C-reactive protein levels and cognitive decline after acute ischemic stroke: An Systematic Review and Meta-analysis Supplementary

Content to the manuscript

Contents of Supplementary Content

Supplementary Content S1

Search strategy and results

Number of citations by each database

Databases and Trial registers:	**Citations**
Databases:	
PubMed	1523
Cochrane	641
Embase	2075
Web of Science	600
Total (databases)	**4839**

Full search strategy for each database

PubMed

#1 ((Cerebrovascular Disorders [MeSH Major Topic]) OR (Hemiplegia [MeSH Major Topic])) OR (Paresis[MeSH Major Topic])

#2 hemipleg*[Title] OR hemipar*[Title] OR paresis[Title] OR paretic[Title] OR stroke[Title] OR poststroke[Title] OR post?stroke[Title] OR cerebrovasc*[Title] OR brain vasc*[Title] OR cerebral vasc*[Title] OR cva*[Title] OR apoplex*[Title] OR SAH[Title]

#3 ((brain*[Title] OR cerebr*[Title] OR cerebell*[Title] OR intracran*[Title] OR intracerebral) [Title]) AND ((isch*emi*[Title] OR infarct*[Title] OR thrombo*[Title] OR emboli*[Title] OR occlus*))[Title])

#4 ((brain*[Title] OR cerebr*[Title] OR cerebell*[Title] OR intracerebral [Title] OR intracranial [Title] OR subarachnoid) [Title]) AND ((haemorrhage*[Title] OR hemorrhage*[Title] OR haematoma*[Title] OR hematoma*[Title] OR bleed*) [Title])

#5 (((#1) OR (#2)) OR (#3)) OR (#4)

#6 (Dementia [MeSH Major Topic]) OR (Cognition Disorders [MeSH Major Topic])

#7 Agnosia [Title/Abstract] OR amnesia [Title/Abstract] OR confusion [Title/Abstract] OR inattention [Title/Abstract] OR Dementia [Title/Abstract]

#8 ((cogniti*[Title/Abstract] OR arous*[Title/Abstract] OR orientat*[Title/Abstract] OR attention*[Title/Abstract] OR concentrat*[Title/Abstract] OR memor*[Title/Abstract] OR recall[Title/Abstract] OR percept*[Title/Abstract] OR think*[Title/Abstract] OR sequenc*[Title/Abstract] OR algorithm*[Title/Abstract] OR judg?ment*[Title/Abstract]

OR awareness[Title/Abstract] OR problem solving[Title/Abstract] OR generali?ation[Title/Abstract] OR transfer[Title/Abstract] OR comprehension[Title/Abstract] OR learning)[Title/Abstract] AND (disorder*[Title/Abstract] OR declin*[Title/Abstract] OR dysfunct*[Title/Abstract] OR impair*[Title/Abstract] OR deficit*[Title/Abstract] OR abilit*[Title/Abstract] OR problem*))[Title/Abstract]

#9 dysexecutive syndrome*[Title/Abstract] OR mental process* [Title/Abstract] OR impulsive behavio?r*[Title/Abstract] OR executive function*[Title/Abstract]

#10 (((#6) OR (#7)) OR (#8)) OR (#9)

#11 Psd [Title/Abstract] OR psci [Title/Abstract]

#12 (#10) AND (#5)

#13 (#11) OR (#12)

#14 ((Cytokines [MeSH Major Topic]) OR (C-reactive protein [MeSH Major Topic]))

#15 Cytokine* OR Inflammat* OR Pro-inflammat* or CRP or C-reactive protein or hs-CRP or hsCRP

#16 (#14) OR (#15)

#17 ((#13) AND (#16))

#18 plasma or blood or serum

#19 ((#17) AND (#18))

Cochrane

#1 MeSH descriptor: [Cerebrovascular Disorders] explode all trees

#2 MeSH descriptor: [Hemiplegia] explode all trees

#3 MeSH descriptor: [Paresis] explode all trees

#4 (hemipleg* or hemipar* or paresis or paretic or stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc* or cva* or apoplex* or SAH): ti

#5 (hemipleg* or hemipar* or paresis or paretic or stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc* or cva* or apoplex* or SAH): ab

#6 ((brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid) near/5 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)): ti

#7 ((brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid) near/5 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)): ab

#8 (((brain* or cerebr* or cerebell* or intracran* or intracerebral) near/5 (isch*emi* or infarct* or thrombo* or emboli* or occlus*))): ti

#9 (((brain* or cerebr* or cerebell* or intracran* or intracerebral) near/5 (isch*emi* or infarct* or thrombo* or emboli* or occlus*))): ab

#10 (((cogniti* or arous* or orientat* or attention* or concentrat* or memor* or recall or percept* or think* or sequenc* or algorithm* or judg?ment* or awareness or problem solving or generali?ation or transfer or comprehension or learning) near/10 (disorder* or declin* or dysfunct* or impair* or deficit* or abilit* or problem*))):ti OR (((cogniti* or arous* or orientat* or attention* or concentrat* or memor* or recall or percept* or think* or sequenc* or algorithm* or judg?ment* or awareness or problem solving or generali?ation or transfer or comprehension or learning) near/10 (disorder* or declin* or dysfunct* or impair* or deficit* or abilit* or problem*))):ab

#11 ((dysexecutive syndrome* or mental process* or impulsive behavio?r* or executive

function*)):ti OR ((dysexecutive syndrome* or mental process* or impulsive behavio?r* or executive function*)):ab

#12 (Psd or psci): ti OR (Psd or psci): ab

#13 MeSH descriptor: [Cytokines] explode all trees

#14 MeSH descriptor: [C-reactive protein] explode all trees

#15 (CRP or C-reactive protein or hs-CRP or hsCRP): ti OR (CRP or C-reactive protein or hs-CRP or hsCRP): ab

#16 #1 OR #2 OR #3 OR #4 OR #5 OR #6

#17 10 OR #11

#18 #16 AND #17

#19 #18 OR #12

#20 #13 OR #14 OR #15

#21 #18 AND #20

#22 (plasma or blood or serum): ti AND (plasma or blood or serum): ab

#23 #21 AND #22

Embase

#1 'cerebrovascular disease'/exp OR 'hemiplegia'/exp OR 'paresis'/exp

#2 hemipleg*: ti OR hemipar*: ti OR paresis: ti OR paretic: ti OR stroke: ti OR poststroke: ti OR post-stroke: ti OR cerebrovasc*: ti OR' brain vasc*': ti OR' cerebral vasc*': ti OR cva*: ti OR apoplex*: ti OR sah: ti

#3 'cognitive defect'/exp OR' dementia'/exp

#4 agnosia: ti OR amnesia: ti OR confusion: ti OR inattention: ti OR dementia: ti

#5 psd: ti OR psci: ti

#6 'cytokine'/exp OR' creactive protein'/exp

#7 cytokine*: ab,ti OR inflammat*: ab,ti OR' pro inflammat*': ab,ti OR' tumor necrosis factor-alpha': ab,ti OR' tumor necrosis factor-α': ab,ti OR' tnf alpha': ab,ti OR' tnf α': ab,ti OR interleukin*: ab,ti OR' il 1*': ab,ti OR' il 2*': ab,ti OR' il 3*': ab,ti OR' il 4': ab,ti OR' il 5': ab,ti OR' il 6': ab,ti OR' il 7': ab,ti OR' il 8': ab,ti OR' il 9': ab,ti OR crp: ab,ti OR' c-reactive protein': ab,ti OR' hs crp': ab,ti OR hscrp: ab,ti

#8 plasma: ab,ti OR blood: ab,ti OR serum: ab,ti

#9 #1 OR #2

#10 #3 OR #4

#11 #9 AND #10

#12 #5 OR #11

#13 #6 OR #7

#14 #8 AND #12 AND #13

Web of Science

#1 TI=(Cerebrovascular Disorders or Hemiplegia or Paresis or hemipleg* or hemipar* or paresis or paretic or stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc* or cva* or apoplex* or SAH）

#2 TI=((brain* or cerebr* or cerebell* or intracran* or intracerebral) and (isch*emi* or infarct* or thrombo* or emboli* or occlus*)) OR TI=（(brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid) and (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*))

#3 TI = (Cognition Disorders or Dementia) OR AB = (Cognition Disorders or Dementia)

#4 TI = (agnosia or amnesia or confusion or inattention or Dementia) OR AB = (agnosia or amnesia or confusion or inattention or Dementia)

#5 TI=((cogniti* or arous* or orientat* or attention* or concentrat* or memor* or recall or percept* or think* or sequenc* or algorithm* or judg?ment* or awareness or problem solving or generali?ation or transfer or comprehension or learning) AND (disorder* or declin* or dysfunct* or impair* or deficit* or abilit* or problem*)) OR AB=((cogniti* or arous* or orientat* or attention* r concentrat* or memor* or recall or percept* or think* or sequenc* or algorithm* or judg?ment* or awareness or problem solving or generali?ation or transfer or comprehension or learning) AND (disorder* or declin* or dysfunct* or impair* or deficit* or abilit* or problem*))

#6 TI = (dysexecutive syndrome* or mental process* or impulsive behavio?r* or executive function*) OR AB=(dysexecutive syndrome* or mental process* or impulsive behavio?r* or executive function*)

#7 TI = (Psd or psci) OR AB = (Psd or psci)

#8 AB = (Cytokines or C-reactive protein) OR TI = (Cytokines or C-reactive protein)

#9 TI = (Cytokine* OR Inflammat* OR Pro-inflammat* OR Tumor Necrosis Factor-alpha OR Tumor Necrosis Factor-α OR TNF-alpha OR TNF-αOR interleukin* OR il-1* OR il-2* OR il-3* OR il-4 OR il-5 OR il-6 OR il-7 OR il-8 OR il-9 OR CRP or C-reactive protein or hs-CRP or hsCRP) OR AB = (Cytokine* OR Inflammat* OR Pro-inflammat* OR Tumor Necrosis Factor-alpha OR Tumor Necrosis Factor-α OR TNF-alpha OR TNF-αOR interleukin* OR il-1* OR il-2* OR il-3* OR il-4 OR il-5 OR il-6 OR il-7 OR il-8 OR il-9

OR CRP or C-reactive protein or hs-CRP or hsCRP)

#10 TI = (plasma or blood or serum) OR AB = (plasm or blood or serum)

#11 #2 OR #1

#12 #6 OR #5 OR #4 OR #3

#13 #12 AND #11

#14 #13 OR #7

#15 #9 OR #8

#16 #15 AND #14 AND #10

Supplementary Content S2

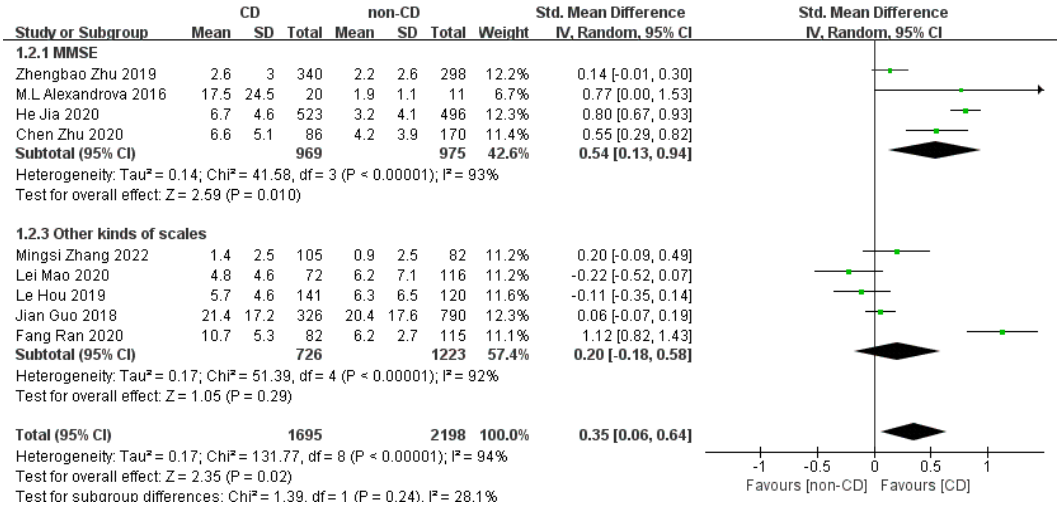
Methodological quality of cohort studies included in the meta-analysis

Study ID	Representative of the exposed group	Selection of the unexposed group	Confirm the exposure	Outcome of interest not present at the start of study	Control for important factor or additional factor	Outcome assessment	Follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts4	Total quality scores
Chen Zhu 2020	☆	☆	☆	☆	☆☆	☆	☆	-	8
Fang Ran 2020	☆	☆	☆	☆	☆☆	☆	-	☆	8
He Jia 2020	☆	☆	☆	☆	☆☆	☆	-	-	7
Jian Guo 2018	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Le Hou 2019	☆	☆	☆	☆	☆☆	☆	-	☆	8
Lei Mao 2020	☆	☆	☆	☆	☆☆	☆	☆	-	8
M.L Alexandrova 2016	☆	☆	☆	-	☆☆	☆	☆	-	7
Mingsi Zhang 2022	☆	☆	☆	☆	☆☆	☆	☆	-	8
ZhengbaoZhu 2019	☆	☆	☆	☆	☆☆	☆	-	☆	8

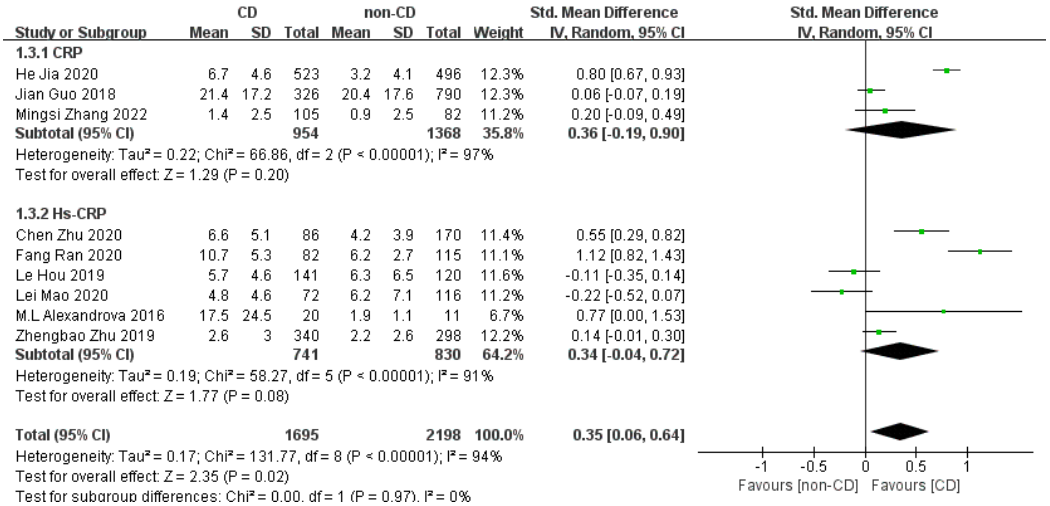
Supplementary Content S3

Forest maps of subgroups

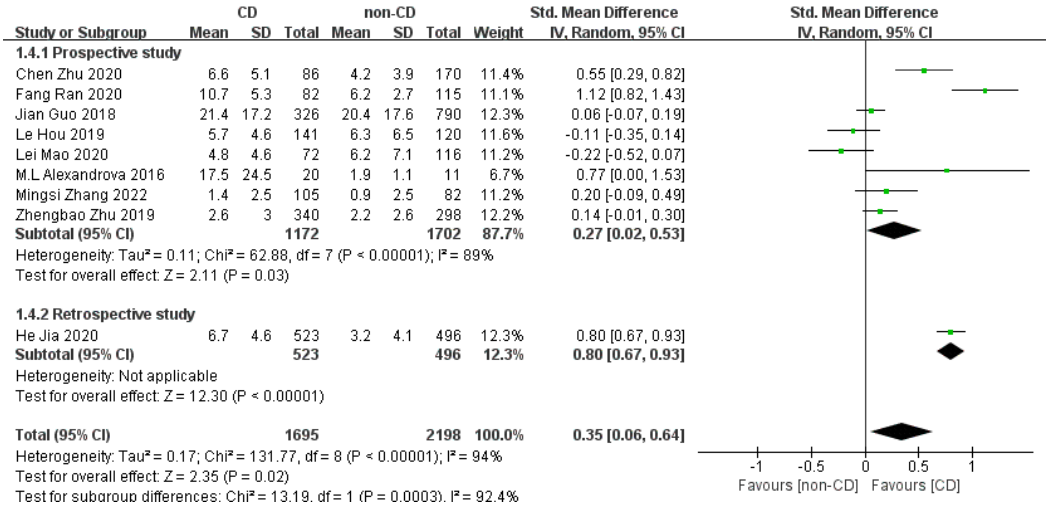
Forest map of scales for cognitive assessment



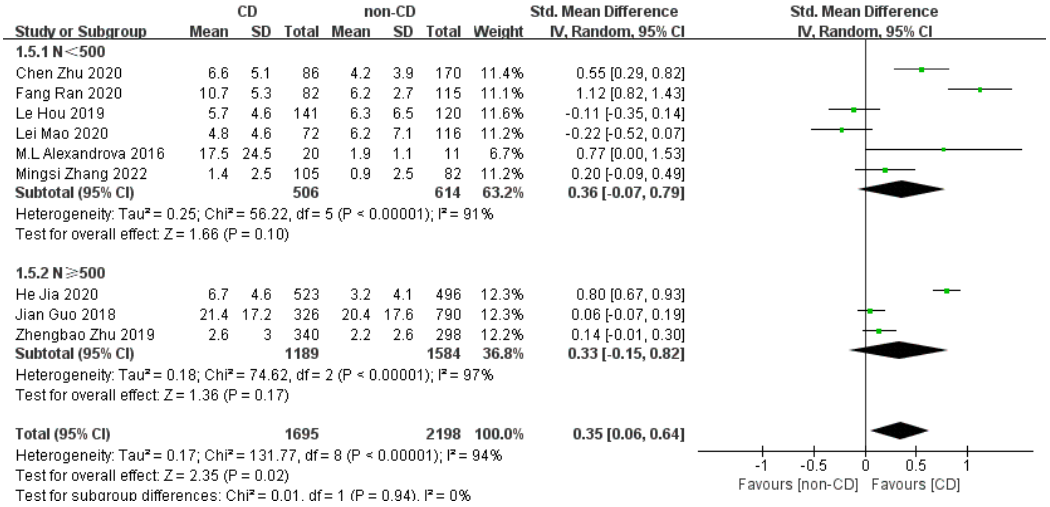
Forest map of detection sensitivity of CRP



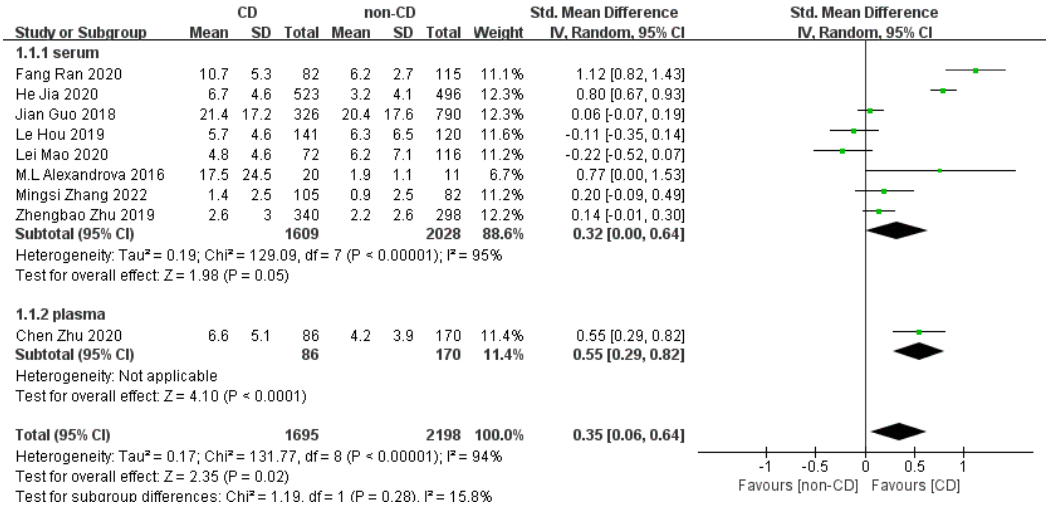
Forest map of research types



Forest map of sample size



Forest map of source of CRP


CD
non-CD
Std. Mean Difference
Std. Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.1.1 serum
Fang Ran 2020 10.7 5.3 82 6.2 2.7 115 11.1% 1.12 [0.82, 1.43]
He Jia 2020 6.7 4.6 523 3.2 4.1 496 12.3% 0.80 [0.67, 0.93]
Jian Guo 2018 21.4 17.2 326 20.4 17.6 790 12.3% 0.06 [-0.07, 0.19]
Le Hou 2019 5.7 4.6 141 6.3 6.5 120 11.6% -0.11 [-0.35, 0.14]
Lei Mao 2020 4.8 4.6 72 6.2 7.1 116 11.2% -0.22 [-0.52, 0.07]
M.L Alexandrova 2016 17.5 24.5 20 1.9 1.1 11 6.7% 0.77 [0.00, 1.53]
Mingsi Zhang 2022 1.4 2.5 105 0.9 2.5 82 11.2% 0.20 [-0.09, 0.49]
Zhengbao Zhu 2019 2.6 3 340 2.2 2.6 298 12.2% 0.14 [-0.01, 0.30]
Subtotal (95% CI) 1609 2028 88.6% 0.32 [0.00, 0.64]
Heterogeneity: Tau² = 0.19; Chi² = 129.09, df = 7 (P < 0.00001); I² = 95%
Test for overall effect: Z = 1.98 (P = 0.05)
1.1.2 plasma
Chen Zhu 2020 6.6 5.1 86 4.2 3.9 170 11.4% 0.55 [0.29, 0.82]
Subtotal (95% CI) 86 170 11.4% 0.55 [0.29, 0.82]
Heterogeneity: Not applicable
Test for overall effect: Z = 4.10 (P < 0.0001)
Total (95% CI) 1695 2198 100.0% 0.35 [0.06, 0.64]
Heterogeneity: Tau² = 0.17; Chi² = 131.77, df = 8 (P < 0.00001); I² = 94%
Test for overall effect: Z = 2.35 (P = 0.02)
Test for subgroup differences: Chi² = 1.19, df = 1 (P = 0.28), I² = 15.8%
-1
-0.5
0
0.5
1
Favours [non-CD]
Favours [CD]