td>
<td>30.0 (8.5)</td>
<td>23.5 (6.3)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>EF</strong></td>
<td>76 (9)</td>
<td>79 (17)</td>
<td>0.63</td>
</tr>
<tr>
<td><strong>EDV, ml</strong></td>
<td>74 (29)</td>
<td>59 (29)</td>
<td>0.26</td>
</tr>
<tr>
<td><strong>ESV, ml</strong></td>
<td>19 (13)</td>
<td>17 (17)</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>MAP, mm Hg</strong></td>
<td>91.5 (14.1)</td>
<td>81.0 (11.2)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>HR, min⁻¹</strong></td>
<td>77.0 (13.9)</td>
<td>65.6 (9.0)</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>AC, ml/mmHg</strong></td>
<td>1.10 (0.46)</td>
<td>1.07 (0.38)</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>SVR, Newton s cm⁻¹</strong></td>
<td>0.02256 (0.00878)</td>
<td>0.02470 (0.00757)</td>
<td>0.27</td>
</tr>
<tr>
<td><strong>RBF, ml/min</strong></td>
<td>569 (242)</td>
<td>382 (197)</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>GFR, ml/min</strong></td>
<td>63.8 (23.6)</td>
<td>40.8 (22.3)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Vu, ml/min</strong></td>
<td>2.42 (1.32)</td>
<td>0.83 (0.69)</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>C_{H2O}, ml/min</strong></td>
<td>2.01 (0.82)</td>
<td>1.30 (0.84)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>C_{Li}, ml/min</strong></td>
<td>15.7 (8.7)</td>
<td>8.4 (6.6)</td>
<td>0.055</td>
</tr>
<tr>
<td><strong>C_{Na}, ml/min</strong></td>
<td>0.80 (0.63)</td>
<td>0.27 (0.46)</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>C_{Cl}, ml/min</strong></td>
<td>0.41 (0.35)</td>
<td>−0.46 (0.35)</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>log serum aldosterone, pmol/l</strong></td>
<td>2.67 (0.60)</td>
<td>3.40 (0.83)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Serum creatinine, mmol/l</strong></td>
<td>81.5 (30.0)</td>
<td>118.7 (51.4)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Results are given as the mean (SD) or median (range).

AC, arterial compliance; C_{H2O}, free water clearance; CI, cardiac index; C_{Li}, lithium clearance; C_{Na}, sodium clearance; CO, cardiac output; C_{osm}, osmolar clearance; EDV, end diastolic volume; EF, ejection fraction; ESV, end systolic volume; GFR, glomerular filtration rate; HR, heart rate; MAP, mean arterial pressure; RBF, renal blood flow; SV, stroke volume; SVR, systemic vascular resistance; Vu, urinary flow rate.
the systemic blood flow and oxygen transport capacity may be deleterious in some patients.

Beta-blockers decrease CI and in patients with ascites and low CI they may potentially worsen haemodynamics and band ligation may therefore be the preferred treatment as prophylaxis against variceal bleeding. Studies in patients with decompensated cirrhosis and hepato-renal syndrome type 2 in whom CI is monitored both with and without beta-blocker are highly relevant.

In conclusion, our study demonstrates that in patients with cirrhosis and ascites those with the lowest CI had the most impaired renal function and the poorest survival. Hence, the development of hepato-renal syndrome, and poor outcome in these patients seem to be related to a cardiac systolic dysfunction.

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Competing interests: None.

Ethics approval: The Regional Medical Ethics Committee approved the study (KF 02–059/04), which was carried out in accordance with the Helsinki Declaration II after informed consent. No complications were encountered during the study.

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REFERENCES