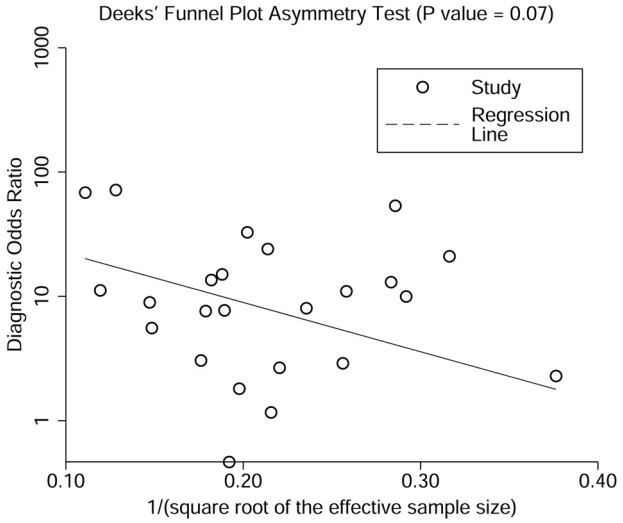
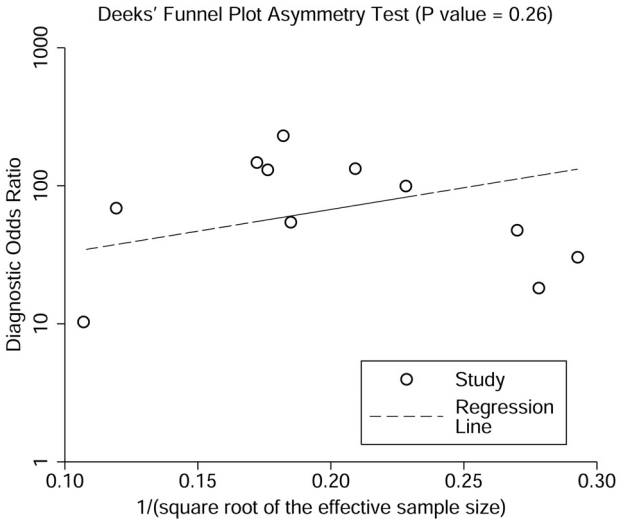


ON-LINE FIG 1. Funnel plot of Deeks et al [40] based on the data of ^{18}F-FDG-PET for differentiating brain tumors.



ON-LINE FIG 2. Funnel plot of Deeks et al [40] based on the data of ^{11}C-MET PET for differentiating brain tumors.

ON-LINE APPENDIX

Search Strategies

The search strategy was based on the combination of the key words: brain neoplasms; ^{18}F-FDG or fluorodeoxyglucose; ^{11}C-MET or methionine; and PET, or positron emission tomography.

PubMed

((“Brain Neoplasms”[MeSH Terms] OR “Glioma”[MeSH Terms] OR glioma* OR (glioblastoma* OR “glioblastoma multiforme”) OR (astrocytoma* OR “anaplastic astrocytoma”) OR (oligodendrocytoma* OR “anaplastic oligodendrocytoma”) OR (brain AND (tumor* OR tumour*)) OR (neuroectodermal AND (tumor* OR tumour*)) OR ependymoma* OR oligodendroglioma*)) AND (“fdg”[All Fields] OR “fluorodeoxyglucose”[All Fields] OR “MET”[All Fields] OR “methionine”[All Fields]) AND (“Tomography, Emission-Computed”[MeSH Terms] OR (positron AND emission AND tomograph*) OR pet) AND “humans”[MeSH Terms].

Scopus

(TITLE-ABS-KEY(glioma) OR TITLE-ABS-KEY(astrocytoma) OR TITLE-ABS-KEY(oligodendrocytoma) OR TITLE-ABS-KEY(neuroectodermal) OR TITLE-ABS-KEY(ependymoma) OR TITLE-ABS-KEY(glioblastoma) OR TITLE-ABS-KEY(oligodendroglioma) OR TITLE-ABS-KEY(brain tumor) AND TITLE-ABS-KEY(pet) OR TITLE-ABS-KEY(positron emission tomography) AND TITLE-ABS-KEY(fluorodeoxyglucose) OR TITLE-ABS-KEY(fdg) AND TITLE-ABS-KEY(methionine) OR TITLE-ABS-KEY(met)).

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(PET or positron emission tomography) AND (brain tumor) AND ((^{18}F-FDG OR fluorodeoxyglucose) OR (^{11}C-MET or methionine)) AND (diagnosis) (keywords were translated into Chinese).

Meta-Analysis Commands in STATA 12.0

1) For testing pooled diagnostic performance and heterogeneity: midas tp fp fn tn, es(x) res(all).
2) For plotting HSROC curves: metandi tp fp fn tn, plot.
3) For testing publication bias: midas tp fp fn tn, pubbias.
4) For estimating covariate effect (meta-regression): midas tp fp fn tn type, es(x) covars.

On-line Table 1: Study and patient characteristics of eligible studies

Study	Country	Design	Patient No.	M/F	Mean/Median Age (yr)	Type of Brain Tumors	Disease Status	PET Tracer	Prior Imaging Tests	Reference Standard	Clinical/Radiologic Follow-Up after PET (Mean/Median, mo)
Chen et al 2006[1]	United States	Prospective	30	18:12	45.2	Glioma, brain metastasis	SPBT and SRBT	FDG	MRI	Histology or clinical follow-up	20
Ricci et al 1998[2]	United States	Retrospective	31	17:14	46	Glioma, unknown (2 pts)	SRBT	FDG	MRI	Histology only	ND
Zuo et al 2001[5]	China	Retrospective	15	10:5	36	Glioma	SRBT	FDG	MRI	Histology or clinical follow-up	ND
Gómez-Río et al 2008[6]	Spain	Prospective	76	43:33	47.7	Glioma	SRBT	FDG	MRI	Histology or clinical follow-up	31
Choi et al 2005[7]	Korea	Prospective	26	15:11	34	Glioma, lymphoma, brain metastasis	SPBT and SRBT	FDG	MRI	Histology, clinical and radiologic follow-up	>6
Pauleit et al 2009[8]	Germany	Prospective	52	36:16	46	Glioma, lymphoma	SPBT	FDG	MRI	Histology only	ND
Lau et al 2010[9]	Australia	Prospective	21	14:7	37	Gliomas, meningioma, lymphoma	SPBT and SRBT	FDG	MRI	Histology, MRI, and clinical follow-up	20
Estrada et al 2008[10]	Mexico	Prospective	30	20:10	43	Glioma	SRBT	FDG	MRI	Histology, imaging, and clinical follow-up	>6
McCarthy et al 2008[11]	Australia	Retrospective	38	15:23	45	Glioma, lymphoma	SPBT and SRBT	FDG	MRI	Histology or clinical follow-up	9.1
Kahn et al 1994[12]	United States	Prospective	19	10:9	40	Glioma, esthesioblastoma, brain metastasis	SRBT	FDG	MRI or CT	Histology or clinical follow-up	12
Thompson et al 1999[13]	United States	Retrospective	15	ND	52	Glioma	SRBT	FDG	MRI	Histology only	ND
Sun et al 2004[14]	China	Prospective	32	21:11	34	Glioma, brain metastasis	SRBT	FDG	ND	Histology, clinical and radiologic follow-up	ND
Santra et al 2012[15]	India	Prospective	90	ND	36.8	Glioma	SRBT	FDG	ND	Histology, imaging, and clinical follow-up	ND
Hong et al 2011[16]	Korea	Prospective	20	10:10	32	Glioma, choroid plexus carcinoma, PNET, DNET	SRBT	FDG	MRI	Histology, clinical and radiologic follow-up	10
Tan et al 2011[17]	China	Retrospective	55	45:10	56.6	Glioma, lymphoma, neuroblastoma, germinoma, brain metastasis	SRBT	FDG	MRI	Histology, clinical and radiologic follow-up	>11
Enslow et al 2012[18]	United States	Prospective	15	9:6	22–75[a]	Glioma	SRBT	FDG	Gd-MRI	Longitudinal observation by Gd-MRI	2–23
Belohlávek et al 2002[19]	Czech	Prospective	29	21:8	17–65[a]	Glioma	SRBT	FDG	MRI	Histology, radiologic and clinical follow-up	>12
Spence et al 2009[20]	United States	Prospective	19	13:6	45.2	Glioma	SRBT	FDG	MRI	Histology, clinical and radiologic follow-up	3–31
Janus et al 1993[21]	United States	Retrospective	50	32:18	38.3	Glioma, ependymoma	SRBT	FDG	MRI	Histology, clinical follow-up	12
Kim et al 2010[22]	Korea	Retrospective	10	8:2	46.1	Glioma	SRBT	FDG, MET	MRI	Histology and clinical follow-up	6.5 (recurrence), 28 (necrosis)
Cai et al 2009[23]	China	Retrospective	41	23:18	49.2	Glioma, neuroblastoma, craniopharyngioma, brain metastasis	SPBT	FDG, MET	MRI	Histology, clinical and radiologic follow-up	>6
Tripathi et al 2012[24]	India	Prospective	35	23:12	33.7	Glioma	SRBT	FDG, MET	MRI	Histology, clinical and radiologic follow-up	>18
Li et al 2012[25]	China	Retrospective	44	26:18	38.6	Glioma	SPBT and SRBT	FDG, MET	ND	Histology and clinical follow-up	>6
Ye et al 2009[26]	China	Prospective	28	21:7	47.3	Glioma	SRBT	FDG, MET	MRI (not all pts)	Histology and clinical follow-up	10–18
Chung et al 2002[29]	Korea	Prospective	45	ND	ND	Glioma, meningioma, germ cell tumor, chordoma, brain metastasis	SPBT and SRBT	FDG[b] MET	ND	Histology, radiologic and laboratory investigations and follow-up	ND
Nakajima et al 2009[30]	Japan	Retrospective	18	12:6	45	Glioma	SRBT	MET	MRI	Histology, imaging, and clinical follow-up	66.8
Terakawa et al 2008[41]	Japan	Retrospective	77	46:31	54.1	Glioma, brain metastasis	SRBT	MET	MRI	Histology, clinical and radiologic follow-up	ND
Galldiks et al 2010[42]	Germany	Prospective	39	ND	15	Glioma, medulloblastoma, DNET, ATRT	SPBT and SRBT	MET	MRI	Histology, clinical and radiologic follow-up	25.5
Sonoda et al 1998[43]	Japan	Retrospective	10	6:4	36	Glioma	SRBT	MET	MRI	Histology, clinical and radiologic follow-up	ND
Tsuyuguchi et al 2004[44]	Japan	Retrospective	11	8:3	35.5	Glioma	SRBT	MET	MRI	Histology, clinical and radiologic follow-up	>5

Note:—ND indicates no data; PNET, primitive neuroectodermal tumors; DNET, dysembryoplastic neuroepithelial tumor; ATRT, atypical teratoid rhabdoid tumor; pts, patients; Gd, gadolinium.

[a] Age range.

[b] Data for ^{18}F-FDG-PET in this study were not extractable and were excluded for the analysis for ^{18}F-FDG-PET.

On-line Table 2: PET characteristics and diagnostic criteria of eligible studies

Study	PET Tracer	Type of PET Scanner	Administered PET Tracer Activity (MBq)	Time of Scanning after Injection (min)	Scan Time (min)	Analysis Method for Diagnostic Performance	Positive Criteria of Visual Assessment	Quantitative Parameters (Cutoff Value)
Chen et al 2006[1]	FDG	PET	2.4/kg	60	30	Qualitative	FDG activity above background level	–
Ricci et al 1998[2]	FDG	PET	370	30	25	Qualitative	Hypermetabolic relative to normal contralateral white matter	–
Zuo et al 2001[5]	FDG	PET	185	30	10	Qualitative	Increased metabolism above adjacent white matter	–
Gómez-Río et al 2008[6]	FDG	PET	185	45	ND	Qualitative	Unexplainable metabolic activity, increased FDG uptake relative to immediately adjacent tissue or closest adjacent white matter	–
Choi et al 2005[7]	FDG	PET	370	60	20	Qualitative	FDG uptake above normal white matter	–
Pauleit et al 2009[8]	FDG	PET	240	30–60	ND	Qualitative	FDG uptake above white matter	–
Lau et al 2010[9]	FDG	PET/CT	400	60	ND	Qualitative	Not clearly mentioned	–
Estrada et al 2008[10]	FDG	PET	185	30–40	30	Qualitative	With uptake in a region showing enhancing areas on postcontrast T1-weighted MRI	–
McCarthy et al 2008[11]	FDG	PET	370 × BSA/1.88	30–40	ND	Qualitative	FDG uptake greater than background	–
Kahn et al 1994[12]	FDG	PET	370	0	45	Qualitative	Increased FDG uptake relative to the immediately adjacent tissue	–
Thompson et al 1999[13]	FDG	PET	ND	40	30	ND	ND	–
Sun et al 2004[14]	FDG	PET	185–370	30–60	20	Qualitative	FDG uptake greater than contralateral white matter	–
Santra et al 2012[15]	FDG	PET/CT	370	45–60	6–10	Qualitative	A definite lesion on CT images (hypermetabolic/isometabolic/ hypometabolic on PET images) or an increased focal FDG uptake without any clearly discernible lesion on CT	–
Hong et al 2011[16]	FDG	PET	370	60	15	Qualitative	FDG uptake greater than normal white matter	–
Tan et al 2011[17]	FDG	PET/CT	275–370	60	ND	Qualitative	Increased FDG uptake relative to the surrounding background radioactivity	–
Enslow et al 2012[18]	FDG	PET	370	45	30	Both[a]	ND	L/WM (1.83), SUVmax (6.2)
Belohlávek et al 2002[19]	FDG	PET	3/Kg	30	20–25	Qualitative	Clearly apparent focal accumulation of FDG	–
Spence et al 2009[20]	FDG	PET	3.7/Kg	75	15	Quantitive	ND	T/C (0.4). T/WM (0.61)[b]
Janus et al 1993[21]	FDG	PET	185–370	ND	About 20	Qualitative	Increased FDG uptake relative to the contralateral hemisphere or adjacent area	–
Kim et al 2010[22]	FDG, MET	PET	370–555 (FDG) 550–740 (MET)	40 (FDG) 10 (MET)	20 (both)	Quantitive	ND	Lmax/Rmax (1.45, FDG; 2.64, MET)
Cai et al 2009[23]	FDG, MET	PET/CT	222–370 (FDG) 555–740 (MET)	60 (FDG) 20 (MET)	ND	Qualitative	Tracer uptake grater than white matter	–
Tripathi et al 2012[24]	FDG, MET	PET/CT	222–296 (FDG) 550–740 (MET)	60 (FDG) 20 (MET)	20 (both)	Quantitive	ND	T/N (0.75, FDG; 1.9, MET)
Li et al 2012[25]	FDG, MET	PET/CT	259–444 (FDG) 370–555 (MET)	50–60 (FDG) 10 (MET)	10 (both)	Qualitative	Not clearly mentioned	–
Ye et al 2009[26]	FDG, MET	PET/CT	4.4–7.4/kg (FDG) 5.5–7.4/kg (MET)	50–60 (FDG) 10 (MET)	10 (both)	Quantitive	ND	SUV (2.5, FDG and MET)
Chung et al 2002[29,c]	MET	PET	555–740 (MET)	10 (MET)	20	Qualitative	MET uptake greater than contralateral gray matter without any morphologic abnormalities	–
Nakajima et al 2009[30]	MET	PET	200–550	20	10	Quantitive	ND	L/R (2.0)
Terakawa et al 2008[41]	MET	PET	6/kg	20	10	Quantitive	ND	L/Nmean (1.41, brain metastasis; 1.58, glioma)
Galldiks et al 2010[42]	MET	PET	11/kg	0/20	60/40	Quantitive	ND	Relative MET uptake (1.48)
Sonoda et al 1998[43]	MET	PET	111–555	30	10	Qualitative	Increased uptake	–
Tsuyugui et al 2004[44]	MET	PET	370	20	10	Qualitative	MET accumulation in the lesion	–

Note:—ND indicates no data; BSA, body surface area; L/WM, ratio of ^{18}F-FDG lesion to contralateral white matter; SUV, standard uptake value; SUVmax, maximum standard uptake value; T/C, ratio of SUV/SUVmax of tumor to that of cortex; T/WM, ratio of SUV/SUVmax of tumor to that of white matter; Lmax/Rmax, the uptake ratio of the maximum uptake of the lesion to the maximum uptake of the referential contralateral cerebral white matter; T/N, tumor-to-normal contralateral cortex ratio: L/R, the mean counts per pixel in the lesion ROI divided by the mean counts per pixel in the reference ROI; L/Nmean, the SUVmean of the lesion to the SUVmean of the contralateral normal frontal lobe gray matter; –, not available.

[a] Data from visual assessment was used for analysis.

[b] Used for diagnostic performance.

[c] Data for ^{18}F-FDG-PET in this study were not extractable and excluded for the analysis for ^{18}F-FDG-PET.

On-line Table 3: Quality assessment of eligible studies[a]

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total Score
Chen et al 2006[1]	Y	Y	Y	N	Y	N	Y	Y	Y	Y	U	Y	Y	Y	23
Ricci et al 1998[2]	Y	U	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	N	24
Zuo et al 2001[5]	N	U	U	U	Y	N	Y	Y	U	Y	U	Y	U	U	17
Gómez-Río et al 2008[6]	N	Y	Y	N	Y	N	Y	N	Y	Y	U	Y	U	U	17
Choi et al 2005[7]	Y	Y	Y	N	Y	N	Y	Y	Y	Y	U	Y	Y	Y	23
Pauleit et al 2009[8]	Y	Y	Y	U	Y	Y	Y	N	Y	Y	U	U	Y	Y	23
Lau et al 2010[9]	Y	Y	Y	N	Y	U	Y	N	Y	Y	U	Y	Y	U	21
Estrada et al 2008[10]	N	Y	U	N	Y	N	N	Y	Y	U	U	U	U	Y	15
McCarthy et al 2008[11]	Y	Y	Y	N	Y	N	Y	N	Y	Y	U	Y	U	Y	20
Kahn et al 1994[12]	Y	Y	Y	N	Y	N	Y	Y	Y	Y	U	Y	Y	Y	23
Thompson et al 1999[13]	N	U	Y	Y	Y	N	Y	N	Y	U	U	U	U	U	16
Sun et al 2004[14]	Y	U	U	U	Y	N	Y	Y	U	Y	U	Y	U	U	19
Santra et al 2012[15]	N	Y	Y	U	Y	N	U	Y	U	Y	U	Y	U	Y	19
Hong et al 2011[16]	Y	Y	Y	N	Y	N	Y	Y	Y	Y	U	Y	Y	Y	23
Tan et al 2011[17]	Y	Y	Y	N	Y	N	Y	N	Y	Y	U	Y	U	U	19
Enslow et al 2012[18]	N	Y	U	N	Y	U	Y	Y	N	Y	U	U	Y	U	17
Belohlávek et al 2002[19]	N	U	Y	N	Y	N	Y	Y	Y	Y	U	Y	Y	U	19
Spence et al 2009[20]	N	Y	U	N	Y	N	N	Y	Y	N	N	Y	N	Y	13
Janus et al 1993[21]	Y	Y	U	N	Y	N	Y	N	Y	Y	U	Y	U	U	18
Kim et al 2010[22]	N	Y	Y	N	Y	N	Y	Y	Y	Y	U	Y	Y	Y	21
Cai et al 2009[23]	Y	Y	Y	N	Y	N	Y	N	Y	Y	U	Y	Y	U	20
Tripathi et al 2012[24]	N	Y	Y	N	Y	N	Y	Y	Y	Y	U	Y	Y	Y	21
Li et al 2012[25]	N	Y	Y	U	Y	N	Y	Y	Y	Y	U	U	U	U	19
Ye et al 2009[26]	N	U	Y	N	Y	N	Y	Y	Y	Y	U	Y	U	U	18
Chung et al 2002[29]	Y	Y	Y	U	Y	N	Y	Y	U	Y	U	Y	U	U	21
Nakajima et al 2009[30]	N	Y	Y	N	Y	N	Y	Y	Y	Y	U	Y	Y	Y	21
Terakawa et al 2008[41]	Y	Y	Y	U	Y	N	Y	Y	U	Y	U	Y	U	Y	22
Galldiks et al 2010[42]	Y	Y	Y	N	Y	N	Y	Y	Y	Y	U	Y	U	Y	22
Sonoda et al 1998[43]	N	Y	U	U	Y	N	Y	Y	U	Y	U	Y	Y	Y	20
Tsuyuguchi et al 2004[44]	N	Y	Y	N	Y	N	Y	Y	Y	Y	U	Y	Y	Y	21

Note:—Y indicates yes or bias avoided; N, no or bias not avoided; U, unclear.

[a] 1, Spectrum bias: was the spectrum of patients representative of the patients who will receive the test in practice? 2, Selection criteria: were selection criteria clearly described? 3, Reference standard: is the reference standard likely to correctly classify the target condition? 4, Disease progression bias: is the time between the reference standard and index test short enough to be reasonably sure that the target condition did not change between the 2 tests? 5, Partial verification: did the whole sample or a random selection of the sample receive verification using a reference standard of diagnosis? 6, Differential verification bias: did patients receive the same reference standard regardless of the index test result? 7, Incorporation bias: was the reference standard independent of the index test (ie, the index test did not form part of the reference standard)? 8, Index test execution: was the execution of the index test described in sufficient detail to permit replication of the test? 9, Reference standard execution: was the execution of the reference standard described in sufficient detail to permit its replication? 10, Test/diagnosis review bias: were the index test results interpreted without knowledge of the results of the reference standard? 11, Reference standard review bias: were the reference standard results interpreted without knowledge of the results of the index test? 12, Clinical review bias: were the same clinical data available when test results were interpreted as would be available when the test was used in practice? 13, Uninterpretable test results: were uninterpretable/intermediate test results reported? 14, Withdrawal: were withdrawals from the study explained?

On-line Table 4: Influence of individual studies for diagnostic performance of ^{18}F-FDG-PET in brain tumors

Excluding Study One by One	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)	Comparison with Overall (*P* Value)[a]
Overall	0.71 (0.63–0.78)	0.77 (0.67–0.85)	
Chen et al 2006[1]	0.72 (0.63–0.79)	0.78 (0.68–0.86)	>.05
Ricci et al 1998[2]	0.70 (0.62–0.77)	0.79 (0.70–0.86)	>.05
Zuo et al 2001[5]	0.70 (0.62–0.77)	0.77 (0.66–0.85)	>.05
Gómez-Río et al 2008[6]	0.71 (0.62–0.78)	0.75 (0.65–0.84)	>.05
Choi et al 2005[7]	0.72 (0.63–0.79)	0.76 (0.65–0.84)	>.05
Pauleit et al 2009[8]	0.73 (0.66–0.79)	0.78 (0.68–0.86)	>.05
Lau et al 2010[9]	0.72 (0.65–0.79)	0.77 (0.66–0.85)	>.05
Estrada et al 2008[10]	0.72 (0.63–0.79)	0.77 (0.66–0.85)	>.05
McCarthy et al 2008[11]	0.71 (0.63–0.78)	0.78 (0.66–0.86)	>.05
Kahn et al 1994[12]	0.71 (0.62–0.78)	0.78 (0.68–0.86)	>.05
Thompson et al 1999[13]	0.72 (0.64–0.79)	0.77 (0.66–0.85)	>.05
Sun et al 2004[14]	0.71 (0.62–0.78)	0.77 (0.66–0.85)	>.05
Santra et al 2012[15]	0.71 (0.63–0.79)	0.75 (0.65–0.83)	>.05
Hong et al 2011[16]	0.71 (0.63–0.78)	0.77 (0.66–0.85)	>.05
Tan et al 2011[17]	0.71 (0.62–0.78)	0.78 (0.67–0.86)	>.05
Enslow et al 2012[18]	0.70 (0.62–0.77)	0.78 (0.68–0.86)	>.05
Belohlávek et al 2002[19]	0.72 (0.63–0.79)	0.77 (0.66–0.85)	>.05
Spence et al 2009[20]	0.70 (0.62–0.77)	0.78 (0.68–0.86)	>.05
Janus et al 1993[21]	0.71 (0.63–0.78)	0.78 (0.66–0.86)	>.05
Kim et al 2010[22]	0.71 (0.63–0.78)	0.77 (0.67–0.85)	>.05
Cai et al 2009[23]	0.72 (0.64–0.79)	0.78 (0.67–0.86)	>.05
Tripathi et al 2012[24]	0.71 (0.63–0.78)	0.77 (0.66–0.85)	>.05
Li et al 2012[25]	0.72 (0.64–0.79)	0.76 (0.65–0.84)	>.05
Ye et al 2009[26]	0.70 (0.62–0.77)	0.78 (0.68–0.86)	>.05

[a] For both sensitivity and specificity.