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Meta-analysis on Radiofrequency Ablation in Combination with Transarterial Chemoembolization for the Treatment of Hepatocellular Carcinoma

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Summary: To evaluate the efficacy and safety of transcatheter arterial chemoembolization (TACE) combined with radiofrequency ablation (RFA) and TACE alone for hepatocellular carcinoma (HCC), Pubmed, Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI) and Wanfang Datebases were searched for the randomized controlled trials (RCTs) and retrospective cohort studies from the establishment of the databases to January 2014. The bibliographies of the included studies were searched, too. After study selection, assessment, data collection and analysis were undertaken, we performed this meta-analysis by using the RevMan5.2 software. Seventeen studies involving 1116 patients met the inclusion criteria with 530 treated with RFA-plus-TACE and 586 with TACE alone. The results of meta-analysis showed that the combination of TACE and RFA was obviously associated with higher 1-, 2-, and 3-year overall survival rates ($OR_{1\text{-year}}$=3.98, 95% CI 2.87–5.51, P<0.00001; $OR_{2\text{-year}}$=3.03, 95% CI 2.10–4.38, P<0.00001; $OR_{3\text{-year}}$=7.02, 95% CI 4.14–11.92, P<0.00001) than TACE alone. The tumor complete necrosis rate in patients treated with TACE and RFA was higher than that of TACE alone (OR=13.86, 95% CI 8.04–23.89, P<0.00001). And there was a significant difference in local recurrence rate between two different kinds of treatment (OR=0.24, 95%CI 0.14–0.44, P<0.00001). Additionally, combination of TACE and RFA was associated with higher complete tumor necrosis rates than TACE mono-therapy in the treatment of HCC. However, RFA plus TACE was found to be associated with a lower local recurrence rate than TACE monotherapy. TACE-plus-RFA treatment was associated with a higher response rate (RR) than the TACE-alone treatment (OR=3.90, 95% CI=2.37–6.42, P<0.00001). TACE-plus-RFA treatment did not differ from the TACE-alone treatment in terms of stable disease (SD) rate (OR=0.38, 95% CI=0.11–1.26, P=0.11). Meta-analyses showed that the combination of RFA and TACE was associated with a significantly lower progressive disease (PD) rate (OR=0.15, 95% CI=0.05–0.43, P=0.0005). The rate of AFP reducing or returning to normal in serum in RFA plus TACE group was obviously lower than TACE alone group (OR=4.62, 95% CI 2.56–8.34, P<0.00001). The effect of TACE plus RFA for HCC is better than TACE mono-therapy. The combined therapy can elevate the patients' overall survival rate, tumor necrosis rate and the rate of AFP reducing or returning to normal in serum and decrease local recurrence rate, PD rate compared with TACE alone.

Key words: hepatocelluar carcinoma; transarterial chemoembolization; radiofrequency ablation; meta-analysis

Hepatocellular carcinoma (HCC) is the fifth most common malignant disorder and causes nearly one million deaths each year worldwide, and the incidence of HCC is dramatically increasing especially in the USA, Europe and Asia[1]. Hepatitis B virus (HBV), hepatitis C virus (HCV)- and alcohol-related cirrhosis is the leading factor associated with HCC carcinogenesis[2]. The incidence of hepatitis is high in China, and the treatment of liver cancer has been a great challenge to Chinese clinicians. Hepatic resection (HR) is considered to be the preferred treatment for early HCC. Unfortunately, 70% of HCC patients are not suitable for liver resection because of such contraindications as late-stage, unfavorable location, large number, big size of the tumor and poor liver function[3, 4]. Liver transplantation is another treatment option, especially for patients with advanced cancer, but patients on the waiting list for transplantation far outnumber potential cadaveric or living hepatic donors[5]. Transcatheter arterial chemoembolization (TACE) is recommended as a first-line, non-curative therapy for non-surgical patients with large, multi-focal HCC[6, 7]. However, the incomplete necrosis of the tumor after TACE makes the long-term outcome, in the treatment for HCC, unsatisfactory. Radiofrequency thermal ablation (RFA) has now become a new alternative for the treatment of HCC because of its economy, safety, ease of operation and less adverse effects[7]. RFA has been demonstrated to be effective for treating focal malignancies in the liver with minimal invasiveness. A recent study[8–10] showed that RFA, for the treatment of small

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hepatic tumors in patients, is similar to surgical resection with regard to local efficacy as well as long-term survival. Nevertheless, its application is limited by the size of lesions, which tends to result in a high rate of local recurrence, particularly with larger tumors[10, 11]. A previous investigation[12] showed that the successful rate of RFA for liver cancer less than 3 cm was 100%, but for those with diameter ranging from 3 cm to 5 cm, especially those larger than 5 cm, failure was common even if RFA was performed repeatedly. To achieve a better survival for HCC patients, the multimodal therapy was designed in the previous studies. In recent years, TACE plus RFA has been more and more widely performed for HCC in clinical trials. In view of this, this meta-analysis was aimed to investigate whether TACE in combination with RFA is more effective than TACE alone for patients with HCC. In this study, the overall survival rate, complete tumor necrosis rate, local recurrence rate, curative effect evaluation and the rate of AFP reducing or returning to normal of HCC patients were compared between the two groups to provide information for clinical decision-making.

Table 1 Baseline features of trials included in the meta-analysis

Study (Reference)	Year	Arms	Sample size (*n*)	Mean age (y)	Tumor size (cm, $\bar{x}\pm s$)	Number of tumors (*n*)	Child-Pugh class (A/B/C)	TACE times for each case
Zhou *et al*[13]	2007	TCAE+RFA	22	56.2	6.5	NR	NR	NR
		TACE	25	56.2	6.5	NR	NR	NR
Fang *et al*[14]	2012	TACE+RFA	19	46.4±8.7	NR	37	NR	2.4
		TACE	24	48.1±8.3	NR	47	NR	3.5
Tan *et al*[15]	2013	TACE+RFA	38	47.6±10.8	5.32	72	11/19/8	NR
		TACE	38	49.1±11.3	5.11	70	10/17/11	NR
Dai *et al*[6]	2010	TACE+RFA	58	50.1	5.25	75	25/29/4	NR
		TACE	54	48.2	5.62	78	20/28/6	NR
Zheng *et al*[16]	2013	TACE+RFA	36	52.7±7.1	5.2±2.2	79	NR	NR
		RFA	44	52.3±4.0	5.2±2.3	97	NR	NR
Wu *et al*[17]	2003	TACE+RFA	42	53±15	6.4±2.4	61	36/4/2	NR
		TACE	43	53±14	6.5±1.8	63	35/6/2	NR
Deng *et al*[18]	2012	TACE+RFA	32	49±21.6	9.8	43	15/17/0	NR
		TACE	30	50±20.4	10.3	40	14/16/0	NR
He *et al*[19]	2013	TACE+RFA	20	54±14	3.4±1.6	NR	NR	NR
		RFA	25	54±13	3.4±1.4	NR	NR	NR
Tang *et al*[20]	2005	TACE+RFA	10	63.2	7.0	13	A/67B13	NR
		TACE	20	62.0	6.8	25	A/76B/11	NR
Cai *et al*[9]	2013	TACE+RFA	26	48	NR	36	NR	1-3
		TACE	22	48	NR	30	NR	3-6
Kang *et al*[21]	2007	TACE+RFA	19	55.6	6.8±1.3	NR	12/7/0	NR
		TACE	21	52.2.	6.7±1.1	NR	12/9/0	NR
Xiong *et al*[22]	2013	TACE+RFA	35	73.4±4.5	6.3±2.1	NR	7/28/0	NR
		TACE	35	74.2±5.6	6.5±2.0	NR	8/27/0	NR
Huang *et al*[10]	2013	TACE+RFA	33	35.7±6.3	5.33±0.31	NR	12/12/9	NR
		TACE	33	37.1±5.9	5.41±0.25	NR	10/12/11	NR
Zhang *et al*[23]	2011	TACE+RFA	96	NR	NR	NR	NR	NR
		TACE	90	NR	NR	NR	NR	NR
Song *et al*[11]	2008	TACE+RFA	14	58.8±11.2	5.9±0.7	NR	7/6/1	2.6
		TACE	25	56.9±11.7	5.9±0.7	NR	8/6/1	3.7
Liang *et al*[24]	2011	TACE+RFA	31	59.1±11.4	5.6±0.6	NR	21/9/1	2.6
		TACE	24	57.6±11.8	6.4±0.1	NR	15/7/2	3.5
Bloomston *et al*[25]	2002	TACE+RFA	13	NR	NR	NR	NR	NR
		TACE	24	NR	NR	NR	NR	NR

NR: not reported

1 MATERIALS AND METHODS

1.1 Inclusion Criteria

Eligible studies included in this meta-analysis should satisfy the following criteria: (1) Trials compared TACE in combination with RFA and TACE alone; (2) Diagnosis of HCC was established pathologically or radiologically (Radiological diagnosis was based on at least 2 coincident imaging findings indicating HCC in high-risk patients), or the serum AFP level ⩾400 μg/L; (3) Information on the overall survival rate, local recurrence rate, complete tumor necrosis rate, curative effect evaluation or the rate of AFP reducing or returning to normal was provided; (4) The studies examined consecutive patients with sample size greater than or equal to 10 patients; (5) The follow-up time of the studies lasted for more than 1 year.

1.2 Exclusion Criteria

A study would be exclude if (1) No comparison was made between two groups; (2) The subjects received surgical or other therapeutic interventions, such as percutaneous ethanol injection (PEI); (3) Sample size was

less than 10 patients; (4) The publication was duplicate in terms of the patient sample.

1.3 Search Strategy

Pubmed, Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI) and Wanfang Datebases were searched. Studies eligible for this meta-analysis was last updated on January 2014. The search terms included HCC, HCC intervention, hepatic tumor, TACE, RFA, TACE plus RFA. Randomized controlled trials and retrospective cohort studies that compared RFA plus TACE with TACE alone for HCC published in English or Chinese were included. All eligible studies were retrieved, and their references were examined for other pertinent publications. Each full-text article was evaluated by a single investigator, but was reviewed by two investigators independently when data were extracted. Any disagreement among reviewers was resolved by mutual discussion. The articles selected were assessed for relevance against aforementioned inclusion criteria (table 1).

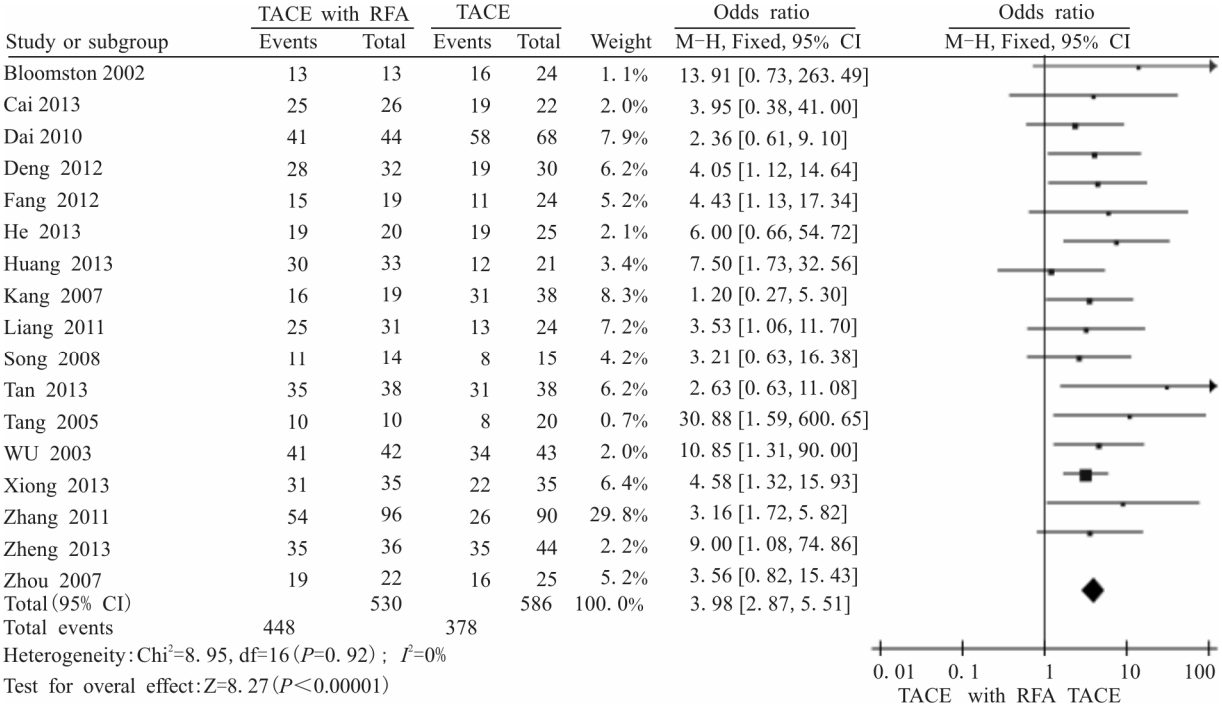

Fig. 1 One-year overall survival rate of TACE with RFA versus TACE (fixed-effects model)

1.4 Quality Assessment

The quality of each available study was independently assessed by three investigators by employing the Jaded scoring criteria[26]. First, the randomization was judged on a 0–2 scale, with those involving randomization and presenting the randomization method in detail being awarded 2 points; those only mentioning the term of random but without detailing the process of randomization 1 point; those that didn't use randomization 0 point. (2) Studies using blind design in terms of participants, personnel and outcome assessors were also assessed on a 0–2 scale, with those using appropriate blind design awarded 2 points; those only referring to it but without providing detailed procedures scoring 1 point; those failing to use blind design 0 point. (3) Follow-up was scored on a 0–1 scale, with those studies mentioning the follow-up process, the reason, number, time of subjects being lost to follow-up being awarded 1 point and those without the information 0 point. The score of overall quality of the studie ranged from 1 to 5 points. By this standard, studies scoring 3–5 points were categorized as high-quality studies and those scoring 1 to 2 points as low-quality article. In this meta-analysis, only 4 studies were of high quality and the others were of low quality.

Publication bias was evaluated by funnel plots.

1.5 Statistical Analysis

For meta-analysis, both the random-effects model and the fixed-effects model were employed. Heterogeneity across trials was first assessed by the Cochrane's Q statistic. A random-effects model was used if a $P<0.05$ and $I^2>50\%$. Otherwise, data were pooled by using the fixed-effects model. In data pooling, we used odds ratios (OR) with 95% confidence intervals (CI) to indicate the effectiveness of research results. When a $P<0.05$, the outcome was considered to be statistically significant. Statistical analyses were conducted by using the software package Review Manager (Version 5.2).

2 RESULTS

2.1 Search Results

Initial literature search preliminarily yielded a total of 316 studies. After reviewing of the titles and abstracts, 197 studies were excluded as they were reviews, animal studies, or bore no association with this study, or involved other interventions such as surgery or PEI, or dealt with only combination treatment. Then, after further assessment, 84 studies were eliminated and 35 studies were selected for screening. In the end, a total of 17 eligible studies[6, 9–11, 13–25] were identified (9 lacking survival data, and the other 9 provided survival rate but

without adequate follow-up). All studies were retrospectively analyzed, 4 of which were randomized controlled trials[10, 14, 15, 22], and the other were retrospective observational studies fulfilling the inclusion criteria[6, 9, 11, 13, 16–21, 23–25]. Collectively, the RFA plus TACE group involved 530 patients, against 586 patients who received TACE alone.

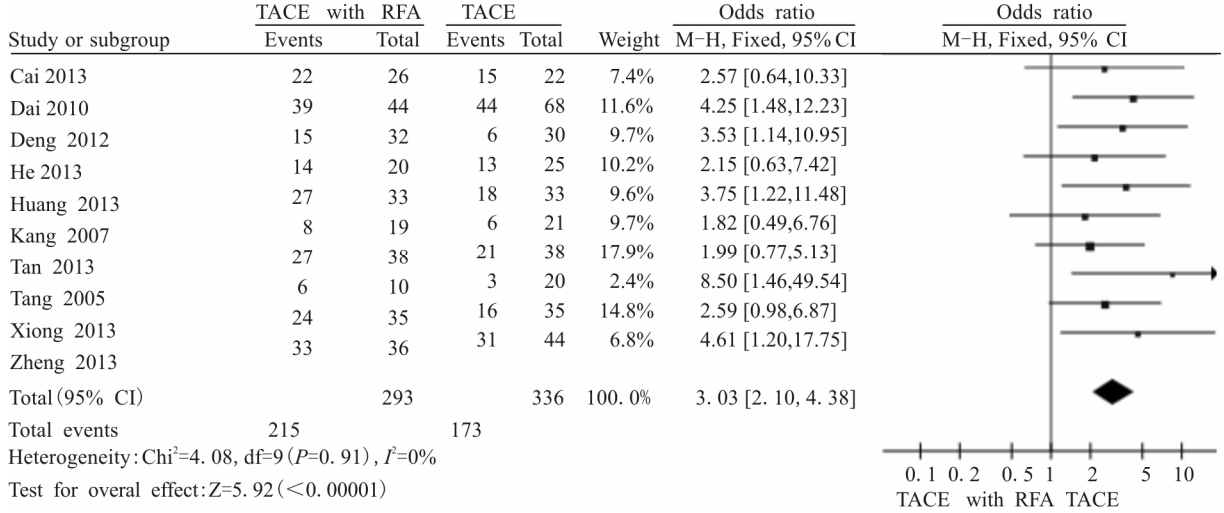

Fig. 2 Two-year overall survival rate of TACE with RFA versus TACE (fixed-effects model)

2.2 Meta-analysis Results

2.2.1 Overall Survival Rate

2.2.1.1 One-year Overall Survival Rate Fifteen trials (involving 1116 participants) reported data on the 1-year overall survival rate[6, 9–11, 13–25]. Analysis indicated that there was no heterogeneity among the trials ($P_{1\text{-year}}$=0.92, I^2=0%), and therefore the fixed-effects model was used to pool the outcomes. A significant difference in 1-year overall survival rate was found between RFA-plus-TACE group and TACE-alone group, and analysis revealed that TACE-plus-RFA treatment was associated with a significantly higher 1-year overall survival rate than TACE-alone treatment (fixed-effects OR=3.98, 95% CI 2.87–5.51, P<0.00001) (fig. 1).

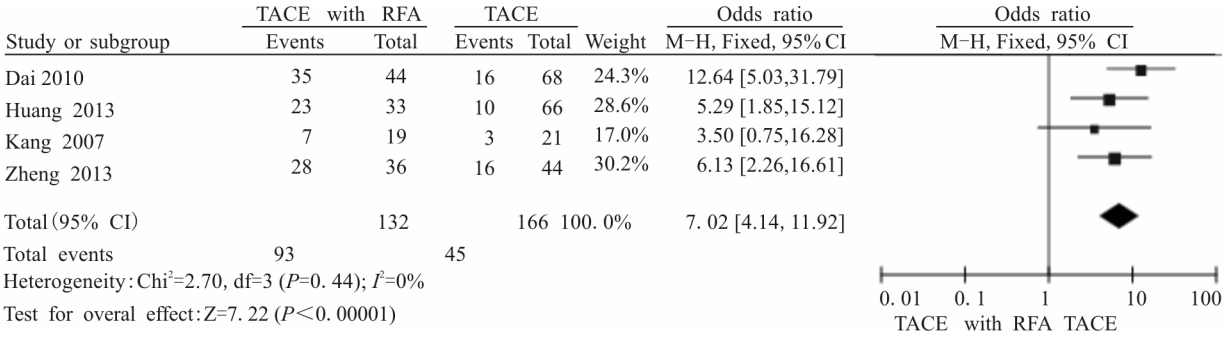

Fig. 3 Three-year overall survival rate of TACE with RFA versus TACE (fixed-effects model)

2.2.1.2 Two-year Overall Survival Rate Ten eligible studies involving 629 participants reported data concerning 2-year overall survival rate[6, 9, 10, 15, 16, 18–22], and the meta-analysis revealed no heterogeneity among the trials ($P_{2\text{-year}}$=0.91, I^2=0%), and the fixed-effects model was used. Sensitivity analysis showed that TACE-plus-RFA treatment was associated with a significantly higher 2-year overall survival rate than TACE-alone treatment (fixed-effects OR=3.03, 95% CI 2.10–4.38, P<0.00001) (fig. 2), suggesting that TACE-plus-RFA had a significantly better benefit for HCC patients in terms of the 2-year overall survival rate than the TACE-alone treatment.

2.2.1.3 Three-year Overall Survival Rate Four studies, involving 298 participants, reported data on 3-year overall survival rate. Since there was no obvious heterogeneity among them ($P_{3\text{-year}}$=0.44, I^2=0%), the fixed-effects model was used to pool the results. A significant difference in 3-year overall survival rate was found between RFA-plus-TACE treatment and TACE-alone treatment and analysis suggested that the RFA-plus-TACE treatment was associated with a higher 3-year overall survival rate than the TACE-alone treatment (fixed-effects OR=7.02, 95% CI 4.14–11.92, P<0.00001) (fig. 3).

2.2.2 Tumor Complete Necrosis Rate Seven trials (including 362 participants) mentioned the data on the tumor complete necrosis rate[9, 11, 17, 20, 24]. Analysis indicated that there was also no apparent heterogeneity among the trials (P=0.31, I^2=16%), and the fixed-effects model was used. There existed a significant difference in tumor complete necrosis rate between RFA-plus-TACE treatment and TACE-alone treatment and the meta-analysis showed that TACE-plus-RFA treatment was

associated with a significantly higher tumor complete necrosis rate than the TACE-alone treatment (fixed-effects OR=13.86, 95% CI 8.04–23.89, $P<0.00001$) (fig. 4).

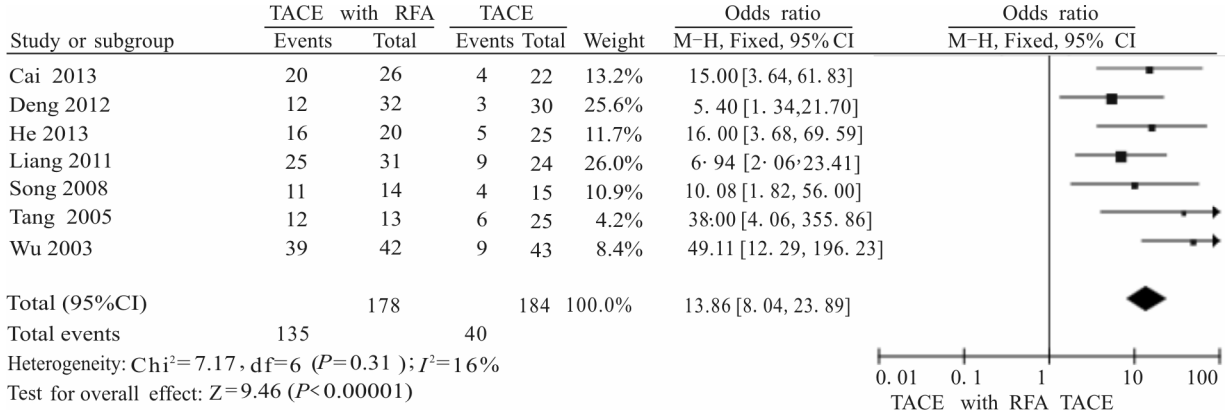

Fig. 4 Tumor complete necrosis rate of TACE with RFA versus TACE (fixed-effects model)

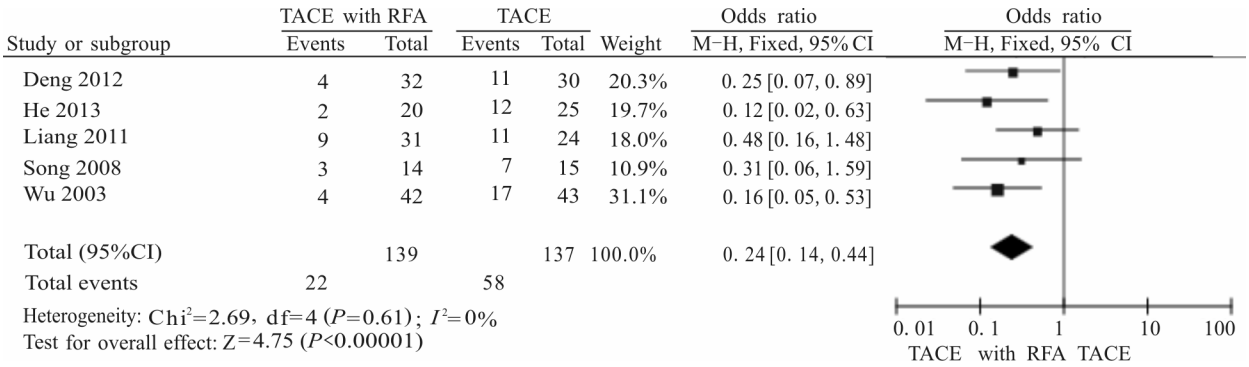

Fig. 5 Local recurrence rate of TACE with RFA versus TACE (fixed-effects model)

2.2.3 Local Recurrence Rate Five trials[11, 18–19, 17, 24] provided data on the local recurrence rate and a statistically significant difference was observed among these trials. Collectively, the five studies showed that TACE-plus-RFA treatment was associated with a significantly lower local recurrence rate than TACE-alone treatment, without any heterogeneity found among the studies ($P=0.61$, $I^2=0\%$). The pooled results by using the fixed-effects model showed that combination therapy decreased tumor recurrence more than TACE monotherapy (fixed-effects OR=0.24, 95% CI 0.14–0.44, $P<0.00001$) (fig. 5).

2.3 Curative Effect Evaluation

According to the therapeutic effect evaluation standard of solid tumor (liver cancer)[16] the response ranged from complete response (CR), partial response (PR), stable disease (SD), to progressive disease (PD). The response rate (RR) was defined as the sum of the CR and PR cases divided by the total case number[22]. Data for therapeutic effect evaluation, including the RR, SD and CR, were provided in all 5 studies[6, 10, 16, 18, 22]. There was no significant heterogeneity in RR among these 5 studies ($P=0.51$, $I^2=0\%$) and the fixed effects model was utilized to pool the results. Analysis exhibited that TACE-plus-RFA treatment was associated with a higher RR than the TACE-alone treatment (OR=3.90, 95% CI=2.37–6.42, $P<0.00001$) (fig. 6). The same five studies reported data on the SD rate. Heterogeneity was revealed among those 5 studies ($P=0.006$, $I^2=72\%$) and the random-effects model was used. Our analysis indicated that TACE-plus-RFA treatment did not differ from the TACE-alone treatment in terms of SD rate (OR=0.38, 95% CI=0.11–1.26, $P=0.11$) (fig. 7). Moreover, there was no significant heterogeneity in PD rate ($P=0.28$, $I^2=15\%$) and the fixed effects model was chosen to pool the results. There was a significant difference in PD rate between RFA-plus-TACE treatment and TACE-alone treatment and the meta-analysis suggested that RFA-plus-TACE treatment was associated with a significantly lower PD rate than the TACE-alone treatment (OR=0.15, 95 % CI=0.05–0.43, $P=0.0005$) (fig. 8).

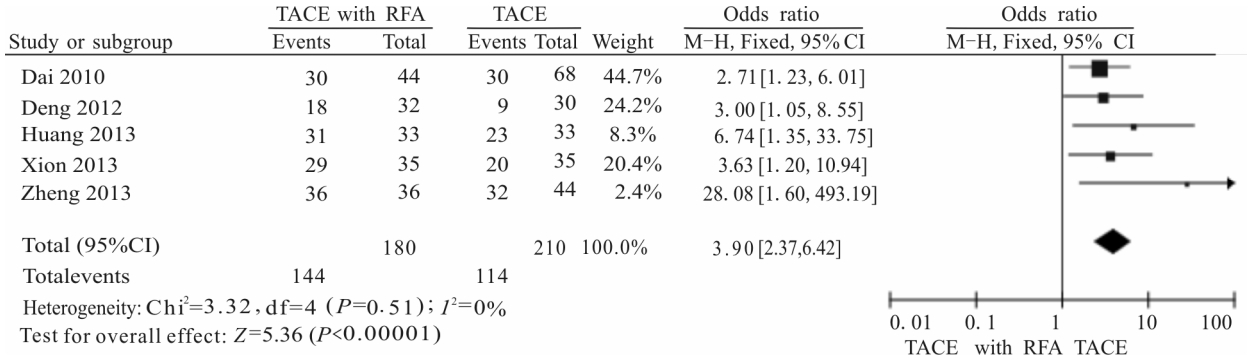

Fig. 6 Response rate of TACE with RFA versus TACE (fixed-effects model)

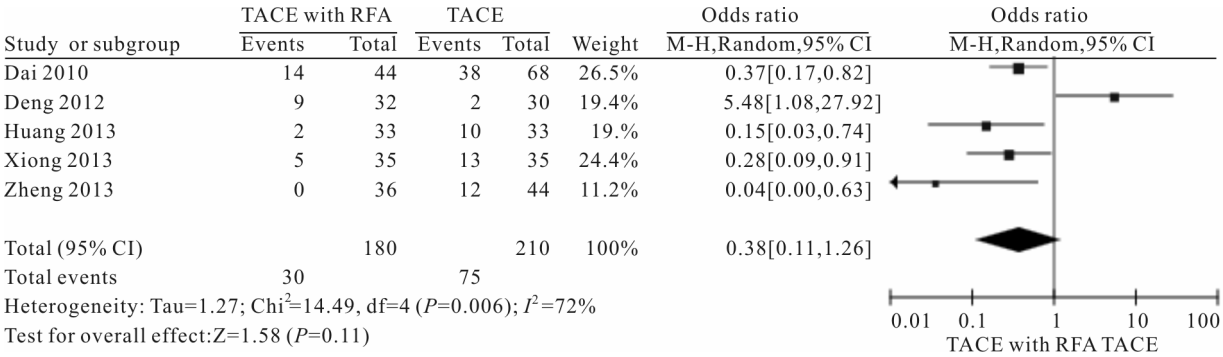

Fig. 7 Stable disease rate of TACE with RFA versus TACE (random-effects model)

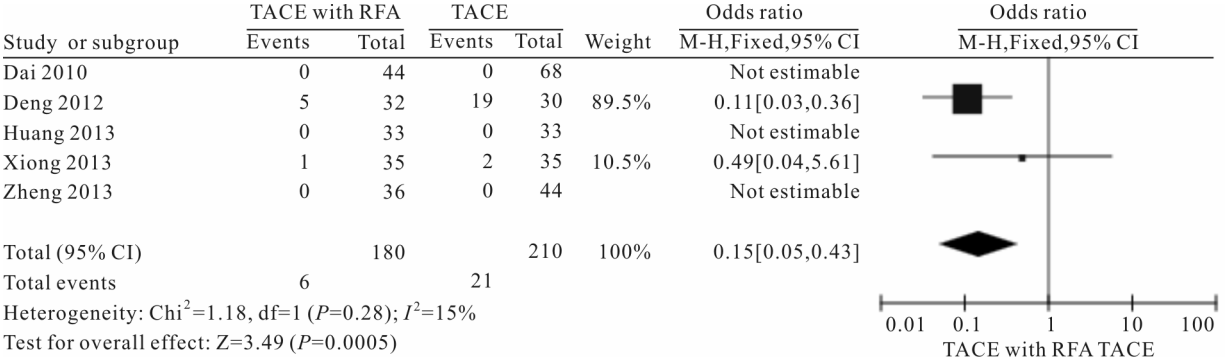

Fig. 8 Progressive disease rate of TACE with RFA versus TACE (fixed-effects model)

2.4 The Rate of AFP Reducing or Returning to Normal

Five trials reported changes in serum AFP in the patients[13, 16, 18, 19, 22]. There was no heterogeneity in the rate among those trials (P=0.51, I^2=0%) and the fixed-effects model was used to pool data. Meta-analysis showed that there was a remarkable difference in terms of AFP reducing rate among the five studies (OR=4.62, 95% CI 2.56–8.34, P<0.00001) (fig. 9).

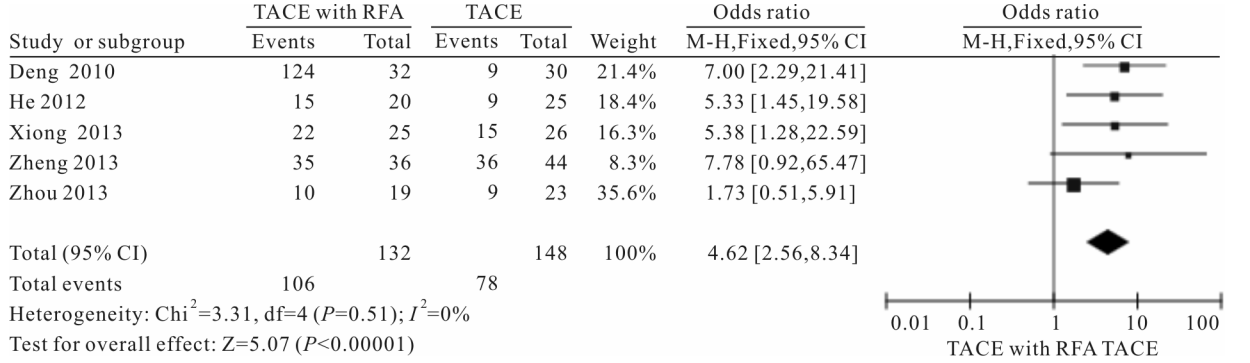

Fig. 9 Rate of AFP reducing or returning to normal rate of TACE with RFA versus TACE (fixed-effects model)

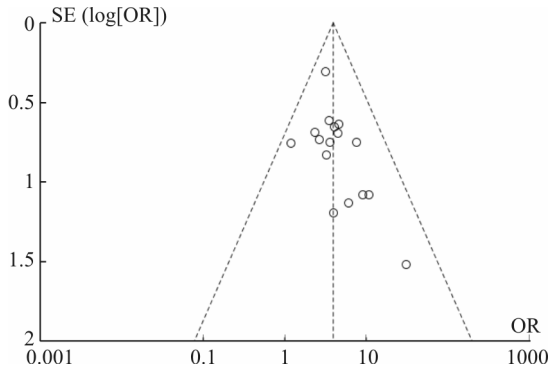

Fig. 10 Funnel plot for one-year survival rates in studies

2.5 Publication Bias

The publication bias was detected by using the funnel plot to evaluate the reliability of the meta-analysis results. Since all data were provided on the one-year overall survival rate, the symmetry of the funnel plot plotted on the basis of these data showed that the publication bias was not evident in this meta-analysis (fig. 8).

3 DISCUSSION

Liver cancer is one of the most common malignancies and with the development of technology, minimally invasive interventional treatment has been increasingly used for the treatment of advanced HCC. When surgical resection or liver transplantation is not a suitable option, TACE has been evidenced as the best therapeutic alternative for patients with HCC. Over the past two decades, the efficacy and safety of TACE in the treatment of HCC have been clinically tested. Nonetheless, it is only a palliative treatment, since complete tumor eradication could not be achieved for the vast majority of malignant tumors[9] and some disadvantages of TACE have been reported[27]. The main reason for the shortcomings is that the tumor blood supply is uniquely different. The blood supply system consists of the hepatic artery and portal vein. After TACE treatment, the blood supply to cancer from hepatic artery can be reduced by 90%[22], but because the blood supply for the periphery of the carcinoma is more from portal vein and more active for tumor growth, which leads to re-canalization embolism or formation of collateral circulation. As a result, TACE treatment alone is not sufficient for achieving complete necrosis of the main tumors, the recurrence rate remains high and the long-term survival is unsatisfactory[28]. In addition, some tumors lack blood supply. Repeated TACE inflicts damage on HCC patients, resulting in grave damage of normal liver parenchyma, and decreased short- and long-term survival. Our meta-analysis indicated that TACE combined with RFA is more effective and safer than TACE alone for the treatment for HCC.

RFA represents a new advance in the minimally invasive treatment of liver cancer. RFA induces thermal injury to the tissue through electromagnetic energy deposition[29]. RF-induced thermal ablation has been demonstrated to be a effective and safe modality for the treatment of small hepatic tumors contraindicated for surgical intervention[9, 22, 30]. Kim *et al*[31] reported that 5-year overall survival rate after percutaneous RFA for HCC was comparable to that after surgical resection for small HCC tumors. RFA treatment also has some limitations. For instance, in larger tumors in three-dimensional space, multiple overlapping needle placement misses tumor areas. Also, tumor necrosis induced by RFA coagulation is inadequate due to such local factors as presence of adjacent vessels or important viscera surrounding the tumor, irregular shape (not always spherical shape) or invasive growth. Moreover, blood flow from nearby vessels acts as a heat sink, which renders tumors next to these vessels inadequately treated. The cooling effect of surrounding vessels limits the coagulation-induced necrosis in the presence of peri-vascular tumor adjacent to the large vessels after RFA[32].

The combination therapy of TACE and RFA has been proved to be effective for local tumor control in HCC patients[3, 33], which was further confirmed by our meta-analysis. Theoretically, the combined use of TACE and RFA may have advantages over TACE alone for the treatment of HCC, since they are mutually complementary, thereby significantly improving the efficacy, life quality and long-term survival of HCC patients[9, 10]. Occlusion of hepatic arterial flow by means of TACE can reduce hepatic blood supply and tumor volume. The decreased cooling effect of hepatic blood flow by TACE reduces heat loss, thus increasing the size of the RFA ablative zone[34, 35]. For tumors supplied by portal vein or those without blood supply, areas that are not embolized by TACE may be decreased by a combination of TACE and RFA. The combination therapy might increase the chance of micrometastasis clearance, reduce the possibility of recurrence, and improve the overall survival rate. The TACE in combination with RFA not only increases the sensitivity of cancer cells to chemotherapeutic agents, but also minimizes the damage due to repetitive treatment. Some recent reports demonstrated that combination of TACE and RFA can enhance the therapeutic effect on hepatic tumors in both humans[33, 36, 37] and in animal models[38]. Therefore, the combination of TACE and RFA should be seen as a better treatment option for inoperable HCC than TACE alone. Further trials are warranted to evaluate the advantages of combination therapy over monotherapy.

This meta-analysis revealed that the combination of TACE and RFA was associated with higher 1-, 2-, and 3-year overall survival rate, tumor necrosis rate, RR and the rate of AFP reducing or returning to normal than TACE alone for the treatment of HCC. Moreover, RFA plus TACE treatment was found to be associated with a lower local recurrence rate and PD rate than the TACE alone, with the difference being statistically significant (P<0.05). On the other hand, there was no significant difference in SD rate between combination treatment and monotherapy (P>0.05). Sensitivity analysis demonstrated that TACE-plus-RFA therapy group was obviously superior to TACE-alone treatment group in terms of short- and long-term survival rates. TACE-plus-RFA treatment could obviously decrease the local recurrence rate and PD rate of HCC, and could increase its complete tumor necrosis rate and RR rate, thereby significantly improving the prognosis of HCC patients. Seventeen trials were included in this meta-analysis, and most studies were conducted in China, and publication bias could be expected. The publication bias in this meta-analysis was

assessed by the symmetry of the funnel plot (fig. 10). The funnel plot was fairly symmetric, indicating that there was no significant publication bias in this meta-analysis. However, because of some restraints in clinical practice, appropriate randomization and blinding were difficult to accomplish, only 4 studies included were of high quality[10, 15, 17, 22], and the quality of other studies low. As a result, the overall quality of all pooled results was relatively low. Thus, randomized-controlled trials of high quality involving larger size comparing TACE-plus-RFA treatment and TACE alone in HCC patients are needed.

Our study had several limitations. First, given the differences in demographic features of subjects among different studies, some important factors, such as, diagnostic criteria for liver cancer, were not consistent among the studies and this could result in heterogeneity of the studies. Second, these studies failed to explicitly assess the safety of TACE-plus-RFA treatment. The studies included didn't afford evidence that the combination treatment had no or less adverse effects. Finally, some studies were non-randomized controlled trial and all studies did not use blinding method.

In conclusion, this meta-analysis demonstrated that TACE in combination with RFA was more effective and safer than TACE monotherapy for the treatment of HCC contraindicated for surgical resection or liver transplantation. TACE plus RFA could obviously prolong the overall survival rate, enhance the complete tumor necrosis and curative effect, reduce local tumor recurrence and serum AFP.

Conflict of Interest Statement

The authors declared no potential conflicts of interest in the study.

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