Hemodynamics in the immediate post-transplantation period in alcoholic and viral cirrhosis

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AIM: To study the hemodynamics in the immediate post transplant period and compare patients with alcoholic vs viral cirrhosis.

METHODS: Between 2000-2003, 38 patients were transplanted for alcoholic cirrhosis and 28 for postviral cirrhosis. Heart rate (HR), central venous pressure (CVP), mean arterial pressure (MAP), pulmonary capillary wedge pressure (PCWP), cardiac index (CI), systemic vascular resistance index (SVRI), pulmonary artery pressure (PAP), and pulmonary vascular resistance index (PVRI) were measured immediately and 24 h post transplantation.

RESULTS: Hyperdynamic circulation persisted at 24 h following transplantation with an elevated CI of 5.4 ± 1.3 L/(min × m²) and 4.9 ± 1.0 L/(min × m²) in the viral and alcoholic groups, respectively, and was associated with a decreased SVRI. Within the first 24 h, there was a significant decrease in HR and increase in MAP; the extent of the change was similar in both groups. The CVP, PCWP, and SVRI increased, and CI decreased in the viral patients, but not the alcoholic patients. Alcoholics showed a lower PVRI (119 ± 52 dynes/(cm² × m²) vs 166 ± 110 dynes/(cm² × m²), P < 0.05) and PAP (20 ± 7 mmHg vs 24 ± 7 mmHg, P < 0.05) compared to the viral group at 24 h.

CONCLUSION: Hyperdynamic circulation persists in the immediate post-transplant period with a faster improvement in the viral group. Alcoholic patients have a more pronounced pulmonary vasodilatation.

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Key words: Hemodynamics; Cirrhosis; Alcohol; Viral; Allograft

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INTRODUCTION

Patients with end stage liver disease manifest a hyperdynamic circulation characterized by a decrease in the systemic vascular resistance and arterial pressure, and
an increase in cardiac output. Many patients with advanced cirrhosis also have pulmonary vascular abnormalities, ranging from hepatopulmonary syndrome to pulmonary hypertension. Although several studies have examined these aspects of the circulation in the medium- and long-term postoperative period after liver transplantation (weeks to months), the cardiovascular profile in the immediate postoperative period remains unclear.

To what extent these changes persist following liver transplantation is unclear, and whether patients with alcoholic cirrhosis who are also at risk of alcoholic cardiomyopathy manifest a different hemodynamic pattern compared to patients with post viral cirrhosis is yet to be determined.

Therefore we conducted a retrospective review of orthotopic liver transplantation (OLT) performed at the Alberta Liver Transplant program between 2000-2003 to assess the systemic and pulmonary hemodynamics within the first 24 h following liver transplantation in patients transplanted for both alcoholic and viral induced cirrhosis.

**MATERIALS AND METHODS**

**Patients**

Systemic and pulmonary hemodynamics for 66 patients (38 alcoholic, 28 viral) receiving a cadaveric liver transplantation for end stage liver disease between January 2000 and January 2003 were evaluated immediately following surgery and 24 h later. There were 26 male patients in the alcohol group and seven in the viral group. The average age was 51 years (range 35-57 years) and 49 years (range 41-74 years) in the two groups, respectively. All included patients were thoroughly evaluated for any coexisting cardiovascular or pulmonary disease as part of the pre-transplant workup.

Following liver transplantation, these patients were transferred to the intensive care unit at the University of Alberta hospital. Postoperative care included: (1) Frequent daily rounds conducted by the intensive care team, transplant hepatologist, transplant surgeons, and other consultants as required; (2) Endotracheal intubation and mechanical ventilation to maintain adequate oxygenation with frequent intra-arterial monitoring through a catheter inserted prior to surgery; intubation was discontinued as soon as possible following the transplantation; (3) Continuous monitoring of the heart rate (HR), blood pressure, and oxygenation, as well as a continuous electrocardiographic tracing; (4) Systemic and pulmonary hemodynamics, including cardiac index (CI), systemic vascular resistance index (SVRI), pulmonary capillary wedge pressure (PCWP), central venous pressure (CVP), mean arterial pressure (MAP), pulmonary artery pressure (PAP), and pulmonary vascular resistance index (PVRI) were measured every 8 h during the first 24 h through a pulmonary arterial (Swan Ganz) catheter inserted preoperatively; (5) Laboratory investigations including a complete cell count, electrolytes, kidney function, coagulation profile, liver enzymes, and albumin were obtained twice a day (or more if indicated) for the first few days; and (6) Fluid balance was charted every 8 h with measurements of total fluid input and output, including surgical drains. Patients who suffered a gastrointestinal bleed or who had a sudden unexplained drop in the hemoglobin (> 2 g/L) underwent the appropriate investigation and were not included in the study. Patients were also excluded from the study if they developed sepsis within the first 72 h following transplantation, required dialysis, had an adverse intraoperative or immediate post operative course requiring continuous pressure support, or were being transplanted for the second time. This study was approved by the Research Ethics Committee of the hospital.

**Statistical analysis**

Results were expressed as mean ± SD. Statistical analysis was done using STATA software (Version 8). Analysis was done using Student’s t-test. A P value of less than 0.05 (two-sided test) was considered statistically significant. The correlations of disease severity graded by the model for end-stage liver disease (MELD) score and the various hemodynamic parameters were analyzed using Spearman’s rank correlation coefficient.

**RESULTS**

Hyperdynamic circulation persisted within the first 24 h with an elevated mean CI of 5.4 and 4.9 L/(min × m²), immediately following surgery in the viral and alcoholic group, respectively. The SVRI was also low at 1232 and 1294 dynes/(cm² × m²) in the two groups, respectively; however, these differences were not statistically significant.

Patients with alcoholic cirrhosis manifested a lower PVRI and a lower PAP, compared to the viral group at 24 h post transplant (P = 0.024 and 0.037, respectively) (Figure 1, Table 1). There were no significant differences in CVP, PCWP, HR, and MAP between the two groups at both time periods. The HR decreased significantly in association with an increase in the MAP over the first

| Table 1  Pulmonary and systemic hemodynamics at 24 h |
|-----------------|-----------------|-----------------|
|                | Alcohol         | Viral           |
| MELD score     | 16.2 ± 6.6      | 16.5 ± 7.3      |
| HR (beats/min) | 88 ± 16         | 86 ± 13         |
| MAP (mm Hg)    | 94.0 ± 17.2     | 95.1 ± 11.4     |
| PAP (mm Hg)    | 20.3 ± 6.9      | 24.1 ± 7.5      |
| PCWP (mm Hg)   | 13.5 ± 6.5      | 15.2 ± 4.6      |
| CVP (mm Hg)    | 10.3 ± 4.7      | 13.0 ± 5.0      |
| CI [L/(min × m²)] | 4.8 ± 1.1    | 4.8 ± 0.9      |
| SVRI [dynes/(cm² × m²)] | 1391 ± 425 | 1398 ± 350 |
| PVRI [dynes/(cm² × m²)] | 119 ± 52 | 166 ± 110 |

*P < 0.05. MELD: Model for end-stage liver disease; HR: Heart rate; MAP: Mean arterial pressure; PAP: Pulmonary artery pressure; PCWP: Pulmonary capillary wedge pressure; CVP: Central venous pressure; CI: Cardiac index; SVRI: Systemic vascular resistance index; PVRI: Pulmonary vascular resistance index.*
24 h in both groups. There was also an increase in the CVP, PCWP, SVRI, and a decrease in the CI in both groups over the first 24 h; these changes reached statistical significance only in the viral cirrhosis group (Table 2).

There were weak, insignificant correlations between the pre transplant MELD score and the CO, SVRI, PAP, PVRI with a Spearman’s rank correlation coefficient of 0.0919, -0.1881, 0.0945, -0.0939, respectively.

**DISCUSSION**

In this study, we showed that cirrhosis-associated hyperdynamic circulation persists in the immediate postoperative period, regardless of the etiology of the underlying liver disease. To our knowledge, this is the first study to compare hemodynamic changes in alcohol vs viral induced cirrhosis in the immediate postoperative period. Our results suggest that patients with viral-related cirrhosis have a rapid improvement in systemic hemodynamics, with a decrease in the cardiac output and an increase in the systemic vascular resistance; these changes were lacking in the alcohol group. We also showed that the increase in systemic vascular resistance was associated with a proportionate increase in CVP and PCWP unmasking the cardiac dysfunction of cirrhotic cardiomyopathy.

These results emphasize the additional effect of alcohol on the pathogenesis of the associated hyperdynamic circulation. Autonomic dysfunction has been clearly described in alcoholics, alcoholic liver disease, and to a lesser degree, in non-alcoholic chronic liver disease; the latter is thought to be related to the severity of the underlying liver disease. Liu et al. demonstrated the role of vagal stimulation in the hyperdynamic circulation of cirrhotic rats, and by blocking this pathway the hyperdynamic circulation significantly decreased in the portal hypertensive rats. Lindgren et al. demonstrated that the autonomic, particularly vagal, nerve dysfunction of chronic liver disease is further exaggerated by alcohol abuse, suggesting that in alcoholic liver disease, sympathetic neuropathy adds to the parasympathetic dysfunction, which further contributes to the altered vascular
responsiveness in patients with alcoholic cirrhosis. It has also been suggested that alcohol consumption has a short and long term effect in reducing the vascular responses to endogenous vasoconstrictors\[13,16\]. Other factors that might contribute to the hyperdynamic circulation in both groups include vasoactive substances (such as nitric oxide and carbon monoxide), A-V shunts, increased blood volume, and central neural dysregulation\[13,17-19\].

The consequences of these cardiovascular alterations can lead to significant cardiovascular derangements at the time of transplantation. OLT induces severe stresses on the cardiovascular system, during both intra- and postoperative periods\[20,21\]. Intraoperatively, the sudden reduction in the preload and the impaired cardiac contractility can result in significant reduction in cardiac output. Postoperatively, patients are at risk of hypovolemia from various factors, including hemorrhage, third space losses, and ongoing ascites formation. On the other hand, volume overload from aggressive fluid replacement can also stress the heart. Furthermore, the rapid improvement of systemic vasodilatation can result in a sudden increase in the afterload, adding extra stress to the heart. Metabolic derangements, in the form of acidosis, hypothermia, and electrolyte disturbance in the immediate postoperative period, can also impair the cardiac contractility and lead to hemodynamic instability and fluctuation. Hemodynamic depression caused by hypocalcemia-induced citrate intoxication from massive transfusion, or as a result of the reperfusion syndrome, has been described following OLT.

Cardiac complications following liver transplantation are common, involving 25%-70% of patients; fortunately most of these complications are mild and subclinical, with no significant impact on patient or graft survival\[22-24\]. Pulmonary edema following OLT is the most common cardiovascular complication, with at least 50% of these episodes developing within the first 24 h\[21,23\]. Careful fluid management and continuous cardiac monitoring in the immediate post transplant period is extremely important to avoid cardiac-related complications.

Studies examining hemodynamics after liver transplantation are limited and the results of those studies do not always agree with each other. Glaser\[26\] studied the systemic hemodynamics within the first 96 h following liver transplantation in 21 patients; his results suggested a progressive improvement towards normal within the study period. Navasa et al\[27\] examined hemodynamics at 2 wk and 2 mo following liver transplantation, and suggested that most of the hemodynamic changes reverse. However, the limitations of these two studies are the small number of patients included (21 and 12, respectively), as well as the diverse indications for liver transplantation—thus only three and five patients were transplanted for alcoholic liver disease in the two studies, respectively. In contrast, other studies suggested persistence of hyperdynamic circulation for at least 6 mo\[28-30\]. In our study, we excluded factors that might affect the systemic circulation, such as anemia, sepsis, and renal failure. Patients who were transplanted previously and were receiving their second or third transplant were also excluded; such surgeries disrupt local innervations and blood supply and might impact the vascular hemodynamics.

A low pulmonary vascular resistance has been described in patients with cirrhosis\[31-34\]. This also is thought to be related to endogenous vasodilators, as measured nitric oxide in exhaled air was higher in patients with cirrhosis compared to the general population\[35\]. Our data suggests that this pulmonary vasodilatory effect persists in the immediate post-transplant period. Furthermore, we showed that patients with alcoholic cirrhosis have a more profound decrease in the pulmonary vascular resistance associated with a significantly lower PAP; this could be related to a higher degree of intrapulmonary vascular shunting in patients with alcoholic cirrhosis and could, in part, be related to alcohol-induced depression in the vascular response to endogenous vasoconstrictors\[36\].

In our study the MELD score did not significantly correlate with hemodynamic disturbance. We believe this is because the study cohort had a limited range of dispersion of MELD scores and hyperdynamic circulation, i.e. almost all patients had high MELD scores and also a significantly abnormal extent of hyperdynamic circulation. It is possible that inclusion of a larger range of less sick patients with lower MELD scores and less hyperdynamic circulation might have allowed a correlation to become more evident. However, such patients would not be considered for transplantation.

In conclusion, our data suggests that the systemic hyperdynamic circulation persists in the immediate post-transplant period. The pattern of changes in hemodynamics in the immediate post transplant period, as well as in the pulmonary circulation, differed in the two groups, suggesting an alcohol-related impact on the neurohumoral factors involved in the pathogenesis of hyperdynamic circulation of cirrhosis.

**COMMENTS**

**Background**

Cirrhosis is associated with hyperdynamic circulation and pulmonary vascular abnormalities; whether these abnormalities persist in the immediate post-transplantation, and differ according to the cause of cirrhosis remains unclear. The aim of this study was to compare the hemodynamics in alcoholic vs viral cirrhosis.

**Research frontiers**

Cirrhosis is associated with significant cardiovascular abnormalities including hyperdynamic circulation, systemic vasodilation, and cirrhotic cardiomyopathy. The immediate effect of liver transplantation on these cardiovascular changes has not been adequately studied. Prior studies on the effect of transplantation on the cardiovascular abnormalities were variable and not consistent.

**Innovations and breakthroughs**

This is the first study to compare hemodynamics in the immediate post transplant period in patients with alcoholic and viral related cirrhosis. The results indicate that, although the hyperdynamic circulation persists in the immediate post-transplant period, systemic parameters improve faster in the viral group. Pulmonary hemodynamics differ significantly between alcoholic and postviral patients within the first 24 h, suggesting that alcoholics might have more pronounced pulmonary vasodilation than viral-cirrhotic patients.
Applications
Following liver transplantation, careful patient monitoring and frequent assessment of the cardiac and fluid volume status is essential to avoid any cardiac-related adverse effects.

Peer review
This is a retrospective study comparing the immediate hemodynamic status of patients with viral cirrhosis with that of those with alcoholic cirrhosis after liver transplantation. The authors found that the viral group has better recovery in hyperdynamic circulation after transplant than the alcoholic group, which has more pronounced pulmonary vasodilatation. This finding is interesting, but the clinical importance of this finding has to be further elaborated by the authors.

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