Search strategy

Embase

('bile duct cancer'/exp OR (klatskin* OR cholangiocarcinom* OR ((bile-duct OR bile-tract OR biliar* OR cholangio* OR gall-duct*) NEAR/3 (carcinom* OR cancer* OR neoplas* OR tumo* OR cholangiocarcinom*))):ab,ti) AND ('radiofrequency ablation'/exp OR (radiofrequency-ablation OR radio-frequency-ablation OR RFA):ab,ti) AND ('stent'/de OR 'biliary stent'/de OR 'metal stent'/exp OR 'nitinol stent'/exp OR 'plastic stent'/de OR 'self expanding stent'/exp OR (stent*):ab,ti)

Medline (Ovid)

(exp Biliary Tract Neoplasms/ OR (klatskin* OR cholangiocarcinom* OR ((bile-duct OR bile-tract OR biliar* OR cholangio* OR gall-duct*) ADJ3 (carcinom* OR cancer* OR neoplas* OR tumo* OR cholangiocarcinom*))).ab,ti.) AND (exp Radiofrequency Ablation/ OR (radiofrequency-ablation OR radio-frequency-ablation OR RFA).ab,ti.) AND (exp Stents/ OR (stent*).ab,ti.)

Web of Science

TS=(((klatskin* OR cholangiocarcinom* OR ((bile-duct* OR bile-tract* OR biliar* OR cholangio* OR gall-duct*) NEAR/2 (carcinom* OR cancer* OR neoplas* OR tumo* OR cholangiocarcinom*)))) AND ((((radiofrequency OR radio-frequency) NEAR/2 (ablation*)) OR RFA)) AND ((stent*)))

Cochrane

((klatskin* OR cholangiocarcinom* OR ((bile-duct OR bile-tract OR biliar* OR cholangio* OR gall-duct*) NEAR/3 (carcinom* OR cancer* OR neoplas* OR tumo* OR cholangiocarcinom*))):ab,ti) AND ((radiofrequency-ablation OR radio-frequency-ablation OR RFA):ab,ti) AND ((stent*):ab,ti)

Google Scholar

klatskin|cholangiocarcinoma|'bile|gall duct|tract carcinoma|cancer|neoplasm|tumor|tumour'|'biliary carcinoma|cancer|neoplasm|tumor|tumour' 'radiofrequency|RF ablation'|RFA stent|stents

Supplementary Table S1. Characteristics and outcome measures of studies describing survival and/or stent patency including the single arm studies, that were included for secondary endpoint analysis only.

Study	Country	Period	Study design		CCA type	Intervention	RFA setting	Stent type	N (RFA)	Palliative treatment		Outcome	
			Data collection	Design						pCTx	Other	Survival	Stent patency
Andrasina [1]	Czech Republic	2010-2019	Prospective	RCT	Bismuth II-IV	PTC	10W for 90-120s, Habib	ucSEMS	21	14	BTx: 18	Median 14.7 months (95% CI, 9.6 – 16.6)	Median 9.6 months (range: 5.2 – 12.2) *
Bhadauria [2]	India	NR	Prospective	Cohort	Bismuth I-IV	ERCP	8-10W for 120s, Habib	Plastic	10	NR	NR	Median 15.8 months (95% CI, 8.5 – 23.1)	NR
Bokemeyer [3]	Germany	2006-2011 controls, 2012-2017 cases	Retrospective	Case control	Bismuth III-IV	ERCP	8-10W for 90s, Habib	Both	20	6	NR	Mean 11.3 months (+/- 1.9)	NR
Buerlein [4]	USA	2011-2018	Retrospective	Cohort	Bismuth I-IV	ERCP	NR	NR	20	NR	PDT: 2	Median 10 months (95% CI, 8.5 – 36.8)	NR
Cui [5, 6]	China	2013-2015	Retrospective	Cohort	Bismuth I-IV	PTC	10W for 90s, Habib	ucSEMS	46	NR	NR	NR	Median 7.6 months (95% CI 6.8-9.2)
Gao [7]	China	2013-2017	Prospective	RCT	Bismuth I-III	ERCP, repeat after 3 months	7-10W for 90s, Habib	Plastic	25	NR	NR	HR 0.414 (95% CI, 0.025 – 0.762)	NR

Gou [8]	China	2013-2018	Retrospective	Cohort	Bismuth I-IV	PTC	10W for 120s, Habib	ucSEMS	18	NR	HAIC: 18	HR 1.48 (95% CI, 0.874 – 2.507)	HR 1.173 (95% CI, 0.685 – 2.011)
Han [9]	South Korea	NR	Both	Single	Bismuth III-IV	ERCP	7W for 120s, ELRA Starmed	Both	21	2	NR	Median 4.9 months (range: 1.7 – 16.1)	NR
Kang [10]	South Korea	NR	Prospective	RCT	Bismuth II-IV	ERCP	7W for 60-120s, ELRA Starmed	Plastic → ucSEMS	13	NR	NR	NR	Median 5.9 months (2.0 – 9.8)
Laleman [11]	Belgium	2014-2015	Prospective	Single	Bismuth III-IV	ERCP	7-10W for 120s, ELRA Starmed	Both	9	NR	NR	NR	Median 4.6 months (range: 1.7 – 11.2)
Laquière [12]	France	NR	Retrospective	Single	Bismuth I-IV	ERCP	10W for 90s, Habib	Both	12	3	NR	Mean 12.3 months (range: 3 – 31)	NR
Lee [13]	South Korea	NR	Prospective	Single	NR	ERCP	ELRA Starmed	NR	20	NR	NR	NR	Median 8 months
Sampath [14]	USA	2010-2015	Retrospective	Cohort	Bismuth I-IV	ERCP	NR	Plastic	8	8 (+/- RTx)	NR	Median 11.8 months	NR
								SEMS	2				
Tal [15]	Germany	2012-2013	Prospective	Single	Bismuth IV	ERCP	8-10W for 90 second, Habib	Plastic	7	NR	NR	Median 6.2 months (IQR: 1.3 – 10.3)	NR
Wang [16]	China	2013-2015	Prospective	Single	Bismuth III-IV	PTC	6-10W for 90-120s, Habib	Metal	9	2	NR	Median 5.3 months (95% CI, 2.5 – 8.1)	NR

Xia [17]	China	2012-2019	Retrospective	Matched Cohort	Bismuth I-IV	ERCP	10-12W for 60-120s, Habib	Both	47	NR	NR	Median 10.5 months (95% CI, 8.2 – 12.8)	NR

***** In 6 out of the 20 patients that received a stent (time to occlusion)

Supplementary Table S2. Newcastle-Ottawa Quality assessment scale for cohort studies**.** *Good quality: 7-9, Fair quality: 4-6, Poor quality: 0-3.*

Article	**Bhadauria**	**Bokemeyer**	**Buerlein**	**Cui**	**Gou**	**Sampath**	**Xia**
Selection							
1. Representativeness of the exposed cohort							
a. Truly representative		X	X	X	X	X	X
b. Somewhat representative							
c. Selected groups							
d. No description of derivation of cohort	X						
2. Selection of non-exposed cohort							
a. Drawn from same community		X	X	X	X	X	X
b. Drawn from different source							
c. No description of derivation of non-exposed cohort	X						
3. Ascertainment of exposure							
a. Secure record		X	X	X	X	X	X
b. Structured interview							
c. Written self report							
d. No description	X						
4. Demonstration that outcome was not present at start of study							
a. Yes	X	X	X	X	X	X	X
b. No							
Comparability							
1. Comparability of cohorts on the basis of the design or analysis							
a. The study controls for extent of disease		X	X	X	X	X	X
b. Study controls for any additional factor		X	X	X	X	X	X
Exposure							
1. Ascertainment of exposure							
a. Independent blind assessment							
b. Record linkage	X	X	X	X	X	X	X
c. Self report							
d. No description							
2. Was FU long enough for outcomes to occur?							
a. Yes	X	X	X	X	X	X	X
b. No							
3. Adequacy of FU of cohort							
a. Complete FU	X	X	X	X			X
b. Subject lost to FU unlikely to introduce bias							
c. FU rate <50% and no description						X	
d. No statement					X		
Score	4	9	9	9	8	8	9

Supplementary Table S3. Modified Jadad scale for RCTs. *Good quality: 6-8, Fair quality: 4-5, Poor quality: 0-3.*

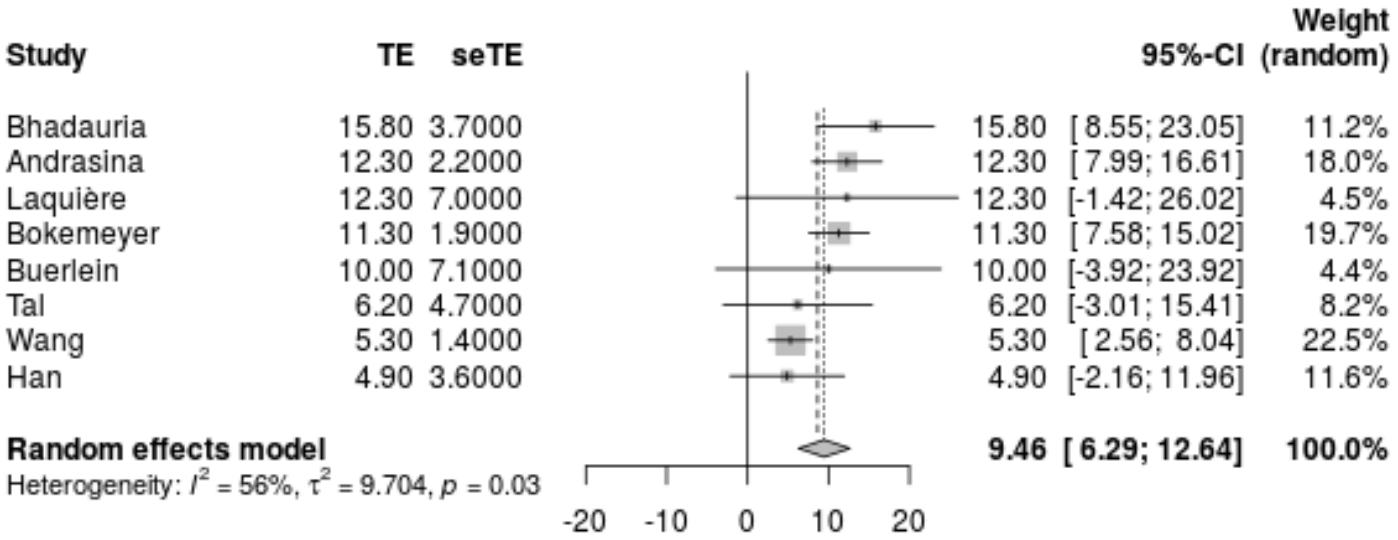
	Andrasina	**Gao**	**Kang ****
Was the study described as randomized?	Yes	Yes	Yes
Was the method of randomization appropriate?	Yes	Yes	Yes
Was the study described as blinded?	No	No*	No
Was the method of blinding appropriate?	Not described	Not described	Not described
Was there as description of withdrawals and drop-outs?	Yes	Yes	Yes
Was there a clear description of the inclusion/exclusion criteria?	Yes	Yes	Yes
Was the method used to assess adverse effects described?	Yes	Yes	Yes
Was the method of statistical analysis described?	Yes	Yes	Yes
Score:	**6**	**6**	**6**

*= Patients and physicians were not blinded, but those responsible for data collection and patients follow-up were.

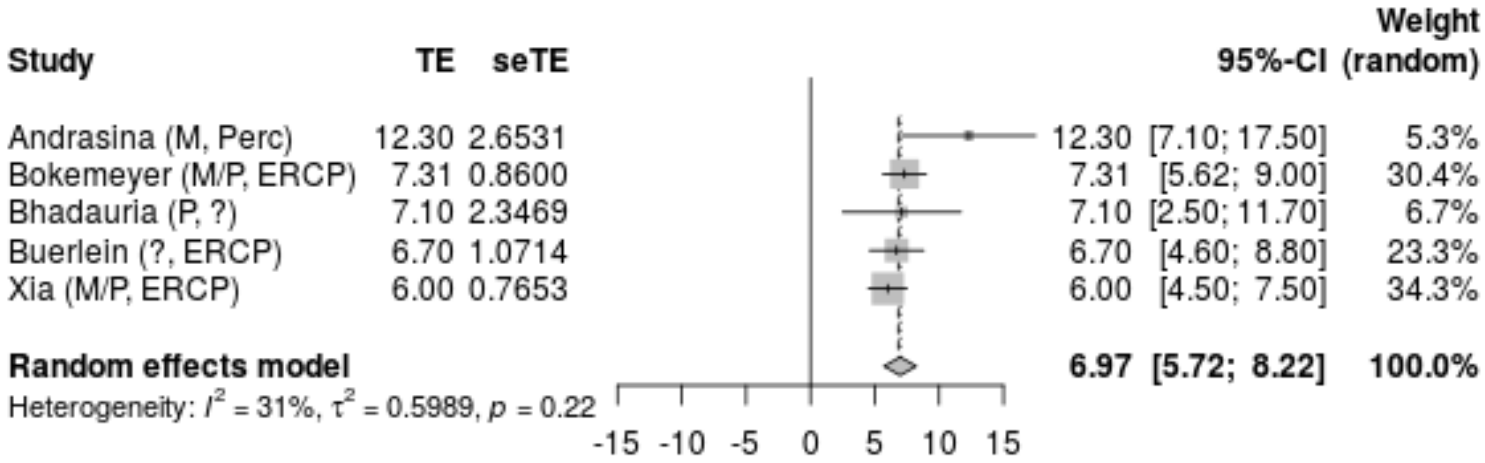
** = Only included in secondary endpoint analysis

Supplementary Table S4. The Joanna Briggs Institute Critical Appraisal Tool for Case Series included in secondary endpoint analysis.

	Han	Laquière	Laleman	Lee	Tal	Wang
1. Were there clear criteria for inclusion in the case series?	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the condition measured in a standard, reliable way for all participants included in the case series?	Yes	Yes	Yes	Unknown	Yes	Yes
3. Were valid methods used for identification of the condition for all participants included in the case series?	Yes	Yes	Yes	Unknown	Yes	Yes
4. Did the case series have consecutive inclusion of participants?	No	Yes	Unknown	Unknown	No	No
5. Did the case series have complete inclusion of participants?	NA	NA	NA	NA	NA	NA
6. Was there clear reporting of the demographics of the participants in the study?	Yes	Yes	Yes	No	Yes	Yes
7. Was there clear reporting of clinical information of the participants?	Yes	Yes	Yes	No	Yes	Yes
8. Were the outcomes or follow up results of cases clearly reported?	Yes	Yes	Yes	No	Yes	Yes
9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information?	Yes	Yes	Yes	No	Yes	Yes
10. Was statistical analysis appropriate?	Yes	Yes	Yes	Yes	Yes	Yes



Supplementary Figure S1. Pooled median survival in months for RFA+stent treatment for studies reporting this in single arm studies specifically for pCCA in combination with articles included in the primary meta-analysis



Supplementary Figure S2. Pooled median survival in months for stent only treatment for all studies included in this primary meta-analysis, with stent type and method of stent placement

M = ucSEMS, P = Plastic stents, Perc = Percutaneous stent, ? = Unknown

Supplementary Table S5. Adverse events reported in included articles.

Study	Analysis		No. per group	Overall AE rate	Cholangitis	Cholecystitis	Pancreatitis	Liver abscess	Bleeding	Abdominal pain	Perforation	P-value
Andrasina	Per patient	RFA	21	NR	NR	NR	NR	NR	NR	NR	NR	0.062
		Stent-only	22									
Bhadauria	Per patient	RFA	17	NR	11.8%	NR	NR	NR	5.9%	More often in RFA	NR	NR
		Stent-only	15	NR	26.7%	NR	NR	NR	0%		NR	NR
Bokemeyer	Per procedure	RFA	54	18.5%	11.1%	3.7%	1.9%	NR	NR	NR	1.9% (intestinal)	NR
		Stent-only	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Buerlein	Per patient	RFA	20	NR	40%	NR	NR	10%	NR	10%	NR	>0.05
		Stent-only	29	NR	41.4%	NR	NR	20.7%	NR	6.9%	NR	
Cui	Per procedure	RFA	50	NR	20%	NR	2%	NR	14%	38%	NR	0.159
		Stent-only	39	NR	15.4%	2.6%	2.6%	NR	5.2%	20.5%	NR	
Gao	Per patient overall	RFA	87	27.6%	11.5%	10.3%	4.6%	1.1%	1.1%	NR	NR	0.211
		Stent-only	87	19.5%	10.3%	0%	5.7%	0%	3.4%	NR	NR	
	Per patient in pCCA specific	RFA	25	NR	NR	28%	NR	NR	NR	NR	NR	NR
		Stent-only	22	NR	NR	0%	NR	NR	NR	NR	NR	
Gou	Per patient	RFA	64	67.2%	12.5%	NR	10.9%	NR	14.1%	21.9%	1.6%	>0.05
		Stent-only	71	60.6%	15.5%	NR	8.5%	NR	8.5%	23.9%	1.4%	
Kang	Per patient	RFA	15	NR	20%	6.7%	0%	0%	0%	20%	0%	>0.05
		Stent-only	15	NR	33.3%	6.7%	6.7%	6.7%	0%	0%	0%	

Lee	Per patient	RFA	21	NR	NR	NR	NR	NR	NR	NR	NR	>0.05
		Stent-only	21									
Sampath	Per patient	RFA	10	NR	30%	NR	NR	NR	NR	NR	0% (bile leak)	NR
		Stent-only	15	NR	0%	NR	NR	NR	NR	NR	6.7% (bile leak)	
Xia *	Per patient	RFA	124	19.5%	6.5%	4.8%	8.9%	NR	1.6%	NR	0.8%	0.804
		Stent-only	396	18.5%	14.2%	0.1%	5.1%	NR	1.2%	NR	0%	

Overall = not specified for cholangiocarcinoma patients, specific = pCCA only.

* = unmatched cohort

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