

SUPPLEMENTAL MATERIAL**Cardiac natriuretic peptides for diagnosis of covert atrial fibrillation after acute****ischemic stroke: a meta-analysis of diagnostic accuracy studies**

Contents

Table I: Search strategy	2
Table II: Characteristics of the included studies	3
Figure I: Study selection	5
Figure II: Risk of bias and applicability concerns graph	5
Figure III: Risk of bias and applicability concerns summary	6
Figure IV: Hierarchical summary receiver operating characteristic curve for the diagnosis of new onset atrial fibrillation using BNP or NT-proBNP	7
Figure V: Deeks' funnel plot asymmetry tests for the diagnosis of new onset atrial fibrillation with BNP or NT-proBNP	8

Table I: Search strategy

Database	Strategy	results
Pubmed	#1: (((("Stroke"[Mesh]) OR (Cerebrovascular Accident)) OR (Brain Vascular Accident)) OR (CVA)) OR (Apoplexy)	331
	#2: (((("Natriuretic Peptide, Brain"[Mesh]) OR (Brain Natriuretic Peptide)) OR (Natriuretic Factor 32)) OR (Type-B Natriuretic Peptide)) OR (Nesiritide)) OR (Natreacor)	
	#3:((((((((("pro-brain natriuretic peptide (1-76)" [Supplementary Concept])) OR (NT-proBNP)) OR (N-terminal pro-BNP)) OR (proBNP(1-76))) OR (NTproBNP)) OR (N-BNP peptide)) OR (NT-BNP))) OR (Amino-terminal pro-brain natriuretic peptide)) OR (aminoterminal pro-B-type natriuretic peptide)	
	#4: ("Atrial Fibrillation"[Mesh]) OR (Auricular Fibrillation)	
	#5 : (#2) OR (#3)	
	#6: ((#1) AND (#4)) AND (#5)	
EMBASE	#1: stroke or Cerebrovascular Accident or CVA or Brain Vascular Accident or Apoplexy	907
	#2: BNP or Brain Natriuretic Peptide or Natriuretic Factor 32 or Type-B Natriuretic Peptide or Nesiritide or Natreacor	
	#3: NT-proBNP or N-terminal pro-BNP or proBNP 76 or NTproBNP or N-BNP peptide or NT-BNP or Amino-terminal pro-brain natriuretic peptide or aminoterminal pro-B-type natriuretic peptide	
	#4: Atrial Fibrillation or Auricular Fibrillation	
	#5 : #2 or #3	
	#6: #1 and #4 and #5	

BNP for diagnosis of covert atrial fibrillation

Table II: Characteristics of the included studies

PMID	Author	Year	Sample size	Age, years (mean)	Men %	Stroke onset	HTN %	DM %	DLP %	Smoking	NIHSS (mean)	AD (cm)	HF %	VD %	TTD, hours	AF %	Method AF diagnosis	BM	Cut-off (pg/mL)	Blood sampling	Method biomarker measurement
31813354	Wasser[1]	2019	373	73	60	na	80	30	42	18	3	4.1	5	na	36	34	EPM or standard of care	BNP	100	randomisation	CLIA
21094497	Okada[2]	2010	165	72	62	<24h	60	30	26	48	7	na	9	na	7.3	13	12-lead ECG, 24h-Holter ECG, Continuous ECG	BNP	85	admission	CLIA
22341921	Shibazaki[3]	2012	584	72	64	<24h	70	30	28	51	4.7	na	0.3	na	3	40	12-lead ECG, 24h-Holter ECG, Continuous ECG	BNP	65	admission	CLIA
23010631	Suissa[4]	2013	300	63	63	na	50	10	29	41	7.1	na	2	17	6.8	52	24h-Holter ECG	BNP	131	admission	CLIA
23803318	Rodríguez-Yáñez[5]	2013	264	73	56	<24h	50	30	30	21	7	na	na	na	na	15	12-lead ECG and 24h-Holter ECG	NT-proBNP	360	admission	ECLIA
23981586*	Fonseca[6]	2014	80	69	69	<72h	70	30	33	9	8.3	na	na	na	na	17	12-lead ECG and 24h-Holter ECG	NT-proBNP	265.5	admission	ECLIA
23981586*	Fonseca	2014	184	62	57	<72h	70	30	45	23	6.7	na	na	na	na	55	12-lead ECG and 24h-Holter ECG	NT-proBNP	265.5	admission	ECLIA

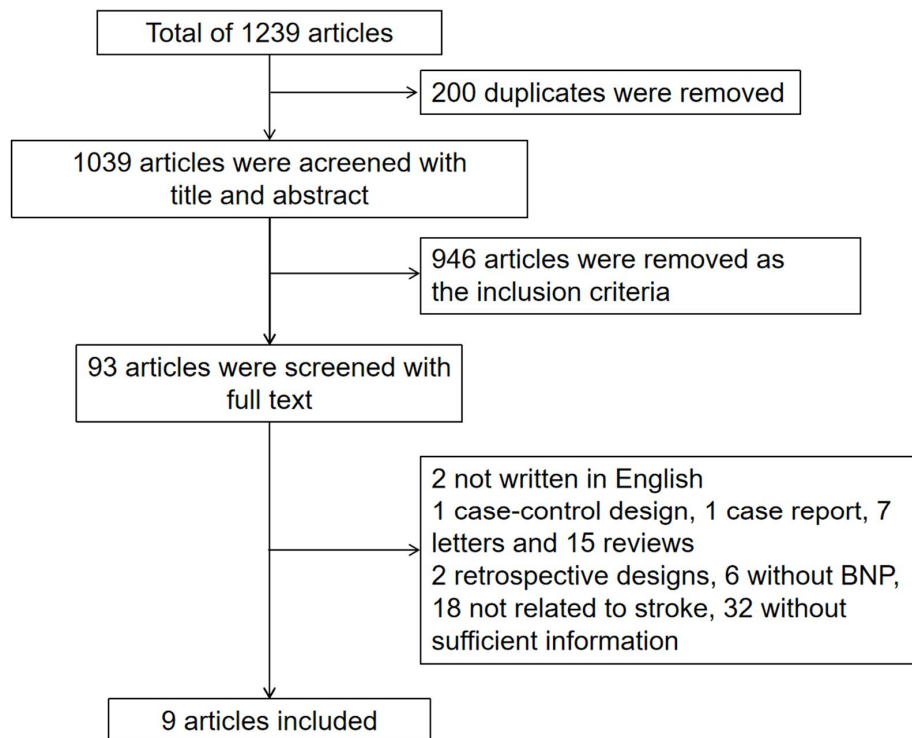
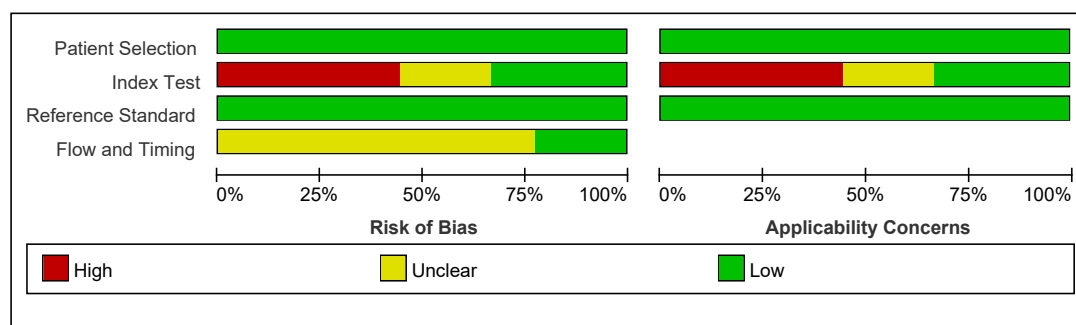
BNP for diagnosis of covert atrial fibrillation

26190307	Yoshioka[7]	2015	288	74	61	<7days	80	30	52	15	na	3.6	2	32	3	45	12-lead ECG, 24h-Holter ECG, Continuous ECG	BNP	90	admission	CLIA
25916280	Sanak[8]	2015	95	41	52	<12h	10	0	14	24	9	3.5	na	na	na	9	3-week ECG monitoring	NT-proBNP	125	admission	ECLIA
22509292	Wachter[9]	2012	220	68	58	<24h	70	20	34	25	3.5	4.1	5	na	na	28	12-lead ECG and 7-day Holter ECG	BNP	118	admission	CLIA

* This study included two cohorts of patients: 184 patients with acute ischemic stroke of known etiology and 80 patients with cryptogenic stroke. Because we did not have access to individual patient data, there was a non-negligible risk of introducing bias by merging data from the two cohorts.

AD indicates atrial diameter ; AF, atrial fibrillation; BM, biomarker ; BNP, B-type natriuretic peptide; CLIA, chemiluminescence immunoassay; DLP, dyslipidemia; DM, diabetes mellitus; ECG, electrocardiogram; ECLIA, electrochemiluminescence immunoassay; HF, heart failure; HTN, hypertension; NIHSS, National Institutes of Health Stroke Scale; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PMID, PubMed accession number; TTD, time to diagnosis of atrial fibrillation; and VD, valvular disease.

BNP for diagnosis of covert atrial fibrillation




Figure I: Study selection**Figure II: Risk of bias and applicability concerns graph**

Authors' judgements about each domain are presented as percentages across included studies.

BNP for diagnosis of covert atrial fibrillation

Figure III: Risk of bias and applicability concerns summary

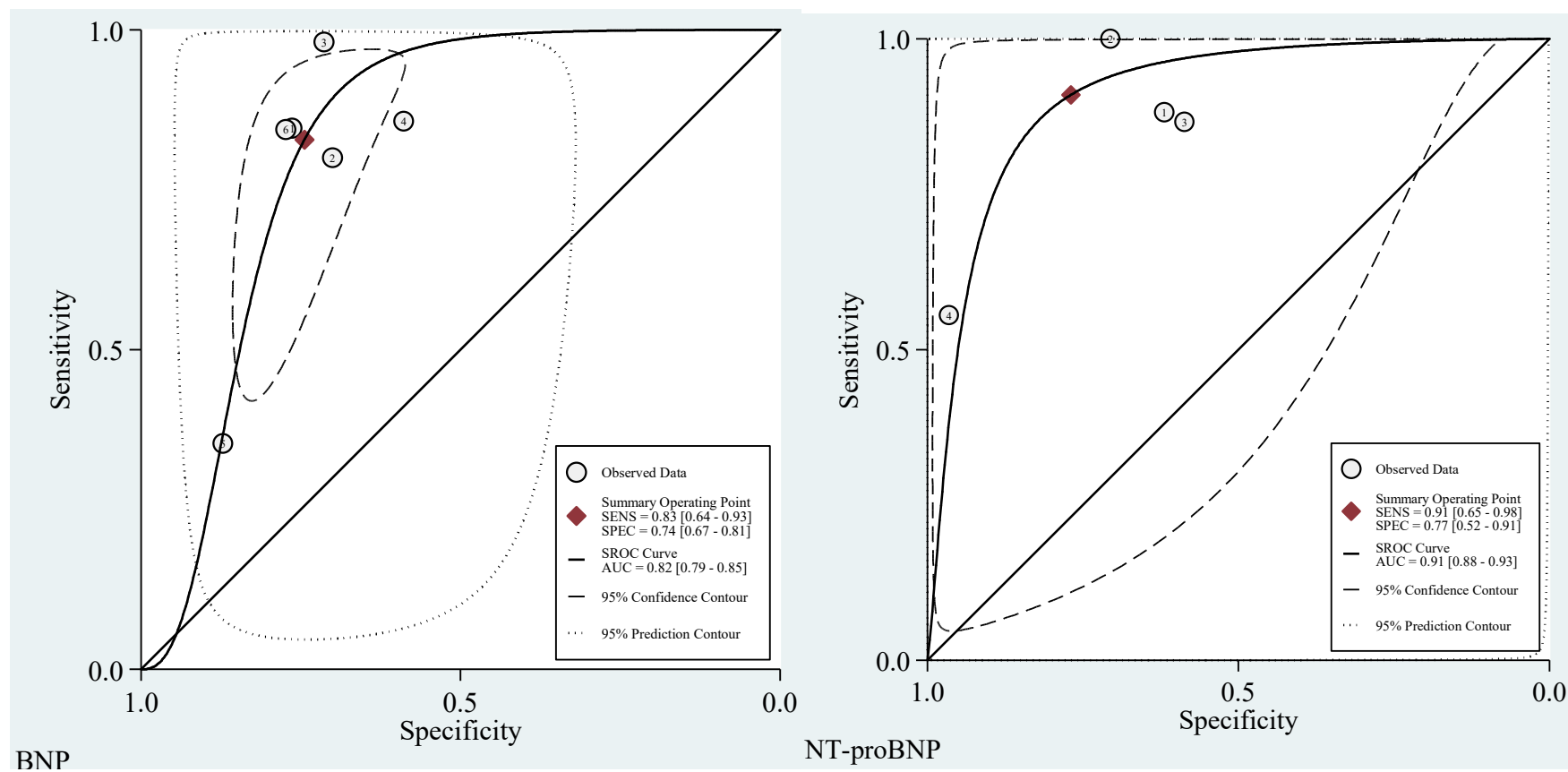
	<u>Risk of Bias</u>				<u>Applicability Concerns</u>		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Fonseca AC2014	+	+	+	?	+	+	+
Okada Y2010	+	-	+	?	+	-	+
Rodríguez-Yáñez2013	+	+	+	?	+	+	+
Sanak D2015	+	?	+	?	+	?	+
Shibazaki K2012	+	-	+	?	+	-	+
Suissa L2013	+	-	+	+	+	-	+
Wachter 2012	+	?	+	+	+	?	+
Wasser K2019	+	+	+	?	+	+	+
Yoshioka, K2015	+	-	+	?	+	-	+

 **High**
  **Unclear**
  **Low**

Authors' judgements about each domain is presented for each included study.

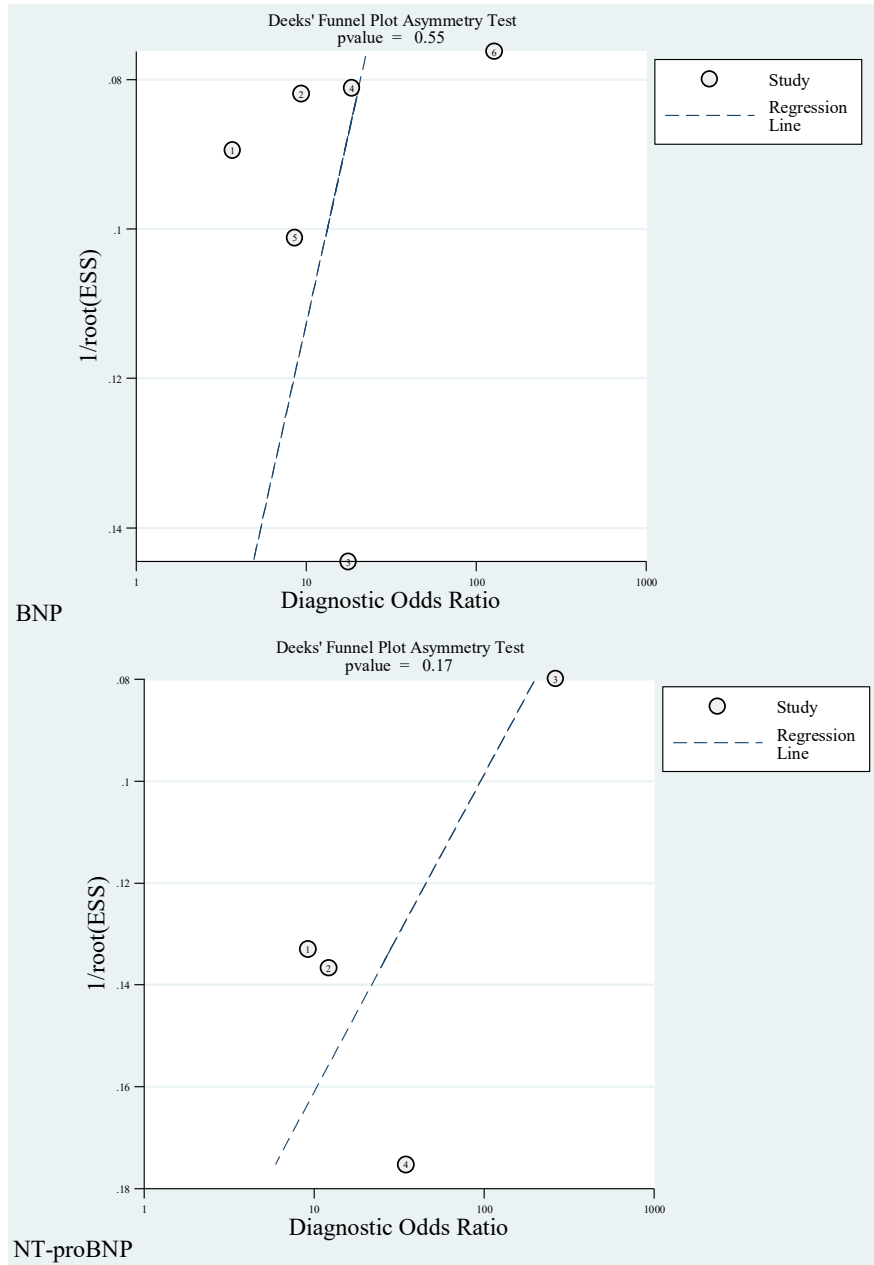
BNP for diagnosis of covert atrial fibrillation

Figure IV: Hierarchical summary receiver operating characteristic curve for the diagnosis of new onset atrial fibrillation using BNP or NT-proBNP



BNP for diagnosis of covert atrial fibrillation

Figure V: Deeks' funnel plot asymmetry tests for the diagnosis of new onset atrial fibrillation with BNP or NT-proBNP



BNP for diagnosis of covert atrial fibrillation