

Supplementary Table 3. Major adverse events in 16 randomized controlled studies

Study name (Country)	Arm	No. of patients	Major complications (%)*	Major complication events
Abdelaziz et al. ²³ 2014 (Egypt)	RFA	45	ND	ND
	MWA	66	ND	ND
Brunello et al. ²⁴ 2008 (Italy)	PEI	69	2.9	Death caused by bowel infarct (n=1),
	RFA	70	2.9	Hemoperitoneum (n=1), hemothorax (n=1)
Chong et al. ²⁵ 2020 (Hong Kong)	MWA	47	ND	ND
	RFA	46	ND	ND
Di Costanzo et al. ²⁶ 2015 (Italy)	RFA	70	1.4	Subcutaneous tumor seeding (n=1)
	LA	70	1.4	Subcutaneous tumor seeding (n=1)
Giorgio et al. ²⁷ 2011 (Italy)	PEI	143	ND	ND
	RFA	142	ND	ND
Kim et al. ⁸ 2021 (South Korea)	PBT	72	0	None
	RFA	72	1.4	Bleeding in the inferior phrenic artery (n=1)
Koda et al. ³⁶ 2001 (Japan)	TACE+PEI	26	7.7	Biloma (n=1), ascites with pleural effusion (n=1)
	PEI	26	0	None
Lencioni et al. ⁶ 2003 (Italy)	RFA	52	0	None
	PEI	50	0	None
Lin et al. ²⁸ 2004 (Taiwan)	RFA	52	0	None
	PEI	52	0	None
Lin et al. ²⁹ 2005 (Taiwan)	RFA	62	4.8	Hemothorax (n=2), gastric bleeding and perforation (n=1)
	PEI	62	0	None
	PAI	63	0	None
Mizuki et al. ³⁷ 2010 (Japan)	PEI	14	0	None
	TACE+PEI	13	0	None
Paul et al. ³⁰ 2020 (India)	PAI	26	7.7	Death caused by hepatic necrosis (n=1), death caused by tumor rupture (n=1)
	RFA	29	6.9	Hydropneumothorax (n=2), hemoperitoneum (n=1)

Supplementary Table 3. Continued

Study name (Country)	Arm	No. of patients	Major complications (%) [*]	Major complication events
Peng et al. ³¹ 2012 (China)	TACE+RFA	69	2.9	Moderate ascites (n=1), liver failure (n=1)
	RFA	70	2.9	Severe ascites (n=1), persistent jaundice (n=1)
Shibata et al. ³² 2009 (Japan)	TACE+RFA	46	2.2	Segmental hepatic infarct (n=1)
	RFA	43	2.3	Pseudoaneurysm of hepatic artery (n=1)
Shiina et al. ³³ 2005 (Japan)	RFA	118	3.4	Transient jaundice (n=1), skin burn (n=1), hepatic infarction (n=1), seeding of malignant cells (n=3)
	PEI	114	2.6	Liver abscess (n=1), neoplastic seeding (n=2)
Tsai et al. ³⁸ 2008 (Taiwan)	PAI	70	1.4	Gross hematuria (n=1)
	PEI	55	0	None
Viotti Violi et al. ³⁴ 2018 (France and Switzerland)	MWA	71	2.8	Arterial bleeding (n=2)
	RFA	73	4.1	Pneumothorax (n=1), lesion of the umbilical vein (n=1), intrahepatic segmental necrosis
Wang et al. ¹⁰ 2015 (China)	CA	180	3.9	Peritoneal hemorrhage (n=2), symptomatic pleural effusion (n=1), septicemia (n=1), hemopneumothorax (n=1), pneumothorax (n=1), worsened jaundice (n=1)
	RFA	180	3.3	Septicemia (n=2), peritoneal hemorrhage (n=1), symptomatic pleural effusion (n=1), intrahepatic abscess (n=1), worsened ascites (n=1).
Zaitoun et al. ³⁵ 2021 (Egypt)	TACE	84	3.6	Severe hepatic dysfunction (n=3)
	MWA	92	2.2	Tumor seeding (n=2)
	TACE+MWA	89	1.1	Severe hepatic dysfunction (n=1)

RFA, radiofrequency ablation; MWA, microwave ablation; PEI, percutaneous ethanol injection; LA, laser ablation; TACE, trans-arterial chemoembolization; PBT, proton beam therapy; PAI, percutaneous acetic acid injections; CA, cryoablation; ND, not described.

^{*}Results for major complications were based on the criteria defined and set by the individual studies. Information corresponding to the reference number listed in Supplementary Table 3 is available in the References for main manuscript.