

SUPPLEMENTAL MATERIAL

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Supplemental Table I. Baseline characteristics of all separate cohorts.

	Juvela et al ¹²		Lindgren et al ²⁰		Mensing et al ¹³		Wermer et al ¹⁶		Molenberg et al ¹⁷		Sonobe et al ¹⁸		Morita et al ¹⁴		Murayama et al ¹⁵		Gondar et al ¹⁹	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Number of patients	75	65	693	488	320	154	70	23	145	53	236	132	3799	1903	1039	522	225	66
Age (mean, SD)	42 ± 11	41 ± 10	57 ± 13	54 ± 11	55 ± 11	57 ± 11	51 ± 10	51 ± 11	56 ± 11	57 ± 11	63 ± 10	60 ± 10	63 ± 10	61 ± 10	66 ± 12	64 ± 11	56 ± 15	53 ± 15
Hypertension	24 (32)	26 (40)	302 (44)	186 (38)	130 (41)	67 (44)	38 (54)	11 (48)	70 (48)	19 (36)	107 (45)	53 (40)	1682 (44)	789 (41)	479 (46)	253 (49)	101 (45)	38 (58)
Smoking	39 (52)	60 (92)	273 (39)	310 (64)	146 (46)	61 (40)	62 (89)	22 (96)	76 (52)	29 (55)	89 (38)	85 (64)	340 (9)	617 (32)	220 (21)	287 (55)	112 (50)	41 (62)
Previous aSAH	67 (89)	62 (95)	21 (3)	23 (5)	0	0	59 (84)	18 (78)	68 (47)	13 (25)	25 (11)	9 (7)	138 (4)	48 (3)	28 (3)	15 (3)	3 (1)	0
Positive family history	12 (16)	15 (23)	161 (23)	87 (18)	44 (14)	18 (12)	23 (33)	6 (26)	42 (29)	18 (34)	24 (10)	12 ((9)	220 (6)	107 (6)	134 (13)	50 (10)	27 (12)	10 (15)
Multiple aneurysms	19 (25)	14 (22)	247 (36)	150 (31)	86 (27)	23 (15)	19 (27)	5 (22)	7 (5)	8 (15)	42 (18)	23 (17)	587 (15)	201 (11)	387 (37)	121 (23)	47 (21)	9 (14)
Size																		
< 7.0 mm	61 (81)	54 (83)	484 (70)	332 (68)	154 (48)	67 (44)	70 (100)	23 (100)	127 (88)	37 (70)	236 (100)	132 (100)	2670 (70)	1402(74)	984 (95)	505 (97)	212 (94)	59 (89)
7.0-9.9 mm	8 (11)	8 (12)	97 (14)	88 (18)	85 (27)	47 (31)	0	0	14 (10)	10 (19)	0	0	651 (17)	306 (16)	24 (2)	10 (2)	8 (4)	5 (8)
10.0-19.9 mm	4 (5)	2 (3)	92 (13)	49 (10)	69 (22)	32 (21)	0	0	4 (3)	4 (8)	0	0	418 (11)	172 (9)	25 (2)	5 (1)	5 (2)	2 (3)
> 20.0 mm	2 (3)	1 (2)	20 (3)	19 (4)	11 (3)	8 (5)	0	0	0	2 (4)	0	0	60 (2)	23 (1)	6 (1)	2 (0)	0	0
Aneurysm location																		
ICA	37 (49)	23 (35)	140 (20)	66 (14)	63 (20)	10 (7)	11 (16)	2 (9)	29 (20)	9 (17)	92 (39)	50 (38)	789 (21)	282 (15)	311 (30)	125 (24)	90 (40)	20 (30)
MCA	30 (40)	32 (49)	321 (46)	230 (47)	106 (33)	68 (44)	29 (41)	10 (44)	62 (43)	23 (43)	82 (35)	49 (37)	1333 (35)	694 (36)	281 (27)	128 (25)	80 (36)	18 (27)
ACA & P	8 (11)	10 (15)	232 (34)	192 (39)	151 (47)	76 (49)	30 (43)	11 (48)	54 (37)	21 (40)	62 (26)	33 (25)	1677 (44)	927 (49)	447 (43)	269 (52)	54 (24)	28 (42)

Phases (median, range)	8 (5-15)	8 (5-14)	9 (5-21)	9 (5-20)	5 (0-15)	5 (0-15)	4 (1-6)	5 (1-6)	4 (0-11)	4 (0-16)	6 (3-10)	5 (3-9)	7 (3-19)	7 (3-19)	7 (3-19)	7 (3-17)	2 (0-12)	4 (0-10)
Phases (mean, SD)	8.3 ± 2.4	8.6 ± 2.2	9.4 ± 3.2	9.6 ± 3.1	5.5 ± 3.3	6.1 ± 3.4	4.0 ± 1.6	4.2 ± 1.7	3.9 ± 2.0	4.6 ± 3.0	5.6 ± 1.8	5.4 ± 1.6	7.6 ± 3.1	7.5 ± 2.8	6.5 ± 2.5	6.5 ± 2.2	2.5 ± 2.1	3.4 ± 2.3
Ruptured aneurysms	22	10	8	6	8	2	0	0	0	1	5	1	79	27	41	14	1	2
Person-years of follow-up	1764.4	1259.2	1163.6	898.09	799.5	377.08	234.1	82.4	150.7	56.6	814.1	485.9	6329.77	3271.89	3858.28	1901.12	706.58	227.3
Follow-up years (median)	23.5 (1-52)	15.4 (1-50)	0.5 (0-18)	0.5 (0-23)	0.7 (0-21)	1 (0-18)	2.2 (1-15)	2.3 (1-10)	1 (0-2)	1 (0-2)	3.2 (0-7)	3.3 (0-7)	1.0 (0-8)	1.0 (0-9)	3.2 (0-11)	3.1 (0-11)	2.5 (0-13)	2.7 (0-10)
Rupture rate	1.25 (0.8-1.9)	0.79 (4.0-14.2)	0.69 (0.32-1.31)	0.69 (0.27-1.39)	1.0 (0.46-1.9)	0.53 (0.09-1.75)	-	-	-	1.77 (0.09-8.71)	0.61 (0.23-1.36)	0.21 (0.01-1.02)	1.25 (0.99-1.55)	0.83 (0.55-1.18)	1.06 (0.77-1.43)	0.74 (0.42-1.21)	0.14 (0.01-0.70)	0.88 (0.15-2.91)

aSAH: aneurysmal subarachnoid hemorrhage, SD: standard deviation, ICA: internal carotid artery, MCA: middle cerebral artery, ACA: anterior cerebral arteries, P: posterior circulation.

Supplemental Table II. Risk of bias assessment tool (QUIPS).

	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis reporting
Juvela et al ¹²	moderate	low	low	moderate	moderate	low
Mensing et al ¹³	low	high	low	moderate	moderate	low
Morita et al ¹⁴	low	moderate	low	moderate	moderate	low
Murayama et al ¹⁵	low	low	low	low	moderate	low
Wermer et al ¹⁶	low	low	low	moderate	low	low
Molenberg et al ¹⁷	low	high	low	low	low	low
Sonobe et al ¹⁸	low	moderate	low	low	low	low
Gondar et al ¹⁹	low	low	low	moderate	low	low
Lindgren et al ²⁰	low	moderate	low	moderate	moderate	low

Table III. Baseline characteristics of patients with and without aneurysm rupture.

Pooled data	No aneurysm rupture (n,%)	Aneurysm rupture (n,%)	Total (n,%)	p-value
Number of patients	9714	226	9940	
Women	6392 (66)	163 (72)	6555 (66)	0.047
Mean age (range)	61.0 (15-100)	63.7 (23-93)	61.1 (15-100)	0.001
Hypertension #	4230 (44)	114 (50)	4344 (44)	0.039
Ever smoker #	2772 (29)	58 (26)	2830 (29)	0.34
Previous aSAH	556 (6)	37 (16)	593 (6)	<0.001
Positive family history for aSAH #	969 (10)	23 (10)	992 (10)	0.92
Population				0.004
Finnish	1275 (13)	46 (20)	1321 (13)	
Japanese	7408 (76)	166 (74)	7574 (76)	
Dutch	743 (8)	11 (5)	754 (8)	
Swiss	228 (3)	3 (1)	291 (3)	
Multiple aneurysms	1960 (0)	58 (0)	2018 (20)	<0.001

Aneurysm size				<0.001
< 7.0 mm	7435 (77)	105 (47)	7540 (76)	
7.0-9.9 mm	1320 (14)	42 (19)	1326 (14)	
10.0-19.9 mm	828 (9)	56 (25)	884 (9)	
> 20.0 mm	131 (1)	23 (10)	154 (2)	
Aneurysm location				<0.001
Internal carotid artery	2107 (22)	28 (12)	2135 (22)	
Middle cerebral artery	3483 (36)	64 (28)	3547 (36)	
Anterior circulation or posterior circulation	4124 (43)	134 (59)	4258 (43)	
Phases score (median, range, mean, standard deviation)	7.0 (0-21) 7.2 ± 3.1	9.0 (2-20) 9.8 ± 4.0	7.0 (0-21) 7.2 ± 3.1	<0.001

aSAH; aneurysmal subarachnoid hemorrhage.

Data are missing for hypertension in 87 persons (1%), for smoking in 235 persons (2%) and for family history of aSAH in 146 persons (1%).

Figure I. Search strings.

Pubmed search string

#1:

"intracranial aneurysm"[Title/Abstract] OR "intracranial saccular aneurysm"[Title/Abstract]
OR
"cerebral aneurysm"[Title/Abstract] OR "intracranial aneurysms"[Title/Abstract] OR
"intracranial
saccular aneurysms"[Title/Abstract] OR "cerebral aneurysms"[Title/Abstract]

#2:

"risk of rupture"[Title/Abstract] OR "aneurysm rupture"[Title/Abstract] OR "risk
factors"[Title/Abstract]
OR "rupture"[Title/Abstract] OR "unruptured"[Title/Abstract] OR "subarachnoid
hemorrhage"[Title/Abstract]

#3:

"follow-up"[Title/Abstract] OR "follow up"[Title/Abstract] OR "natural
history"[Title/Abstract] OR "natural
course"[Title/Abstract]

#1 AND #2 AND #3

Embase search string

#1:

'intracranial aneurysm':ti:ab OR 'intracranial saccular aneurysm':ti:ab OR 'cerebral
aneurysm':ti:ab OR
'intracranial aneurysms':ti:ab OR 'intracranial saccular aneurysms':ti:ab OR 'cerebral
aneurysms':ti:ab

#2:

'risk of rupture':ti:ab OR 'aneurysm rupture':ti:ab OR 'risk factors':ti:ab OR 'rupture':ti:ab
OR
'unruptured':ti:ab OR 'subarachnoid hemorrhage':ti:ab – 339.423

#3:

'follow-up':ti:ab OR 'follow up':ti:ab OR 'natural history':ti:ab OR 'natural course':ti:ab -
688.714

#1 AND #2 AND #3

Supplemental Table II. Complete case analysis: hazard ratio (HR) of the rupture rate in women compared to men adjusted for the PHASES score, smoking and positive family history of aneurysmal subarachnoid hemorrhage, analyzing the data per patient.

