

Table S1. Complete information of inclusion research

1st author(year)	Country	Gold standard	Study design	Subgroup	No. of patients	Males	Females	Age(Mean)	Stage I	Stage II	Stage III	Stage IV	TP	FN	FP	TN	Sensitivity	Specificity	Thresholds	
Zhang et al. (2020)	China	Surgery, Histopathology	retrospective	II (PC/CP, others/HC)	184	114	70	52.09	—	—	—	—	50	11	47	76	0.82	0.618	37.00/ml	
Yoshizawa et al. (2020)	Japan	Histopathology, puncture	retrospective	II (PDAC/CP)	80	—	—	—	12	3	8	20	34	9	7	30	0.791	0.811	37.00/ml	
Chen et al. (2020)	China	—	retrospective	I (PC/HC)	156	103	53	59	27	35	16	0	51	27	12	66	0.654	0.846	—	
Yamada et al. (2020)	Japan	—	retrospective	I (PDAC/HC)	98	41	57	25-96 (63.77)	15	15	11	14	49	6	2	41	0.89	0.95	21.230/ml	
Marta et al. (2019)	Poland	Histopathology	retrospective	II (PC/CP/HC)	226	115	111	21-88	0	13	19	60	65	27	4	130	0.707	0.97	—	
Dou et al. (2019)	China	Surgery, Histopathology	retrospective	II (PC/BPT)	374	219	155	12-84 (60.27)	50	94	102	0	184	62	7	121	0.748	0.9453	37.00/ml	
Kuwatani et al. (2019)	Japan	—	retrospective	II (PC/CP, IPMN/HC)	256	170	86	36-80 (65.41)	1	2	10	85	74	24	12	146	0.76	0.92	37.00/ml	
				II (PC/CP, IPMN)	151	72	79	36-80 (65.91)	1	2	10	85	74	24	10	43	0.76	0.81	37.00/ml	
				II (PC/CP)	119	61	58	36-80 (65.48)	1	2	10	85	74	24	7	14	0.76	0.67	37.00/ml	
				II (PC/IPMN)	130	57	73	44-80 (67.35)	1	2	10	85	74	24	3	29	0.76	0.91	37.00/ml	
				I (PC/HC)	203	144	59	38-80 (65.96)	1	2	10	85	74	24	2	103	0.76	0.98	37.00/ml	
				—	80	—	—	—	—	—	—	—	26	14	6	34	0.65	0.85	37.00/ml	
Zhou et al. (2019)	China	Surgery, Histopathology, puncture	retrospective	II (PDAC/CP, AP)	240	—	—	18-88 (56.9)	7	25	9	20	94	31	9	106	0.752	0.922	37.00/ml	
Traeger et al. (2018)	Germany	Histopathology	retrospective	III (PDAC/CP, IPMN/HC)	142	73	69	34-87.9	—	38	11	16	53	12	18	59	0.81	0.768	—	
Ulutas et al. (2018)	Turkey	—	retrospective	I (PAC/HC)	168	85	83	39-73 (52.48)	83	—	—	—	65	18	8	77	0.78	0.91	20.50/ml	
Choe et al. (2018)	Korea	—	retrospective	II (diabetic populations)	5111	3280	1831	60.3	—	—	—	—	62	25	517	4507	0.713	0.897	37.00/ml	
Murakami et al. (2018)	Japan	—	retrospective	II (diabetic populations)	236	153	83	47-89 (70.7)	—	—	—	—	99	19	21	97	0.839	0.822	37.00/ml	
				II (diabetic populations)	236	153	83	47-89 (70.7)	—	—	—	—	82	36	2	116	0.695	0.982	75.00/ml	
Hogendorf et al. (2018)	Poland	Surgery, Histopathology	retrospective	II (PDAC/CP)	63	28	35	59.95	—	—	—	—	24	18	2	19	0.5714	0.905	36.00/ml	
Zhou et al. (2018)	China	Histopathology	retrospective	I (PC/HC)	108	74	34	21-56	—	—	—	—	48	10	3	47	0.828	0.94	27.00/ml	
Li et al. (2018)	China	Surgery, Histopathology	retrospective	II (PDAC/CP, BPT)	723	442	281	57.6	342	—	289	—	453	178	4	88	0.718	0.957	72.920/ml	
Kakkat et al. (2017)	India	Surgery, Histopathology	prospective	II (PDAC/CP)	61	44	17	49.77	—	—	—	—	19	15	5	22	0.559	0.815	37.00/ml	
				II (PDAC/CP)	61	44	17	49.77	—	—	—	—	25	9	6	21	0.735	0.778	25.30/ml	
				II (PDAC/CP)	61	44	17	49.77	—	—	—	—	16	18	1	26	0.47	0.963	10010/ml	
				II (PDAC/CP)	61	44	17	49.77	—	—	—	—	15	19	0	27	0.44	1	11510/ml	
				III (PDAC/CP,HC)	189	128	61	66.7	8	50	10	13	56	25	0	108	0.6914	1	55.00/ml	
Kim et al. (2017)	United States	—	prospective	III (PDAC/CP, IPMN/HC)	537	284	253	66.1	10	78	41	68	153	44	5	335	0.7766	0.9857	55.00/ml	
Yan et al. (2017)	China	Surgery, Histopathology	retrospective	II (PAC/AIP)	125	90	35	52-70	—	—	—	—	56	44	1	24	0.56	0.96	306.750/ml	
Hirata et al. (2017)	Japan	—	retrospective	I (PDAC/HC)	112	61	51	45-86	7	47	—	—	37	17	4	54	0.685	0.93	37.00/ml	
Zhao et al. (2017)	China	Histopathology	retrospective	I (PC/HC)	138	88	50	55.34	—	—	—	—	52	20	0	66	0.7222	1	39.00/ml	
				I (PC/HC)	53	—	—	—	—	—	—	—	18	6	0	29	0.75	1	39.00/ml	
				II (PC/BPD)	122	—	—	—	—	—	—	—	70	26	8	18	0.7292	0.6923	39.00/ml	
				III (PC/BPD/HC)	217	—	—	—	—	—	—	—	70	26	8	113	0.7292	0.9339	39.00/ml	
Pezzilli et al. (2016)	Germany	—	retrospective	II (PDAC/CP, other)	91	54	37	28-88 (61.6)	—	—	—	—	12	12	19	48	0.5	0.716	37.00/ml	
Yuan et al. (2016)	China	—	retrospective	III (PC/CP, BPT, other cancers/HC)	240	149	91	21-82	4	8	46	18	62	14	11	153	0.816	0.933	—	
				III (PC/CP, BPT, other cancers/HC)	280	147	133	16-88	1	7	51	23	59	23	28	170	0.72	0.859	—	
				II (PC/CP)	98	58	40	21-82	4	8	46	18	62	14	5	17	0.816	0.773	—	
				II (PC/CP+BPT)	132	70	62	16-88	1	7	51	23	59	23	10	40	0.72	0.8	—	
				I (PC/HC)	158	95	63	21-82	4	8	46	18	62	14	0	82	0.816	1	—	
				I (PC/HC)	170	90	80	35-88	1	7	51	23	59	23	4	84	0.72	0.955	—	
Gu et al. (2016)	China	Surgery, Histopathology	retrospective	II (PC/CP)	60	38	22	69	—	—	—	—	35	5	8	12	0.875	0.6	37.00/ml	
Ferri et al. (2016)	Spain	Histopathology	retrospective	II (PDAC/CP)	67	44	23	61.7	1	26	8	12	38	9	1	19	0.809	0.95	37.00/ml	
Mohamed et al. (2016)	Egypt	Histopathology	retrospective	III (PC/CP/HC)	112	70	42	58.8	30	—	20	—	40	10	27	35	0.8	0.564	55.50/ml	
				III (PC/CP/HC)	112	70	42	58.8	30	—	20	—	35	15	26	36	0.7	0.581	60.50/ml	
				III (PC/CP/HC)	112	70	42	58.8	30	—	20	—	33	17	25	37	0.66	0.597	71.50/ml	
				III (PC/CP/HC)	112	70	42	58.8	30	—	20	—	32	18	24	38	0.64	0.613	79.00/ml	
Schonemeier et al. (2016)	Germany	Histopathology	prospective	II (PC/CP)	106	75	31	24-85 (58.6)	—	—	—	—	39	15	9	43	0.72	0.82	37.00/ml	
Choe et al. (2016)	Korea	—	retrospective	II (diabetic populations)	2363	1284	1079	65.38	12	24	8	24	39	29	483	1812	0.574	0.79	37.00/ml	
Ma et al. (2016)	China	Surgery, Histopathology, puncture	retrospective	III (PC/CP, AP/HC)	170	98	72	38-61 (50.4)	—	—	—	—	18	3	6	23	0.857	0.793	—	
Zhong et al. (2016)	China	Surgery, Histopathology	retrospective	II (PC/BPD)	254	159	95	23-84 (58.94)	—	—	—	—	121	28	42	63	0.8121	0.6	37.00/ml	
Gu et al. (2015)	China	—	retrospective	III (PC/CP, BPT/HC)	132	68	64	28-71 (56.5)	—	—	—	—	43	9	33	47	0.827	0.586	37.00/ml	
Kim et al. (2015)	Korea	Surgery	retrospective	II (IPMN-PC, HGD, IPMN-LGD, LGD, IPMA)	367	231	136	63.7	—	—	—	—	40	77	19	231	0.342	0.924	37.00/ml	
Han et al. (2015)	China	—	retrospective	III (PC/CP, BPT/HC)	232	152	80	34-84 (60.48)	16	46	27	51	103	37	15	77	0.7357	0.837	39.30/ml	
				II (PC/CP, BPT)	184	122	62	36-84 (60.84)	16	46	27	51	103	37	8	36	0.7357	0.8181	39.30/ml	
				I (PC/HC)	188	—	—	—	16	46	27	51	103	37	7	41	0.7357	0.8542	39.30/ml	
Rammohan et al. (2015)	India	Histopathology	retrospective	II (PC/CP)	83	56	27	40.6	—	—	—	—	27	1	8	47	0.9643	0.8545	127.00/ml	
Mohamed et al. (2015)	Egypt	Histopathology	retrospective	I (PC/HC)	70	43	27	46-81	5	16	8	21	41	9	7	13	0.82	0.667	55.00/ml	
Bian et al. (2015)	China	Surgery, Histopathology	retrospective	II (PC/BPD)	70	46	24	45-67 (55.15)	—	—	—	—	30	5	10	25	0.857	0.7142	102.10/ml	
Cheng et al. (2015)	China	Surgery, Histopathology	retrospective	II (PC/CP, AIP, others)	118	84	34	38-89	11	26	22	8	38	7	13	14	0.804	0.519	37.00/ml	
Huang et al. (2015)	China	Histopathology	retrospective	III (PC/BPD/HC)	166	101	65	21-78 (51.2)	—	—	—	—	43	11	15	97	0.7963	0.8661	27.00/ml	
Chang et al. (2014)	China	Histopathology	retrospective	II (PC/CP, AIP)	402	212	190	51.3	13	10	23	84	108	22	68	204	0.83	0.75	37.00/ml	
				II (PC/CP)	216	119	97	51	13	10	23	84	108	22	17	69	0.83	0.802	37.00/ml	
				II (PC/AIP)	316	158	158	51.9	13	10	23	84	108	22	51	135	0.83	0.726	37.00/ml	
Chan et al. (2014)	Canada	Histopathology	prospective	II (PDAC/AP, CP, CBDstones, others)	176	—	—	—	7	79	—	—	25	86	25	11	54	0.775	0.831	20.30/ml
				II (PDAC/AP, CP, CBDstones, others)	204	—	—	—	10	105	—	—	24	96	43	13	52	0.691	0.8	20.30/ml
				II (PDAC/CP)	49	—	—	—	7	17	0	0	17	7	8	17	0.708	0.68	20.30/ml	
Lee et al. (2014)	Korea	Histopathology	retrospective	II (PDAC/CP)	52	—	—	—	10	17	0	0	15	12	11	14	0.556	0.56	20.30/ml	
Schultz et al. (2014)	Denmark	Histopathology	prospective	III (PC/CP, other cancers/HC)	185	133	52	56.4	—	—	—	—	33	8	43	101	0.804	0.7	37.00/ml	
				III (PDAC/CP/HC)	230	132	98	33-75	5	25	26	87	126	17	7	80.				

1st author (year)	Country	Gold standard	Study design	Subgroup	No. of patients	Males	Females	Age (Mean)	Stage I	Stage II	Stage III	Stage IV	TP	FN	FP	TN	Specificity	Sensitivity	Thresholds
Liu et al. (2014)	China	Surgery, Histopathology	retrospective	II (PC/BPD)	89	—	—	—	—	—	—	—	50	17	8	14	0.746	0.636	37.00/ml
Yoon et al. (2013)	Korea	Histopathology	retrospective	II (PC/AIP)	316	218	98	61.2	—	—	—	—	142	59	29	86	0.706	0.748	37.00/ml
				II (PC/AIP)	316	218	98	61.2	—	—	—	—	105	96	14	101	0.522	0.878	100.00/ml
Tonack et al. (2013)	United Kingdom	Histopathology	retrospective	II (PDAC/CP, others)	101	—	—	—	—	—	—	—	11	11	8	71	0.5	0.9	—
				II (PDAC, jaundice/CP, others)	117	—	—	—	—	—	—	—	29	9	8	71	0.76	0.9	—
Wang et al. (2013)	China	Histopathology	retrospective	II (PC/BPD)	232	126	106	—	33	54	32	10	94	35	25	78	0.729	0.757	37.00/ml
Poruk et al. (2013)	United States	Histopathology	retrospective	III (PDAC/CP/HC)	220	115	105	29-94	7	35	17	27	72	14	16	118	0.84	0.88	37.00/ml
Kaur S et al. (2013)	United States	Histopathology	retrospective	I (PC/HC)	106	—	—	—	5	37	2	38	68	14	8	16	0.83	0.67	37.00/ml
				II (PC/CP)	105	—	—	—	5	37	2	38	68	14	9	14	0.83	0.61	37.00/ml
				III (PC/CP/HC)	129	—	—	—	5	37	2	38	68	14	17	30	0.83	0.6383	37.00/ml
				II (PC/NPND)	81	41	40	52-77 (67.1)	—	—	—	—	49	9	11	12	0.84	0.52	2221.70/ml
Kaur S et al. (2013)	United States	—	prospective	II (PC/CP)	82	51	31	54-77 (66.8)	—	—	—	—	32	26	10	14	0.55	0.58	5868.20/ml
				II (PDAC/BPD)	317	—	—	—	—	—	—	—	180	54	22	61	0.77	0.73	37.00/ml
				II (PDAC/CP)	284	—	—	—	—	—	—	—	180	54	16	34	0.77	0.68	37.00/ml
Xie et al. (2012)	China	Histopathology	retrospective	III (PC/BPT, AP/HC)	137	—	—	—	—	—	—	—	33	16	5	83	0.673	0.943	41.610/ml
Molina et al. (2012)	Spain	—	prospective	II (PC/BPT, AP)	465	—	—	—	36	73	110	170	317	72	21	55	0.815	0.724	37.00/ml
				III (PC/CP/HC)	313	205	108	57	27	39	17	55	112	26	12	163	0.812	0.931	37.00/ml
Liu et al. (2012)	China	Surgery, Histopathology	retrospective	II (PC/CP)	245	160	85	56.03	27	39	17	55	112	26	12	95	0.812	0.89	37.00/ml
				I (PC/HC)	206	133	73	61.37	27	39	17	55	112	26	0	68	0.812	1	37.00/ml
Hirono et al. (2012)	Japan	Histopathology	retrospective	II (IPMN-PC, HGD/IPMN-LGD, LGD, IPMA)	134	74	60	32-84 (68.9)	—	—	—	—	27	51	6	50	0.346	0.893	—
Gu et al. (2012)	China	Surgery, Histopathology, puncture	retrospective	II (PC/CP)	60	38	22	31-80 (58.5)	—	—	—	—	35	5	8	12	0.875	0.6	37.00/ml
Wu et al. (2012)	China	Surgery, Histopathology	retrospective	II (PC/BPD)	96	59	37	39-77 (54.9)	17	—	—	39	42	14	14	26	0.75	0.65	35.00/ml
Li et al. (2012)	China	Histopathology	retrospective	III (PC/BPD/HC)	90	—	—	51.4	—	—	—	—	18	12	4	56	0.6	0.933	35.00/ml
				II (PC/BPD)	102	—	—	—	—	—	—	—	67	11	5	19	0.86	0.79	35.00/ml
				II (PC/BPD)	102	—	—	—	—	—	—	—	32	46	3	21	0.41	0.87	100.00/ml
				II (PC/BPD)	102	—	—	—	—	—	—	—	18	60	1	23	0.23	0.96	200.00/ml
Sivaraman et al. (2011)	India	Radiological diagnosis	prospective	II (PC/BPD)	102	—	—	—	—	—	—	—	7	71	0	24	0.08	1	300.00/ml
				II (PDAC/BPT)	49	—	—	—	—	—	—	—	11	10	8	20	0.524	0.714	37.00/ml
				II (PC/CP, AP)	122	75	47	32-80	—	21	24	22	54	13	9	46	0.806	0.836	37.00/ml
				II (PDAC/IPMN)	142	82	60	31-87	—	—	—	—	37	13	13	79	0.74	0.859	37.00/ml
Hwang et al. (2011)	Korea	Histopathology	retrospective	II (IPMN-PC, HGD/IPMN-LGD, LGD, IPMA)	237	137	100	38-83 (63)	—	—	—	—	11	28	20	178	0.282	0.9	37.00/ml
Xu et al. (2011)	China	Histopathology	retrospective	II (IPMN-PC, HGD/IPMN-LGD, LGD, IPMA)	86	62	24	41-76 (62)	15	45	3	1	45	19	3	19	0.7031	0.8636	37.00/ml
				III (PC/BPD/HC)	858	485	373	22-88 (55.6)	9	59	251	203	323	199	28	308	0.619	0.916	37.00/ml
				II (PC/BPD)	658	—	—	22-88	9	59	251	203	323	199	22	114	0.619	0.8382	37.00/ml
				I (PC/HC)	722	429	293	22-88 (54.7)	9	59	251	203	323	199	6	194	0.619	0.97	37.00/ml
Huang et al. (2011)	China	Surgery, Histopathology	retrospective	III (PC/BPD/HC)	215	113	102	21-79 (54.6)	—	3	21	51	62	13	27	113	0.827	0.807	37.00/ml
Chi et al. (2011)	China	Surgery, Histopathology	retrospective	II (PC/BPD)	59	40	19	15-82 (57.09)	3	1	12	22	34	4	8	13	0.895	0.619	32.00/ml
Joergensen et al. (2010)	Denmark	—	prospective	II (PDAC/CP, BPT, CBD stones, others)	103	55	48	36.4-83.8	—	6	22	23	44	7	14	38	0.863	0.731	37.00/ml
				II (IPMN-PC, HGD/IPMN-LGD, LGD, IPMA)	195	—	—	—	—	—	—	—	21	28	11	135	0.4286	0.9247	37.00/ml
Wang et al. (2010)	China	Surgery, Histopathology	prospective	II (PDAC/CP, others)	67	37	30	30-78 (60.39)	—	—	—	—	39	10	3	10	0.7959	0.7692	37.00/ml
Hu et al. (2010)	China	Surgery, Histopathology	retrospective	I (PC/BPD)	156	85	71	64.47	11	4	22	35	63	10	48	35	0.863	0.4216	37.00/ml
Liao et al. (2009)	China	Histopathology	retrospective	I (PC/HC)	160	97	63	60.6	3	29	12	14	47	11	9	93	0.81	0.912	37.00/ml
				III (PC/CP, BPT/HC)	299	175	124	30-94	4	31	17	23	58	17	20	204	0.773	0.911	37.00/ml
				II (PC/BPT)	117	66	51	41-92	4	31	17	23	58	17	10	32	0.773	0.762	37.00/ml
				II (PC/CP)	107	63	44	32-92	4	31	17	23	58	17	2	30	0.773	0.9375	37.00/ml
Bedi et al. (2009)	India	Surgery, Histopathology	prospective	I (PC/HC)	225	138	87	30-94	4	31	17	23	58	17	8	142	0.773	0.947	37.00/ml
				II (PC/CP)	84	—	—	—	—	—	—	—	23	11	15	35	0.68	0.7	37.00/ml
				II (PC/CP)	84	—	—	—	—	—	—	—	14	20	7	43	0.41	0.86	100.00/ml
				II (PC/CP)	84	—	—	—	—	—	—	—	8	26	2	48	0.24	0.96	200.00/ml
				II (PC/CP)	84	—	—	—	—	—	—	—	5	29	0	50	0.15	1	300.00/ml
Zhao et al. (2009)	China	Histopathology	retrospective	II (PC/BPD)	185	—	—	—	—	—	—	—	14	4	42	125	0.778	0.75	22.00/ml
Lu et al. (2009)	China	Surgery, Histopathology	retrospective	II (PC/BPD)	102	—	—	—	—	2	11	21	28	6	15	53	0.824	0.779	37.00/ml

Notes:

- ① Subgroup analysis: I: studies with healthy controls; II: studies with benign (non-cancer) pancreatic disease controls; III: studies with mixed (non-cancer patients and healthy individuals) controls
- ② Pancreatic cancer stage: Stage I: TNM stage is T1~2 N0 M0; Stage II: TNM stage is T3 N0 M0, T1~3 N1 M0; Stage III: TNM stage is T1~3 N2 M0, T4 N0~2 M0; Stage IV: TNM stage is T1~4 N0~2 M1
- ③ Diagnostic accuracy measurements: TP: true positive; FN: false negative; FP: false positive; TN: true negative

Abbreviation:

AIP: autoimmune pancreatitis; AP: acute pancreatitis; BPD: benign pancreatic disease; BPT: benign pancreatic tumor; CBD stones: common bile duct stones; CP: chronic pancreatitis; HC: healthy controls; IPMA : intraductal papillary mucinous adenoma of the pancreas ; IPMN: intraductal papillary mucinous neoplasm; IPMN-HGD
IPMN-LGD : IPMN with intermediate-grade dysplasia; IPMN-LGD :IPMN with low-grade dysplasia; IPMN-PC : IPMN with invasive carcinoma; NPNH: not pancreatic cancer and not health; PAC: pancreatic adenocarcinoma; PC: pancreatic cancer; PDAC: pancreatic ductal adenocarcinoma; PNET: Pancreatic neuroendocrine tumor;