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ORIGINAL ARTICLE

Evaluation of drug-eluting beads versus conventional transcatheter arterial chemoembolization in patients with unresectable hepatocellular carcinoma: A systematic review and meta-analysis

Peng Chen [1], Peng Yuan [1], Bo Chen, Jingchang Sun, Hang Shen, Yeben Qian [*]

Department of General Surgery, First Affiliated Hospital of Anhui Medical University, Hefei 230000, China

Summary

Background and objectives: Transcatheter arterial chemoembolization (TACE) is the first-line treatment for unresectable hepatocellular carcinoma (HCC). It consists of conventional TACE (cTACE) and drug-eluting beads TACE (DEB-TACE). The comparative outcomes of the two methods remain controversial. The study aim to research the optimal TACE strategy for unresectable HCC.

Methods: A systematic search of keywords, including 'HCC' and 'drug-eluting beads' was performed including four electronic databases: PubMed, Embase, China Biological Medicine Database (CBM), and Cochrane library databases from the date of inception to December 25, 2015. Review Manager 5.3 was used to calculate the pooled relative risks (RRs) and 95% confident intervals (CIs).

Results: Sixteen cohort studies (4 RCTs, 3 prospective cohorts, 9 retrospective cohorts) were included comprising a total of 1832 patients: 822 patients with DEB-TACE therapy and 1010 patients undergoing cTACE. The 1-, 2-, and 3-year overall survival (OS) rates and 1- and 2-year relapse-free survival (RFS) rates were significantly higher in DEB-TACE group, with pooled RRs of 1.12 (95% CI = 1.03–1.23, $P = 0.007$), 1.26 (95% CI = 1.03–1.54, $P = 0.02$), 1.69 (95% CI = 1.00–2.84, $P = 0.04$), 1.21 (95% CI = 1.01–1.44, $P = 0.03$) and 1.68 (95% CI = 1.17–2.43, $P = 0.005$). There was no statistical significance in 3-year RFS, tumor response and treatment-related adverse events.

* Corresponding author.
E-mail address: qianyeben@hotmail.com (Y. Qian).
[1] These authors contributed equally to this work.

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Conclusion: Compared with cTACE, DEB-TACE therapy significantly improved 1-, 2-, and 3-year OS rates and the 1- and 2-year RFS rates.

Introduction

Hepatocellular carcinoma (HCC) is a common worldwide malignancy of the digestive system [1,2]. According to the World Health Organization (WHO), HCC ranks second in cancer-related mortality. The 1-, 3- and 5-year overall survival (OS) rates of intermediate stage patients are 80%, 65% and 50%, respectively, while the corresponding survival rates of patients in advanced stages are much lower at 29%, 16% and 8%, respectively [3]. Despite the progress in the field of early HCC diagnosis, over 50% of these patients were found with late-stage carcinoma refractory to curative therapies including hepatic resection, liver transplantation and radiofrequency ablation [4,5]. Furthermore, the recurrence rate of patients receiving curative therapies is still high — up to 70% within 5 years, and a large number of HCC-relapsed patients are not candidates for secondary surgery [6,7]. Therefore, adaptation to novel treatments for this large group of patients with unresectable HCC is crucial.

Until now, transcatheter arterial chemoembolization (TACE) has been widely used as first-line therapy for patients with unresectable HCC clinically [8]. Conventional TACE (cTACE) and drug-eluting bead TACE (DEB-TACE) are two different chemotherapy modalities, which use lipiodol and DEB as chemotherapy drug carriers, respectively [9,10]. Numerous studies [11—15] have shown that both cTACE and DEB-TACE benefit patients. However, the comparative efficacy of either intervention is still unclear. Four retrospective studies [16—19] have suggested the significant superiority of DEB-TACE in terms of overall survival (OS) or tumor response or less adverse events. However, a few studies [20—23] suggested that the two modalities were equally effective and safe. Meta-analyses to select a better TACE yielded different results [24—28]. We performed this meta-analysis for the following reasons:

- the most recent and the largest RCT conducted by Golerfier may affect the results of previous meta-analyses. However, there are no meta-analyses that had completely included this RCT and other studies;
- a few studies demonstrated differences in outcomes with the two methods of treatment when the patients were in different Child-Pugh grading or Barcelona Clinic Liver Cancer (BCLC) classification [16,18,29]. However, there is no consensus on the TACE recommended for patients at different liver function or tumor stages. Song et al. [18] indicated lack of significant differences in OS between the two groups of patients when patients were in early stage HCC. By contrast, Dhanasekaran et al. [16] concluded that in both BCLC A and B HCC, the OS rate was significantly higher in the DEB-TACE group compared with the cTACE group. However, there was no previous meta-analysis conducted;
- to our knowledge, four studies reported relapse-free survival (RFS) with different results [18,20,21,30].

This present meta-analysis, which combined the overall analysis and subgroup analyses, was designed to summarize the current evidence for a comprehensive comparison of DEB-TACE and cTACE.

Material and methods

Study selection

This meta-analysis was based on four electronic databases, including PubMed, Embase, China Biological Medicine Database (CBM), and Cochrane library databases, from the date of inception until December 25, 2015. The search was performed based on MeSH terms combined with free text, using the following main keywords: (''DEB'' OR ''drug eluting'' OR ''drug eluting microsphere'' OR ''doxorubicin eluting'') AND (''TACE'' OR ''transcatheter arterial chemoembolization'') AND (''hepatocellular carcinoma'') OR (''adenocarcinoma'' OR ''carcinoma'' OR ''cancer'' OR ''neoplasm'' OR ''tumour'' OR ''tumor''). The gray literature (i.e. reports, reference lists for relevant reviews, congress abstracts and conference proceedings), which was not found in the computer search, was manually searched.

Eligible studies were selected based on published literature without language restriction as long as they met the following inclusion criteria:

- study design: randomized controlled trials (RCTs), prospective or retrospective cohort studies;
- patients with confirmed unresectable HCC who were diagnosed radiologically or histopathologically in addition to alpha-fetoprotein;
- DEB-TACE treatment used in the experimental group;
- cTACE treatment used in the control group;
- the following outcomes: OS, RFS, tumor response or adverse events.

Exclusion criteria were as follows:

- duplicates;
- commentaries and editorials;
- reviews;
- case reports;
- animal studies;

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