Percutaneous ablation for adrenal metastases: a systematic review and meta-analysis

Jian-Hua Zhang[1], **Yu-Fei Fu**[2], **Jing-Ya Wang**[2]

[1]Department of Interventional Radiology, Fengjie People's Hospital, Chongqing, China
[2]Department of Radiology, Xuzhou Central Hospital, Xuzhou, China

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Abstract

Introduction: *Imaging-guided percutaneous ablation (PA) is commonly employed for the treatment of patients diagnosed with adrenal metastasis (AM), but comprehensive analyses are essential to validate the efficacy and safety of this approach.*
Aim: *The present meta-analysis was designed to evaluate the safety, efficacy, and long-term outcomes associated with the imaging-guided PA treatment of AM.*
Material and methods: *Relevant studies in the PubMed, Embase, and Wanfang databases published as of June 2022 were identified, and pooled endpoint analyses were performed with Stata 12.0.*
Results: *This meta-analysis included 15 studies. Overall, the respective pooled primary technical success, secondary technical success, local hemorrhage, pneumothorax, hypertension crisis, local recurrence, 1-year overall survival (OS), and 3-year OS rates in study participants were 88%, 93%, 3%, 6%, 6%, 19%, 80%, and 46%. High levels of heterogeneity were evident for the 1-year OS (I^2 = 79.6%) and 3-year OS endpoints (I^2 = 67.1%), but meta-regression analyses failed to identify predictors of these OS rates. Low heterogeneity was observed for subgroups of patients who had undergone cryoablation (I^2 = 0%) or patients with multiple primary cancers (I^2 = 0%) with respect to 1-year OS. Similarly, low heterogeneity for the 3-year OS endpoint was detected in subgroups of patients who had undergone cryoablation (I^2 = 0%), ultrasound-guided PA (I^2 = 0%), individuals with AMs secondary to hepatocellular carcinoma (I^2 = 0%), and patients with multiple primary cancers (I^2 = 0%).*
Conclusions: *These results suggest imaging-guided PA to be a safe and effective treatment for AM associated with satisfactory long-term patient outcomes.*

Key words: *ablation, imaging, adrenal, metastasis.*

Introduction

The adrenal glands are a common site of tumor metastasis, and such adrenal metastasis (AM) is often associated with poor patient outcomes [1]. While adrenalectomy can improve the survival of patients with isolated AMs [2–5], patients with some comorbidities are ineligible for this procedure [1]. Imaging-guided percutaneous ablation (PA) is often implemented as an alternative to adrenalectomy [6, 7], with several studies having reported these two techniques to exhibit comparable levels of clinical efficacy for benign adrenal tumors, with PA additionally being associated with reduced intraoperative blood loss, a shorter operative duration, and more rapid postoperative recovery [6, 7].

Imaging-guided PA is commonly utilized as a treatment for AM, and reported technical success, local

Address for correspondence
Jing-Ya Wang, Department of Radiology, Xuzhou Central Hospital, Xuzhou, China, e-mail: wjyhetao@163.com

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recurrence, and complication rates associated with this procedural approach are in the range of 96–97%, 8.8–25%, and 8.6–18%, respectively [8, 9]. Moreover, the 3-year rates of local recurrence-free survival and overall survival (OS) associated with such PA-based treatment are reported to be in the range of 52–69% and 34–52%, respectively [8, 9]. However, the guidance approaches, PA methods, and primary tumor types included in these studies have the potential to influence the conclusions of associated studies. Hence, comprehensive analyses of the safety and clinical efficacy of imaging-guided PA for the treatment of AMs are warranted, as is confirmation of the factors that influence such safety and efficacy.

Aim

Here, a meta-analysis was performed with the goal of assessing the clinical efficacy, safety, and long-term outcomes associated with imaging-guided PA-based treatment of AMs.

Material and methods

Study selection

Study selection was conducted based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklists [10].

Relevant studies in the PubMed, Embase, and Wanfang databases published as of June 2022 were identified with the following strategy: ((ablation) AND (adrenal)) AND ((metastasis) OR (metastatic)). This meta-analysis was registered at INPLASY.COM (No. INPLASY202270032).

Studies eligible for meta-analysis were:

a) studies focused on computed tomography (CT)- or ultrasound (US)-guided PA treatment of AM;
b) studies with > 20 patients;
c) studies on inoperable patients or patients who refused surgery;
d) studies reporting a minimum of one of the following: PA technical success, local hemorrhage, pneumothorax, hypertensive crisis, local recurrence, 1-year OS, and/or 3-year OS rates;
e) no language limitations were imposed.

Studies were not eligible for inclusion if they:

a) utilized multiple guidance methods;
b) employed multiple PA methods;
c) performed chemical ablation;
d) were case reports, letters, or reviews.

Data extraction

Two authors were responsible for the independent extraction of relevant data from eligible studies, and any discrepant data were resolved through discussion with a third investigator. Extracted baseline data included first author, publication year, country, patient number, study design, number of AMs, patient age, imaging guidance approach, tumor diameter, and PA methodology. Outcome data extracted from these studies included rates of technical success, local hemorrhage, hypertensive crisis, local recurrence, pneumothorax, 1-year OS, and 3-year OS.

Quality assessment

The Newcastle-Ottawa scale [11] was used to evaluate observational study quality. Studies were assigned points according to selection (4 points), comparability (2 points), and outcome (3 points) criteria, with studies exhibiting a NOS score ≥ 7 being considered of high quality.

Endpoints

Technical success was defined by the completion of PA-based AM treatment as per the planned treatment protocol without any visible evidence of tumor enhancement on contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) performed 2–5 days after treatment, given that the targeted ablation zone in the surrounding fat tissue is difficult to detect on CT or MRI [8, 9]. Hypertensive crisis was defined by systolic blood pressure ≥ 180 mm Hg or diastolic blood pressure ≥ 110 mm Hg [6, 7].

Statistical analysis

Random-effects models were used for all pooled analyses owing to the presumption of heterogeneity, with weighting being performed in accordance with the inverse variance of these studies. Heterogeneity was assessed with the Q test and the I^2 statistic, with $I^2 > 50\%$ corresponding to high levels of heterogeneity. Sources of heterogeneity were investigated with meta-regression and subgroup analyses. Egger's test was used to assess publication bias, with $p < 0.05$ as the threshold of significance. Stata 12.0 was used for all pooled analyses.

Results

Study selection

The study selection process is detailed in Figure 1. In total, 15 articles were included in this meta-analysis [12–26], all of which were retrospective (Table I). These studies included 538 patients with 562 AMs who underwent treatment via imaging-guided PA. Of these 15 articles, 8 employed radiofrequency ablation (RFA) [14–16, 18, 20, 22, 25, 26], 5 employed cryoablation (CA) [12, 13, 17, 23, 24], and 2 employed microwave ablation (MWA) [19, 21]. In addition, 10 studies employed CT guidance [12, 13, 15, 19, 20, 22–26], while 5 employed US guidance [14, 16–18, 21]. Of these studies, 9 included patients with multiple primary cancers [12, 14, 15, 17, 18, 21, 23, 25, 26], while 3 included patients with AMs secondary to lung cancer (LC) [13, 19, 24], and 3 studies enrolled individuals with AMs secondary to hepatocellular carcinoma (HCC) [16, 20, 22]. All articles reported NOS scores in the range 7–8.

Primary technical success

Primary technical success rates were reported in all studies, with a pooled primary technical success rate of 88% (95% CI: 0.85–0.91, Figure 2 A). While these studies exhibited low heterogeneity for this endpoint (I^2 = 18.6%, p = 0.246), a high risk of publication bias was detected (Egger's test: $p < 0.01$).

Secondary technical success

Secondary technical success rates were reported in four studies [12, 15, 16, 18], with a pooled secondary technical success rate of 93% (95% CI: 0.88–0.97, Figure 2 B). While these studies exhibited low heterogeneity for this endpoint (I^2 = 0%, p = 0.508), a high risk of publication bias was detected (Egger's test: p = 0.005).

Local hemorrhage

Local hemorrhage rates were reported in four studies [15, 19, 25, 26], with a pooled rate of 3% (95% CI: 0.01–0.05, Figure 2 C). These studies exhibited low heterogeneity for this endpoint (I^2 = 0%, p = 0.495), and Egger's test failed to detect any publication bias.

Pneumothorax

Pneumothorax rates were reported in four studies [20, 22, 25, 26], with an overall pooled rate of 6% (95% CI: 0.02–0.09, Figure 2 D). These studies exhibited low heterogeneity for this endpoint (I^2 = 0%, p = 0.996), and Egger's test failed to detect any publication bias.

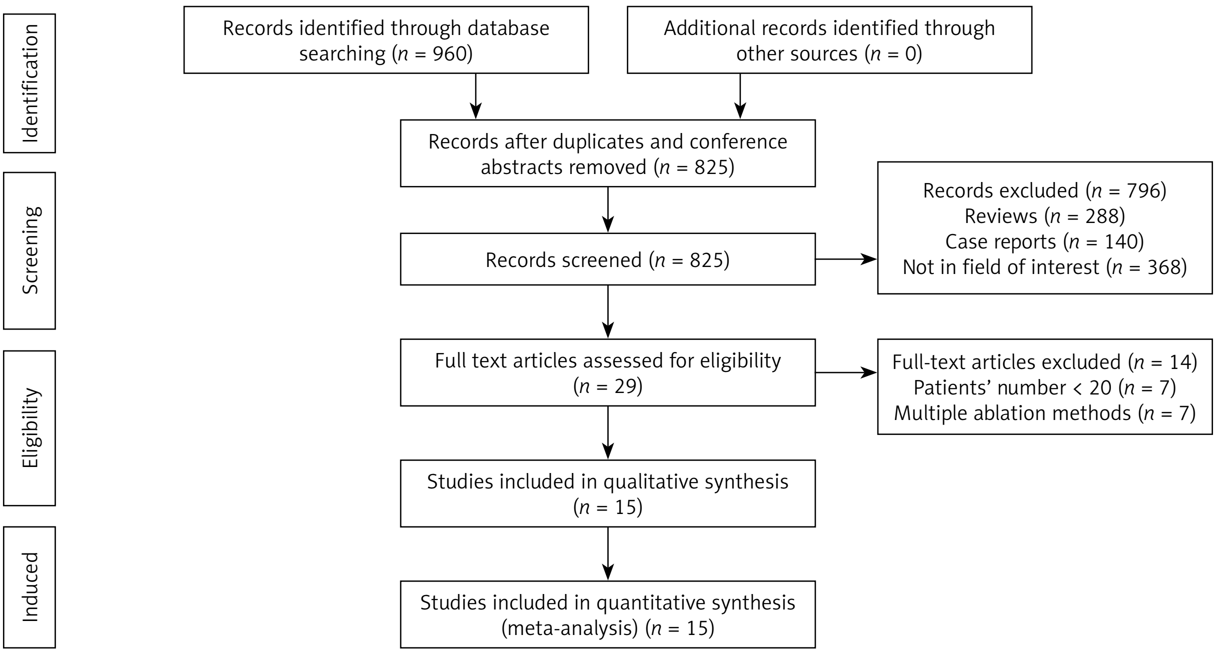

Figure 1. Study selection flow chart

Table I. Baseline data of the included studies

Author [ref.]	Year	Country	Number of patients	Number of AMs	Mean age [years]	Mean diameter [cm]	Primary tumor	Ablation methods	Guidance	Mean follow-up [m]
Aoun [12]	2021	USA	34	40	63	3.2	Multiple	CA	CT	21.3
Cheng [13]	2021	China	34	34	58.4	3.0	LC	CA	CT	28.8
Gao [14]	2020	China	43	43	60.9	Not given	Multiple	RFA	US	28.6
Hasegawa [15]	2015	Japan	35	41	64.7	3.3	Multiple	RFA	CT	30.1
Huang [16]	2019	China	22	22	53.0	4.0	HCC	RFA	US	10
Li [17]	2013	China	30	30	64.2	4.2	Multiple	CA	US	Not given
Liu [18]	2020	China	29	29	52.9	Not given	Multiple	RFA	US	24.5
Men [19]	2016	China	31	31	64.9	3.46	LC	MWA	CT	11.1
Sui [20]	2019	China	70	70	Not given	Not given	HCC	RFA	CT	Not given
Sun [21]	2010	China	23	24	49.35	4.1	Multiple	MWA	US	Not given
Yuan [22]	2018	China	38	38	54.2	3.3	HCC	RFA	CT	26.3
Zhang [23]	2018	China	31	31	57.9	3.0	Multiple	CA	CT	30.5
Zhang [24]	2021	China	39	39	58.4	3.0	LC	CA	CT	33
Zhou [25]	2018	China	33	38	60	Not given	Multiple	RFA	CT	22.8
Zhou K [26]	2018	China	46	52	64.4	3.31	Multiple	RFA	CT	11.5

AM – adrenal metastasis, CA – cryoablation, CT – computed tomography, HCC – hepatocellular carcinoma, LC – lung cancer, MWA – microwave ablation, RFA – radiofrequency ablation, US – ultrasound.

Hypertensive crisis

Hypertensive crisis rates were reported in 11 studies [12, 14–22, 25, 26], with a pooled rate of 6% (95% CI: 0.03–0.08, Figure 2 E). Low heterogeneity was detected among these studies (I^2 = 20.4%, p = 0.249), as well as a low risk of publication bias (Egger's test: p = 0.935).

Local recurrence

Local recurrence rates were reported in 12 studies [12, 13, 15–19, 22–26], with a pooled local recurrence rate of 19% (95% CI: 0.15–0.23, Figure 2 F). This endpoint was associated with low levels of heterogeneity (I^2 = 0%, p = 0.87), as well as a low risk of publication bias (Egger's test: p = 0.744).

1-year overall survival

Patient 1-year OS was reported in nine studies [13–15, 18–20, 22–24], with an overall pooled 1-year OS of 80% (95% CI: 0.71–0.88, Figure 2 G). This endpoint exhibited high levels of heterogeneity (I^2 = 79.6%, p < 0.001), as well as a high risk of publication bias (Egger's test: p = 0.003).

Meta-regression analyses failed to identify predictors of 1-year OS rates (Table II), and details pertaining to subgroup analyses for this endpoint are provided in Table III. Low heterogeneity was evident in subgroups of patients who had undergone CA (I^2 = 0%) and patients with multiple primary cancers (I^2 = 0%).

3-year overall survival

Patient 3-year OS was reported in seven studies [14, 15, 18, 20, 22–24], with an overall pooled 3-year OS of 46% (95% CI: 0.36–0.56, Figure 2 H). This endpoint exhibited high levels of heterogeneity (I^2 = 67.1%, p = 0.006), as well as a high risk of publication bias (Egger's test: p = 0.007).

Meta-regression analyses failed to identify predictors of 3-year OS rates (Table II) and details pertaining to subgroup analyses for this endpoint are provided in Table IV. Low heterogeneity was evident in subgroups of patient who had undergone CA (I^2 = 0%), patients who had undergone US-guided PA (I^2 = 0%), patients with AMs secondary to HCC (I^2 = 0%), and patients with multiple primary cancers (I^2 = 0%).

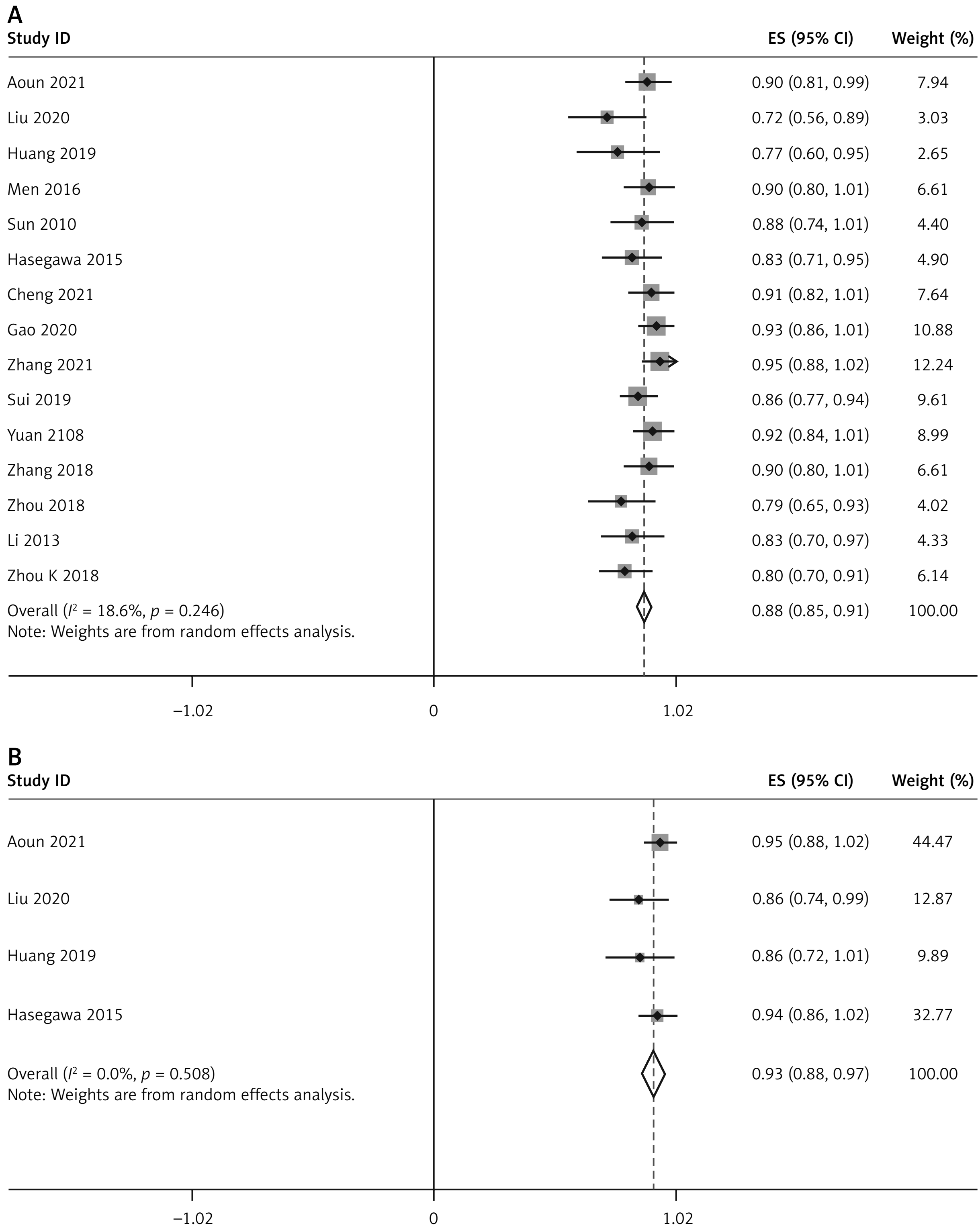

Figure 2. Pooled results for primary technical successful rate (**A**), secondary technical successful rate (**B**)

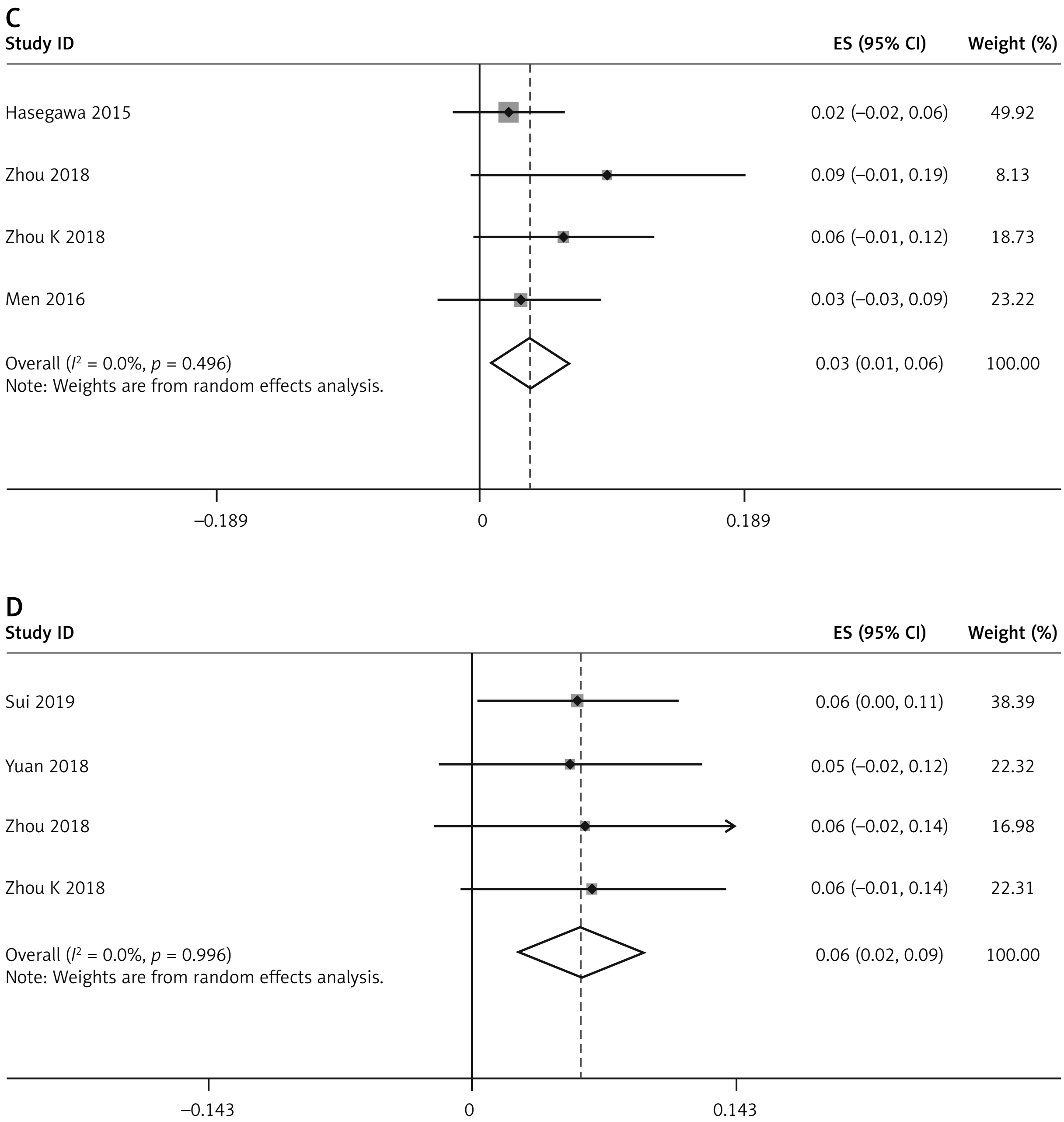

Figure 2. Cont. local hemorrhage rate (**C**), pneumothorax rate (**D**)

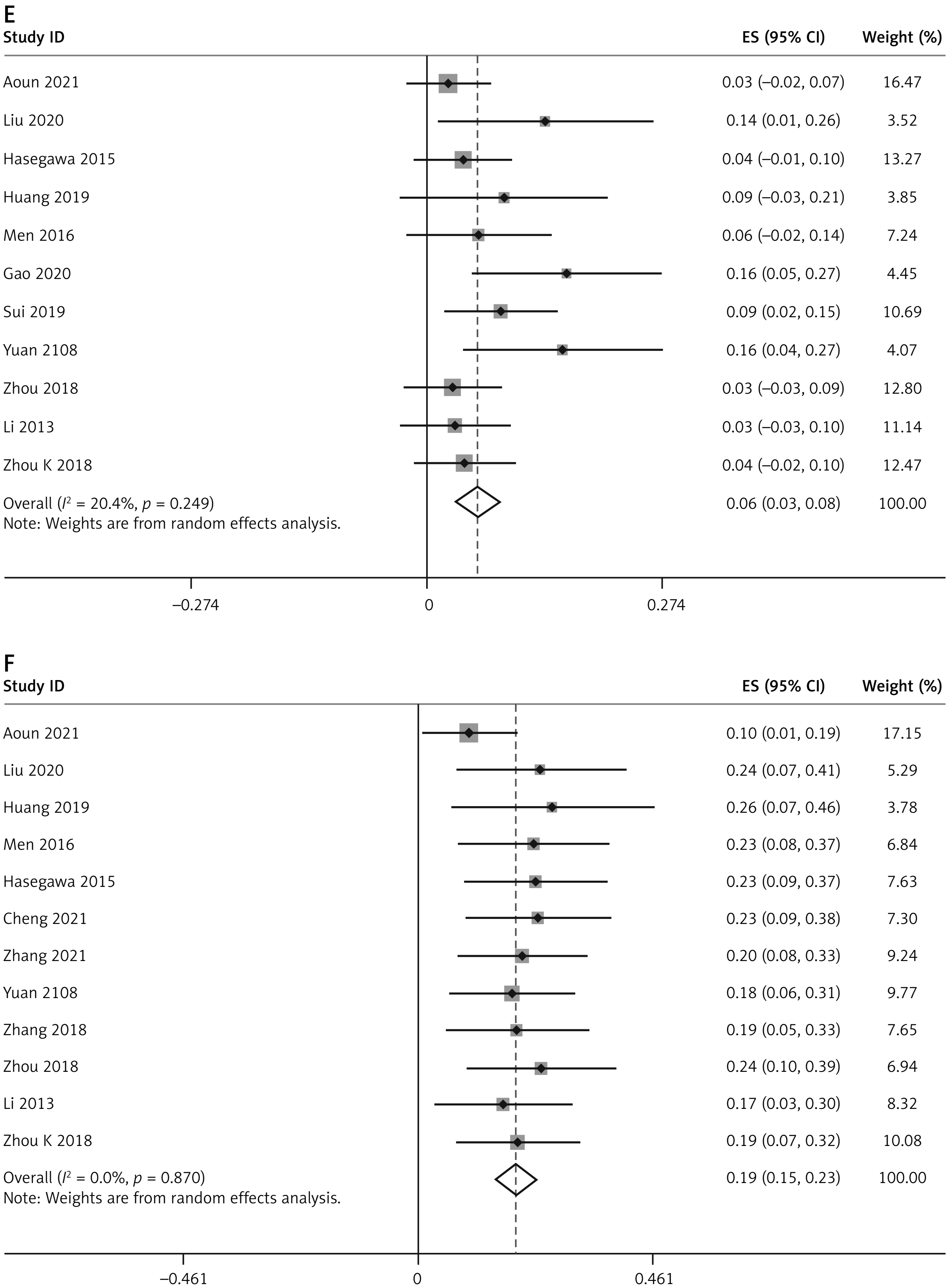

Figure 2. Cont. hypertension crisis rate (**E**), local recurrence rate (**F**)

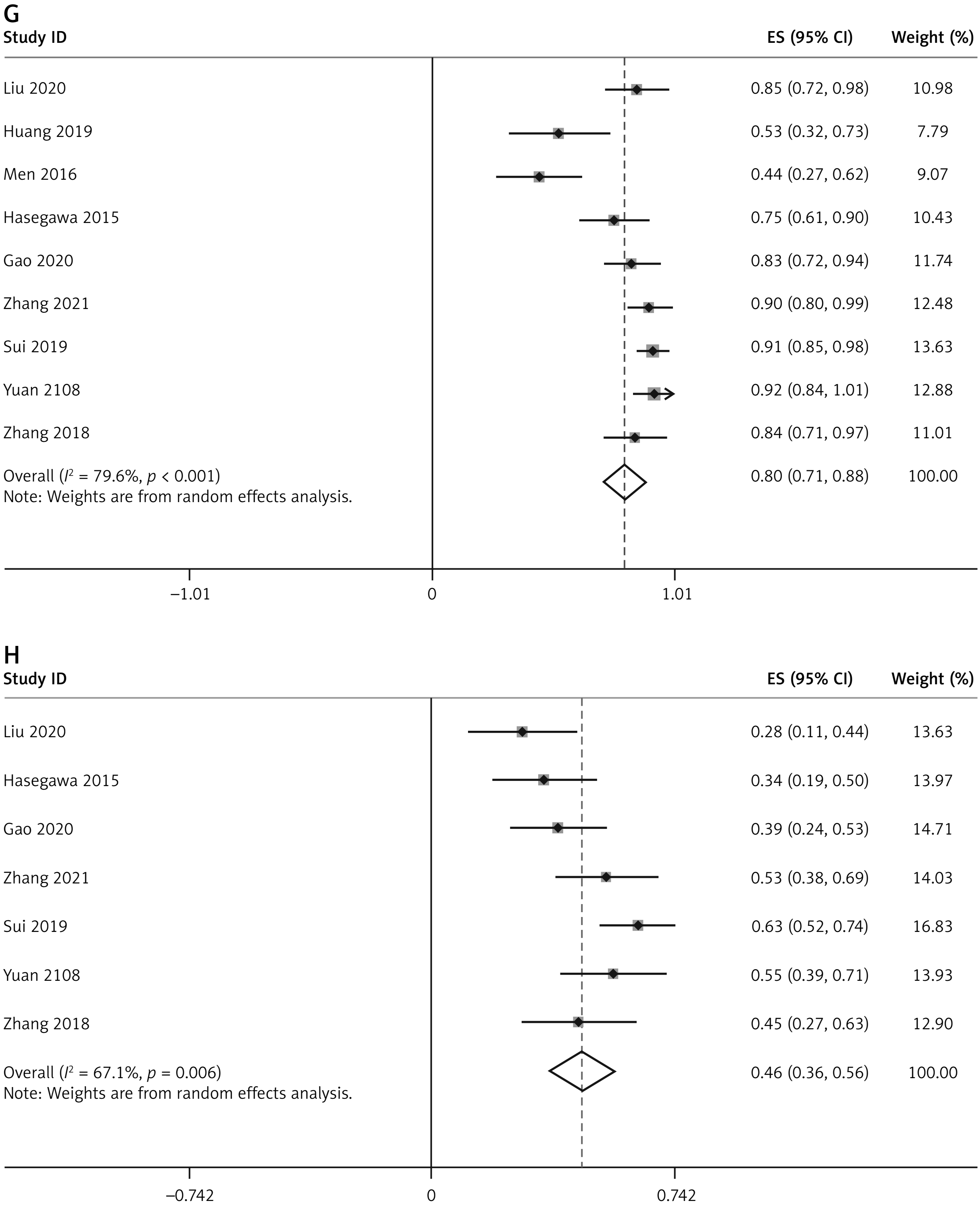

Figure 2. Cont. 1-year OS rate (**G**), and 3-year OS rate (**H**)

Subgroup analyses based on primary LC

Three studies focused on patients with primary LC [13, 19, 24]. The pooled rates of primary technical success, local hemorrhage, hypertensive crisis, local recurrence, 1-year OS, and 3-year OS were 93% (95% CI: 0.88–0.98), 3% (95% CI: –0.03–0.09), 6% (95% CI: –0.02–0.14), 22% (95% CI: 0.14–0.30), 79% (95% CI: 0.71–0.88), and 53% (95% CI: 0.38–0.69), respectively (Table V).

Subgroup analyses based on primary HCC

Three studies focused on the patients with primary HCC [16, 20, 22]. The pooled rates of primary technical success, secondary technical success, pneumothorax, hypertensive crisis, local recurrence, 1-year OS, and 3-year OS were 88% (95% CI: 0.82–0.93), 86% (95% CI: 0.72–1.01), 6% (95% CI: 0.01–0.10), 10% (95% CI: 0.05–0.15), 21% (95% CI: 0.10–0.31), 89% (95% CI: 0.84–0.94), and 60% (95% CI: 0.51–0.70), respectively (Table VI).

Table II. Meta-regression results

Variable	1-year OS rate		3-year OS rate	
	P-value	95% CI	*P*-value	95% CI
Ablation methods	0.838	–0.37; 0.32	0.382	–0.54; 0.43
Guidance methods	0.652	–0.76; 1.04	0.466	–0.76; 1.04
Primary tumors	0.361	–0.26; 0.52	0.611	–0.80; 0.72
Sample size	0.780	–0.86; 1.05	0.392	–1.33; 1.66
Countries	0.489	–1.21; 0.73	0.301	–1.62; 1.19

CI – confidential interval.

Table III. Subgroup analysis of 1-year OS rates

Variable	Studies (*n*)	1-year OS rate	95% CI	I^2
Total	9	80%	0.71–0.88	79.6%
Ablation methods:				
RFA	5	87%	0.83–0.92	75.2%
MWA	2	71%	0.62–0.81	92.4%
CA	2	88%	0.80–0.95	0.0%
Guidance method:				
US	3	79%	0.71–0.87	73.0%
CT	6	87%	0.83–0.91	82.8%
Primary tumor:				
LC	2	79%	0.71–0.88	95.0%
HCC	3	89%	0.84–0.94	84.2%
Multiple	4	82%	0.76–0.88	0.0%
Sample size:				
< 30	2	76%	0.65–0.87	85.0%
≥ 30	7	86%	0.83–0.90	79.6%
Countries:				
Japan	1	75%	0.61–0.90	–
China	8	86%	0.82–0.90	81.2%

CA – cryoablation, CI – confidence interval, CT – computed tomography, HCC – hepatocellular carcinoma, LC – lung cancer, MWA – microwave ablation, OS – overall survival, RFA – radiofrequency ablation, US – ultrasound.

Table IV. Subgroup analysis of 3-year OS rates

Variable	Studies (*n*)	3-year OS rate	95% CI	I^2
Total	7	46%	0.36–0.56	67.1%
Ablation methods:				
RFA	4	49%	0.42–0.56	81.4%
MWA	1	39%	0.23–0.53	–
CA	2	50%	0.38–0.61	0.0%
Guidance method:				
US	2	34%	0.23–0.45	0.0%
CT	5	52%	0.46–0.59	56.0%
Primary tumor:				
LC	1	53%	0.38–0.69	–
HCC	2	60%	0.51–0.70	0.0%
Multiple	4	36%	0.28–0.44	0.0%
Sample size:				
< 30	1	28%	0.11–0.44	–
≥ 30	6	50%	0.44–0.56	57.9%
Countries:				
Japan	1	34%	0.19–0.50	–
China	6	49%	0.43–0.55	67.2%

CA – cryoablation, CI – confidence interval, CT – computed tomography, HCC – hepatocellular carcinoma, LC – lung cancer, MWA – microwave ablation, OS – overall survival, RFA – radiofrequency ablation, US – ultrasound.

Table V. Meta-analysis based on the patients with primary lung cancers

Variable	Studies (*n*)	Pooled rate	95% CI	I^2
Primary technical success	3	93%	0.88–0.98	0.0%
Local hemorrhage	1	3%	–0.03–0.09	–
Hypertensive crisis	1	6%	–0.02–0.14	–
Local recurrence	3	22%	0.14–0.30	0.0%
1-year OS	2	79%	0.71–0.88	95.0%
3-year OS	1	53%	0.38–0.69	–

CI – confidence interval, OS – overall survival.

Table VI. Meta-analysis based on the patients with primary hepatocellular carcinoma

Variable	Studies (*n*)	Pooled rate	95% CI	I^2
Primary technical success	3	88%	0.82–0.93	22.9%
Secondary technical success	1	86%	0.72–1.01	–
Pneumothorax	2	6%	0.01–0.10	0.0%
Hypertensive crisis	3	10%	0.05–0.15	0.0%
Local recurrence	2	21%	0.10–0.31	0.0%
1-year OS	3	89%	0.84–0.94	84.2%
3-year OS	2	60%	0.51–0.70	0.0%

CI – confidence interval, OS – overall survival.

Discussion

Here, the safety, short-term efficacy, and long-term outcomes associated with imaging-guided PA-based treatment of AMs were assessed. Overall these analyses yielded positive results, with respective pooled primary and secondary technical success rates of 88% and 93%, suggesting that PA can readily achieve instant efficacy when used to treat AMs. While some patients exhibit residual tumors following an initial PA procedure, this approach can be repeated as an efficacious supplementary treatment.

In these analyses, the primary and secondary technical success rates exhibited low heterogeneity, suggesting that they are unlikely to be impacted by the different PA methods, imaging guidance approaches, or primary tumor types in different patients and studies. The most common PA methods at present are RFA, MWA, and CA. RFA and MWA have previously been reported to exhibit comparable complete ablation rates in several tumor types [27–29]. CA can also achieve efficacy similar to that of RFA and MWA in many malignancies [30–32]. CT and US guidance were not associated with any significant differences in PA-associated therapeutic efficacy [33].

Overall, the imaging-guided PA approach was found to be a safe approach to AM patient treatment, as evidenced by the low pooled local hemorrhage, pneumothorax, and hypertensive crisis rates (3%, 6%, and 6%, respectively). Hypertensive crisis is the most critical adverse event to consider when performing the PA-based treatment of adrenal disease, with incidence rates in the range of 15.2–67.5% for patients with primary adrenal tumors undergoing PA, particularly among pheochromocytoma patients [6, 7, 34]. In contrast, PA is much safer when used to treat AMs.

Pooled long-term outcome analyses of patient local recurrence, 1-year OS, and 3-year OS were also conducted. As the pooled local recurrence rate was just 19%, this may suggest that PA can achieve good local control of AMs, and this local control was stable across analyses (I^2 = 0%). Frenk *et al.* [9] have previously reported local AM recurrence to be unrelated to primary tumor histology, tumor size, or PA modality, while Liu *et al.* [18] found PA to be associated with significantly higher rates of local recurrence relative to adrenalectomy (24% vs. 6.5%, p = 0.048). However, owing to the minimally invasive nature of the PA procedure, it could be repeated following local AM recurrence.

In this meta-analysis, the respective pooled rates of 1- and 3-year OS were 80% and 46%, suggesting that imaging-guided PA represents an effective disease control strategy in patients harboring AMs. Prior work has suggested primary LC to be a risk factor linked to shorter patient OS [9, 15], but meta-regression analyses conducted herein failed to detect any OS-related risk factors in the present meta-analysis. Subgroup analyses revealed lower levels of 1- and 3-year OS endpoint heterogeneity when evaluating patients who underwent CA or had multiple primary cancer types. Over half of the analyzed studies included multiple primary cancer types, highlighting the need for more studies focused on specific cancers.

There are certain limitations to this meta-analysis. For one, all studies were retrospective. In addition, the 1- and 3-year OS endpoints were subject to high levels of heterogeneity. While some subgroup analyses were conducted for these endpoints, other factors with the potential to impact patient OS such as age, gender, tumor stage, tumor size, the extent of disease, and systematic treatment use were not evaluated as the included studies did not provide sufficient information to stratify patient data based on these parameters. Third, many of the included endpoints exhibited evidence of publication bias. Fourth, this study did not include any control group. Consequently, it was not possible to gauge the relative clinical efficacy of PA and other treatments or to compare different PA modalities.

Conclusions

These results suggest that imaging-guided PA is a safe and effective approach to AM treatment associated with satisfactory long-term patient outcomes.

Conflict of interest

The authors declare no conflict of interest.

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