

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Choueiri 2012	+	+	+	+	+	+	+
Fradet 2019	+	?	+	+	+	+	-
Gallagher 2010	?	?	+	+	+	+	-
Herbst 2019	-	-	+	+	+	+	-
Jones 2017	+	+	+	+	+	+	+
Parikh 2018	?	?	+	+	+	+	-
Petrylak 2016	+	+	+	+	+	+	-
Petrylak 2020	+	+	+	+	+	+	-
Powles 2018	+	+	+	+	+	+	-
Rosenberg 2018	+	+	+	+	+	+	+
Sharma 2019	+	-	+	+	+	+	-
Wong 2012	+	+	+	+	+	+	+

Figure S1 The quality assessment by Cochrane risk of bias tool.

Table S1 Meta-analysis of the relationship between prognostic indicators and OS event in the subgroup analysis of CNA group

Groups	OS event, %	OR (95% CI)	P value	I ²
Male	73.8% versus 76.0%	1.30 (0.73–2.30)	0.372	0.0%
Versus				
Female				
Age (years) <65	75.6% versus 71.3%	1.29 (0.80–2.06)	0.300	0.0%
Versus				
Age (years) ≥65				
ECOG-PS =0	68.5% versus 77.5%	0.64 (0.40–1.04)	0.069	0.0%
Versus				
ECOG-PS ≥1				
Liver metastases	83.2% versus 70.6%	1.57 (0.92–2.68)	0.099	0.0%
Versus				
Non-Liver metastases				
Haemoglobin <10 (g/dL)	84.8% versus 72.2%	2.17 (0.93–5.06)	0.072	0.0%
Versus				
Haemoglobin ≥ 10 (g/dL)				

CNA, combined therapy based on novel agents; CI, confidence interval; OR, odds ratio; OS, overall survival; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; OS event was defined as death.

Table S2 Meta-analysis of the relationship between prognostic indicators and PFS event in the subgroup analysis of CNA group

Groups	PFS event, %	OR (95% CI)	P value	I ²
Male	80.7% versus 76.5%	1.38 (0.43–4.44)	0.593	0.0%
Versus				
Female				
Age (years) < 65	92.3% versus 73.1%	2.89 (0.88–9.54)	0.081	0.0%
Versus				
Age (years) ≥ 65				
ECOG-PS = 0	77.8% versus 80.4%	0.91 (0.33–2.49)	0.85	0.0%
Versus				
ECOG-PS ≥ 1				
Liver metastases	87.1% versus 77.4%	2.16 (0.65–7.15)	0.206	0.0%
Versus				
Non-Liver metastases				
Haemoglobin < 10 (g/dL)	89.0% versus 77.7%	3.23 (0.39–26.51)	0.274	0.0%
Versus				
Haemoglobin ≥ 10 (g/dL)				

CNA, combined therapy based on novel agents; CI, confidence interval; OR, odds ratio; PFS, progression-free survival; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; PFS event was defined as disease progression or death.

Table S3 Meta-analysis of the relationship between prognostic indicators and ORR in the subgroup analysis of CNA group

Groups	ORR, %	OR (95% CI)	P value	I ²
Male	26.1% versus 27.0%	0.75 (0.20–2.76)	0.666	0.0%
Versus				
Female				
ECOG-PS =0	46.7% versus 18.3%	5.55 (1.33–23.22)	0.019	40.9%
Versus				
ECOG-PS ≥1				
Liver metastases	33.3% versus 24.5%	1.81 (0.48–6.75)	0.379	0.0%
Versus				
Non-Liver metastases				
Bellmunt risk factors (n) =0	48.0% versus 22.8%	4.11 (0.94–18.06)	0.061	46.3%
Versus				
Bellmunt risk factors (n) ≥1				
UT	17.7% versus 43.3%	0.31 (0.94–18.06)	0.066	0.0%
Versus				
LT				

CNA, combined therapy based on novel agents; CI, confidence interval; OR, odds ratio; ORR, objective response rate; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; UT, upper urinary tract; LT, lower urinary tract.

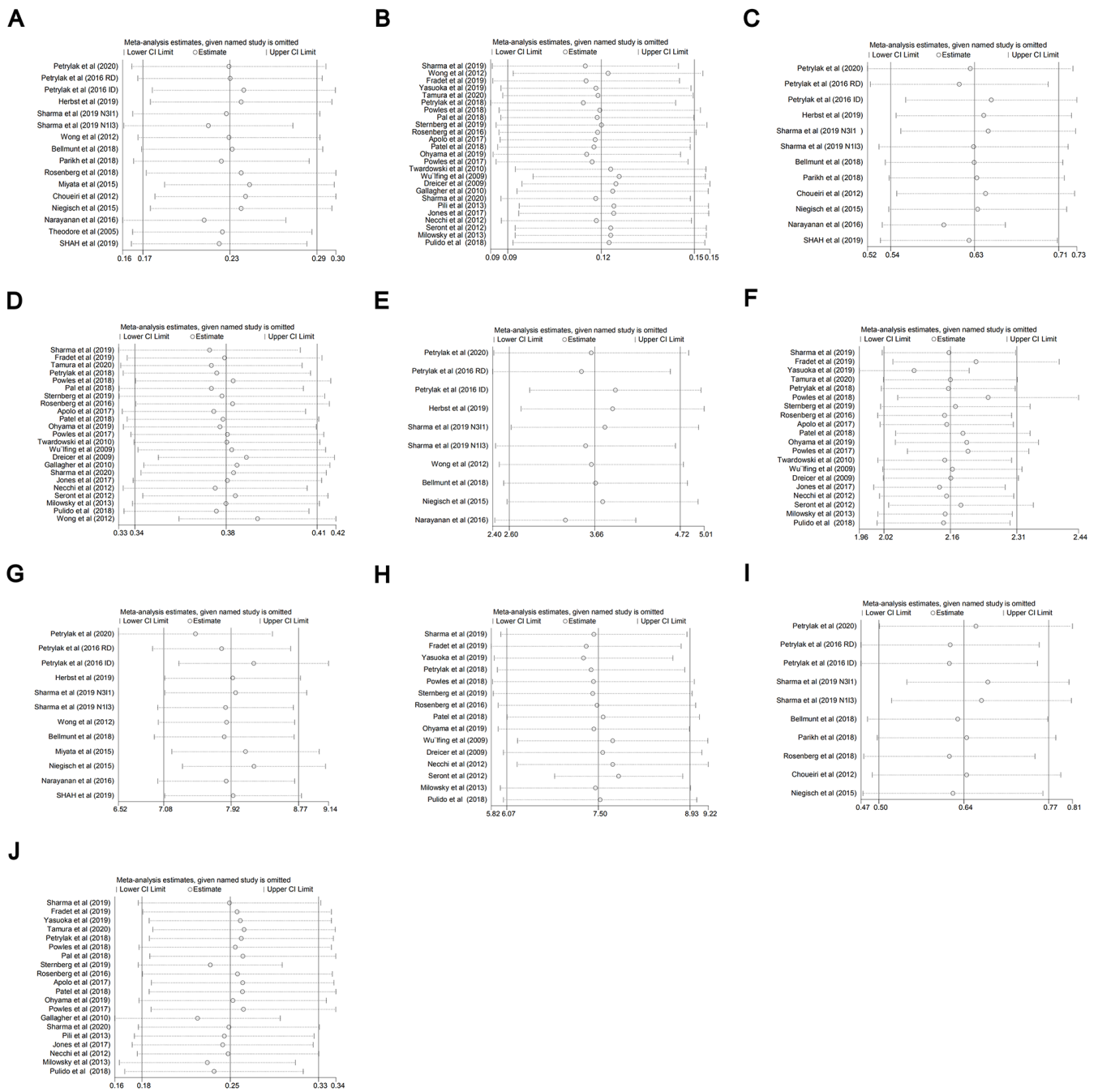
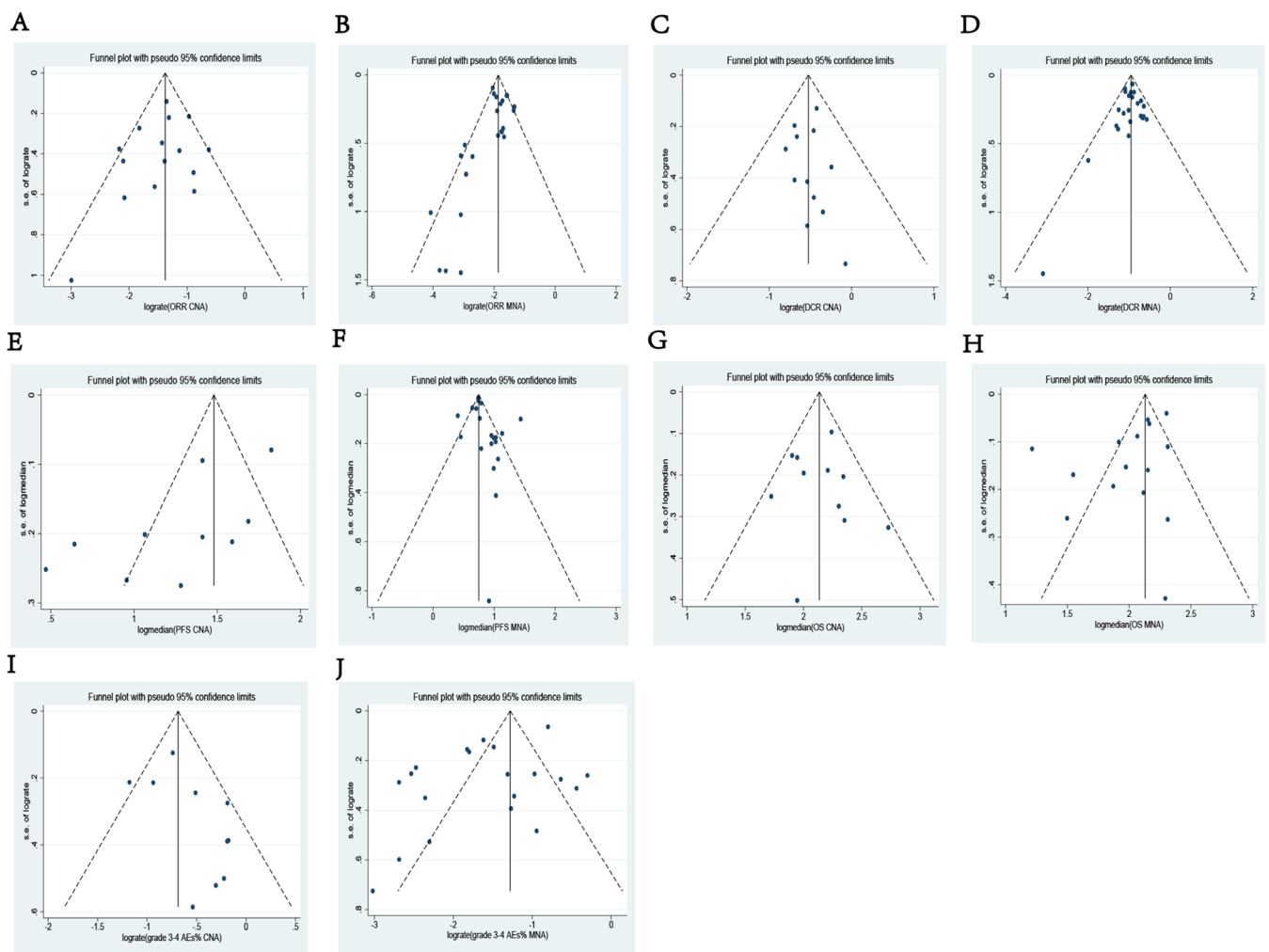


Figure S2 Sensitivity analyses. (A) ORR of CNA. (B) ORR of MNA. (C) DCR of CNA. (D) DCR of MNA. (E) median PFS of CNA. (F) median PFS of MNA. (G) median OS of CNA. (H) median OS of MNA. (I) grade 3-4 AEs% of CNA. (J) grade 3-4 AEs% of MNA. CNA, combined therapy of novel agents; MNA, monotherapy of novel agents; ORR, objective response rate; DCR, disease control rate; PFS, progression-free survival; OS, overall survival; grade 3-4 AEs%, grade 3 or 4 adverse events rate.



K

Quantitative assessment for publication bias					
	ORR	DCR	median PFS	median OS	Grade 3-4 AEs%
Number of studies					
CNA	16	12	10	12	10
MNA	25	23	20	15	20
P value for Egger's tests					
CNA	0.641	0.123	0.039	0.269	0.494
MNA	0.011	0.588	0.607	0.003	P<0.001

CNA, combined therapy based on novel agents; MNA, monotherapy of novel agents; ORR, objective response rate; DCR, disease control rate; PFS, progression-free survival; OS, overall survival; AEs%, adverse effects rate.

Figure S3 Publication bias diagnoses. (A) ORR of CNA. (B) ORR of MNA. (C) DCR of CNA. (D) DCR of MNA. (E) median PFS of CNA. (F) median PFS of MNA. (G) median OS of CNA. (H) median OS of MNA. (I) grade 3-4 AEs% of CNA. (J) grade 3-4 AEs% of MNA. (K) Egger' tests. CNA, combined therapy of novel agents; MNA, monotherapy of novel agents; ORR, objective response rate; DCR, disease control rate; PFS, progression-free survival; OS, overall survival; grade 3-4 AEs%, grade 3 or 4 adverse events rate.