ABSTRACT

Background. The aim of this study was to investigate the changes in oxygen consumption during liver transplantation and to examine the relationship between intraoperatively elevated systemic oxygen consumption and postoperative liver function.

Methods. This study was performed in 33 adult patients undergoing liver transplantation between September 2011 and March 2014. We measured intraoperative oxygen consumption through the use of indirect calorimetry, preoperative and intraoperative data, liver function tests, and postoperative complications and outcomes.

Results. The mean age of patients was 52 ± 9.7 years; 14 (42%) of them were women. Average Model for End-Stage Liver Disease scores were 20 ± 8.9. Oxygen consumption significantly increased after reperfusion from 172 ± 30 mL/min during the anhepatic phase to 209 ± 30 mL/min (P < .0001). We divided patients into 2 groups according to the increase in oxygen consumption after reperfusion (oxygen consumption after reperfusion minus anhepatic phase oxygen consumption: 40 mL/min increase as cutoff). The higher consumption group had a longer cold ischemia time and higher postoperative aspartate aminotransferase and alanine aminotransferase levels as compared with the lower oxygen consumption group. There were no statistically significant differences in major postoperative complications, but the higher oxygen consumption group tended to have shorter hospital stays than the lower consumption group (58 versus 95 days).

Conclusions. We have demonstrated that oxygen consumption significantly increased after reperfusion. Furthermore, this increased oxygen consumption was associated with a longer cold ischemia time and shorter hospital stays.
different anatomical sites. Oxygen consumption can also be measured by use of indirect calorimetry [14–19]. This requires only exhaled gas sampling and can be measured continuously. This is useful for nutritional management in critically ill patients [17].

In the present study, with the use of indirect calorimetry, we aimed to measure the changes in oxygen consumption during liver transplantation. Thereafter, we also examined the relationship between the increased intraoperative oxygen consumption after reperfusion and the results of postoperative liver enzyme tests.

METHODS

This study was performed in 33 adult patients undergoing liver transplantation for hepatic insufficiency between September 2011 and March 2014 at our hospital. Patients who underwent multiple organ transplantsations and re-transplantations were included, but children younger than 18 years of age were excluded. The study was approved by the institutional review board of our hospital, and informed consent was obtained from patients or their guardians. The study was performed in accordance with the ethical standards of the Declaration of Helsinki.

All patients received anesthesia with the use of inhalational anesthetics. Before induction, the patients were monitored for arterial blood pressure, electrocardiogram, and oxygen saturation (SpO2). Anesthesia was induced with intravenous propofol (1 to 2 mg/kg) and fentanyl (2 to 4 μg/kg) and rocuronium (0.6 mg/kg) to facilitate tracheal intubation. Anesthesia was maintained with inhalational anesthesia, infusion of 0.1 to 0.2 μg/kg/min remifentanil, and intermittent injection of fentanyl. Muscle relaxation was achieved with rocuronium. After tracheal intubation, the patients’ lungs were mechanically ventilated by means of the pressure-controlled mode with 40% to 60% oxygen and with a positive end-expiratory pressure to maintain the partial pressure of arterial oxygen (PaO2) above 80 mm Hg. After the induction, partial pressure of arterial carbon dioxide (PaCO2) within the normal range. After the induction, PA and central venous catheters were placed. We aimed to achieve a mean arterial pressure of >60 mm Hg by monitoring cardiac index, SVo2, and central venous pressure without any specific targets. Lactated Ringer’s solution, albumin, and fresh-frozen plasma administration was guided by cardiovascular performance and requirements for clotting factors, respectively. Blood losses were replaced with packed red cells to maintain hemoglobin above 7 g/dL, according to our anesthesia protocol.

With the use of a Deltatrac metabolic monitor (Datex-Ohmeda), we measured systemic oxygen consumption (VO2) intraoperatively at the following times: at induction of anesthesia, in the pre-anheptic phase, anheptic phase, 1 hour after reperfusion, and at the end of skin closure. The Deltatrac metabolic monitor is an open-system, indirect calorimetry device equipped with a fast paramagnetic oxygen sensor to measure a differential signal between inspired and expired gases and a gas dilution system to measure flow [19].

Measurements were commenced when the patient was in a stable state shortly after intubation over a period of 5 minutes. After that, the measurements were continuous (every minute). The mean of these single measurements was calculated and compared with the assumed VO2 values [18,19]. On the basis of the increased rate of VO2 after reperfusion, calculated as the difference between oxygen consumption after reperfusion and anhepic phase oxygen consumption, in relation to assumed oxygen consumption values, we classified the patients into 2 groups: the higher increase rate group (H group) and the lower increase rate group (L group) (according to the calculation of oxygen consumption after reperfusion minus anheptic phase oxygen consumption: 40 mL/min increase as cutoff).

We noted preoperative data (age, sex, height, weight, body mass index [BMI], the underlying disease, Model for End-Stage Liver Disease [MELD] scores, Child-Pugh scores, and the use of preoperative hemodialysis and plasma exchange) from the patients’ charts as the clinical variables. Intraoperative factors (use of venovenous bypass, surgical time, cold and warm ischemia time, anheptic time, transfusions, and graft weight/recipient weight ratio [GW/WRB (%)]) were also noted. We also obtained data on conventional liver function parameters (serum aspartate aminotransferase [AST] and alanine aminotransferase [ALT]), preoperatively and on postoperative days (POD) 1, 2, 3, and 7. The occurrence of major postoperative complications was recorded, including use of postoperative hemodialysis, reoperation for bleeding, acute rejection, duration of ventilation above 1 week, vasopressor requirement, infections, intensive care unit (ICU) stay, hospital stay, and survival at 6 months.

The changes in VO2 were assessed by use of the paired t test, and the two groups were compared by use of the unpaired t test. We also investigated associated factors for increased oxygen consumption after reperfusion and compared the two groups regarding postoperative liver enzyme levels. All data are expressed as mean values ± standard deviation. We considered a value of P < .05 to indicate a significant difference.

RESULTS

From September 2011 to March 2014, 33 patients, 19 men and 14 women (mean age, 52 ± 9.7 years; mean BMI, 22 ± 4.5), underwent living donor liver transplantation (LDLT) at our hospital. Underlying diseases of the recipients included liver cirrhosis by viral hepatitis in 25 patients, alcoholic hepatitis in 2 patients, primary biliary cirrhosis in 2 cases, and other diseases in 4 cases. The average MELD score of these patients was 20 ± 8.9, and average Child-Pugh score was 11 ± 2.1. Preoperative donor evaluation revealed normal liver biochemistry and bilirubin levels. The surgical time of the recipients was 587 ± 135 minutes; and cold and warm ischemia times of the graft were 201 (127 to 275) minutes and 49 ± 23 minutes, respectively. Average anheptic time was 161 ± 63 minutes. The GW/WRB ratio was 1.61 ± 0.82, and average blood loss during the recipient operation was 7190 ± 5280 mL.

Intraoperative oxygen consumption changed significantly during LDLT (P < .0001). VO2 was 205 ± 33 mL/min at the induction of anesthesia, 197 ± 33 mL/min in the pre-anheptic phase, and 172 ± 30 mL/min in the anheptic phase. Thus, during LDLT, VO2 appears to decrease until the anheptic phase. VO2 increased significantly to 209 ± 30 mL/min after reperfusion (P < .05) compared with the anheptic phase (Fig 1). Furthermore, this increase in oxygen consumption was unrelated to changes in mean arterial pressure, cardiac index, and SVo2.

Classification of the patients according to the difference in oxygen consumption between reperfusion and the
Intraoperative oxygen consumption increased after reperfusion compared with the anhepatic phase. VO2-1, induction of anesthesia; VO2-2, pre-anhepatic phase; VO2-3, anhepatic phase; VO2-4, 1 hour after reperfusion; VO2-5, end of wound closure.

We also compared the values of conventional liver function parameters preoperatively and on POD 0, 1, 2, 3, and 7 between the two groups (Fig 2). The H group tended to have higher AST and ALT values on POD 1, 2, and 3 compared with the L group. In the H group, AST and ALT values peaked on POD 1 and then decreased to preoperative values. On the other hand, the L group had stable AST and ALT levels during the observation period (Fig 2).

We also investigated major postoperative variables, including the incidence of kidney dysfunction requiring postoperative hemodialysis, reoperation due to bleeding, acute rejection, need for mechanical ventilation for over 1 week, ICU stay, hospital stay, and survival at 6 months. There were no statistically significant differences in these variables between the two groups (Table 1). However, the H group tended to have a shorter hospital stay than did the L group (58 versus 95 days).

### DISCUSSION

In the present study, we prospectively measured systemic oxygen consumption during liver transplantation with the use of indirect calorimetry. We also examined the relationship between intraoperative VO2 after reperfusion and postoperative liver enzyme levels. We found that oxygen consumption significantly increased after reperfusion and that this increase in oxygen consumption was associated with a longer cold ischemia time and higher liver enzyme levels postoperatively and with a shorter hospital stay.

VO2 significantly increased after reperfusion during liver transplantation. Some previous reports that used the Fick method suggested similar trends. Takaya et al. [12] reported that oxygen consumption significantly increased in 88 patients who underwent primary liver transplantation. Steltzer et al. [11] also suggested increased VO2 after reperfusion in 99 patients undergoing orthotopic liver transplantation.

In this study, however, we used a new noninvasive indirect calorimetry method and continuously measured total body VO2 by monitoring expired gas [15–19]. This method has been validated in several different situations [13–16]. Gonzalez-Arevalo et al. [16] measured VO2 in 21 critically ill, mechanically ventilated patients. Stuart-Andrews et al. [15] reported continuous monitoring of VO2 in 30 patients undergoing cardiopulmonary bypass surgery. Compared with the Fick method, indirect calorimetry is easier, safer, and can provide continuous measurements [19].

In the present study, this increased VO2 was associated with a longer cold ischemia time. It has been previously reported that VO2 significantly decreases when the ischemia time is shortened by use of veno-venous bypass [13].
also suggested that VO\textsubscript{2} significantly decreased after hepatic artery clamping and that reperfusion causes a dramatic initial increase in VO\textsubscript{2}, depending on the ischemia time. In the present study, we also confirmed this relationship between ischemia time and VO\textsubscript{2} after reperfusion. We believe that the increase in VO\textsubscript{2} may be based on recovery of metabolic activity in the transplanted liver [10].

We studied the association between the increased VO\textsubscript{2} and postoperative liver enzymes and clinical outcomes. This increased VO\textsubscript{2} was associated with higher liver enzyme levels after surgery and with a shorter hospital stay. This study shows that increased VO\textsubscript{2} can affect postoperative liver function. Some reports suggested that systemic VO\textsubscript{2} after reperfusion in patients with successful liver transplantation was higher than that in patients with graft dysfunction [11,12]. With the use of the Fick method, Steltzer [11] reported the relationship between VO\textsubscript{2} and graft function in 99 patients who underwent liver transplantation. They showed that patients with primary non-function had much smaller increases in VO\textsubscript{2} than did patients with normal liver function after reperfusion. These results suggest that VO\textsubscript{2} after reperfusion could be a useful marker of the function of the grafted liver. The multi-factors could be associated with longer hospital stay. The relationship between ischemic time and hospital stay would be controversial.

Our study has certain limitations. We analyzed only 33 patients who underwent liver transplantation, which is a relatively small number. In this study, there were no significant differences in the clinical outcomes between the two groups. A larger sample size will be needed to determine the significance of post-perfusion VO\textsubscript{2} in relation to clinical outcome.

We measured systemic VO\textsubscript{2} with the use of indirect calorimetry. This measurement might not directly reflect local liver VO\textsubscript{2} [20]. Actually, a higher VO\textsubscript{2} after reperfusion in recipients of cadaveric whole liver grafts was associated with a poorer prognosis [20]. Further study is needed to clarify the exact significance of the increased systemic VO\textsubscript{2} after reperfusion.

CONCLUSIONS
In the present study, we prospectively measured VO\textsubscript{2} during liver transplantation by use of indirect calorimetry. We found that systemic VO\textsubscript{2} significantly increased after reperfusion. Furthermore, we also found that this increased VO\textsubscript{2} was associated with a longer cold ischemia time, higher liver enzyme levels after surgery, and shorter hospital stays.

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REFERENCES


