

Table S1 Search strategies

Search strategies for PubMed

- #1. Dickkopf-1[All Fields] AND gastrointestinal[All Fields] AND ("carcinoma"[MeSH Terms] OR "carcinoma"[All Fields])
- #2. DKK-1[All Fields] AND gastrointestinal[All Fields] AND ("carcinoma"[MeSH Terms] OR "carcinoma"[All Fields]) AND ("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields])
- #3. #1 and #2
- #4. DKK-1[All Fields] AND ("gastrointestinal neoplasms"[MeSH Terms] OR ("gastrointestinal"[All Fields] AND "neoplasms"[All Fields]) OR "gastrointestinal neoplasms"[All Fields] OR ("digestive"[All Fields] AND "cancer"[All Fields]) OR "digestive cancer"[All Fields])
- #5. DKK-1[All Fields] AND alimentary[All Fields] AND ("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields])
- #6. #4and #5
- #7. #3 OR#6

Search strategies for EMBase

- #1 'Dickkopf-1\$:ab,ti
- #2 'DKK-1\$:ab,ti
- #3 'gastrointestinal':it
- #4 'digestive':it
- #5 'carcinoma':it
- #6 ' cancer':it
- #8 #1or#2
- #9#3or#4
- #10 #5or#6
- #11 #5 and #6 and #7

Search strategies for Cochrane library

- #1. Dickkopf-1 or DKK-1, gastrointestinal cancer or digestive cancer
- #2. MeSH descriptor

Table S2 Main characteristics of DKK-1 in GIC

Table S2A Main characteristics of diagnosis value of DKK-1 in GIC

Study	Country	Cancer type	Control type	Case count(age, male/female)	Control count	Test method	DKK-1 Cut-off values	Treatment	All Mark used	Data extra-ction type	TP	FP	FN	TN
Zheng X, 2019[A1]	China	HCC	Benign diseases+Healthy control	liver (56.62 ±6.83)	70 82	ELISA	≥2.0 ng/ml	Untreated	AFP+TK1+DKK1	Reported in text	47	7	23	75
Zekri AR, 2020[A3]	Egypt	HCC	Cirrhotic +Cirrhotic +Healthy control	78(58.27 ±9.7)	160	ELISA	2000 pg/ml	Untreated	AFP+DKK1	Estimated	73	21	5	139
Chen Z, 2019[1]	China	HCC	B1:Benign diseases B2:Healthy control	liver 120(49.6 ±2.3,68/52)	B1:90(49.2 ±2.0, 50/40) B2:80(48.6 ±1.9,45/35)	ELISA	≥2.0 ng/ml	Untreated	AFP+TK1+DKK1	Reported in text	66	54	15	75
NAM Hassan(a), 2019[2]	Egypt	HCC	B1:liver cirrhosis B2:Healthy control	40	B1:24 B2:16	ELISA	more than 331 pg/ml	Untreated	AFP+DKK1	Estimated	28	5	12	35
NAM Hassan(b), 2019[2]	Egypt	HCC	liver cirrhosis	40	24	ELISA	more than 331 pg/ml	Untreated	AFP+DKK1	Estimated	28	3	12	21
NAM Hassan(c), 2019[2]	Egypt	Early HCC	B1:liver cirrhosis B2:Healthy control	20	B1:24 B2:16	ELISA	more than 331 pg/ml	Untreated	AFP+DKK1	Estimated	14	5	6	35

NAM Hassan(d), 2019[2]	Egypt	Early HCC	liver cirrhosis	20	24	ELISA	more than 331 pg/ml	Untreated	AFP+D KK1	Estimated	14	3	6	21
Xi L(a), 2019[3]	China	HCC	B1:liver cirrhosis B2:HBV B3:Healthy control	122(54.9 ± 6.0, 105/17)	B1:152(54.9 ± 6.2, 119/33) B2:105(55.5 ± 6.7, 81/24) B3:101(54.9 ± 5.7, 80/21)	ELISA	0.431	Untreated	AFP+C KAP4+ DKK1	Estimated	80	8	42	350
Xi L(b), 2019[3]	China	HCC	B1:liver cirrhosis B2:HBV B3:Healthy control	76	B1:152(54.9 ± 6.2, 119/33) B2:105(55.5 ± 6.7, 81/24) B3:101(54.9 ± 5.7, 80/21)	ELISA	0.431	Untreated	AFP+C KAP4+ DKK1	Estimated	55	8	21	350
Chen S, 2017[6]	China	PC	B1:Benign pancreatic disease B2:Healthy control	122	B1:58 B2:62	ELISA	2.0 ng/mL	Untreated	CA19-9 +CA242 +DKK1	Estimated	96	16	9	111
Liu DJ, 2017 [7]	China	PC	Healthy control	311	311	IHC	-	Unknown	DKK1	Reported in text	205	106	188	123
Qin QF, 2017 [8]	China	HCC	Benign liver diseases	86	100	ELISA	2.0 ng/mL	Untreated	AFP+D CP+DK K1	Reported in text	63	23	56	44
Xie H, 2017[9]	China	GC	B1:Benign gastrosia diseases B2:Healthy control	75(60.3 ± 9.5, 49/26)	B1:70(61.6 ± 6.9, 48/22) B2:50(56.8 ± 7.7, 39/11)	ELISA	26.5 pg/mL	Untreated	CA72-4 +TFF3+ DKK1	Estimated	70	15	5	105

Xu Y,2017[10]	China	Adenocarcinoma of esophago-gastric junction	Healthy control	79(38-78,65/14)	101(32-75,78/23)	ELISA	2615.9 pg/mL	Untreated	DKK1	Estimated	27	49	52	52
Yao F H,2017[11]	China	HCC	B1:HBV group B2:Healthy control	117(55.9 ± 8.2, 81/36)	B1:80(52.0 ± 7.9, 50/30) B2:80(53.8 ± 9.5, 49/31)	ELISA	2.153 µg/L	Untreated	DKK1+AFP+G P73	Reported in text	89	17	28	63
Erdal H(a),2016[12]	Turkey	HCC	liver cirrhosis	40(64.2 ± 8.9, 36/4)	54(58.4 ± 10.0, 33/21)	ELISA	1.4µg/L	Untreated	AFP+D KK1+D KK3	Estimated	29	18	11	36
Erdal H(b),2016[12]	Turkey	HCC	Healthy control	40(64.2 ± 8.9, 36/4)	39(58.4 ± 7.3, 10/29)	ELISA	1.4µg/L	Untreated	AFP+D KK1+D KK3	Estimated	29	15	11	24
Erdal H(c),2016[12]	Turkey	Early HCC	liver cirrhosis	29	54(58.4 ± 10.0, 33/21)	ELISA	1.4µg/L	Untreated	AFP+D KK1+D KK3	Estimated	22	18	7	36
Erdal H(d),2016[12]	Turkey	Early HCC	Healthy control	29	39(58.4 ± 7.3, 10/29)	ELISA	1.4µg/L	Untreated	AFP+D KK1+D KK3	Estimated	22	15	7	24
Fouad YM,2016[13]	Egypt	HCC	B1:Chronic HCV group B2:liver cirrhosis group	50(59.3 ± 8.7, 34/16)	B1:20(42.7 ± 9.8, 13/7) B2:20(54.3 ± 5.1, 14/6)	ELISA	1.53 ng/mL	Untreated	DKK1+AFP	Estimated	34	4	16	36
Mao L,2016[14]	China	HCC	B1:liver cirrhosis Group B2:HBV group B3:Healthy	48(56.1, 37/11)	B1:20(52.3, 16/4) B2:20(37.8, 13/7)	ELISA	565ng/L	Untreated	DKK1	Estimated	45	18	3	42

			control		B3:20(47.3,14/6)										
Su R,2016[15]	China	HCC	B1:HBV group B2:liver cirrhosis Group B3:Healthy control	120(55.6 ± 14.2,84/36)	B1:60(47.7 ± 15.3, 32/28) B2:60(53.5 ± 13.9, 36/24) B3:60(50.5 ± 4.8, 35/25)	ELISA	10.13ng/mL	Untreated	DKK1+ AFP	Reported in text	58	9	62	171	
Zhao P,2016[16]	China	HCC	B1:HBV group B2:liver cirrhosis Group B3:Healthy control	60(55.6 ± 5.5, 54/6)	B1:40(44.2 ± 7.3, 31/9) B2:40(58.6 ± 7.3, 27/13) B3:40(48.6 ± 5.7, 28/12)	ELISA	2.153μg/L	Untreated	DKK1+ AFP	Estimated	48	12	12	108	
Fu Y,2015[17]	China	HCC	adjacent tissue	75(52.47 ± 10.62, 64/11)	75	IHC	More than 50% of the cells were positive	Surgery	C-MET+GolpII 2+EZH2 +DKK1	Reported in text	63	24	12	51	
Ge T(a),2015[18]	USA	HCC	B1:liver cirrhosis Group B2:HBV group B3:Healthy control	89	B1:36 B2:65 B3:200	ELISA	1.31 ng/mL	Untreated	AFP+D KK1+O PN	Estimated	71	32	18	269	
Ge T(b),2015[18]	USA	HCC	B1:liver cirrhosis Group B2:HBV group	89	B1:36 B2:65	ELISA	1.31 ng/mL	Untreated	AFP+D KK1+O PN	Estimated	71	7	18	94	
Ge T(c),2015[18]	USA	Early HCC	B1:liver cirrhosis Group B2:HBV group	56	B1:36 B2:65 B3:200	ELISA	1.31 ng/mL	Untreated	AFP+D KK1+O PN	Estimated	44	32	12	269	

			B3:Healthy control											
Ge T(d),2015[18]	USA	Early HCC	B1:liver cirrhosis Group	56	B1:36	ELIS A	1.31 ng/mL	Untreated	AFP+D KK1+O PN	Estimated	44	7	12	94
Han SX(a),2015[19]	China	PC	B1:Benign pancreatic tumor	140(61.7 ± 10.8, 88/52)	B1:18(58.8 ± 12.1, 12/6)	ELIS A	39.3U/ml and 1560.02p g/ml	Untreated	DKK1+ CA19-9	Estimated	125	19	15	73
			B2:Chronic pancreatitis		B2:26(57.6 ± 11.3, 22/4)									
			B3:Healthy control		B3:48(59.1 ± 11.0, 30/18)									
Han SX(b),2015[19]	China	PC	B1:Benign pancreatic tumor	140(61.7 ± 10.8, 88/52)	B1:18(58.8 ± 12.1, 12/6)	ELIS A	39.3U/ml and 1560.02p g/ml	Untreated	DKK1+ CA19-9	Estimated	125	12	15	32
			B2:Chronic pancreatitis		B2:26(57.6 ± 11.3, 22/4)									
Han SX(c),2015[19]	China	Early PC	B1:Benign pancreatic tumor	62	B1:18(58.8 ± 12.1, 12/6)	ELIS A	39.3U/ml and 1560.02p g/ml	Untreated	DKK1+ CA19-9	Estimated	53	19	9	73
			B2:Chronic pancreatitis		B2:26(57.6 ± 11.3, 22/4)									
			B3:Healthy control		B3:48(59.1 ± 11.0, 30/18)									
Han SX(d),2015[19]	China	Early PC	B1:Benign pancreatic tumor	62	B1:18(58.8 ± 12.1, 12/6)	ELIS A	39.3U/ml and 1560.02p g/ml	Untreated	DKK1+ CA19-9	Estimated	53	12	9	32
			B2:Chronic pancreatitis		B2:26(57.6 ± 11.3, 22/4)									
Peng Y,2015[22]	China	EPC	Healthy control	126(40-80, 102/24)	60(37-76,47/13)	ELIS A		Non-surgery	DKK1+ P53	Estimated	78	3	48	57
Wang	China	PC	Benign	44	19	IHC	More	Untreated	DKK1+	Reported	30	1	14	18

Q,2014[25]			pancreatic tumor				than 50% of the cells were positive	ated	CA19-9	ted in text				
Zhou Y,2014[26]	China	PC	Healthy control	50(65.04 ± 13.55, 31/19)	50(53.42 ± 10.66, 27/23)	ELISA	22.5μg / L	Untreated	DKK1+ CA19-9	Estimated	26	4	24	46
Peng L,2013[27]	China	HCC	B1:HBV group B2:liver cirrhosis Group	35	B1:38 B2:105	ELISA	2.13 ng/mL	Untreated	AFP+D KK1	Estimated	28	29	7	117
Yang H(a),2013[28]	China	Early stage HCC	liver cirrhosis Group	104(54.5,91/13)	102(45,77/25)	IHC	6.25 ng/mL	Untreated	AFP+D KK1	Estimated	61	21	43	81
Yang H(b),2013[28]	China	Early stage HCC	liver cirrhosis Group	80(51.5, 71/9)	72(43,58/14)	IHC	6.25 ng/mL	Surgery	AFP+D KK1	Estimated	44	13	36	59
Shen Q(a),2012[31]	China	HCC	B1:HBV group B2:liver cirrhosis Group B3:Healthy control	424	B1:98 B2:96 B3:213	ELISA	0.03 ng/mL	Untreated	AFP+D KK1	Estimated	293	38	131	369
Shen Q(b),2012[31]	China	HCC	B1:HBV group B2:liver cirrhosis Group	424	B1:98 B2:96	ELISA	0.03 ng/mL	Untreated	AFP+D KK1	Estimated	293	30	131	164
Shen Q(c),2012[31]	China	HCC	B1:HBV group B2:liver cirrhosis Group B3:Healthy control	209	B1:73 B2:72 B3:99	ELISA	0.03 ng/mL	Untreated	AFP+D KK1	Estimated	149	31	60	213

Shen Q(d),2012[31]	China	HCC	B1:HBV group B2:liver cirrhosis Group	209	B1:73 B2:72	ELIS A	0.03 ng/mL	Untreated	AFP+D KK1	Estimated	149	14	60	131
Zhang Y,2012[33]	China	A1:EPC A2:precancerous lesions	Healthy control	A1:72 A2:13	30	ELIS A	13.4µg/ L	Untreated	DKK1	Reported in text	63	1	22	29
Soydinc HO,2011[34]	Turkey	CRC	Healthy control	295(59)	90(50)	ELIS A	29.36 ng/mL	Untreated	DKK1	Estimated	175	45	120	45
Zhou Y, 2011[36]	China	PC	Benign pancreatic disease	24	7	IHC	More than 5% of the cells were positive	Untreated	DKK1	Reported in text	21	0	3	7
Zhang X,2010[37]	China	GC	Healthy control	34(28-87, 23/11)	38(22-75, 25/13)	ELIS A	3.539µg/ L	Untreated	DKK1	Estimated	21	6	13	32
Li B,2009[38]	China	EPC	Healthy control	80(45-79, 68/12)	35	ELIS A	14.54ng/ mL	Untreated	DKK1	Reported in text	53	6	27	29
Yamabuki T,2007[40]	Japan	EPC	Healthy control	81	207	IHC	3.3µg/ L	Untreated	DKK1	Reported in text	51	197	30	10

A:Cancer case group; B: Control case group; ELISA:enzyme-linked immunosorbent assay;IHC: Immunohistochemistry;

HCC:hepatocellular carcinoma; PC:pancreatic carcinoma ; GC:gastric carcinoma ; EPC:esophageal carcinoma; CRC: Colorectal carcinoma

FN = false negative; FP = false positive; TN = true negative; TP = true positive.

29researches, 46analysis

Table S2B Main characteristics of prognostic value of DKK-1 in GIC

Study	Count	High/Low (age, male/female)	Cancer type	Control type	Patient treatment	Research type	Test method	Cut-off values	All Mark used	Tumor size(<5/>5cm)	TNM stage(I+II/II I+IV)	Differentiation grade (Well and moderate/Poor)	Lymphatic invasion (Yes/No)	Lymph node metastasis (Yes/No)	Vascular invasion (Yes/No)	Distant metastasis (Yes/No)	Data extraction type
Hu W,2020[A2]	China	H:21 L:26	GC	adjacent tissue+Healthy control	Surgey	Case-control study	IHC	Unknown	DKK-1	H:14/7 L:18/8	H:3/18 L:17/9			H:18/3 L:15/12			
Gu L,2018[4]	China	H:28(14/14) L:132(80/52)	GC	B1: adjacent tissue B2:Normal gastric mucosa		Case-control study	IHC	More than 25% of the cells were positive	OPN, sLAG-3, DKK-1		H:18/10 L:10/82	H:10/18 L:80/52	-	H:16/12 L:84/48	-	-	Reported in text
Hong SA, 2018[5]	Korea	H:73(53/20) L:85(60/25)	GC	-	Surgey	Case-control study	IHC	More than 60 H scores,	DKK1 expressi on with β-catenin positivitiy		H:27/46 L:41/44	H:26/47 L:20/65	H:62/11 L:65/20	-	H:7/66 L:5/80		Reported in text
Liu DJ, 2017[7]	China	H:205(122/83) L:106(54/52)	PC	Healthy control	Unknown	Case-control study	IHC	Unknown	DKK-1		H:20/185 L:19/87	H:128/77 L:66/40		H:120/85 L:75/31	H:182/23 L:98/8	H:181/24 L:100/6	Reported in text
Xu	China	H:27(22)	Adenoc	-	Surgey	Case-control study	ELIS	2615.9	DKK-1	H:10/1	H:5/22	-	-	H:22/5	-	H:8/19	Estima

Y,2017 [10]		/5) L:52(43/ 9)	arcinom a of esophag o-gastri c junction		y	ontrol study	A	pg/mL		5 L:25/2 1	L:9/43		L:32/1 0	L:5/47	ted	
Fu Y,2015 [17]	China	H:63(51. 2 ± 11.6, 56/7) L:12(52. 7 ± 10.5,8/4)	HCC	-	Surger y	Case-c ontrol study	IHC	More than 50% of the cells were positive	C-MET+ Golpl12+ EZH2+D KK1	H:42/2 1 L:6/6			H : 7/56 L : 2/10	H:26/3 7 L:5/7	Report ed in text	
Ma G,201 5[20]	China	H:133(1 02/31) L:195(1 33/62)	GC	-	Surger y+che mother apy	Case-c ontrol study	IHC	More than 50% of the cells were positive	DKK1	H:76/5 7 L:116/ 79	H:75/3 6 L:71/1 46	H:35/9 2 L:61/1 37	H:52/8 1 L:150/ 45	H:27/1 06 L:100/ 95	H:6/12 7 L:40/1 55	Report ed in text
Ma X,201 5[21]	China	H:18(13 /5) L:54(43/ 11)	HCC	-	Surger y	Case-c ontrol study	ELIS A	1769 pg/mL	DKK1	H:12/6 L:33/2 1	H:15/3 L:42/1 2			H:10/8 L:22/3 2	Report ed in text	
Peng Y,2015 [22]	China	H:57(42 /15) L:69(60/ 9)	EPC	-	Non-s urgery	Case-c ontrol study	ELIS A	More than 50% of the cells were positive	DKK1+ P53		H:35/2 2 L:28/4 1		H:33/2 4 L:51/1 6		Report ed in text	
Tan J,2015	China	H:35(28 /7)	EPC	-	Surger y	Case-c ontrol	IHC	More than 50%	DKK1		H:19/1 6	H:24/1 1	H:17/1 8		Report ed in	

[23]		L:15(10/5)				study		of the cells were positive		L:14/1	L:14/1	L:10/5		text		
Cai L,2014 [24]	China	H:27(60 ± 14.93, 19/8) L:126(58.11 ± 12.07, 83/43)	GC	-	Surgey	Case-control study	IHC	60 pg/mL	DKK1+ CEA+C A19-9	H:15/12 L:100/26	H:11/16 L:88/38	H:22/59 L:117/12	H:16/11 L:114/12	H:22/59 L:117/9	Reported in text	
Wang Q,2014 [25]	China	H:30 L:14	PC	-	Untreated	Case-control study	IHC	More than 50% of the cells were positive	DKK1+ CEA+C A19-9	H:8/22 L:10/4	H:15/15 L:2/12	H:24/6 L:7/7		Reported in text		
Gao C,2012 [29]	China	H:195(57.2 ± 9.6, 133/62) L:133(61.9 ± 11.8, 102//31)	GC	-	Surgey	Case-control study	IHC	More than 50% of the cells were positive	DKK1	H:116/79 L:76/57	H:49/146 L:97/36	H:61/132 L:35/88	H:150/45 L:52/81	H:100/95 L:27/106	H:40/155 L:6/127	Reported in text
Lee HS,2012 [30]	Korea	H:27(60 ± 14.93, 19/8) L:126(58.11 ±	GC	Healthy control	Surgey	Case-control study	IHC	60 pg/mL	DKK1+ CEA+C A19-9	H:15/12 L:100/26	H:11/16 L:88/38	H:13/14 L:81/45	H:16/11 L:114/12	H:22/59 L:117/9	Reported in text	

Zhang X,2012[32]	China	12.07, 83/43) H:19(10/9) L:31(18/13)	Intrahepatic cholangiocarcinoma	Healthy control	Untreated	Case-control study	IHC	More than 25% of the cells were positive	DKK1	H:7/12 L:14/17	H:11/8 L:27/4	H:14/5 L:20/11	H:5/14 L:2/29	H:4/14 L:1/29	Reported in text
Tung EK, 2011[35]	China	H:23(19/4) L:77(63/14)	HCC	-	Untreated	Case-control study	ELISA	1500 pg/mL	DKK1	H:5/17 L:39/37	H:4/18 L:30/44		H:6/6 L:15/22		Reported in text
Li B,2009[38]	China	H:53 L:27	EPC	Healthy control	Untreated	Case-control study	ELISA	14.54ng/mL	DKK1+ CEA+C YFRA21 -1		H:17/3 L:16/11	H:40/1 L:18/9	H:43/1 L:15/12		Reported in text
Makinoto T,2009[39]	Japan	H:72(63/9) L:98(89/9)	EPC	-	Chemotherapy	Case-control study	IHC	More than 10% of the cells were positive	DKK1		H:28/4 L:45/53	H:13/5 L:28/70			Reported in text

H:High expression group; L: Low expression group; ELISA:enzyme-linked immunosorbent assay;IHC: Immunohistochemistry;
HCC:hepatocellular carcinoma; PC:pancreatic carcinoma ; GC:gastric carcinoma ; EPC:esophageal carcinoma; CRC: Colorectal carcinoma

Table S3 Quality assessment of included of studies by QUADAS-2 scales.

Study	PATIENT SELECTION				INDEX TEST(S)			REFERENCE STANDARD			FLOW AND TIMING				
	Was a consecutive or random sample of patients enrolled?	Was a case-control design avoided?	Did the study avoid inappropriate exclusions?	Is there concern that the included patients do not match the review question?	Were the index test results interpreted without knowledge of the reference standard?	If a threshold was used, was it pre-specified?	Is there concern that the index test, its conduct, or interpretation differ from the review question?	Is the reference standard likely to correctly classify the target condition?	Were the reference results interpreted without knowledge of the index test?	Is there concern that the target condition as defined by the reference standard does not match the review question?	Was there an appropriate interval between index test(s) and reference standard?	Did all patients receive the same reference standard?	Did patients receive the same reference standard?	Were all patients included in the analysis?	Could the patient flow have introduced bias?
Chen Z, 2019[1]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
NAM Hassan, 2019[2]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Xi L, 2019[3]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Chen S, 2017[6]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Qin QF,2017[8]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Xie H, 2017[9]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Xu Y,2017[10]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Yao F H,2017[11]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Erdal H,2016[12]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Fouad YM,2016[13]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear

Mao L,2016[14]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Su R,2016[15]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Zhao P,2016[16]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Fu Y,2015[17]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Ge T,2015[18]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Han SX,2015[19]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Peng Y,2015[22]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Wang Q,2014[25]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Zhou Y,2014[26]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Peng L,2013[27]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Yang H,2013[28]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Shen Q,2012[31]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Zhang Y,2012[33]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Soydinc HO,2011[34]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Zhou Y, 2011[36]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Zhang X,2010[37]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Li B,2009[38]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Yamabuki T,2007[40]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Zheng X, 2019[A1]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear
Zekri AR, 2020[A3]	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear

Table S4 Quality assessment of included of studies by Critical Appraisal Skills Programme (CASP) scales.

Study, Year	1. Did the study address a clearly focused issue?	2. Was the cohort recruited in an acceptable way?	3. Was the exposure accurately measured to minimise bias?	4. Was the outcome accurately measured to minimise bias?	5. (a) Have the authors identified all important confounding factors?	5. (b) Have they taken account of the confounding factors in the design and/or analysis?	6. (a) Was the follow up of subjects complete enough?	6. (b) Was the follow up of subjects long enough?	7. What are the results of this study?	8. How precise are the results?	9. Do you believe the results?	10. Can the results be applied to the local population?	11. Do the results of this study fit with other available evidence?	12. What are the implications of this study for practice?
Gu L,2018[4]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Can't tell	Yes	Can't tell	Yes	Yes	Yes	Yes
Hong SA, 2018[5]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
Xu Y,2017[10]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Can't tell	Yes	Can't tell	Yes	Yes	Yes	Yes
Fu Y,2015[17]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Can't tell	Yes	Can't tell	Yes	Yes	Yes	Yes
Ma G,2015[20]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Can't tell	Yes	Can't tell	Yes	Yes	Yes	Yes
Ma X,2015[21]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Can't tell	Yes	Can't tell	Yes	Yes	Yes	Yes
Peng Y,2015[22]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Can't tell	Yes	Can't tell	Yes	Yes	Yes	Yes
Tan J,2015[23]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Can't tell	Yes	Can't tell	Yes	Yes	Yes	Yes
Cai L,2014[24]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Can't tell	Yes	Can't tell	Yes	Yes	Yes	Yes

Wang Q,2014[25]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	No	Yes	Can't tell	Yes	Yes	Yes	Yes
Gao C,2012[29]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Can't tell	Yes	Can't tell	Yes	Yes	Yes	Yes
Lee HS,2012[30]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
Zhang X,2012[32]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
Tung EK, 2011[35]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Can't tell	Yes	Can't tell	Yes	Yes	Yes	Yes
Li B,2009[38]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
Makino T,2009[39]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
Hu W,2020[A2]	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes

==	No.of Analyses	No. of participa nts	Sensitivity, (95% CI)	Specificity, (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Diagnostic Odds Ratio (95% CI)	Area Under the Curve	Meta-reg ression	Publicati on bias	GRADE
			DKK-1+AFP								
HCC	12 (30)	7683	0.91 (0.82-0.96)	0.88 (0.87-0.89)	6.39 (5.26-7.77)	0.19 (0.16-0.23)	36.57 (26.30-50.86)	0.9211*		0.945	High
Compare d with LC±HB V±HCV in HCC	5(12)	2654	0.80(0.78-0.82)	0.82(0.79-0.84)	4.36(3.69-5.17)	0.23(0.17-0.29)	20.26(14.22-28.87)	0.8876	0.14	0.582	High
Early HCC	5(13)	3138	0.84(0.82-0.86)	0.87(0.85-0.88)	5.56(4.20-7.37)	0.19(0.14-0.26)	30.33(18.37-50.09)	0.9109*	0.88	0.524	High
			AFP								
HCC	11(17)	4872	0.65 (0.63-0.67)	0.73 (0.71-0.75)	3.17 (2.35-4.28)	0.41(0.35-0.49)	8.30(5.33-12.93)	0.7941		0.180	High
			DKK-1								
HCC	17 (35)	9080	0.71 (0.69-0.72)	0.87 (0.86-0.88)	5.12 (4.08-6.41)	0.33 (0.29-0.37)	17.08 (12.83-22.74)	0.8515		0.208	High

Table S6 SUCRA score from network meta-analysis for TNM stage and lymph node metastasis.

Sub-type	TNM stage	Lymph node metastasis
EPC	83.7	61.1
GC	51.4	60
AEGJ	52	62.3
HCC	53.3	0
IHCC	51	43.7
PC	26.7	31.8
IHC	83.7	61.1
ELISA	51.4	60
Low group	38.2	9