Anesthesia Management of Modified Ex Vivo Liver Resection and Autotransplantation

B Fujun Cheng*
BE Zhiyong Yang*
C Jing Zeng
F Jianteng Gu
DF Jian Cui
CF Jiaonin Ning
AE Bin Yi

* These authors contributed equally to this work and should be considered co-first authors

Corresponding Author: Bin Yi, e-mail: yibin1974@163.com
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Background: Ex situ liver surgery allows liver resection and vascular reconstruction in patients who have liver tumors located in critical sites. Only a small series of studies about ex situ liver surgery is available in the literature. No anesthesia management experience has been previously published. The aim of the current study was to summarize our experience with anesthetic management of patients during ex vivo liver surgery.

Material/Methods: The first 43 patients who received ex vivo liver surgery between January 2007 and April 2012 were included. A pulmonary artery catheter (PAC), transesophageal echocardiography (TEE), and pulse indicator continuous cardiac output (PiCCO) were used intraoperatively in the patients to monitor the hemodynamic changes. Thromboelastogram and the plasma coagulation test were used to monitor the coagulation changes.

Results: All patients received general anesthesia with rapid sequence induction. The data obtained by PAC, TEE, and PiCCO in these cases showed large changes in hemodynamics during the stages of the first or second vessel reconstruction. The CI decreased about 59%/63% and the MPAP decreased about 49%/37% during the first/second vessel reconstruction. Accurate judgment of the dosage of active drug for vascular support is the key for the stabilization of hemodynamics as quickly as possible. However, a high incidence (35.5%) of prophase fibrinolysis in a long anhepatic phase should be monitored and managed.

Conclusions: Ex vivo liver surgery is no longer experimental and is a therapeutic option for patients with liver cancer in critical sites. Good anesthesia support is an essential element of liver autotransplantation.

MeSH Keywords: Autografts • Liver Transplantation • Patient Care Management

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Background
Surgical resection of tumors in most cancer cases is the only effective modality of treatment that is capable of offering a chance of a cure [1]. However, for many patients with liver cancer in a critical site, such as adjacent to a large vessel region or a difficult-to-expose area, normal surgical options are not possible. In the past, receiving a liver allotransplantation was the only choice for these patients. However, the number of liver donors is not sufficient to meet the demand of the increasing number of patients. Ex situ ex vivo liver resection and autotransplantation was developed by Pichlmayr et al. and Oldhafer et al. to expand the surgical treatment to otherwise non-resectable liver tumors [2,3]. This approach allows better access to difficult tumor locations and complex extended resections, and some institutions have performed such procedures.

The modified ex vivo surgery does not use veno-venous bypass, which is its main difference from classical ex vivo liver surgery. Ex situ liver surgery without veno-venous bypass simplified the surgical procedure and decreased the postoperative complications, but increased the difficulty and complexity of the anesthesia management. Many pathophysiologival changes in the modified ex vivo surgery were different from the classical ex vivo surgery and traditional liver transplantation. The surgical success depends on the anesthesia management throughout the entire operation. Thus, this procedure is challenging for both surgeons and anesthetists due to the intensity of the hemodynamic changes, massive blood volume loss, and administration of large amounts of blood products and vasoactive agents within a short time. Several institutions have performed such operations [4–8]. A large series, however, has not yet been published. The existing reports have focused on the technical feasibility or short/long-term results of the ex situ surgery. Reports on the anesthesia management experiences of ex situ surgery are lacking.

This paper shows our current management procedures during the ex situ surgery and presents the first experience with anesthesia management.

Material and Methods
Patient
The records of 43 liver cancer (hepatocellular carcinoma and cholangiocarcinoma) patients who underwent ex vivo liver surgery with the same surgical and anesthesiological staff at our hospital between January 2007 and April 2012 were retrospectively studied. The study protocol was approved by the Committee on Human Research of Southwest Hospital of the Third Military Medical University (Army Medical University) of China PR. All patients received a comprehensive evaluation, including a general examination and the analysis of all test results to exclude cirrhosis, cholestatic, and liver malfunction. The degree of the inferior vena cava and/or main hepatic vein involvement was assessed by preoperative radiographic inspection and verified when the liver was explored in the operation. The tumor diameter was 6–13 cm, the extent of involved IVC was 79–100° circumferentially and 4–7 cm longitudinally, which were unresectable by conventional techniques. Patients weighing 45–68 kg and aged 44–69 years accepted the ex vivo liver surgery. They were not allowed access to water or food for 6 h before the surgery.

Anesthesia
All patients who underwent the ex vivo liver surgery received general anesthesia with rapid endotracheal intubation. After intramuscular injection (IM) premedication with midazolam (0.1 mg/kg) and atropine sulfate (0.5 mg), an intravenous catheter was inserted in a forearm vein to administer Ringer’s solution followed by propofol (2 mg/kg), fentanyl (2–3 µg/kg), and vecuronium (0.08–0.1 mg/kg) for induction and intubation. After tracheal intubation, the lungs were ventilated (Servo 99c ventilator, Siemens, Munich, Germany) with an oxygen-air mixture (FIO₂=0.4) to maintain end-expiratory carbon dioxide at 30–40 mmHg. Anesthesia was maintained with a continuous infusion of propofol (50–150 µg/kg/min) and remifentanil (0.1–0.5 µg/kg/min) and with bolus injections of vecuronium (0.08–0.1 mg/kg/30 min). The left radial artery was cannulated for blood sampling and blood pressure monitoring. Two central venous catheters were inserted in the right internal jugular vein: one (7F double-lumen catheter, Arrow International, Pennsylvania, USA) for intravenous fluid infusion, drug administration, and monitoring the central venous pressure (CVP), and the other (8.5F; Arrow International) for pulmonary artery catheterization. A femoral vein catheter was inserted for monitoring the CVP of the inferior vena cava. A warming pad was used to maintain body temperature at approximately 37°C. Metabolic acidosis was corrected by the administration of sodium bicarbonate. Bolus doses of calcium chloride were given to maintain an optimal plasma concentration of ionized calcium. Dopamine was infused intravenously at 5–10 µg/kg/min to maintain a mean blood pressure of 60–80 mmHg when necessary. All patients received colloids, blood, and fresh frozen plasma during the surgery.

Surgical procedures (Figure 1)
Our procedure for ex vivo liver surgery was modified from the classic ex vivo liver surgery. The bilateral subcostal incisions which provided adequate exposure were used for all cases. After separating adhesions,
mobilization of liver, the tumor location and extent of tumor involvement was carefully reassessed through both intraoperative palpation and ultrasonography. All patients underwent the total vascular exclusion (TVE) in view of the tumor location and extent of tumor involvement: the suprahepatic and infrahepatic vena cava were exposed and controlled as well as the portal vein and hepatic artery. After the portal vein, hepatic artery, and common bile duct were clamped and divided, approximately 8 cm inferior, the vena cava, including the conjunctive port with the liver vessels, was dissociated and clamped (defined as the first vascular reconstruction). Thus, the organ can be completely removed from the body with the inferior vena cava segment.

Figure 1. The images show the typical surgery procedures of a modified ex situ ex vivo liver resection and autotransplantation.
(A) The large convex lump in the top portion of the liver was liver cancer; (B) The first porta hepatis structures after the liver were removed from the body; (C) The inferior vena cava was rebuilt with a vascular prosthesis; (D) The portal vein was anastomosed with the vascular prosthesis; (E) Ex situ ex vivo liver cancer resection in the HTK preservative fluid; (F) The liver cancer was resected from the liver, and the vessel stumps were ligatured; (G) The porta hepatis structures after the liver were autotransplanted. a: inferior vena cava or vascular prosthesis; b: hepatic artery; c: portal vein.
Immediately after the successful procurement of the whole liver, in 1 surgical group we reconstructed the inferior vena cava (IVC) with an 8-cm vascular prosthesis (2 cm in diameter). After that, the IVC was unclamped, and then the stump of the portal vein was anastomosed with the side of the vascular prosthesis for portosystemic shunt (defined as the first reperfusion).

Another surgical group was scheduled to have bench resection simultaneously. The liver was adequately perfused with preservation solution [histidine-tryptophan-ketoglutarate (HTK)-Bretschneider] at 4°C through the cannulation of the portal and arterial systems and immediately packed with ice, then the tumor was meticulously dissected under intraoperative ultrasonographic guide.

After carefully examining for any leaks, the suprahepatic and infrahepatic vena cava were clamped and the prosthetic graft was removed, then the autograft was reimplanted orthotopically. The suprahepatic vena cava, hepatic IVC, PV, HA, and biliary tract were successively reconstructed. When the suprahepatic and infrahepatic vena cava were reclamped, the temporal shunt was interrupted (defined as the second vessel reconstruction). After finishing the portal anastomosis, reperfusion was then commenced (defined as the second reperfusion).
Finally, the wound was closed after meticulous hemostasis.

A rapid infusion pump (Terumo Terufusion syringe pump TE-312, Japan) was used to administer fluids, all of which, including the blood and plasma, had been prewarmed in an incubator at 37°C. The volume and speed of fluid administration were guided by the hemodynamic parameters.

Monitoring

The central venous pressure (CVP), mean pulmonary arterial pressure (MPAP), and pulmonary capillary wedge pressure (PCWP) were monitored via a PAC using a Marquette Eagle 4000 monitor (GE, New York, USA). In all cases, a TEE was used, including an ultrasound probe with combined M-mode and Doppler transducers. It was placed in the esophagus and positioned at proximity to the aortic walls to evaluate cardiac output (CO), stroke volume (SV), ejection fraction (EF), and left ventricular end-diastolic volume (LEDV). Sample images obtained from the patients are shown in Figure 2. In the first 3 cases, we wanted more information on the systemic vascular resistance index (SVRI), extravascular lung water (EVLW), and intrathoracic blood volume (ITBV) to guide the fluid transfusion. Thus, the PICCO was also used in the remaining cases: A 5-Fr PiCCO thermodilution arterial catheter (FT-Pulsion-cath, Pulsion Medizintechnik, Munich, Germany) was inserted into the femoral artery.

Other physiological parameters, including urine volume, acid-base balance (blood gases i-STAT portable clinical analyzer, Heska, USA), electrolytes, clotting profile, and nasopharyngeal temperature (Marquette Eagle 4000, GE), were also monitored throughout the surgery.

The parameters were recorded at the following times: after intubation and cannulation (T0), 5 min before the first vessel reconstruction (T1), immediately after starting the first vessel reconstruction (T2), 5 min after starting the first vessel reconstruction (T3), 5 min after the first reperfusion (T4), 5 min before the second vessel reconstruction (T5), immediately after starting the second vessel reconstruction (T6), 5 min after starting the second vessel reconstruction (T7), 5 min after the second reperfusion (T8), and at the end of surgery (T9).

Data analysis

The parameter/laboratory value was obtained in all patients; unfortunately, 9 patients died of liver dysfunction and sepsis after surgery. All data are expressed as the mean values ± SD, except those measured by PICCO (only in 1 case are data presented) for analysis by one-way ANOVA followed by the Student-Newman-Keuls test, when appropriate. P<0.05 was considered statistically significant.

Results

General data of patients and anesthetic management data

Table 1. General data of patients and anesthetic management data (N=43).

| Parameters                     | Values       |
|--------------------------------|--------------|
| Body weight (kg)               | 57±6         |
| Operative time (h)             | 8.2±2.3      |
| First vessel reconstructive time (min) | 22.9±5.6 |
| Second vessel reconstructive time (min) | 24.9±3.4 |
| Anhepatic phase (min)          | 250±45       |
| Concentrated red cell infusion volume (ml) | 863±234 |
| Fresh frozen plasma            | 1276±320     |
| Human albumin (g)              | 35±9         |
| Colloidal volume (ml)          | 1200±344     |
| Crystalloid volume (ml)        | 1500±46      |
| Urine volume (ml)              | 1300±400     |
| Blood loss (ml)                | 1587±434     |
| Hospital stay (day)            | 26.1±10.3    |

Vessel reconstructive time: the time between the inferior vena cava crossclamp for initiation of reconstruction with a vascular prosthesis, and the end of the termino-lateral porto-caval (to caval graft) anastomosis.

Finally, the wound was closed after meticulous hemostasis. A rapid infusion pump (Terumo Terufusion syringe pump TE-312, Japan) was used to administer fluids, all of which, including the blood and plasma, had been prewarmed in an incubator at 37°C. The volume and speed of fluid administration were guided by the hemodynamic parameters.

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Table 2. Postoperative complications data(N=43).

| Complications     | Number (ratio) |
|-------------------|----------------|
| Bleeding          | 5 (11.6%)      |
| Liver failure     | 8 (18.6%)      |
| Biliary leakage   | 10 (23.2%)     |
| Renal failure     | 4 (9.3%)       |
| Pneumonia         | 3 (6.9%)       |

Table 3. Data for 9 cases of death in-hospital.

| Cause of death | Number (ratio) |
|----------------|----------------|
| Liver failure  | 5 (55.5%)      |
| Renal failure  | 1 (11.1%)      |
| Sepsis         | 3 (33.3%)      |

Table 1 summarizes the general data of the patients and anesthetic management, including the average consumption of concentrated red blood cells, platelets, and fresh frozen plasma.
Ex vivo surgery is of necessity a long surgical procedure. The operative time was 8.2±2.3 h. However, it was shorter compared with that reported by Oldhafer et al. [2]. Postoperative complications are summarized in Table 2. Data for 9 cases of in-hospital death are summarized in Table 3.

Changes in hemodynamic parameters and the dosages of vasoactive agents

Almost all hemodynamic parameters were stable from inductive anesthesia to the start of the first vascular reconstruction. Two minutes before the clamping the inferior vena cava, 5–8 µg/kg/min dopamine and 0.2–0.7 µg/kg/min norepinephrine were used to prevent excessive hemodynamic changes. Dosage of 5 µg/kg/min dopamine and 0.2 µg/kg/min norepinephrine were suitable for most cases. When the inferior vena cava and portal vein were clamped for liver removal (T2 time point), the hemodynamic parameters changed significantly. The HR increased from 72.5±8.2 to 122.2±10.1 bpm (p<0.05) (Figure 2A). The MAP decreased from 86.8±9.3 to 45.3±5.3 mmHg (p<0.05) (Figure 2B). The CVP of the inferior vena cava increased from 8.2±0.6 to 32.9±3.2 mmHg. The CVP of the superior vena cava decreased from 7.2±0.6 to 1.9±0.2 mmHg (Figure 2C). The CI decreased from 4.2±0.5 to 1.7±0.2 L/min·m² (p<0.05) (Figure 2D). The MPAP decreased from 18.1±1.9 to 9.2±0.8 mmHg (p<0.05) (Figure 2G). The dosages of dopamine and norepinephrine were regulated to 5–8 µg/kg/min and 0.2–0.7 µg/kg/min, respectively, to ensure that MAP was not less than 60 mmHg. An injection of 10 mg esmolol hydrochloride was used if the HR was over 130 bpm (Figure 2J).

All of these parameters returned to their baseline values after 110.9±20.3 ml of 5% sodium bicarbonate solution was given when the second vessel reconstruction was finished and during the reperfusion of the inferior vena cava and portal vein. In addition, 48.3±5.3 ml of 10% glucuronic acid calcium infusion was given routinely to all patients to maintain normal calcium levels when they were switched to FFP or concentrated red blood cells.

Coagulation changes monitored by thromboelastogram

The TEG variables were: reaction time (R), the time to clot initiation; kinetics time (K), the time to reach a certain threshold of clot strength; alpha (α) angle, slope between R and K; maximum amplitude (Ma), the maximum strength of the clot; and CL30 (LY30), the degree of thrombolysis at 30 min.

The analysis (Figure 3A–3G) showed that the coagulation index increased from +3.45±0.25 at T0 to +5.46±0.47 at T1 and decreased to +1.22±0.20 at T3 (p<0.05), −2.34±0.21 at T5 (p<0.05), and −5.14±0.46 at T7 (p<0.05). The R time and K time were maintained until T3 and then increased significantly at T3, T5, T7, and T9 (p<0.05). The α corner and Ma remained stable until T7 and T9, when it decreased significantly compared with T0. The CL30 did not change significantly throughout the operation. There were no fibrinolysis cases until T3, and there were 3 cases at T5 and 4 cases each at T7 and T9.

Coagulation changes monitored by the plasma coagulation test

The analysis (Figure 4A–4D) showed that the fibrinogen level decreased slowly from 3.24±0.28 g/L at the beginning of the operation to 2.96±0.19 g/L at T1, 2.12±0.21 g/L at T3 (p<0.05), 1.82±0.15 g/L at T5 (p<0.05), 1.63±0.14 g/L at T7 (p<0.05), and 1.42±0.15 g/L at the end of the operation (p<0.05). The APTT, PT, and TT did not change significantly throughout the operation.

Changes in electrolytes and blood gas analysis

The analysis (Figure 5A–5D) showed that almost all electrolyte levels remained stable during the entire operation (p>0.05). In addition, PCO₂ and PO₂ did not change significantly (p>0.05). However, the pH value decreased from the beginning of the operation to 7.26±0.03 at T8. After the use of the sodium bicarbonate solution, the pH value returned to the normal range. The lactic acid level increased gradually during the operation and reached a minimum 7.26±0.03 at T8. After the use of the sodium bicarbonate solution, the pH value returned to the normal range. The lactic acid level increased gradually (p<0.05), which might be the main source of the unstable pH value.

The analysis (Figure 5E–5H) showed that 110.9±20.3 ml of 5% sodium bicarbonate solution was given when the second vessel reconstruction was finished and during the reperfusion of the inferior vena cava and portal vein. In addition, 48.3±5.3 ml of 10% glucuronic acid calcium infusion was given routinely to all patients to maintain normal calcium levels when they received FFP or concentrated red blood cells.
Discussion

Many clinical centers have shared their experiences with the anesthesia management of orthotopic liver transplantation patients [9–13]. Although 1324 cases of successful orthotopic liver transplantation in our hospital provided much experience as a basis, the anesthesia management of modified ex vivo liver surgery was still challenging because little was known about the involved pathophysiological changes during the entire operation. Previous studies reported that the ex vivo liver surgery used veno-venous bypass, which had more complications, such as increased bleeding and hemolysis [2]. In addition, no
anesthesia management experience had been previously published for either classic or modified ex vivo liver surgery. Our experiences with modified ex vivo surgery without veno-venous bypass were sufficient to ensure patient safety and were helpful for improving the clinical practice.

The maintenance of hemodynamic stability during surgery is crucial for surgical success [14]. Liver surgery is associated with large fluid shifts due to massive blood loss, dehydration, vascular clamping, long ischemic time, and intraoperative visceral exposure. The hemodynamic changes during the dissection phase were mainly due to blood loss during liver removal. The intense hemodynamic changes occurred during the first and second vessel reconstruction because of the occlusion of the inferior vena cava and portal vein. These intense hemodynamic changes impaired the functions of the heart, lung, kidney, and brain. Regulating the hemodynamics by using vasoactive agents as soon as possible was very important for patient safety.

However, there were many factors that influenced the degree of hemodynamic change at this time. The main influencing factors were body height, body weight, and collateral circulation of the inferior vena cava. In addition, each patient has an obviously different sensitivity to the vasoactive agents. All of these factors make it difficult for the anesthetist to decide on the appropriate dosage of vasoactive agents. In our experience, the first step is a sufficient infusion of blood products, such as erythrocytes, FFP, cryoprecipitation, or albumin prepared from human plasma selected according to the patient’s coagulation state prior to vessel reconstruction. Then, 2 min before the inferior vena cava was clamped, appropriate doses of dopamine and norepinephrine were used to decrease the excessive change in the hemodynamics. Although some patients with rich collateral circulation have a stable hemodynamic situation, most patients lack sufficient collateral circulation due to the fast growth pattern of the tumor, so we also asked the surgeon who exploratorily clamped the inferior vena cava to observe the severe dilation of the infrahepatic vena cava or the condition of the intestines, which greatly helped the anesthetist to decide on the prophylactic dose of vasoactive agents. The prophylactic use of 5 µg/kg/min dopamine and 0.2 µg/kg/min norepinephrine 2 min before the complete clamping of the inferior vena cava was used to avoid severe hemodynamic fluctuations in most cases. During the first vascular reconstruction, the dosages of dopamine and norepinephrine were regulated to 5–8 µg/kg/min and 0.2–0.7 µg/kg/min, respectively, to ensure that the hemodynamic parameters met the needs of the patient. Two minutes before the first reperfusion, the dosage of dopamine decreased to 2–3 µg/kg/min and norepinephrine was stopped to avoid high hemodynamics evoking pulmonary injury or edema due to the absence of bleeding. Although the use of dopamine in the perioperative support of liver transplant recipients remains controversial, especially in

![Figure 4. Coagulation changes measured by the plasma coagulation test. (A) Thrombin time (TT); (B) Fibrinogen (Fib); (C) Activated coagulation time of whole blood (APTT); (D) Prothrombin time (PT). T0: after intubation and cannulation; T1: 5 min before the first vessel reconstruction; T3: 5 min after starting the first vessel reconstruction; T5: 5 min before the second vessel reconstruction; T7: 5 min after starting the second vessel reconstruction; and T9: at the end of the surgery. P<0.05 vs. baseline (T0).]
Figure 5. The changes in electrolytes and blood gas analysis. (A) Hydrogen-Ion concentration (PH); (B) Partial pressure of carbon dioxide (PCO₂); (C) Partial pressure of oxygen (PO₂); (D) Lactic acid concentration; (E) Natrium ion concentration (Na⁺); (F) Potassium ion concentration (K⁺); (G) Calcium ion concentration (Ca²⁺); (H) Chlorine ion concentration (Cl⁻). T0: after intubation and cannulation; T1: 5 min before the first vessel reconstruction; T2: immediately after starting the first vessel reconstruction; T3: 5 min after before the first vessel reconstruction; T4: 5 min after the first reperfusion; T5: 5 min before the second vessel reconstruction; T6: immediately after starting the second vessel reconstruction; T7: 5 min after starting the second vessel reconstruction; T8: 5 min after the second reperfusion; and T9: at the end of the surgery. P<0.05 vs. baseline (T0).

the role of renal protection, small doses of dopamine are still thought to be helpful in the protection of microcirculation during liver transplantation [15,16]. We also found that the dosage of norepinephrine could be decreased, avoiding hemodynamic fluctuation during the modified ex vivo liver surgery. However, the role of dopamine remains ambiguous and demands further study. In our study, the hemodynamics were relative stable because of the fluid replacement and the application of vasoactive agents guided by the PCA, TEE and PiCCO. The intraoperative transfusion requirement was 4880±243 ml, and
pulmonary complications (pneumonia) occurred in 3 patients (6.9%). Among the 9 patients who died after surgery, 1 died of respiratory failure related to fluid overload.

The anhepatic phase lasted 250±45 min and gradually induced severe lactic acidosis. Five minutes after starting the first vessel reconstruction, the lactic acid content increased significantly compared with the baseline (p<0.05). However, the hemodynamics were stable during the anhepatic phase, and the lactic acidosis did not need to be addressed. In orthotopic liver transplantation, lactic acidosis was constantly serious, requiring large doses of sodium bicarbonate [17,18]. In contrast, the acidosis situation in the modified ex vivo liver surgery did not require aggressive treatment due to the inferior vena cava being rebuilt and the portal vein being anastomosed with a vascular prosthesis.

Compared with the first vascular reconstruction, the condition of the patient in the second vascular reconstruction was more serious because of the increased lactic acidosis and the disturbance of other electrolytes. Additionally, the massive hemorrhage in the raw surface of the liver aggravated the hemodynamic inhibition during the second reperfusion. Occasionally, judging whether acidosis or hemorrhage was the main cause of the hemodynamic inhibition was difficult. Our experience was that a sufficient fluid content should be given slowly to achieve a CVP value of 7–9 mmHg during the anhepatic phase. The dosages of dopamine and norepinephrine in the second vascular reconstruction increased by 3–5 µg/kg/min compared with the dosages in the first vascular reconstruction. When the second vascular reconstruction was finished, we asked the surgeon to reopen the inferior vena cava first. The bleeding from the anastomoses of the inferior vena cava was carefully stopped. Then, the portal vein was reopened, and the hemorrhage was addressed from its anastomoses. Thus, the volume of hemorrhage could be obviously decreased. When the portal vein was reperfused, 110.9±20.3 ml of 5% sodium bicarbonate solution was given immediately. The change of hemodynamic was sometimes drastic because of the low volume and acidosis, so epinephrine was recommended to avoid cardiac arrest.

From 5–10 min after the second reperfusion, the hemodynamics recovered, and only small dosages of dopamine and norepinephrine were needed. Our data show that the most important aspect during this phase was the regulation of coagulation.

Patients who received large amounts of blood intraoperatively have been shown to have a higher risk of many complications, such as infection, lung injury, severe allergic reaction, and anaphylaxis. Thus, decreases in the administration of FFP, platelets, and cryoprecipitate have been the main methods used to regulate coagulation function. We used TEG and the normal coagulation test to direct the infusion of blood products during the entire operation. The benefits of thromboelastography (TEG)-based transfusion algorithms have been known for many years [19,20], and its use permits the assessment of both absent components of whole-blood coagulation and fibrinolysis, instead of singular parameters of procoagulation or anticoagulation. The TEG data showed that the patients, at the beginning of the operation, had shorter r and k times and higher alpha angle and MA values compared to the normal values of a healthy adult because patients with a liver tumor are in a hypercoagulable state [21]. Following the surgery, the coagulation state of the patients remained decreased because of bleeding, hypothermia, or other pathophysiological changes. Under the direction of TEG, we carefully regulated the infusion rate of cryoprecipitate, FFP, and platelets to ensure that the TEG parameters reached a suitable level, which was slightly lower (~10—20%) than the normal value, but satisfied the needs of surgery (i.e., no obvious blood oozing from the wound surface). Thus, this state could help decrease the incidence of complications that are feared by surgeons, such as hematoma thrombosis and other thromboembolic events. Compared with TEG, the normal coagulation function test is not sufficient to determine whether a decrease in coagulation factors is the result of hemodilution or coagulopathy (factor deficiency and fibrinolysis), but it was also used in vitro to assess the effect of treatments such as antifibrinolytic therapy. During the anhepatic phase, a rapid rise in tissue-type plasminogen activator occurs in the absence of a2-antiplasmin and plasminogen activator inhibitor, with the net result being an increase in plasmin activity and a hyperfibrinolytic state [22–24]. The TEG data showed 35.5% (11 cases) prophase fibrinolysis cases in the whole operation, with 22.6% (7 cases) at the anhepatic phase (T5 plus T7) and 12.9% (4 cases) at the end of the operation. In our experience, the appropriate use of tranexamic acid (2–3 g) or EACA (0.25–0.5 g) at the dissection phase was valuable in decreasing the incidence of fibrinolysis and did not obviously influence the coagulation state. Tranexamic acid is a synthetic derivative of the amino acid lysine, which exerts its antifibrinolytic effect through the reversible blockade of lysine-binding sites on plasminogen molecules. Bleeding and anastomotic vessel thrombosis are common complications in association with the ex situ procedure. In our study, bleeding occurred in 5 (11.6%) patients and no surgical intervention was required. No anastomotic vessel thrombosis was found.

Conclusions

The participation of a multidisciplinary team in ex vivo liver surgery is of utmost importance. In optimized anesthetic management of circulation, coagulation function is an essential part. Anesthetic management during ex vivo liver surgery is a rapidly growing field that has evolved dramatically over time. Our management may be appropriate for this surgery considering...
the low early postoperative mortality (20.9%) and the low incidence of early complications of bleeding, pulmonary complications, and embolization. However, long-term results are needed for further analysis.

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