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REVIEW ARTICLE

Recent advances in surgical strategies for alveolar echinococcosis of the liver

Toshiya Kamiyama[1]

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Abstract

Liver resection is the safest intervention for alveolar echinococcosis (AE), because the only potentially curative treatment is complete removal of the lesion. In combination with medical anthelmintic treatment, a safe distance of at least 1 mm is permissible in this procedure. Even when liver resection does not cure AE, good long-term survival outcomes can be achieved if most of the lesion has been removed and the disease is controlled with lifelong benzimidazole treatment. If the residual lesion is comparatively small and does not contain a closed space that may adhere to the surrounding tissue and form an abscess, complications such as sepsis arising from an abscess on the cut surface can be prevented and the required biliary drainage might be relatively simple. Larger AE lesions that invade the inferior vena cava can be treated effectively with the recent advances in reduction surgical techniques. An effective concentration of albendazole (ABZ) is found only in the periphery of AE lesions, because this drug penetrates the lesions passively. Liver transplantation, with adjuvant ABZ and the administration of appropriate immunosuppressive agents such as cyclosporin A, is indicated for patients with end-stage AE.

Keywords Alveolar echinococcosis · Liver · Hepatectomy

Abbreviations

AE	Alveolar echinococcosis
WHO	World Health Organization
IWGE	Informal Working Group on Echinococcosis
TNM	Tumor–node–metastasis
IVC	Inferior vena cava
ABZ	Albendazole
LT	Liver transplantation
LDLT	Living-donor liver transplantation
IS	Immunosuppressive status

Background

Alveolar echinococcosis (AE) is a zoonosis caused by the larval stage of *Echinococcus multilocularis*. Cystic echinococcosis (CE) is caused by *E. granulosus*. AE is prevalent in the northern hemisphere, including Central Europe and Japan, and many researchers have focused on its endemicity [1–3], whereas CE has a global distribution. However, over the past 2 decades, extensive epidemiological research has revealed a significant expansion of AE into Northern, Eastern, and Western Europe [4]. In Japan, a gene associated with AE was recently detected in the feces of wild dogs in Saitama Prefecture (2005) [5] and Aichi Prefecture (2018) [6], although Hokkaido was the previous endemic area. AE causes liver tumors that result in infiltrative growth and distant metastases. Clinically, AE behaves like a malignant tumor and the prognosis is generally poor. AE is a serious disease with a greater than 90% mortality rate in untreated patients [7]. Chemotherapy using albendazole (ABZ) and mebendazole and surgical hepatectomy are the accepted treatment options for AE. These drugs have contributed remarkably to the improved survival of patients with AE [8], particularly of those whose lesions cannot be removed completely [9, 10]. Although hepatectomy is currently the only curative treatment for AE, some lesions are too large at the time of diagnosis for complete resection; however, the surgical benefits of reduction hepatectomy in these patients are unclear. For patients with severe disease in which the lesions exceed the level of resectability or those with decompensated liver dysfunction caused by AE, liver transplantation (LT) gives the only possibility of survival and cure. The aim of the present review was to describe the effectiveness

✉ Toshiya Kamiyama
t-kamiya@med.hokudai.ac.jp

[1] Department of Gastroenterological Surgery I, Hokkaido University Graduate School of Medicine, North 5, West 7, Kita-ku, Sapporo 060-8638, Japan

of surgical therapeutic strategies, including hepatectomy and LT, as treatments for AE.

Hepatectomy for AE treatment

Hepatectomy offers the only curative treatment for AE if the lesions are completely resectable at their location of origin and liver function is well preserved by this procedure. According to many studies [11–14], complete resection of an AE lesion is curative and should always be the goal. Unfortunately, curative resection is not feasible for approximately 70% of patients at the time of AE diagnosis, resulting in a resection rate of only 20–40% [11, 12, 15].

The resectability of AE depends on the stage of disease and the number and size of the lesions, as well as the extent of invasion of neighboring organs, including the inferior vena cava (IVC), hepatic hilum, diaphragm, and retroperitoneal space. If AE has invaded the hepatic hilum, comprising the hepatic artery, portal vein, and biliary tract, surgery for hilum cholangiocarcinoma is required, which involves major hepatectomy and is technically challenging. Major hepatectomy is also required for very large lesions or lesions that have invaded the major hepatic vein (right, middle, or left hepatic trunk). The number and volume of AE lesions are important indicators for hepatic resection: if multiple lesions are present, major hepatectomy, multiple partial resection, or combined major and partial resection approaches are considered. When such surgery is necessary, precise evaluation of liver function and future remnant liver volume is essential. Specific criteria have been proposed by Japanese researchers to establish the resectability of the liver. These include the Makuuchi criteria, which are classified mainly based on the indocyanine green retention rate at 15 min [16, 17]. The resection criteria for AE are the same as that for other liver tumors. It was recently demonstrated that the future remnant liver volume could be calculated from the DICOM data obtained from computed tomography images using computer applications. If the rate of the resected liver volume to the whole liver is larger than ideal for a right

Table 1 Recent outcomes of surgical strategies for alveolar echinococcosis

Study	Total patients	Mortality (%)	OS (%) of all patients	Surgical strategy (*n*)	OS (%) or survival period according to surgical strategy		PFS (%) or time of recurrence according to surgical strategy	
Joliat et al. (2015) [14]	59	2	97% at 100 months	R0 (42)	NS		97.6% at 200 months	
				R1 (14) R2 (3)	100% during the follow-up (median: 84 months)		64.3% at 200 months 33.3% at 200 months	
Chen et al. (2018) [23]	115	3.5	NS	Radical (77)	94% overall median survival rate		NS	
				Transplantation (17)	81% overall median survival rate		NS	
				Non-radical (81)	70.6% overall median survival rate		NS	
Hillenbrand et al. (2017) [22]	92	0	100 at 20 years	SD: ≥ 10 mm (28)	NS		100% at 20 years	
				SD: > 1–10 mm (21)	NS		95% at 20 years	
				SD: 1 mm (10)	NS		90% at 20 years	
				SD: < 1 mm (33)	NS		61% at 20 years	
Buttenschoen et al. (2009) [28]	36	3	NS	Radical (18)	48 (15–277) months*		First relapse at 42, 54 months	
				Palliative (18)	184 (14–237) months*			
Kadry et al. (2005) [29]	113	NS	NS	R0 (46)	NS		NS	
				R1 (24)	NS		NS	
				Benzimidazole alone (43)	NS		NS	
Kawamura et al.(2011) [21]	182	0	NS	Complete resection (119)	98.9% at 10 years	98.9% at 20 years	96.5% at 10 years	94.4% at 20 years
				Reduction surgery (63)	92.8% at 10 years	61.9% at 20 years	87.1% at 10 years	61.4% at 20 years
Koch et al. (2003) [46]	45	2.2	49% at 10 years	Transplantation (44)	49% at 10 years		45% at 10 years	
Aydinli et al. (2015) [47]	27	22.2	77.8%**	Transplantation (27)	77.8%**		3.7%**	
Ozdemir et al. (2015) [48]	10	30	19.5%***	Transplantation (10)	19.5%***		Local recurrence 10%*** Distant metastasis 20%***	

OS overall survival, *PFS* progression-free survival, *SD* safe distance, *NS* not stated

*Interval between surgery and the last follow-up; median (min–max)

**After a mean follow-up of 16.1 months (range 6–39 months)

***Interval between surgery and the last follow-up; (min–max 0–54)

hepatectomy, extended right hepatectomy with right and left tri-sectionectomy and portal vein embolization is necessary for hepatectomy [16]. The reported operative mortality rates for patients undergoing hepatic resection were greater than 5% before 2000 [18]; however, recent data indicate substantial improvement in operative mortality, with rates as low as 0–0.1% [16, 19, 20]. The operative mortality rates of hepatic resection for AE were recently reported as 0–3.5%, excluding those of liver transplantation (Table 1) [14, 21–23].

Surgical indications for AE according to the WHO classification

The PNM staging system for AE was proposed in 2006 by the European Network for Concerted Surveillance of AE and the World Health Organization (WHO) Informal Working Group on Echinococcosis (IWGE) [24]. This staging system was based on the tumor–node–metastasis (TNM) system that is currently used to classify malignant tumors, and on the following three main factors. The P-factor defines the location and extension of the primary (original) parasitic lesion within the liver. The N-factor denotes the involvement of neighboring organs, that is, whether the larvae have spread to nearby tissues, including the lymph nodes. The M-factor indicates the presence or absence of metastasis, that is, whether the larvae have spread to distant areas of the body (Table 2). PNM staging comprises five stages: stages I, II, IIIa, IIIb, and IV (Table 3). The WHO IWGE recommends that the general indications to treat AE should principally follow the PNM staging in each case [25]. Accordingly, radical resection is limited to patients with P1N0M0 and P2N0M0 AE, in which the lesions do not extend beyond one lobe.

Table 3 PNM stage grouping of alveolar echinococcosis

Stage I	P1	N0	M0
Stage II	P2	N0	M0
Stage IIIa	P3	N0	M0
Stage IIIb	P1–3	N1	M0
	P4	N0	M0
Stage IV	P4	N1	M0
	Any P	Any N and/or	M1

Curative resection

The surgical procedures to treat AE are classified as R0, R1, and R2 (R0, no parasitic residue; R1, microscopic parasitic residue; and R2, macroscopic parasitic residue). R1 resection with a safety margin < 1 cm and possible microscopic remnants was recently reported to achieve an overall survival rate approximately equal to that of R0 resection, with nearly 100% disease-free survival rates achieved when this procedure was followed by continuous ABZ chemotherapy [21]. In a previous study by Joliat et al., the progression-free survival following R0 resection was 97.6% vs. 64.3% for R1 resection and vs. 33.3% for R2 resection at 200 months.

Table 2 PNM classification of alveolar echinococcosis

P	Hepatic localization of the parasite
PX	Primary tumor cannot be assessed
P0	No detectable tumor in the liver
P1	Peripheral lesions without proximal vascular and/or biliary involvement
P2	Central lesions with proximal vascular and/or biliary involvement of one lobe[a]
P3	Central lesions with hilar vascular or biliary involvement of both lobes and/or with involvement of two hepatic veins
P4	Any liver lesion with extension along the vessels[b] and the biliary tree
N	Extra hepatic involvement of neighboring organs [diaphragm, lung, pleura, pericardium, heart, gastric and duodenal wall, adrenal glands, peritoneum, retroperitoneum, parietal wall (muscles, skin, bone), pancreas, regional lymph nodes, liver ligaments, kidney]
NX	Not evaluable
N0	No regional involvement
N1	Regional involvement of contiguous organs or tissues
M	The absence or presence of distant metastasis [lung, distant lymph nodes, spleen, CNS, orbital, bone, skin, muscle, kidney, distant peritoneum and retroperitoneum]
MX	Not completely evaluated
M0	No metastasis[c]
M1	Metastasis

[a]For classification, the plane projecting between the bed of the gall bladder and the inferior vena cava divides the liver into two lobes

[b]Vessels refer to the inferior vena cava, portal vein and arteries

[c]Chest X-ray and cerebral computed tomography (CT), negative

After R0 resection, there was no intrahepatic recurrence and lung metastasis was identified in only 2% of the patients. After R1 and R2 resections, 41.2% (7/17, R1:5/14, R2: 2/3) of the patients exhibited intrahepatic disease progression, but none had extrahepatic lesions [14]. The disease in 64% of the patients with AE and R1 status was stabilized by long-term (> 1 year) benzimidazole treatment and the overall survival rate of the study cohort was 97% at 100 months after surgery. According to Chen et al., patients with all stages of hepatic AE should undergo active surgical interventions with radical hepatic resection considered as the first-choice treatment for early stage disease, while palliative surgery is still useful to relieve symptoms and improve the quality of life of patients with advanced AE [23]. Table 1 summarizes the recent outcomes of hepatectomy treatment for AE based on articles documenting survival rates.

From the perspective of the safety margin, 2 cm was previously recommended for radical resection as no recurrence was observed if the minimal distance was at least 2 cm [15]. However, that study was only a retrospective analysis and a surgical margin of this size would be difficult to achieve due to the anatomy of the Couinaud classification, IVC, and hepatic vessels. Moreover, because the reported outcomes of R1 resection combined with ABZ have been acceptable, a 2 cm margin may be not necessary. Hillenbrand et al. reported that a safe distance of at least 1 mm in combination with medical anthelmintic treatment for 2 years may optimize the chance of a good long-term disease-free outcome [22]. Further investigations are required to verify these results.

Palliative resection

Echinococcosis lesions can invade the hepatic hilum, IVC, and neighboring organs, in which case, the lesion may not be completely resectable and palliative resection may be performed. However, palliative surgery has been consistently associated with biliary drainage and liver abscess complications that impaired quality of life. Moreover, the reported outcomes of palliative surgery were not better than those of ABZ treatment [14, 26, 27]. Therefore, the use of surgical intervention, including palliative resection has decreased. Buttenschoen et al. [28] reported that the rates of surgical intervention for AE lesions have changed dramatically based on data from the WHO Collaborating Center. Between 1983 and 1999, the rate of R2 resection was reported to be approximately 79%, whereas between 2000 and 2006, it was only 7%. On the other hand, Buttenschoen et al. observed increased rates of R0 resection in patients with AE. Between 1983 and 1999, the rate of R0 resection was 21% and between 2000 and 2006, it had increased to 87%. Moreover, palliative resection for AE was performed in 18 patients between 1983 and 2006, 16 patients between 1983 and 1999, and 2 patients between 2000 and 2006. Of the 16 patients who underwent palliative resection between 1983 and 1999, 5 (31.25%) died, although neither of the 2 who underwent palliative resection between 2000 and 2006 died.

Severe postoperative complications derive from remnant lesions, including sepsis arising from abscesses on the cut surface and cholangitis. Kadry et al. reported that the long-term survival of patients who underwent debulking procedures ($p = 0.061$) and curative resection ($p = 0.002$) was better than that of patients treated with benzimidazole therapy alone [29]. However, after adjusting for the patient's age, year of initial treatment, and PNM stage, an increased survival rate was evident only for patients who had undergone curative resection. Debulking surgery resulted in higher progression rates than curative resection and the same rates of parasite-related complications as benzimidazole therapy alone. Hence, the authors concluded that debulking surgery was not advantageous for patients with AE. Because AE can be treated either alone or in combination with ABZ and nonsurgical treatment with biliary drainage, as endoscopic biliary drainage and percutaneous transhepatic biliary drainage [30, 31], clinicians believe that palliative surgery should be avoided because of the high prevalence of complications [32]. Moreover, the rates of AE recurrence ranged from 2 to 25% after either inadequate cyst removal or the growth of previously undetected cysts [11].

Because the volume of the AE lesion reduced by debulking surgery was not described in the aforementioned reports, residual lesions with a substantial volume might have affected the surgical outcomes. If the residual lesion is comparatively small, complications, including sepsis arising from an abscess on the cut surface, might be prevented because of the lack of a closed space adhering to the surrounding tissue that might result in an abscess, and the required biliary drainage might be relatively simple. Although conservative approaches are less technically demanding, radical approaches, including resection, result in better outcomes with less chance of recurrence when performed by experienced surgeons. Resection, as either hepatectomy or total cystopericystectomy, rather than partial cystectomy and drainage, is currently the procedure of choice for liver hydatid disease [33]. Recent reports have also described technical developments in the hepatectomy procedure for malignant liver tumors that involve external circulation, including veno-venous bypass [34, 35]. A combination of liver resection and reconstruction of the IVC is feasible in a certain subset of patients, with acceptable morbidity and mortality rates and reasonable long-term results [36]. Hence, large AE lesions invading neighboring organs and the IVC can now be resected with low mortality rates [37]. Huang et al. reported the successful treatment of a case in which the IVC was occluded, with stricture of the biliary tree and portal vein at the hilum [38]. A combination of liver

resection and reconstruction of the IVC can be performed safely in certain patients with in situ, ante situm, and ex vivo resection [39]. However, controversy exists about whether IVC resection is justified for patients with hepatic echinococcosis, particularly CE [40]. Over the last 10 years, the outcomes of palliative treatment for AE have been satisfactory and almost comparable to those of complete resection (Table 1). In a report by Kawamura [21], a reduction rate of more than 90% was recommended for AE lesions in reduction surgery and the importance of postoperative ABZ was stressed. Because ABZ sulfoxide enters *E. multilocularis* cysts passively, an effective concentration of ABZ may not reach the center of an AE lesion [41]. ABZ may be more effective if the remnant AE lesion is smaller, when more effective levels of ABZ sulfoxide are obtainable. When a relatively large lesion remains, ABZ is less effective because the required concentration levels may not be obtained.

Repeated complications from biliary drainage following palliative surgery may be overcome by recent developments in radiological and endoscopic techniques and equipment. If very large hepatic lesions comparable to cysts remain, these should not be managed by tube drainage because of the high viscosity of the content, which can lead to sepsis as a result of infection and abdominal distension. This complication can result in anorexia and general fatigue, and impair the patient's quality of life. After late biliary complications develop in patients with unresectable AE, the median survival is only 3 years, which shows that these complications lead to a poor prognosis [30]. In another study, the average survival following the onset of hepatobiliary complications and interventional treatment was 8.8 years [31]. Reduction surgery removing greater than 90% of the tissue, as recommended by Kawamura et al., is necessary and could alleviate the symptoms of abdominal distension related to a large mass and delay the onset of late biliary complications. Even if the biliary tract remains obstructed, this can be treated with an internal and/or external fistula with tube stents due to the remarkable recent progress of radiological and endoscopic techniques for biliary drainage. However, for some patients, bile drainage might be necessary as a permanent external drain that is changed regularly to prevent obstruction. Chen et al. reported that palliative surgery is still helpful to relieve symptoms and improve the quality of life of patients with advanced AE [23].

Adjuvant chemotherapy using albendazole

The drugs that are generally used to treat AE are benzimidazoles, ABZ, or mebendazole. The 'Expert Consensus 2010' guidelines [25] recommend these drugs as systematic chemotherapy for all patients with AE. ABZ is the drug used most commonly to treat AE and is given intermittently from the initial presentation. Continuous ABZ treatment of AE is recommended based on reports that it is well tolerated and has been taken for more than 20 years by some patients; therefore, intermittent treatments should no longer be given. In terms of the adjuvant use of ABZ, the Expert Consensus 2010 report states that irrespective of the type of procedure, concomitant benzimidazole treatment is mandatory for at least 2 years. When the lesions are completely removed, a 2-year course of ABZ is recommended. When complete resection is not performed, the patient must take ABZ for the rest of their life. Ishizu et al. reported favorable responses to ABZ [10], such as decreases in lesion size, changes in cyst morphology, and amelioration of clinical symptoms or signs, in 11 (55%) of the patients they evaluated. They also observed these effects in AE patients who had undergone noncurative resection and palliative surgery and concluded that palliative or mass reduction surgery combined with ABZ therapy may be a viable strategy for patients with advanced disease, particularly when complete resection might result in morbidity or mortality.

Kawamura et al. reported on the surgical outcomes of complete resection in patients with AE. The progression-free survival rates recorded 10 years after ABZ had been administered for 1 year postoperatively were described as favorable, with a 95% rate for patients who had undergone reduction surgery, and with 90% of patients treated with lifelong ABZ showing a comparable rate [21]. Joliat also recommended a combination of surgery and ABZ treatment [14]. Hence, when dissection of an AE lesion is not radical but palliative, lifelong ABZ is recommended.

Notably, side effects have been reported with the continuous administration of ABZ. Because the ABZ sulfoxide level in human plasma is typically measured using liquid chromatography–tandem mass spectrometry [42], clinicians can assess patient adherence to treatment by evaluating drug efficacy/blood concentrations, as well as side effect/blood concentration ratios [43]. Plasma ABZ sulfoxide levels must be monitored to assess adherence to treatment. The effective serum ABZ sulfoxide levels are estimated to be an average of 1–3 μmol/L, 4 h after the morning drug intake, which appears to be a good balance between activity and toxicity [25]. Based on unpublished data showing that the concentration of ABZ in AE lesions should be higher than that in plasma, Vuitton et al. supported reducing the dose of ABZ because of side effects [44].

Transplantation for AE

Indications and outcomes of LT for AE

Because of the high overall operative mortality rate of patients with AE in previous studies, strict criteria for

surgical intervention have been established. Now, dissections are performed only if fewer than three segments are involved, the hepatic hilum is not extensively involved, and the IVC has not been invaded [45]. LT has been performed for patients with AE not meeting the criteria for hepatectomy, namely, those with inoperable lesions and/or chronic liver failure. Brunetti et al. described the following conditions that qualify patients with AE for LT [25]: severe liver insufficiency (secondary biliary cirrhosis or Budd–Chiari syndrome) or recurrent life-threatening cholangitis; ineligibility for radical liver resection; and the absence of an extrahepatic AE location.

Koch et al. evaluated 45 patients with AE from 65 European centers, who underwent LT [46]. The analysis was performed on 44 patients who underwent transplantation. They reported a 5-year survival rate of 71%, but LT was curative in only 50% of these patients. Twenty patients (45%) died, including three with AE recurrence in the brain, one with pulmonary recurrence, and one with liver graft failure. Aydinli et al. reported the clinical characteristics and outcomes of LT in 27 patients with AE [47]. Most of these patients underwent living-donor liver transplantation (LDLT), and the overall survival rate was 77.8% after a mean follow-up of 16.1 months. No local AE recurrence was detected in the cohort, but one patient suffered cerebral AE recurrence approximately 1 year after LT. Although the operative mortality rate was 22.2% (6/27 patients), with death caused by *Klebsiella* sepsis (3 patients), intracranial hemorrhage (1 patient), and primary nonfunction (2 patients), no deaths were attributed to recurrent AE. Ozdemir et al. reported an analysis of ten patients who underwent LDLT for AE [48]. The mean survival time was 19.5 months (range, 0–54 months) and the mortality rate was 30%. In this series, local recurrence developed in one patient and distant metastatic lesions were detected in two patients (Table 1).

The success rate of LT for AE with invasive characteristics was much lower given that the surgery is considerably more difficult. The outcomes also differ from those of LT for cirrhosis and the mortality rates are high. The intracystic abscess and cholangitis caused by AE must be treated first with medical and percutaneous methods before transplantation is attempted, to decrease the difficulty of the operation and reduce the postoperative mortality rate [47]. On the other hand, because benzimidazoles can control residual/recurrent AE lesions after LT, the risk of recurrence, particularly in patients with residual or metastatic AE lesions, should not be regarded as a contraindication for LT when AE is considered fatal in the short term [43]. High doses of immunosuppressive drugs, the late introduction of benzimidazoles, withdrawal of benzimidazoles due to side effects, and nonadherence to this therapy are all factors that adversely affect the prognosis.

Immunosuppression after LT for AE

LT for AE has one specific problem: the regrowth or recurrence of lesions caused by immunosuppression. Immunosuppressant therapy also results in an increase in the size of metastases. The immune status of the intermediate host is crucial for the development of the metacestode. In humans, immunosuppression may enhance silent lesion growth and increase the rate of progression. In the French AE registry (1982–2012, 509 cases), AE was more frequently an incidental finding (78% vs. 42%) and was diagnosed at earlier stages (41% vs. 23%) in patients with immunosuppressive status (IS)/AE than in patients with non-IS/AE. The patients with IS included 30 with cancer, 9 with malignant hematological disorders, 14 with chronic inflammatory diseases, 5 transplant recipients, and 1 with acquired immune deficiency syndrome [49]. Rituximab-induced B-cell depletion may have contributed to the negative serology in some of the patients who underwent LT for AE, as reported in renal transplant recipients. Rapidly progressive hepatic AE was observed in an ABO-incompatible renal transplant recipient [50]. However, not all immunosuppressive agents are likely to enhance the progression of AE lesions, as outlined in the following case report.

A patient with AE, who was commencing TNF inhibitor treatment, was found to have small hepatic cysts on sonography performed by the treating rheumatologist. About 6 months later, the patient started losing weight and 2 months after that, a painful mass developed in the right upper abdomen. The immunosuppressive agent was changed from etanercept to abatacept and cyclosporin A (CsA) in combination with albendazole. The size of the lesion decreased, indicating that abatacept is safe to use in combination with albendazole [51]. CsA was reported to kill *E. granulosus* protoscoleces in vitro *[*52]. All activated protoscoleces were killed in the culture following exposure to 100 μg/ml of CsA for 3 days or 50 or 20 μg/ml of CsA for 5 days.

The progression of AE caused by immunosuppressive agents has limited the clinical practice of performing allogeneic LT to treat this condition. On the other hand, immunosuppressive agents are not required for ex vivo liver resection and autotransplantation, which is an alternative approach to allogeneic LT that has been used successfully in many patients [53]. The major indications for ex vivo liver resection are an unresectable lesion that has invaded the hepatocaval region involving three hepatic veins and the retrohepatic vena cava, and that has also invaded the tertiary portal and arterial supply. These conditions require complex reconstruction and an extended duration that the liver cannot tolerate.

Conclusions

Hepatic resection is considered safe and the only curative treatment for AE when the lesion is able to be removed completely. Even if resection is noncurative for AE, good long-term survival and stabilization of the disease can be achieved with benzimidazole therapy if the lesion volume is reduced by 90%. Very large AE lesions that have invaded the IVC and neighboring organs can be treated by reduction surgery due to the recent advances in operative techniques. LT, along with adjuvant benzimidazole and appropriate immunosuppressive therapy, is indicated for patients with end-stage AE. However, current reports on hepatectomy for AE are based on a retrospective design and a relatively small sample size. Therefore, large-scale, multi-institutional studies of patients with AE across international boundaries are needed.

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Compliance with ethical standards

Conflict of interest No potential financial or other conflicts of interest are declared. No financial support was received.

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