Supplemental data

Table of contents

Abbreviations

CSF: cerebrospinal fluid

DCI: delayed cerebral ischemia

h: hours

MD: microdialysate

POD: post-operative day

SAH: subarachnoid hemorrhage

Search strategy

PubMed:

#	Searches	Results
1	Validat$.tw. or Predict$.ti. or Rule$.tw. or (Predict$ and (Outcome$ or Risk$ or Model$)).tw. or ((History or Variable$ or Criteria or Scor$ or Characteristic$ or Finding$ or Factor$) and (Predict$ or Model$ or Decision$ or Identif$ or Prognos$)).tw. or (Decision$.tw. and ((Model$ or Clinical$).tw. or logistic models/)) or (Prognostic and (History or Variable$ or Criteria or Scor$ or Characteristic$ or Finding$ or Factor$ or Model$)).tw. or ("Stratification" or "Discrimination" or "Discriminate" or "c-statistic" or "c statistic" or "Area under the curve" or "AUC" or "Calibration" or "Indices" or "Algorithm" or "Multivariable").tw.	5050668
2	exp VASOSPASM, INTRACRANIAL/ or ((Delayed or Secondary or symptomatic) adj2 (Ischemia or infarc*)).ti,ab,kf. or ((intracranial or cerebral or cerebrovascular) adj (vasospasm* or angiospasm* or vascular spasm*)).ti,ab,kf. or ((Delayed or Secondary) adj3 (Ischemic or neurological) adj Deficit*).ti,ab,kf. or (DCI or Vasospasm).ti,ab,kf.	18111
3	1 or 2	5064922
4	exp Biomarkers/ or exp Peptides/ or exp "Genetic Phenomena"/ or exp Genes/ or exp Proteins/ or exp "Polymorphism, Single Nucleotide"/ or exp "Genome-Wide Association Study"/ or exp MicroRNAs/ or exp "Sequence Analysis, DNA"/ or exp DNA/ or (biomarker* or Marker* or Surrogate Endpoint* or Polypeptides or Neuropeptide or (Genetic adj (Concept* or Phenomenon* or Process* or material*)) or Gene or Genes or Cistron* or SNP or SNPs or "Single Nucleotide Polymorphism" or MicroRNA or miRNA* or stRNA or "Small Temporal RNA" or Genome-Wide Association or (Sequence adj (Analys?s or determinaion*)) or Sequencing or Sequence or "Deoxyribonucleic Acid" or ds-DNA).ti,ab,kf.	9819019
5	exp Cerebrospinal Fluid/ or exp CYTOKINES/ or exp C-Reactive Protein/ or exp SEROLOGY/ or exp Feces/ or exp urine/ or (micro-particle* or microparticle* or spinal fluid or cerebrospinal fluid or serology or serum or plasma or urine or stool or crp or cytokine* or interleukin* or adhesion).ti,ab,kf. or (level* or levels or concentration or value).ti,ab.	7835561
6	4 or 5	13711807
7	exp Subarachnoid Hemorrhage/ or (SAH or (subarachnoid adj (h?emorrhage or h?ematoma or bleeding))).ti,ab,kf.	34848
8	6 and 7	11317
9	3 and 8	5607
10	(exp animals/ not humans/) or (mice or mouse or rat or rats or rodent or canine or dog or rabbit or dogs or murine or cat or cats or rabbits or rodents or canines).ti.	5204407
11	9 not 10	4209

Embase:

#	Searches	Results
1	Validat$.mp. or Predict$.ti. or Rule$.mp. or (Predict$ and (Outcome$ or Risk$ or Model$)).tw. or ((History or Variable$ or Criteria or Scor$ or Characteristic$ or Finding$ or Factor$) and (Predict$ or Model$ or Decision$ or Identif$ or Prognos$)).tw. or (Decision$.tw. and ((Model$ or Clinical$).tw. or statistical model/)) or (Prognostic and (History or Variable$ or Criteria or Scor$ or Characteristic$ or Finding$ or Factor$ or Model$)).tw. or ("Stratification" or "Discrimination" or "Discriminate" or "c-statistic" or "c statistic" or "Area under the curve" or "AUC" or "Calibration" or "Indices" or "Algorithm" or "Multivariable").tw. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]	6992976
2	exp brain vasospasm/ or ((Delayed or Secondary or symptomatic) adj2 (Ischemia or infarc*)).ti,ab,kw. or ((intracranial or cerebral or cerebrovascular) adj (vasospasm* or angiospasm* or vascular spasm*)).ti,ab,kw. or ((Delayed or Secondary) adj3 (Ischemic or neurological) adj Deficit*).ti,ab,kw. or (DCI or Vasospasm).ti,ab,kw.	28604
3	1 or 2	7014925
4	exp biological marker/ or exp peptide/ or exp heredity/ or exp gene/ or exp protein/ or exp single nucleotide polymorphism/ or exp genome-wide association study/ or exp genetic association/ or exp microRNA/ or exp circulating microRNA/ or exp sequence analysis/ or exp DNA/ or (biomarker* or Marker* or Surrogate Endpoint* or Polypeptides or Neuropeptide or (Genetic adj (Concept* or Phenomenon* or Process* or material*)) or Gene or Genes or Cistron* or SNP or SNPs or "Single Nucleotide Polymorphism" or MicroRNA or miRNA* or stRNA or "Small Temporal RNA" or Genome-Wide Association or (Sequence adj (Analys?s or determinaion*)) or Sequencing or Sequence or "Deoxyribonucleic Acid" or ds-DNA).ti,ab,kw.	7506594
5	exp cerebrospinal fluid/ or exp cytokine/ or exp C reactive protein/ or exp serology/ or exp feces/ or exp feces analysis/ or exp urine/ or (micro-particle* or microparticle* or spinal fluid or cerebrospinal fluid or serology or serum or plasma or urine or stool or crp or cytokine* or interleukin* or adhesion).ti,ab,kw. or (level* or levels or concentration).ti,ab.	10030196
6	4 or 5	14546244
7	exp Subarachnoid Hemorrhage/ or (SAH or (subarachnoid adj (h?emorrhage or h?ematoma or bleeding))).ti,ab,kw.	57415
8	6 and 7	16360
9	3 and 8	7769
10	((exp experimental organism/ or animal tissue/ or animal cell/ or exp animal disease/ or exp carnivore disease/ or exp bird/ or exp experimental animal welfare/ or exp animal husbandry/ or animal behavior/ or exp animal cell culture/ or exp mammalian disease/ or exp mammal/ or exp marine species/ or nonhuman/ or animal.hw.) not human/) or (mice or mouse or rat or rats or rodent or canine or dog or rabbit or dogs or murine or cat or cats or rabbits or rodents or canines).ti.	7923711
11	9 not 10	6182
12	limit 11 to embase	4135

Methods used for classification of biomarkers which are measured by more than one study.

If a biomarker was investigated by more than one study, the classification into significant and non-significant was either based on a biomarker-specific meta-analysis, if methodologically possible (similar type of analyses and timing of measurement), or by descriptive comparison.

Meta-analyses were performed using Review Manager 5.4. For continuous data we used the inverse variance method with random effects model to calculate weighted mean differences with 95% confidence intervals. For dichotomous data we used the Mantel-Haenszel method with random effects model to calculate estimated odds ratio with 95% confidence intervals.

Descriptive comparison of the studies was done by summarizing the results of all relevant studies in a biomarker-specific figure, which was then used to classify the biomarkers into significant, inconclusive and non-significant.

The biomarker-specific figures display the author, year, number of patients with and without DCI, the type of analyses and the results. Results were divided into categories of sampling timing (day 0-3, 4-8, 9-13 and >14 after SAH). Results could also cover more than one time period (e.g. repeated measures).

Classification into significant, inconclusive and non-significant was done as follows:

1) If all results within the biomarker-specific figure were **significant**, the biomarker was considered significant. Similarly, biomarkers with exclusively non-significant results were considered **non-significant**.

2) In case the biomarker-figure contained both significant and non-significant results, we evaluated the results within each time intervals (day 0-3, 4-8, 9-13 and >14 after SAH) to determine whether a biomarker was deemed significant.
    a. A time interval was considered non-significant if the results of all studies within that time interval showed non-significant results
    b. A time interval was considered significant if the results of all studies within that time interval showed significant results, pointing in the same direction (e.g. all studies show higher biomarker levels in DCI compared to no DCI patients).
    c. In case of both significant and non-significant results, the time interval was considered inconclusive.
    d. In case of multiple significant results, however the results point in opposite directions (study A shows higher biomarker levels, whereas study B shows lower levels in DCI), the time interval was considered inconclusive.
    e. As long as at least one time interval was considered significant, the biomarker was deemed **significant**. Otherwise, the biomarker was classified as **inconclusive**.

Table S1 - Baseline characteristics of included studies

1st author, year	Method[1]	Study Design	SAH n	Age[2] mean (SD)	Female n (%)	Poor grade[3] n (%)	Fisher 3-4[4] n(%)	DCI n (%)	DCI definition[5]	Risk of bias
Cohen, 2021[1]	Pro	Cohort	356	57 (13)	241 (68)	WFNS 134 (38)	-	142* (40)	C	4/8
Albanna, 2021[2]	Pro	Cohort	66	55 (1)	51 (77)	WFNS: 18 (27)	mF: 34 (52)	33 (50) 9 (14)	C R	6/9
Helbok, 2021[3]	Pro	Cohort	36	57 (48-67)	26 (72)	HH: 26 (72)	33 (91)	9* (25)	R	4/8
Veldeman, 2021[4]	Pro	Cohort	30	54 (14)	17 (57)	HH: 7 (23)	mF: 16 (53)	13 (43)	C	4/8
Krenzlin, 2021[5]	Pro	Cohort	29	55 (12)	19 (66)	mean HH: 3	mean: 4	13 (45)	C	2/9
Darkwah, 2021[6]	Retro	Cohort	633	55 (14)	422 (67)	WFNS: 300 (47)	mF: 538 (91)	153 (24)	R	7/8
Park, 2021[7]	Retro	Cohort	510	56	348 (68)	HH: 83 (16)	-	47* (9)	C	4/8
Zhang, 2021[8]	Retro	Cohort	439	-	304 (69)	WFNS: 93 (21)	mF: 123 (28)	84 (24)	C	7/8
Veldeman, 2021[9]	Retro	Cohort	24	59 (12)	19 (79)	HH: 10 (42)	mF: 18 (75)	14 (58)	C	2/8
Neumaier, 2021[10]	-	Cohort	96	54 (12)	71 (74)	HH: 21 (22)	mF: 55 (57)	48 (50)	C	5/8
Heinsberg, 2020[11]	Pro	Cohort	591	53 (11)	423 (72)	WFNS: 142 (24)	350 (59)	103* (34)	C	5/8
Heinsberg, 2020[12]	Pro	Cohort	474	54	343 (72)	WFNS: 111 (23)	272 (57)	179* (39)	C	6/8
Luo, 2020[13]	Pro	Cohort	418	58 (49-66)	242 (58)	HH: 127 (30)	mF: 217 (52)	89 (21)	C	6/9
Veldeman, 2020[14]	Pro	Cohort	132	56 (12)	91 (96)	HH: 31 (24)	mF: 80 (61)	64 (46)	C	5/9
Chaudhry, 2020[15]	Pro	Cohort	80	58 (12)	49 (61)	HH: 27 (34)	77 (96)	28* (35)	C	5/9
Chaudhry, 2020[16]	Pro	Cohort	76	59 (12)	46 (61)	HH: 24 (31)	73 (96)	16* (21)	R	3/9
Kim, 2020[17]	Pro	Cohort	76	56	50 (66)	HH: 27(36)	59 (78)	25 (33)	C	3/8
Bache, 2020[18]	Pro	Cohort	63	59 (11)	49 (78)	WFNS: 40 (63)	61 (97)	17* (49)	C	5/9
Wang, 2020[19]	Pro	Cohort	61	55 (6)	36 (59)	WFNS: 15 (25)	19 (31)	19 (31)	C	7/9
Park, 2020[20]	Pro	Cohort	52	61	26 (50)	HH: 23 (44)	26 (50)	18 (52)	C	4/8
Kofler, 2020[21]	Pro	Cohort	51	59 (50-67)	36 (71)	HH: 35 (69)	mF: 46 (90)	16 (31)	R	4/8
Wisniewski, 2020[22]	Pro	Cohort	38	59	24 (63)	HH: 0	26 (68)	19 (50)	C	6/9
Rzeplinski, 2020[23]	Pro	Cohort	37	56 (40-67)	22 (60)	WFNS: 14 (38)	mF: 24 (65)	8 (22)	C	6/8
Youn, 2020[24]	Pro	Cohort	33	61	15 (45)	HH3-5: 17 (52)	-	12 (36)	C	2/8
Manner, 2020[25]	Pro	Case-control	18	57 (13)	9 (50)	WFNS: 12 (67)	16 (89)	7 (44)	R	4/9
Torne, 2020[26]	Pro	Cohort	16	58 (7)	-	WFNS: 16 (100)	15 (94)	5 (31)	R	2/8
Roa, 2020[27]	Pro	Cohort	13	56	8 (62)	WFNS: 7 (54)	mF: 9(69)	5 (39)	C	3/8

Liu, 2020[28]	Retro	Cohort	887	-	562 (63)	HH: 123 (14)	mF: 158 (18)	224 (25)	C	6/8
Arleth, 2020[29]	Retro	Cohort	384	56 (48-64)	275 (72)	WFNS3-5: 163 (44)	-	102* (35)	C	5/8
Chen, 2020[30]	Retro	Cohort	197	60 (51-67)	114 (58)	HH: 49 (25)	mF: 135 (69)	58 (29)	C	6/8
Hurth, 2020[31]	Retro	Cohort	138	53	104 (75)	WFNS: 62 (45)	119 (86)	27 (20)	R	5/8
Li, 2020[32]	Retro	Cohort	75	59 (2)	50 (67)	HH: 21 (28)	mean: 4	37 (40)	R	5/8
Xie, 2020[33]	Retro	Cohort	66	58 (10)	47 (71)	HH: 66 (100)	-	26 (39)	R	6/8
Matzen, 2020[34]	Retro	Cohort	63	59 (11)	49 (78)	WFNS: 39 (62)	62 (98)	18* (29)	C	6/9
Wang, 2020[35]	Retro	Cohort	54	59 (51-63)	31 (57)	HH: 11 (20)	28 (52)	19* (33)	C	4/9
Jayamanoharan, 2020[36]	Retro	Cohort	30	59	16 (53)	WFNS: 11 (37)	-	13 (43)	C	5/8
Guresir, 2020[37]	-	Cohort	231	54 (14)	-	WFNS: 0 (0)	F3: 207 (90)	22 (10)	R	5/8
Al-Mufti, 2019[38]	Pro	Cohort	1067	-	731 (69)	HH3-5: 645 (61)	560 (52)	202* (19) 170* (16)	C R	6/8
Zhang, 2019[39]	Pro	Cohort	535	54 (11)	325 (60)	HH: 65 (12)	-	161 (30)	C	6/9
Giede-Jeppe, 2019[40]	Pro	Cohort	319	-	221 (60)	-	-	112 (35)	R	6/8
Bevers, 2019[41]	Pro	Cohort	240	58	162 (68)	-	-	86* (45)	C	5/9
Zhu, 2019[42]	Pro	Cohort	196	58 (10)	103 (53)	WFNS: 55 (28)	mF: 102 (52)	41 (21) 57 (29)	C R	6/8
Kanamaru, 2019[43]	Pro	Cohort	109	65 (13)	77 (71)	WFNS: 39 (36)	mF: 96 (77)	16 (15)	C	7/9
Chen, 2019[44]	Pro	Cohort	104	52 (36-61)	61 (69)	median WFNS: 3	median mF: 2	35 (34)	C	5/9
Tanioka, 2019[45]	Pro	Cohort	95	66	66 (69)	WFNS: 30 (32)	88 (93)	13 (14) 24 (25)	C R	7/8
Rasmussen. 2019[46]	Pro	Cohort	90	53 (22-77)	74 (82)	WFNS: 13 (15)	90 (100)	24 (27)	C	5/8
Ahn, 2019[47]	Pro	Cohort	60	52 (13)	46 (77)	median WFNS: 2	median mF: 3	14 (23)	C	6/8
Hviid, 2019[48]	Pro	Cohort	44	58 (10)	13 (30)	WFNS: 20 (45)	33 (75)	9 (20)	C	5/9
Kim, 2019[49]	Pro	Cohort	42	58	30 (71)	HH: 17 (40)	33 (79)	14 (33)	C	3/8
Kwan, 2019[50]	Pro	Cohort	25	56 (10)	15 (60)	mean WFNS: 3	mean mF: 4	9 (36)	C	4/9
Qi, 2019[51]	Retro	Cohort	252	53 (13)	108 (43)	median HH: 1	-	53 (21)	C	6/8
Wu, 2019[52]	Retro	Cohort	122	55 (11)	74 (61)	HH: 24 (20)	109 (89)	43 (35)	C	7/8
Lin, 2019[53]	-	Cohort	146	-	-	-	-	34 (23) 31 (21)	C R	5/9
Aida, 2019[54]	-	Cohort	27	58	20 (74)	HK: 2 (7)	23 (85)	7 (26)	C	3/8
Hostettler, 2018[55]	Pro	Cohort	548	55 (13)	67 (67)	WFNS: 145 (26)	485 (89)	127 (23)	R	5/8
Ayling, 2018[56]	Pro	Cohort	413	51 (11)	289 (70)	WFNS: 100 (24)	-	72* (19)	C	5/8

Griessenauer, 2018[57]	Pro	Cohort	149	55 (13)	114 (77)	HH: 34 (23)	126 (85)	34 (23) 31* (21)	C R	7/9
Hendrix, 2018[58]	Pro	Cohort	149	55 (13)	114 (77)	HH: 34 (23)	126 (85)	34 (23) 31* (21)	C R	7/9
Nakatsuka, 2018[59]	Pro	Cohort	109	65 (12)	76 (70)	WFNS: 32 (29)	mF4: 37 (34)	17 (16) 14 (13)	C R	8/9
Yang, 2018[60]	Pro	Cohort	108	53 (38-61)	63 (58)	median WFNS 3	median mF: 2	36 (33)	C	5/9
Cai, 2018[61]	Pro	Cohort	60	56 (12)	38 (63)	HH: 13 (21)	mF: 31 (52)	17 (28)	R	5/8
Thomas, 2018[62]	Pro	Cohort	21	-	9 (43)	-	-	4 (19)	R	6/9
Halawa, 2018[63]	Pro	Cohort	19	61 (43-79)	14 (74)	HH: 4 (21)	17 (89)	7 (37)	C	3/8
Kim, 2018[64]	Pro	Cohort	87	60	56 (64)	HH: 46 (53)	60 (69)	38 (44)	C	3/8
Matano, 2018[65]	Retro	Cohort	333	60	210 (63)	HK: 104 (31)	-	41 (12)	R	5/8
Ray, 2018[66]	Retro	Cohort	169	53 (13)	114 (68)	WFNS: 67 (40)	mF: 106 (63)	38 (25)	C	4/8
Suzuki, 2018[67]	Retro	Cohort	156	64	116 (74)	WFNS: 67 (43)	122 (78)	21 (13)	C	8/9
Chaudhry, 2018[68]	Retro	Cohort	53	58 (12)	35 (66)	-	F3: 43 (81)	20* (38)	R	5/9
Tao, 2017[69]	Pro	Cohort	247	56 (12)	159 (64)	median WFNS 2	median mF: 3	47 (19)	C	5/8
Griessenauer, 2017[70]	Pro	Cohort	149	55 (13)	144 (77)	HH: 34 (23)	126 (85)	34 (23) 31* (21)	C R	6/8
Hendrix, 2017[71]	Pro	Cohort	149	55 (13)	144 (77)	HH: 34 (23)	126 (85)	34 (23) 31* (21)	C R	6/8
Hendrix, 2017[72]	Pro	Cohort	149	55 (13)	144 (77)	HH: 34 (23)	126 (85)	34 (23) 31* (21)	C R	7/9
Hendrix, 2017[73]	Pro	Cohort	149	55 (13)	144 (77)	HH: 34 (23)	126 (85)	34* (23) 31* (21)	C R	6/9
Hendrix, 2017[74]	Pro	Cohort	149	55 (13)	144 (77)	HH: 34 (23)	126 (85)	34 (23) 31* (21)	C R	6/8
Frontera, 2017[75]	Pro	Cohort	106	55	63 (59)	HH: 24 (23)	-	-	C	5/9
Chamling, 2017[76]	Pro	Cohort	89	54	58 (65)	WFNS: 38 (43)	75 (84)	24 (27)	C	6/8
Beseoglu, 2017[77]	Pro	Cohort	87	57 (11)	57 (66)	39 (45)	61 (69)	36 (41) 14 (16)	C R	4/8
Hollig, 2017[78]	Pro	Cohort	81	54 (13)	51 (63)	WFNS: 37 (45)	67 (82)	18 (22)	C	5/8
Chaudhry, 2017[79]	Pro	Cohort	80	58 (12)	49 (61)	HH: 27 (34)	77 (96)	28 (35) 17 (21)	C R	5/9
Chaudhry, 2017[80]	Pro	Cohort	80	57 (12)	50 (63)	HH: 28 (35)	77 (96)	28 (35) 16 (20)	C R	5/9
Bache, 2017[81]	Pro	Cohort	27	57 (13)	19 (70)	WFNS:29 (70)	26 (96)	8* (47)	C	5/9

Griessenauer, 2017[82]	Pro	Cohort	27	55 (22-85)	14 (52)	HH: 11 (41)	25 (93)	9 (33)	R	6/8
Wisniewski, 2017[83]	Pro	Cohort	20	60	11 (55)	HH: 2 (10)	13 (65)	9 (45)	C	6/9
Spitzer, 2017[84]	Pro	Cohort	15	51 (9)	9 (60)	WFNS: 4 (27)	11 (73)	8 (53)	C	4/8
Xu, 2017[85]	Retro	Cohort	386	56	243 (63)	HH: 115 (30)	139 (36)	23 (6)	C	6/8
Fukuda, 2017[86]	Retro	Cohort	187	64	150 (80)	WFNS: 65 (35)	-	24 (13) 12 (6)	C R	6/8
Li, 2017[87]	-	Cohort	83	60 (5)	38 (46)	HH: 18 (22)	-	31 (37)	C	3/8
Lu, 2017[88]	-	Case-control	40	59	22 (55)	WFNS3-5: 13 (33)	40 (100)	20 (50)	R	3/9
Ewelina, 2017[89]	-	Cohort	24	59	11 (46)	WFNS median 2	median: 3	6 (25)	C	5/9
Srinivasan, 2016[90]	Pro	Cohort	246	50	129 (52)	WFNS: 44 (18)	211 (86)	94 (38) 62 (25)	C R	6/8
Ding, 2016[91]	Pro	Cohort	125	52 (13)	76 (61)	WFNS median 3	median: 2	38 (30)	C	5/9
Jiang, 2016[92]	Pro	Cohort	118	42 (12)	48 (41)	WFNS median 3	median: 3	33* (30)	C	5/9
Rasmussen, 2016[93]	Pro	Cohort	90	53	74 (82)	WFNS: 13 (15)	90 (100)	24 (27)	C	5/8
Mijiti, 2016[94]	Retro	Cohort	343	-	210 (61)	HH:117 (34)	mF: 149 (43)	99 (29) 87 (25)	C R	7/8
van Donkelaar, 2016[95]	Retro	Cohort	285	55 (47-65)	189 (66)	WFNS: 141 (49)	-	84 (29)	R	7/8
Behrouz, 2016[96]	Retro	Cohort	142	55 (13)	85 (60)	-	142 (100)	54 (38)	C	5/8
Wu, 2016[97]	-	Cohort	57	58 (10)	24 (42)	HH: 8 (14)	-	27 (47)	C	5/9
Donnelly, 2015[98]	Pro	Cohort	332	53	239 (72)	HH3-5:141 (42)	224 (67)	183* (55)	C	6/8
Donnelly, 2015[99]	Pro	Cohort	332	53	239 (72)	HH3-5: 141 (42)	224 (67)	183* (55)	C	5/8
Chen, 2015[100]	Pro	Cohort	120	41 (12)	49 (41)	WFNS mean 2.6	mean 2.8	36 (30) 15 (13)	C R	5/9
Shen, 2015[101]	Pro	Cohort	118	42 (12)	48 (41)	WFNS mean 3	mean: 3	33 *(30) 14 (12)	C R	4/9
Crago, 2015[102]	Pro	Cohort	99	50 (10)	62 (63)	HH: 24 (24)	63 (64)	45* (47)	C	6/8
Helbok, 2015[103]	Pro	Cohort	26	55 (47-67)	15 (58)	HH: 18 (69)	mF: 20 (77)	6 (23)	R	4/8
Kofler, 2015[104]	Pro	Cohort	25	55 (47-68)	14 (56)	HH: 18 (72)	mF: 19 (76)	5 (20)	R	4/8
Leclerc, 2015[105]	Both	Cohort	74	55 (15)	54 (73)	WFNS mean 2.5	43 (58)	22 (30)	C	5/8
Sun, 2015[106]	Retro	Cohort	218	-	139 (64)	HH3-5: 31 (14)	91 (42)	78 (36)	C	8/8
Tang, 2015[107]	-	Cohort	58	53 (11)	34 (59)	HH: 8 (14)	mF: 22 (38)	12 (21)	C	4/9
Suzuki, 2015[108]	-	Cohort	30	63 (2)	23 (77)	WFNS: 13 (43)	30 (100)	14* (47)	C	6/9
Helbok, 2015[109]	-	Cohort	22	56 (47-68)	15 (68)	HH: 17 (77)	mF: 16 (73)	4 (18)	R	4/8
Cai, 2014[110]	Pro	Cohort	120	41 (12)	49 (41)	WFNS mean 2.6	mean 2.8	36 (30)	C	5/8

Martini, 2014[111]	Pro	Cohort	95	55 (-)	66 (69)	HH: 36 (38)	87 (92)	28 (29)	R	5/8
Bergstrom, 2014[112]	Pro	Cohort	48	-	39 (81)	-	43 (90)	15* (32)	C	4/9
Zanier, 2014[113]	Pro	Cohort	39	56 (13)	25 (64)	WFNS: 21 (54)	38 (97)	14 (34) 6 (15)	C R	4/9
Radolf, 2014[114]	Pro	Cohort	18	52	10 (55)	WFNS: 8 (44)	median 3	8 (45)	C	5/8
Gomes, 2014[115]	Pro	Cohort	12	58 (6)	10 (83)	WFNS median 3.5	mF median: 4	7 (58)	C	3/8
Beseoglu, 2014[116]	Retro	Cohort	274	54	187 (68)	WFNS: 132 (48)	-	- -	C R	6/8
Uekusa, 2014[117]	-	Cohort	20	-	15 (75)	WFNS: 16 (80)	-	7* (41)	R	2/8
De Rooij, 2013[118]	Pro	Cohort	371	44 (22-67)	261 (70)	WFNS: 104 (28)	mF: 324 (87)	110 (30)	R	6/8
Bian, 2013[119]	Pro	Cohort	239	53 (12)	123 (51)	WFNS: 25 (11)	127 (53)	34* (15)	C	7/8
Gallek, 2013[120]	Pro	Cohort	235	53	165 (70)	HH: 44 (19)	161 (69)	113* (48)	C	3/8
Nakagawa, 2013[121]	Pro	Cohort	103	66	68 (66)	HK: 41 (40)	57 (55)	13 (13)	C	4/8
Ohnishi, 2013[122]	Pro	Cohort	95	62	53 (56)	HK: 39 (41)	86 (91)	22 (23) 18 (19)	C R	6/8
July, 2013[123]	Pro	Cohort	44	52 (11)	24 (55)	WFNS: 6 (14)	F4: 11 (25)	29 (66)	C	4/8
Barges-Coll, 2013[124]	Pro	Cohort	40	47 (2)	22 (55)	WFNS: 0 (0)	33 (83)	17* (43)	C	6/9
Lanterna, 2013[125]	Pro	Cohort	26	53 (13)	19 (73)	HH: 0 (0)	9 (35)	12* (46)	C	3/8
Fischer, 2013[126]	Pro	Cohort	20	52	16 (80)	WFNS: 7 (35)	18 (90)	7* (35)	R	5/9
Kim, 2013[127]	-	Cohort	245	54	172 (70)	-	-	109* (45)	C	2/8
Aggarwal, 2013[128]	-	Cohort	74	50	-	WFNS: 16 (22)	61 (82)	39 (53)	C	3/8
Maimaitili, 2013[129]	-	Cohort	49	53 (13)	27 (57)	HH: 12 (24)	27 (55)	19 (39)	C	3/9
Zanier, 2013[130]	-	Cohort	38	54	31 (82)	WFNS: 24 (63)	37 (97)	11* (31) 10 (26)	C R	4/9
Nyquist, 2013[131]	-	Case-control	28	-	-	-	-	14 (50)	C	4/9
Juvela, 2012[132]	Pro	Cohort	178	50 (13)	90 (51)	WFNS: 37 (21)	129 (72)	48 (26) 50 (28)	C R	6/8
Papanikolaou, 2012[133]	Pro	Cohort	37	43 (2)	23 (62)	HH: 23 (62)	23 (62)	12* (33)	R	6/8
Yang, 2012[134]	Pro	Cohort	20	52	10 (50)	HH mean: 3	Mean mF: 3	10 (50)	R	8/9
Zhu, 2012[135]	Retro	Cohort	303	44 (12)	172 (57)	WFNS mean 2.3	mean mF: 2.7	131 (43)	C	6/9
Jeon, 2012[136]	Retro	Cohort	93	57	60 (65)	HH: 31 (33)	F3: 37 (40)	26 (29)	C	5/8
Vrsajkov, 2012[137]	Retro	Cohort	82	53	60 (73)	WFNS mean 2.4	-	39 (48)	C	5/8
Watanabe, 2012[138]	Retro	Cohort	34	64	21 (62)	27 979)	34 (100)	6 (18)	C	4/8

Jung, 2012[139]	Retro	Cohort	24	51 (11)	19 (79)	WFNS: 7 (29)	24 (100)	4 (17)	C	4/9
Sarrafzadeh, 2012[140]	Retro	Cohort	21	55 (46-62)	11 (52)	WFNS: 12 (57)	median: 4	12 (57)	C	5/8
Beeftink, 2011[141]	Pro	Cohort	67	57	47 (70)	WFNS: 13 (19)	-	10 (15)	C	8/8
Zanier, 2011[142]	Pro	Cohort	38	54 (2)	31 (82)	WFNS: 24 (63)	37 (97)	14* (47)	C	3/9
Dietmann, 2011[143]	Pro	Cohort	20	52	16 (80)	WFNS: 7 (35)	-	7 (35)	R	4/9
Fischer, 2011[144]	Pro	Cohort	20	52	16 (80)	WFNS: 7 (35)	18 (90)	7 (35)	R	6/9
Zheng, 2011[145]	Retro	Cohort	383	56 (-)	66	WFNS: 124 (32)	-	54 (24)	R	5/8
Zhu, 2011[146]	Retro	Cohort	303	44 (12)	172 (57)	WFNS mean 2.3	mean mF: 2.7	131 (43)	C	7/9
Nakae, 2011[147]	Retro	Cohort	142	61 (12)	85 (60)	HH3-5: 113 (80)	71 (50)	28 (20)	R	3/8
Taub, 2011[148]	Retro	Cohort	119	57 (-)	90 (76)	HH: 19 (16)	49 (41)	46 (39)	R	6/8
Zanier, 2011[149]	-	Cohort	35	-	-	-	35 (100)	10 (29)	R	4/9
Hirashima, 2011[150]	-	Cohort	28	62	19 (68)	WFNS3-5: 15 (54)	F3: 19 (68)	14 (50)	C	3/8
Wang, 2011[151]	-	Cohort	21	46	11 (52)	-	-	7 (33)	C	7/9
Naidech, 2010[152]	Pro	RCT	44	57	33 (75)	WFNS: 13 (30)	43 (98)	10 (23) 20 (45)	C R	3/7
Lackner, 2010[153]	Pro	Cohort	20	52	16 (80)	WFNS: 7 (35)	18 (90)	7 (35)	R	6/9
Kasius, 2010[154]	Retro	Cohort	106	54	71 (67)	WFNS: 25 (24)	-	14* (15)	C	6/8
Ruigrok, 2010[155]	-	Cohort	208	60 (15)	149 (72)	WFNS: 41 (20)	-	49 (24)	C	6/9
Vergouwen, 2010[156]	-	Cohort	31	53 (11)	19 (61)	WFNS median 2	-	11 (35)	C	5/8
Juvela, 2009[157]	Pro	Cohort	105	48 (11)	52 (50)	WFNS: 20 (19)	73 (70)	24 (23) 29* (28)	C R	7/8
Vergouwen, 2009[158]	Pro	Cohort	31	53 (11)	19 (61)	WFNS median 2	-	11 (35)	C	5/8
Oddo, 2009[159]	Pro	Cohort	20	51	13 (65)	WFNS: 14 (70)	19 (95)	8 (40)	C	5/8
Kruyt, 2008[160]	Pro	Cohort	265	56	175 (66)	49 (18)	-	86* (33)	C	5/8
van den Bergh, 2008[161]	Pro	Cohort	167	56 (15)	110 (66)	WFNS: 47 (28)	-	49 (29)	C	7/8
Starke, 2008[162]	Pro	Cohort	77	54	49 (64)	HH: 13 (17)	42 (55)	24 (30) 8 (10)	C R	7/8
Lewis, 2008[163]	-	Cohort	30	56	22 (73)	WFNS: 15 (50)	30 (100)	17 (57)	C	4/9
Isman, 2008[164]	Pro	Cohort	20	46 (13)	9 (45)	HH: 1 (5)	9 (45)	14 (70)	C	4/9
Dorhout Mees, 2007[165]	Pro	Cohort	155	56	102 (66)	WFNS: 33 (21)	-	27 (17)	C	6/8
Tseng, 2007[166]	Pro	Cohort	80	53 (12)	44 (55)	WFNS: 26 (19)	69 (86)	14 (18)	C	5/8
Igarashi, 2007[167]	Pro	Cohort	67	55	44 (66)	HK: 7 (10)	58 (87)	12 (18)	C	4/8
Oh, 2007[168]	Retro	Cohort	158	51	98 (62)	HH: 0 (0)	F3: 73 (46)	46 (31)	C	5/8
Schebesch, 2007[169]	Retro	Cohort	88	53	54 (61)	HH: 22 (25)	-	37 (42)	C	3/8

Schoch, 2007[170]	Retro	Cohort	64	55 (12)	49 (77)	WFNS: 39 (61)	60 (94)	17 (27)	R	3/8
Siironen, 2007[171]	-	Cohort	105	48	52 (50)	WFNS: 20 (19)	F3: 73 (70)	24 (23)	C	6/8
Lewis, 2007[172]	-	Cohort	20	54	15 (75)	WFNS: 13 (65)	20 (100)	13 (65)	C	4/9
Juvela, 2006[173]	Pro	Cohort	136	50	67 (49)	WFNS: 27 (20)	99 (73)	37 (27) 37* (30)	C R	5/8
Rothoerl, 2006[174]	Pro	Cohort	15	47	10 (66)	HH: 2 (13)	-	5 (33)	C	3/8
Rothoerl, 2006[175]	Retro	Cohort	88	53	54 (61)	HH: 22 (25)	-	37 (42)	C	3/8
Frijns, 2006[176]	-	Cohort	106	54	72 (68)	WFNS: 25 (24)	-	12* (13)	C	6/8
Frijns, 2006[177]	-	Cohort	86	55	62 (72)	WFNS: 19 (22)	-	9 (14)	C	5/8
Oertel, 2006[178]	-	Cohort	51	52 (11)	32 (63)	WFNS: 28 (45)	34 (67)	26 (51)	C	5/8
Lanterna, 2005[179]	Pro	Cohort	101	52 (8)	53 (53)	HH: 0 (0)	50 (50)	37 (37)	C	5/8
Kastner, 2005[180]	Pro	Cohort	20	58 (10)	11 (55)	WFNS: 5 (25)	13 (65)	7 (35) 7 (35)	C R	4/9
Asaeda, 2005[181]	-	Cohort	34	63	22 (65)	-	30 (88)	15 (44)	R	3/8
Dohi, 2005[182]	-	Cohort	15	62 (15)	4 (27)	HH: 6 (40)	-	7 (47)	C	4/8
Tanriverdi, 2005[183]	-	Cohort	12	47	8 (67)	HH: 3 (25)	7 (58)	4 (33)	C	5/9
Juvela, 2005[184]	Pro	Cohort	175	51	88 (50)	WFNS: 36 (21)	127 (73)	46* (26) 46* (30)	C R	6/8
Khurana, 2004[185]	Pro	Case-control	51	54 (12)	35 (69)	WFNS: 5 (10)	41 (80)	12 (24)	C	7/9
McGirt, 2004[186]	Pro	Cohort	40	53 (12)	32 (80)	HH median: 2	26 (65)	16 (40)	C	8/8
Sarrafzadeh, 2004[187]	Pro	Cohort	13	46 (14)	9 (69)	WFNS: 4 (31)	10 (77)	10 (77)	C	3/9
Collignon, 2004[188]	-	Cohort	128	54	83 (65)	HH: 40 (31)	-	55* (43)	C	3/8
Hendryk, 2004[189]	-	Cohort	30	-	-	-	-	14 (47)	C	3/8
van den Bergh, 2003[190]	Pro	Cohort	107	-	66 (62)	WFNS: 45 (42)	-	21 (20)	C	8/8
Qureshi, 2002[191]	Pro	Cohort	298	52	218 (73)	-	-	-	C	6/8
Juvela, 2002[192]	Pro	Cohort	51	51	23 (45)	WFNS: 12 (24)	35 (69)	13* (26) 9 (18)	C R	6/8
Nissen, 2001[193]	Pro	Cohort	36	-	23 (64)	WFNS: 0 (0)	-	13 (36)	C	2/8
Mascia, 2001[194]	Pro	Cohort	20	55 (16)	13 (65)	WFNS median 3	19 (95)	4 (20)	C	4/8
Hirashima, 2001[195]	-	Cohort	28	61	17 (61)	-	-	10 (36)	R	4/9
Nam, 2001[196]	-	Cohort	24	55	15 (63)	HH: 6 (25)	-	11 (46)	C	3/8
Juvela, 2000[197]	Pro	Cohort	70	46	34 (49)	HH: 12 (17)	44 (63)	20* (31)	R	2/9
Gruber, 2000[198]	Pro	Cohort	44	51 (14)	26 (60)	HH: 23 (52)	35 (80)	17 (39)	R	4/8
Takenaka, 2000[199]	-	Cohort	20	56	13 (65)	HH: 2 (10)	-	7 (35)	C	3/9

Mayer, 1999[200]	Retro	Cohort	72	51 (13)	47 (65)	HH: 14 (20)	36 (50)	27 (36)	C	6/8
Fuji, 1997[201]	-	Cohort	117	58	67 (57)	HH: 37 (32)	-	18 (15)	C	4/8
Hirashima, 1997[202]	-	Cohort	21	58	8 (38)	HH: 8 (38)	14 (67)	9 (43)	C	3/9
Hirashima, 1997[203]	-	Cohort	19	61	11 (58)	HH: 5 (26)	15 (83)	6* (33)	R	3/9
Okuchi, 1996[204]	Pro	Cohort	17	60	-	HH: 0	-	4 (24)	C	3/8
Hirashima, 1995[205]	Pro	Cohort	32	59	18 (56)	WFNS: 4 (13)	23 (72)	18 (56) 7 (22)	C R	3/8
Hirashima, 1994[206]	-	Cohort	32	58	16 (50)	WFNS: 11 (34)	19 (59)	9 (28)	R	3/8
Hirashima, 1994[207]	-	Cohort	21	59	13 (62)	HH: 5 (24)	14 (67)	6 (29)	R	2/8
Suzuki, 1989[208]	-	Cohort	14	64	11 (79)	-	-	11 (79)	C	3/9
Rodriguez, 1988[209]	-	Cohort	40	-	-	HH: 0 (0)	-	16 (40)	C	4/9

[1] Retro: retrospective study, pro: prospective study.
[2]Age is given in mean with SD or median with quartile 1 – quartile 3, if available.
[3]Poor outcome is defined as WFNS 4-5, HH 4-5 or HK 4-5.
[4] F3: fisher 3 score, F4: fisher 4 score, mF: modified Fisher scale.
[5] C: clinical DCI, R: radiological DCI
* data on DCI development was not available of the entire SAH cohort

Table S2 - Biomarker classification table of all 724 biomarkers studied for clinical or radiological DCI.

				Clinical DCI		Radiological DCI	
Biomarker	**Abbreviation**	**Biomarker (sub-)group**	**Medium**	**Studies**	**Conclusion**	**Studies**	**Conclusion**
Brain injury							
A-II Spectrin Breakdown Product 120	SBPD120	Brain injury	CSF	172	Significant		
A-II Spectrin Breakdown Product 145	SBPD145	Brain injury	CSF	172	Significant		
A-II Spectrin Breakdown Product 150	SBPD150	Brain injury	CSF	172	Significant		
CD45-positive mitochondrial particles		Other	CSF	24	Non-significant		
Glutamate-aspartate transporter-allophycocyanin positive mitochondrial particles	GLAST-positive	Other	CSF	24	Significant		
Glycerol		Brain injury	MD	187	Non-significant		
extracellular JC-1 red/green ratio	JC-1	Brain injury	CSF	24	Significant		
Lactate dehydrogenase	LDH	Brain injury	Blood	90	Non-significant	90	Non-significant
Myelin basic protein	MBP	Brain injury	CSF			195	Significant
phosphorylated axonal Neurofilament subunit H	pNF-H	Brain injury	Blood	163	Non-significant		
phosphorylated axonal Neurofilament subunit H	pNF-H	Brain injury	CSF	163	Significant		
Neurofilament light chain	NFL	Brain injury	Blood	48	Non-significant		
Neurofilament light chain	NFL	Brain injury	CSF	63	Non-significant	149	Non-significant
Neuron specific enolase	NSE	Brain injury	Blood	178	Non-significant		
S-100B		Brain injury	Blood	112, 178	Significant		
Tau protein	Tau	Brain injury	CSF	63, 130	Significant	130	Non-significant
Tau protein	Tau	Brain injury	MD			109	Non-significant
Taurine		Brain injury	Blood	124	Non-significant		
Taurine		Brain injury	MD			104	Significant
Coagulation cascade							
α_2-antiplasmin	A2-PI	Coagulation cascade	Blood	201	Non-significant		
Activated partial thromboplastin time	APTT	Coagulation cascade	Blood	201	Non-significant	134	Non-significant
ADAM Metallopeptidase with thrombospondin type 1 motif 13	ADAMTS13	Coagulation cascade	Blood	87,107,158	Significant		
Antiphospholipid antibodies	aPLs	Coagulation cascade	Blood	205	Non-significant	205	Non-significant
Antithrombin III	AT III	Coagulation cascade	Blood	201	Non-significant		
D-dimer		Coagulation cascade	Blood	28, 35, 86, 146, 166, 173, 201	Significant	31, 86, 173	Significant
D-dimer		Coagulation cascade	CSF	36	Significant		
D-dimer/plasminogen ratio	D-dimer/PLG	Coagulation cascade	CSF	36	Significant		
Enhancement of platelet sensitivity	EPS	Coagulation cascade	Blood	201	Non-significant		

Fibrinogen		Coagulation cascade	Blood	8, 35, 166, 201	Significant	33	Non-significant
International normalized ratio	INR	Coagulation cascade	Blood			134	Non-significant
Mean platelet volume	MPV	Coagulation cascade	Blood	8, 23, 30	Significant		
Mean platelet volume/platelet count ratio	MPV-PLT ratio	Coagulation cascade	Blood	23, 30, 66	Significant		
Plasmin-α_2-antiplasmin complex	PAP	Coagulation cascade	Blood	201	Non-significant		
Plasminogen	PLG	Coagulation cascade	Blood	201	Non-significant		
Plasminogen	PLG	Coagulation cascade	CSF	36	Non-significant		
Platelet activating factor	PAF	Coagulation cascade	Blood	202	Significant	206	Significant
Platelet activating factor	PAF	Coagulation cascade	CSF			207	Significant
Platelet activating factor - acetylhydrolase	PAF-AH	Coagulation cascade	Blood			206	Non-significant
Platelet activating factor - acetylhydrolase	PAF-AH	Coagulation cascade	CSF	150	Non-significant	207	Significant
Platelet aggregation		Coagulation cascade	Blood			206	Non-significant
Platelet count	PC	Coagulation cascade	Blood	23, 28, 30, 35, 69, 128, 136, 151, 154, 169, 193, 201	Inconclusive	134, 206	Significant
Platelet factor 4	PF4	Coagulation cascade	Blood	202	Non-significant	206	Significant
Platelet membrane glycoprotein-140	GMP-140	Coagulation cascade	Blood	87	Significant		
CD41+/A+ platelet microparticle	PMP	Coagulation cascade	Blood			153	Significant
CD41/CD61-positive mitochondrial particles		Other	CSF	24	Non-significant		
Platelet/large cell ratio	P-LCR	Coagulation cascade	Blood	23	Non-significant		
Protein C		Coagulation cascade	Blood	201	Non-significant		
Prothrombin fragment F1+2	PF 1+2	Coagulation cascade	Blood	201	Non-significant		
Prothrombin time	PT	Coagulation cascade	Blood	28, 35, 201	Non-significant	134	Non-significant
Signal peptide-Cub-Egf domain-containing protein-1	SCUBE1	Coagulation cascade	Blood	91	Significant		
Thrombin-antithrombin III complex	TAT	Coagulation cascade	Blood	201, 202	Significant		
Thrombin-antithrombin III complex	TAT	Coagulation cascade	CSF			203	Significant
Thromboelastography maximal amplitude	TEG-MA	Coagulation cascade	Blood	75	Significant		
Tissue factor	TF	Coagulation cascade	Blood	202	Non-significant		
Membrane-bound tissue factor	mTF	Coagulation cascade	CSF			195	Significant
von Willebrand factor	vWF	Coagulation cascade, Endothelial injury	Blood	87, 107, 176, 202	Significant		
von Willebrand factor antigen	vWF antigen	Coagulation cascade, Endothelial injury	Blood	158	Significant		
von Willebrand factor propeptide	vWF propeptide	Coagulation cascade, Endothelial injury	Blood	158, 176	Significant		
von Willebrand factor ristocetin cofactor activity	vWFRiCof	Coagulation cascade, Endothelial injury	Blood	158	Non-significant		

Cortical spreading depressions							
Glutamate		Cortical spreading depressions	CSF	19	Significant		
Glutamate		Cortical spreading depressions	MD	187	Non-significant		
Endothelial injury							
Angiopoetin 1	Ang-1	Endothelial injury	Blood			144	Significant
Angiopoetin 2	Ang-2	Endothelial injury	Blood			144	Non-significant
CD105+/A+ endothelial microparticle	EMP	Endothelial injury, Vascular tone	Blood			153	Significant
Extra domain 1-Fibronectin	ED1-FN	Endothelial injury	Blood	176	Non-significant		
Homocysteine	Hcy	Endothelial injury	Blood	28	Significant		
Sphingosine 1-phosphate	S1P	Endothelial injury	CSF			25	Non-significant
von Willebrand Factor positive mitochondrial particles	vWF-positive	Endothelial injury	CSF	24	Significant		
Genetic							
Apolipoprotein E ε2 allele	ApoE ε2	Genetic - Genomic	Buccal swabs	157	Non-significant	157	Non-significant
Apolipoprotein E ε3 allele	ApoE ε3	Genetic - Genomic	Buccal swabs	157	Non-significant	157	Non-significant
Apolipoprotein E ε4 allele	ApoE ε4	Genetic - Genomic	Buccal swabs	157	Non-significant	157	Non-significant
Apolipoprotein E ε4 allele	ApoE ε4	Genetic - Genomic	Blood	179	Significant		
Platelet activating factor - acetylhydrolase genotype	PAF-AH	Genetic - Genomic	Blood	150	Non-significant		
microRNA 1. miR-15a 2. miR-27a 3. miR-27b 4. miR-93-5p 5. miR-125a 6. miR-132 7. miR-297 8. miR-324 9. miR-339-5p 10. miR-421 11. miR-574 12. miR-1268 13. miR-1290 14. miR-3178	miRNA	Genetic - microRNA	Blood			88	 1. Non-significant 2. Non-significant 3. Non-significant 4. Significant 5. Non-significant 6. Significant 7. Significant 8. Non-significant 9. Non-significant 10. Significant 11. Significant 12. Significant 13. Significant 14. Significant

15. miR-3651							15. Significant
16. miR-4433							16. Non-significant
17. miR-4440							17. Non-significant
18. miR-4449							18. Significant
19. miR-4454							19. Non-significant
20. miR-4459							20. Significant
21. miR-4463							21. Significant
22. miR-4492							22. Significant
23. miR-4497							23. Significant
24. miR-4532							24. Significant
25. miR-4674							25. Significant
26. miR-4689							26. Significant
27. miR-4690							27. Significant
28. miR-4793							28. Significant
microRNA	miRNA	Genetic – MicroRNA	CSF	[18, 81]			
1. miR-9-3p					1. Non-significant		
2. miR-9-5p					2. Non-significant		
3. miR-10b-3p					3. Non-significant		
4. miR-15a-5p					4. Non-significant		
5. miR-15b-5p					5. Non-significant		
6. miR-16-5p					6. Non-significant		
7. miR-19a-3p					7. Non-significant		
8. miR-19b-3p					8. Non-significant		
9. miR-20a-5p					9. Non-significant		
10. miR-21-5p					10. Non-significant		
11. miR-22-3p					11. Non-significant		
12. miR-23a-3p					12. Non-significant		
13. miR-24-3p					13. Non-significant		
14. miR-25-3p					14. Non-significant		
15. miR-26a-5p					15. Non-significant		
16. miR-27a-3p					16. Non-significant		
17. miR-27b-3p					17. Non-significant		
18. miR-29a-3p					18. Non-significant		
19. miR-29b-3p					19. Non-significant		
20. miR-29c-3p					20. Non-significant		
21. miR-30a-5p					21. Non-significant		
22. miR-30d-5p					22. Non-significant		
23. miR-32-5p					23. Non-significant		
24. miR-34a-5p					24. Non-significant		
25. miR-34b-3p					25. Non-significant		
26. miR-92a-3p					26. Non-significant		

27. miR-93-5p 28. miR-125b-5p 29. miR-130a-3p 30. miR-130b-3p 31. miR-132-3p 32. miR-143-3p 33. miR-146a-5p 34. miR-152-3p 35. miR-185-5p 36. miR-193a-5p 37. miR-204-5p 38. miR-208a-3p 39. miR-221-3p 40. miR-222-3p 41. miR-223-3p 42. miR-328-3p 43. miR-361-5p 44. miR-451a 45. miR-483-5p 46. miR-486-5p 47. miR-490-3p 48. miR-520h 49. miR-553 50. miR-643 51. miR-let-7b-5p					27. Non-significant 28. Non-significant 29. Non-significant 30. Non-significant 31. Non-significant 32. Non-significant 33. Non-significant 34. Non-significant 35. Non-significant 36. Non-significant 37. Non-significant 38. Non-significant 39. Non-significant 40. Non-significant 41. Non-significant 42. Non-significant 43. Non-significant 44. Non-significant 45. Non-significant 46. Non-significant 47. Non-significant 48. Non-significant 49. Non-significant 50. Non-significant 51. Non-significant			
Cadherin related family member 5 – DNA methylation CpG-site cg11464053	CDHR5	Genetic - Methylation	Blood	[17]	Significant			
DNA methylation intensity of distal intergenic region upstream of Inositol 1-,4-,5-trisphosphate receptor	ITPR3	Genetic - Methylation	Blood	[49]	Significant			
DNA methylation CpG-sites 1. Cg0268232 2. Cg00074576 3. Cg00789789 4. Cg01141087 5. Cg01620248 6. Cg01834661 7. Cg02180699 8. Cg02750582 9. Cg03297297 10. Cg06479032	CpG	Genetic - Methylation	Blood	[17]	 1. Significant 2. Significant 3. Significant 4. Significant 5. Significant 6. Significant 7. Significant 8. Significant 9. Significant 10. Significant			

11. Cg06502011 12. Cg07259358 13. Cg08789159 14. Cg09217327 15. Cg11337626 16. Cg12601633 17. Cg14592104 18. Cg14916658 19. Cg15090337 20. Cg16837008 21. Cg18101414 22. Cg19132447 23. Cg19751670 24. Cg21222185 25. Cg21486195 26. Cg21808832 27. Cg23222472 28. Cg23407997 29. Cg25058463 30. Cg25934800 31. Cg26306080 32. Cg26826512 33. Cg089669578					11. Significant 12. Significant 13. Significant 14. Significant 15. Significant 16. Significant 17. Significant 18. Significant 19. Significant 20. Significant 21. Significant 22. Significant 23. Significant 24. Significant 25. Significant 26. Significant 27. Significant 28. Significant 29. Significant 30. Significant 31. Significant 32. Significant 33. Significant		
Hepcidin antimicrobial peptide gene DNA methylation CpG-site 1. cg02131995 2. cg04085447 3. cg04668516 4. cg17907567 5. cg18149657 6. cg23677000 7. cg26283059 8. cg27273033	HAMP	Genetic - Methylation	CSF	[11]	1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant		
Insulin Receptor DNA methylation CpG-site cg00441765	INSR	Genetic - Methylation	Blood	[17]	Significant		
Soluble Epoxide Hydrolase 2 polymorphism 1. K55R 2. R287Q	EPHX2	Genetic - Polymorphism	Blood			[111]	1.Significant 2. Non-significant
Factor XIII subunit A polymorphism 1. Pro564Leu 2. Tyr204Phe	FXIII A	Genetic - Polymorphism	Blood	[155]	1. Non-significant 2. Non-significant		

3. Val34Leu					3. Non-significant		
Factor XIII subunit B polymorphism His95Arg	FXIII B	Genetic - Polymorphism	Blood	155	Non-significant		
Haptoglobin polymorphism 1. 1-1 2. 2-1 3. 2-2	Hp	Genetic - Polymorphism	Blood	64, 105, 122	 1. Non-significant 2. Significant 3. Significant	122	 1. Non-significant 2. Non-significant 3. Non-significant
Haptoglobin 2-1 subunit 1. a1 2. a2	Hp	Genetic – Polymorphism	Blood	64	 1. Significant 2. Non-signficant		
Single nucleotide polymorphism 1. rs999662 2. rs3849943 3. rs6805782 4. rs10967965	SNP	Genetic - Polymorphism	Blood	127	 1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant		
Activating Signal Cointegrator 1 Complex subunit 2 mRNA	ASCC2	Genetic - RNA	Blood	17	Non-significant		
Cadherin related family member 5 - mRNA	CDHR5	Genetic - RNA	Blood	17	Significant		
DNA methyltransferase mRNA	DNMT1	Genetic - RNA	Blood	49	Significant		
Interleukin-1B RNA	IL-1B RNA	Genetic - RNA	Blood	196	Significant		
Immunoglobulin like domain containing receptor 1 mRNA	ILDR1	Genetic - RNA	Blood	17	Non-significant		
inositol 1-,4-,5trisphosphate receptor mRNA	ITPR3	Genetic - RNA	Blood	49	Significant		
Insulin receptor mRNA	INSR	Genetic - RNA	Blood	17	Significant		
Leucine rich single-plass membrane protein 1 mRNA	LSMEM1	Genetic - RNA	Blood	17	Non-significant		
Mitogen-activated protein kinase kinase kinase 13 mRNA	MAP3K13	Genetic - RNA	Blood	17	Non-significant		
Nucleolar protein 4 like mRNA	NOL4L	Genetic - RNA	Blood	17	Non-significant		
Ten-eleven translocation enzyme 1 mRNA	TET1	Genetic - RNA	Blood	49	Significant		
Ten-eleven translocation enzyme 2 mRNA	TET2	Genetic - RNA	Blood	49	Non-significant		
Ten-eleven translocation enzyme 3 mRNA	TET3	Genetic - RNA	Blood	49	Non-significant		
Tumor necrosis factor a RNA	TNF-α	Genetic - RNA	Blood	196	Non-significant		
Zinc finger protein 706 mRNA	ZNF706	Genetic - RNA	Blood	17	Non-significant		
20-Hydroxyeicosatetraenoic acid SNP CYP4F2 SNP rs3093089 g.4593T>C	20-HETE SNP CYP4F2	Genetic – SNP	CSF & Blood	99	Significant		
Aconitase 1 SNPs 1. rs1028932 2. rs2026739 3. rs4879583 4. rs7866419	ACO1	Genetic - SNP	Blood	12	 1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant		

5. rs10435797 6. rs10738885 7. rs10813816 8. rs10970972 9. rs13292540 10. rs13302577					5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant 9. Non-significant 10. Non-significant		
Aconitase 2 SNPs 1. rs2076196 2. rs9611598	ACO2	Genetic - SNP	Blood	[12]	 1. Non-significant 2. Non-significant		
Amyloid precursor protein SNPs 1. rs3991 2. rs128648 3. rs216763 4. rs216772 5. rs216780 6. rs373521 7. rs429410 8. rs436587 9. rs454017 10. rs465853 11. rs466609 12. rs1701000 13. rs1783016 14. rs1787438 15. rs2026225 16. rs2070652 17. rs2234988 18. rs2242683 19. rs2829970 20. rs2829979 21. rs2830012 22. rs2830036 23. rs2830042 24. rs2830045 25. rs2830048 26. rs2830050 27. rs2830051 28. rs2830053 29. rs2830066 30. rs2830104 31. rs9305268	APP	Genetic - SNP	Blood	[12]	 1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant 9. Non-significant 10. Non-significant 11. Non-significant 12. Non-significant 13. Non-significant 14. Non-significant 15. Non-significant 16. Non-significant 17. Non-significant 18. Non-significant 19. Non-significant 20. Non-significant 21. Non-significant 22. Non-significant 23. Non-significant 24. Non-significant 25. Non-significant 26. Non-significant 27. Non-significant 28. Non-significant 29. Non-significant 30. Non-significant 31. Non-significant		

32. rs9980729 33. rs9981258 34. rs11087985					32. Non-significant 33. Non-significant 34. Non-significant		
Angiotensin 2 receptor type 1 SNP rs5186 A>C	AT1	Genetic - SNP	Blood	[70]	Non-significant	[70]	Non-significant
Angiotensin 2 receptor type 2 SNP rs11091046 A>C	AT2	Genetic - SNP	Blood	[70]	Non-significant	[70]	Non-significant
Angiotensin 2 receptor type 2 SNP rs1403543 G>A	AT2	Genetic - SNP	Blood	[70]	Non-significant	[70]	Non-significant
Angiotensin converting enzyme SNP rs4340 I/D	ACE	Genetic - SNP	Blood	[70]	Non-significant	[70]	Non-significant
Angiotensinogen SNP rs699 C>T	AGT	Genetic - SNP	Blood	[70]	Non-significant	[70]	Non-significant
Brain-derived neurotrophic factor SNP Val66Met	BNDP	Genetic - SNP	Blood	[171]	Non-significant		
Ceruloplasmin SNP 1. rs701755 2. rs772908 3. rs773050 4. rs3816893 5. rs9853335 6. rs13072552 7. rs13075921 8. rs16861579 9. rs16861634 10. rs17787768 11. rs17838831	CP	Genetic - SNP	Blood	[12]	 1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant 9. Non-significant 10. Non-significant 11. Non-significant		
Cubilin SNP 1. rs703064 2. rs780810 3. rs780837 4. rs780839 5. rs780846 6. rs796667 7. rs1276711 8. rs1276722 9. rs1398431 10. rs1687702 11. rs1797081 12. rs1914172 13. rs2087631 14. rs2130806 15. rs2356823	CUBN	Genetic - SNP	Blood	[12]	 1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant 9. Non-significant 10. Non-significant 11. Non-significant 12. Non-significant 13. Non-significant 14. Non-significant 15. Non-significant		

16. rs2603796					16. Non-significant		
17. rs2883972					17. Non-significant		
18. rs3012477					18. Non-significant		
19. rs3012501					19. Non-significant		
20. rs3740169					20. Non-significant		
21. rs3847364					21. Non-significant		
22. rs3847369					22. Non-significant		
23. rs3914238					23. Non-significant		
24. rs4335444					24. Non-significant		
25. rs6602163					25. Non-significant		
26. rs7071422					26. Non-significant		
27. rs7072049					27. Non-significant		
28. rs7075040					28. Non-significant		
29. rs7082270					29. Non-significant		
30. rs7098659					30. Non-significant		
31. rs7100290					31. Non-significant		
32. rs7893395					32. Non-significant		
33. rs7893507					33. Non-significant		
34. rs7897704					34. Non-significant		
35. rs7898283					35. Non-significant		
36. rs7900486					36. Non-significant		
37. rs7904146					37. Non-significant		
38. rs7906242					38. Non-significant		
39. rs7917400					39. Non-significant		
40. rs10508517					40. Non-significant		
41. rs10508518					41. Non-significant		
42. rs10752063					42. Non-significant		
43. rs10795440					43. Non-significant		
44. rs10795445					44. Non-significant		
45. rs10904831					45. Non-significant		
46. rs10904850					46. Significant		
47. rs11254235					47. Non-significant		
48. rs11254238					48. Non-significant		
49. rs11254248					49. Non-significant		
50. rs11254308					50. Non-significant		
51. rs11591673					51. Non-significant		
52. rs12146414					52. Non-significant		
53. rs12244831					53. Non-significant		
54. rs12354787					54. Non-significant		
55. rs17139666					55. Non-significant		
56. rs17347211					56. Non-significant		

57. rs41335345 58. rs41517646 59. rs41526049					57. Non-significant 58. Non-significant 59. Non-significant		
Cystathionine b-synthase SNP 1. rs1801181 1080C>T 2. rs234706 699G>A, c.699C>T 3. 844ins68	CBS	Genetic - SNP	Blood	58	1. Non-significant 2. Non-significant 3. Non-significant	58	1. Non-significant 2. Non-significant 3. Non-significant
Divalent metal transporter 1 SNP 1. rs2928672 2. rs2978475 3. rs7015818 4. rs7833754 5. rs7834536 6. rs11781222 7. rs12548753 8. rs13266950	SLC11A2	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant		
Duodenal cytochrome b SNP 1. rs12476341 2. rs13009270 3. rs13392902	CYBRD1	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant		
Endothelin receptor type A SNP 1. rs5333 2. rs5335 3. rs5342 4. rs1801708 5. rs6537484 6. rs6812093 7. rs6841799 8. rs10008744 9. rs10305860	ET_A	Genetic - SNP	Blood	57, 120	1. Non-significant 2. Significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant 9. Non-significant	57	1. Non-significant 2. Non-significant 4. Non-significant
Endothelin receptor type B SNP 1. rs5351 2. rs3027111 3. rs3818416 4. rs4885491 5. rs4885493 6. rs9574124	ET_B	Genetic - SNP	Blood	57, 120	1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant	57	1. Non-significant 3. Non-significant
Endothelin-1 SNP 1. rs5369 2. rs5370 3. rs5371	ET1	Genetic - SNP	Blood	57, 120	1. Non-significant 2. Non-significant 3. Non-significant	57	2. Non-significant

4. rs1476046 5. rs1626492 6. rs1800541 7. rs2070699 8. rs2071943 9. rs3087459 10. rs6912834					4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant 9. Non-significant 10. Non-significant		6. Non-significant 7. Non-significant
Epoxyeicosatrienoic acid metabolic pathway SNP 1. CYP2C8 SNP rs1058930 g.16136C>G Ile264Met 2. CYP2J2 SNP rs1155002 g.30354600T>G	EET SNP CYP2C8 CYP2J2	Genetic - SNP	Blood & CSF	98	1. Significant 2. Significant		
Factor V Leiden SNP G1691A	FV Leiden	Genetic - SNP	Blood	155	Non-significant		
Feline Leukemia Virus Subgroup C Receptor SNP 1. rs963328 2. rs6674933 3. rs7553536 4. rs12404754	FLVCR1	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant		
Mitochondrial ferritin SNP rs1560550	FTMT	Genetic - SNP	Blood	12	Non-significant		
Ferrochelatase SNP 1. rs317806 2. rs317807 3. rs492274 4. rs533952 5. rs1041951 6. rs1736439 7. rs1788002 8. rs2269219 9. rs8095390 10. rs12454808 11. rs12969847	FECH	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant 9. Non-significant 10. Non-significant 11. Non-significant		
Frataxin SNP 1. rs1411675 2. rs2498432 3. rs3793451 4. rs4069737 5. rs7847872 6. rs7851458 7. rs7870295 8. rs7871596	FXN	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant		

9. rs10126006 10. rs10869867 11. rs11145194 12. rs11790543 13. rs12001326					9. Non-significant 10. Non-significant 11. Non-significant 12. Non-significant 13. Non-significant		
Glutaredoxin 5 SNP 1. rs716315 2. rs1007813 3. rs4905335 4. rs10131473	GLRX5	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant		
Heme-oxygenase 1 SNP 1. rs2269533 2. rs2285112 3. rs5995097	HMOX1	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant		
Heme-oxygenase 2 SNP rs2160567	HMOX2	Genetic - SNP	Blood	12	Non-significant		
Hemoglobin scavenger receptor SNP 1. rs3210140 2. rs6488336 3. rs6488338 4. rs7487755 5. rs7954492 6. rs10743939 7. rs10845265 8. rs11054074 9. rs12304718	CD163	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant 9. Non-significant		
Hemopexin SNP rs2035675	HPX	Genetic - SNP	Blood	12	Non-significant		
Hepcidin antimicrobial peptide gene SNP 1. rs7251432 2. rs10421768	HAMP	Genetic - SNP	Blood	11	1. Non-significant 2. Non-significant		
Hephaestin SNP 1. rs1264215 2. rs6624875 3. rs12689282	HEPH	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant		
High-mobility group box 1 SNP rs2249825 3814C>G	HMGB1	Genetic - SNP	Blood	72	Non-significant	72	Significant
Human hemochromatosis protein SNP 1. rs707889 2. rs1800562 3. rs2071303	HFE	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant		
Iron responsive element binding protein 2 SNP	IREB2	Genetic - SNP	Blood	12			

1. rs924840 2. rs8041628 3. rs11636431 4. rs16969899 5. rs17483721					1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant		
Low-density lipoprotein receptor related protein SNP 1. rs1799986 2. rs2306692 3. rs4759277 4. rs7975818 5. rs10876966	LRP1	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant		
Methylenetetetrahydrofolate reductase SNP C677T	MTHFR	Genetic - SNP	Blood	155	Non-significant		
Endothelial Nitric oxide synthase SNP 1. 27VNTR 2. G894T	eNOS SNP	Genetic - SNP	Blood	185	1. Non-significant 2. Non-significant		
Endothelial Nitric oxide synthase SNP rs2070744 T-786C	eNOS SNP	Genetic - SNP	Blood	74, 185	Inconclusive	74	Significant
Endothelial Nitric oxide synthase SNP rs2070744 T-786C	eNOS SNP	Genetic - SNP	Buccal swab	162	Significant	162	Non-significant
Progesterone receptor membrane SNP 1. rs2428744 2. rs2428757 3. rs5909608	PGRMC1	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant		
Prothrombin SNP rs1799963 G20210A		Genetic - SNP	Blood	155	Non-significant		
Ryanodine Receptor 1 SNP rs35364374 c.6178G>T	RYR1	Genetic - SNP	Blood	73	Non-significant	73	Non-significant
Serine proteinase inhibitor family E member 1 SNP 1. rs6090 G/A 2. rs6092 G/A 3. rs7242 T/G 4. rs2227631 G/A 5. rs2227684 G/A 6. rs1799889 4G/5G 7. rs2227631 + rs1799889 8. rs6092+rs6090+rs2227684+rs7242 9. rs2227631+rs1799889+rs6092+ rs6090+rs2227684+rs7242	SERPINE1	Genetic - SNP	Blood	53, 71	1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant 9. Significant	53, 71	1. Non-significant 2. Non-significant 3. Non-significant 5. Non-significant 7. Significant 8. Non-significant 9. Significant

Solute carrier family 11 member 1 SNP 1. rs2276631 2. rs2695343	SLC11A1	Genetic - SNP	Blood	12	 1. Non-significant 2. Non-significant		
Solute carrier family 25 member 37 SNP (Mitoferrin 1) 1. rs150909 2. rs224446 3. rs224572 4. rs224589 5. rs2269683	SLC25A37	Genetic - SNP	Blood	12	 1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant		
Solute carrier family 40 member 1 SNP (Ferropontin) 1. rs930373 2. rs1123109 3. rs1123110 4. rs1439816 5. rs2304704 6. rs4667287	SLC40A1	Genetic - SNP	Blood	12	 1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant		
Solute carrier family 48 member 1 SNP 1. rs3782908 2. rs4760636	SLC48A1	Genetic - SNP	Blood	12	 1. Non-significant 2. Non-significant		
STEAP3 metalloreductase SNP 1. rs838079 2. rs838083 3. rs838090 4. rs838102 5. rs838103 6. rs865688 7. rs1867749 8. rs1867856 9. rs3769659 10. rs6720040 11. rs10188946 12. rs11694139 13. rs12990907	STEAP3	Genetic - SNP	Blood	12	 1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant 6. Non-significant 7. Non-significant 8. Non-significant 9. Non-significant 10. Non-significant 11. Non-significant 12. Non-significant 13. Non-significant		
Transferrin SNP 1. rs1049296 2. rs1799852 3. rs4241357 4. rs7645538 5. rs8177191	TF	Genetic - SNP	Blood	12	 1. Non-significant 2. Non-significant 3. Non-significant 4. Non-significant 5. Non-significant		

6. rs8177201 7. rs8177224 8. rs8177235 9. rs8177248 10. rs8177277 11. 1rs12493168					6. Non-significant 7. Non-significant 8. Non-significant 9. Non-significant 10. Non-significant 11. Non-significant		
Transferrin receptor 1 SNP 1. rs3933 2. rs3804141 3. rs17788379	TFRC	Genetic - SNP	Blood	12	1. Non-significant 2. Non-significant 3. Non-significant		
Tumor necrosis factor a SNP 863C>A	TNF-α	Genetic - SNP	Blood	141	Non-significant		
Inflammation and Immune system							
CD45+ Hematopoetic cells	CD45+ HSC	Inflam & Immune System	Blood	27	Non-significant		
Calprotectine	S100A8/A9	Inflam. & Immune system	Blood	35	Significant		
C-C Motif Chemokine Ligand 2	CCL2	Inflam. & Immune system	Blood	47	Non-significant		
C-C Motif Chemokine Ligand 5	CCL5	Inflam. & Immune system	Blood	15, 47	Inconclusive		
C-C Motif Chemokine Ligand 5	CCL5	Inflam. & Immune system	CSF	15	Significant		
C-C Motif Chemokine Ligand 7	CCL7	Inflam. & Immune system	Blood	47	Non-significant		
Soluble CD40L ligand	sCD40L	Inflam. & Immune system	Blood	47, 100	Inconclusive	100	Non-significant
C-reactive protein	CRP	Inflam. & Immune system	Blood	35, 43, 75, 76, 131, 132, 136, 141, 146, 154, 175	Inconclusive	31, 37, 55, 65, 132	Significant
high-sensitivity C-reactive protein	hs-CRP	Inflam. & Immune system	Blood	46, 90	Non-significant	90	Non-significant
Erythrocyte sedimentation rate	ESR	Inflam. & Immune system	Blood	154	Non-significant		
E-selectin		Inflam. & Immune system	Blood	76, 151, 176, 193	Inconclusive		
E-selectin		Inflam. & Immune system	CSF	183	Non-significant		
Ficolin-1	FCN1	Inflam. & Immune system	Blood	34, 113	Non-significant	113	Non-significant
Ficolin-1	FCN1	Inflam. & Immune system	CSF	34	Non-significant		
Ficolin-2	FCN2	Inflam. & Immune system	Blood	34, 113	Non-significant	113	Non-significant
Ficolin-2	FCN2	Inflam. & Immune system	CSF	34	Non-significant		
Ficolin-3	FCN3	Inflam. & Immune system	Blood	34, 113	Inconclusive	113	Significant
Ficolin-3	FCN3	Inflam. & Immune system	CSF	34	Non-significant		
Galectin-3	Gal3	Inflam. & Immune system	Blood	45	Non-significant	45	Non-significant
Granulocyte colony-stimulating factor	G-CSF or CSF3	Inflam. & Immune system	Blood	47	Non-significant		
Granulocyte-macrophage colony-stimulating factor	GM-CSF or CSF2	Inflam. & Immune system	Blood	47	Non-significant		
Soluble Growth Stimulation Expressed Gene 2	sST2	Inflam. & Immune system	Blood	41	Significant		
High-mobility group box 1	HMGB1	Inflam. & Immune system	Blood	135	Significant	68	Non-significant

Interleukin-1 receptor antagonist	IL-1Ra	Inflam. & Immune system	Blood	47	Non-significant		
Interleukin-1B	IL-1B	Inflam. & Immune system	Blood	47, 202	Non-significant		
Interleukin-1B	IL-1B	Inflam. & Immune system	CSF	189	Significant		
Interleukin-2	IL-2	Inflam. & Immune system	Blood	47	Non-significant		
Interleukin-5	IL-5	Inflam. & Immune system	Blood	47	Non-significant		
Interleukin-6	IL-6	Inflam. & Immune system	Blood	46, 47, 76, 80, 107, 202	Inconclusive	80	Significant
Interleukin-6	IL-6	Inflam. & Immune system	CSF	27, 97, 142, 189	Inconclusive	170	Significant
Interleukin-6	IL-6	Inflam. & Immune system	MD			103	Significant
Interleukin-8	IL-8	Inflam. & Immune system	Blood	46, 47	Non-significant		
Interleukin-9	IL-9	Inflam. & Immune system	Blood	47	Non-significant		
Interleukin-10	IL-10	Inflam. & Immune system	Blood	47	Non-significant	16	Non-significant
Interleukin-17	IL-17	Inflam. & Immune system	Blood	79	Significant	79	Significant
Interleukin-23	IL-23	Inflam. & Immune system	Blood	79	Non-significant	79	Non-significant
Interferon alpha-2	IFN-a2	Inflam. & Immune system	Blood	47	Non-significant		
Interferon gamma	IFN-y	Inflam. & Immune system	Blood	46, 47	Non-significant		
Interferon gamma-induced protein 10	IP-10 or CXCL10	Inflam. & Immune system	Blood	47	Significant		
Intercellular Adhesion Molecule 1	ICAM-1	Inflam. & Immune system	Blood	46, 76 , 151, 174, 176, 193	Inconclusive		
Intercellular Adhesion Molecule 1	ICAM-1	Inflam. & Immune system	CSF	174	Non-significant		
Functional Lectin complement pathway activity	LCP activity	Inflam. & Immune system	Blood	113	Significant	113	Significant
Leukemia inhibitor factor	LIF	Inflam. & Immune system	Blood	76	Non-significant		
Leukocytes	WBC	Inflam. & Immune system	Blood	28, 51, 52, 69, 76, 90, 94, 136, 141, 151, 154, 168, 175, 193, 201	Inconclusive	31, 37, 65, 90, 94, 134, 147	Inconclusive
L-selectin		Inflam. & Immune system	Blood	151, 193	Significant		
Monocyte lymphocyte function-associated antigen-1	LFA-1	Inflam. & Immune system	Blood			134	Significant
Neutrophil lymphocyte function-associated antigen-1	LFA-1	Inflam. & Immune system	Blood			134	Significant
Lymphocytes		Inflam. & Immune system	Blood	28, 51, 52, 69, 151	Inconclusive		
CD8+CD161+ "Tc17" lymphocytes		Inflam. & Immune system	CSF	27	Significant		
Monocyte macrophage antigen-1	Mac-1	Inflam. & Immune system	Blood			134	Significant
Neutrophil macrophage antigen-1	Mac-1	Inflam. & Immune system	Blood			134	Significant
Macrophage CD163 expression	CD163	Inflam. & Immune system	CSF			62	Non-significant
Macrophage imigration inhibitory factor	MIF	Inflam. & Immune system	CSF	50	Significant		
Macrophage inflammatory protein 1a	MIP-1a	Inflam. & Immune system	Blood	47	Significant		

Macrophage inflammatory protein 1b	MIP-1b	Inflam. & Immune system	Blood	47	Non-significant		
Mannose-binding lectin	MBL	Inflam. & Immune system	Blood	34, 113	Non-significant	113	Non-significant
Mannose-binding lectin	MBL	Inflam. & Immune system	CSF	34	Non-significant		
Matrix metalloproteinase-3	MMP-3	Inflam. & Immune system	Blood			126	Non-significant
Matrix metalloproteinase-9	MMP-9	Inflam. & Immune system	Blood	78	Non-significant	126	Significant
Matrix metalloproteinase-9	MMP-9	Inflam. & Immune system	CSF	27	Non-significant		
Matrix metalloproteinase-9	MMP-9	Inflam. & Immune system	MD	140	Non-significant	103	Non-significant
Pro-matrix metalloproteinase-9	Pro-MMP9	Inflam. & Immune system	MD	140	Significant		
CD45dimCD11b+ Microglia		Inflam. & Immune system	CSF	27	Non-significant		
Monocytes		Inflam. & Immune system	Blood	151	Non-significant		
Activated $CD16_{bright}CD56_{dim}$ *cytotoxic* natural killer cells		Inflam. & Immune system	CSF	84	Significant		
CD3-CD161 + natural killer cells		Inflam. & Immune system	CSF	27	Non-significant		
Netrin-1		Inflam. & Immune system	Blood	44	Non-significant		
Neutrophil/albumin ratio	NAR	Inflam. & Immune system	Blood	8	Significant		
Neutrophil/lymphocyte ratio	NLR	Inflam. & Immune system	Blood	28, 38, 52, 69	Significant	38, 40	Inconclusive
Neutrophil elastase	NE	Inflam. & Immune system	Blood	202	Significant		
Neutrophils		Inflam. & Immune system	Blood	28, 52, 69, 75, 151	Inconclusive		
(Neutrophil/lymphocyte) / (platelet/lymphocyte) ratio	NLR-PLR	Inflam. & Immune system	Blood	69	Significant		
Osteopontin	OPN	Inflam. & Immune system	Blood	59	Significant	59	Significant
Pentraxin 3	PTX3	Inflam. & Immune system	Blood	142	Non-significant		
Pentraxin 3	PTX3	Inflam. & Immune system	CSF	142	Significant		
Periostin	POSTN	Inflam. & Immune system	Blood	43	Significant	45	Non-significant
Platelet-endothelial adhesion molecule	PECAM	Inflam. & Immune system	Blood	193	Non-significant		
Platelet/lymphocyte ratio	PLR	Inflam. & Immune system	Blood	69	Significant		
Procalcitonin	PCT	Inflam. & Immune system	Blood	14	Significant	31, 37	Non-significant
P-selectin		Inflam. & Immune system	Blood	107, 151, 176, 177, 193	Significant		
Monocyte P-selectin glycoprotein ligand-1	PSGL-1	Inflam. & Immune system	Blood			134	Significant
Neutrophil P-selectin glycoprotein ligand-1	PSGL-1	Inflam. & Immune system	Blood			134	Significant
cleaved Receptor for advanced glycation end-products	cRAGE	Inflam. & Immune system	Blood	60	Significant		
soluble Receptor for advanced glycation end-products	sRAGE	Inflam. & Immune system	Blood	54	Significant		
CD3+ T cells		Inflam. & Immune system	CSF	27	Non-significant		
Tenascin-C	TNC	Inflam. & Immune system	Blood	67	Significant		
Tenascin-C	TNC	Inflam. & Immune system	CSF	108	Significant		
Tissue inhibitors of metalloproteinases-3	TIMP-3	Inflam. & Immune system	Blood			126	Non-significant

Tumor necrosis factor a	TNF-α	Inflam. & Immune system	Blood	46, 47, 141, 202	Non-significant		
Tumor necrosis factor a	TNF-α	Inflam. & Immune system	CSF	27, 97, 142	Inconclusive		
Vascular cell adhesion protein 1	VCAM-1	Inflam. & Immune system	Blood	46 , 151, 174, 193	Inconclusive		
Vascular cell adhesion protein 1	VCAM-1	Inflam. & Immune system	CSF	174	Non-significant		
Alkaline phosphotase	AP	Inflam. & Immune system, Vascular tone	Blood	42	Significant	42	Non-significant
Oxidative stress							
8-iso-Prostaglandin F_{2a} (free)	8-iso-PGF_{2a}	Oxidative stress	CSF	150	Significant		
8-iso-Prostaglandin F_{2a} (free + esterified)	8-iso-PGF_{2a}	Oxidative stress	CSF			181	Significant
Bilirubin		Oxidative stress	Blood	35	Non-significant		
Ceruloplasmin	CP	Oxidative stress	CSF	115	Non-significant		
Diacron reactive oxygen metabolites	d-ROMs	Oxidative stress	Blood			117	Significant
Diacron reactive oxygen metabolites	d-ROMs	Oxidative stress	CSF			117	Non-significant
F2-isoprostane	F2-IsoPs	Oxidative stress	Urine	22, 83	Significant		
Ferritin		Oxidative stress	CSF	115	Non-significant		
Gamma-glutanyl transferase	GGT	Oxidative stress	Blood	85	Non-significant		
Pro-Hepcidin		Oxidative stress	CSF	115	Non-significant		
Free Hydroxyeicosatetraenoic acids	HETE	Oxidative stress	CSF	150	Non-significant		
Free Hydroxyoctadecadienoic acids	HODE	Oxidative stress	CSF	150	Non-significant		
Iron		Oxidative stress	Blood	39	Significant		
Iron		Oxidative stress	MD			3	Non-significant
non-transferrin bound Iron	NTBI	Oxidative stress	CSF	115	Significant		
Lactoferrin	LF	Oxidative stress	CSF	115	Non-significant		
Reactive oxygen species	ROS	Oxidative stress	Blood	89	Significant		
Redox-active iron	REDOX-Fe	Oxidative stress	CSF	115	Non-significant		
Total antioxidant capacity	TAC	Oxidative stress	Blood	5	Non-significant		
Total antioxidant capacity	TAC	Oxidative stress	CSF	5	Significant		
Transferrin	TF	Oxidative stress	CSF	115, 199	Inconclusive		
Zinc		Oxidative stress	Blood	29	Significant		
Vascular tone							
20-Hydroxyeicosatetraenoic acid	20-HETE	Vascular tone	CSF	99	Significant		
6-keto-prostaglandin F_{1a}	6-keto-PGF_{1a}	Vascular tone	CSF	209	Non-significant		
Asymmetric dimethyl-arginine	ADMA	Vascular tone	CSF	139	Non-significant		
Big endothelin-1	Big ET-1	Vascular tone	Blood	192	Significant	192, 198	Non-significant
Big endothelin-1	Big ET-1	Vascular tone	CSF			198	Significant
Calcitonin gene-related peptide	CGRP	Vascular tone	CSF	208	Non-significant		
Calcium	Ca	Vascular tone	Blood	161	Non-significant		
Carbon dioxide partial pressure	pCO_2	Vascular tone	Blood			6, 147	Inconclusive
Dihydroxyeicosatetraenoic acid	DHET	Vascular tone	CSF	98	Non-significant		

Endothelin-1	ET1	Vascular tone	Blood	180, 192	Significant	180, 192, 197	Non-significant
Endothelin-1	ET1	Vascular tone	CSF	139, 180, 194	Inconclusive	180	Non-significant
Endothelin-1	ET1	Vascular tone	MD	180	Non-significant	180	Non-significant
Endothelin-1/big endothelin-1 ratio	ET1/big-ET1	Vascular tone	Blood	192	Non-significant	192	Non-significant
Endothelin-1/nitric oxide ratio	ET1/NO	Vascular tone	Blood	123	Non-significant		
Endothelin-converting enzyme 1 activity	ECE-1	Vascular tone	Blood	192	Non-significant	192	Non-significant
Epoxyeicosatrienoic acid	EET	Vascular tone	CSF	98	Non-significant		
Leukotriene C4	LTC4	Vascular tone	CSF	209	Significant		
Magnesium	Mg	Vascular tone	Blood	165, 188, 190	Inconclusive		
Neuropeptide Y	NPY	Vascular tone	Blood	93	Significant		
Neuropeptide Y	NPY	Vascular tone	CSF	208	Non-significant		
Parathyroid hormone	PTH	Vascular tone	Blood	161	Non-significant		
Prostaglandin D2	PGD2	Vascular tone	CSF	209	Significant		
Thromboxane B2	TxB2	Vascular tone	CSF	209	Non-significant		
Adrenomedulin	ADM	Vascular tone	Blood	110	Significant		
Bioactive Adrenomedulin	Bio-ADM	Vascular tone	Blood	4	Significant		
Bioactive Adrenomedulin	Bio-ADM	Vascular tone	CSF	4	Significant		
Volemic status							
Albumin		Volemic status	Blood	28, 35, 51, 96	Inconclusive		
Aldosterone		Volemic status	Blood	204	Non-significant		
Antidiuretic hormone	ADH	Volemic status	Blood	204	Non-significant		
Atrial natriuretic peptide	ANP	Volemic status	Blood	204	Non-significant		
Atrial natriuretic peptide	ANP	Volemic status	CSF	208	Non-significant		
Brain natriuretic peptide	BNP	Volemic status	Blood	186	Significant	133, 148	Significant
Copeptin	CP	Volemic status	Blood	146	Significant		
Renin		Volemic status	Blood	204	Non-significant		
Sodium		Volemic status	Blood	1, 28, 35, 116, 129, 137, 167, 191, 204	Inconclusive	71, 116, 145, 147	Significant
Sodium		Volemic status	Urine	121, 167, 204	Inconclusive		
Other							
Soluble Endoglin	sEng	Angiogenesis	Blood			82, 143	Significant
Soluble Endoglin	sEng	Angiogenesis	CSF			82	Non-significant
Soluble Fms-like tyrosine kinase 1	sFlt-1	Angiogenesis	Blood			82	Non-significant
Soluble Fms-like tyrosine kinase 1	sFlt-1	Angiogenesis	CSF			82	Non-significant
Thrombospondin-1	TSP-1	Angiogenesis	Blood	101, 131	Inconclusive	101	Non-significant
Hematocrit	Ht	Blood viscosity	Blood	35, 138, 201	Non-significant	147	Non-significant
Cardiac troponin 1	cTnI	Cardiac	Blood			133	Non-significant
Creatine kinase-myoglobin binding	CK-MB	Cardiac	Blood	200	Non-significant		
Heart-Fatty acid-binding protein	H-FABP	Cardiac	CSF	130	Non-significant	130	Non-significant

Glucose		Cerebral metabolism	MD	187	Non-significant	21	Significant
Lactate		Cerebral metabolism	MD	114, 187	Significant		
Lactate/pyruvate ratio	LPR	Cerebral metabolism	MD	114, 187	Inconclusive	21, 26	Significant
Estradiol	E1	Gender	Blood	102	Significant		
Estrone	E1	Gender	Blood	102	Significant		
Fibroblast growth factor 2	FGF-2	Growth factors	Blood	47	Non-significant		
Platelet derived growth factor AA	PDGF-AA	Growth factors	Blood	47	Non-significant		
Platelet derived growth factor AB/BB	PDGF-ABBB	Growth factors	Blood	47	Significant		
Transforming growth factor a	TGF-a	Growth factors	Blood	47	Non-significant		
Transforming growth factor B1	TGF-B1	Growth factors	Blood			143	Non-significant
Vascular endothelial growth factor	VEGF	Growth factors	CSF	27	Non-significant		
Apolipoprotein A1	ApoA	Lipid metabolism	Blood	131	Significant		
Total cholesterol	TC	Lipid metabolism	Blood	51	Significant	32, 134	Non-significant
Fatty acid–binding protein 4	FABP4	Lipid metabolism	Blood	13	Significant		
High-density lipoprotein	HDL	Lipid metabolism	Blood			32	Significant
Low-density lipoprotein	LDL	Lipid metabolism	Blood			32	Non-significant
Triglycerides	TG	Lipid metabolism	Blood	94	Non-significant	32, 94	Non-significant
Base excess	BE	Metabolism	Blood			147	Non-significant
Hydrogencarbonate	HCO_3^-	Metabolism	Blood			147	Non-significant
Lactate		Metabolism	Blood			95, 147	Non-significant
pH	pH	Metabolism	Blood			147	Non-significant
Glycated Hemoglobin	HbA1C	Metabolism	Blood	7, 77	Inconclusive	77	Non-significant
Hemoglobin	Hb	Oxygen-carrying capacity	Blood	20, 28, 35, 56, 69, 106, 152, 159	Significant	61, 147, 152	Inconclusive
Hemoglobin	Hb	Oxygen-carrying capactiy	CSF	115	Non-significant		
Oxygen partial pressure	pO_2	Oxygen-carrying capacity	Blood			147	Non-significant
Red blood cells	RBC	Oxygen-carrying capacity	Blood	151	Non-significant	134	Non-significant
Red cell distribution width	RCDW	Oxygen-carrying capacity	Blood	28	Non-significant		
Cortisol		Stress response	Blood	123, 125, 156	Significant		
Free Cortisol		Stress response	Blood	123	Significant		
Cortisol-binding globulin	CBG	Stress response	Blood	123	Non-significant		
Glucose	BG	Stress response	Blood	28, 35, 69, 77, 94, 119, 160, 184	Inconclusive	65, 77 , 94, 95, 118, 134, 147, 184	Inconclusive
Glucose/potassium ratio		Stress response	Blood			65	Significant
Potassium		Stress response	Blood	35	Non-significant	65 , 147	Inconclusive
Adrenocorticotropic hormone	ACTH	Stress response	Blood	123	Non-significant		
Leptin		Nutrition	Blood	9	Non-significant		
Leptin		Nutrition	CSF	9	Non-significant		
circulatory Dipeptidyl peptidase 3	cDPP3	Other	Blood	10	Significant		

Hyaluranidase	Hyal	Other	Blood	[164]	Non-significant		
Hypocretin-1		Other	CSF	[182]	Significant		
Pituitary adenylate cyclase-activating polypeptide	PACAP	Other	Blood	[92]	Significant		
Pituitary polypeptide 7B2	7B2	Other	CSF	[208]	Non-significant		
Total protein		Other	CSF	[182]	Significant		
Urea/creatinine ratio	UCR	Other	Blood	[2]	Significant	[2]	Significant

Biomarker-specific figures of biomarkers of clinical DCI which have been studied by more than one study

Figure S1: ADAM Metallopeptidase with Thrombospondin Type 1 Motif 13 (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Li, 2017[87,†]	31	52	Mean ± SD day 1, 4, 10	↓†	ns†	ns	
Tang, 2015[107, †]	12	46	Mean ± SD day 1, 4, 9	↓†	ns†	ns	
Vergouwen, 2009[158]	11	20	Trend in time during day 2, 4, 7, 10, 14, 17	sign. bigger decrease			

† meta-analysis possible of 2 of 2 studies with measurements on day 1 and 4, see below

Figure S1.1:

Study or Subgroup	DCI Mean	DCI SD	DCI Total	no DCI Mean	no DCI SD	no DCI Total	Weight	Mean Difference IV, Random, 95% CI
9.1.1 Day 1								
Li 2017	32.1	14.6	31	64.4	15.5	52	25.7%	-32.30 [-38.95, -25.65]
Tang 2015	29.8	14.6	12	63.1	17.4	46	24.9%	-33.30 [-42.97, -23.63]
Subtotal (95% CI)			**43**			**98**	**50.6%**	**-32.62 [-38.10, -27.14]**
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%								
Test for overall effect: Z = 11.67 (P < 0.00001)								
9.1.2 Day 4								
Li 2017	56.3	15.6	31	57.9	14.6	52	25.7%	-1.60 [-8.38, 5.18]
Tang 2015	65.9	19.6	12	59.6	22	46	23.8%	6.30 [-6.48, 19.08]
Subtotal (95% CI)			**43**			**98**	**49.4%**	**0.41 [-6.33, 7.16]**
Heterogeneity: Tau² = 3.96; Chi² = 1.15, df = 1 (P = 0.28); I² = 13%								
Test for overall effect: Z = 0.12 (P = 0.90)								

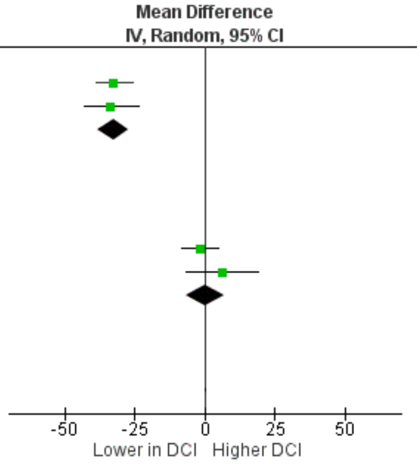

Figure S2: Albumin (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Liu, 2020[28]	224	663	DCI in hypoalbuminemia & no hypoalbuminemia in pre-operative levels (threshold: unknown)	↑DCI in hypo-			
Wang, 2020[35]	19	39	Levels <48h	ns			
Qi, 2019[51]	53	199	Mean (SD) <24h	ns*			
Behrouz, 2016[96]	54	88	% DCI in hypoalbuminemia & normal albumin at admission (threshold: 3.4)	ns			

Figure S3: C-C Motif Chemokine Ligand 5 (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Chaudhry, 2020[15]	28	52	Median (IQR) on day 1 and 7	ns	ns		
Ahn, 2019[47]	14	46	Median (IQR) <24h, 24-48h, 3-5 and 6-8 days	ns/↑*	↑*/ns		

Figure S4: ***soluble*** **CD40 ligand** (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Ahn, 2019[47]	14	46	Median (IQR) <24h, 24-48h, 3-5 and 6-8 days	ns	ns		
Chen, 2015[100]	36	84	Levels at admission	significa nt			

Figure S5: Cortisol (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
July, 2013[123]	29	15	Mean (SD) pre-operative and post-operative day 2, 4, 7, 10	↑*			
Lanterna, 2013[125]	12	14	% DCI in hypo- & normocortisolism between day 1-15 (threshold: 10)	ns			
			Mean on day 5		↑		
Vergouwen, 2010[156]	11	20	Trend in time during day 2, 4, 7, 10, 14, 17	↑			

Figure S6: C-reactive protein (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Wang, 2020[35]	19	39	Levels <48h	ns*			
Kanamaru, 2019[43]	16	93	Mean (SEM) on day 1-3, 4-6, 7-9, 10-12 after onset	ns	ns	ns	
Chamling, 2017[76]	16	65	Mean <24h	↑*			
			Maximum during day 0, 1, 4, 7, 10, 14	maximum: ns*			
Frontera, 2017[75]	?	?	Levels at 0-24, 24-48 & 48-72h	ns			
Nyquist, 2013[131]	14	14	Antibody array by ELISA on day (0-3)	↑			
Jeon, 2012[136]	26	65	Mean (SD) levels pre-operative and post-operative day (1-2) & (3-7)	↑*/ns	↑		
Juvela, 2012[132]	no DCI: 132 RIND[1]: 17 FIND[1]: 29		Mean (SD) at admission, after surgery (mean day 2), at discharge (mean day 10)	ns		ns	
Zhu, 2011[146]	131	172	Mean at admission	ns*			
Beeftink, 2011[141]	10	57	% DCI in high & low mean levels of day 0-12 (threshold: median)	↑DCI in high CRP*			
			% DCI in high & low mean levels of day 0-21 (threshold: median)	ns*			
Kasius, 2010[154]	11	40	Levels <72h	ns*			
			Difference "before → after DCI onset" vs. paired samples in non-DCI	ns difference during DCI onset			
Rothoerl, 2006[175]	37	51	Mean on day 1-8	ns	ns/↑		

[1] RIND: reversible ischemic neurological deficit, FIND: fixed ischemic neurological deficit

Figure S7: *high-sensitivity* **C-reactive protein** (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Rasmussen, 2019[46]	24	65	Mean (95% C.I.) on day 3 and 8.	ns	ns		
			Ratio day 8/3	ns			
Srinivasan, 2016[90]	94	152	Mean (SD) levels at admission	ns			

Figure S8: D-dimer (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Liu, 2020[28]	224	663	Pre-operative levels	ns			
Wang, 2020[35]	19	39	Levels <48h	ns			
Fukuda, 2017[86]	24	163	Median (IQR) at admission	ns			
Zhu, 2011[146]	131	172	Mean (SD) at admission	ns*			
Tseng, 2007[166]	14	66	Mean (SD) day 6 decrease	sign. bigger decrease			
Juvela, 2006[173]	37	99	Median (IQR) after surgery & at discharge	ns		↑	
Fuji, 1997[201]	18	99	Mean (SD) on day 0, 3, 6, 14, 30	ns/↑	ns		↑/ns

Figure S9: Endothelin-1 (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Kastner, 2005[180]	7	13	Medians day 1-8	ns	ns		
Juvela, 2002[192]	13	37	Mean (SD) at admission, after surgery (mean day 2) and at discharge (mean day 10)	↑*		↑*	

Figure S10: Endothelin-1 (CSF)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI Day 0-3	Day 4-8	Day 9-13	Day ≥14
Jung, 2012[139]	4	20	Mean (SD) on day 0-14	ns	ns	ns	ns
Kastner, 2005[180]	7	13	Medians on day 1-8	ns	ns		
Mascia, 2001[194]	4	16	Levels on day 1, 4, 7	ns	ns/↑		

Figure S11: Endothelin-1 SNP rs1800541

Study	DCI	no DCI	Comparison	**Results** DCI per allele Day 0-3	Day 4-8	Day 9-13	Day ≥14
Griessenauer 2018[57]	34	115	T/G alleles	ns (all days)			
Gallek, 2013[120]	113	122	genotype TT/GT/GG	ns			

Figure S12: Endothelin-1 SNP rs2070699

Study	DCI	no DCI	Comparison	**Results** DCI per allele Day 0-3	Day 4-8	Day 9-13	Day ≥14
Griessenauer 2018[57]	34	115	G/T alleles	ns (all days)			
Gallek, 2013[120]	113	122	GG/TT/GT alleles	ns			

Figure S13: E-selectin (blood)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI Day 0-3	Day 4-8	Day 9-13	Day ≥14
Chamling, 2017[76]	16	65	Maximum during day 0, 1, 4, 7, 10, 14	maximum: ns* (all days)			
Wang, 2011[151]	7	14	Median (IQR) <24h	ns			
			Difference "before → after DCI" vs. paired samples in non-DCI	sign. bigger increase during DCI onset (all days)			
Frijns, 2006[176]	12	55	DCI in high & low levels <72h (threshold 41.5)	ns*			
Nissen, 2001[193]	13	23	Mean (SE) of means during hospitalization	ns (all days)			

Figure S14: F2-isoprostane (urine)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI Day 0-3	Day 4-8	Day 9-13	Day ≥14
Wisniewski, 2020[22]	19	19	Mean on day 3	↑			
			Mean and peak of day 2-6	ns (day 0-8)			
Wisniewski, 2017[83]	9	11	Mean on day 3	↑			
			Mean and peak of day 2-6	ns (day 0-8)			

Cohorts were independent

Figure S15: Fibrinogen (blood)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI Day 0-3	Day 4-8	Day 9-13	Day ≥14
Zhang, 2021[8]	84	355	Median (IQR) at admission	ns			
Wang, 2020[35]	19	39	Levels <48h	ns			
Tseng, 2007[166]	14	66	Mean increase from admission to day 3	sign. bigger increase (day 0-8)			
Fuji, 1997[201]	18	99	Mean (SD) on day 0, 3, 6, 14, 30	ns/↑	↑		ns

Figure S16: Ficolin-1 (blood)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI Day 0-3	Day 4-8	Day 9-13	Day ≥14
Matzen, 2020[34]	13	20	Mean (SD) per day, day 0-9 after SAH	ns	ns	ns	
			Trend in time from day 0 – 9 after SAH	ns* (day 0-13)			
Zanier, 2014[113]	14	25	Median (IQR) of early (day 1-3, median: 2) and late (day 4-14, median: 7) sample	ns	ns (day 4-13)		

Figure S17: Ficolin-2 (blood)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI Day 0-3	Day 4-8	Day 9-13	Day ≥14
Matzen, 2020[34]	13	20	Mean (SD) per day, day 0-9 after SAH	ns	ns	ns	
			Trend in time from day 0 – 9 after SAH	ns* (day 0-13)			
Zanier, 2014[113]	14	25	Median (IQR) of early (day 1-3, median: 2) and late (day 4-14, median: 7) sample	ns	ns (day 4-13)		

Figure S18: Ficolin-3 (blood)

Results DCI compared to no DCI

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Matzen, 2020[34]	13	20	Mean (SD) per day, day 0-9 after SAH	ns/↑	↑/ns	ns	
			Trend in time from day 0 – 9 after SAH	ns*			
Zanier, 2014[113]	14	25	Median (IQR) of early (day 1-3, median: 2) and late (day 4-14, median: 7) sample	ns	↓		

Figure S19: Glucose (blood)

Results DCI compared to no DCI

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Liu, 2020[28]	224	663	% DCI in high & low pre-operative levels (threshold: 6.1)	ns			
Wang, 2020[35]	19	39	Levels <48h	ns			
Beseoglu, 2017[77]	36	51	Relative risk for DCI in hyperglycemia vs. no hyperglycemia <72h (threshold: 7.9)	ns			
Tao, 2017[69]	47	200	Median (IQR) <24h	↑*			
Mijiti, 2016[94]	99	244	% DCI in high & low levels at admission (threshold: 7.0)	ns*			
Bian, 2013[119]	34	194	% DCI in patients with increasing and decreasing glucose between admission and day 14	ns			
Kruyt, 2008[160]	86	169	% DCI in high & low glucose <48h (threshold: median)	ns*			
			% DCI in high & low mean fasting glucose in the first week (threshold: median)	↑*			
Juvela, 2005[184]	No DCI: 128 RIND*: 17 FIND*: 29		Mean (SD) at admission & after surgery (mean day 1.9)	ns			

Figure S20: Haptoglobin 1-1 polymorphism

Study or Subgroup	Hp1-1 Events	Hp1-1 Total	Hp2-1/2-2 Events	Hp2-1/2-2 Total	Weight	Odds Ratio M-H, Random, 95% CI
Kim 2018	3	12	35	75	38.7%	0.38 [0.10, 1.52]
Leclerc 2015	3	11	19	63	36.1%	0.87 [0.21, 3.64]
Ohnishi 2013	2	7	20	88	25.2%	1.36 [0.25, 7.55]
Total (95% CI)		**30**		**226**	**100.0%**	**0.71 [0.30, 1.67]**
Total events	8		74			

Heterogeneity: Tau² = 0.00; Chi² = 1.41, df = 2 (P = 0.49); I² = 0%
Test for overall effect: Z = 0.79 (P = 0.43)

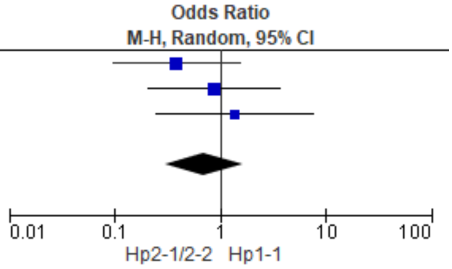

Figure S21: Haptoglobin 2-1 polymorphism

Study or Subgroup	Hp2-1 Events	Hp2-1 Total	Hp1-1/2-2 Events	Hp1-1/2-2 Total	Weight	Odds Ratio M-H, Random, 95% CI
Kim 2018	14	36	24	51	42.4%	0.72 [0.30, 1.70]
Leclerc 2015	9	39	13	35	31.1%	0.51 [0.18, 1.40]
Ohnishi 2013	5	39	17	56	26.4%	0.34 [0.11, 1.01]
Total (95% CI)		**114**		**142**	**100.0%**	**0.53 [0.30, 0.93]**
Total events	28		54			

Heterogeneity: Tau² = 0.00; Chi² = 1.12, df = 2 (P = 0.57); I² = 0%
Test for overall effect: Z = 2.22 (P = 0.03)

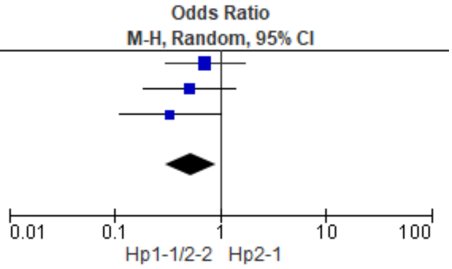

Figure S22: Haptoglobin 2-2 polymorphism

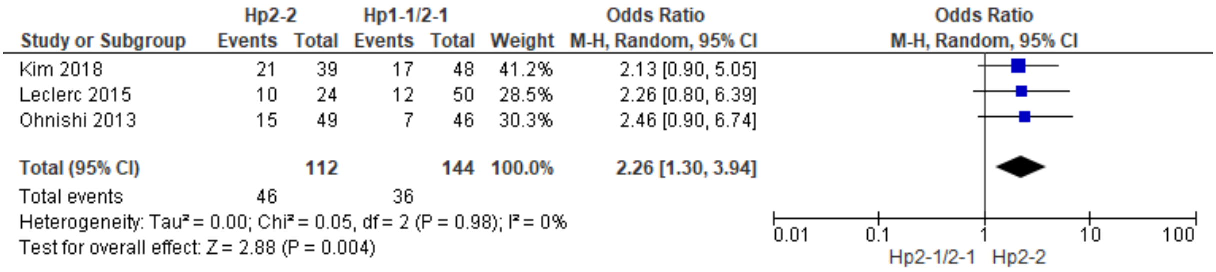

Figure S23: Hematocrit (blood)

Study	DCI	no DCI	Comparison	Results DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Wang, 2020[35]	19	39	Levels <48h	ns			
Watanabe, 2012[138]	6	34	Mean (SEM) on 2 days pre-DCI, 1 day pre-DCI and day of DCI-onset[1]	ns			
Fuji, 1997[201]	18	99	Mean (SD) on day 0, 3, 6, 14, 30	ns	ns		ns

[1] day of DCI-onset is used for both the DCI and no DCI group, calculated by the mean day of DCI occurrence

Figure S24: Hemoglobin (blood)

Study	DCI	no DCI	Comparison	Results DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Liu, 2020[28]	224	663	Pre-operative levels	ns			
Wang, 2020[35]	19	39	Levels <48h	ns			
Park, 2020[20]	18	34	Mean (SD), timing of measurement unknown	ns			
Ayling. 2018[56]	72	303	% DCI in high or low levels on day 1-3 and day 5-9. Threshold: 10 g/dL.	↑DCI in low	↑DCI in low		
Tao, 2017[69]	47	200	Median (IQR) <24h	ns			
Sun, 2015[106]	78	140	% DCI in mean (post-operative to day 21) levels categorized into ≤11, 11-12, 12-13, >13	Hb-group 11-12: significantly lower risk on DCI compared to other Hb groups			
Naidech, 2010[152]	10	34	% DCI in goal level ≥11.5 and ≥10, day 0-13	ns			
Oddo, 2009[159]	8	12	Mean (SD) of day (1-7)	↓			

Figure S25: *glycated* Hemoglobin (blood)

Study	DCI	no DCI	Comparison	Results DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Park, 2021[7]	47	463	% DCI in high & low levels at admission (threshold: 6.0%)	↑			
Beseoglu, 2017[77]	36	51	% DCI in high & low levels <72h (threshold: 39 mmol/mol)	ns			

Figure S26: Intercellular Adhesion Molecule 1 (blood)

Study	DCI	no DCI	Comparison	Results DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Rasmussen, 2019[46]	24	65	Mean (95% C.I.) on day 3 and 8.	ns	ns		
			Ratio day 8/3	ns			
Chamling, 2017[76]	16	65	Levels <24h	ns			
			Delta (maximum – baseline) value of day 0-14	delta: ↓*			
Wang, 2011[151]	7	14	Median (IQR) <24h	↓			
			Difference "before → after DCI" vs. paired samples in non-DCI	ns difference during DCI onset			
Frijns, 2006[176]	12	55	DCI in high & low levels <72h (threshold 376.5)	ns*			
Rothoerl, 2006[174]	5	10	Mean level on day 1-9	ns	ns	ns	
			Maximum level during day 1-9	maximum: ns			
Nissen, 2001[193]	13	23	Mean (SE) of means during hospitalization	ns			

Figure S27: Interferon gamma (blood)

Study	DCI	no DCI	Comparison	Results DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Rasmussen, 2019[46]	24	65	Mean (95% C.I.) on day 3 and 8.	ns	ns		
			Ratio day 8/3	ns			
Ahn, 2019[47]	14	46	Median (IQR) <24h, 24-48h, 3-5 and 6-8 days	ns	ns*		

Figure S28: Interleukin-1B (blood)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Ahn, 2019[47]	14	46	Median (IQR) <24h, 24-48h, 3-5 and 6-8 days	ns	ns		
Hirashima, 1997[202]	9	12	Mean (SD) on day 0-4, 5-9, 10-14	ns	ns	ns	

Figure S29: Interleukin-6 (blood)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Rasmussen, 2019[46]	24	65	Mean (95% C.I.) on day 3 and 8.	ns	ns		
			Ratio day 8/3	ns			
Ahn, 2019[47]	14	46	Median (IQR) <24h, 24-48h, 3-5 and 6-8 days	ns	ns		
Chamling, 2017[76]	16	65	Levels <24h	↓*			
			Maximum and delta (maximum – baseline) value of day 0-14	maximum: ns, delta: ns			
Chaudhry, 2017[80]	28	52	Mean (SE) on day 1, 3, 5, 7, 9, 11, 13	ns/↑*	↑*	↑*	
Tang, 2015[107]	12	46	Mean (SD) on day 1, 4, 9	↑	ns	ns	
Hirashima, 1997[202]	9	12	Mean (SD) on day (0-4), (5-9), (10-14)	ns	ns	ns	

Figure S30: Interleukin-6 (CSF)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Roa, 2020[27]	5	8	Mean (SEM) on day (0–1), (2–4), (5–9) and >10	ns	ns	ns	ns
Wu, 2016[97]	27	30	Mean (SD) on day 2	↑			
Zanier, 2011[142]	14	16	Levels during ICU-admission	ns			
Hendryk, 2004[189]	8	7	Mean (SD) at day (0-3), (4-7), (8-15)	↑	ns	ns	

Figure S31: Interleukin-8 (blood)

Study	DCI	no DCI	Comparison	Results DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Rasmussen, 2019[46]	24	65	Mean (95% C.I.) on day 3 and 8.	ns	ns		
			Ratio day 8/3	ns			
Ahn, 2019[47]	14	46	Median (IQR) <24h, 24-48h, 3-5 and 6-8 days	ns	ns		

Figure S32: Lactate (microdialysate

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Radolf, 2014[114]	8	10	Median on day 1-11	ns	↑/ns	ns	
			Variance on day 8-11		↑*		
Sarrafzadeh, '04[187]	10	3	Mean (SD) of 3 day medians	ns			

Figure S33: Lactate/pyruvate ratio (microdialysate)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI: Day 0-3	Day 4-8	Day 9-13	Day ≥14
Radolf, 2014[114]	8	10	Median on day 1-11	ns	ns	ns	
Sarrafzadeh, '04[187]	10	3	Mean (SD) of 3 day medians	↑			

Figure S34: Leukocytes (blood)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI Day 0-3	Day 4-8	Day 9-13	Day ≥14
Liu, 2020[28]	224	663	Pre-operative levels	↑			
Qi, 2019[51]	53	199	Mean (SD) <24h	ns*			
Wu, 2019[52]	43	79	Mean (SD) <72h	ns*			
			DCI in high vs low levels (threshold: 11.5*10^9/L)	↑*			
Tao, 2017[69]	47	200	Mean (SD) <24h	ns			
Chamling, 2017[76]	16	65	Levels <24h	↑*			
			Delta (maximum – baseline) value of day 0-14	delta: ns*			
Mijiti, 2016[94]	99	244	% DCI in high & low levels at admission (threshold: 11.0x10^9)	↑DCI in high*			
Srinivasan,2016[90]	94	152	Mean (SD) at admission	↑			
Jeon, 2012[136]	26	65	Mean (SD) levels on pre-operative and post-operative day 0 & (1-2)	↑/ns			
Beeftink, 2011[141]	10	57	DCI in high & low mean levels mean levels of day 0-12 and 0-21 (threshold: median)	ns*			
Wang, 2011[151]	7	14	Median (IQR) <24h	↑			
Kasius, 2010[154]	11	40	Levels <72h	ns*			
			Difference "before → after DCI onset" vs. paired samples in non-DCI	sign. bigger increase during DCI onset			
Oh, 2007[168]	46	112	% with leukocytosis (WBC>11.000) in DCI vs. no DCI on admission & POD 1,3,5,7	↑*/ns	ns		
			% with severe leukocytosis (WBC>15.000) in DCI & no DCI on POD 7		ns		
Rothoerl, 2006[175]	37	51	Mean on day 1-8	↑/ns	↑/ns		
Nissen, 2001[193]	13	23	Mean (SE) of means during hospitalization	ns			
Fuji, 1997[20]	18	99	Mean (SD) on day 0, 3, 6, 14, 30	ns	ns		ns

POD: post-operative day

Figure S35: L-selectin (blood)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI Day 0-3	Day 4-8	Day 9-13	Day ≥14
Wang, 2011[151]	7	14	Median (IQR) <24h	↑			
			Difference "before → after DCI" vs. difference in paired samples in non-DCI	sign. bigger increase during DCI onset			
Nissen, 2001[193]	13	23	Mean (SE) of means during hospitalization	↓			

Figure S36: Lymphocytes (blood)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI Day 0-3	Day 4-8	Day 9-13	Day ≥14
Liu, 2020[28]	224	663	Pre-operative levels	ns			
Qi, 2019[51,†]	53	199	Mean (SD) <24h	ns*			
Wu, 2019[52]	43	79	Mean (SD) <72h	ns*			
			DCI in high vs low levels (threshold: 1.5*10^9/L)	ns*			
Tao, 2017[69,†]	47	200	Mean (SD) <24h	↓*			
Wang, 2011[151]	7	14	Median (IQR) <24h	↑			

Figure S37: Magnesium (blood)

Study	DCI	no DCI	Comparison	**Results** DCI compared to no DCI Day 0-3	Day 4-8	Day 9-13	Day ≥14
Dorhout Mees, 2007[165]	27	128	Mean (SD) of day 4 to 20/discharge		ns		
			Mean (SD) "latest before DCI"-levels	latest before DCI: ns			
	% DCI per quartile of "latest before DCI"-levels in mmol/L): 1) ≥1.10≤1.28, 2) ≥1.28 ≤1.40, 3) >1.40 ≤1.62, 4) >1.62.			↑DCI in Q1*			
Collignon, 2004[188]	55	72	Admission levels	ns			
	Mean, minimum and maximum during day (0-4), (4-14), (>14)			mean, minimum and maximum: ns			
	% DCI per hypo- & normo- and hypermagnesemia (threshold: 1.7 and 2.1 mg/dL) during hospitalization			ns			
Van den Bergh, 2003[190]	20	69	% DCI per hypo- & normomagnesemia <48h and between day 2-12 (threshold: 0.70 mmol/L)	ns*	↑DCI in hypo*		

Figure S38: Mannose-binding lectin (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Matzen, 2020[34]	13	20	Mean (SD) per day, day 0-9 after SAH	ns	ns	ns	
			Trend in time from day 0 – 9 after SAH	ns*			
Zanier, 2014[113]	14	25	Median (IQR) of early (day 1-3, median: 2) and late (day 4-14, median: 7) sample	ns	ns		

Figure S39: Mean platelet volume (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Zhang, 2021[8]	84	355	Median (IQR) at admission	ns			
Chen, 2020[30]	58	139	Median (IQR) on day (1-3), (3-5), (5-7), (7-9)	↑	↑*	↑	
Rzeplinski, 2020[23]	8	29	Levels at admission	ns			

Figure S40: Mean platelet volume/platelet count ratio (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Chen, 2020[30]	58	139	Median (IQR) on day (1-3), (3-5), (5-7), (7-9)	↑	ns*/↑	↑	
Rzeplinski, 2020[23]	8	29	Levels at admission	ns			
Ray, 2018[66]	38	131	Admission levels	ns			
			Mean increase from admission to day 3	↑			

Figure S41: Neutrophils (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Liu, 2020[28]	224	663	Pre-operative levels	ns			
Wu, 2019[52]	43	79	Mean (SD) <72h	↑*			
			DCI in high vs low levels (threshold: $7.5*10^9$/L)	ns*			
Tao, 2017[69]	47	200	Mean (SD) <24h	ns			
Frontera, 2017[75]	?	?	Levels at 0-24, 24-48 & 48-72h	ns			
Wang, 2011[151]	7	14	Median (IQR) <24h	↑			

Figure S42: Neutrophil/lymphocyte ratio (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Liu, 2020[28]	224	663	% DCI in high & low pre-operative ratio (threshold: 5.9)	↑DCI in high			
Al-mufti, 2019[38]	202	836	% DCI in high & low admission ratio (threshold: 5.9)	↑DCI in high *			
Wu, 2019[52]	43	79	Mean (SD) <72h	↑*			
Tao, 2017[69]	47	200	Mean (SD) <24h	↑*			

Figure S43: ***endothelial*** **Nitric oxide synthase SNP rs2070744 T-786C**

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results			
Hendrix, 2017[74]	34	115	-	ns			
Khurana, 2004[185]	no VS[#]: 7 as-VS: 10 S-VS: 11		% no/asymptomatic/symptomatic vasospasm per CC/CT/TT	CT and C allele significantly associated with higher rates of symptomatic vasospasm†			

#: no VS: no vasospasm, as-VS: asymptomatic vasospasm, S-VS: symptomatic vasospasm (defined as DCI)

Figure S44: Platelet count (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Liu, 2020[28]	224	663	Pre-operative levels	ns			
Chen, 2020[30]	58	139	Median (IQR) on day (1-3), (3-5), (5-7), (7-9)	ns	ns*/↑	↑	
Wang, 2020[35]	19	39	Levels <48h	ns			
Rzeplinski, 2020[23]	8	29	Levels at admission	ns			
Tao, 2017[69]	47	200	Mean (SD) <24h	ns			
Aggarwal, 2013[128]	39	35	DCI in patients with vs. without absolute thrombocytopenia (<150.000) on day 1 & 7	↑ DCI in trombo-cytopenia day 1, 7			
			DCI in patients with vs. without relative thrombo-cytopenia (<80% of baseline) on day 5, 7, 9		↑ DCI in thrombo-cytopenia day 5, 7, 9		
Jeon, 2012[136]	26	65	Mean (SD) levels pre-operative and post-operative day 0 & (1-2)	ns			
Wang, 2011[151]	7	14	Median (IQR) <24h	ns			
Kasius, 2010[154]	11	36	Levels <72h	ns*			
			Difference "before → after DCI onset" vs. paired samples in non-DCI	ns difference during DCI onset			
Schebesch, 2007[169]	37	55	Mean on day 1-10	ns	ns	ns	
Nissen, 2001[193]	13	23	Mean (SE) of means during hospitalization	↑			
Fuji, 1997[201]	18	99	Mean (SD) on day 0, 3, 6, 14, 30	ns	ns		ns

Figure S45: Prothrombin time (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Liu, 2020[28]	224	663	Pre-operative levels	ns			
Wang, 2020[35]	19	39	Levels <48h	ns			
Fuji, 1997[201]	18	99	Mean (SD) on day 0, 3, 6, 14, 30	ns	ns		ns

Figure S46: P-selectin (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Tang, 2015[107]	12	46	Mean (SD) on day 1, 4, 9	ns	↑	ns	
Wang, 2011[151]	7	14	Median (IQR) <24h	↓			
			Difference "before → after DCI" vs. paired samples in non-DCI	↑ increase during DCI onset			
Frijns, 2006[176,#]	9	58	DCI in high & low levels <72h (threshold: 92.5)	ns*			
Frijns, 2006[177,#]	12	55	Difference "before → after DCI" vs. paired samples in non-DCI	↑ increase during DCI onset			
Nissen, 2001[193]	13	23	Mean (SE) of means during hospitalization	↑			

[#] two studies with overlapping patient cohorts, though different comparison between DCI and no DCI

Figure S47: s-100B (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Bergstrom, 2014[112]	15	32	Mean (SD) on day (0-2), (3-5), (6-8), (9-11), (12-15)	ns	ns	ns/↑	↑
Oertel, 2006[178]	26	25	Mean (SD) of day 1, 2, 3	↓*			

Figure S48: Sodium (urine)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Nakagawa, 2013[121]	13	90	% DCI in groups with/without excess sodium excretion on day 2, 3, 7, 14	ns	ns		ns
Igarashi, 2007[167]	12	55	Mean sodium excretion from 3 days before to 3 days after DCI	DCI-3 to DCI-1: ns DCI to DCI+3: ↑			
			Mean sodium balance (sodium intake – sodium excretion) from 3 days before to 3 days after DCI	DCI-3,-2, +0-2: ns DCI-1,DCI+3: ↓			
Okuchi, 1996[204]	4	13	Mean (SE) sodium balance on POD 1-10	ns	↓/ns	ns	
			Mean negative peak and accumulative sodium balance of day POD 0-10	↓			

POD = postoperative day

Figure S49: Sodium (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Cohen, 2021[1]	142	214	Mean sodium during ICU admission	ns*			
			Mean sodium variability during ICU admission	ns*			
Liu, 2020[28]	224	663	Pre-operative hyponatremia vs no hyponatremia	ns			
Wang, 2020[35]	19	39	Levels <48h	ns			
Beseoglu, 2014[116]	total: 274		Levels every 8h on day 0-5	ns			
Maimaitili, 2013[129,†]	19	30	% DCI per normo- & hyponatriemia on day 1-3 (threshold: 135)	↑DCI in hyponatremia †			
Vrsajkov, 2012[137,†]	39	43	% DCI per normo- & hyponatriemia during hospitalization (threshold: 135)	↑DCI in hyponatremia*†			
Igarashi, 2007[167]	12	55	Difference during 3 days before DCI → day of DCI	ns difference around DCI onset			
Qureshi, 2002[191]	54	244	% DCI in patients with and without hypo- (<135) and hypernatriemia (>145) between admission and day 9	hypo: ns, hyper: ns			
Okuchi, 1996[204]	4	13	Mean (range) of day 1-10	↓			
			Mean (SD) per day on day 1-10	ns	↓/ns	ns/↓	

Figure S50: Tau protein (CSF)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Halawa, 2018[63]	7	12	Mean on day 4, 10		ns	ns	
			Ratio day 10 : day 4		ratio: ↑		
Zanier, 2013[130]	11	24	Acute (<48h) and delayed (>48h) peak	ns			

Figure S51: Thrombin-antithrombin III complex (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Fuji, 1997[201]	18	99	Mean (SD) on day 0, 3, 6, 14, 30	ns	↑		ns
Hirashima, 1997[202]	9	12	Levels at day (5-9)		↑		

Figure S52: Thrombospondin-1 (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Shen, 2015[101]	33	85	Levels at admission	sign.			
Nyquist, 2013[131]	14	14	Levels on day (0-3)	ns			

Figure S53: Tumor necrosis factor a (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Rasmussen, 2019[46]	24	65	Mean (95% C.I.) on day 3 and 8.	ns	ns		
			Ratio day 8/3	ns			
Ahn, 2019[47]	14	46	Median (IQR) <24, 24-48 hours, 3-5 and 6-8 days	ns	ns		
Beeftink, 2011[141]	10	57	DCI in high & low mean levels mean levels of day 0-12 and 0-21 (threshold: median)	ns			
Hirashima, 1997[202]	9	12	Levels at day (0-4), (5-9), (10-14)	ns	ns	ns	

Figure S54: Tumor necrosis factor a (CSF)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Roa, 2020[27]	5	8	Mean (SEM) on day (0–1), (2–4), (5–9) and >10	ns	ns	ns	ns
Wu, 2016[97]	27	30	Mean (SD) on day 2	↑			
Zanier, 2011[142]	14	16	Levels during ICU-admission	ns			

Figure S55: Transferrin (CSF)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Gomes, 2014[115]	7	5	Mean (SE) on day 1, 3 ,5	ns	ns		
Takenaka, 2000[199]	7	13	Mean (SD)	↑ (unknown when measured)			

Figure S56: Vascular cell adhesion protein 1 (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Rasmussen, 2019[46]	24	65	Mean (95% C.I.) on day 3 and 8.	ns	ns		
			Ratio day 8/3	ns			
Wang, 2011[151]	7	14	Median (IQR) <24 hours	↑			
			Difference "before → after DCI" vs. paired samples in non-DCI	ns difference during DCI onset			
Rothoerl, 2006[174]	5	10	Mean level on day 1-9	ns	ns	ns	
			Maximum level during day 1-9	ns			
Nissen, 2001[193]	13	23	Mean (SE) of means during hospitalization	ns			

Results DCI compared to no DCI

Figure S57: von Willebrand Factor (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Li, 2017[87,†]	31	52	Mean (SD) on day 1, 4, 10 (U/mL)	↑	↑	ns	
Tang, 2015[107, †]	12	58	Mean (SD) on day 1, 4, 9 (U/mL)	↑	↑	ns	
Frijns, 2006[176]	12	55	DCI in high & low levels <72h (threshold 93.0)	ns*			
Hirashima, 1997[202]	9	12	Mean (SD) on day (5-9)		↑		

Results DCI compared to no DCI

† meta-analysis possible of 2 of 2 studies with measurements on day 1 and 4, see below.

Figure S57.1:

Study or Subgroup	DCI Mean	DCI SD	DCI Total	no DCI Mean	no DCI SD	no DCI Total	Weight	Mean Difference IV, Random, 95% CI
10.1.1 Day 1								
Li 2017	3.4	1.7	31	2.2	1.5	52	31.9%	1.20 [0.48, 1.92]
Tang 2015	4.8	2.7	12	2.4	2.4	58	21.9%	2.40 [0.75, 4.05]
Subtotal (95% CI)			**43**			**110**	**53.8%**	**1.56 [0.48, 2.64]**
Heterogeneity: Tau² = 0.30; Chi² = 1.71, df = 1 (P = 0.19); I² = 41%								
Test for overall effect: Z = 2.84 (P = 0.005)								
10.1.2 Day 4								
Li 2017	5.3	1.5	31	2.2	1.7	52	32.1%	3.10 [2.40, 3.80]
Tang 2015	5.1	4.5	12	1.7	1.1	58	14.1%	3.40 [0.84, 5.96]
Subtotal (95% CI)			**43**			**110**	**46.2%**	**3.12 [2.44, 3.80]**
Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = 0.82); I² = 0%								
Test for overall effect: Z = 9.04 (P < 0.00001)								

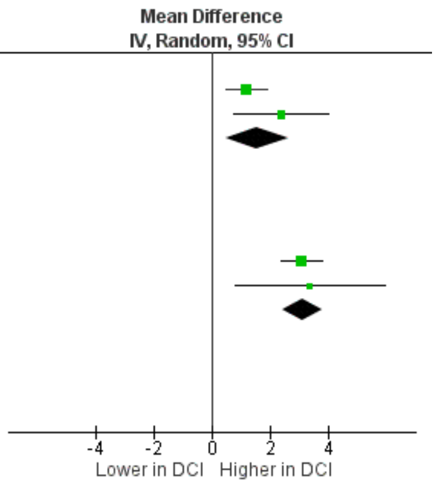

Figure S58: von Willebrand Factor propeptide (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Vergouwen, 2009[158]	11	20	Trend in time during day 2, 4, 7, 10, 14, 17	↑ increase first few days			
Frijns, 2006[176]	12	55	DCI in high & low levels <72h (threshold 7.70)	ns*			

Results DCI compared to no DCI

Biomarkers of radiological DCI which have been studied by more than one study

Figure S59: Big endothelin-1 (blood) — **Results** DCI compared to no DCI

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Juvela, 2002[192]	?	?	Mean (SD) at admission, after surgery and at discharge	ns		ns	
Gruber, 2000[198]	17	27	Mean (SD) of day 0-14	ns			

Figure S60: Brain natriuretic peptide (blood) — **Results DCI compared to no DCI**

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Papanikolaou 2012[133]	12	24	Mean (SE) before repair surgery	↑*			
Taub, 2011[148]	46	73	Quartile analysis of levels after admission, mean day 5.5 ± 3 (top quartile vs other)	↑*			

Figure S61: Carbon dioxide partial pressure (blood) — **Results DCI compared to no DCI**

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Darkwah, 2021[6]	153	480	Mean daily highest and lowest values of day 0-13	lowest: ns, highest: ns			
			% DCI in optimal pCO_2 (30-38) vs. non-optimal pCO_2 (<30/>38) during day 0-13	↑ DCI in non-optimal*			
Nakae, 2011[147]	28	114	Mean (SD), unknown when measured	ns (unknown when measured)			

Figure S62: ***total*** **Cholesterol** (blood) — **Results** DCI compared to no DCI

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Li, 2020[32]	37	38	% DCI in high & low levels at admission (threshold: 160)	ns*			
Yang, 2012[134]	10	10	Mean (SD) <48h	ns			

Figure S63: C-reactive protein (blood) — **Results** DCI compared to no DCI

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Guresir, 2020[37]	22	209	% DCI in high & low levels at admission (threshold: 5)	↑DCI in high			
Hurth, 2020[31]	27	111	Median (IQR) at admission, after treatment, on day 4, 9, 14 after SAH and at discharge from ICU	ns	ns	↑	↑
Matano, 2018[65]	41	292	Mean (SD) at admission	ns			
Hostettler, 2018[55]	186	168	DCI in high & low CRP on day 1 (threshold: 23)	↑DCI in high			
Juvela, 2012[132]	no ischemia: 69 early ischemia: 59 DCI: 50		Mean(SD) no/early/late ischemic lesion at admission, after surgery (mean day 2), at discharge (mean day 10)	ns		ns	

Figure S64: D-dimer (blood) — **Results** DCI compared to no DCI

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
Hurth, 2020[31]	27	111	Median (IQR) at admission, after treatment, day 4, 9 and 14 after SAH and at discharge from ICU	ns	ns	ns	↑
Fukuda, 2017[86]	12	175	Median (IQR) at admission	ns*			
Juvela, 2006[173]	no ischemia: 69 other ischemia: 59 DCI: 37		Median (IQR) of DCI / other ischemia /no ischemia at surgery & at discharge	ns		ns	

Figure S65: *soluble* **Endoglin** (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Griessenauer, 2017[82]	9	18	Mean on day 1, 6	ns	ns		
Dietman, 2011[143]	7	13	Mean(SE) on day 1-7, 9, 11, 13, 15	↓	↓	↓	↓

Figure S66: Endothelin-1 (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Kastner, 2005[180]	7	13	Medians day 1-8	ns	ns		
Juvela, 2002[192]	9	37	Mean (SD) at admission, after surgery and at discharge	ns		ns	
Juvela, 2000[197]	20	35	Mean (SE) day (1-5), (6-14), (15-28)	ns	ns		ns

Figure S67: Glucose (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Matano, 2018[65,†]	41	292	Mean (SD) at admission	↑			
Beseoglu, 2017[77]	14	73	Relative risk for DCI in high vs low glucose <72h (threshold: 7.8 mmol/L)	ns			
Mijiti, 2016[94]	87	256	% DCI per dichotimized glucose at admission (threshold: 7.0 mmol/L)	ns*			
van Donkelaar, 2016[95]	84	201	Median (IQR) maximum level <24h	↑*			
De Rooij, 2013[118]	110	261	Hyperglycemia at admission	ns*			
Yang, 2012[134,†]	10	10	Mean (SD) <48h	ns			
Nakae, 2011[147]	28	114	Mean (SD), timing of measurement unknown	ns (timing unknown)			
Juvela, 2005[184]	No ischemia: 55 Other ischemia: 54 DCI: 46		Mean (SD) at admission and after surgery (mean day 1.9)	ns*/ns			

Figure S68: Hemoglobin (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Cai, 2018[61]	17	43	% DCI in high vs. low "lowest level" (threshold: 10g/dL), timing of measurement unknown	↑ DCI in low (timing unknown)			
Nakae, 2011[147]	28	114	Mean (SD), timing of measurement unknown	ns (timing unknown)			
Naidech, 2010[152]	20	24	% DCI in goal level ≥11.5 and ≥10, day 0-13	ns			

Figure S69: Lactate (blood)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Van Donkelaar, 2016[95]	84	201	Median (IQR) maximum level <24h	ns*			
Nakae, 2011[147]	28	114	Mean (SD), timing of measurement unknown	ns (timing unknown)			

Figure S70: Lactate/pyruvate ratio (microdialysate)

Study	DCI	no DCI	Comparison	Day 0-3	Day 4-8	Day 9-13	Day ≥14
				Results DCI compared to no DCI			
Kofler, 2020[21]	16	35	Levels on day (0-3), (4-7), >7	↑			
			Occurrence of metabolic distress (levels >40) on day (0-3), (4-7), >7	↑			
Torne, 2020[26]	5	16	Hours of lactate pyruvate ratio >40, day 0-13	↑			

Figure S71: Leukocytes (blood)

Results DCI compared to no DCI

Study	**DCI**	**no DCI**	**Comparison**	**Day 0-3**	**Day 4-8**	**Day 9-13**	**Day ≥14**
Guresir, 2020[37]	22	209	% DCI in high vs. low levels at admission (threshold: 12.1)	ns			
Hurth, 2020[31]	27	111	Median (IQR) at admission, after treatment, day 4, 9 and 14 after SAH and at discharge from ICU	ns	ns	ns	ns
Matano, 2018[65,†]	41	292	Mean (SD) at admission	ns			
Mijiti 2016[94]	87	256	% DCI per dichotimized levels at admission (threshold: 11.0x10^9)	↑*			
Srinivasan 2016[90†]	62	184	Mean (SD) at admission	ns*			
Yang 2012[134†]	10	10	Mean (SD) <48h	ns			
Nakae, 2011[147]	28	114	Mean (SD), timing of measurement unknown	ns (timing unknown)			

Results

Figure S72: Neutrophil/lymphocyte ratio (blood)

Results DCI compared to no DCI

Study	**DCI**	**no DCI**	**Comparison**	**Day 0-3**	**Day 4-8**	**Day 9-13**	**Day ≥14**
Giede-Jeppe, 2019[40]	112	217	% DCI in high vs low levels at admission (threshold: 7.05)	ns*			
Al-Mufti, 2019[38]	170	862	% DCI in high vs low levels at admission (threshold: 5.9)	↑ DCI in high			

Figure S73: Platelet count (blood)

Results DCI compared to no DCI

Study	**DCI**	**no DCI**	**Comparison**	**Day 0-3**	**Day 4-8**	**Day 9-13**	**Day ≥14**
Yang, 2012[134]	10	10	Mean(SD) <48h	ns			
Hirashima, 1994[206]	9	23	Minimum during at least 11 days	minimum: ↓			

Figure S74: Potassium (blood)

Results DCI compared to no DCI

Study	**DCI**	**no DCI**	**Comparison**	**Day 0-3**	**Day 4-8**	**Day 9-13**	**Day ≥14**
Matano, 2018[65]	41	292	Mean (SD) at admission	↓			
Nakae, 2011[147]	28	114	Mean (SD), timing of measurement unknown	ns (timing unknown)			

Figure S75: Procalcitonin (blood)

Results DCI compared to no DCI

Study	**DCI**	**no DCI**	**Comparison**	**Day 0-3**	**Day 4-8**	**Day 9-13**	**Day ≥14**
Guresir, 2020[37]	22	209	% DCI in high & low levels at admission (threshold: 0.5)	ns			
Hurth, 2020[31]	27	111	Median (IQR) at admission, after treatment, day 4, 9, 14 after SAH and at discharge from ICU	ns	ns	ns	ns

Figure S76: Sodium (blood)

Results DCI compared to no DCI

Study	**DCI**	**no DCI**	**Comparison**	**Day 0-3**	**Day 4-8**	**Day 9-13**	**Day ≥14**
Hendrix, 2017[71]	31	115	DCI in patients with and without hyponatremia <72h of admission (threshold: unknown)	↑DCI in hypo*			
Beseoglu, 2014[116]	total: 274		Correlation of DCI with hypernatremia (>145) at 56h after ictus	ns			
Zheng, 2011[145]	94	289	% DCI in patients with and without hyponatremia during day 0-9 (threshold: 135)	↑ DCI in hypo			
Nakae, 2011[147]	28	114	Mean (SD), timing of measurement unknown	ns (timing unknown)			

Figure S77: Triglycerides (blood)

Results DCI compared to no DCI

Study	**DCI**	**no DCI**	**Comparison**	**Day 0-3**	**Day 4-8**	**Day 9-13**	**Day ≥14**
Li, 2020[32]	37	38	DCI in low vs. high levels at admission (threshold: 100 mg/dL)	ns			
Mjiti, 2016[94]	87	256	% DCI in high vs. low levels at admission (threshold: 2.26 mmol/L)	ns			

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