

Clinical Burden of Angiographic Vasospasm and Its Complications after Aneurysmal Subarachnoid Hemorrhage: a Systematic Review

Authors

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Supplementary Material

Table S1. Embase and Medline search strategy (searched via Embase.com)

No.	Query
#1	'subarach-id hemorrhage'/exp
#2	(subarach-id NEXT/2 (hemorrhage OR haemorrhage)):ti,ab
#3	'intracranial aneurysm'/exp
#4	'intracranial aneurysm':ti,ab OR 'aneurysm':ti,ab OR 'aneurysmal':ti,ab OR 'brain infarction':ti,ab OR 'brain ischemia':ti,ab OR 'cerebral infarction':ti,ab OR 'cerebral ischemia':ti,ab
#5	(#1 OR #2) AND (#3 OR #4)
#6	'aneurysmal subarach-id hemorrhage':ti,ab OR 'aneurysmal subarach-id haemorrhage':ti,ab
#7	#5 OR #6
#8	'vasospasm':ti,ab OR 'brain vasospasm':ti,ab
#9	#7 OR #8
#10	'glasgow outcome scale':ti,ab OR 'glasgow coma score':ti,ab
#11	'national institutes of health stroke scale':ti,ab OR 'nihss':ti,ab
#12	'rankin scale':ti,ab
#13	'functional status examination'
#14	'functional status assessment'
#15	'disability rating scale' OR 'drs'
#16	'functional independence measure' OR 'fim'
#17	'mini mental state examination' OR 'mmse'
#18	'montreal cognitive assessment'
#19	'delayed cerebral ischemia' OR dci
#20	'brain infarction':ti,ab OR 'cerebral infarction':ti,ab
#21	'delayed ischemic neurological deficit'
#22	'mortality'
#23	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
#24	#9 AND #23
#25	#24 -T ('animal'/de -T 'human'/de)
#26	#25 -T ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [-te]/lim)
#27	#26 -T 'case report'
#28	#27 -T (review:it -T ((systematic:ti,ab OR meta:ti,ab) AND analy*:ti,ab OR ((indirect:ti,ab OR mixed:ti,ab) AND 'treatment comparison':ti,ab)))
#29	'randomised controlled trial':de OR 'controlled clinical trial':de OR 'pragmatic trial':de OR 'equivalence trial':de OR 'phase 3 clinical trial':de OR 'randomization':de OR 'double blind procedure':de OR 'single blind procedure':de OR 'placebo':de OR 'controlled study':de

No.	Query
#30	random*:ti,ab OR sham:ti,ab OR placebo*:ti,ab
#31	((singl* OR doubl* OR tripl* OR trebl*) NEXT/1 (blind* OR dumm* OR mask*)):ti,ab
#32	(control* NEAR/3 (study OR studies OR trial* OR group*)):ti,ab
#33	-nrandom*:ti,ab OR '-n random*':ti,ab OR '-n-random*':ti,ab OR 'quasi-random*':ti,ab OR quasirandom*:ti,ab
#34	allocated:ti,ab
#35	('open label' NEAR/5 (study OR studies OR trial*)):ti,ab
#36	((equivalence OR superiority OR '-n-inferiority' OR -ninferiority) NEAR/3 (study OR studies OR trial*)):ti,ab
#37	'pragmatic stud*':ti,ab
#38	((pragmatic OR practical) NEAR/3 trial*):ti,ab
#39	((quasiexperimental OR 'quasi-experimental') NEAR/3 (study OR studies OR trial*)):ti,ab
#40	(phase NEAR/3 (iii OR '3') NEAR/3 (study OR studies OR trial*)):ti,ab
#41	#29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40
#42	'clinical study'/exp
#43	'case control study'/exp
#44	'family study'/exp
#45	'longitudinal study'/exp
#46	'retrospective study'/exp
#47	'prospective study'/exp
#48	'randomized controlled trial'/exp
#49	#47 -T #48
#50	'cohort analysis'/exp
#51	(cohort NEXT/1 (study OR studies)):ti,ab
#52	('case control' NEXT/1 (study OR studies)):ti,ab
#53	('follow up' NEXT/1 (study OR studies)):ti,ab
#54	(observational NEXT/1 (study OR studies)):ti,ab
#55	(epidemiologic* NEXT/1 (study OR studies)):ti,ab
#56	('cross sectional' NEXT/1 (study OR studies)):ti,ab
#57	#42 OR #43 OR #44 OR #45 OR #46 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56
#58	'register'/exp
#59	'register':ti,ab OR 'registry':ti,ab
#60	'real world evidence'/exp OR 'real world data'/exp
#61	'real world':ti,ab
#62	#57 OR #58 OR #59 OR #60 OR #61
#63	#41 OR #62

No.	Query
#64	#28 AND #63

Table S2. Cochrane search strategy

ID	Search
#1	MeSH descriptor: [Subarachnoid Hemorrhage] explode all trees
#2	(subarachnoid NEXT/2 (hemorrhage OR haemorrhage)):ti,ab
#3	MeSH descriptor: [Intracranial Aneurysm] explode all trees
#4	('intracranial aneurysm' OR 'aneurysm' OR 'aneurysmal' OR 'brain infarction' OR 'brain ischemia' OR 'cerebral infarction' OR 'cerebral ischemia'):ti,ab
#5	(#1 OR #2) AND (#3 OR #4)
#6	('aneurysmal subarachnoid hemorrhage' OR 'aneurysmal subarachnoid haemorrhage'):ti,ab
#7	#5 OR #6
#8	('vasospasm' OR 'brain vasospasm'):ti,ab
#9	#7 OR #8
#10	(conference OR 'conference paper'):pt
#11	review:pt
#12	((systematic OR meta) AND analy* OR ((indirect OR mixed) AND 'treatment comparison')):ti,ab
#13	#11 NOT #12
#14	#9 NOT (#10 OR #13)

Table S3. Summary of data extraction variables

Study objective	As stated in the publication	
Study characteristics	Author, year Design (e.g. randomized, observational, survey) Randomization & blinding methods (if RCTs) Selection criteria and study design for non-RCTs Baseline stratification Years of study conduct	Follow up duration Country Key inclusion/exclusion criteria Study phase Sample size
Patient characteristics	Age Sex Race/ethnicity Body weight, BMI Comorbidities	Morbidity score on admission Days between admission and treatment Treatment modality (coiling, clipping)
Medication	Drugs (such as prophylactic “triple-H” therapy, clazosentan, and intraarterial papaverine calcium channel blockers, milrinone, tirilazad, fasudil, cilostazol, albumin, eicosapentaenoic acid, erythropoietin, corticosteroids, minocycline, deferoxamine, intrathecal thrombolytics)	
Study outcomes	Measure of clinical events <ul style="list-style-type: none"> •Delayed Cerebral Ischemia (DCI) •Cerebral Infarction •Delayed Ischemic Neurological Deficits (DIND) Measure of cognitive status <ul style="list-style-type: none"> •Mini-Mental State Exam (MMSE) •Montreal Cognitive Assessment (MoCA) Measure of functional status <ul style="list-style-type: none"> •Glasgow Outcome Scale (GOS) •Glasgow Outcome Scale Extended (GOSE) •Abbreviated National Institutes of Health Stroke Scale (NIHSS) •modified Glasgow Coma Score (mGCS) •modified Rankin Scale •Functional Status Examination (FSE) •Disability Rating Scale (DRS) •Functional Independence Measure (FIM) Mortality	

Table S4. Study characteristics of the 59 studies included in the clinical burden systematic literature review

Author (date) Study ID	Country	Data Source	No. of centers	Study design	No. pts	Data collection		Consecutive recruitment
						Start	End	
Comparative studies								
Abulhasan et al. (2020) [21]	Canada	Montreal Neurological Institute and Hospital	1	RLC	322	01-Apr-10	Mar-2016	Yes
Appel et al. (2018) [22]	Germany	Department of Intensive Care Medicine, University Medical Center Hamburg-Eppendorf	1	PLC	34	2012	2014	Unclear
Athiraman et al. (2020) [23]	USA	Washington University School of Medicine	1	RLC	181	Jan-10	Dec-13	Yes
Brown et al. (2013) [24]	USA	Neurology/Neurosurgery Intensive Care Unit, Barnes-Jewish Hospital	1	RLC	134	Jul-07	Jun-11	Yes
Budohoski et al. (2012) [25]	Poland	Brodno Mazovia Hospital	1	PLC	98	Jun-10	Jan-12	Yes
Ding et al. (2020) [26]	China	First Affiliated Hospital of Fujian Medical University	1	PLC	103	Mar-17	Dec-17	Yes
Ehlert et al. (2016) [27]	Germany	University Hospital Münster	1	RCC	74	-	-	Yes
Filipce and Caparoski (2015) [28]	North Macedonia	University Department of Neurosurgery Skopje	1	RLC	224	2011	2015	Unclear
Haegens et al. (2018) [29]	Netherlands	Academic Medical Center Amsterdam, University Medical Center Groningen, University Medical Center Utrecht	3	RLC	1,647	2006	2015	Unclear

Author (date) Study ID	Country	Data Source	No. of centers	Study design	No. pts	Data collection		Consecutive recruitment
						Start	End	
Hurth et al. (2020) [30]	Germany	University Hospital Tuebingen	1	RLC	138	2010	2015	Yes
Jeon et al. (2012) [31]	South Korea	Seoul National University Hospital	1	RLC	93	Jul-07	Jun-10	Yes
Karamchandani et al. (2014) [32]	USA	University of Michigan	1	RLC	259	Jan-05	Feb-12	Unclear
Konczalla et al. (2016) [33]	Germany	Goethe-University Hospital	1	RLC	106	2003	2012	Unclear
Lee et al. (2019) [34]	Canada	Ottawa Hospital	1	RLC	463	Jun-02	2011	Yes
Mortimer et al. (2015) [35]	Australia	Royal North Shore Hospital	1	RCT (post hoc)	80	01-Apr-05	01-Feb-10	-
Sakr et al. (2016) [36]	Germany	Friedrich-Schiller university hospital surgical intensive care unit (ICU)	1	RCC	142	Mar-04	Nov-10	Yes
Sanelli et al. (2012) [37]	USA	Weill Cornell Medical College/NewYork-Presbyterian Hospital	1	RLC	137	Jan-02	May-09	Yes
Tekle et al. (2014) [38]	USA	Academic institutions	2	RCC	41	Jun-06	Apr-10	Yes
Uozumi et al. (2017) [39]	Japan	Steel Memorial Hirohata Hospital & Hyogo Brain and Heart Center	2	RLC	97	Apr-07	Jun-16	Unclear
Vrsajkov et al. (2016) [40]	Serbia	Clinical centre of Vojvodina	1	PLC	54	Mar-11	Jan-13	Unclear
Regression-based studies								

Author (date) Study ID	Country	Data Source	No. of centers	Study design	No. pts	Data collection		Consecutive recruitment
						Start	End	
Aldakkan et al. (2017) [41]	Multiple	Subarachnoid Hemorrhage International Trialists data repository	Multiple	RCT (post hoc)	4,125	-	-	-
Ali et al. (2018) [42]	Turkey	Istanbul Medical Faculty, Istanbul	1	PLC	82	Jan-13	Jun-15	Yes
AlMatter et al. (2018) [43]	Germany	Klinikum Stuttgart	1	RLC	693	01-Jan-07	31-Dec-16	Yes
Al-Mufti et al. (2017) [44]	USA	Neurological Intensive Care Unit of Columbia University Medical Center	1	PLC	1,286	Aug-96	Jun-13	Yes
Ayling et al. (2016) [45] CONSCIOUS-1	Multiple	CONSCIOUS-1	52	RCT (post hoc)	413	2005	2006	-
Barges-Coll et al. (2013) [46]	Mexico	National Institute of Neurology and Neurosurgery	1	PLC	40	-	-	Yes
Beadell et al. (2012) [47]	USA	Oregon Health & Science University	1	RLC	28	Jan-05	Dec-10	Unclear
Brawanski et al. (2017) [49]	Germany	Goethe-University Hospital	1	RLC	191	Jun-99	Jun-14	Unclear
Brawanski et al. (2019) [48]	Germany	Goethe-University Hospital	1	RLC	471	1999	Jun-14	Yes
Chotai et al. (2021) [50]	USA	NIS database	1	RCC	5,353	Jan-12	Sep-15	Yes
Chou et al. (2010) [51]	USA	Duke University Medical Center database	1	RCC	189	Feb-99	Oct-04	Yes
Cinotti et al. (2019) [52]	France	Centre Hospitalier Universitaire de Nantes	1	PLC	208	Mar-10	Dec-12	Yes

Author (date) Study ID	Country	Data Source	No. of centers	Study design	No. pts	Data collection		Consecutive recruitment
						Start	End	
Darkwah Oppong et al. (2018) [53]	Germany	University Hospital, University of Duisburg-Essen	1	RLC	994	Jan-03	Jun-16	Yes
Dinc et al. (2019) [54]	Germany	Goethe University Hospital	1	RLC	74	Jan-16	Dec-16	Unclear
Drazin et al. (2015) [55]	USA	Cedars Sinai Medical Center	1	RCC	107	-	-	Yes
Dumont et al. (2010) [56] CONSCIOUS-1	Multiple	CONSCIOUS-1	52	RCT (post hoc)	413	2005	2006	-
Fontana et al. (2018) [57]	Belgium	Erasme Hospital, Université Libre de Bruxelles	1	RLC	270	Jan-11	May-16	Yes
Geraghty et al. (2020) [58]	USA	University of Illinois Hospital	1	RLC	105	Jan-13	Jul-19	Yes
Hosmann et al. (2018) [59]	Austria	Medical University of Vienna	1	RLC	80	1997	2017	Yes
Ibrahim et al. (2012) [61] CONSCIOUS-1	Multiple	CONSCIOUS-1	52	RCT (post hoc)	413	2005	2006	-
Ibrahim and Macdonald (2013) [60] CONSCIOUS-1	Multiple	CONSCIOUS-1	52	RCT (post hoc)	413	2005	2006	-
Ido et al. (2020) [62]	Japan	J-ASPECT Study Diagnosis Procedure Combination database	579	RLC	17,343	Apr-10	Mar-14	Yes
Jabbarli et al. (2016) [63]	Germany	University Medical Center Freiburg	1	RLC	531	Jan-05	Dec-12	Yes

Author (date) Study ID	Country	Data Source	No. of centers	Study design	No. pts	Data collection		Consecutive recruitment
						Start	End	
Kilbourn et al. (2013) [64]	USA	Hartford Hospital Stroke Center	1	RLC	299	Jan-06	Jun-11	Unclear
Konczalla et al. (2016) [65]	Germany	Goethe-University Hospital	1	RLC	193	1999	2013	Unclear
Lannes et al. (2012) [66]	Canada	Montreal Neurological Hospital	1	RLC	88	Apr-99	Apr-06	Yes
Macdonald et al. (2012) [67] CONSCIOUS-1	Austria, Canada, Finland, France, Germany, Israel, Italy, Sweden, Switzerland, UK, USA	CONSCIOUS-1	52	RCT (post hoc)	409	2005	2006	-
Mahajan et al. (2014) [68]	India	-	1	RCT	66	-	-	Unclear
Matano et al. (2019) [69]	Japan	Tama Nagayama Hospital	1	RLC	333	Jan-06	2016	Unclear
Matsukawa et al. (2015) [70]	Japan	Abashiri Neurosurgical Rehabilitation Hospital and Teishinkai Hospital	2	RLC	460	Apr-96	Apr-14	Unclear
Mortimer et al. (2015) [71]	Australia	Royal North Shore Hospital & Westmead Hospital	2	RLC	57	Nov-09	Dec-13	Unclear
Orakdogan et al. (2016) [72]	Turkey	Haydarpasa Numune Training and Research Hospital	1	RLC	104	Jan-08	Feb-14	Unclear
Ozono et al. (2020) [73]	Japan	mWFNS Scale Project	38	RLC	1,124	Oct-10	Mar-13	Unclear
Pegoli et al. (2015) [74]	USA	St. Mary's Hospital-Mayo Medical Center	1	RLC	381	Feb-01	Jun-13	Yes

Author (date) Study ID	Country	Data Source	No. of centers	Study design	No. pts	Data collection		Consecutive recruitment
						Start	End	
Rass et al. (2019) [75]	Austria	Medical University of Innsbruck	1	RLC	237	2010	2016	Yes
Sokolowski et al. (2018) [76]	USA	University of Virginia Health System	1	RLC	159	Aug-99	Mar-15	Yes
Szmuda et al. (2013) [77]	Poland	Neurosurgery Department, Medical University of Gdansk	1	RCC	206	1997	2006	Unclear
Voellger et al. (2019) [78]	Germany	University Hospital Marburg	1	RLC	176	2009	2017	Unclear
Wong et al. (2012) [79]	Hong Kong	-	4	PLC	90	-	-	Yes

Abbreviations: aSAH, aneurysmal subarachnoid hemorrhage; CONSCIOUS-1, Clazosentan to Overcome Neurological Ischemia and Infarction Occurring after Subarachnoid Hemorrhage; NIS, Nationwide Inpatient Sample; No., number; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; VSP, vasospasm.

Table S5. VSP diagnosis per study

Author (date) Study ID	Study design	VSP diagnosis			
		Angiographic	DCI	TCD	VSP combined with DCI or cerebral infarction
Comparative studies					
Abulhasan et al. (2020) [21]	RLC	✓	✓	-	✓
Appel et al. (2018) [22]	PLC	✓	-	✓	✓
Athiraman et al. (2020) [23]	RLC	✓	✓	-	✓
Brown et al. (2013) [24]	RLC	✓	-	-	-
Budohoski et al. (2012) [25]	PLC	-	✓	✓	✓
Ding et al. (2020) [26]	PLC	✓	-	-	-
Ehlert et al. (2016) [27]	RCC	-	✓	✓	-
Filipce and Caparoski (2015) [28]	RLC	Not reported	Not reported	Not reported	Not reported
Haegens et al. (2018) [29]	RLC	-	-	-	✓
Hurth et al. (2020) [30]	RLC	✓	-	✓	-
Jeon et al. (2012) [31]	RLC	✓	✓	-	-
Karamchandani et al. (2014) [32]	RLC	✓	✓	-	✓
Konczalla et al. (2016) [33]	RLC	✓	-	✓	-
Lee et al. (2019) [34]	RLC	✓	✓	✓	✓
Mortimer et al. (2015) [35]	RCT (post hoc)	✓	-	-	-
Sakr et al. (2016) [36]	RCC	✓	-	✓	-
Sanelli et al. (2012) [37]	RLC	✓	✓	-	-
Tekle et al. (2014) [38]	RCC	-	-	✓	-

Author (date) Study ID	Study design	VSP diagnosis			
		Angiographic	DCI	TCD	VSP combined with DCI or cerebral infarction
Uozumi et al. (2017) [39]	RLC	✓	-	-	-
Vrsajkov et al. (2016) [40]	PLC	✓	-	-	-
Regression-based studies					
Aldakkan et al. (2017) [41]	RCT (post hoc)	✓	✓	✓	-
Ali et al. (2018) [42]	PLC	-	✓	-	-
AlMatter et al. (2018) [43]	RLC	✓	-	✓	-
Al-Mufti et al. (2017) [44]	PLC	✓	-	-	-
Ayling et al. (2016) [45] CONSCIOUS-1	RCT (post hoc)	✓	-	-	-
Barges-Coll et al. (2013) [46]	PLC	✓	✓	✓	✓
Beadell et al. (2012) [47]	RLC	✓	-	✓	-
Brawanski et al. (2017) [49]	RLC	✓	-	-	-
Brawanski et al. (2019) [48]	RLC	✓	✓	✓	-
Chotai et al. (2021) [50]	RCC	Not reported	Not reported	Not reported	Not reported
Chou et al. (2010) [51]	RCC	-	✓	✓	-
Cinotti et al. (2019) [52]	PLC	✓	-	-	-
Darkwah Oppong et al. (2018) [53]	RCC	✓	✓	✓	-
Dinc et al. (2019) [54]	RLC	✓	-	✓	-
Drazin et al. (2015) [55]	RCC	-	-	✓	-
Dumont et al. (2010) [56] CONSCIOUS-1	RCT (post hoc)	✓	-	-	-
Fontana et al. (2018) [57]	RLC	✓	✓	✓	-

Author (date) Study ID	Study design	VSP diagnosis			
		Angiographic	DCI	TCD	VSP combined with DCI or cerebral infarction
Geraghty et al. (2020) [58]	RLC	✓	✓	✓	✓
Hosmann et al. (2018) [59]	RLC	✓	✓	✓	-
Ibrahim et al. (2012) [61] CONSCIOUS-1	RCT (post hoc)	✓	-	-	-
Ibrahim and Macdonald (2013) [60] CONSCIOUS-1	RCT (post hoc)	✓	-	-	-
Ido et al. (2020) [62]	RLC	Not reported	Not reported	Not reported	Not reported
Jabbarli et al. (2016) [63]	RLC	✓	-	✓	-
Kilbourn et al. (2013) [64]	RLC	✓	-	✓	✓
Konczalla et al. (2016) [65]	RLC	✓	-	-	-
Lannes et al. (2012) [66]	RLC	✓	✓	✓	-
Macdonald et al. (2012) [67] CONSCIOUS-1	RCT (post hoc)	✓	-	-	-
Mahajan et al. (2014) [68]	RCT	-	-	✓	-
Matano et al. (2019) [69]	RLC	✓	-	-	-
Matsukawa et al. (2015) [70]	RLC	✓	✓	-	✓
Mortimer et al. (2015) [71]	RLC	✓	-	-	-
Orakdogan et al. (2016) [72]	RLC	-	✓	✓	-
Ozono et al. (2020) [73]	RLC	✓	✓	-	-
Pegoli et al. (2015) [74]	RLC	✓	✓	✓	✓
Rass et al. (2019) [75]	RLC	✓	✓	✓	✓
Sokolowski et al. (2018) [76]	RLC	✓	-	-	-

Author (date) Study ID	Study design	VSP diagnosis			
		Angiographic	DCI	TCD	VSP combined with DCI or cerebral infarction
Szmuda et al. (2013) [77]	RCC	✓	✓	-	-
Voellger et al. (2019) [78]	RLC	✓	-	-	-
Wong et al. (2012) [79]	PLC	✓	-	-	-

Abbreviations: CONSCIOUS-1, Clazosentan to Overcome Neurological Ischemia and Infarction Occurring after Subarachnoid Hemorrhage; DCI, delayed cerebral ischemia; PLC, prospective longitudinal cohort; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; TCD, transcranial Doppler; VSP, vasospasm.

Table S6. Multivariate adjustments for regression-based studies

Author (date) Study ID	Study design	Endpoint	Adjusted Prognostic Factor			
			Age	Hypertension	WFNS grade	Fisher grade
Ali et al. (2018) [42]	PLC	mRS score	✓	-	-	✓
AlMatter et al. (2018) [43]	RLC	DCI	✓	-	-	-
Al-Mufti et al. (2017) [44]	PLC	MoCA	-	✓	-	-
Ayling et al. (2016) [45] CONSCIOUS-1	RCT (post hoc)	Cerebral infarction	-	✓	✓	-
		GOS-E	✓	✓	✓	-
Barges-Coll et al. (2013) [46]	PLC	GOS	✓	-	✓	✓
		GOS	✓	-	-	✓
Beadell et al. (2012) [47]	RLC	Cerebral infarction	✓	-	-	✓
		Cerebral infarction	✓	-	-	✓
Brawanski et al. (2017) [49]	RLC	mRS score	-	-	✓	✓
Brawanski et al. (2019) [48]	RLC	mRS score	✓	-	✓	-
Chou et al. (2010) [51]	RCC	Death	✓	-	✓	-
Cinotti et al. (2019) [52]	PLC	mRS score	✓	-	-	-
Darkwah Oppong et al. (2018) [53]	RLC	mRS score	✓	-	✓	✓
		DCI	✓	-	✓	✓
Dinc et al. (2019) [54]	RLC	mRS score	-	-	✓	✓
Drazin et al. (2015) [55]	RCC	Death	✓	-	✓	-
		Death	✓	-	✓	-
Fontana et al. (2018) [57]	RLC	GOS	✓	-	✓	-
		GOS	✓	-	✓	-
Hosmann et al. (2018) [59]	RLC	Cerebral infarction	-	-	-	-
Ibrahim et al. (2012) [61] CONSCIOUS-1	RCT (post hoc)	DCI	-	-	✓	-
		GOS-E	-	-	✓	-
Ibrahim and Macdonald (2013) [60] CONSCIOUS-1	RCT (post hoc)	mRS score	✓	✓	✓	-

Author (date) Study ID	Study design	Endpoint	Adjusted Prognostic Factor			
			Age	Hypertension	WFNS grade	Fisher grade
Jabbarli et al. (2016) [63]	RLC	mRS score	✓	-	-	✓
Kilbourn et al. (2013) [64]	RLC	Death	✓	-	-	-
Konczalla et al. (2016) [65]	RLC	mRS score	✓	-	✓	✓
Lannes et al. (2012) [66]	RLC	mRS score	✓	-	-	-
Macdonald et al. (2012) [67] CONSCIOUS-1	RCT (post hoc)	MMSE	✓	✓	-	-
Mahajan et al. (2014) [68]	RCT	MMSE	Not reported	Not reported	Not reported	Not reported
Matsukawa et al. (2015) [70]	RLC	GOS	✓	-	-	-
Mortimer et al. (2015) [71]	RLC	Cerebral infarction	✓	-	-	-
		mRS score	✓	-	✓	-
Orakdogan et al. (2016) [72]	RLC	Death	✓	-	✓	-
Ozono et al. (2020) [73]	RLC	mRS score	✓	-	✓	-
		Death	✓	-	✓	-
Rass et al. (2019) [75]	RLC	mRS score	✓	-	-	✓
Sokolowski et al. (2018) [76]	RLC	mRS score	✓	✓	-	-
Szmuda et al. (2013) [77]	RCC	GOS	✓	✓	-	✓
Voellger et al. (2019) [78]	RLC	Death	✓	-	-	✓
		GOS	✓	-	-	✓
Wong et al. (2012) [79]	PLC	MMSE	✓	-	✓	✓
		MoCA	✓	-	✓	✓
		mRS score	✓	-	✓	✓

Abbreviations: CONSCIOUS-1, Clazosentan to Overcome Neurological Ischemia and Infarction

Occurring after Subarachnoid Hemorrhage; DCI, delayed cerebral ischemia; GOS, Glasgow Outcome Scale; GOS-E, extended Glasgow Outcome Scale; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; mRS, modified Rankin scale; TCD, transcranial Doppler; VSP, vasospasm; WFNS, World Federation of Neurosurgical Societies.

Table S7. Patient characteristics at baseline: Age

Author (date) Study ID	Study design	Subgroup	No. pts	n	%	Mean	Median	SD	Range	IQR
Comparative studies										
Abulhasan et al. (2020) [21]	RLC	No DCI	212	-	-	-	57	-	-	49–69
		With aVSP/DCI + standard therapy	89	-	-	-	54	-	-	48–62
		With aVSP/DCI + rescue therapy	21	-	-	-	52	-	-	49–56
Appel et al. (2018) [22]	PLC	-	34	-	-	53.1	-	12.5	-	-
Athiraman et al. (2020) [23]	RLC	aVSP	97	-	-	55	-	13	-	-
		No aVSP	60	-	-	59	-	15	-	-
Brown et al. (2013) [24]	RLC	-	134	-	-	55	-	14	-	-
Budohoski et al. (2012) [25]	PLC	DCI	32	-	-	56	-	10	-	-
		No DCI	66	-	-	57	-	12	-	-
Ding et al. (2020) [26]	PLC	-	103	-	-	52.48	-	10.1	-	-
Ehlert et al. (2016) [27]	RCC	Molsidomine	29	-	-	49	-	-	26–77	-
		Standard therapy with TCD-defined VSP	25	-	-	52	-	-	16–76	-
		Standard therapy no TCD-defined VSP	20	-	-	64	-	-	42–86	-
Haegens et al. (2018) [29]	RLC	-	1647	-	-	56	-	13	-	-
Hurth et al. (2020) [30]	RLC	-	138	-	-	-	53	-	-	-
Jeon et al. (2012) [31]	RLC	No aVSP	65	-	-	58	-	14	-	-
		aVSP	26	-	-	54	-	14	-	-
Karamchandani et al. (2014) [32]	RLC	-	259	-	-	55	-	13	23–90	-
Konczalla et al. (2016) [33]	RLC	Long-lasting cerebral VSP	106	-	-	53	-	12	-	-
Lee et al. (2019) [34]	RLC	DCI	97	-	-	54.62	-	11.6	-	-
		No DCI	366	-	-	56.35	-	13.6	-	-
Mortimer et al. (2015) [35]	RCT (post hoc)	None/mild aVSP	63	-	-	56.5	-	3.5	-	-
		Severe aVSP	17	-	-	48.9	-	6.2	-	-

Author (date) Study ID	Study design	Subgroup	No. pts	n	%	Mean	Median	SD	Range	IQR
Sakr et al. (2016) [36]	RCC	-	142	-	-	54	-	14	-	-
Sanelli et al. (2012) [37]	RLC	-	137	-	-	-	52	-	24–88	-
Tekle et al. (2014) [38]	RCC	No new symptomatic TCD-defined VSP	30	-	-	52	-	12.8	-	-
		New symptomatic TCD-defined VSP	11	-	-	43	-	11.2	-	-
Uozumi et al. (2017) [39]	RLC	No aVSP	70	-	-	56.6	-	-	25–85	-
		aVSP	27	-	-	65	-	-	46–87	-
Vrsajkov et al. (2016) [40]	PLC	aVSP	29	-	-	53.3	-	9.2	-	-
		No aVSP	25	-	-	55.4	-	10.6	-	-
Regression-based studies										
Aldakkan et al. (2017) [41]	RCT (post hoc)	-	4125	-	-	51.33	-	13.3	-	-
Ali et al. (2018) [42]	PLC	-	82	-	-	49.6	-	9.1	-	-
AlMatter et al. (2018) [43]	RLC	<20 years	693	3	0.4	-	-	-	-	-
		20-30 years	693	16	2.3	-	-	-	-	-
		31-40 years	693	58	8.4	-	-	-	-	-
		41-50 years	693	166	24	-	-	-	-	-
		51-60 years	693	202	29	-	-	-	-	-
		61-70 years	693	114	17	-	-	-	-	-
		71-80 years	693	95	14	-	-	-	-	-
		>80 years	693	39	5.6	-	-	-	-	-
Al-Mufti et al. (2017) [44]	PLC	With ultra-early aVSP, >53 years	59	22	37	-	-	-	-	-
		No ultra-early aVSP, >53 years	1227	675	55	-	-	-	-	-
Ayling et al. (2016) [45] CONSCIOUS-1	RCT (post hoc)	Early infarct	76	-	-	51.14	-	10.7	-	-
		Delayed infarct	79	-	-	51.66	-	11.2	-	-
		Both early & delayed infarcts	36	-	-	52.22	-	10.8	-	-
		No infarct	222	-	-	50.5	-	10.7	-	-
Barges-Coll et al. (2013) [46]	PLC	-	40	-	-	47.3	-	2	-	-

Author (date) Study ID	Study design	Subgroup	No. pts	n	%	Mean	Median	SD	Range	IQR
Beadell et al. (2012) [47]	RLC	Methamphetamine users	28	-	-	45.2	-	7.3	-	-
		Non-methamphetamine users	346	-	-	55.9	-	12.9	-	-
		Control	28	-	-	45.2	-	7.3	-	-
Brawanski et al. (2017) [49]	RLC	-	471	-	-	53.7	-	13.7	-	-
Chotai et al. (2021) [50]	RCC	-	5353	-	-	-	55	-	46–64	-
Chou et al. (2010) [51]	RCC	TCD-defined VSP	116	-	-	50.6	-	13	-	-
		No TCD-defined VSP	73	-	-	58.8	-	15.3	-	-
Cinotti et al. (2019) [52]	PLC	-	208	-	-	-	55	-	-	45–65
Darkwah Oppong et al. (2018) [53]	RLC	-	994	-	-	55	-	14	-	-
Drazin et al. (2015) [55]	RCC	Direct-admit	31	-	-	57.2	58	-	32–90	44–66
		Transfer	76	-	-	54.9	54	-	23–83	45–66
Dumont et al. (2010) [56] CONSCIOUS-1	RCT (post hoc)	-	413	-	-	51	-	11	-	-
Fontana et al. (2018) [57]	RLC	-	270	-	-	-	54	-	-	45–66
Geraghty et al. (2020) [58]	RLC	-	105	-	-	51.6	-	11.9	-	-
Hosmann et al. (2018) [59]	RLC	-	80	-	-	46.9	-	8.9	-	-
Ibrahim and Macdonald (2013) [60] CONSCIOUS-1	RCT (post hoc)	Received colloids	41	-	-	55.3	9.6	-	-	-
		Did not receive colloids	82	-	-	55.8	9.6	-	-	-
Ido et al. (2020) [62]	RLC	Age <75 years	13548	-	-	57	-	11.3	-	-
		Age ≥75 years	3885	-	-	80.9	-	4.5	-	-
Jabbarli et al. (2016) [63]	RLC	-	531	-	-	55.4	-	-	21-94	-
Kilbourn et al. (2013) [64]	RLC	-	299	-	-	55	-	13.8	-	-
Konczalla et al. (2016) [65]	RLC	-	193	-	-	55.2	-	-	-	-

Author (date) Study ID	Study design	Subgroup	No. pts	n	%	Mean	Median	SD	Range	IQR
Lannes et al. (2012) [66]	RLC	-	88	-	-	53.4	-	11.5	34–78	-
Macdonald et al. (2012) [67] CONSCIOUS-1	RCT (post hoc)	Total population	409	-	-	51.1	-	10.7	-	-
Mahajan et al. (2014) [68]	RCT	No propofol	32	-	-	44.2	-	12.6	-	-
		Propofol	34	-	-	44.9	-	9.6	-	-
Matano et al. (2019) [69]	RLC	-	333	-	-	59.7	-	-	24–93	-
Matsukawa et al. (2015) [70]	RLC	-	460	-	-	62	-	14	-	-
Mortimer et al. (2015) [71]	RLC	-	57	-	-	50.4	-	3	-	-
Orakdogan et al. (2016) [72]	RLC	-	104	-	-	51.79	51.5	12.8	16–84	-
Ozono et al. (2020) [73]	RLC	Age <65	613	-	-	52.5	55	9.1	-	46–60
		Age ≥65	511	-	-	74.3	74	6.6	-	68–79
Pegoli et al. (2015) [74]	RLC	-	381	-	-	55.8	-	13.3	-	-
Rass et al. (2019) [75]	RLC	-	237	-	-	-	57	-	-	47–67
Sokolowski et al. (2018) [76]	RLC	-	159	-	-	51.8	-	11.9	-	-
Szmuda et al. (2013) [77]	RCC	-	206	-	-	51.6	-	12.5	-	-
Voellger et al. (2019) [78]	RLC	-	176	-	-	56	-	-	22–90	-
Wong et al. (2012) [79]	PLC	-	90	-	-	54	-	11	-	-

Abbreviations: aVSP, angiographic vasospasm; CONSCIOUS-1, Clazosentan to Overcome Neurological Ischemia and Infarction Occurring after Subarachnoid Hemorrhage; DCI, delayed cerebral ischemia; IQR, interquartile range; n, number; No., number; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; SD, standard deviation; TCD, transcranial Doppler; VSP, vasospasm.

Table S8. Patient characteristics at baseline: Pre-existing hypertension

Author (date) Study ID	Study design	Subgroup	No. pts	n	%
Comparative studies					
Appel et al. (2018) [22]	PLC	DCI	14	5	36
		No DCI	20	9	45
Brown et al. (2013) [24]	RLC	Delayed infarct	20	8	40
		No infarct	114	53	47
Ding et al. (2020) [26]	PLC	aVSP	52	28	54
		No aVSP	51	19	37
Jeon et al. (2012) [31]	RLC	No aVSP	65	34	52
		aVSP	26	11	42
Karamchandani et al. (2014) [32]	RLC	No DCI	165	72	44
		DCI	94	49	52
Lee et al. (2019) [34]	RLC	DCI	97	42	43
		No DCI	366	171	47
Mortimer et al. (2015) [35]	RCT (post hoc)	None/mild aVSP	63	20	32
		Severe aVSP	17	5	29
Tekle et al. (2014) [38]	RCC	No new symptomatic TCD-defined VSP	30	11	37
		New symptomatic TCD-defined VSP	11	7	64
Vrsajkov et al. (2016) [40]	PLC	aVSP	29	18	62
		No aVSP	25	11	44
Regression-based studies					
Al-Mufti et al. (2017) [44]	PLC	With ultra-early aVSP	59	27	46
		No ultra-early aVSP	1227	585	49
Ayling et al. (2016) [45] CONSCIOUS-1	RCT (post hoc)	Early infarct	76	36	47
		Delayed infarct	79	40	51
		Both early & delayed infarcts	36	17	47
		No infarct	222	82	37
Chou et al. (2010) [51]	RCC	TCD-defined VSP	116	61	52.6
		No TCD-defined VSP	73	34	46.6
Cinotti et al. (2019) [52]	PLC	-	208	75	36
Drazin et al. (2015) [55]	RCC	Direct-admit	31	16	53.3
		Transfer	76	43	57.3

Author (date) Study ID	Study design	Subgroup	No. pts	n	%
Comparative studies					
Dumont et al. (2010) [56] CONSCIOUS-1	RCT (post hoc)	-	413	172	42
Fontana et al. (2018) [57]	RLC	-	270	114	42
Ibrahim and Macdonald (2013) [60] CONSCIOUS-1	RCT (post hoc)	-	413	175	42
Ido et al. (2020) [62]	RLC	Age <75 years	13548	7421	55
		Age ≥75 years	3885	2231	57
Kilbourn et al. (2013) [64]	RLC	-	299	128	43
Lannes et al. (2012) [66]	RLC	-	88	16	18
Mahajan et al. (2014) [68]	RCT	No propofol	32	9	28.1
		Propofol	34	12	35.3
Mortimer et al. (2015) [71]	RLC	-	57	18	32
Pegoli et al. (2015) [74]	RLC	-	381	212	56
Sokolowski et al. (2018) [76]	RLC	-	103	79	77

Abbreviations: aVSP, angiographic vasospasm; CONSCIOUS-1, Clazosentan to Overcome Neurological Ischemia and Infarction Occurring after Subarachnoid Hemorrhage; DCI, delayed cerebral ischemia; n, number; No., number; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; TCD, transcranial Doppler; VSP, vasospasm.

Table S9. Patient characteristics at baseline: Fisher grade

Author (date) Study ID	Study design	Subgroup	No. pts	Mean	Median	Range	Grade (%)						
							1	2	3	4	1-2, 4	<1mm	>1mm
Comparative studies													
Appel et al. (2018) [22]	PLC	DCI	14	-	-	-	-	-	-	64	-	-	-
		No DCI	20	-	-	-	-	-	-	50			
Ehlert et al. (2016) [27]	RCC	Molsidomine	29	4	-	1-4	-	-	-	-	-	-	-
		Standard therapy with TCD-defined VSP	25	4	-	2-4	-	-	-	-	-	-	-
		Standard therapy no TCD-defined VSP	20	4	-	1-4	-	-	-	-	-	-	-
Hurth et al. (2020) [30]	RLC	-	138	-	-	-	0.7	13	27	59	-	-	-
Jeon et al. (2012) [31]	RLC	No aVSP	65	-	-	-	-	-	34	-	66	-	-
		aVSP	26	-	-	-	-	-	58	-	42	-	-
Konczalla et al. (2016) [33]	RLC	-	106	-	-	-	-	-	76	-	-	-	-
Sakr et al. (2016) [36]	RCC	-	142	-	-	-	0.7	12	23	65	-	-	-
Uozumi et al. (2017) [39]	RLC	No aVSP	70	-	-	-	-	-	80	20	-	-	-
		aVSP	27	-	-	-	-	-	74	26	-	-	-
Regression-based studies													
Aldakkan et al. (2017) [41]	RCT (post hoc)	-	190	-	-	-	31		70				-
Ali et al. (2018) [42]	PLC	-	82	-	-	-	13	60	22	4.9	-	-	-

Author (date) Study ID	Study design	Subgroup	No. pts	Mean	Median	Range	Grade (%)						
							1	2	3	4	1-2, 4	<1mm	>1mm
AlMatter et al. (2018) [43]	RLC	-	693	-	-	-	4.5	10.1	16.5	68.8	-	-	-
Barges-Coll et al. (2013) [46]	PLC	-	40	-	-	-	5	13	40	43	-	-	-
Beadell et al. (2012) [47]	RLC	Methamphetamine users	28	-	4	-	-	-	-	-	-	-	-
		Non-methamphetamine users	346	-	3	-	-	-	-	-	-	-	-
		Control	28	-	3	-	-	-	-	-	-	-	-
Brawanski et al. (2017) [49]	RLC	-	471	-	-	-	-	-	72.2	-	-	-	
Chou et al. (2010) [51]	RCC	TCD-defined VSP	116	-	-	-	5.2	7.8	57.8	29.3	-	-	-
		No TCD-defined VSP	73	-	-	-	9.6	13.7	54.8	21.9	-	-	-
Cinotti et al. (2019) [52]	PLC	Good neurological recovery	138	-	-	-	4.3	26.1	16.7	52.9	-	-	-
		Poor neurological recovery	70	-	-	-	0	1.4	12.9	85.7	-	-	-
Darkwah Oppong et al. (2018) [53]	RLC	-	994	-	-	-	-	-	86.5	-	-	-	
Dinc et al. (2019) [54]	RLC	-	74	-	-	-	35		65	-	-	-	
Drazin et al. (2015) [55]	RCC	Direct-admit	31	-	-	-			77.4				
		Transfer	76	-	-	-			75				
Fontana et al. (2018) [57]	RLC	-	270	-	4	-	-	-	-	-	-	-	
Konczalla et al. (2016) [65]	RLC	-	193	-	-	-	-	-	-	-	-	-	
Mahajan et al. (2014) [68]	RCT	No propofol	32	-	-	-	18.8	40.6	18.8	21.9	-	-	-
		Propofol	34	-	-	-	14.7	44.1	11.8	29.4	-	-	-

Author (date) Study ID	Study design	Subgroup	No. pts	Mean	Median	Range	Grade (%)						
							1	2	3	4	1-2, 4	<1mm	>1mm
Mortimer et al. (2015) [71]	RLC	-	57	-	-	-	0	1.8	87.7	10.5	-	-	-
Orakdogan et al. (2016) [72]	RLC	-	104	-	-	-	-	-	-	-	-	37	29
Ozono et al. (2020) [73]	RLC	Age <65	613	-	-	-	4.9	14	80.8	0.3	-	-	-
		Age ≥65	511	-	-	-	5.7	12.4	81.5	0.4	-	-	-
Sokolowski et al. (2018) [76]	RLC	-	157	-	-	-	3.8	14	19.1	63.1	-	-	-
Szmuda et al. (2013) [77]	RCC	-	206	-	-	-	3.4	59	31	2.9	-	-	-
Wong et al. (2012) [79]	PLC	-	90	-	-	-	-	-	100	-	-	-	-

Abbreviations: aVSP, angiographic vasospasm; DCI, delayed cerebral ischemia; No., number; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; TCD, transcranial Doppler; VSP, vasospasm.

Table S10. Patient characteristics at baseline: Modified Fisher grade

Author (date) Study ID	Study design	Subgroup	No. pts	Median	IQR	Grade (%)				
						0	1	2	3	4
Comparative studies										
Abulhasan et al. (2020) [21]	RLC	No DCI	211	-	-	-	-	-	81	
		With aVSP/DCI + standard therapy	89	-	-	-	-	-	93	
		With aVSP/DCI + rescue therapy	21	-	-	-	-	-	81	
Athiraman et al. (2020) [23]	RLC	aVSP	97	3	3-4	-	-	-	-	-
		No aVSP	60	3	3-4	-	-	-	-	-
		DCI	63	3	3-4	-	-	-	-	-
		No DCI	94	3	3-4	-	-	-	-	-
Brown et al. (2013) [24]	RLC	Delayed infarct	20	-	-	5			95	
		No infarct	114	-	-	12			88	
Budohoski et al. (2012) [25]	PLC	DCI	32	-	-	-	13	13	59	16
		No DCI	66	-	-	-	27	7.6	39	26
Ding et al. (2020) [26]	PLC	aVSP	52	3	2-4	-	-	-	-	-
		No aVSP	51	2	2-3	-	-	-	-	-
Karamchandani et al. (2014) [32]	RLC	No DCI	165	-	-	-	-	11	73	16
		DCI	94	-	-	-	-	3	53	44
Lee et al. (2019) [34]	RLC	DCI	97	-	-	11		8.3	22	59
		No DCI	366	-	-	30		21	13	37
Regression-based studies										
Geraghty et al. (2020) [58]	RLC	-	105	3	3	-	-	-	-	-

Lannes et al. (2012) [66]	RLC	-	88	-	-	-	4.6	11.5	37.9	46
Rass et al. (2019) [75]	RLC	-	237	-	-	-	12	16	25	47
Voellger et al. (2019) [78]	RLC	-	176	-	-	3.4	8.5	6.3	32	50

Abbreviations: aVSP, angiographic vasospasm; DCI, delayed cerebral ischemia; No., number; PLC, prospective longitudinal cohort; pts, patients; RLC, retrospective longitudinal cohort; VSP, vasospasm.

Table S11. Patient characteristics at baseline: WFNS grade

Author (date) Study ID	Study design	Subgroup	No. pts	Mean (SD)	Median (IQR)	WFNS grade (%)				
						1	2	3	4	5
Comparative studies										
Abulhasan et al. (2020) [21]	RLC	No DCI	212	-	-	-	-	47		
		With aVSP/DCI + standard therapy	89	-	-	-	-	67		
		With aVSP/DCI + rescue therapy	21	-	-	-	-	43		
Appel et al. (2018) [22]	PLC	DCI	14	-	-	-	-	-	71	
		No DCI	20	-	-	-	-	-	40	
Brown et al. (2013) [24]	RLC	Delayed infarct	20	-	-	60			40	
		No infarct	114	-	-	70			30	
Budohoski et al. (2012) [25]	PLC	DCI	32	-	-	34	22	3.1	31	9.4
		No DCI	66	-	-	35	33	7.6	17	7.6
Ding et al. (2020) [26]	PLC	-	103	-	-	43	2.9	12	25	17
Haegens et al. (2018) [29]	RLC	-	1647	-	-	-	-	-	45	
Hurth et al. (2020) [30]	RLC	-	138	-	-	31	20	4	20	25
Jeon et al. (2012) [31]	RLC	No aVSP	65	-	-	72	11		17	
		aVSP	26	-	-	46	19		35	
Konczalla et al. (2016) [33]	RLC	-	106	-	-	21.7	17	4.7	14.2	42.5
Lee et al. (2019) [34]	RLC	DCI	97	-	-	36	19	8.3	21	17
		No DCI	366	-	-	54	12	4.1	17	12
	RCT (post hoc)	None/mild aVSP	63	-	-	-	30	-	-	-

Author (date) Study ID	Study design	Subgroup	No. pts	Mean (SD)	Median (IQR)	WFNS grade (%)				
						1	2	3	4	5
Mortimer et al. (2015) [35]		Severe aVSP	17	-	-	-	65	-	-	-
Sakr et al. (2016) [36]	RCC	-	142	-	-	25	23	9.2	20	23
Uozumi et al. (2017) [39]	RLC	No aVSP	70	-	-	46		54		-
		aVSP	27	-	-	33		67		-
Vrsajkov et al. (2016) [40]	PLC	aVSP	29	2.14 (1.22)	-	-	-	-	-	-
		No aVSP	25	1.68 (0.98)	-	-	-	-	-	-
Regression-based studies										
Aldakkan et al. (2017) [41]	RCT (post hoc)	-	191	-	-	51	49	-	-	-
Ali et al. (2018) [42]	PLC	-	82	-	-	38	38	24	-	-
Ayling et al. (2016) [45] CONSCIOUS-1	RCT (post hoc)	Early infarct	76	-	-	71			-	-
		Delayed infarct	79	-	-	67			-	-
		Both early & delayed infarcts	36	-	-	67			-	-
		No infarct	222	-	-	82			-	-
Barges-Coll et al. (2013) [46]	PLC	-	40	-	-	100		-	-	-
Brawanski et al. (2017) [49]	RLC	-	471	-	-	63.5			-	-
Cinotti et al. (2019) [52]	PLC	Good neurological recovery	138	-	-	44.9	21	8	13.8	12.3
		Poor neurological recovery	70	-	-	4.3	7.1	2.9	31.4	54.3
Darkwah Oppong et al. (2018) [53]	RLC	-	994	-	-	-	-	-	43.2	

Author (date) Study ID	Study design	Subgroup	No. pts	Mean (SD)	Median (IQR)	WFNS grade (%)				
						1	2	3	4	5
Dinc et al. (2019) [54]	RLC	-	74	-	-	-	-	-	51	
Dumont et al. (2010) [56] CONSCIOUS-1	RCT (post hoc)	-	413	-	-	76			24	
Fontana et al. (2018) [57]	RLC	Favourable outcome	161	-	1 (1-2)	-	-	-	-	-
		Unfavourable outcome	109	-	5 (2-5)	-	-	-	-	-
Konczalla et al. (2016) [65]	RLC	-	193	-	-	59			-	-
Matsukawa et al. (2015) [70]	RLC	-	460	-	-	19	33	11	24	14
Mortimer et al. (2015) [71]	RLC	-	57	-	-	19.3	14	10.5	22.8	33.3
Orakdogan et al. (2016) [72]	RLC	-	104	-	-	82.7			17.3	
Pegoli et al. (2015) [74]	RLC	-	381	2.3 (1.5)	-	-	-	-	-	-
Sokolowski et al. (2018) [76]	RLC	-	128	-	-	39.1	27.3	7.8	14.8	10.9
Szmuda et al. (2013) [77]	RCC	-	206	-	-	67	4.9	5.3	19	3.9
Wong et al. (2012) [79]	PLC	-	90	-	-	78		22		

Abbreviations: aVSP, angiographic vasospasm; CONSCIOUS-1, Clazosentan to Overcome Neurological Ischemia and Infarction Occurring after Subarachnoid Hemorrhage; DCI, delayed cerebral ischemia; IQR, interquartile range; n, number; No., number; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; SD, standard deviation; VSP, vasospasm; WFNS, World Federation of Neurosurgical Societies.

Table S12. Clinical burden: The occurrence of DCI in patients with angiographic VSP or its related complications

Author (date)	Study Design	Subgroup	No. pts	n	%	Odds ratio	95% CI	p-value
Comparative studies								
Budohoski et al. (2012) [25]	PLC	DCI	32	28*	87.5	-	-	0.0001
		No DCI	66	24*	36.4	-	-	
Hurth et al. (2020) [30]	RLC	aVSP	49	17	34.7	-	-	0.001
		No aVSP	87	10	11.5	-	-	
Vrsajkov et al. (2016) [40]	PLC	aVSP	29	20	69.0	-	-	0.001
		No aVSP	25	5	20.0	-	-	
Regression-based studies								
Aldakkan et al. (2017) [41]	RCT (post hoc)	Severe aVSP	4125	-	-	9.5	2.07–43.50	0.004**
Al-Mufti et al. (2017) [44]	PLC	Ultra-early aVSP†	1286	-	-	2.3	1.4–3.9	0.002**
						1.9	1.1–3.3	0.02‡
Darkwah Oppong et al. (2018) [53]	RCC	aVSP	994	-	-	3.27		0.001**

Abbreviations: aVSP, angiographic vasospasm; DCI, delayed cerebral ischemia; n, number; No., number; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; TCD, transcranial Doppler. *number of patients with TCD-defined VSP; **univariate analysis; †ultra-early aVSP (defined as angiographic VSP within the first 48 hours of aSAH); ‡multivariate analysis adjusting for age, Hunt-Hess grade, aSAH thickness, aneurysm location, and mean arterial pressure.

Table S13. Clinical burden: The occurrence of cerebral infarction in patients with angiographic VSP or its related complications

Author (date)	Study Design	Subgroup	No. pts	n	%	Odds ratio	95% CI	p-value
Comparative studies								
Jeon et al. (2012) [31]	RLC	aVSP	26	9	34.6	-	-	-
		No aVSP	65	0	0.0	-	-	
Sanelli et al. (2012) [37]	RLC	DCI	81	46	56.8	-	-	<0.0001
		No DCI	56	0	0.0	-	-	
Regression-based studies								
Al-Mufti et al. (2017) [44]	PLC	Ultra-early aVSP [†]	1286	-	-	2.0	1.0–3.9	0.04*
Hosmann et al. (2018) [59]	RLC	aVSP before intervention	80	-	-	-	-	0.02*
			80	-	-	2.04	0.88–4.73	0.1**
		aVSP after intervention	80	-	-	-	-	0.03*
			80	-	-	1.25	0.61–2.59	0.54**
Mortimer et al. (2015) [71]	RLC	aVSP	57	-	-	-	-	0.0042*
			57	-	-	4.2	0.9–18	0.0634‡

Abbreviations: aVSP, angiographic vasospasm; DCI, delayed cerebral ischemia; n, number; No., number; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort. *univariate analysis; **multivariate analysis, adjusting for Hunt-Hess grade, days of aneurysm treatment, number of interventions; [†]ultra-early aVSP (defined as angiographic VSP within the first 48 hours of aSAH); [‡]multivariate analysis, adjusting for delayed presentation, aneurysm management, age, sex, intraventricular hemorrhage, hydrocephalus, intraparenchymal extension of hemorrhage, use of transluminal balloon angioplasty, and maximal clot thickness.

Table S14. Clinical burden: Functional outcome (mRS) in patients with VSP or VSP-related complications compared with patients without VSP or VSP-related complications from comparative studies

Author (date)	Study Design	Subgroup	Assessment	mRS score	No. pts	n	%	Median mRS	IQR	p-value
Tekle et al. (2014) [38]	RCC	New symptomatic TCD-defined VSP	At discharge	3–6	11	9	82	-	-	0.58
		No new symptomatic TCD-defined VSP		3–6	30	21	70	-	-	
Jeon et al. (2012) [31]	RLC	aVSP	At discharge	0–3	28	19	67.9	-	-	0.303
		No aVSP		0–3	65	51	78.5	-	-	
		aVSP		4–6	28	9	32.1	-	-	
		No aVSP		4–6	65	14	21.5	-	-	
Athiraman et al. (2020) [23]	RLC	aVSP	At discharge	-	97	-	-	2	1-3	0.76
		No aVSP		-	60	-	-	2	1-4	
		DCI	At discharge	-	63	-	-	2	1-4	0.15
		No DCI		-	94	-	-	2	1-3	
Budohoski et al. (2012) [25]	PLC	DCI	At discharge	-	32	-	-	2	-	0.65
		No DCI		-	66	-	-	2	-	
Uozumi et al. (2017) [39]	RLC	aVSP	Month 3	0–2	27	5	18.5	-	-	<0.01
		No aVSP		0–2	70	44	62.9	-	-	
		aVSP		3–5	27	18	66.7	-	-	
		No aVSP		3–5	70	23	32.9	-	-	
		aVSP		6	27	4	14.8	-	-	
		No aVSP		6	70	3	4.2	-	-	

Author (date)	Study Design	Subgroup	Assessment	mRS score	No. pts	n	%	Median mRS	IQR	p-value
Ehlert et al. (2016) [27]	RCC	Standard therapy with TCD-defined VSP	Month 3	-	25	-	-	5	2-6	0.0011*
		Standard therapy no TCD-defined VSP		-	20	-	-	4	2-5	0.006*
		Molsidomine-treated TCD-defined VSP		-	29	-	-	1	0-3	reference
Mortimer et al. (2015) [35]	RCT (post hoc)	Severe aVSP	Month 3	0-2	17	15	88.2	-	-	0.7224
		None/mild aVSP		0-2	63	51	81	-	-	
Haegens et al. (2018) [29]	RLC	DCI-related infarct	Month 3	4-6	65	48	74.0	-	-	<0.001
		No DCI-related infarct		4-6	179	64	36	-	-	
Ding et al. (2020) [26]	PLC	aVSP	Month 6	3-6	52	32	61.54	-	-	<0.001
		No aVSP		3-6	51	12	23.53	-	-	
Konczalla et al. (2016) [33]	RLC	Cerebral VSP lasting >14 days	Month 6	0-2	106	64	60	-	-	<0.01
		Cerebral VSP lasting ≤14 days		0-2	106	52	49	-	-	
Abulhasan et al. (2020) [21]	RLC	DCI + standard therapy	Month 18	0-2	87	61	70	-	-	0.221**
		DCI + rescue therapy		0-2	21	14	67	-	-	0.715**
		No DCI		0-2	206	129	63	-	-	reference

Abbreviations: aVSP, angiographic vasospasm; DCI, delayed cerebral ischemia; IQR, interquartile range; mRS, modified Rankin Scale; n, number; No., number; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; TCD, transcranial Doppler; VSP, vasospasm. *versus TCD-defined VSP treated with molsidomine; **versus no DCI.

Table S15. Clinical burden: Functional outcome (GOS) in patients with VSP or VSP-related complications compared with patients without VSP or VSP-related complications from comparative studies

Author (date)	Study Design	Subgroup	Assessment	GOS score	No. pts	n	%	OR (95% CI)	p-value
Appel et al. (2018) [22]	PLC	DCI	At discharge	Poor (1–3)	14	-	-	5.4 (1.2–24)	0.03
		No DCI		Poor (1–3)	20	-	-	-	Reference
		DCI	Month 3	Poor (1–3)	14	-	-	10 (2–49)	<0.01
		No DCI		Poor (1–3)	20	-	-	-	Reference
Filipce et al. (2015) [28]	RLC	Cerebral VSP	At discharge	Good	38	16	42.1	-	<0.001
		No cerebral VSP		Good	186	121	65.1	-	
		Cerebral VSP	At discharge	Moderate disability	38	1	2.6	-	
		No cerebral VSP		Moderate disability	186	31	16.7	-	
		Cerebral VSP	At discharge	Severe disability	38	3	7.9	-	
		No cerebral VSP		Severe disability	186	12	6.5	-	
		Cerebral VSP	At discharge	Vegetative state	38	7	18.4	-	
		No cerebral VSP		Vegetative state	186	10	5.4	-	
		Cerebral VSP	At discharge	Death	38	11	28.9	-	
		No cerebral VSP		Death	186	12	6.5	-	
Mortimer et al. (2015a) [35]	RCT (post hoc)	None/mild aVSP	At discharge	Good (4–5)	63	35	55.5	-	0.591
		Severe aVSP		Good (4–5)	17	8	47.1	-	
		None/mild aVSP	Month 3	Good (4–5)	63	52	82.5	-	0.4444
		Severe aVSP		Good (4–5)	17	16	94.1	-	
	RCC	Mild TCD-defined VSP	Month 3	Poor (1–3)	55	5	9.1	-	<0.001

Sakr et al. 2016 [36]		Moderate TCD-defined VSP	Poor (1–3)	24	43.6	-	<0.001	
		Severe TCD-defined VSP	Poor (1–3)	26	47.3	-		
		Mild TCD-defined VSP	Good (4–5)	16	47.1	-		
		Moderate TCD-defined VSP	Good (4–5)	34	15	44.1		-
		Severe TCD-defined VSP	Good (4–5)	3	8.8	-		
		Mild TCD-defined VSP	Poor (1–3)	5	9.6	-		
		Moderate TCD-defined VSP	Poor (1–3)	52	23	44.2		-
		Severe TCD-defined VSP	Poor (1–3)	24	46.2	-		
	Month 6	Mild TCD-defined VSP	Good (4–5)	16	43.2	-		
		Moderate TCD-defined VSP	Good (4–5)	37	16	43.2		-
		Severe TCD-defined VSP	Good (4–5)	5	13.5	-		
		Mild TCD-defined VSP	Poor (1–3)	5	10.2	-		
		Moderate TCD-defined VSP	Poor (1–3)	46	21	42.9		-
		Severe TCD-defined VSP	Poor (1–3)	23	46.9	-		
	Month 12	Mild TCD-defined VSP	Good (4–5)	16	40.0	-		
		Moderate TCD-defined VSP	Good (4–5)	40	18	45.0		-
		Severe TCD-defined VSP	Good (4–5)	6	15.0	-		

Abbreviations: aVSP, angiographic vasospasm; CI, confidence interval; DCI, delayed cerebral ischemia; GOS, Glasgow outcome scale; n, number; No., number; OR, odds ratio; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; VSP, vasospasm.

Table S16. Clinical burden: Functional outcome (GOS-E) in patients with VSP or VSP-related complications compared with patients without VSP or VSP-related complications from comparative studies

Author (date)	Study Design	Subgroup	Assessment	GOS-E	No. pts	n	%	Mean	SD	p-value
Hurth et al. (2020) [30]	RLC	aVSP	At discharge	I-IV	49	36	73.5	-	-	0.01
		No aVSP			87	44	50.6	-	-	
		aVSP		V-VIII	49	13	26.5	-	-	
		No aVSP			87	43	49.4	-	-	
		aVSP	Month 3-6	I-IV	49	12	24.5	-	-	0.72
		No aVSP			87	16	18.4	-	-	
		aVSP		V-VIII	49	30	61.2	-	-	
		No aVSP			87	47	54.0	-	-	
		DCI	At discharge	I-IV	27	25	92.6	-	-	<0.001
		No DCI			111	57	51.4	-	-	
		DCI		V-VIII	27	2	7.4	-	-	
		No DCI			111	54	48.6	-	-	
		DCI	Month 3-6	I-IV	27	11	55.0	-	-	0.002
		No DCI			111	18	20.9	-	-	
		DCI		V-VIII	27	9	45.0	-	-	
		No DCI			111	68	79.1	-	-	
Vrsajkov et al. (2016) [40]	PLC	aVSP	Month 6	-	29	-	-	4.52	2.66	0.01
		No aVSP		-	25	-	-	6.16	2.11	

Abbreviations: aVSP, angiographic vasospasm; DCI, delayed cerebral ischemia; GOS-E, Glasgow outcome scale extended; n, number; No., number; PLC, prospective longitudinal cohort; pts, patients; RLC, retrospective longitudinal cohort; SD, standard deviation; VSP, vasospasm.

Table S17. Clinical burden: Cognitive impairment (MoCA and MMSE) in patients with VSP or VSP-related complications

Author (date) Study ID	Study Design	Predictor	Assessment	Endpoint	No. pts	Odds ratio (95% CIs)	β -coefficient	R ² value	p-value
MoCA									
Geraghty et al. (2020) [58]	RLC	Cerebral VSP	At discharge	MoCA <22	105	1.27 (0.554–2.908)	-	-	0.572
		DCI	At discharge	MoCA <22	105	3.079 (1.173–8.082)	-	-	0.022
Wong et al. (2012) [79]	PLC	Cerebral infarction due to DCI	Month 3	MoCA <26	90	-	-4.189	0.384	Significant
Ali et al. (2018) [42]	PLC	DCI*	Year 1	MoCA <21	82	3.9 (1.9–7.8)	-	-	<0.001
MMSE									
Macdonald et al. (2012) [67] CONSCIOUS-1	RCT (post hoc)	Severe aVSP	Week 12	MMSE	409	-	-	-	<0.0001**
Wong et al. (2012) [79]	PLC	Cerebral infarction due to DCI	Month 3	MMSE <27	90	-	-3.832	0.314	Significant

Abbreviations: aVSP, angiographic vasospasm; DCI, delayed cerebral ischemia; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; No., number; PLC, prospective longitudinal cohort; pts, patients; RCT, randomized controlled trial; RLC, retrospective longitudinal cohort; VSP, vasospasm. *number of days with DCI; **versus pts with no aVSP after adjustment for age and WFNS grade (Kruskal-Wallis one-way comparison across aVSP categories)

Table S18. Clinical burden: Mortality in patients with VSP or VSP-related complications compared with patients without VSP or VSP-related complications

Author (date)	Study design	Mortality	Subgroup	No. pts	No. deaths	% died	p-value
Jeon et al. (2012) [31]	RLC	In hospital	aVSP	28	0	0.0	1
			No aVSP	65	1	1.5	
Konczalla et al. (2016) [33]	RLC	In hospital	Cerebral VSP lasting >14 days	106	2	1.9	<0.0001
			Cerebral VSP lasting ≤14 days	106	24	22.6	
Mortimer et al. (2015) [35]	RCT (post hoc)	In hospital	Severe aVSP	17	0	0	1
			None/mild aVSP	63	2	3.2	
Appel et al. (2018) [22]	PLC	In hospital	DCI	14	2	14.3	0.08
			No DCI	20	0	0	
Sanelli et al. (2012) [37]	RLC	In hospital	DCI	81	9	11.0	<0.0001
			No DCI	56	1	2.0	
Lee et al. (2019) [34]	RLC	In hospital	DCI	97	nr	16.5	nr
			No DCI	366	nr	13.7	
Abulhasan et al. (2020) [21]	RLC	In hospital	DCI + standard therapy	89	8	9	0.357
			No DCI	212	27	13	
Brown et al. (2013) [24]	RLC	In hospital	Delayed infarction	20	2	10	0.134
			No infarction	114	3	2	
Budohoski et al. (2012) [25]	PLC	Day 21	DCI	32	3	9.375	nr
			No DCI	66	3	4.545	
Ehlert et al. (2016) [27]	RCC	Month 3	Standard therapy with TCD-defined VSP	25	9	36.0	nr
			Standard therapy no TCD-defined VSP	20	3	15.0	
			Molsidomine-treated TCD-defined VSP	29	1	3.4	0.0034*
Ding et al. (2020) [26]	PLC	Month 6	aVSP	52	26	50	<0.001
			No aVSP	51	10	19.61	
Konczalla et al. (2016) [33]	RLC	Month 6	Cerebral VSP lasting >14 days	106	9	8	<0.001
			Cerebral VSP lasting ≤14 days	106	29	27	

Abbreviations: aVSP, angiographic vasospasm; DCI, delayed cerebral ischemia; No., number; nr, not reported; PLC, prospective longitudinal cohort; pts, patients; RCC, retrospective case control; RCT,

randomized controlled trial; RLC, retrospective longitudinal cohort; TCD, transcranial Doppler; VSP, vasospasm. *versus standard therapy with VSP

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