

Received: 2015.08.03
Accepted: 2015.10.28
Published: 2016.05.26

Improvement of Survival Rate for Patients with Hepatocellular Carcinoma Using Transarterial Chemoembolization in Combination with Three-Dimensional Conformal Radiation Therapy: A Meta-Analysis

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

A 1 **Houqiao Bai***
B 1 **Peng Gao***
C 2 **Hao Gao**
C 1 **Guangxi Sun**
D 1 **Chonghai Dong**
F 3 **Jian Han**
E 4 **Guosheng Jiang**

1 Department of Internal Medicine, Maternity and Child Care, Weihai, Shandong, P.R. China
2 Department of Imaging, Tumor Branch of Municipal Hospital, Weihai, Shandong, P.R. China
3 Department of Bone Cancer, Yantai Hospital, Yantai, Shandong, P.R. China
4 Medical Sciences of Shandong, Jinan, Shandong, P.R. China

* These authors contributed equally to this work

Guosheng Jiang, e-mail: jiangguosheng_sd@sina.com

Departmental sources

Corresponding Author:

Source of support:

Background: Transarterial chemoembolization (TACE) has been used alone or in combination with three-dimensional conformal radiation therapy (3DCRT) for treating hepatocellular carcinoma (HCC). The overall survival rate of HCC patients undergoing both treatments, however, has not been systematically studied. The aim of this meta-analysis-based study was to evaluate the overall efficacy of the combined therapy or monotherapy, thereby providing information for clinical treatment.

Material/Methods: We searched Google Scholar, PubMed, and Chinese National Knowledge Infrastructure (CNKI) for eligible studies, and a total of 17 case-control studies (including HCC patients treated by TACE plus 3DCRT or TACE alone) were included to perform the meta-analysis. Based on the available data, we assessed the improvements of 1-year, 2-year, and 3-year survival rate for the combination therapy of TACE and 3DCRT or TACE alone. Furthermore, the analysis was also stratified by the tumor response: complete response (CR), partial response (PR), no response (NR) and progressive disease (PD). Statistical analysis was performed using STATA 12 (Stata Statistical Software: Release 12).

Results: The results show that HCC patients receiving combination therapy have significantly increased overall survival rate when compared to those receiving TACE alone (1-year survival rate: OR=1.95, 95% CI 1.54–2.47, $p=7.3 \times 10^{-8}$; 2-year survival rate: OR=1.87, 95% CI 1.49–2.34, $p=1.6 \times 10^{-7}$; 3-year survival rate: OR=2.00, 95% CI 1.52–2.64, $p=1.8 \times 10^{-6}$).

Conclusions: Assessment of tumor response demonstrates that the combination therapy can efficiently increase the tumor response rate (CR+PR: OR=2.29, 95% CI 1.70–3.08, $p=1.1 \times 10^{-7}$), with a lower rate of subsequent tumor development (PD: OR=0.25, 95% CI 0.15–0.40, $p=5.5 \times 10^{-8}$).

MeSH Keywords: **Carcinoma, Hepatocellular • Chemoembolization, Therapeutic • Meta-Analysis**

Full-text PDF: <http://www.medscimonit.com/abstract/index/idArt/895548>

 2202

 3

 5

 30



Background

Hepatocellular cancer (HCC), a primary malignancy of the liver, is one of the most common malignancies worldwide, especially in East Asian countries. For example, China, which has the highest overall mortality rate as well as a high incidence, has around 35 cases per 100 000 persons [1]. Numerous treatment strategies, including surgical resection, which is a widely accepted mainstay therapy, have been developed for HCC treatment [2]. Resection is able to remove the part of the liver that contains the hepatocellular carcinoma or malignant hepatoma surgically, and it largely depends on the size, number, and locations of the tumors [3]. For instance, hepatic resection is not suitable for patients with large tumors (>3 cm) or extensive disease progression [3]. Moreover, surgery is frequently accompanied by recurrence due to the intrahepatic dissemination of the multicentric carcinoma [3]. Among the various treatment strategies, TACE was developed for treating unresectable hepatocellular tumors or intermediate-stage HCC, thereby providing an additional option for patients [4,5]. TACE is a minimally invasive, real-time, image-guided technology that prevents tumor progression and improves survival through inducing tumor necrosis, which represses tumors locally. Compared with traditional surgery, TACE has lower risk of complications and takes less recovery time [4,5].

It has been documented that TACE frequently becomes ineffective due to tumor regression, even if TACE is currently considered as one of the primary approaches, especially for large tumors and metastatic liver cancer [6,7]. Therefore, it is necessary to develop other treatment options for favorable clinical outcomes. Previous work has demonstrated that three-dimensional conformal radiation therapy (3DCRT) is an effective adjunct for parallel treatment for HCC [8]. 3DCRT is a complex technology for creating a digitally reconstructed 3-D image of the tumor and normal adjacent tissue based on computers in conjunction with CT scans, initially developed to provide precise data for targeting the tumor and to reduce adverse events of other traditional treatments, such as radiotherapy [9]. To date, numerous clinical trials have been conducted to assess the efficacy of the combination of 3DCRT and TACE for HCC [10–26], and these studies have provided considerable evidence that the combination therapy is beneficial for HCC, whereas it remains unclear whether the combination therapy can improve overall patient survival. A previous meta-analysis [27] including several clinical trials has evaluated the efficacy of the combination of TACE and radiation therapy or TACE alone, but it did not specifically focus on TACE and 3DCRT. In the present study, we performed a meta-analysis to evaluate the efficacy of the combination of 3DCRT and TACE on the overall survival for HCC patients, thereby providing a reference for HCC therapy.

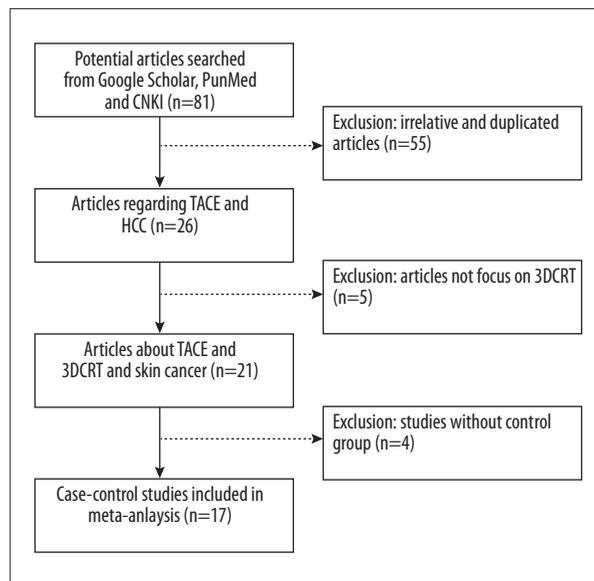


Figure 1. Flow diagram of eligible studies included in the meta-analysis.

Material and Methods

Data collection

PubMed, Google Scholar, and Chinese National Knowledge Infrastructure (CNKI) databases were searched with the following terms: “hepatocellular cancer”, “transarterial chemoembolization”, and “Three-dimensional conformal radiation therapy”. The search included studies published before September 2014. A total of 81 results (8 from PubMed, 58 from Google Scholar, and 15 from CNKI) were retrieved. Only studies meeting the following inclusion criteria were pooled for our meta-analysis: (i) case-control studies that focused on hepatocellular cancer and TACE/3dCRT therapy; (ii) source information available for both case and control groups; (iii) the diagnosis of hepatocellular cancer confirmed by clinical examinations; (v) studies published in English. The exclusion criteria were: (i) irrelevant and duplicated articles; (ii) study without case-control information; (iii) survival rate and tumor response information was unavailable; (iv) article type such as meta-analysis, letter, or editorial. A total of 17 studies were analyzed in our meta-analysis. From eligible articles, the following data were collected: the first author’s last name, year of publication, number of patients, overall survival rate (1-, 2-, and 3-year survival rates), and tumor response information. The procedure for study collection is shown in Figure 1.

Statistical methods

In this study, STATA software (Release 12 College Station, TX: StataCorp LP) was used for data analyses. The improvement between case group (the combination therapy of 3DCRT and

Table 1. Characteristics of studies included in the meta-analysis.

Author	Year	Survival rate (%) in (TACE+3dCRT)/TACE			No. of patients	Tumor response in TACE			
		1-year	2-year	3-year		CR	PR	NR	PD
Lu	2014	62.4/56.5	20.8/18.8	N/A	30/33	5/5	16/10	6/11	3/7
Gong	2011	79.2/58.3	54.2/33.3	25/16.7	24/24	1/0	16/13	5/8	2/3
Xiao	2011	45/25	27.5/12.5	N/A	40/40	6/4	24/14	8/14	2/8
Ning	2009	61.8/46.9	41.2/18.8	29.4/6.3	34/32	0/0	26/15	5/11	3/6
Zhao	2009	95/78	N/A	N/A	40/50	7/4	28/30	4/12	1/4
Zhang	2009	32.5/6.9	N/A	N/A	16/29	N/A	N/A	N/A	N/A
Xiao	2008	86.7/53.3	53.3/36.7	33.3/16.7	30/30	5/1	22/18	2/7	1/4
Shang	2007	78/50	60/32	34/18	40/36	14/1	16/12	8/7	2/9
Chung	2006	65/58	35/44	26/35	64/276	N/A	N/A	N/A	N/A
Zhao	2006	82/55	63/28	43/15	49/47	17/8	18/11	9/17	5/11
Liu	2005	66.5/53.9	48.4/37.2	37.4/17.8	54/60	N/A	N/A	N/A	N/A
Lan	2005	57.1/61.7	40.5/30	26.2/16.7	42/60	3/0	20/22	19/38	0/0
Shim	2005	N/A	36.8/14.3	N/A	38/35	0/0	N/A	N/A	1/8
Zeng	2004	71.5/59.6	42.3/26.5	24/11.1	54/149	3/1	38/45	13/68	0/35
Wu	2004	90.2/89.7	75.6/58.7	44.6/24	41/40	7/4	28/22	4/6	2/8
Li	2003	73.2/54.8	58.7/27.3	41.9/12.8	41/41	4/1	32/23	3/14	2/3
Cheng J	2001	N/A	58/56	N/A	17/16	N/A	N/A	N/A	N/A

TACE) and control group (TACE alone) was assessed by pooled odds ratios (ORs) and 95% confidence intervals (CIs). Three overall survival rates (1-, 2-, and 3-year survival rates) were used to evaluate the efficacy. Subgroup analysis was conducted with respect to tumor response (complete response, partial response, no response, and progressive disease). The heterogeneity was assessed by I^2 index; a higher I^2 indicates more significant heterogeneity. When $I^2 \leq 25\%$, we assumed that there was no significant heterogeneity between pooled data. $I^2 > 75\%$ was regarded as significant heterogeneity. We used a Mantel-Haenszel (M-H) fixed-effects model for calculation unless there was a significant heterogeneity, in which case a DerSimonian and Laird (D-L) random-effects model was used. In our meta-analysis, we used an M-H fixed-effects model to test the heterogeneity first, and then we chose a different model based on the test results. Forest plots were generated to summarize the results. Begg's funnel plots and Egger's regression asymmetry test were used to evaluate potential publication bias. All reported P values were two-sided, and $P < 0.05$ was considered to be statistically significant.

Results

Characteristics of studies

A total of 17 eligible case-control studies [10–26] were included for our meta-analysis, and the characteristics of these studies

are shown in Table 1. A total of 1652 patients that had been randomized into combined or monotherapy groups were enrolled in this analysis, and among them, 654 cases received the combination therapy of TACE and 3DCRT (case group) and 998 received TACE alone (control group). The overall survival rates are presented in Table 1 with period length from 1 year to 3 years. Irrespective of the None-Applicable cases (N/A cases), in case groups, the 1-year survival rate ranged from 32.5% to 86.7%, 2-year survival rate ranged from 20.8% to 60%, and 3-year survival rate ranged from 25% to 34%. In control groups, the 1-year survival rate ranged from 25% to 78%, 2-year survival rate ranged from 12.5% to 44%, and 3-year survival rate ranged from 6.3% to 35%.

The results for tumor response are shown in Table 1, which contain 4 types of responses: complete response (CR, complete clearance of the lesion), partial response (PR, lesion decreased more than 50%), no response (NR, lesion decreased less than 50% or increased less than 25%), and progressive disease (PD, lesion increased more than 25%). Specifically, despite the N/A cases, 72, 309, 98, and 24 of 654 patients had CR, PR, NR, and PD, respectively, in case groups and the percentage in each arm was 11.01%, 47.25%, 14.98%, and 3.67%, respectively. However, 29, 235, 213, and 106 of 998 patients had CR, PR, NR, and PD, respectively, in control groups, and the percentage in each arm was 2.91%, 23.55%, 21.34%, and 10.62%, respectively. Based on the data, the patients in case

Table 2. Meta-analysis of entire database with respect to different survival rates.

Survival rate	No. of studies	Analysis method	Heterogeneity		Overall	OR		p-value*	Publication bias	
			I ² (%)	p-value [#]		Lower	Upper		Begg	Egger
1-year	15	Fixed	16.9	0.264	1.95	1.54	2.47	7.3×10 ⁻⁸	0.075	0.028
2-year	15	Fixed	41.5	0.047	1.87	1.49	2.34	1.6×10 ⁻⁷	0.921	0.075
3-year	11	Fixed	51.8	0.023	2.00	1.52	2.64	1.8×10 ⁻⁶	0.436	0.013

[#] P-value from heterogeneity test; * P-value from OR test.

Table 3. Meta-analysis of entire database for tumor response.

Tumor response	No. of studies	Analysis method	Heterogeneity		Overall	OR		p-value*	Publication bias	
			I ² (%)	p-value [#]		Lower	Upper		Begg	Egger
CR+PR	12	Fixed	28.3	0.167	2.29	1.70	3.08	1.1×10 ⁻⁷	0.193	0.008
CR	11	Fixed	0.0	0.580	3.02	1.92	4.77	5.0×10 ⁻⁶	0.350	0.039
PR	12	Fixed	0.8	0.435	2.35	1.81	3.05	4.7×10 ⁻¹⁰	0.837	0.151
PD	11	Fixed	0.0	0.811	0.25	0.15	0.40	5.5×10 ⁻⁸	0.586	0.165

[#] P-value from heterogeneity test; * P-value from OR test.

groups had higher percentages in CR and PR categories, but lower percentages in NR and PD compared with control groups.

Survival rates

We further compared the survival rates between case and control groups and the results are shown in Table 2. We used random-effects models, and the 1-, 2-, and 3-year survival rates were analyzed. Overall, we found significant survival rate improvement for the combination of TACE and 3DCRT over TACE alone. Specifically, the combination of TACE plus 3DCRT was associated with higher 1-year (OR=1.95, 95% CI 1.54–2.47, p=7.3×10⁻⁸), 2-year (OR=1.87, 95% CI 1.49–2.34, p=1.6×10⁻⁷), and 3-year survival rates (OR=2.00, 95% CI 1.52–2.64, p=1.8×10⁻⁶) compared with TACE treatment. These results indicate that the HCC patients with the additive treatment of 3DCRT generally had nearly 2-fold better survival rate than those who received TACE treatment alone. Also, we noted that the largest overall OR occurred in 3-year survival rate, implying that this advantage becomes more apparent with longer observation. Forest plots for survival rates are shown in Figure 2.

Tumor response

We performed tumor response analysis, and results are shown in Table 2 and Figure 3. Twelve trials were identified with outcome measurements of CR+PR. The results of pooled analysis showed a significant improvement of the tumor response rate

in the case group (OR=2.29, 95% CI 1.70–3.08, p=1.1×10⁻⁷) compared with the control group (Figure 3A). Specifically, the case group had significant improvement of CR (OR=3.02, 95% CI 1.92–4.77, p=5.0×10⁻⁶) in 11 trials (Figure 3B). Similarly, significant improvement of PR was also noticed in the patients receiving combined treatment (OR=2.35, 95% CI 1.81–3.05, p=4.7×10⁻¹⁰) (Figure 3C) in 12 trials. However, patients treated with additive 3DCRT presented a significantly decreased progressive disease rate compared with those receiving TACE alone (PD: OR=0.25, 95% CI 0.15–0.40, p=5.5×10⁻⁸) (Figure 3D). All these analyses demonstrated that the combination of TACE and 3DCRT was more effective than TACE alone for the HCC treatment.

Evaluation of heterogeneity and publication bias

Statistically significant heterogeneity was observed in the 2- and 3-year survival rates, since the I² indexes were larger than 25%, with P-value less than 0.05 (Table 2). However, no significant heterogeneity was found in the analyses of tumor response (Table 3). Funnel plot and Egger’s test were performed to assess publication bias (Figure 4). No significant publication bias was found based on the funnel plot of 2-year survival rates (P-value of Egger’s test >0.05), but significant publication bias was shown in 1- and 3- year survival rates (P-value of Egger’s test=0.028 and 0.013, respectively (Table 2). For tumor response, the publication bias was found in the cases of CR+PR and CR, with Egger’s test P-value of 0.008 and 0.039, respectively, and the funnel plot for the tumor response is shown in Figure 5.

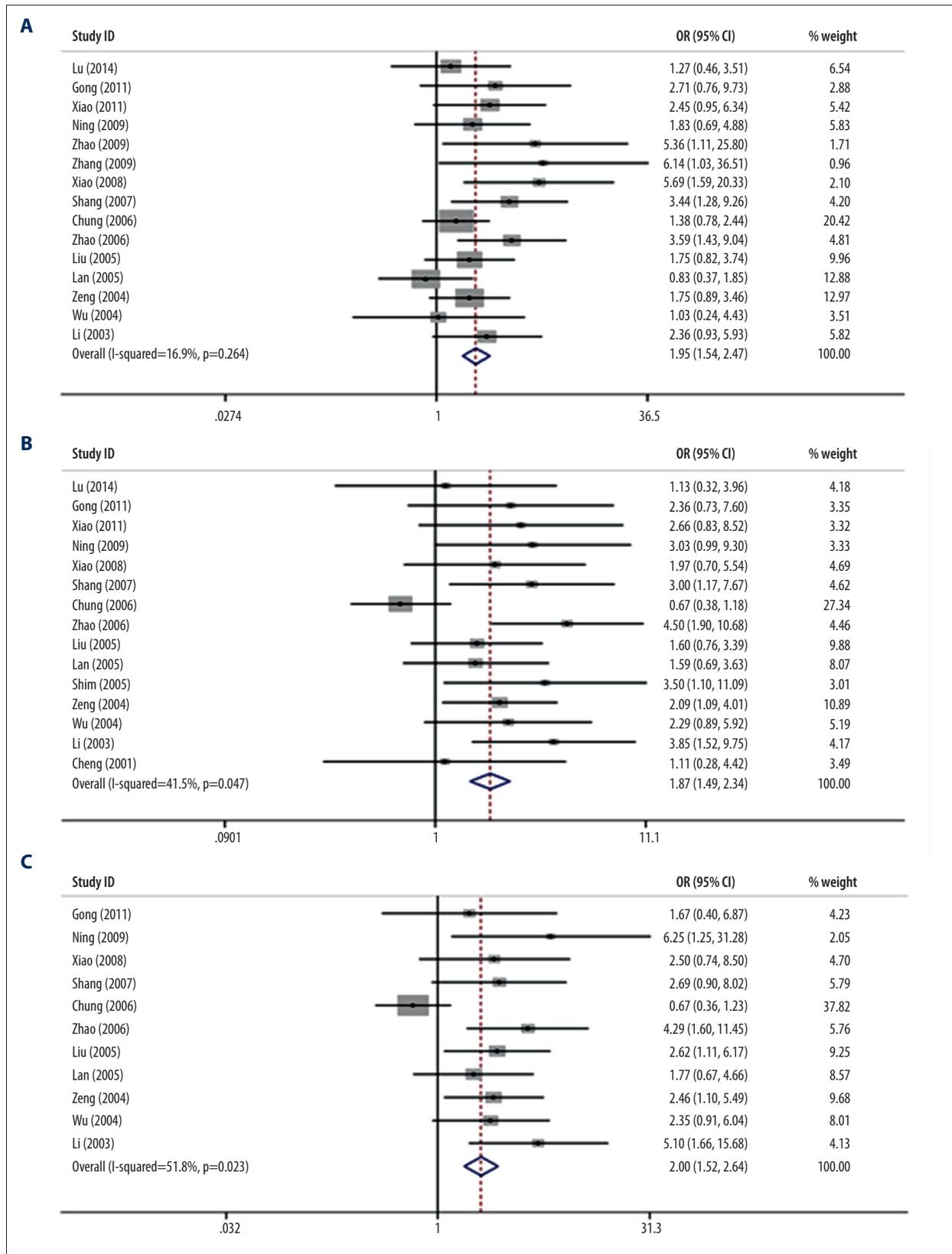


Figure 2. Forest plot of meta-analysis for the comparison of the combined therapy with TACE alone in terms of overall survival rates. (A) Meta-analysis of 1-year survival. (B) Meta-analysis of 2-year survival. (C) Meta-analysis of 3-year survival.

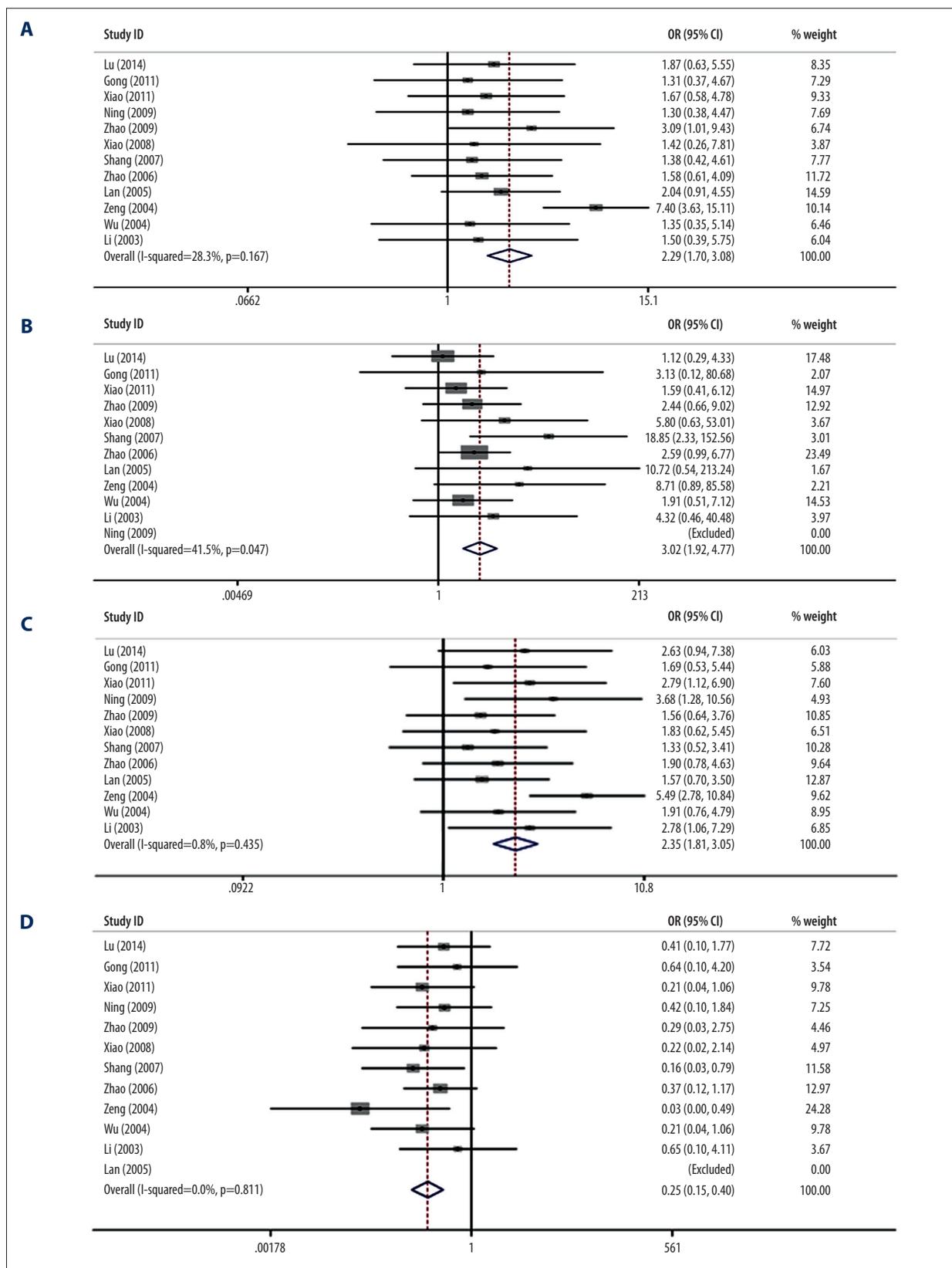


Figure 3. Forest plot of meta-analysis for the comparison of the combined therapy with TACE alone on tumor response. (A) Meta-analysis of CR+PR. (B) Meta-analysis of CR. (C) Meta-analysis of PR. (D) Meta-analysis of PD.

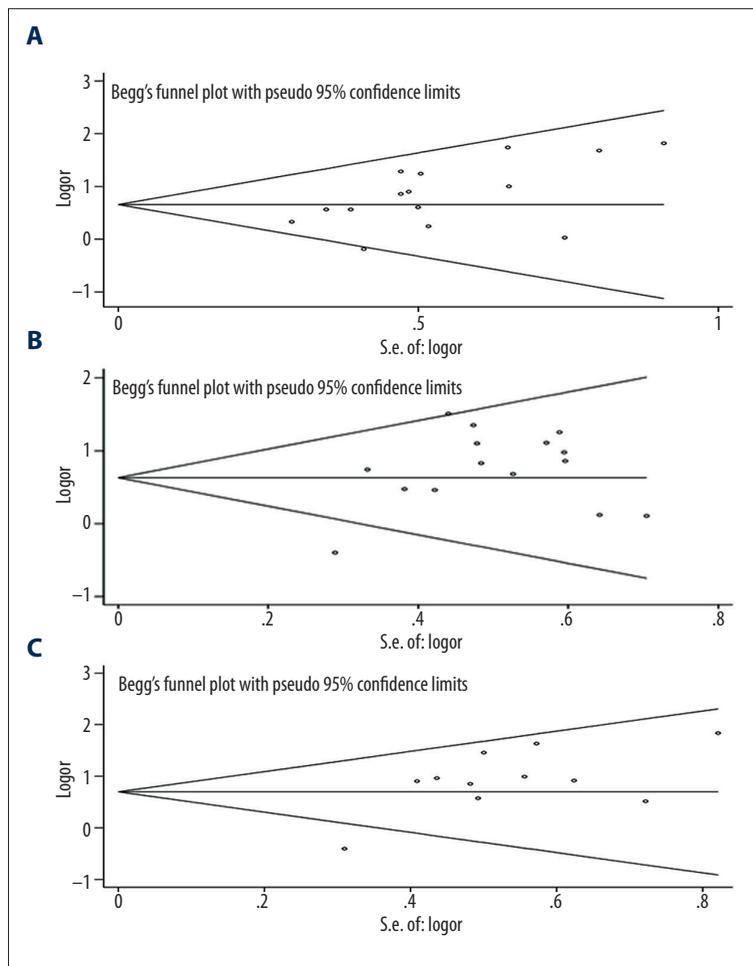


Figure 4. Begg's funnel plot of meta-analysis for the comparison of the combined therapy with TACE alone in terms of overall survival rates. (A) One-year survival. (B) Two-year survival. (C) Three-year survival.

Discussion

In this study we performed a meta-analysis based on the published data to compare the overall survival rates and tumor responses for patients who received the combination therapy of TACE and 3DCRT or TACE alone. TACE is the most commonly offered treatment, which is performed clinically by delivering a highly concentrated dose of chemotherapeutic drugs, including doxorubicin, cisplatin, or mitomycin, into the tumor through cannulating a feeding artery to reduce systemic toxicity [28,29]. In addition to TACE and the hepatectomy mentioned above, which are frequently utilized to treat HCC, radiotherapy is also an option for HCC treatment. Although radiotherapy has been used as an effective therapy for HCC for over 40 years, liver toxicity from the ionizing radiation limits its use [30]. The newly developed technology, 3DCRT, significantly and accurately minimizes the normal tissues exposed to irradiation during the treatment in combination with radiotherapy, although the application of radiotherapy still largely depends on the individual tolerance of the liver to radiation-induced damage [9]. The combined treatment, 3DCRT plus TACE, was thus designed and used clinically for patients

with unresectable HCC, as well as those who are sensitive to irradiation. However, there has been less research on whether the introduction of 3DCRT into TACE is able to substantially increase the overall survival rate of HCC patients.

In spite of the heterogeneity and publication bias, the present study shows that the strategy of combination therapy exhibited distinctly higher survival rates than the monotherapy, which is consistent with a previous study [27]. Specifically, in our study, improvements of survival rates were observed at 1 year (OR=1.95, 95% CI 1.54–2.47), 2 years (OR=1.87c, 95% CI 1.49–2.34), and 3 years (OR=2.00, 95% CI 1.52–2.64) after treatment with TACE+3DCRT for 654 patients. The increased survival rates were also supported by more positive tumor responses in the combination therapy. The assessment of tumor response demonstrated that combined treatment was able to increase the tumor response rate (CR+PR: OR=2.29, 95% CI 1.70–3.08), and simultaneously decrease the rate of further development of tumor tissue (PD: OR=0.25, 95% CI 0.15–0.40). Thus, the 2 clinical efficacies indicated a better outcome with the combination therapy. Importantly, heterogeneity of 2-year survival rate was moderate ($I^2=41.5\%$), and the I^2 index of

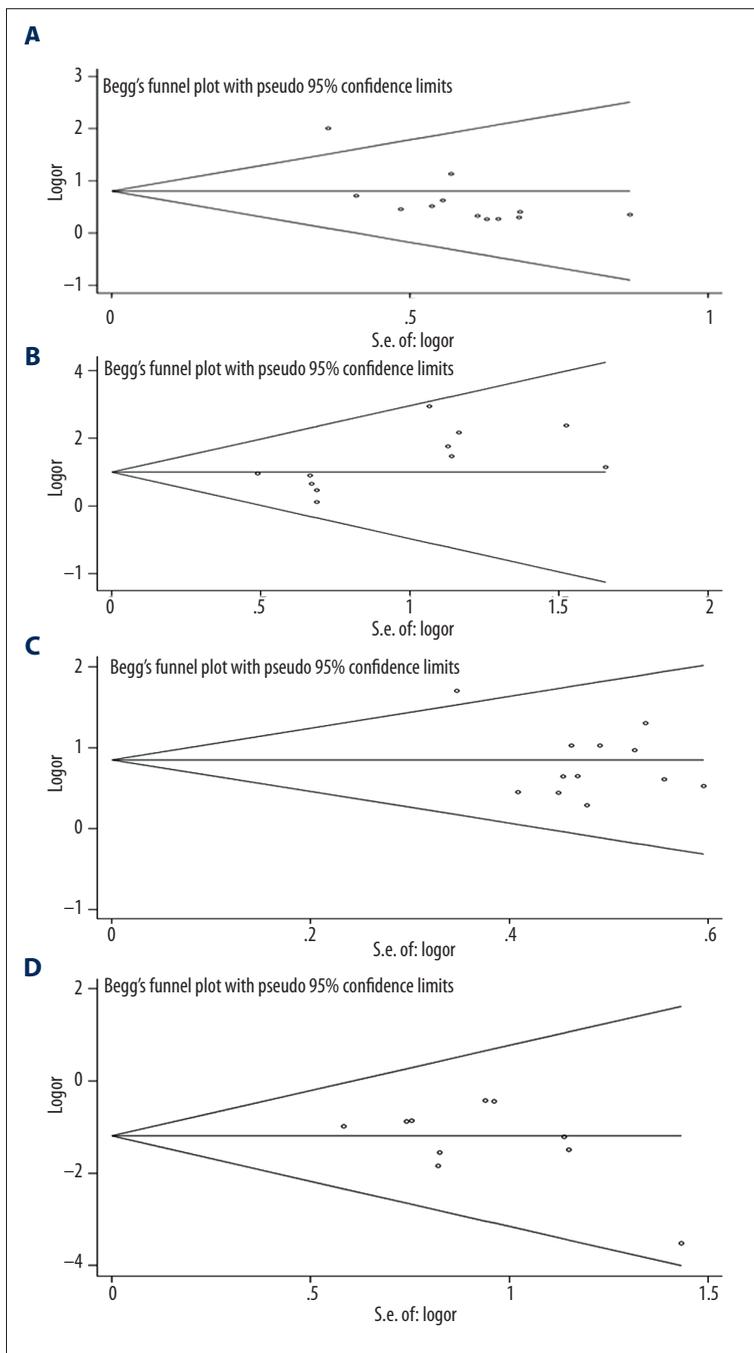


Figure 5. Begg's funnel plot of meta-analysis for the comparison of the combined therapy with TACE alone on tumor response. **(A)** CR+PR. **(B)** CR. **(C)** PR. **(D)** PD.

3-year survival rate was over 50% (51.8%). The value of I^2 index between 25% and 75% usually cannot be directly interpreted as significant heterogeneity. In this scenario, P-value is used to assess heterogeneity because it yields more information (e.g., sample size, case-control proportion, and, more importantly, data from examination). Here, since the P-values for 2- and 3-year survival rates are 0.047 and 0.023, respectively, and both of them are larger than 0.01, we assume the heterogeneity is acceptable.

There are several limitations that may affect the reliability of the conclusions regarding the positive effects of TACE plus 3DCRT on patients in these trials. Firstly, the data in this study were restricted to the population of China, although the restriction was unexpected prior to the analysis; therefore, the results are probably applicable with ethnic specificity. Secondly, publication bias was shown in 1- and 3- year survival rates (P-value of Egger's test was 0.028 and 0.013, respectively) and the tumor responses CR+PR and CR (P-value of Egger's test was 0.008 and 0.039, respectively). Lastly, factors such as age,

sex, genetic background, and tumor size were not considered during the analysis. Given these limitations, a well-designed meta-analysis with large sample size among different ethnicities needs to be performed. The results of our study should be interpreted with caution.

References:

1. Xu H, He Y-T, Zhu J-Q: Liver cancer mortality trends during the last 30 years in Hebei province: Comparison results from provincial death surveys conducted in the 1970's, 1980's, 1990's and 2004–2005. *Asian Pac J Cancer Prev*, 2012; 13(5): 1895–99
2. Heinow HS, Brockmann JG, Köhler M et al: Liver transplantation versus suprahepatic transarterial chemoembolization in palliative patients with hepatocellular carcinoma exceeding the Milan Criteria – is it time for a more individual approach? *Ann Transplant*, 2013; 18: 515–24
3. Roayaie S, Jibara G, Tabrizian P et al: The role of hepatic resection in the treatment of hepatocellular cancer. *Hepatology*, 2015; 62(2): 440–51
4. Murata S, Mine T, Sugihara F et al: Interventional treatment for unresectable hepatocellular carcinoma. *World J Gastroenterol*, 2014; 20(37): 13453–65
5. Cheng YC, Chen TW, Fan HL et al: Transarterial chemoembolization for intrahepatic multiple recurrent HCC after liver resection or transplantation. *Ann Transplant*, 2014; 19: 309–16
6. Rahbari NN, Mehrabi A, Mollberg NM et al: Hepatocellular carcinoma: current management and perspectives for the future. *Ann Surg*, 2011; 253(3): 453–69
7. Yu YQ, Xu DB, Zhou XD et al: Experience with liver resection after hepatic arterial chemoembolization for hepatocellular carcinoma. *Cancer*, 1993; 71(1): 62–65
8. Tse RV, Guha C, Dawson LA: Conformal radiotherapy for hepatocellular carcinoma. *Crit Rev Oncol Hematol*, 2008; 67(2): 113–23
9. Merle P, Mornex F, Trepo C: Innovative therapy for hepatocellular carcinoma: three-dimensional high-dose photon radiotherapy. *Cancer Lett*, 2009; 286(1): 129–33
10. Liu MZ, Wang XS, Cai L et al: [External radiation and combined transcatheter arterial chemoembolization for unresectable primary liver cancer]. *Ai Zheng*, 2005; 24(1): 82–86 [in Chinese]
11. Shim SJ, Seong J, Han KH et al: Local radiotherapy as a complement to incomplete transcatheter arterial chemoembolization in locally advanced hepatocellular carcinoma. *Liver Int*, 2005; 25(6): 1189–96
12. Zeng ZC, Tang ZY, Fan J et al: A comparison of chemoembolization combination with and without radiotherapy for unresectable hepatocellular carcinoma. *Cancer J*, 2004; 10(5): 307–16
13. Meihong Z, Fengping L, Qi'an J et al: Three-dimensional conformal radiotherapy combined with transcatheter arterial chemoembolization for inoperable primary liver cancer. *Chin J Radiat Oncol*, 2006; 15: 39–41
14. Lan D, Gong X, Wei X: The efficacy analysis of transcatheter hepatic arterial chemoembolization combined with radiotherapy for primary liver cancer. *Chin J Radiat Oncol*, 2005; 14: 152–53
15. Li Y, Ying Y, Haibo Z et al: Threedimensional conformal radiation combined with transarterial chemoembolization for unresectable primary liver cancer. *Chin J Radiat Oncol*, 2003; 12: 30–32
16. Shang Y et al: Prospective randomized clinical study of transcatheter arterial chemoembolization, combined with three-dimensional conformal radiotherapy for primary liver cancer: An analysis of 40 cases. *World Chin J Digestology*, 2007; 15: 3140–42
17. Wu DH, Zhi FZ, Chen LH: Evaluating the efficacy of transcatheter arterial chemoembolization combined with hypofractionated 3-dimensional conformal radiotherapy for hepatocellular carcinoma. *Chin J Dig*, 2004; 24: 353–59
18. Chung YL, Jian JJ, Cheng SH et al: Sublethal irradiation induces vascular endothelial growth factor and promotes growth of hepatoma cells: implications for radiotherapy of hepatocellular carcinoma. *Clin Cancer Res*, 2006; 12(9): 2706–15
19. Lu DH, Fei ZL, Zhou JP et al: A comparison between three-dimensional conformal radiotherapy combined with interventional treatment and interventional treatment alone for hepatocellular carcinoma with portal vein tumour thrombosis. *J Med Imaging Radiat Oncol*, 2015; 59(1): 109–14
20. Zhang XB, Wang JH, Yan ZP et al: Hepatocellular carcinoma with main portal vein tumor thrombus: treatment with 3-dimensional conformal radiotherapy after portal vein stenting and transarterial chemoembolization. *Cancer*, 2009; 115(6): 1245–52
21. Chia-Hsien Cheng J, Chuang VP, Cheng SH et al: Unresectable hepatocellular carcinoma treated with radiotherapy and/or chemoembolization. *Int J Cancer*, 2001; 96: 243–52
22. Qiao-ying G, Jin-gao L, Gong-li K: Effects of transcatheter arterial chemoembolization (TACE) versus TACE combined with three dimensional radiation (3-DCRT) in the treatment of patients with primary hepatocellular carcinoma. *Practical Journal of Cancer*, 2011; 26(6): 634–36
23. Sihai N et al: Three-dimensional conformal radiotherapy combined with transcatheterarterial chemoembolization for hepatocellular carcinoma. *Sichuan Medical Journal*, 2009; 30(12): 1896–98
24. Zemin X et al: Transcatheter arterial chemoembolization combined with 3-dimensional conformal radiotherapy for patients with unresectable primary hepatic carcinoma. *Chinese Journal of Clinical Oncology*, 2008; 35(1): 18–21
25. Peng X et al: Effect comparison of TACE plus 3DCRT and TACE alone in the treatment of primary hepatic cancer. *Journal of Basic and Clinical Oncology*, 2011; 24(6): 506–7
26. Zhao C, Ren Y, Wen S et al: Analysis of the curative effect of interventional therapy plus 3 dimensional conformal radiation therapies for hepatic cell carcinoma. *West China Medical Journal*, 2009; 24(7): 1686–89
27. Meng MB, Cui YL, Lu Y et al: Transcatheter arterial chemoembolization in combination with radiotherapy for unresectable hepatocellular carcinoma: a systematic review and meta-analysis. *Radiother Oncol*, 2009; 92(2): 184–94
28. Wiggermann P, Sieron D, Brosche C et al: Transarterial chemoembolization of Child-A hepatocellular carcinoma: drug-eluting bead TACE (DEB TACE) vs. TACE with cisplatin/lipiodol (cTACE). *Med Sci Monit*, 2011; 17(4): 189–95
29. Chung GE, Lee JH, Kim HY et al: Transarterial chemoembolization can be safely performed in patients with hepatocellular carcinoma invading the main portal vein and may improve the overall survival. *Radiology*, 2011; 258(2): 627–34
30. Zou LQ, Zhang BL, Chang Q et al: 3D conformal radiotherapy combined with transcatheter arterial chemoembolization for hepatocellular carcinoma. *World J Gastroenterol*, 2014; 20(45): 17227–34

Conclusions

Our meta-analysis of 17 studies including total 1652 patients suggests survival and tumor response advantages of combined therapy of TACE plus 3DCT over TACE alone. We believe our study may help further HCC treatment research.