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A pooled analysis of treatment and prognosis of hepatic angiosarcoma in adults

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ABSTRACT

Background: Hepatic angiosarcoma is a rare malignant vascular tumor presenting unique treatment challenges. The aim of the present study was to determine the treatment and prognosis of this entity.
Data sources: A systematic literature search was conducted using PubMed, Embase and Chinese Biomedical Literature database, to identify articles published from January 1980 to July 2017. Search terms were "hepatic angiosarcoma" and "liver angiosarcoma". Additional articles were retrieved through manual search of bibliographies of the relevant articles. Pooled individual data concerning the prognosis following various therapeutic modalities were analyzed.
Results: A total of 75 articles involving 186 patients were eligible for inclusion. The median overall survival (OS) was 8 months, with 1-, 3-, and 5-year OS rates of 36.6%, 22.3%, and 12.0%, respectively. The median OS after partial hepatectomy ($n=86$), chemotherapy ($n=36$), liver transplantation ($n=17$), and supportive care ($n=46$) were 15, 10, 5 and 1.3 months, respectively. Small tumor size (<10 cm) was the only significant favorable factor for OS after partial hepatectomy ($P=0.012$).
Conclusions: Despite the dismal prognosis, partial hepatectomy could prolong the survival of hepatic angiosarcoma patients, particularly those with tumors <10 cm. Chemotherapy could be an option for unresectable disease. Liver transplantation is not a recommendable option for the management of this malignancy.

Introduction

Hepatic angiosarcoma (HAS) is a rare malignancy of vascular origin representing less than 2% of all primary liver tumors. Unlike most primary hepatocellular carcinomas (HCC) occurring in a background of chronic liver disease, the etiologic factors for HAS remain unclear in most cases, and only a few cases were reported to be associated with exposure to chemical carcinogens such as thorium dioxide, vinyl chloride, arsenic and radiation. However, most HAS cases had no known etiology [1]. Partial hepatectomy, chemotherapy, and liver transplantation have been used in the treatment of HAS patients. But given the rarity of this entity, it is difficult to provide sufficient evidence to draw a conclusion about the efficacy of a particular therapy. The aim of this systematic review is to evaluate the prognosis following various therapeutic modalities by pooling data from all individually documented patients with HAS.

Methods

The present study was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [2]. The level of evidence of each study was classified according to the Oxford Centre for Evidence-Based Medicine levels of evidence [3].

Literature review

A systematic literature search was conducted using PubMed, Embase and Chinese Biomedical Literature database, to identify articles published from January 1980 to July 2017. Search terms were "hepatic angiosarcoma" and "liver angiosarcoma". Additional articles were retrieved through manual search of bibliographies of the relevant articles.

Inclusion criteria: (i) articles that included patients who underwent partial hepatectomy, or any other treatments for HAS; (ii) original data published; (iii) availability of survival data; and (iv) articles published in either the Chinese or English language.

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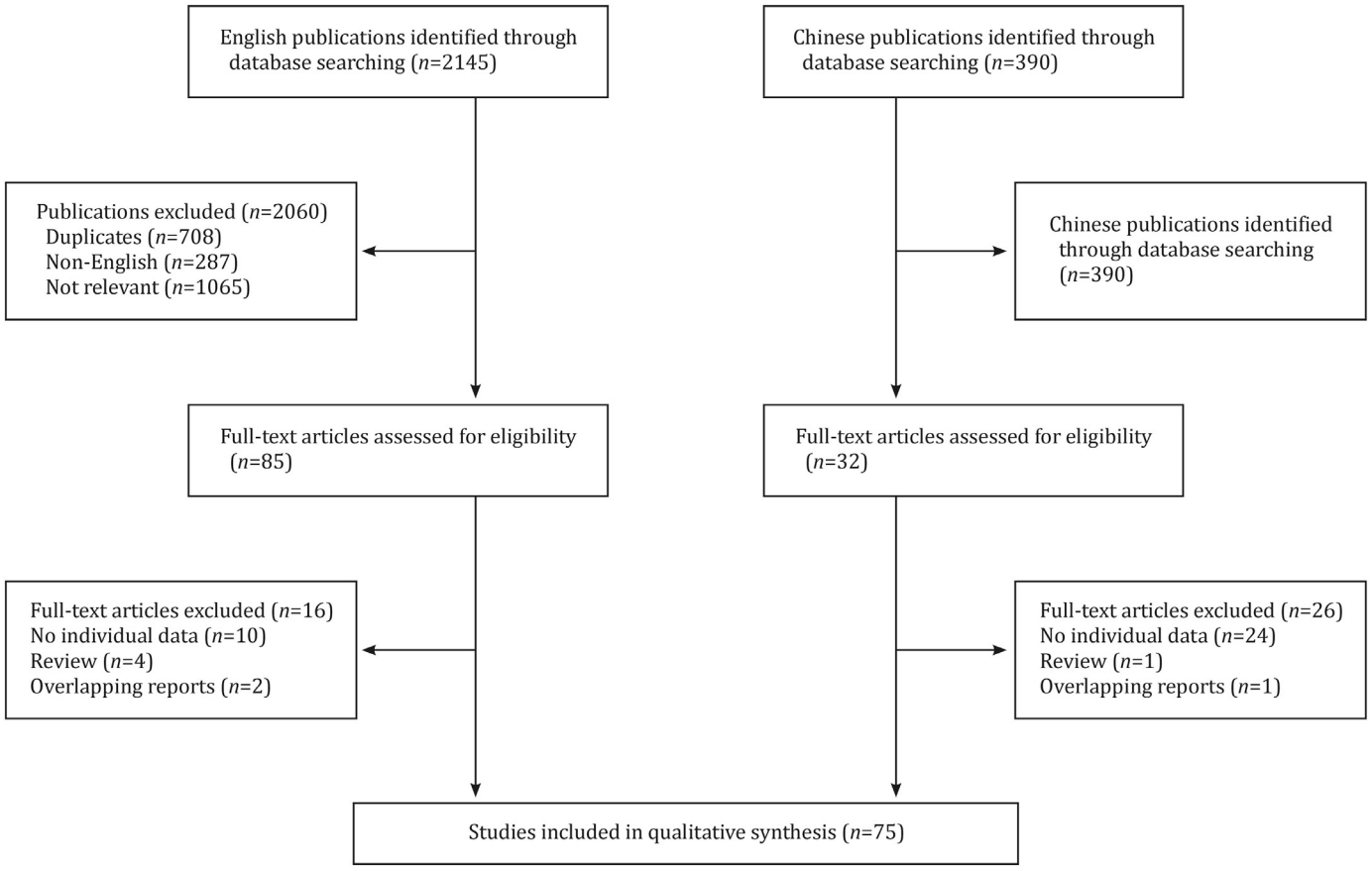

Fig. 1. Flow diagram for the selection of studies.

Exclusion criteria: (i) studies published in a language other than English and Chinese; (ii) reviews without original data and animal studies; (iii) the absence of individual patient data; (iv) multiple studies reported in the same population; (v) the absence of survival outcome data; and (vi) data for childhood HAS.

Data extraction and statistical analysis

Two investigators independently reviewed all the retrieved studies that met the inclusion and exclusion criteria. Discrepancies between the two reviewers were resolved by discussion and consensus. The primary outcome was overall survival (OS) following various therapeutic modalities.

Categorical data are presented as proportions and continuous data are presented as mean ± SD. OS was analyzed by the Kaplan–Meier method, and the log-rank test was used for univariate analysis of prognostic factors. Variables with P value of <0.1 in univariate analysis were entered in the multivariable Cox proportional hazards regression to investigate independent predictors of survival. All statistical analyses were performed using SPSS version 18.0 (SPSS, Chicago, IL, USA).

Results

Characteristics of the study population

The database searches identified 2535 potentially relevant articles. After screening, a total of 75 articles met election criteria and were included in the current study (Fig. 1). All studies were retrospective by design and classified as level-4 evidence [4–78]. The 75 studies contained data on 186 patients. The overall patient characteristics are presented in detail in Table 1. These patients were treated with partial hepatectomy ($n=86$), chemotherapy ($n=36$), liver transplantation ($n=17$), supportive care ($n=46$), and cyberknife ($n=1$). Chemotherapy regimen data was available for 19 patients, including adriamycin + cytoxan + methotrexate ($n=3$); cisplatin ($n=4$); doxorubicin + carboplatin + 5-fluorouracil ($n=3$); doxorubicin + ifosfamide ($n=3$); adriamycin + dacarbazine ($n=1$); etoposide + ifosfamide ($n=1$); ifosfamide + doxorubicin ($n=1$); adriamycin + taxotere or ifosfamide ($n=1$); thalidomide ($n=1$); and adriamycin ($n=1$).

Long-term results of treatment

The 1-, 3-, and 5-year OS rates in the whole group of 186 patients were 36.6%, 22.3%, and 12.0%, respectively, with a median OS of 8 months (Fig. 2). Table 2 shows the survival of patients treated by different modalities. The partial hepatectomy group had the best survival, followed by chemotherapy, liver transplantation, and supportive care groups.

Small tumor size (<10 cm) was the only significant favorable factor for OS after partial hepatectomy ($P=0.012$) under univariate analysis. Multivariable analysis was not performed for OS because univariable analysis revealed only one variable with $P<0.1$ (Table 3). Univariate analysis of prognostic factors for OS in patients who underwent other treatments was not performed due to small cohorts.

Discussion

Although HAS is an uncommon clinical entity, it constitutes the most common malignant mesenchymal tumor of the liver. The

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