THE LANCET Neurology

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Greving JP, Wermer MJH, Brown RD Jr, et al. Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies. *Lancet Neurol* 2013; published online Nov 27. http://dx.doi.org/10.1016/S1474-4422(13)70263-1.

Appendix

The absolute 5-year risk of aneurysm rupture (%) was calculated as $1 - S(t_5)^{\exp(ß)}$, where ß = A - B and the baseline survival for 5 years [$S(t_5)$] is 0.97754.

The beta coefficients from our final Cox regression model are used to calculate a linear function (A). The latter is corrected for the averages of the patients' risk factors (B), and the subsequent result [ß] is exponentiated and used to calculate a 5-year probability of aneurysm rupture after insertion into a survival function.

A = 0.362 (if age 70+) + 0.302 (if hypertension present) + 0.368 (if history SAH present) + 0.822 (if size 7-10 mm) + 1.705 (if size 10-20 mm) + 3.046 (if size ≥ 20 mm) + 0.530 (if ACA location) - 0.617 (if ICA location) + 0.698 (if posterior communicating artery or posterior location) + 1.017 (if Japanese) + 1.348 (if Finnish).
B = 1.601

As an example how to use this formula: consider a 55-year-old American man, no hypertension, no previous SAH, with one medium-sized (8 mm) posterior circulation aneurysm. In this instance, A = 0 (for age 55) + 0 (for hypertension not present) + 0 (for history SAH not present) + 0.822 (for size 8.0) + 0.698 (for posterior location) + 0 (for American) = 1.520
ß = 1.520 – 1.601 = -0.081
exp (ß) = 0.922
$1 - S(t_5)^{0.922} = 1 – 0.97754^{0.922} = 1 – 0.979 = 0.021 = 2.1\%$
He will have a 2% chance of rupture over 5 years.

Webtable 1 – 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**

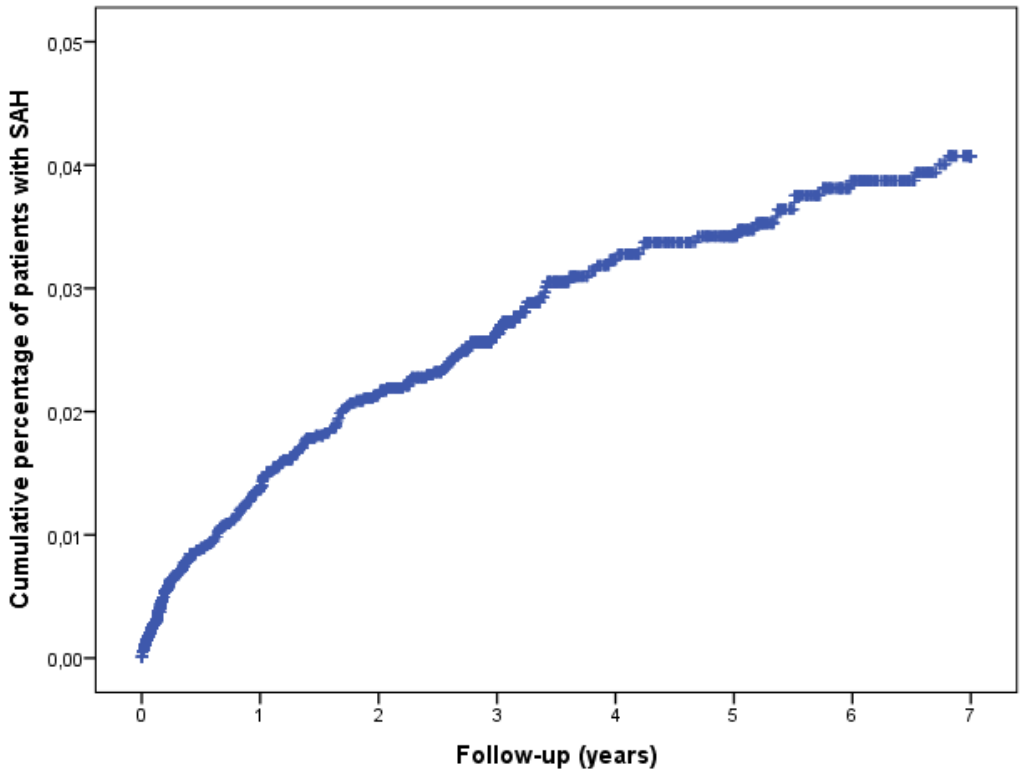
Webtable 2 - Baseline characteristics of all separate cohorts

	ISUIA		Juvela		SUAVe*		Ishibashi		Wermer		UCAS	
	n	%	n	%	n	%	n	%	n	%	n	%
	1691		142		374		419		93		5720	
Patient characteristics												
Women	1260	75%	76	54%	238	64%	280	67%	70	75%	3805	67%
Age (in years; mean±SD)	55.2	13.1	41.8	10.1	62.5	10.5	59.8	11.4	50.5	10.5	62.5	10.3
< 40	210	12%	58	41%	9	2%	23	5%	13	14%	119	2%
40-49	387	23%	52	37%	30	8%	49	12%	28	30%	463	8%
50-59	413	24%	30	21%	108	29%	123	29%	33	35%	1552	27%
60-69	422	25%	2	1%	138	37%	139	33%	19	20%	2009	35%
70+	259	15%	0	0%	89	24%	85	20%	0	0%	1577	28%
Hypertension	731	44%	51	36%	163	44%	-		46	52%	2480	43%
Ever smoking	1294	77%	85	69%	75	41%	-		80	92%	960	17%
Prior SAH	615	36%	131	92%	36	10%	14	3%	77	83%	187	3%
Number of aneurysms												
Single	1218	72%	109	77%	313	84%	298	71%	69	74%	4927	86%
Multiple	473	28%	33	23%	61	16%	121	29%	24	26%	793	14%
Aneurysm characteristics												
Total of unruptured aneurysms at baseline	2362		181		442		529		125		6697	
Size of aneurysms (in mm; mean±SD)	6.4	5.7	4.7	3.4	3.3	0.9	4.5	3.5	2.9	1.0	5.7	3.6
< 5.0	1217	52%	112	62%	424	96%	392	74%	116	93%	3132	47%
5.0-6.9	439	19%	42	23%	18	4%	83	16%	9	7%	1854	28%
7.0-9.9	279	12%	17	9%			24	5%			1016	15%
10.0-19.9	314	13%	7	4%			22	4%			611	9%
>= 20.0	103	4%	3	2%			8	2%			84	1%

Aneurysm location												
Anterior cerebral arteries and branches	242	10%	15	8%	75	17%	107	20%	16	13%	1381	21%
Internal carotid artery	1222	52%	79	44%	172	39%	216	41%	39	31%	2282	34%
posterior communicating artery	341	14%	-		-		92	17%	20	16%	1037	15%
other ICA	881	37%	-		-		124	23%	19	15%	1245	19%
Middle cerebral artery	644	27%	82	45%	157	36%	141	27%	53	42%	2425	36%
Posterior circulation	254	11%	5	3%	38	9%	65	12%	17	14%	609	9%
Ruptured aneurysms	59		34		7		19		1		111	
Person-years of follow-up	14005		3064		1336		1050		316		9596	

* 193 patients in the SUAVe study[12] had missing smoking status. This variable was introduced one year after the start of the cohort study. SAH, subarachnoid haemorrhage.

Webfigure 1 – Kaplan-Meier estimation of aneurysm rupture.



Webfigure 2 – Calibration plot for 5-year risk of aneurysm rupture. Values depict observed and predicted event-free survival with 95% confidence intervals. The dotted 45° line denotes ideal agreement between predicted and observed
risk.