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ORIGINAL RESEARCH

Impact of Multimodal Fast-Track Protocols on Recovery in End-Stage Hepatic Alveolar Echinococcosis Patients Undergoing ex vivo Liver Resection and Autotransplantation: a Preliminary Study

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Background: While ex vivo liver resection combined with autotransplantation has been reported from various perspectives, the use of fast-track protocols for this procedure in treating end-stage hepatic alveolar echinococcosis has not been documented.

Methods: We retrospectively analyzed the outcomes of 21 patients with end-stage hepatic alveolar echinococcosis who underwent ex vivo liver resection and autotransplantation, followed by a fast-track recovery protocol at our institution between 2014 and 2017.

Results: All patients successfully underwent liver autotransplantation with no intraoperative mortality. Postoperative hospital stays ranged from 4 to 51 days, with an average of 23.5 days. Hospital costs averaged $3 million (range $1.94–4.07 million). Twelve patients experienced postoperative complications, with four classified as Clavien-Dindo grade III or higher. Two patients died due to intra-abdominal bleeding and acute cerebral hemorrhage, respectively. Nineteen patients were followed for a median of 16.2 months (range 3–38 months), with no recurrence of hepatic alveolar echinococcosis.

Conclusion: Fast-track protocols are safe and effective in the context of ex vivo liver resection and autotransplantation.

Keywords: fast-track surgery, autotransplantation, *ex vivo* resection

Introduction

Fast-track surgery, theoretically defined as an approach that accelerates the recovery process from preoperative preparation through surgery to early hospital discharge, has gained widespread acceptance across various surgical disciplines, including liver transplantation (LT).[1,2] It has been demonstrated that fast-track protocols can be safely applied to select patients undergoing LT.[3–7] However, the application of multimodal fast-track protocols in the context of ex vivo liver resection and autotransplantation (ERAT) for end-stage hepatic alveolar echinococcosis (AE) remains uncertain. Our previous studies have shown that the parenchymal transection technique used in ERAT closely resembles that of liver graft harvesting from living donors, suggesting that similar recovery protocols might be beneficial.[8] This study aims to explore whether multimodal fast-track protocols can enhance recovery in patients with end-stage hepatic AE undergoing ERAT.

Hepatic alveolar echinococcosis is a rare, life-threatening parasitic disease characterized by a slow-growing neoplasm with infiltrative growth, closely mimicking the behavior of liver malignancies, hence its designation as "worm cancer".[9] China bears more than 90% of the global burden of AE, with over 16,000 new cases diagnosed annually, prompting significant governmental efforts to control, prevent, and treat this zoonosis.[10,11] The technique of ex situ liver resection, first described by Pichlmayr in 1988, laid the foundation for subsequent developments in ERAT.[12] Wen et al, and others

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Table 1 FAST Track Surgery Protocol Elements in Peri-Operative Management

Preoperative	Detailed bilingual preoperative consultation and education with Tibetan and Chinese
	Preoperative fasting (solid food up to 6 h + clear fluids up to 2 h)
	No intestinal preparation or prophylactic use of antibiotics
	No routine nasogastric tube;
Intraoperative	Shorten the time of anesthesia
	Prevention of hypothermia: Body temperature was maintained with warming blankets and intravenous fluid warmers with a target temperature of 36°C to 37°C.
	CVP monitoring (central venous pressure <5 mmHg)
	Limit quantity of infusions
Postoperative	ICU treatment: early tracheal extubation after patients are fully awake; return to general ward early
	Early mobilization
	Antithrombotic prophylaxis: (a) A low-molecular-weight heparin sodium injection (0.4 mL q12 hours) was used after surgery with no signs of postoperative bleeding. (b)
	According to the weight and the INR of the patient adjusting Warfarin dosage for at least half a year. (c) No more than 2 hours of exercise near the bed on the 1st postoperative day, then
	gradually increasing.
	Oral enteral nutrition agent 6 hours after returning to the general ward;
	Clear liquid diet until the 5th postoperative day;
	Postoperative nausea and vomiting (PONV) prophylaxis
	Remove urine catheter on the morning of postoperative day 1 after returning to the general ward

have since focused primarily on refining the surgical techniques involved in this procedure.[13,14] However, there is a paucity of data regarding perioperative management, postoperative complications, and long-term outcomes when ERAT is combined with multimodal fast-track protocols, especially for advanced, complex cases of AE.

In this report, we retrospectively analyzed 21 cases of ERAT combined with multimodal fast-track protocols performed at our center. Our objective was to assess the feasibility, indications, perioperative preparation, and post-operative outcomes of this approach. The details of the perioperative program are summarized in Table 1.

Materials and Methods

Patient Recruitment and Data Collection

From January 2014 to June 2017, we prospectively collected data on consecutive patients undergoing ex vivo liver resection and autotransplantation, who were admitted to the fast-track unit of the Department of Liver Surgery & Liver Transplantation Center at West China Hospital of Sichuan University. The study involved a multidisciplinary team (MDT) consisting of six hepatobiliary surgeons, a vascular surgeon, a nutritionist, three nurses, and an anesthesiologist. Data was extracted using a standardized form and method. All patients followed a fast-track protocol and were managed by the MDT. Before surgery, comprehensive communication was conducted with patients and their families in their native language to explain the advantages of the fast-track protocol and potential surgical complications. Baseline data, imaging characteristics, and surgical outcomes for each patient were documented (see Table 2). This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of West China Hospital (approval number: No. 2017–38). The requirement for individual informed consent was waived by the ethics committee due to the retrospective nature of the study and the analysis used anonymous clinical data.

Fast-Track Procedures and Perioperative Management

Pretransplant Evaluation

The decision to implement a fast-track protocol was jointly made by the transplant surgeon and anesthesiologist. Preoperative imaging, including computed tomography (CT) and magnetic resonance imaging (MRI), was routinely performed to assess lesion location, extent, hepatocaval and portal hilum involvement, and the presence of extrahepatic metastases.[15] Three-dimensional (3D) imaging[16] was utilized to determine remnant liver volume (RLV) and visualize the

Table 2 Autotransplantation Characteristics of the 21 Patients

Patient	Sex	Age (y)	Nation	Pre-ERAT PTCD (n)	Lesion Size (cm)	PNM stage	Duration of Surgery (h)	Autograft Mass(g)	Current Status
1	F	43	Tibetan	1	17.0	P4N0M0	15.8	360	Alive
2	F	17	Tibetan	0	15.5	P4N0M0	11.0	400	Alive
3	M	29	Tibetan	2	20.0	P4N1M0	16.8	630	Alive
4	M	48	Tibetan	0	16.0	P4N1M0	17.0	540	Lost
5	M	28	Hui	0	18.9	P4N1M1	15.3	800	Alive
6	F	30	Tibetan	0	13.6	P3N1M0	17.0	650	Alive
7	F	57	Han	0	15.0	P4N1M0	12.8	636	Dead
8	F	34	Tibetan	0	18.0	P4N1M0	14.2	720	Alive
9	F	41	Tibetan	1	15.0	P4N1M0	16.7	870	Alive
10	F	33	Tibetan	1	12.8	P4N0M0	12.5	560	Alive
11	F	35	Tibetan	0	15.9	P4N0M0	11.0	520	Alive
12	F	42	Tibetan	1	22.0	P4N0M0	9.7	1300	Alive
13	M	37	Tibetan	0	20.0	P4N1M1	19.5	1095	Dead
14	F	27	Tibetan	1	18.3	P4N1M1	14.0	850	Alive
15	F	26	Han	1	16.0	P4N1M0	13.0	750	Alive
16	F	28	Tibetan	0	13.9	P4N1M0	10.5	610	Alive
17	F	39	Tibetan	0	15.0	P4N0M0	10.3	788	Alive
18	F	23	Tibetan	0	15.5	P4N1M0	11.8	720	Alive
19	F	31	Tibetan	0	12.2	P4N1M0	13.2	440	Alive
20	F	41	Tibetan	0	20.0	P4N1M0	9.4	950	Alive
21	F	52	Tibetan	0	16.5	P4N1M0	13.8	540	Alive

Abbreviations: PTCD, percutaneous transhepatic cholangial draina; PNM stage, the classifications P (parasitic in the liver), N (extension to neighboring organs); and M (distant metastasis).

vascular and biliary tract anatomy, as well as the spatial location of large masses. The criteria for proceeding with ex vivo liver resection and autotransplantation included: (a) No extrahepatic disease on CT scan; (b) Multidisciplinary discussion and successful percutaneous transhepatic cholangial drainage (PTCD); and (c) Preoperative Child-Pugh classification of liver function as grade A or B.

Preoperative Management

Given that most patients were from minority groups, communication with patients and their families was conducted in their native language, accompanied by written materials. Patients received a checklist and an information booklet detailing the operation and postoperative rehabilitation, emphasizing the importance of early mobilization and oral intake. Preoperative treatment included eliminating bowel preparation, administering prophylactic antibiotics, fasting from solid food for 6 hours, and fasting from liquids for 2 hours before surgery. Patients received intravenous glucose administration, and a nasogastric tube was not used.

Anesthetic and Surgical Practice

Anesthetic management included hemodynamic monitoring through an arterial line, central venous catheter, and pulmonary artery catheter. Body temperature was maintained between 36°C and 37°C using warming blankets and intravenous fluid warmers. Patients received patient-controlled morphine analgesia, and pain was assessed daily using a visual analogue scale (VAS) ranging from 0 to 10.

The surgical procedure, based on liver transplantation techniques, required close collaboration among the liver surgery center, liver transplantation center, and vascular center. Our transplantation center has performed nearly 1400 liver transplants, including about 400 living donor liver transplants. During the anhepatic phase, an artificial vascular graft (InterGard, InterVascular SAS, Inc., La Ciotat, France) was used to temporarily reconstruct the inferior vena cava (IVC). Meanwhile, a separate surgical team performed the ex vivo liver resection. Once the liver was completely resected, the liver graft was perfused with 4–8 liters of 0–4°C HTK solution (histidine-tryptophan-ketoglutarate, HTK,

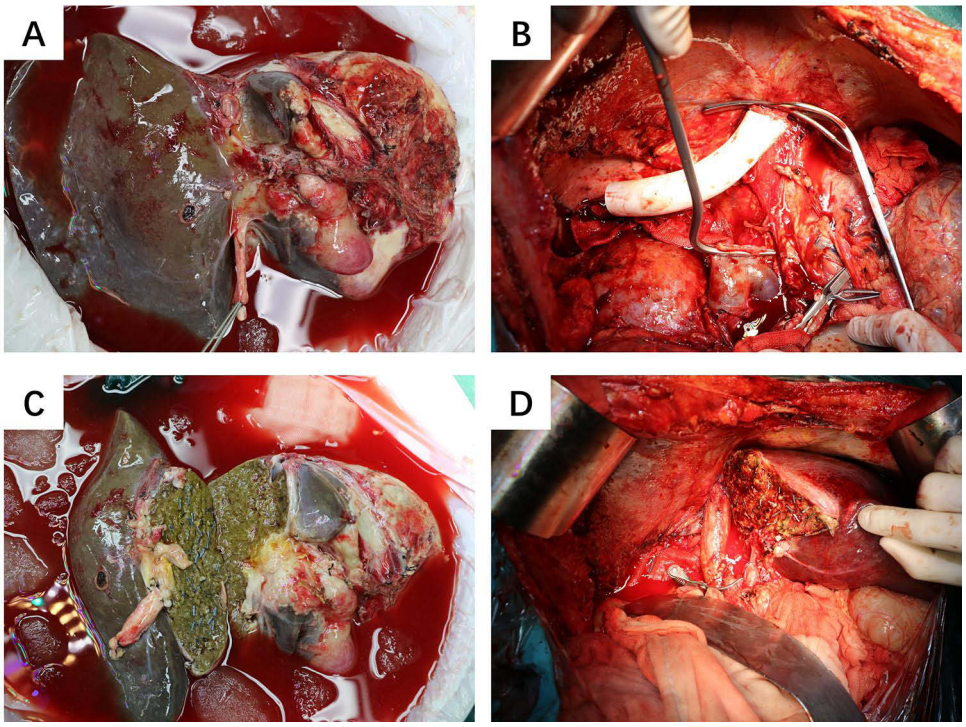

Figure 1 Operative Steps of ELRA Surgery. (**A**) The liver is completely removed and placed in an ice bath for hypothermic preservation; (**B**) During bench resection, the inferior vena cava is temporarily reconstructed; (**C**) Radical excision of the lesion and vascular repair are performed under hypothermic conditions; (**D**) The reconstructed liver is reimplanted into the body.

Custodiol, Dr. Franz Kohler Chemie, Germany) via the portal vein while being cooled in an ice bath. After bench resection, the temporary IVC and portocaval shunt were removed, and IVC reconstruction was completed before replacing the autograft in situ. The key surgical site is illustrated in Figure 1.

Postoperative Management

Reduction in Complications and Stress Response

The fast-track pathway for surgery has been shown to improve perioperative care and reduce complications by up to 50%.[16] After surgery, patients were transferred to the liver transplantation intensive care unit (ICU). Drains were removed as soon as no hemorrhage or bile leakage was observed, and the urinary catheter was removed on the morning of postoperative day 1 when patients returned to the general ward. Regular monitoring of liver and kidney function, autograft ultrasound, and thrombosis prevention measures were implemented. Thrombosis prevention included: (a) Low-molecular-weight heparin sodium injection (0.4 mL every 12 hours) postoperatively, barring signs of bleeding; (b) Warfarin dosage adjustment based on patient weight and INR for at least six months; and (c) Gradual mobilization, starting with up to 2 hours of exercise near the bed on postoperative day 1, with normal ambulation resumed by day 5. Early mobilization was emphasized to prevent pulmonary dysfunction and thromboembolism.

Managing Endocrine, Metabolic, and Inflammatory Responses

The traditional view of the endocrine, metabolic, and inflammatory responses as essential for surviving major surgery has evolved. Massive catecholamine release, protein loss, hyperglycemia, systemic inflammatory response, and immunosuppression are now recognized as hindrances to recovery. To mitigate these responses, we employed strategies such as preemptive analgesia, multimodal analgesia, and early oral nutrition. Patients began oral enteral nutrition 6 hours after returning to the general ward, with diets advanced as tolerated and intravenous infusions minimized. Patients were

followed up every 3–6 months post-discharge, with most returning to normal work. Serum C-reactive protein (CRP) levels were used to evaluate the surgical stress response.

Results

The study included 21 patients, consisting of 4 males and 17 females, with a mean age of 36 years (range, 17–57 years). The ethnic distribution was predominantly Tibetan (18 cases), with 2 han and 1 hui. All patients had a documented history of exposure in endemic regions. Preoperatively, 7 patients underwent percutaneous transhepatic cholangial drainage (PTCD), successfully reducing total bilirubin (TBIL) levels to meet the criteria for surgery. The preoperative Child-Pugh classification of liver function was grade A in 20 patients, with one patient classified as grade B. Inferior vena cava (IVC) reconstruction was performed in 17 patients (80.95%), with 3 cases (14.29%) utilizing artificial blood vessels and 1 case (4.76%) using an allogeneic vessel.

The median operative time was 13.6 hours (range, 9.4–19.5 hours), and the median anhepatic time was 314 minutes (range, 180–455 minutes). The median weight of the autograft was 701.4 g (range, 360–1300 g). Intraoperative blood loss ranged from 1200 to 6000 mL, with a mean loss of 2379 mL. The time to first flatus postoperatively was a median of 3.84 days (range, 3–7 days). The median postoperative hospital stay was 23.5 days (range, 4–51 days), and the median ICU stay was 5 days (range, 3–9 days). Hospital costs averaged $3 million (range, $1.94–4.07 million), and there was only one case of readmission. Detailed parameters are presented in Table 3.

Postoperative complications occurred in 12 patients, with 4 patients experiencing complications classified as Clavien-Dindo grade III or higher.[17] There were two postoperative deaths: one due to severe abdominal hemorrhage on postoperative day (POD) 4 and the other due to acute cerebral hemorrhage on POD 7. Two patients required reoperation—one for jejunostomy bleeding and the other for hepatic vein stent placement and angioplasty after being diagnosed with mild stenosis of the left hepatic vein. Severe pulmonary infections developed in two patients, and biliary leakage occurred in four patients. Postoperative pain scores, serum C-reactive protein (CRP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), and direct bilirubin (DBIL) levels normalized soon after surgery (Figure 2).

During a mean follow-up period of 16.2 months (range, 3–38 months), 20 patients were followed up, and no recurrence or extrahepatic metastasis of hepatic alveolar echinococcosis (HAE) was detected. One patient, originally from the Tibetan plateau, was lost to follow-up after one year.

Table 3 Intraoperative and Postoperative Parameters

Parameters	Value
Operation time, h, median (range)	13.6 (9.4–19.5)
Anhepatic time, min, median (range)	314 (180–455)
Autograft mass, g, median (range)	701.4 (360–1300)
Blood loss volume, mL, median (range)	2379 (1200–6000)
Erythrocyte suspension requirement, mL, Median (range)	2120 (0–7900)
Time to first flatus, d, median (range)	3.84 (3–7)
ICU stay, d, median (range)	5 (3–9)
Postoperative hospital stay, d, median (range)	23.5 (4–51)
Hospital costs,$, million, median (range)	3(1.94–4.07)
Follow-up, mo, mean (range)	16.2 (3–38)
Readmission, n (%)	1 (4.7)

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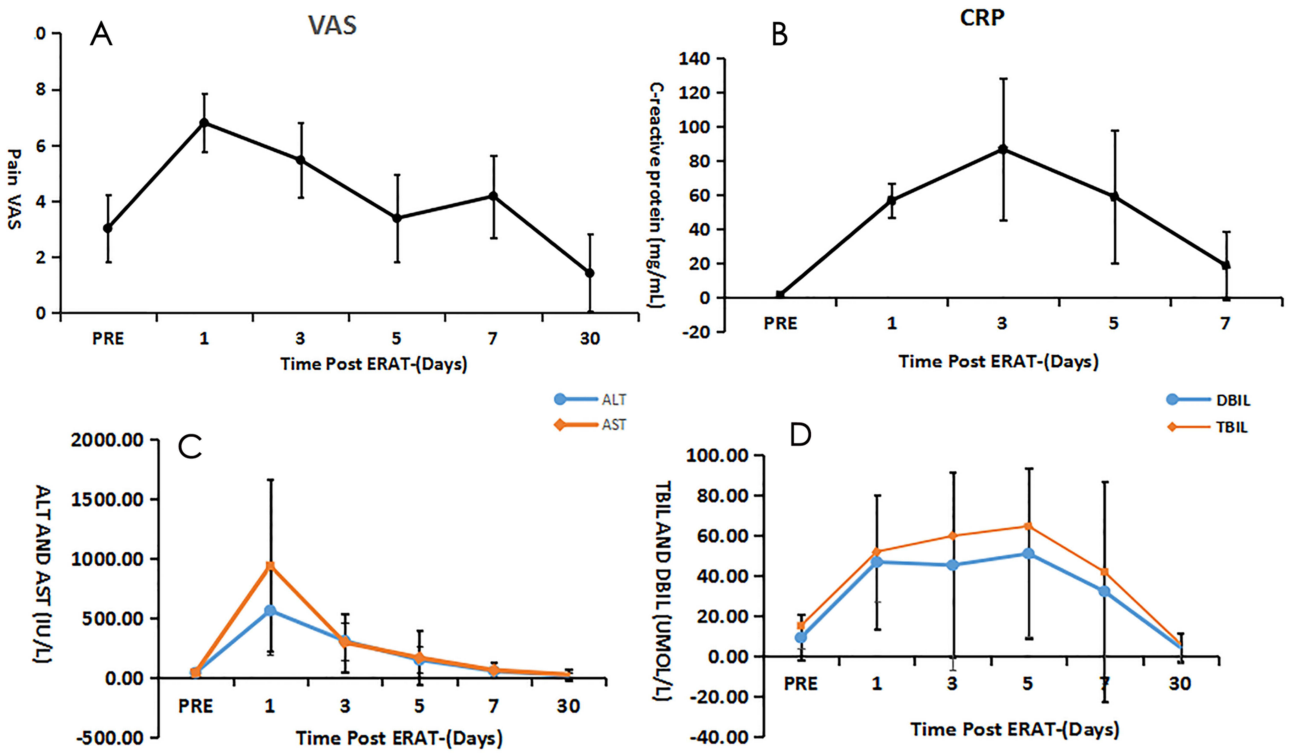

Figure 2 Preoperative and postoperative pain score, serum C-reactive protein (CRP) and biochemical examination of the patients with hepatic alveolar echinococcosis for liver autotransplantation. (**A**) VAS pain score in the after surgery. VAS score was moderate 3 days after operation and returned to mild 5 days after surgery. (**B**) The C-reactive protein (CRP) were used to evaluate the surgical stress response. The serum level was highest on the third day after operation, which returned gradual decline to normal. (**C** and **D**) The patient's liver function (AST, ALT, TBIL, DBIL) was poor 3 days after surgery and gradually returned to normal 7 days after surgery.

Discussion

Ex vivo liver resection combined with autotransplantation is an emerging treatment for end-stage hepatic alveolar echinococcosis (HAE), offering a potentially curative approach. Although global experience with this technique remains limited, initial clinical outcomes are promising. Several centers, including ours, have demonstrated that ex vivo liver resection and autotransplantation provide a radical treatment option for advanced HAE, with low early postoperative mortality, no requirement for organ donors, and the avoidance of immunosuppressive therapy.[14,18] Our case series represents the largest reported cohort of patients undergoing liver autotransplantation for AE within a fast-track protocol framework. The outcomes were encouraging, with a mortality rate of 9.5% (2/21) and a morbidity rate of 19.05% (4/21) for complications classified as Clavien-Dindo grade III or above. The average postoperative hospital stay was 23.5 days, with a median ICU stay of 5 days, and the average hospital cost was $3 million. Only one patient required readmission. These results are comparable to or better than those reported for allotransplantation and previously reported autotransplantation cases.[19–21]

The goal of the fast-track program is to enhance recovery through a combination of preoperative education, improved surgical techniques, multidisciplinary care, early extubation, and enteral nutrition.[22,23] This approach ensures smoother treatment outcomes. A significant portion of our patients were Tibetan (18/21, 85.7%), and language barriers posed challenges for pre-surgery counseling and perioperative cooperation. To address this, we provided preoperative counseling in both Tibetan and Mandarin, which helped improve patient understanding and postoperative recovery.

Given the unique growth pattern of the parasite, which often invades the portal trunk, advanced imaging techniques such as CT, MRI, and 3D reconstruction were essential for preoperative planning. These tools allowed us to accurately estimate residual liver volume and ensure complete removal of the lesion while preserving critical structures.[24] The multidisciplinary team, including transplant surgeons, hepatologists, medical imaging experts, anesthesiologists, and nurses, played a crucial role in enhancing the safety and predictability of the procedure. Rigorous preoperative

evaluation, including assessments of disease progression, imaging, lung function, and liver and kidney function, was vital. In particular, serum bilirubin levels were prioritized. In our study, 33.3% of patients (7/21) improved to Child-Pugh grade A liver function through preoperative PTCD, which likely enhanced the regenerative capacity of the liver graft and made ex situ liver surgery feasible.[25,26]

Postoperative management and the prevention of complications were also key factors in the success of autologous liver transplantation. Early ambulation helped prevent pulmonary infections, bedsores, and thromboembolic events, while early enteral nutrition facilitated gastrointestinal recovery and minimized the risk of intestinal paralysis.[27] We encouraged patients to ambulate near the bed on the first postoperative day, gradually increasing activity, and we implemented a diet plan developed by a dietitian. Other measures, such as early removal of drainage tubes and urethral catheters, further supported early ambulation and reduced the risk of retrograde infections.[28] Our multimodal fast-track protocols also included patient education, intraoperative temperature control, and postoperative analgesia, all of which contributed to improved perioperative outcomes.

The overall complication rate in this study was 57.1% (12/21), with 19.05% (4/21) classified as Clavien-Dindo grade III or higher. This compares favorably to historical data from Wen et al,[13] who reported a 20% biliary leakage rate in similar procedures without fast-track protocols. The reduced incidence of severe complications in our cohort (eg, 12.9% biliary leakage vs 20% in Wen's series) may be attributed to the multimodal fast-track interventions, particularly early mobilization and enteral nutrition, which likely mitigated systemic inflammatory responses and promoted tissue healing.[27] Furthermore, the integration of advanced preoperative imaging modalities, as emphasized by Aydin et al,[15] allowed precise surgical planning and contributed to minimizing intraoperative vascular injuries—a critical factor in achieving lower reoperation rates (9.5% vs 15–25% in conventional approaches).[19,20]

Two patients experienced unexpected deaths: one from hemorrhagic shock due to intercostal artery hemorrhage, likely related to the extent of diaphragm resection and surgical technique, and another from acute cerebral hemorrhage. Detailed preoperative evaluation and rigorous anticoagulant therapy post-surgery may help prevent such catastrophic events in the future. After discharge, all patients were treated with oral albendazole until liver function normalized. Regular follow-up included abdominal and chest CT scans every six months. Only one patient developed significant ascites due to anastomotic stenosis of the left hepatic vein three months postoperatively. The remaining patients resumed normal daily activities, with no evidence of hepatic insufficiency or failure.

In conclusion, multimodal fast-track protocols for ex vivo liver resection and autotransplantation in patients with end-stage hepatic alveolar echinococcosis are safe and feasible. Further studies with larger sample sizes and control groups are necessary to fully evaluate the therapeutic effects of these protocols in clinical practice.

Abbreviation

LT, liver transplantation; HAE, Hepatic Alveolar echinococcosis; MDT, Multidisciplinary team; CT, Computed tomography; MRI, Magnetic resonance imaging; 3D, Three-dimensional; PTCD, Percutaneous transhepatic cholangial drainage; VAS, Visual analogue scale; CRP, C-reactive protein; AE, Alveolar echinococcosis; RLV, Remnant liver volume; HTK, Histidine-tryptophan-ketoglutarate; IVC, Inferior vena cava.

Data Sharing Statement

All data used to perform the study, including the information downloaded from the database as well as that derived from the treatment of the bibliographic entries, are available in the Dataverse Project, an open access public repository.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of West China Hospital (approval number: No. 2017-38). The requirement for individual informed consent was waived by the ethics committee due to the retrospective nature of the study and the analysis used anonymous clinical data.

Consent for Publication

The authors give consent to publish the manuscript.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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