

## Original Article

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## Long-term experience with debulking surgery in extensive hepatic alveolar echinococcosis: A case series and literature review

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## ABSTRACT

**Objective:** To assess the role of debulking surgery in extensive hepatic alveolar echinococcosis (HAE).

**Methods:** Five cases of extensive HAE undergoing debulking surgery with their long-term follow-ups were reported. Additionally, a systematic review was carried out.

**Results:** The average age of patients in the study was (50.8±17.1) years (range 36 to 77 years). Three cases were female. The median follow-up period was 61 months (range 12 to 84 months). Left liver resections were performed in 2 cases and right hemihepatectomies were undertaken in 2 cases. Two patients (cases 2 and 4) developed early surgical complications, while one of them (case 4) who suffered from the recurrent sub-hepatic abscess died at 12 months postoperatively.

**Conclusions:** This study highlights the importance of debulking surgery for the management of complex symptomatic HAE lesions in patients with no curative option available.

**KEYWORDS:** Alveolar echinococcosis; Debulking surgery; Reduction; Palliative; *Echinococcosis multilocularis*; Case series

## 1. Introduction

Hepatic alveolar echinococcosis (HAE) is a considerably fatal infection seeded by the larvae of tapeworm *Echinococcus multilocularis*. HAE essentially affects the liver as a malignant tumor-like lesion, with devastating tissue growth often invading neighboring structures and metastasizing distant organs[1–3]. HAE mainly affects the liver, it can also affect the lung, diaphragm, lymphatics, peritoneum, spleen, or bone[4]. The introduction of benzimidazoles (BZM) has significantly improved the prognosis of patients with HAE, with survival rates rising near that of healthy controls (80%-89% improvement in outcomes)[5]. However, surgical

resection still remains the pillar of treatment of extensive HAE infections[6–8]. Unfortunately, patients with extensive lesions are receptive to cure in only one third of all cases upon diagnosis, and those deriving benefits from surgery are limited[9].

Based on the World Health Organization (WHO) recommendation, radical resection of the entire parasitic lesion is the standard of curative treatment; but whether it should include vast resection of neighboring organs or distant metastases remains unclear[10]. As conservative modalities have progressed, the role of palliative surgical procedures has to be redefined[11]. Recent studies have shown that overall survival after debulking is estimated within 50%-97% based on the follow-up period[12].

Western studies are deficient, and include a combination of debulking, medical treatment with BMZ, and radical resection[7,13]. Conflicting results are based on heterogeneous series reporting different surgical approaches which have been attempting to close the gap of knowledge.

## Significance

In advanced stages of hepatic alveolar echinococcosis (HAE), debulking of the parasitic mass can be an effective alternative. There is scarcity of data on the role of palliative surgery. In this study, over 10 years, the outcomes of debulking in HAE were almost equivalent to complete resection. With exclusion of two cases, three stayed asymptomatic in an average 61 months of follow-ups.

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We present our experience with 5 cases of HAE who underwent debulking surgery and their long-term follow-ups.

## 2. Patients and methods

### 2.1. Introduction of 5 cases

This case series has been reported in line with the PROCESS Guideline. All cases were symptomatic, presented with a confirmed diagnosis of HAE, based on preoperative imaging [computed tomography (CT) scan] and preoperative specimen analysis. A short description of patients' manifestations and their follow-up is summarized in Table 1.

Debulking (incomplete resection) is defined as surgical removal of as much of a pathological tissue as possible. The scope of surgical interventions was based on the removal of HAE mass with preservation of healthy and functional liver tissue, including anatomic and non-anatomic hepatic resections [Two cases of left lobectomy (case 1 and case 5); two cases of right lobectomy (case 2 and case 4); and segmentectomy in case 3].

Patients who were submitted to debulking received albendazole 10-15 mg per kg of the body weight per day for the lifetime period.

### 2.2. Ethical approval

This study was conducted and approved by the ethics committee of Mashhad University of Medical Sciences, Mashhad, Iran (IR.MUMS.fm.REC.1396.460); and the written informed consents were received from all patients.

### 2.3. Literature review

#### 2.3.1. Search strategy

MEDLINE, Scopus, Web of Science databases, and Google Scholar were searched for published articles up to the 31st of December 2021. Different combinations of the following key terms were searched: alveolar echinococcosis, echinococcus multilocularis, liver surgery, liver resection, debulking.

#### 2.3.2. Selection criteria

Studies providing information on liver resection in HAE were included. For references that seemed to meet the criteria, the full text was retrieved. Two independent investigators screened full texts of the included publications. We included English-language publications, which were based on specifically debulking as the surgical modality of treatment for HAE. Studies with insufficient data or studies in which patients underwent any other treatment modalities were excluded.

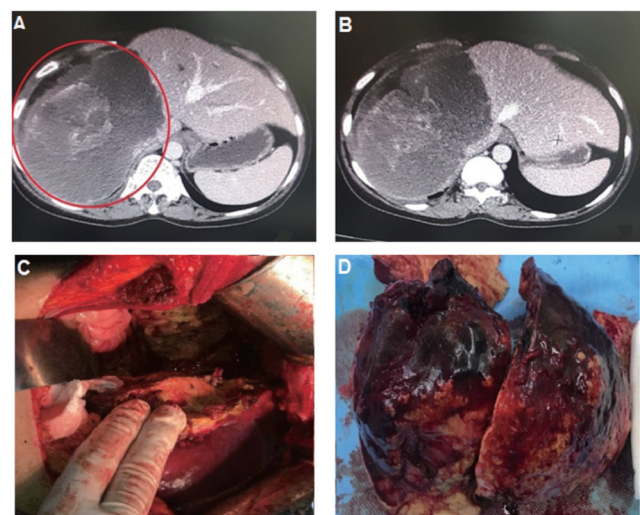
A recent clinical classification of HAE was used to stage primary lesion, neighboring organs, and metastases[14]. Additionally, we employed the stage classification of HAE as previously reported by Sato *et al*[15].

## 3. Results

### 3.1. Clinical case presentations

Case 1: A 36-year-old woman presented with dyspepsia and epigastric pain. Abdominal CT scan revealed an infiltrative solid mass in the hepatic left lobe with a central 70 mm × 45 mm × 45 mm cystic part. In June 2014, she underwent a left hepatectomy. Invasions to the pericardium, diaphragm, Inferior Vena Cava (IVC), and hepatic veins were noted intraoperatively. Multilocularis hydatid cyst was confirmed by pathological evaluation. In the postoperative CT scan, a 35 mm × 82 mm × 30 mm cystic lesion had remained in the right lobe and right sub-diaphragmatic area; however, at 84 months of follow-up, she had not developed any symptoms and the lesion remained stable in size.

Case 2: A 46-year-old woman presented with nonspecific abdominal pain. Abdominal CT scan confirmed a 133 mm × 102 mm × 160 mm mass with cystic and necrotic central area displacing the right lobe inferolaterally. The mass tightly adhered to the hepatic veins and diaphragm. Due to vascular invasion, the complete resection was not technically possible; thus debulking surgery was performed with a margin of 10 mm from the healthy liver. Postoperatively, the patient developed a wound infection and a subhepatic abscess that required additional intervention. At 60 months of follow-up, the patient remained asymptomatic with a small lesion in the left lobe <6 mm (Figure 1).



**Figure 1.** A and B CT scan shows multilocularis hydatid cyst in the right lobe of the liver in a 46-year-old female (Patient #2) with infiltration of hepatocaval area and diaphragm. C and D show right hepatic lobectomy.

**Table 1.** Patients' characteristics and operative parameters.

Case No.	Sex/age (years)	Date of surgery	Lesion area	Lesion size (mm)	Invasion	Margin (mm)	PNM staging I	Operation	Postoperative complication	Residue/recurrence	Survival	Clinical assessment	Further surgery
1	Female/36	June 2014	Left lobe	70×45×45	Pericard/diaphragm/ Inferior Vena Cava and hepatic vessels	NA	III b	Left hepatectomy	-	35×82×30 mm in right lobe	No symptom	Alive (7.5 years)	-
2	Female/46	June 2016	Right lobe	133×102×160	Hepatic vessels /diaphragm	5	III b	Partial right lobectomy	Surgical site infection/ subhepatic collection	<6 mm in left lobe	No symptom	Alive (5.5 years)	-
3	Male/58	May 2017	Right lobe (seg V, VI) left lobe (seg II, III)	70×55×50	-	18	III a	Segmentectomy	-	Normal findings	No symptom	Alive (4.5 years)	-
4	Male/77	June 2019	Right lobe abscess and mass	130×80×55	Hepatic vessels	NA	III b	Partial right lobectomy and drainage of abscess	Subhepatic collection	84×70 mm, and 95×83 mm	Died	Died due to sepsis (June 2020)	-
5	Female/37	July 2015	Left lobe	150×70×60	-	10	III a	Left hepatectomy	-	54×43×12 mm before liver transplantation	No symptom	Alive (5.5 years); Died due to sepsis caused by recurrent pulmonary transplantation and hepatic abscess (Jan 2021)	Liver

I PNM stage (P, hepatic parasite localization; N, neighbouring structure involvement; M, metastases).

**Table 2.** Patients characteristics and demographic of eligible studies.

Author (publication year)	Country of origin	Time frame	Sample size (n)	Reductive surgery group (n)	Mean age in reductive surgery group (years)	Recurrence rate in reductive surgery group	Overall survival in reductive surgery group
Emre et al. (2003)[16]	Turkey	1990-2000	32	1	NA	N/A	N/A
Kadry et al. (2005)[7]	Switzerland	1976-2003	113	24	49	11/24	19/24 during the follow-up (median: 12.3 years)
Buttenschoen et al. (2009)[6]	Germany	1982-2006	36	18	NA	N/A	184 (14-237) months
Kawamura et al. (2011)[12]	Japan	1984-2009	188	63	53	87.1% at 10 years, 61.4% at 20 years	92.8% at 10 years, 61.9% at 20 years
Joliat et al. (2015)[10]	Switzerland	1992-2013	59	3	60	41%	100% during the follow-up (median: 84 months)
Du et al. (2016)[17]	China	2004-2015	144	60	41.50	N/A	5-year: 89.7% and 10-year: 73.4%
Grüner et al. (2017)[18]	Germany	1992-2011	312	50 (R2 resection)	N/A	52%	N/A
Qu et al. (2017)[19]	China	1998-2009	42	15 (palliative resection)	40.53	N/A	1-year: 86.7% 3-year: 53.3% 5-year: 40.0%
Chen et al. (2018)[20]	China	2004-2016	115	17	47	N/A	70.6%

Case 3: A 58-year-old man presented with a history of vague abdominal pain. Abdominal CT scan demonstrated a 70 mm × 55 mm × 50 mm mass involving the segments V and VI of the right lobe plus segments II and III in the left lobe of the liver. Due to the difficult access to the anatomical plane of the tumor, he received atypical resection in the form of debulking. The mass vanished in the postoperative CT scan and the patient remained asymptomatic, with no evidence of recurrence in 48 months postoperatively.

Case 4: A 77-year-old male patient presented with a history of fever and malaise as well as few hepatic necrotic lesions in the abdominal ultrasonography. The percutaneous liver biopsy confirmed an infection from *Echinococcus multilocularis*. Abdominal CT scan revealed a 130 mm × 80 mm × 55 mm mass compounded with abscess formation, involving the right lobe of the liver with invasions of the hepatic veins. The patient underwent a partial right lobectomy as well as abscess drainage. At a 6-month follow-up, the patient still suffered from night fevers and was diagnosed with recurrent intra-abdominal abscess; hence he underwent a re-operation for drainage. Unfortunately, the patient was not compliant with post-operative recommendations and follow-up; and one year later, eventually he died in an episode of septic shock caused by a recurrent intra-abdominal abscess.

Case 5: The last case was a 37-year-old woman with the initial diagnosis of HAE, based on pathological evaluation of liver biopsy. Due to the extensive lesion involving the left lobe and partially right lobe of the liver, she received an extended left hepatectomy. Postoperative CT scan revealed a 54 mm × 43 mm × 12 mm residual lesion. Due to extensive loss of liver parenchyma, she underwent

liver transplantation at 12th month of post-operation.

The average age of patients in the study was (50.8±17.1) years (range from 36 to 77 years). The median period of follow-up was 61 months (range from 12 to 84 months). Three cases were female. A single lesion was detected in 80% (4/5) patients, as well as multiple lesions in one case (case 3) with the involvement of multiple segments. Three cases had invasions to adjacent structures, including IVC and hepatic veins. Since the entire resection of the pseudotumor was not feasible in present cases, the operations were performed based on initial palliative intentions. Left liver resections were performed in 2 cases and right hemihepatectomies were undertaken in 2 cases. Two patients (cases 2 and 4) developed early surgical complications, while one of them (case 4) who suffered from the recurrent sub-hepatic abscess, died at 12th month postoperatively.

In brief, the most common stage in the screened patients was stage III b (60%, 3/5) in those with adjacent vascular invasions, followed by stage III a in 40% (2/5) of patients. One case (case 5) underwent liver transplantation one year after initial debulking surgery. None of our cases had developed distant metastasis.

### 3.2. Literature comparison

The initial search retrieved 45 records from different sources. After removing 16 duplicates, 33 eligible records were screened *via* title and abstract review. Excluding 16 irrelevant studies and adding 6 records by manual searching, the full-text articles of 23 records were reviewed, of which 14 were excluded due to study design (2 systematic reviews) and different treatment modalities (8 studies

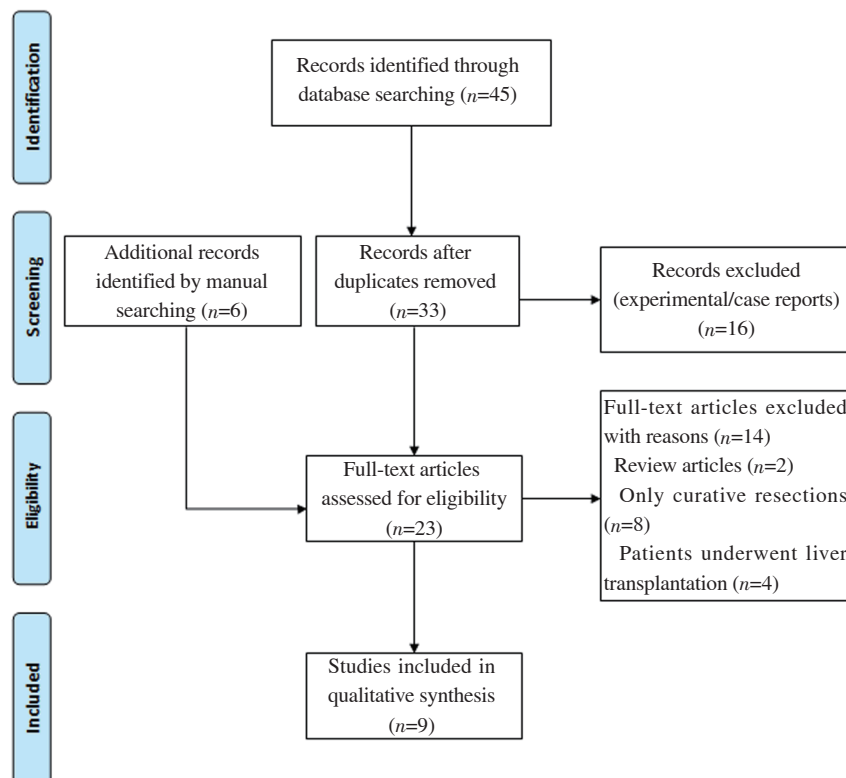


Figure 2. PRISMA flowchart of the study.

assessed only curative intentions, 4 studies evaluated only liver transplantation). Finally, 9 studies with a pooled population of 251 patients with alveolar echinococcosis who specifically underwent debulking surgery were included in this literature review (Figure 2).

Characteristics of the included studies, including first author and publication date, country of origin, time frame, total sample size, and explicitly debulking surgery sample size, as well as patient demographics in debulking group and recurrence rate and overall survival in population are illustrated in Table 2.

#### 4. Discussion

Clinical aspects of HAE are restricted by its scarcity accompanied by the subsequent insufficiency of patients in a timeframe. Herein, available evidence on potential debulking resections was reassessed. Such approaches ought to be claimed in the background of available data across diverse healthcare systems[12].

Predominantly, these lesions potentially invade the hepatocaval structure and adjacent tissue, where the parasitic process has progressed to an unresectable stage at the time of diagnosis. Nevertheless, resections even if incomplete are suggested to decompress the biliary system or restrain a huge mass. Palliative reduction combined with BMZ therapy may be a treatment strategy, especially when radical resection might lead to significant morbidity and mortality[10,20,21].

The most extensive surgical series issued previously was a study by Kawamura *et al.*[12]. who showed the debulking surgery, removing more than 90% of the lesion volume, is essential and could alleviate the symptoms caused by a large mass and postpone the biliary complications. The overall survival rate after reductive surgery was reported approximately 92.8% based on a 20-year follow-up (Table 2). Although the tumor size, portal and hepatic vein invasion, lung lesions, and curability were measured as risk factors negatively impacting survival, only curability, defined as complete resection, was an independent factor in multiple analyses.

Since the 10-year survival rate of HAE cases that received debulking surgery was shown to be just around 73.4% in 1980s[17], treatment for HAE has progressed dramatically.

Based on information of the WHO Collaborating Center, Buttenschoen *et al.*[6] highlighted the significant changes in the rate of interventions performed for the hepatic cysts. Before the 2000s, the rate of debulking was detailed to be roughly 79%, while this rate dropped to 7% by 2006. On the other hand, only 2 patients received palliative resection between 2000 and 2006, in comparison to 16 cases prior to 2000.

Since the extent of the HAE lesion reduced by debulking was not outlined in the aforementioned series, residues with a considerable volume could have impacted the survival. Thus, residual lesion

might lead to formation of an abscess which could be potentially treatable[10,21].

We applied the debulking approach for the extensive HAE lesions based on the vast lesion size and its invasion to neighboring structures in this existing case series. Over 10 years, the main results of reductive resection for HAE have been acceptable and approximately equivalent to those of radical resection. In this study, with the exclusion of one case that died at 12-month postoperatively and one that needed liver transplantation, the rest of cases stayed asymptomatic during an average of 61 months of follow-up (60%, 3/5).

Over the years, strategies have switched from palliation to more curative plans. Although most studies observed no significant benefits for debulking strategy in comparison to the medical treatment, some paradoxically presented higher prevalence of recurrence and complications[6,7,20].

Kadry *et al.*[7] stated the long-term survival of cases undergoing debulking ( $P=0.061$ ) and radical resection ( $P=0.002$ ) was better in comparison with those treated with medical treatment alone. Debulking surgery yielded higher recurrence rates than radical resection; thus, the authors came to the conclusion that debulking cannot be rewarding for all patients with HAE.

On the other hand, reductive surgery has been closely linked with complications induced by the biliary infections[10,21]. In our experience, two patients developed postoperative complications, of whom only one case died due to sepsis caused by recurrent hepatic and sub-hepatic abscesses.

Patients included in recent studies often undergo liver transplantation as a surrogate to palliative surgery for late stages with numerous biliary complications. Likewise, early recurrence post-transplantation notably restrained the results[10,22].

In our previous attempt, we showed that liver transplant with pre- and post-operative BMZ shown to be advantageous for morbid HAE[23]. In this case series, one case underwent liver transplant 12 months after initial reductive surgery.

Further investigations should deal with the disease severity as a relevant confounding, plus the indication of surgery arisen from applied conservative strategies.

In conclusion, debulking of extensive hepatic HAE lesions, especially in cases of central necrosis and abscess formation, in combination with BMZ, should be considered in symptomatic patients as it could be associated with long symptom-free interval and stable disease.

#### Conflict of interest statement

The authors declare that they have no conflicts of interest and nothing to disclose.

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## Authors' contributions

M.A and S.S. did the concept and design of the study; S.S. did data acquisition; S.S and M.D did statistical analysis; S.S. analyzed the data and drafted the manuscript. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

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