

Original Article

Clinical application of color Doppler flow imaging in prediction of postoperative complications in patients with end-stage hepatic alveolar echinococcosis undergoing autologous liver transplantation: a review of the literature and case reports

Lingfei Yang¹, Jian Dong¹, Xuewen Ji², Hui Liu³, Tao Song¹, Hao Wen²

¹Department of Ultrasonography, First Affiliated Hospital of Xinjiang Medical University, Urumqi 830011, China;

²Hepatobiliary and Hydatid Department, Digestive and Vascular Surgery Centre, First Teaching Hospital of Xinjiang Medical University, Urumqi 830011, China; ³Xinjiang Key Laboratory of Echinococcosis, Urumqi 830011, China

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Abstract: Objective: To investigate the clinical application of color Doppler flow imaging (CDFI) in the diagnosis of postoperative complications in patients with end-stage hepatic alveolar echinococcosis (HAE) undergoing autologous liver transplantation (ALT). Methods: We described 27 patients with end-stage HAE examined by CDFI to observe the presence of short- and long-term complications after ALT. Normal and abnormal images of the hepatic parenchyma, biliary tract, hepatic artery, portal vein, hepatic vein, inferior vena cava, and splanchnocoele were observed and analyzed. Results: The average follow-up was 0.1-31 months (mean duration: 4.02 ± 6.37 months). Among the 27 patients, 25 patients revealed various abnormal ultrasonographic findings after ALT (25/27, 92.6%). Twelve patients (44.4%) showed disseminated/regional changes in the echogenicity of the hepatic parenchyma, 4 patients (14.8%) showed biliary abnormalities, 4 cases (14.8%) showed hepatic artery abnormalities, 9 patients (33.3%) presented portal vein complications, 2 cases (7.4%) showed hepatic vein abnormalities, 3 patients (11.1%) revealed inferior vena cava abnormalities, 19 patients (70.4%) had ascites, 26 patients (96.3%) had hydrothorax, 1 patient (3.7%) recurred, and 7 patients (25.9%) died. Conclusion: CDFI is valuable for dynamic monitoring of postoperative complications in patients with end-stage HAE undergoing ALT, especially for the early stages after the operation.

Keywords: Color Doppler flow imaging, postoperative complications, end-stage hepatic alveolar echinococcosis, autologous liver transplantation

Introduction

Hepatic alveolar echinococcosis (HAE) is a rare parasitic infection caused by the zoonotic agent *Echinococcus multilocularis* [1, 2]. It has been reported that the disease is epidemic in some parts of the world, such as North America, Central Europe (e.g. Germany, Austria, and Switzerland) and Asia [3, 4]. HAE is a potentially serious life-threatening disease if not diagnosed early and managed appropriately [5, 6]. It is characterized by tumor-like infiltrative growth and the potential for metastasis, with high mortality rate and poor prognosis [7].

Surgical removal of the lesions is one of most important treatments for HAE [8]. However, the boundary between the HAE lesion and adjacent tissues is often indistinct, which greatly increases the difficulty of surgical resection. In addition, the long duration, large size and invasive growth of the lesion causes internal anatomical change and the formation of collateral vessels, which also increases the difficulty and complexity of the surgical procedure. A growing body of evidence has suggested that autologous liver transplantation (ALT), a treatment strategy that combines liver resection and organ transplantation technology, has been reported to be a

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Table 1. Postoperative complications in patients

Postoperative complications		Numbers	%
Abnormal liver parenchymal echogenicity	Diffuse change	5	18.5
	Focal change	7	25.9
Biliary abnormalities	Bile embolism formation	1	3.7
	Biliary pneumatosis	1	3.7
	Hepatolith	1	3.7
	Intrahepatic bile duct dilation	1	3.7
Hepatic artery complications	Abnormal blood flow	1	3.7
	Abnormal flow rate	2	7.4
	Abnormal frequency	1	3.7
Portal vein complications	Abnormal flow rate	5	18.5
	Stenosis	3	11.1
	Thrombus	1	3.7
Hepatic venous complications	Abnormal blood flow	1	3.7
	Abnormal flow rate	1	3.7
Inferior vena cava complications	Abnormal flow rate	1	3.7
	Stenosis	1	3.7
	Thrombus	1	3.7
Seroperitoneum		19	70
Hydrothorax		26	96.3
Recurrence		1	3.7
Colonic fistula		1	3.7
Death		7	25.9

good way to improve the clinical outcome, especially for the patients with end-stage HAE [9-11]. Nevertheless, various complications may occur after the surgery, greatly affecting the prognosis of the patients. Therefore, postoperative monitoring is extremely important to identify the potential complications and outcomes of surgery.

Color Doppler flow imaging (CDFI) is a relatively new noninvasive ultrasound technique to assess vascular function and morphology [12]. It is characterized by high resolution and rapid diagnostic capability, and is especially useful for patients requiring intensive care [13]. Recently, CDFI has been considered to be the preferred examination method in diagnosing HAE [14], as well as in evaluating the potential complications of patients undergoing liver transplantation [15]. However, little information is available regarding the clinical application of CDFI in prediction of postoperative complications in patients with end-stage HAE undergoing ALT.

Therefore, in this present study, the postoperative CDFI results of 27 patients with HAE who underwent ALT were analyzed in order to evaluate the clinical application of CDFI in the diagnosis of complications after the procedure of ALT. Our study might provide a new insight into clinical usefulness of CDFI.

Materials and methods

Patients

We described 27 patients (15 males and 12 females, mean age of 35.7 ± 11.8 years, range: 17-55 years) who underwent ALT at the Department of xxx in the First Affiliated Hospital of Xinjiang Medical University (Urumqi, China) between December 2013 and June 2015 for incurable HAE. Patients had no history of extrahepatic hydatidosis and all patients received liver resection *in vitro* and ALT. The diagnosis of HAE was confirmed by postoperative pathological examination and serology. The study was approved by the Ethics Committee of the the First Affiliated Hospital of Xinjiang Medical

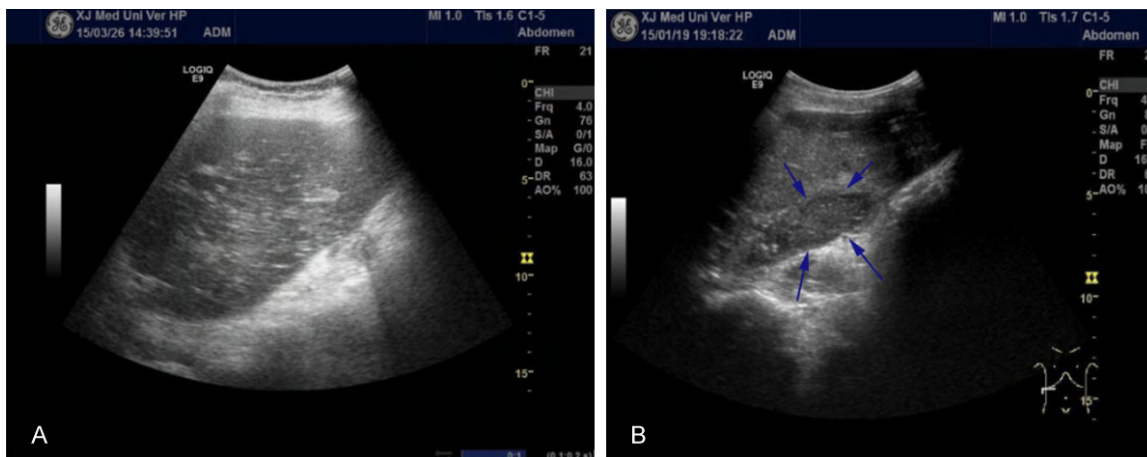


Figure 1. Abnormal liver parenchymal echogenicity. A. Diffuse change of abnormal liver parenchymal echogenicity at 10 days after surgery in a 30-year-old female patient; B. 40-year-old female patient with reduction of multi-slice echo-planar presented liquefaction necrosis (arrow) at 28 days after surgery.

University, and informed consent was obtained from each subject.

Postoperative CDFI examination and follow-up

All patients underwent first CDFI examination within 24 hours after the surgery to obtain baseline data. Daily CDFI was performed to all patients after first week of surgery, and this testing was repeated if necessary. For the second week, CDFI was performed every other day. Afterwards, CDFI was applied according to the patient's clinical manifestations, and laboratory test results. The average follow-up was 0.1-31 months (mean duration: 4.02 ± 6.37 months).

CDFI examination

CDFI examination was performed to all the subjects in supine or left lateral position with a LOGIQ E9 or LOGIQ S8 ultrasound system (GE Healthcare, Milwaukee, WI, USA) using a C1-5 convex transducer with the frequency of 2.5-5 MHz. Patients underwent the ultrasound examination after at least 8 to 12 h of fasting. The ultrasonographic examination included the following assessment: (1) The volume and morphology of the transplanted liver, the echo level of liver parenchyma; (2) The diameter, flow rate, frequency and resistance index of the hepatic artery, portal vein, and hepatic vein, and the presence/absence of stenosis, blood flow interruption, and the formation of collateral circulation; (3) The presence/absence of stenosis and

the condition of blood flow in the lumen of the inferior vena cava, and anastomotic stenosis; (4) The presence/absence of intrahepatic bile duct dilatation; and (5) Liver wounds, the presence/absence of empyema, ascites, and hydrothorax.

Statistical analysis

The data are presented as mean \pm standard deviation (SD) and percentage out of total numbers.

Results

The average number of ultrasound examinations was 8.3 ± 4.1 (range: 6-21). A total of nine different types of postoperative complications were observed in 25 cases among all the patients (**Table 1**).

Abnormal liver parenchymal echogenicity

Abnormal liver parenchymal echogenicity was noted in 12 patients (12/27, 44.4%) including five cases of diffuse change and seven cases of focal change. Of the five cases of diffuse change, four cases were identified within 3 days after the surgery, including two cases of local echo reduction and ischemic changes. In the remaining case, diffuse hepatic parenchyma echogenicity was detected at 10 days after surgery, and a reduced focal parenchymal echo and a clear boundary with the surrounding liver parenchyma was identified at 21 days after sur-

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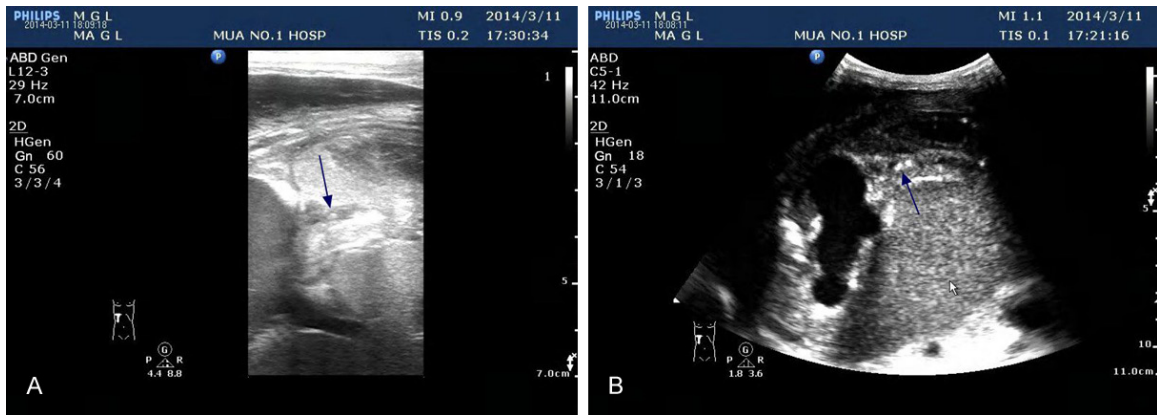


Figure 2. Biliary complications. A. A 27-year-old male patient developed into biliary embolism 2 months after the surgery. CDFI showed poor penetrability of the intrahepatic bile duct lumen (arrow), flocculent and lumpy medium echogenicity and upper bile duct dilatation; B. Biliary pneumatosis (arrow) were detected at 1 month after surgery in the same patient.

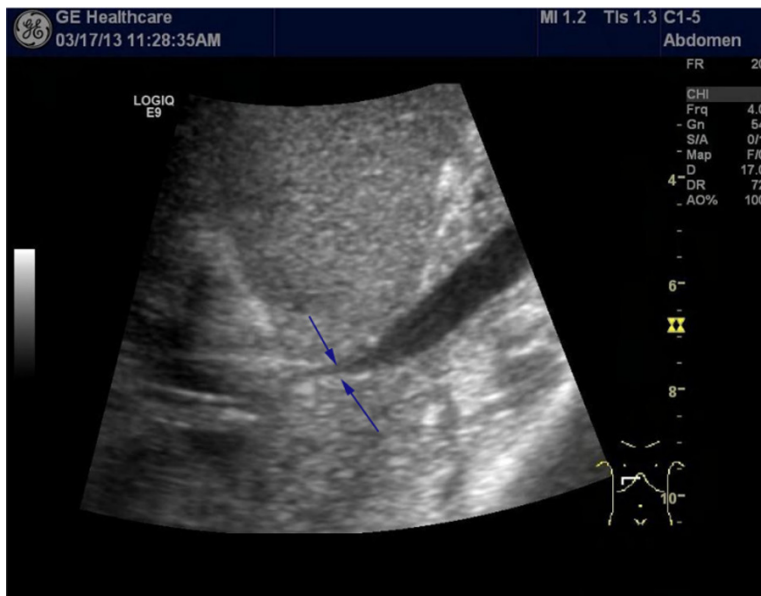


Figure 3. Portal vein complications. Anastomotic stenosis was detected in this case at 21 week after surgery in a 20-year-old male patient. Local amplification ultrasound image showed the local narrowing portal vein (arrow).

gery. Of the seven cases with focal change, there were 3 cases exerting a diffuse change in liver parenchymal echogenicity, followed by focal change. In the remaining four cases, multi-slice echo-planar reduction was detected with two cases presenting liquefaction necrosis (Figure 1A and 1B).

Biliary complications

There were a total of 4 patients (14.8%) presenting postoperative biliary abnormalities. One patient developed into biliary embolism 2

months after the surgery. The ultrasonographic examination exhibited poor penetrability of the intrahepatic bile duct lumen. Flocculent, lumpy medium echogenicity was detected, as well as upper bile duct dilatation (Figure 2A). One patient developed into biliary pneumatosis during the first month after surgery, and one patient presented hepatolithiasis at 1 month after surgery (Figure 2B). In the remaining case, intrahepatic bile duct dilatation was detected at 6 months after surgery. The stenosis was located at the hilar bile duct, and the patient subsequently underwent ultrasound-guided percutaneous transhepatic bile duct drainage.

Hepatic artery complications

Hepatic artery abnormalities were detected in four cases (4/27, 14.8%). Two cases showed an increased blood flow rate in the hepatic artery within 3 days after surgery. But the flow rate returned to normal by the 6th day and 11th day after surgery, respectively. One patient showed abnormal spectrum of hepatic artery (waveform and messy burr-shaped spectrum). For the rest one, no signal of blood flow was detected during the first ultrasonographic examination. All patients with hepatic artery abnormali-

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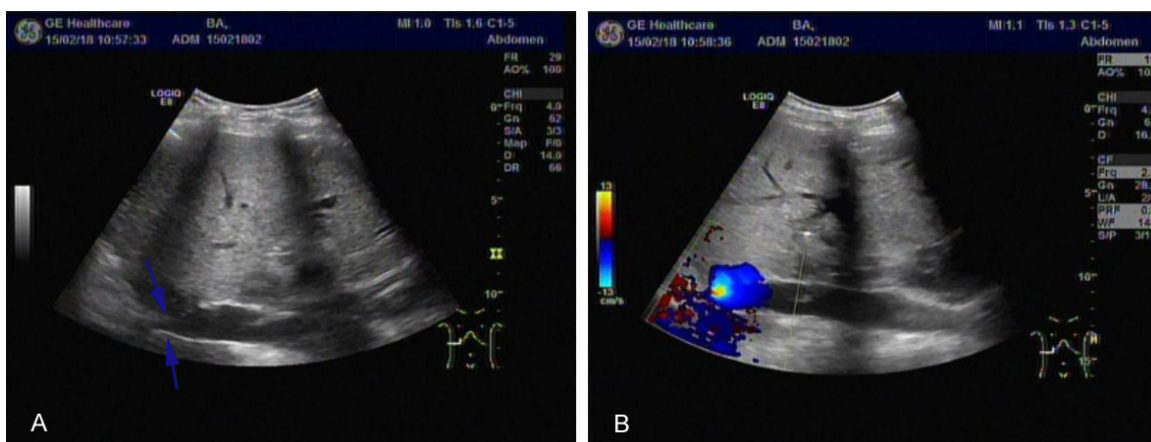


Figure 4. Postcava complications. A. The ultrasonogram showed anastomotic stenosis (arrow) with an inner diameter less than 0.7 cm in 51-year-old female patient; B. The upstream postcava lumen was broadened.

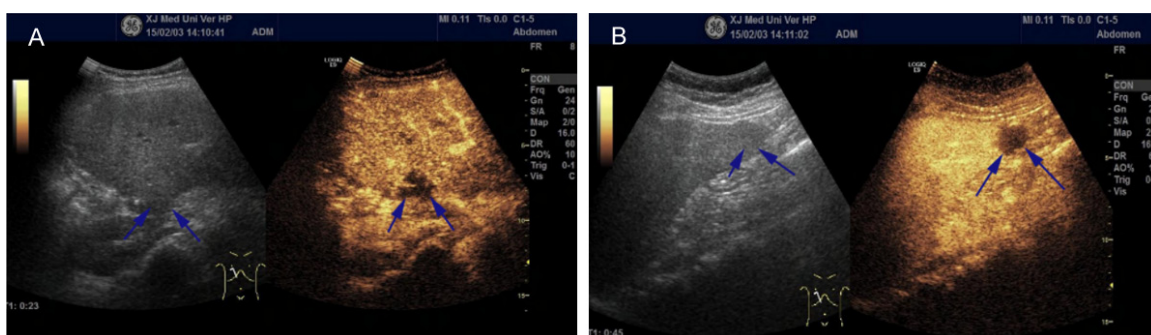


Figure 5. Recurrence. A and B. A 55 year-old female patient recurred at the 16th month after the surgery. Two alveolar hydatidosis lesions (arrow) were observed, with a diameter of 4.4 cm and 2.7 cm, respectively.

ties showed similar clinical manifestations such as different degrees of fever, jaundice, and increased total bilirubin (T-BIL) and aspartate aminotransferase (AST)/alanine aminotransferase (ALT).

Portal vein complications

A total of nine patients (9/27, 33.3%) developed into portal vein abnormalities including 5 cases of abnormal blood flow rate, 3 cases of anastomotic stenosis, and 1 case of mural thrombus. Among the 5 cases with abnormal blood flow rate, 3 cases revealed an increased portal vein blood flow rate after 3 days of the surgery, but returned to normal by the 7th day. Another two cases emerged decreased postoperative portal vein blood flow during the first day after surgery, and 1 case recovered the rate within 3 days and the other patient died. Moreover, anastomotic stenosis was detected in two cases within 3 days of after surgery and

in one case at 21 week after surgery (**Figure 3**). Besides, we found one patient showed mural thrombus in portal vein at 32 days after surgery with the hypoechoogenicity in the portal vein wall.

Hepatic vein complications

Hepatic vein complications were observed in two patients (2/27, 7.4%): one patient showed no blood flow signal in the hepatic vein and died within 2 days after surgery; and one revealed increased postoperative blood flow in the hepatic vein at the first day after surgery but had returned to the normal at day 10.

Postcava complications

Postcava complications were detected in three cases (3/27, 11.1%). One patient developed into postcava thrombosis, as suggested by a flocculent, mass-shaped hypoechoic area in the postcava lumen. In one case, anastomotic

stenosis was detected. The inner diameter was less than 0.7 cm (**Figure 4A**), with widened upstream postcava lumen and a bright signal of blood flow (**Figure 4B**). In one case, the signal was not detectable owing to a slow flow rate.

Others

Nineteen patients developed into ascites (19/27, 70.3%). Ascites were present in the graft wound area, right subphrenic region, right/left subhepatic region, and intersegmental fissure. Moreover, a total of 26 patients (26/27, 96.3%) developed into hydrothorax, and most of the hydrothorax was on the right side. One patient recurred at the 16th month after the surgery. Two alveolar hydatidosis lesions were observed, with a diameter of 4.4 cm and 2.7 cm, respectively (**Figure 5A** and **5B**). One patient developed into colonic fistula at the 8th day after surgery and received puncture and catheter drainage and anti-infective drugs, but died of multiple organ failure on day 43.

Death

A total of seven patients (7/27, 25.9%) died after liver transplantation: two died of intestinal fistula, one due to chronic liver failure, one own to acute liver failure, and three died of multiple organ failure.

Discussion

In the present study, we elevated the clinical application of CDFI in the diagnosis of postoperative complications in patients with end-stage HAE undergoing ALT. The results revealed that among the 27 patients, 25 patients revealed various abnormal ultrasonographic findings after ALT. Therefore, we concluded that CDFI is valuable for dynamic monitoring of postoperative complications in patients with end-stage HAE undergoing ALT, especially for the early stages after the operation.

ALT was first reported in 1990 for the treatment of primary or secondary carcinoma or benign liver tumors by Pichlmayer *et al.* [16]. Then, Sauvanet *et al.* improved and simplified the technique and achieved more satisfactory results [17]. Most patients with HAR showed no obvious clinical symptoms at the early stage. However, in late-or end-stage of the disease, large lesions often develop and converge towards to the porta hepatis, compressing the

intrahepatic vascular and biliary systems. These lesions cannot be completely removed by conventional surgery, and ALT has become the only way to be able to treat patients with end-stage inoperable HAE. Moreover, the contralateral liver underwent compensatory hyperplasia in 3-12 months, and can meet the needs of liver function in these patients. However, the surgery is involved in reconstruction of vascular and biliary tract and anatomical change of the hepatic artery and portal vein. Hence, various types of postoperative complications may occur early or late in the postoperative period, leading to a high perioperative mortality rate. Therefore, early diagnosis and treatment of postoperative complications is crucial for the success of ALT. CDFI is characterized by its high resolution and rapid diagnostic capability, which has been used as a convenient tool to detect changes in the organs or postoperative complications and/or risk factors after different types of operations including liver surgery [18-21]. In addition, it is particularly applicable for dynamic monitoring for patients who are in intensive care unit (ICU).

The ultrasonographic features of liver parenchymal abnormalities after ALT are similar to those in orthotopic liver transplantation [22]. In the present study, the incidence of abnormal liver parenchyma was 44.4% (12/27). Either focal or diffuse changes were detected in these cases, but the reasons were different. Focal changes were normally associated with local intrahepatic ischemia due to vascular anastomotic stenosis or vascular distortion. In our study, we found that the hypoechoic ischemic areas were all located at the edge of the liver parenchyma. However, in some cases, different types of hepatic artery anomalies concurrently developed with the liver parenchymal abnormalities. Changes of intrahepatic hemodynamics after early hepatic arterial perfusion leads to ischemia-reperfusion injury, and followed by ischemic necrosis. In addition, although hypoechoic ischemic areas were detected at the edge of the liver parenchyma, no hepatic artery abnormalities were observed, suggesting that CDFI is limited for detection of peripheral arteries. Therefore, contrast enhanced ultrasound (CEUS) can be used as an alternative to detect focal parenchymal ischemia.

It has been reported that the incidences of postoperative biliary complications were respectively 41.9% (161/384) and 24.5% (53/216)

in recipients who underwent living donor liver transplantation (LDLT) and deceased donor liver transplantation (DDLT), [23]. In contrast, in our study, the incidence of biliary complications after ALT was 14.8% (4/27). One of the main reasons for the lower incidence in our study might be the lower immunological rejection of organ transplantation. It is well known that biliary complications are associated with several factors such as repair of the residual liver, biliary anastomosis technique, biliary blood supply, ischemia-reperfusion injury, stenosis of bile duct, biliary tract infections, and impaired peribiliary vascular plexus [24-26]. In one of our patients, biliary sludge had been observed in the intrahepatic bile duct of the left lateral lobe, probably as a result of condensation of bile or the accumulation of collagenous tissue on the inner surface of the injured bile duct. Moreover, a concurrent early abnormal hepatic arterial spectrum and increased blood flow rate were also detected, suggesting that it is very important to ensure sufficient blood supply to the bile duct to prevent biliary complications.

Hepatic artery complication has been known as the most serious vascular complication after liver transplantation [27]. In this study, neither postoperative hepatic artery blood flow nor two-dimensional intraluminal thrombosis echo was detected in one case, which might be related to liver artery spasm due to prolonged hypoxia or the surgical procedure. Another patient exhibited burr-like changes in the ultrasonographic spectrum of the hepatic artery and the patient developed into focal parenchymal ischemic changes. A liver abscess was found after 60 days of surgery and died of secondary infection and multi-organ failure at 180 days after surgery. These findings suggested that hepatic arterial insufficiency may induce ischemic changes of the liver parenchyma and abnormalities of the biliary system.

In the present study, the complications in the portal vein and inferior vena cava were mainly anastomotic stenosis and thrombosis, which was in line with a previous study after liver transplantation [22]. It has been acknowledged that alveolar hydatid diseases often affect hepatic hilar [28], resulting in hilar adhesion. Therefore, it is hard to separate the adhesion area during surgery. Bypass is sometimes required in some patients with limited length of blood vessels. Anastomotic contracture or scar can also lead to anastomotic vascular stenosis. In this study, mural thrombus in portal vein and

inferior vena cava wall were detected in two cases. The results demonstrated that the thrombus can be easily formed owing to the rough intima and vortex flow near the anastomosis site, which should be checked carefully after surgery. Additionally, it is also critical to detect postoperative effusion formation. In contrast to conventional orthotopic liver transplantation, repair of the residual liver is a critical step. The liver wound hemostasis plays a significant role during the repair. Moreover, patients who underwent ALT are prone to develop blood coagulation dysfunction vascular ligature exfoliation, and incomplete intraoperative hemostasis, which can cause abdominal hemorrhage. Peritoneal effusion is easy to appear in subhepatic area, liver wound, right subphrenic and hepatic fissural. Dynamic ultrasound observation of changes in effusion range, together with the observation of effusion color, can effectively prevent intra-abdominal hemorrhage. Furthermore, recurrence of HAE was reported in one case, indicating the importance of postoperative follow-up.

Conclusions

In conclusion, CDFI is convenient and valuable for dynamic monitoring of postoperative complications in patients with end-stage HAE undergoing ALT, especially for the early stages after the operation.

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Disclosure of conflict of interest

None.

Address correspondence to: Tao Song, Department of Ultrasonography, The First Affiliated Hospital of Xinjiang Medical University, No. 137 Liyushan Road, Urumqi 830011, China. Tel: +86-1599912-3925; E-mail: doctorsongtao@163.com

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