ORIGINAL ARTICLE

Novel techniques and preliminary results of ex vivo liver resection and autotransplantation for end-stage hepatic alveolar echinococcosis: A study of 31 cases

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Ex vivo liver resection combined with autotransplantation is a recently introduced approach to cure end-stage hepatic alveolar echinococcosis (HAE), which is considered unresectable by conventional radical resection due to echinococcal dissemination into the crucial intrahepatic conduits and adjacent structures. This article aims discuss the manipulation details and propose reasonable indications for this promising technique. All patients successfully underwent liver autotransplantation with no intraoperative mortality. The median weight of the autografts was 636 g (360-1300 g), the median operation time was 12.5 hours (9.4-19.5 hours), and the median anhepatic phase was 309 minutes (180- 460 minutes). Intraoperative blood loss averaged 1800 mL (1200-6000 mL). Postoperative complications occurred in 13 patients during hospitalization; 5 patients experienced postoperative complications classified as Clavien-Dindo grade III or higher, and 2 patients died of intraabdominal bleeding and acute cerebral hemorrhage, respectively. Twenty-nine patients were followed for a median of 14.0 months (3-42 months), and no HAE recurrence was detected. The technique requires neither an organ donor nor any postoperative immunosuppressant, and the success of the treatment relies on meticulous preoperative assessments and precise surgical manipulation.

KEYWORDS
autotransplantation, clinical research/practice, liver transplantation/hepatology, liver transplantation: living donor, liver transplantation: split

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1 | INTRODUCTION

Hepatic alveolar echinococcosis (HAE) is a life-threatening parasitic disease caused by the larvae of *Echinococcus multilocularis*, leading to comprehensive invasion of multiple intrahepatic structures.[1] Untreated HAE patients are estimated to have a 10-year mortality of 94%.[2] Alveolar echinococcosis (AE) is endemic in the northern hemisphere, where its extensive range includes the central part of western Europe, parts of the near East, Russia, and the central Asian Republics, China, northern Japan, and Alaska.[3] China alone endures 90% of the global burden of AE, with over 16 000 primarily diagnosed cases every year.[4,5] To date, radical hepatectomy accompanied by albendazole therapy is deemed to be the best solution for HAE.[6] Unfortunately, the insidious onset and slow progression of HAE usually result in delayed diagnosis. Thus most patients miss their chance for radical resection due to multiple lesions and severe intrahepatic structure invasion; only 35% of patients are eligible for radical hepatectomy.[7] Palliative surgery, such as lesion reduction surgery or cholangial drainage, does not notably benefit patient survival. Oral chemotherapy, such as albendazole, may postpone HAE progression, but the results are still far from satisfactory.[8-10] Liver transplantation (LT) has been applied as the last-resort therapy and as the only opportunity for radical cure of HAE since 1985.[7,11] This application has been expanded through living donor liver transplantation (LDLT)[12,13]; however, the limitations are obvious: post-LT complications, recurrence associated with the management of immunosuppressive drugs, the shortage of organ donations, and the intolerably high expense of treatment have impaired the wide application of LT.[7,14]

In 1988, Pilchmayr et al[15] pioneered and presented the concept of extracorporeal liver surgery, which was applied for advanced malignant tumors. However, the outcome of this brilliant technique was not satisfactory due to the high incidence of unmanageable complications and postoperative recurrence.[16,17] End-stage HAE is a relatively benign disease characterized by single or multiple large lesions that have extensively invaded crucial intrahepatic conduits or even hilum, thus making conventional hepatectomy impossible because the liver cannot tolerate the length of time required for the reconstruction procedure following resection. The above-mentioned limitations prompted us to apply ex vivo liver resection and autotransplantation (ERAT) for HAE. We conducted the first reported ERAT for advanced HAE with replacement of the retrohepatic inferior vena cava (IVC) using autologous vein grafting.[18] The result was satisfactory and encouraged us to explore more details of ERAT. In this report, we retrospectively studied 31 cases of ERAT performed at our center with the aim of discussing the feasibility, indications, preparation, technical details, and postoperative outcomes of this promising technique.

2 | MATERIALS AND METHODS

2.1 | Patient selection

From January 2014 to June 2017, 31 patients were selected to undergo ERAT. The study was approved by the ethics committee of West China Hospital of Sichuan University (No. 2017-38) and conducted in accordance with the Declaration of Helsinki. After the strict evaluation for ERAT by a multidisciplinary team (MDT) that included hepatobiliary surgeons, a vascular surgeon, a radiologist, and an anesthetist, 31 patients with the following chief distinguishing features underwent ERAT: (1) evaluation of advanced HAE as "unresectable" with the use of traditional techniques when there was difficulty exposing or removing the lesions, and a lack of reconstruction techniques and materials; (2) involvement of the hepatocaval region, 3 hepatic veins, and the retrohepatic vena cava (RHVC) or invasion of the tertiary branches of the portal veins (PV) and portal arteries requiring a complex reconstruction for prolonged ischemic time that the liver cannot tolerate; (3) good physiological state of the patient, with normal liver and kidney function and extrahepatic echinococcosis lesions that could be surgically removed or controlled by albendazole. Before the operation, we communicated fully with the patients and their families in their native language and explained the advantages of surgery and possible complications. The patients' baseline data, imaging features,[6] and surgical results were collected in Table 1.

2.2 | Pretransplant evaluation

All patients were evaluated by imaging tools, including MRI and computed tomography (CT) (Figure 1A), to assess the characteristics of the lesions, the portal hilum involvement, and the length and diameter of RHVC invasion, as well as to evaluate whether there was evidence of extrahepatic metastasis. A 3-dimensional (3D) imaging analysis system [19] calculated remnant liver volume (RLV) and visualized the vascular and biliary tract anatomy and the spatial location of the large masses (Figure 1B). The standard liver volume (SLV) was calculated following the experience of Urata et al[20,21] For patients with highly suspected extrahepatic metastases, positron emission tomography-computed tomography (PET-CT) was essential to determine whether there were any potential surgical contraindications. Ultrasonography (US) evaluation of the large abdomen vessels was necessary to assess the vascular flow status and the presence or absence of "rich collateral circulation."[22] US of the bilateral great saphenous vein (GSV) was performed to evaluate its diameter and length for the reconstruction of the RHVC. If patients had persistent obstructive jaundice and biliary dilatation before the operation, X-ray- or US-guided percutaneous transhepatic cholangial drainage (PTCD) was performed to alleviate the bilirubin level and biliary obstruction. Patients with cholestatic jaundice were eligible for ERAT if the total bilirubin (TBIL) level was less than twice the upper limit of normal. After meticulous preoperative assessment and repetitive MDT discussions concerning the difficulties of conduit reconstruction and potential liver failure, the ERAT procedure would be conducted with the preparation of a blood type–matched donation after cardiac death (DCD) liver graft. In addition, the evaluation of the patient's family members as donors for LDLT would be initiated when DCD LT was not available, or if the waiting period was too long.
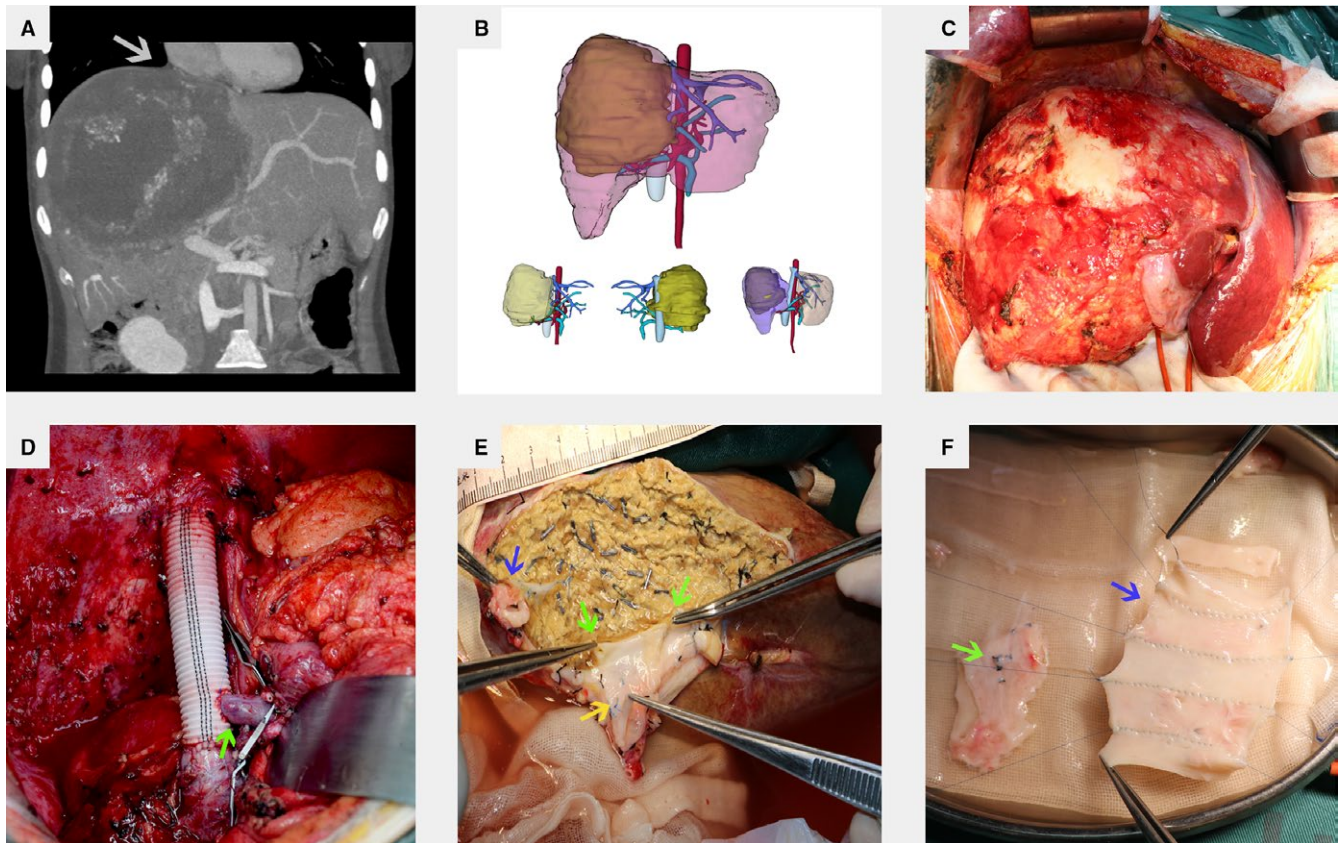
2.3 | Surgical procedures

2.3.1 | Exploratory surgery

The surgical procedure was based on LDLT,[23] and the Mercedes incision was employed to ensure adequate exposure of the liver. The liver

TABLE 1 Clinical, radiological, and autotransplantation characteristics of the 31 patients

Patient	Sex	Age (y)	Pre-ERAT PTCD (n)	Pre-ERAT surgery (h)	Lesion size (cm)	PNM stage	Duration of surgery (h)	Duration of anhepatic phase (min)	RLV (mL)	RLV/SLV	Autograft mass (g)	Current status
1	F	43	1	0	17.0	P4N0M0	15.8	420	390	0.36	360	Alive
2	F	17	0	0	15.5	P4N0M0	11.0	180	420	0.40	400	Alive
3	M	29	2	2	20.0	P4N1M0	16.8	330	700	0.63	630	Alive
4	M	48	0	1	16.0	P4N1M0	17.0	400	500	0.42	540	Lost
5	M	28	0	0	18.9	P4N1M1	15.3	360	750	0.58	800	Alive
6	F	30	0	2	13.6	P3N1M0	17.0	290	800	0.79	650	Alive
7	F	57	0	1	15.0	P4N1M0	12.8	310	600	0.49	636	Dead
8	F	34	0	0	18.0	P4N1M0	14.2	397	700	0.52	720	Alive
9	F	41	1	0	15.0	P4N1M0	16.7	345	850	0.70	870	Alive
10	F	33	1	0	12.8	P4N0M0	12.5	305	700	0.63	560	Alive
11	F	35	0	0	15.9	P4N0M0	11.0	249	480	0.43	520	Alive
12	F	42	1	0	22.0	P4N0M0	9.7	226	1300	1.01	1300	Alive
13	M	37	0	0	20.0	P4N1M1	19.5	455	1363	1.11	1095	Dead
14	F	27	1	0	18.3	P4N1M1	14.0	309	850	0.76	850	Alive
15	F	26	1	0	16.0	P4N1M0	13.0	337	1000	0.92	750	Alive
16	F	28	0	0	13.9	P4N1M0	10.5	286	600	0.57	610	Alive
17	F	39	0	0	15.0	P4N0M0	10.3	278	900	0.74	788	Alive
18	F	23	0	0	15.5	P4N1M0	11.8	307	800	0.76	720	Alive
19	F	31	0	0	12.2	P4N1M0	13.2	281	500	0.47	440	Alive
20	F	41	0	0	20.0	P4N1M0	9.4	205	1000	0.81	950	Alive
21	F	52	0	0	16.5	P4N1M0	13.8	331	550	0.40	540	Alive
22	F	39	0	0	16.0	P4N1M0	10.3	294	550	0.45	560	Alive
23	F	26	0	0	15.0	P4N0M0	12.3	460	550	0.50	600	Alive
24	F	17	0	0	13.6	P4N0M0	12.5	250	800	0.83	800	Alive
25	M	23	0	0	19.2	P4N0M1	10.2	277	435	0.36	440	Alive
26	M	25	0	0	11.3	P4N1M0	11.0	322	600	0.50	610	Alive
27	M	32	1	0	14.1	P4N1M0	12.0	304	600	0.55	565	Alive
28	F	38	1	0	15.9	P4N1M0	13.2	292	980	0.94	920	Alive
29	M	21	0	0	17.4	P4N1M0	12.0	384	680	0.58	650	Alive
30	M	25	0	0	12.7	P4N0M0	11.3	327	560	0.44	540	Alive
31	F	41	0	1	16.5	P4N0M0	15.1	428	900	0.81	880	Alive

ERAT, ex vivo liver resection and autotransplantation; PTCD, percutaneous transhepatic cholangial drainage; PNM stage, the classifications P (parasitic in the liver), N (extension to neighboring organs), and M (distant metastasis) were recently developed by the European Echinococcosis Registry Network of the WHO Informal Working Group on Echinococcosis[6]; RLV, estimated remnant liver volume; SLV, estimated standard liver volume. SLV = 706.2 × BSA + 2.4, BSA = 0.007184 × BW(kg)$^{0.425}$ × Height(cm)$^{0.725}$ × BW(kg)$^{0.425}$.[20] Patient 4 was lost to follow-up after 1 year, so his current state is unknown.

FIGURE 1 The key preoperative assessment and surgical procedures for ex vivo liver resection and autotransplantation for patients with advanced alveolar echinococcosis. (A) Preoperative CT revealed a large lesion in the right liver in patient 14 that involved the diaphragm (white arrow), retrohepatic inferior vena cava, and portal veins. (B) The preoperative 3D reconstruction of the HAE lesions, which provided information concerning the anatomy, estimated future liver volume (FLV), and surgical planning. (C) The large HAE lesion seen during surgery, which severely violated the first hepatic hilum. (D) The temporary inferior vena cava reconstruction and portocaval shunt (green arrow) in anhepatic phase. (E) Repair and reconstruction of the inflow and outflow tracts of the liver autograft in bench resection; the hepatic vein (blue arrow), bile ducts (green arrow), and portal vein (yellow arrow) are shown. (F) A new inferior vena cava was reconstructed with the bilateral saphenous vein (blue arrow) and with an HAE-free patch of RHVC (green arrow) after the vessel was reshaped

was subsequently carefully mobilized from any adjacent adhesions. The incision line for ex vivo liver resection (bench resection) was then determined by US. The large HAE lesion frequently involved extensive adhesions to the adjacent organs and invasion into the RHVC, which presented an additional challenge for the bench resection procedure (Figure 1C). With the aim of radical resection, the diaphragm, right lung, right adrenal gland, or right kidney were resected if invasion was present. Patient 5 underwent right nephrectomy. For patients 5 and 13, the right lungs were partially removed. Patients 5, 6, 7, and 13 had an artificial patch to repair the resected portions of the diaphragm. The liver was moved into an ice bath for bench resection after the successful procurement of the entire liver.

2.3.2 | Anhepatic phase management

In the anhepatic phase, an artificial vascular graft (InterGard, InterVascular SAS, Inc., La Ciotat, France) was applied to temporarily reconstruct the IVC. A portocaval shunt was then established between the portal vein (PV) stump and the temporary IVC. Stable hemodynamics was maintained by these 2 routine procedures[18]

(Figure 1D). Blood gas analysis (including pH, lactate [LAC], and blood oxygen saturation) was performed at 1-hour intervals, and anesthetic adjustments were made accordingly.

2.3.3 | Ex vivo liver resection

The ex vivo liver resection was simultaneously performed by another group of surgeons. The liver was perfused with 4-8 L of 0-4°C HTK solution (histidine-tryptophan-ketoglutarate, HTK, Custodiol, Dr. Franz Kohler Chemie, Germany) via the PV while cooled in an ice bath. Parenchymal transection was performed with a minimum 1.0-cm lesion-free margin using the Cavi-Pulse Ultrasonic Surgical Aspirator (CUSA, Valleylab, Boulder, CO). The procedure for the parenchyma transaction was similar to that of liver graft harvesting from living donors, which was introduced in our previous studies.[24,25] Notably, the left hepatic vein (HV), hepatic artery (HA), hepatic bile duct (HD), and the PV were carefully protected for subsequent reconstruction (Figure 1E). To ensure a radical removal of the lesion, frozen-section specimens of the transection margin were frequently sent for pathological examination, which revealed no evidence of HAE invasion. In addition,, the autograft was

inspected by repeated perfusion to avoid any potential bile leakage or vascular rupture. The volume and weight of the autograft were recorded before it was stored in a 4°C refrigerator.
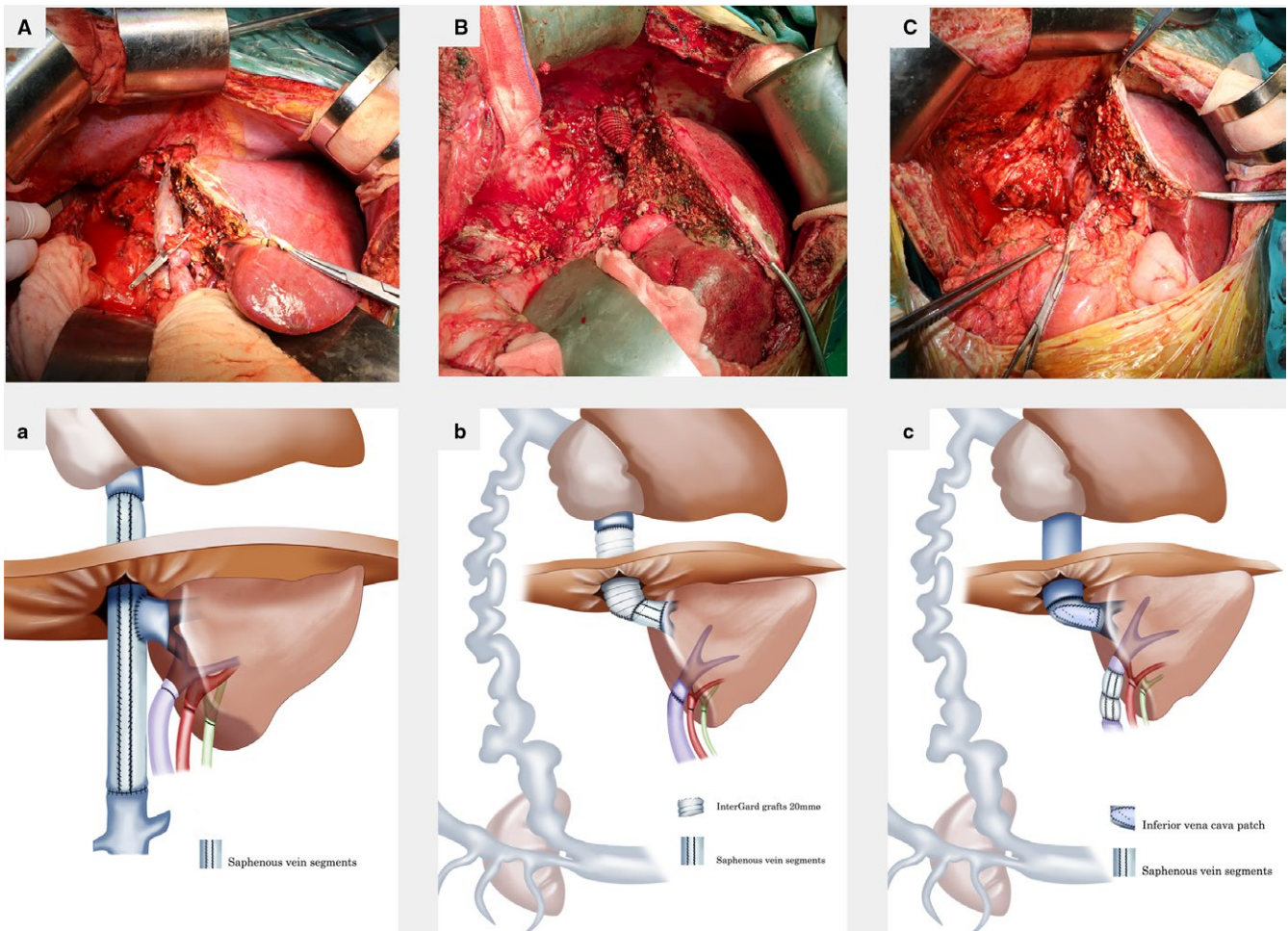
2.3.4 | IVC reconstruction

After the completion of bench resection, the temporary IVC and portocaval shunt were removed. IVC reconstruction is the final process prior to replacing the autograft in situ. The materials for reconstruction included artificial vessels, autologous vessels, and allogenic vessels. The autologous vessels (including the GSV, portions of the HAE-free hepatic vein, a posterior segment of the RHVC, and the inferior mesenteric vein) were selected primarily.[18,26] Typically, the autologous veins were vertically split and annularly assembled as the graft of IVC [18] (Figure 1F). For patient 26, the new IVC was extended above the mediastinum because the HAE lesion had invaded the pericardium (Figure 2A, a). It is notable that for patient 27 (Figure 2B, b)

and patient 31 (Figure 2C, c), the entire IVC was not reconstructed. In the other 5 cases, the temporary IVC, which was rebuilt using an artificial graft, was not removed because the bilateral GSV was too short to be the source of the IVC reconstruction.

2.3.5 | Bile duct and PV reconstruction

The maneuvers and materials for PV and HV revascularization (Figure 3A, B, C) were similar to those used for the IVC (Figure 2). After the outflow and PV were successfully reconstructed, the anhepatic period ended. Warming water was administered to the surface of the autograft to accelerate reperfusion. Subsequently, HA anastomosis and biliary duct reconstruction were performed. The number of segmental HDs in the autograft varied from 1 to 4 and necessitated diverse approaches for reconstruction, including left HD and common bile duct (CBD) anastomosis, Roux-en-Y hepaticojejunostomy, or a combination of these 2 approaches (Figure 3D, E, F). A careful

FIGURE 2 Three complex inferior vena cava reconstruction methods and state of the liver autograft implanted. (A and a) For patient 26, the new IVC was extended above the mediastinum, which was rebuilt using bilateral GSVs. Left PV to portal trunk, end-to-end anastomosis; left HD to CBD, end-to-end anastomosis. The left hepatic artery was anastomosed to the end of the hepatic proper artery. (B and b) For patient 27, the IVC was partially rebuilt using an artificial vascular graft due to the rich collateral circulation. The GSV patches were adopted to rebuild the outflow. The hepatic hilum reconstructions were similar in patient 27 as in patient 26. (C and c) For patient 31, the IVC was not rebuilt due to the rich collateral circulation, and an HAE-free piece of IVC was used to repair the left hepatic vein. The hepatic artery and bile duct reconstructions were similar to those used for patient 26, but the portal vein was extended by 2 GSV loop patches to the portal trunk

examination of the autograft for any possible bile leakage and bleeding was the final step.

2.3.6 | Postoperative management

The patients were admitted to a special ward for ERAT after surgery. Liver and kidney function, autograft ultrasound, and complete blood count were examined regularly. Once postoperative bleeding was excluded, a low-molecular-weight heparin sodium injection (0.4 mL q12 hours, with the individual dosage adjusted according to the weight of the patient and the blood international normalized ratio [INR]) was administered to prevent thrombotic complications from the postoperative day (POD)2 to discharge. The patients subsequently need to take warfarin sodium tablets (the individual dosage should be adjusted according to the weight and the INR of the patient; the INR reference value is 2.0-3.0) for at least half a year. Drainage was extended in cases in which hemorrhage or bile leakage occurred. All patients were administered albendazole (15 mg/kg/day) routinely for 1 year after ERAT.[27] The patients returned for follow-up visits every 3-6 months after discharge.

3 | RESULTS

Thirty-one patients underwent ERAT successfully after MDT discussion, and there were no intraoperative deaths. The 31 patients included 9 males and 22 females, and the mean age was 33.2 years (range, 17-57 years). Nine patients underwent preoperative PTCD, and their TBIL level reduced successfully to reach compliance with standards. Patient 24 refused PTCD, although she had a TBIL level of 174.7 μmol/L. She eventually underwent ERAT because the duration of cholestatic jaundice was less than 7 days and the estimated RLV was 820 mL. Four patients had undergone palliative hepatectomy prior to admission to our center. The preoperative Child-Pugh classification of liver function was grade A in 27 patients and grade B in 4 patients. The mean value of the estimated RLV was 723 mL (range 390-1363 mL), and the corresponding average RLV/SLV was 0.63 (range 0.36-1.11).

All patients underwent temporary IVC reconstruction and portocaval shunts in the anhepatic phase. The artificial grafts were applied for IVC reconstruction in 5 patients, whereas the allograft vessel was
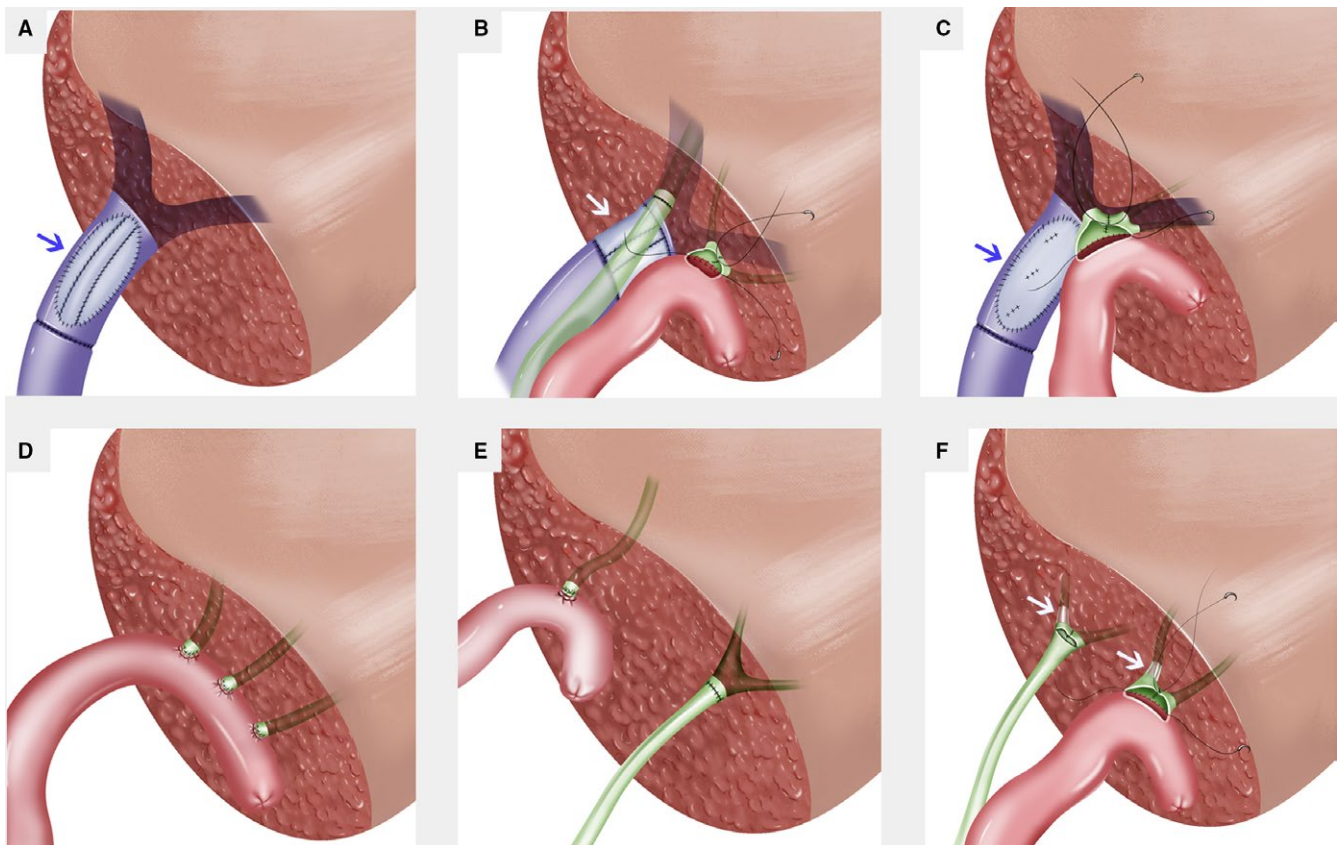
FIGURE 3 Several patterns of reconstruction of the portal vein and bile duct. (A) A GSV patch (blue arrow) was used to repair the orifice the portal veins of the S2 and S3 segment; subsequently, the left PV to portal trunk were end-to-end anastomosed. (B) A GSV loop patch (white arrow) was utilized to lengthen the portal vein. The biliary tract was reconstructed by anastomosis between the left HD and CBD and Roux-en-Y hepaticojejunostomy. (C) An HAE-free piece of RHVC (blue arrow) was used to reconstruct the portal vein. Two bile ducts were first reshaped to form a general opening, and a Roux-en-Y hepaticojejunostomy was performed. (D) Three bile ducts were independently reconstructed by Roux-en-Y hepaticojejunostomy. (E) The anastomosis between the left HD and the CBD and Roux-en-Y hepaticojejunostomy were performed. (F) The hepatic ducts of the S3 segment were anastomosed to the CBD with a small anesthetic tube (white arrow), and hepaticojejunostomy was performed on the hepatic ducts of the S2 segment with a small anesthetic tube (white arrow)

used in 1 patient. The remaining 23 patients (74.2%) underwent autologous revascularization of the IVC. Details of conduit reconstruction are presented in Figure 3 and Table 2. The median operative time was 12.5 hours (range 9.4-19.5 hours), the median anhepatic time was 309 minutes (range 180-460 minutes). The median weight of the autograft was 636 g (range 360-1300g). The rest of intraoperative parameters were reported in Table 2.

Postoperative complications occurred in 13 patients, and complications classified as Clavien-Dindo grade[28] III or higher appeared in 5 patients (Table 3). Two patients died: 1 due to severe abdominal hemorrhage in POD4 and 1 due to acute cerebral hemorrhage on POD7. Patient 12 underwent re-laparotomy because the jejunojejunostomy revealed hemorrhaging through hemafecia. Two patients developed severe pulmonary infection, and biliary leakage occurred in 4 patients. Most unexpectedly, persistent ascites and hypoproteinemia occurred in patient 16 after postoperative 2 months, and she was diagnosed with mild stenosis of the left HV. The other patient experienced pleural effusion, and the pyoperitoneum gradually recovered under careful management with no need for surgery. The changes in the LAC levels during the perioperative and postoperative periods are presented in Figure 4A. The alanine aminotransferase (ALT), aspartate aminotransferase (AST), TBIL, Direct bilirubin (DBIL), and creatinine (CREA) levels returned to normal soon after surgery (Figure 4B, C, D).

Patients were administered albendazole regularly for at least 1 year after surgery. US, CT (Figure 5), and the blood parameters were examined every 3 months to study liver function and long-term outcomes of ERAT. No evidence of HAE recurrence or extrahepatic metastasis was found. Five patients who received artificial blood vessels were in good condition and had no complications. Only patient 31 experienced a transient lower extremity edema and recovered in POD7. No renal dysfunction or gastrointestinal symptoms were observed in patients 28 and 31, who did not have their RHVCs rebuilt. Twenty-nine patients were regularly followed. Unfortunately, patient 4, who came from the Tibetan plateau, was lost to follow-up after 1 year. During the mean 14.0-month follow-up (range, 3-42 months), 28 patients were alive with normal daily work.

4 | DISCUSSION

HAE is a rare and deadly parasitic disease in the northern hemisphere, especially in western China.[4,5] In recent years, HAE cases have been expanding rapidly in Europe, Australia, and the United States from the countryside to urban areas, largely due to the increasing fox populations, the increasing encroachment of foxes into urban areas, and other factors such as spillover of *Echinococcus multilocularis* infection from wild carnivores to domestic dogs.[29] The World Health Organization has made great efforts to improve the management of HAE and the quality of life of patients with HAE, but many of these patients fail to receive timely treatment.[30] HAE is alluded to as "parasitic cancer," which exhibits tumor-like features with infiltrative growth.[27] Radical

TABLE 2 Intraoperative and postoperative parameters of the 31 patients

| Parameters	Value
Operation time, h, median (range)	12.5 (9.4-19.5)
Anhepatic time, min, median (range)	309 (180-460)
Temporary IVC and portocaval shunts	
Reconstruction time, min, median (range)	54 (30-94)
Duration time, min, median (range)	176 (63-353)
Autograft mass, g, median (range)	636 (360-1300)
Blood loss volume, mL, median (range)	1800 (1200-6000)
Erythrocyte suspension requirement, mL, median (range)	7 (0-39.5)
Fresh-frozen plasma requirement, mL, median (range)	800 (0-6050)
ICU stay, d, median (range)	4 (2-9)
Postoperative hospital stay, d, median (range)	19 (4-50)
Inferior vena cava reconstruction materials	
Autologous blood vessels, n (%)	23 (74.2)
Artificial blood vessel, n (%)	5 (16.1)
None, n (%)	2 (6.5)
Allogenic vessel, n (%)	1 (3.2)
Biliary tract reconstruction	
HD to CBD, end-to-end[L], n (%)	16 (51.6)
Roux-en-Y hepaticojejunostomy[R], n (%)	9 (29.0)
L+R, n (%)	6 (19.4)
Follow-up, mo, mean (range)[a]	14.0 (3-42)

IVC, inferior vena cava; HD, hepatic bile duct; CBD, common bile duct; follow-up[a], the follow-up period excluded 2 deaths.

TABLE 3 Postoperative complications and Clavien-Dindo classification for the 31 patients

Parameters	N (%)
Postoperative complications	
None	18 (58.1)
Biliary leakage	4 (12.9)
Pleural effusion	3 (9.6)
Pulmonary infection	2 (6.5)
Dead	2 (6.5)
Hemorrhage of jejunojejunostomy	1 (3.2)
Mild stenosis of left hepatic vein	1 (3.2)
Clavien-Dindo classification	
Grade I	2 (6.5)
Grade II	6 (19.4)
Grade IIIa	2 (3.2)
Grade IIIb	1 (3.2)
Grade IV	0 (0.0)
Grade V	2 (6.5)

The Clavien-Dindo classification of surgical complications based on the report of Clavien PA, et al.[28]
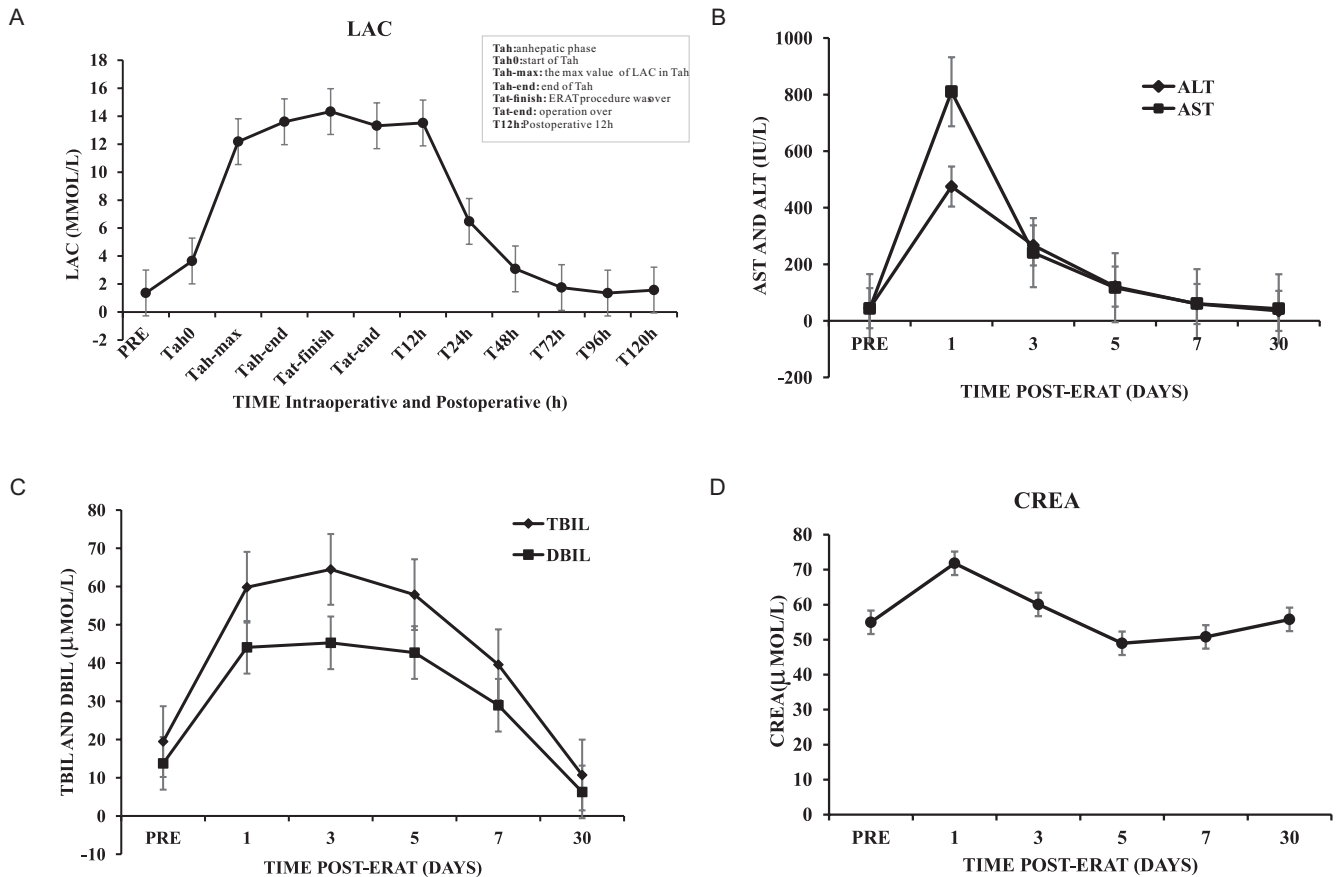
FIGURE 4 Intraoperative and postoperative biochemical examination of the patients with hepatic alveolar echinococcosis for liver autotransplantation. (A) Changes in blood lactate (LAC) values in the operation period and after surgery. In the anhepatic phase, LAC began to rise gradually because anaerobic glycolysis increased, which returned to normal until 48 hours after operation. (B and C) The patient's liver function (AST, ALT, TBIL, DBIL) was poor 3 days after surgery and gradually returned to normal 7 days after surgery; (D) Blood creatinine (CREA) is a key parameter to assess renal function impairment; although the creatinine values increased slightly after the operation, no renal dysfunction was indicated

resection is the first-line treatment for HAE patients. However, patients in the Chinese endemic areas frequently have lack of medical resources. More seriously, many patients lack the inclination to visit a hospital for therapy because HAE is considered a benign disease with no significant symptoms. Therefore, these patients lose the best chances for radical resection in the early stage HAE, and they must undergo treatment with oral albendazole tablets or palliative external drainage without an alternative treatment option.[8-10]

Liver transplantation has provided a life-saving technique for patients with "unresectable" but not metastatic HAE lesions.[11,13,14,31-35] Several centers had reported their work, which was summarized in Table 4. According to the experience of a European collaborative report, severe infection and recurrence of HAE are primarily responsible for early postoperative mortality (9/45, 20%),[35] which is consistent with the outcomes from our center.[31,34] Multiple elements, for instance, the shortage of graft donors and high incidence of postoperative recurrence associated with mandatory immunosuppressive therapy, eventually led to limited utilization of LT. These limitations prompted us to explore an alternative that could overcome these impediments. Thus ERAT was introduced. Since Wen et al [36] reported a

case with such a technique in 2011, a few centers have also started using this approach.[18,22,36,37] Two deaths were reported previously, 1 from PV thrombosis [37] and 1 from acute liver failure in POD12.[22] Nonetheless, the details of indication, manipulation, and postoperative management remain controversial. According to our experience, this promising technique is feasible for end-stage HAE with a convincing outcome; in our hands, it had a mortality rate of only 6.5% and a 16.1% morbidity rate classified as Clavien-Dindo grade III or above, and no recurrence was detected up to the writing of this article. To the best of our knowledge, this case series constitutes the world's largest series of patients with end-stage HAE who underwent ERAT with multiple novel surgical technical details.

The meticulous selection of candidates is the basis for ensuring a smooth treatment outcome. HAE is preferably considered a benign disease; despite its tumor-like infiltrative growth, a relatively long time between primary infection and presentation of symptoms enables adequate compensatory function of the disease-free lobe of the liver. We consider it as the result of the obstruction of the PV branch and the biliary tract caused by the lesion pressure, which increases the blood inflow of the disease-free lobes. In our study, the ratio of RLV to
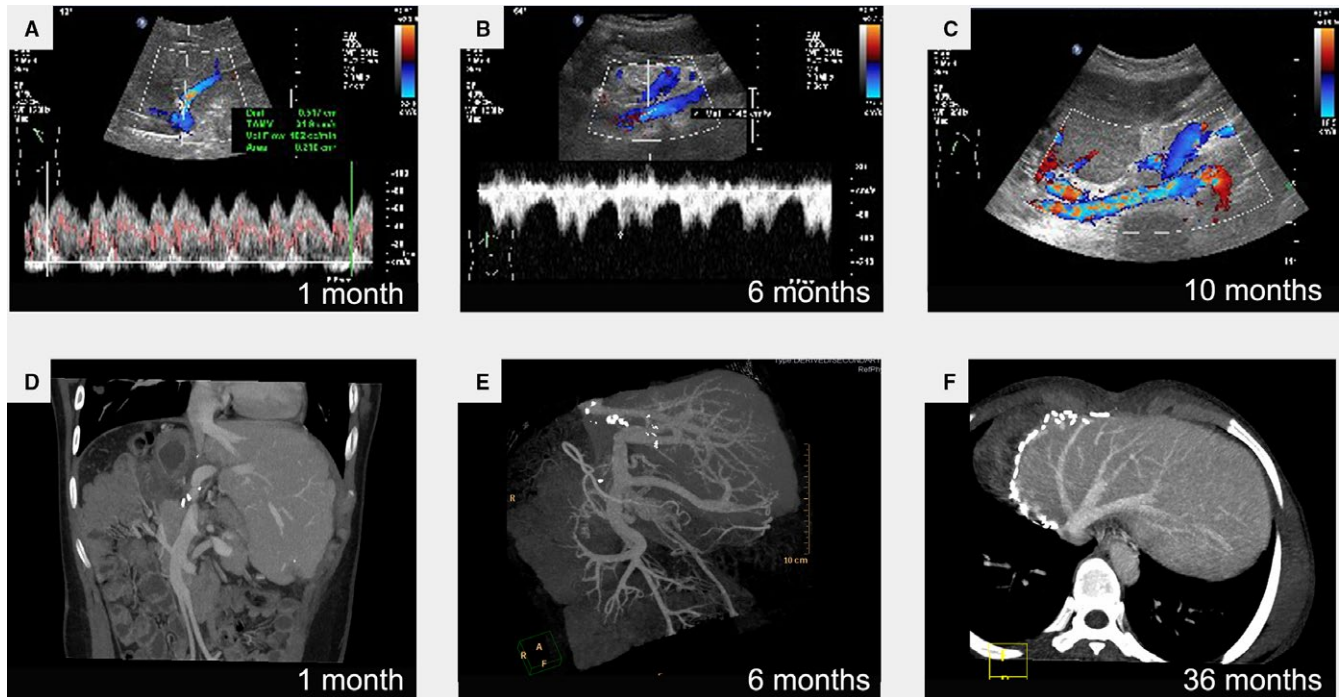
FIGURE 5 Results of postoperative ultrasonography and CT scans. (A) The US of patient 26, 1 month after surgery, which indicated no obstruction or stenosis. The diameter of the HV at the confluence is 5.1 mm. (B) The US of patient 20, 6 months after surgery, which indicated good hepatic outflow; the diameter of the HV at the confluence is 8 mm. (C) The US of patient 14, 10 months after surgery, which indicated no abnormity of hepatic outflow. (D) In patient 23, the obvious hypertrophy of the liver graft was detected by CT scan 1 month after operation. (E) In patient 15, rich vascular flows of the portal vein and hepatic vein were recognized 6 months after surgery. (F) In patient 1, the function of liver normalized, and no HAE recurrence or vascular complications were observed after 3 years of follow-up

SLV of all patients was larger than 35%, which suggested that the RLV was adequate to meet the functional demands.[38] Thus if successful reconstruction of intrahepatic conduits could be managed following complete removal of the lesion, HAE might be a specific indication for ERAT that yields better results than those obtained in malignant tumor. Based on our experience of over 356 cases of LDLT and abundant practice with vascular reconstruction,[23] we propose a preliminary list of indications: (1) the lesions have invaded 2 or more crucial structures including the porta hepatis, second and third porta hepatis; (2) severe invasion and even obliteration of the RHVC (≥3 cm longitudinally and ≥180° circumferentially); (3) severe invasion of the RHVC up to the pericardium/mediastinum/thoracic level; (4) patients with obstructive jaundice but in whom the serum total bilirubin level can be reduced to less than twice the upper limit of the normal value through PTCD; (5) the ratio of RLV to SLV is more than 35%; and (6) patients with remote metastasis, whose extrahepatic AE lesions can be surgically removed or controlled by albendazole.

The preoperative evaluation began with multiple blood examinations, in which serum bilirubin holds the priority. Oldhafer et al[39] suggested that an ex situ liver surgery should be avoided in patients with cholestasis because a high level of serum bilirubin or obstructive jaundice may critically impair the regenerating ability of the graft. In our study, the liver function of 9 patients (29.0%) was improved to Child-Pugh grade A through PTCD, which made it possible for them to receive the procedure. Preoperative US of the GSV was adopted to

determine whether autologous vein grafts could be used for vascular reconstruction. The most important advantage of an autologous graft over an artificial one is better biocompatibility, which greatly reduces the risk of graft rejection while reducing the postoperative anticoagulant therapy, thus reducing the possibility of postoperative bleeding.[40,41] In addition, the GSVs are easy to harvest, and their removal does not cause many adverse effects; all the preceding reasons make the GSV the ideal material for vascular reconstruction.[26,32,35]

The management of the anhepatic phase is another key issue for maintaining an uneventful intraoperative course. Before the successful procurement of the entire liver, complete vena cava occlusion can lead to severe systematic circulation disorders and intestinal congestion. Thus we suggest that regular temporary IVC reconstruction combined with portosystemic shunting should be performed in all patients. A median of 54 minutes (range, 30-94 minutes) is required for temporary reconstruction, and for guaranteeing the stability of hemodynamics and reducing the incidence of postoperative infection caused by bacterial translocation. Eventually, whether the permanent IVC reconstruction is needed depends on the flow of the collateral circulation. In our cases, 2 patients had no reconstruction of the IVC for 4 reasons: (1) rich collateral circulation was detected by preoperative CT; (2) the IVC was found to be totally occluded or seriously cramped; (3) no obvious disturbance of the blood pressure was detected after clamping the vena cava; and (4) the estimated urine volume was >50 mL/h during the period of temporarily reconstructing the IVC and portosystemic shunting. Only

TABLE 4 Indications and results of liver transplantation for hepatic alveolar echinococcosis: a major literature (≥5 cases) overview from 2003 to 2017 in PubMed

Year	Authors	Region	N	Indication for LT	Type of LT	Follow-up (months), mean (range)	Results
2016	Sulima et al. 33	Poland	9	Recurrent cholangitis; Progressive tumoral disease with hilum involvement; Liver failure; PNM staged was IIIa, IIIB, or IV.	DCD	76.8 (7-155)	One patient died due to liver failure. Two patients relapsed.
2015	Ozdemir et al. 13	Turkey	10	Extensive liver disease, hilar involvement, recurrent cholangitis, cholestasis, and recurrent disease after surgical resection.	LDLT	14.5 (2-54)	The local recurrence and distant metastasis rates were 10% and 20%. The mortality rate was 30%.
2015	Aydinli et al. 32	Turkey	27	Severe Hilar invasion, recurring cholangitis, uncontrolled biliary infections, and biliary invasion; Budd-Chiari, portal hypertension and bronchobiliary fistula.	LDLT20 + DCD7	16.1 (6-39)	No recurrence in the graft. One patient was detected brain AE. Six patients died.
2011	Bresson-Hadni et al. 14	France	5	Chronic AE-related Budd-Chiari syndrome;Cholangitis;Cholangitis and biliary cirrhosis; Severe jaundice (2 months of pregnancy).	N/A	>180	All patients alive with residual or recurrent AE.
2007	Li et al. 31	China	7	Tumor syndrome invading both lobes of the liver; Advanced chronic liver disease, including secondary sclerosing cholangitis, obstructive jaundice, hilum invasion, and hepatic vein invasion with or without chronic Budd-Chiari syndrome.	OLT	N/A (4-68)	One patient died 21 days and another patient died 3 months after OLT from heart failure.
2005	Xia et al. 34	China	5	Tumor syndrome invading both lobes of the liver and requiring urgent OLT; Advanced chronic liver disease: secondary sclerosing, cholangitis, obstructive jaundice with or without biliary tract fistula, and hilum invasion.	OLT	31 (25-39)	Two patients died.
2003	Bresson-Hadni et al. 7	Europe	47	Biliary disease, life-threatening cholangitis and/or abscesses, Secondary biliary cirrhosis, related to parasitic involvement of the hilum; Tumoral disease invading both lobes of the liver, with or without chronic parasitic Budd-Chiari syndrome.	N/A	N/A	The nine early deaths and five late deaths. Five-year survival was 71%. Five-year survival without recurrence was 58%.

LT, liver transplantation; DCD, donation after circulatory death; LDLT, living donor liver transplantation; OLT, orthotopic liver transplantation.
PNM stage was developed by the European Echinococcosis Registry Network of the WHO Informal Working Group on Echinococcosis.[6] N/A = data not available or cannot be counted.

patient 31 experienced a transient lower extremity edema and recovered in POD7. None of the patients had renal function impairment. The reconstruction of the inflow and outflow of the autologous graft requires attentive angioplasty because the intrahepatic conduits were frequently invaded by huge HAE lesions; moreover, the actual extent of the invasions was often found to be more serious than estimated by the preoperative assessment. The anastomosis of the PV circumstantially requires extension of the stump to prevent postoperative stenosis and kinking. The scheme for reintegrating the bile duct is difficult. Two or more orifices of bile duct are often found during the bench resection due to various mutations of the biliary system, which is difficult to identify from the orifice of other vessels because the graft is cooled in an ice bath and has no blood flow.

Two mortalities were reported. One patient died from postoperative intraabdominal bleeding originating from intercostal arteries. In this case, a large proportion of the diaphragm was removed and repaired by an artificial patch due to unexpected extensive invasion, which might be primarily responsible for the observed postoperative bleeding and consequent death. The incident might have been prevented by a more detailed preoperative assessment and delicate operative technique. Another patient died of acute cerebral hemorrhage; we speculate that this event was caused by excessive postoperative anticoagulant therapy. The most frequent cause of postoperative morbidity was bile leakage, with an incidence of 12.9% (4/31), which is lower than the incidence of 46.7% reported by Wen et al.[22] Stenosis was detected at the HV in 1 case after 2 months of follow-up, which may be a result of anastomosis scarring or hepatic vein kinking caused by pressure from the enlarged liver graft. Of interest, no hepatic insufficiency or failure was found in our case series; we attribute this to precise preoperative assessment of the graft volume and to the preoperative interventional modalities for mitigating obstructive jaundice.

Our experience from 31 cases indicated that ERAT is feasible for treating end-stage HAE. However, this study is inevitably associated with certain shortcomings, namely, a rather short follow-up period and the lack of a control group. Meanwhile, the advantage of autologous veins over artificial and allogeneic grafts as material for vessel reconstruction remains uncertain, and the intraoperative process of managing the oxygen metabolism, body fluid balance, and inflammatory responses needs to be fully studied. More rigorous experimental designs with large sample sizes are needed to assess the detailed utility of this technology.

ERAT provides a radical treatment option for advanced HAE that does not require an organ donor or immunosuppressive therapy. Accurate preoperative evaluation, delicate reconstruction of intrahepatic conduits, and meticulous postoperative management can improve patient survival and reduce the incidence of complications.

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DISCLOSURE

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