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Influence of thermal ablation of hepatic metastases from gastric adenocarcinoma on long-term survival

Systematic review and pooled analysis

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Abstract

The objectives of this systematic review and pooled analysis were to examine long-term survival, morbidity, and mortality following thermal ablation of gastric cancer hepatic metastases and to identify prognostic factors that improve survival.

Patients with hepatic metastases from gastric cancer are traditionally treated with palliative chemotherapy. Surgical resection is an alternative treatment of hepatic metastases. Whether patients can obtain benefit from thermal ablation of hepatic metastases is still controversial.

A systematic literature search was undertaken (1990–2018). Publications were included if they studied more than 7 patients undergoing thermal ablation for hepatic metastasis from gastric cancer in the absence of peritoneal disease or other distant organ involvement. The primary outcome was the hazard ratio (HR) for overall survival. Comparison between thermal ablation and systematic chemotherapy or hepatic resection had been carried out. The influence of liver metastasis-related factors, such as <3 cm versus >3 cm, single versus multiple and metachronous versus synchronous upon survival was also assessed.

The median survival of thermal ablation for the 12 studies included was 22.93[20.45–25.41] months. Procedures were associated with a median 30-day morbidity of 6% (0%–23%) and with no mortality. The median 1-year, 2-year, 3-year, and 5-year survival were 79.14%, 39.79%, 28.45%, and 19.46%, respectively. Thermal ablation of hepatic metastasis was associated with improved overall survival compared with systematic chemotherapy (HR=2.12; 95% Cl 0.77–3.47; P=.000). Meta-analysis confirmed the additional survival benefit of size <3 cm (HR=1.46; 95% Cl 1.03–1.88; P=.002) and receiving chemotherapy after thermal ablation (HR=2.14; 95% Cl 1.05–3.23; P=.000).

A use of RFA/ microwave ablation (MWA) as a liver-directed treatment may provide greater survival benefit than chemotherapy and is an alternative option for the treatment of liver-only metastases from gastric cancer. With the appropriate selection of patients, such as tumors <3 cm in diameter, thermal ablation may provide better prognosis than hepatic resection of hepatic metastasis with lower morbidity and mortality. Postoperation chemotherapy should be provided to patients with GLM who received thermal ablation.

Abbreviations: GLM = gastric cancer liver metastasis, HR = hazard ratio, MWA = microwave ablation, OR = odds ratio, RFA = radiofrequency ablation.

Keywords: gastric cancer, hepatic metastases, thermal ablation

1. Introduction

Gastric cancer is the fourth most common type of tumor and the second cause of cancer-related death worldwide.^[1] The

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Received: 19 August 2018 / Accepted: 12 November 2018 http://dx.doi.org/10.1097/MD.000000000013525 prevalence of gastric cancer has district and gender differences. The incidence of gastric cancer in the North American women is lowest, with average incidence of 3.4/100000 people, whereas it is highest in Asian men, with average incidence of 26.9/100000, especially in Japan, South Korea, and China.^[2,3] Remote metastases as a sign of systemic disease reduce the overall patient survival. One of the most common sites for gastric cancer metastasis is the liver.^[4] The incidence of gastric cancer liver metastasis (GLM) during the course of the disease varies between 30% and 50%, including both synchronous and metachronous metastases.^[5,6] The first line treatment for GLM is systemic chemotherapy. However, the effect of chemotherapy is unsatisfactory and limited.

Thermal ablation, including radiofrequency ablation (RFA) and microwave ablation (MWA), has become widely used for hepatic metastasis, especially from colorectal cancer, and it has been proposed as an alternative to hepatic resection in patients with limited hepatic involvement or with solitary liver metastasis.^[7,8] More recently, thermal ablation was used for the treatment of liver metastases from gastric cancer and produced variable median survival periods ranging from 10.0 to 20.9 months with better

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survival outcomes in cases with single, small, and unilobar hepatic metastases.^[9–11] In eastern centers, some surgeons may embark on thermal ablation of gastric cancer hepatic metastasis in highly selected cases, but the standard treatment remains as supportive care and/or palliative chemotherapy.

The primary aim of this systematic review and pooled analysis was to examine overall survival following thermal ablation of gastric cancer hepatic metastases. The secondary aim was to identify prognostic factors of hepatic metastases from gastric cancer that may differentially improve survival.

2. Methods

2.1. Literature search strategy

An electronic literature search was undertaken using Embase, Medline, Pubmed, and Cochrane library databases up to July 2018. Search terms included "liver", "ablation", "neoplasm", "metastasis", "stomach", and "gastric cancer". Two authors Tang and Liu performed the electronic search independently in July 2018. Abstracts of the literature were reviewed by authors Tang and Liu to determine their suitability for inclusion in the pooled analysis. Any discordances regarding study inclusion between these 2 authors were settled in discussion with a third independent author Dong. The quality of evidence provided by each study was evaluated using the Oxford levels of evidencebased medicine scoring system (http://www.cebm.net/oxfordcentre-evidence-based-medicine-levels-march-2009/).

Publications were included in this review if they meet the following criteria:

- Cohort or comparative studies of patients undergoing RFA/ MWA for hepatic metastasis from gastric adenocarcinoma, in the absence of peritoneal disease;
- (2) Included more than 7 patients; and
- (3) Survival data for at least median survival time following RFA/ MWA were available.

Publications were excluded if they met any of the following criteria:

- (1) Studies published in a language other than English;
- (2) Case reports or cohort studies including less than 7 patients;
- (3) Studies including patients with peritoneal disease or other non-liver organ involvement including spleen and pulmonary metastases;
- (4) Survival outcome data and data regarding RFA/MWA were unavailable; and
- (5) Malignancy other than gastric adenocarcinoma with secondary liver metastasis.

In the situation in which authors from the same institution had published a primary paper and then an updated analysis with a larger patient cohort, the most recent publication was included in the analysis.

2.2. Outcome measures for meta-analysis of comparative studies

The primary outcome measure evaluated was the hazard ratio (HR) for overall survival. The influence of liver metastasis-related factors: size, unilobar versus bilobar, multiple versus single, and metachronous versus synchronous upon survival was also assessed. Metachronous metastases were identified at least 6 months after the cessation of treatment for the primary gastric

cancer (following surgery or adjuvant chemotherapy). Only studies that provided direct comparison of survival for RFA/ MWA or no ablation, or for the influence of the liver metastasisrelated factors described above, were included in the metaanalysis. Survival was calculated from the time of ablation of the hepatic metastases or time of diagnosis of hepatic metastases in the nonablation group.

2.3. Statistical analysis

Two independent reviewers extracted data from the selected articles by using a predefined data extraction form. To estimate HR and its variance, this was extracted from the study directly or required additional calculation depending on the method of data being presented: annual mortality rates, survival curves, number of deaths, or percentage freedom from death.^[12] The measure of effect of liver metastasis related factors was an odds ratio (OR) of cumulative survival. For each study, the OR was estimated by a method dependent upon the data provided. The simplest method consisted of the direct collection of ORs with 95% CIs mentioned in the original study.

Meta-analysis of data was conducted using a random effects model. Publication bias was explored graphically with funnel plots to detect asymmetry and any outliers. Inter-study heterogeneity was assessed using the x² statistic and the I² value to measure the degree of variation not attributable to chance alone. This was graded as low (I² <25%), moderate (I² 25%– 75%), or high (I² >75%). The significance level was set at P < .05. This meta-analysis is exempt from ethical approval as the analysis involves only already published and anonymized data.

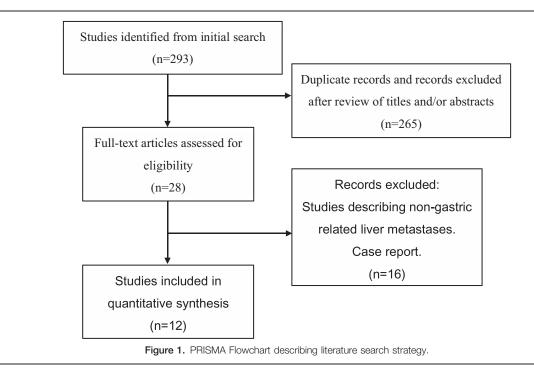
3. Results

3.1. Search results

Figure 1 shows the literature search flowchart. During the literature search, we found 293 studies. After reviewing the titles and abstracts we found 265 articles to be not eligible as they were review articles, editorials, nonhuman studies or non-English articles, not focusing on the review topic, and others not meeting the inclusion criteria. We identified 28 articles as potentially eligible for this review. However, 7 of these articles were case reports and 9 of them were non-gastric related liver metastases. We finally selected 12 eligible articles^[9-11,13-21] (Fig. 1). All these included 12 research articles were observational studies.

3.2. Characteristics of the studies

In our meta-analysis, we included 12 observational studies that evaluated the survival rate in patients affected by thermal ablation for hepatic metastasis from gastric cancer. In Table 1, we report the main characteristics of these studies. The total number of patients considered in the survival analysis of the included studies was 226 with median age of around 63 years. Liver is the only organ metastasis from gastric cancer in the studies included. 8 of the studies were from Korea, 3 from China and 1 from Japan. None of the studies included was from the same institution. 2 of the studies researched about MWA for GLM, the other 10 were about RFA for GLM. Thermal ablation for GLM can be performed for a median 30-day morbidity of 6% (0%–23%) and with no mortality from the studies included. The median 1-year, 2-year, 3-year, and 5-year survival were 79.14%, 39.79%, 28.45%, and 19.46%, respectively, with a median survival time



22.93[20.45-25.41] months for patients undergoing thermal ablation for GLM.

In Table 2, we analyzed factors affecting prognosis in patients undergoing RFA/MWA for GLM. The results suggested that the most important prognostic factors were the size of hepatic metastases, chemotherapy after thermal ablation and T stage of the primary gastric cancer in 58%, 50%, and 50% of studies included. Other important factors in terms of prognosis also included the number of hepatic metastases (42%), age of the patients (42%), distribution of hepatic metastases (unilobar or bilobar) (33%), synchronous versus metachronous hepatic metastases (33%), and lymph node status (25%) of the primary gastric cancer. We also evaluated the survival rate in patients with GLM, comparing thermal ablation with hepatic resection (25%), and systemic chemotherapy (33%).

3.3. Main analysis of comparative studies

3.3.1. Thermal ablation versus surgical resection of hepatic metastases. Pooled analysis of 3 studies^[15,16,18] included 143 patients: 54 in RFA/MWA group and 89 in surgical resection group (Fig. 2A). This pooled analysis demonstrated that surgical resection of hepatic metastases was associated with a significantly improved survival compared with RFA/MWA (HR=0.81; 95% CI 0.75–0.88; P=.271). There was no evidence of significant statistical heterogeneity for this result (I²=23.4%).

3.3.2. Thermal ablation versus systemic chemotherapy. Pooled analysis of 4^[13,14,19,21] studies included 190 patients: 88 in RFA/MWA group and 102 in systemic chemotherapy group (Fig. 2B). This pooled analysis demonstrated that thermal ablation of hepatic metastases was associated with an improved

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								Ove	rall survi	val
Authors	Country	Time period	Quality of evidence [*]	Patient number	Median age	1-year	2-year	3-year	5-year	Median (months) 95% Cl
SE Hwang et al	Korea	1995–2005	2b	15	59	86.70%	73.30%	66.70%	46.70%	22[5.6-38.4]
HR Kim et al	Korea	1995–2008	2b	20	57	66.80%	45.00%	40.10%	16.70%	26.25[14.57-37.92]
T Ryu et al	Japan	1997-2015	2b	13	66	91.70%	46.15%	37.50%	25%	36.95[21.58-52.32]
A Guner et al	Korea	1998–2013	2b	30	60	73.30%	60%	43%	34.40%	35.28[26.67-43.90]
HO Kim et al	Korea	2000-2008	2c	7	66	NR	NR	NR	NR	13.93[3.20-24.56]
CWLee et al	Korea	2000-2013	2b	19	63	73.70%	34.70%	NR	14.50%	20.5[17.8-22.8]
JW Lee et al	Korea	2000-2014	2b	11	66	90.91%	36.36%	27.27%	18.18%	30.1[14.2-46.1]
J Li et al	China	2001-2015	2b	21	60	75%	42.86%	6.30%	NR	22.47[18.07-26.88]
J Chen et al	China	2002-2007	2b	21	65	70%	11%	5%	3%	23.1[17.5,28.8]
BL Yun et al	Korea	2002-2008	2c	10	61	80%	30%	20%	NR	20.5[11.30-29.70]
JEH wang et al	Korea	2002-2011	2b	27	64	81.48%	18.52%	7.41%	NR	20.9[18.4-23.4]
F Zhou et al	China	2008-2016	2b	32	65	80.90%	NR	31.20%	16.70%	25[16.5-33.5]
TOTAL				226	62.7	79.14%	39.79%	28.45%	19.46%	22.93[20.45-25.41]

NR indicates not recorded.

* Oxford Centre for Evidence-based Medicine-Levels of Evidence (March 2009) http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009.

							Hepat	Hepatic metastasis		
Authors	Age	versus HR	versus CTx	Post-treatment CTx	reatment CTx Pathologic stage	Number	Size	Synchronous/metachronous	Distribution	Extrahepatic metastasis
SE Hwang et al	RN	NR	4.79[1.76-13.05]	NR	2.03[1.18-3.49]	NR	1.25[0.43-4.8]	0.8[0.36-1.83]	2.11[1.25–3.56]	2.01[1.10–3.67]
HR Kim et al	3.99[2.97-5.35]	NR	3.19[2.56–3.99]	4.51[3.37-6.04]	0.73[0.63-0.84]	1.17[1.08-1.28]	1.18[1.06–1.32]	1.13[1.04–1.23]	1.18[1.04–1.32]	, NR
T Ryu et al	NR	0.84[0.77-0.92]	NR	NR	NR	NR	NR	NR	NR	NR
A Guner et al	NR	1.113[0.648-1.910]	NR	NR	NR	NR	1.905[1.126–3.223]	0.77[0.71–0.83]	NR	NR
HO Kim et al	1.64[1.22-2.21]	, NR	NR	6.43[1.51–27.36]	0.78[0.59–1.05]	0.99[0.72-1.34]	2.21[1.37–3.59]	NR	NR	NR
CW Lee et al	1[0.34-1.82]	NR	NR	0.75[0.20-1.93]	1.19[0.49–10.75]	NR	1.14[0.57–2.87]	NR	NR	NR
JW Lee et al	0.64[0.62-0.65]	0.75[0.65-0.87]	NR	2.86[2.07–3.95]	M	NR	5.71[3.56–9.16]	NR	NR	NR
J Li et al	NR	NR	1.069 (0.603-1.069)	NR	NR	NR	NR ,	NR	NR	NR
J Chen et al	NR	NR	NR	0.88[0.60-1.30]	1.44[0.60–3.45]	6.174[1.519-25.095]	0.94[0.71-1.26]	1.19[0.60–2.34]	0.536[0.123-2.336]	NR
BL Yun et al	2.99[2.07-4.34]	NR	NR	NR	8.68[4.75-15.87]	NR	NR	NR	NB	NR
JEH wang et al	0.73[0.26-2.12]	NR	NR	2.06[1.40–2.82]	1.10[0.48-2.55]	1.77[0.78–3.40]	1.23[0.31–3.47]	NR	1.87[1.01–3.24]	1.75[1.16–2.52]
F Zhou et al	NR	NR	1.751[1.077–2.845]	NR	NR	2.461[1.365-4.276]	2.437[1.361–4.683]	NR	NR	7.531[4.754–30.768]
Total	1.99[1.02–2.96]	1.99[1.02–2.96] 0.81[0.75–0.88]	2.12[0.77-3.473]	2.14[1.05–3.23]	0.90[0.57-1.24]	1.17[0.92–1.41]	1.46[1.03-1.88]	0.95[0.65–1.26]	1.32[0.81-1.84]	1.82[1.22,2.42]

survival compared with systemic chemotherapy, but without significant differences (HR = 2.12; 95% CI 0.77–3.47; P = .000). The result had significant heterogeneity $(I^2 = 90.9\%)$. For sensitivity analyses, a single study involved in the pooled meta-analysis was excluded each time. The heterogeneity had reduced to 44.4% when 1 study^[14] excluded in the pooled analysis, while the result was unchanged (HR=1.35; 95% CI 0.64–2.05; P=.165). The random-effect model was used in the analysis.

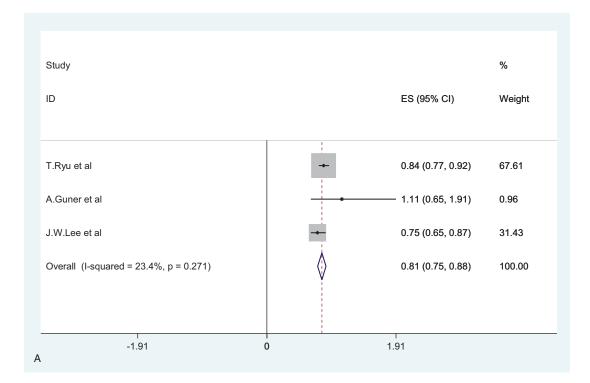
3.3.3. Thermal ablation of <3cm versus >3cm hepatic metastases. There were 9 studies researched about effect of size of hepatic metastases on thermal ablation of GLM. 2 studies were excluded: $1^{[11]}$ is about <2 cm versus >2 cm, the other^[13] is about <4 cm versus >4 cm. Pooled analysis of 7 studies^[9,10,14,16–18,21] included 182 patients receiving thermal ablation. This pooled analysis demonstrated that size of hepatic metastases less than 3 cm was associated with a significantly improved survival compared with larger 1 (HR = 1.46; 95% CI 1.03–1.88; P = .002) (Fig. 3A). The result had significant heterogeneity ($I^2 = 70.5\%$). A random-effect model was used in the analysis.

3.3.4. Thermal ablation with post-operation of chemotherapy versus thermal ablation alone. Pooled analysis of 6 studies^[9-11,14,17,18] included 105 patients to compare whether post-operative chemotherapy can improve survival of patients with GLM. This pooled analysis demonstrated that chemotherapy after thermal ablation was associated with a significantly improved survival compared with thermal ablation alone (HR = 2.14; 95% CI 1.05-3.23; P=.000) (Fig. 3B). The result had significant heterogeneity ($I^2 = 88.8\%$). Some patients in the studies had gastric cancer with synchronous hepatic metastases that might get more benefit from thermal ablation with postoperation of chemotherapy compared with those with metachronous hepatic metastases who had received chemotherapy before. When we compared thermal ablation + post-operation of chemotherapy with thermal ablation alone, we did not distinguish synchronous from metachronous. This may be the main reason of heterogeneity. Kinds of chemotherapy included in the studies may be another reason of heterogeneity.

3.3.5. Thermal ablation of synchronous versus metachronous hepatic metastases. Pooled analysis of 4 studies^[10,13,14,16] included 86 patients to compare thermal ablation of synchronous and metachronous of hepatic metastases. This pooled analysis demonstrated no significant differences between synchronous and metachronous hepatic metastases in overall survival (HR=0.95; 95% CI 0.65–1.26; P=.000) (Fig. 3C). The result had significant heterogeneity ($I^2 = 92.5\%$). For sensitivity analyses, a single study involved in the pooled meta-analysis was excluded each time. The heterogeneity had reduced to 0.0% when 1 study^[14] excluded in the pooled analysis (Figure S1, http://links.lww.com/MD/C678). As a result, the result demonstrated metachronous was associated with a significantly improved survival compared with synchronous. (HR = 0.77; 95% CI 0.71-0.83; P = .639). The fixed-effect model was used in the analysis.

3.4. Other factors

5 studies^[9–11,14,21] were included to analyze the effect of number of hepatic metastases in overall survival. The result demonstrated no significant differences between solitary and multiple hepatic metastases (HR = 1.17; 95% CI 0.92–1.41; P = .216) (Figure S2, http://links.lww.com/MD/C678). The result of pooled analysis of



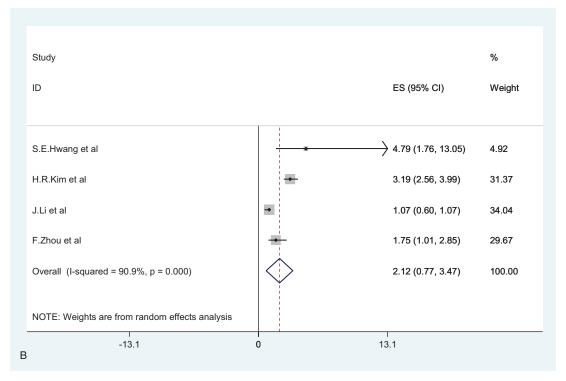
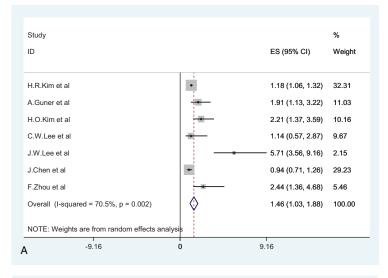
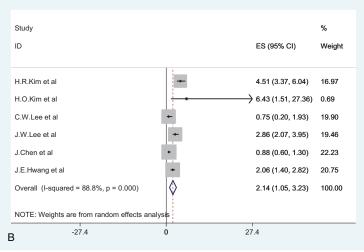


Figure 2. Forrest plot random effects model for (A) thermal ablation of GLM versus hepatic resection (HR=0.81; 95% CI 0.75–0.88); (B) thermal ablation of GLM versus systematic chemotherapy (HR=2.12; 95% CI 0.77–3.47). CI=confidence interval, GLM=gastric cancer liver metastasis, HR=hazard ratio.

4 studies^[10,11,13,14] demonstrated no significant differences between unilobar and bilobar distribution of hepatic metastases (HR = 1.32; 95% CI 0.81–1.84; P=.158) (Figure S3, http://links. lww.com/MD/C678). To compare the effect of different T stage of the primary gastric cancer to thermal ablation of GLM, the result of pooled analysis of 6 studies^[9,11,13,14,17,20] demonstrated

no significant differences between I/II and III/IV in overall survival for thermal ablation of GLM (HR = 0.90; 95% CI 0.57– 1.24; P=.022) (Figure S4, http://links.lww.com/MD/C678). Extrahepatic lymph node metastases and the age of patients with GLM had significant effect on overall survival for thermal ablation of GLM, for no extrahepatic metastases versus





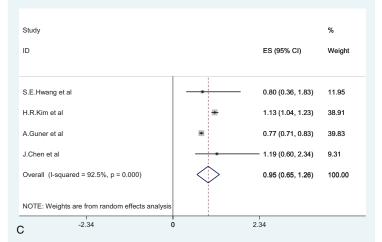
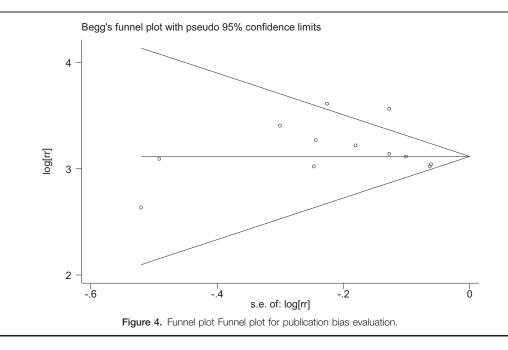


Figure 3. Forrest plot random effects model for the influence of liver metastasis-related factors. (A) size<3cm versus >3cm (HR=1.46; 95% Cl 1.03–1.88; P=.002); (B) thermal ablation +chemotherapy versus thermal ablation alone (HR=2.14; 95% Cl 1.05–3.23; P=.000); (C) synchronous versus metachronous hepatic metastases (HR=0.95; 95% Cl 0.65–1.26; P=.000). Cl=confidence interval, HR=hazard ratio.



extrahepatic metastases, HR = 1.82; 95% CI 1.22–2.42 (Figure S5, http://links.lww.com/MD/C678); for age <64 years versus >64 years, HR = 1.99; 95% CI 1.02–2.96 (Figure S6, http://links.lww.com/MD/C678).

3.5. Bias exploration/sensitivity analyses

Funnel plots were created for combined and the subgroup analysis for the various factors to visual assess the publication bias (Fig. 4). They demonstrated symmetry. In order to uncover the influence of each study's individual dataset, we performed sensitivity analyses for the 4 subgroups mentioned above. A single study involved in the pooled meta-analysis was excluded each time, the results had mentioned above.

4. Discussion

Thermal ablation has been used increasingly as an alternative locoregional treatment for primary and secondary hepatic malignancies and has been frequently used in patients who are poor candidates for surgery or deemed unresectable.^[22,23] Because of great metastasis rate of gastric cancer, whether patients can get benefit from thermal ablation of GLM is still controversial. This systematic review with pooled analysis shows that thermal ablation of GLM in the absence of peritoneal disease is associated with 1-year, 2-year, 3-year, and 5-year survivals of 79.14%, 39.79%, 28.45%, and 19.46% respectively, and a median survival of 23 months. Those survival figures in selected patients are better than the 1-year survival of 46% and the median survival of 11.3 months reported using epirubicin, oxaliplatin, and capecitabine (EOX) in REAL3 randomized controlled phase III trial,^[24] or the median survival of 13.8 months reported using trastuzumab along with chemotherapy in the ToGA randomized controlled phase III trial.^[25] Compared with systematic chemotherapy alone, thermal ablation can destroy hepatic metastases from gastric cancer which has been resistant to chemotherapy. This pooled analysis demonstrated that thermal ablation of hepatic metastases was associated with an improved survival compared with systemic chemotherapy, but without significant differences (HR = 2.12; 95% CI 0.77–3.47).

The result of recent meta-analysis^[26] about hepatic resection of GLM mentioned the median 1-year, 3-year, and 5-year survival were 68%, 31%, and 27%, respectively, with a median survival or 21 (9-52.3) months, which has similar prognosis compared with thermal ablation of GLM. Compared with hepatic resection, thermal ablation is a minimal-invasive technique with lower morbidity and mortality. With the appropriate selection of patients, such as tumors <3 cm in diameter, thermal ablation is a safe and feasible treatment option for GLM, sometimes has better prognosis than hepatic resection.^[16] The result of pooled analysis in this study showed hepatic resection had improved survival compared with thermal ablation (HR=0.81; 95% CI 0.75-0.88). The ideal size for RFA is less than 3 cm in order to achieve a tumor-free ablation margin.^[27] However, patients with large hepatic metastasis also received thermal ablation in studies included. That is may be the reason why thermal ablation had poor prognosis compared with hepatic resection in this metaanalysis.

Diameter of hepatic metastasis less than 3 cm had been the best prognosis in this meta-analysis because of tumor-free margin achieved during thermal ablation of GLM. Other important prognostic factors included whether received chemotherapy after RFA/MWA and extrahepatic lymph node metastases. Interestingly, distribution and number of hepatic metastasis have limited effect on survival of thermal ablation of GLM, which is quite different from hepatic resection. For thermal ablation, the size of hepatic metastasis is the only factor to achieve tumor-free margin. Multiple metastases in bilobar of liver can also be destroyed by thermal ablation with limited damage of liver function, if only the size is less than 3 cm.

Just as mentioned in inclusion criteria, the current analysis did not include patients with peritoneal disease or other nonliver metastatic sites. The prognosis in patients with positive peritoneal cytology or peritoneal metastasis is rather poor and no survival benefits have been observed with thermal ablation. The result of present study should be viewed with caution, as the present study has several limitations. Patients with gastric cancer always have peritoneal metastasis before hepatic metastasis or combined with nonliver metastatic sites. Patients with hepatic metastasis as the only metastatic sites included in the studies are quite few. In the 12 studies included in the meta-analysis, the largest number of patients is 98 patients. Some results of the pooled analysis have methodological heterogeneity which is hard to eliminate. In spite of those limitations, the study has robust statistical analysis and presents a concept that can dramatically change clinical practice. A use of RFA/MWA as a liver-directed treatment may provide greater survival benefit than chemotherapy and is an alternative option for the treatment of liver-only metastases from gastric cancer. With the appropriate selection of patients, such as tumors <3 cm in diameter, thermal ablation may provide better prognosis than hepatic resection of hepatic metastasis with lower morbidity and mortality. Post-operation chemotherapy should be provided to patients with GLM who received thermal ablation.

5. Conclusion

The meta-analysis of multivariate data shows a survival advantage of thermal ablation of hepatic metastases. A use of RFA/MWA as a liver-directed treatment may provide greater survival benefit than chemotherapy and is an alternative option for the treatment of liver-only metastases from gastric cancer. With the appropriate selection of patients, such as tumors <3 cm in diameter, thermal ablation may provide better prognosis than hepatic resection of hepatic metastasis with lower morbidity and mortality. Post-operation chemotherapy should be provided to patients with GLM who received thermal ablation. Studies included in the meta-analysis are with low quality of evidence and patients included in the studies are quite few which is the main limitation of this meta-analysis. At this point, an international prospective study would be needed to clearly assess the feasibility and complications of thermal ablation of GLM. Then, it will possible to plan specific randomized clinical trials to fully understand the effectiveness of thermal ablation of GLM.

Author contributions

Conceptualization: Kezhong Tang, Linping Dong.

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Funding acquisition: Yanmo Liu.

- Investigation: Jian Chen, Zhe Tang.
- Methodology: Zhe Tang.
- Resources: Yanmo Liu, Linping Dong.
- Software: Kezhong Tang, Yanmo Liu, Linping Dong.
- Supervision: Kezhong Tang, Linping Dong.
- Validation: Kezhong Tang, Linping Dong.

Visualization: Linping Dong.

- Writing original draft: Kezhong Tang.
- Writing review & editing: Kezhong Tang.

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