L’aneurisma non rotto: dubbi e certezze

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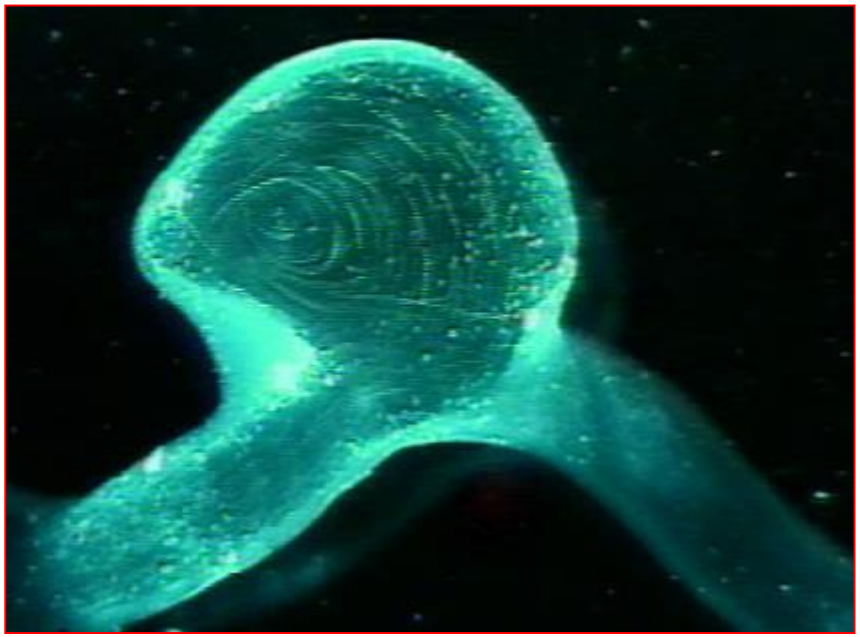
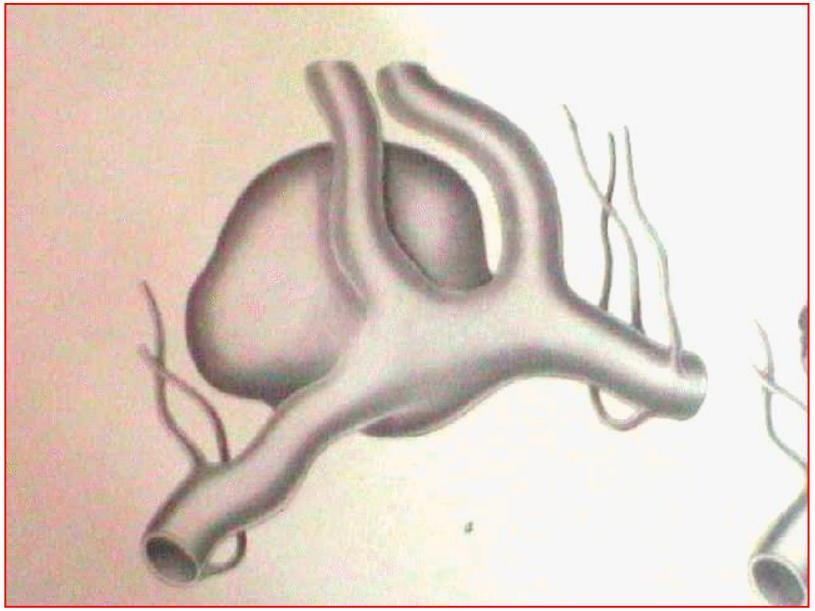
Lancet. 2003 Jul 12;362(9378):103-10.

Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment.

Wiebers DO1, Whisnant JP, Huston J 3rd, Meissner I, Brown RD Jr, Piepgras DG, Forbes GS, Thielen K, Nichols D, O'Fallon WM, Peacock J, Jaeger L, Kassell NF, Kongable-Beckman GL, Torner JC; International Study of Unruptured Intracranial Aneurysms Investigators.





ISUIA 2003

- 4060 pazienti reclutati in Europa, USA e Canada

- 1692 non trattati e seguiti in follow up
- 1917 sottoposti a chirurgia
- 451 a trattamento endovascolare

ISUIA: caratteristiche dei pazienti

	No surgery (n=1692)	Surgery		p*	p†
		Open surgical (n=1917)	Endovascular (n=451)		
Subarachnoid haemorrhage					
No (group 1)	1077	1591	409	<0·0001	<0·0001
Yes (group 2)	615	326	42		
Age (years) (mean [SD])	55·2 (13·1)	51·5 (11·4)	53·7 (13·1)	<0·0001	<0·0001
Women (%)	1261 (74·5%)	1456 (75·9%)	351 (77·8%)	0·302	0·399
White	1550 (91·6%)	1734 (90·4%)	427 (94·7%)	0·015	0·004
Number with unruptured aneurysms					
Single	1006 (59·7%)	1284 (67·5%)	309 (70·7%)	<0·0001	0·298
Multiple	679 (40·3%)	623 (32·5%)	132 (29·3%)		
Total number of unruptured aneurysms	2686	2884	651		
Maximum diameter of aneurysms (mm) (mean [SD])	7·4 (6·9)	9·6 (6·7)	13·1 (9·7)	<0·0001	<0·0001
Size of aneurysm (mm), (number of patients [%])				<0·0001	<0·0001
2–7	1049 (62·0%)	735 (38·6%)	126 (27·9%)		
7–12	390 (23·0%)	758 (39·8%)	137 (30·4%)		
13–24	198 (11·7%)	332 (17·4%)	133 (29·5%)		
⩾25	55 (3·2%)	80 (4·2%)	55 (12·2%)		
Aneurysm location (number of patients [%])				<0·0001	<0·0001
Cavernous part of carotid artery	210 (12·4%)	38 (2·0%)	89 (19·7%)		
Internal carotid artery	387 (22·9%)	681 (35·6%)	145 (32·2%)		
Anterior communicating or anterior cerebral artery	175 (10·3%)	284 (14·8%)	41 (9·1%)		
Middle cerebral artery	475 (28·1%)	650 (34·0%)	54 (12·0%)		
Posterior communicating artery	246 (14·5%)	84 (4·4%)	15 (3·3%)		
Vertebrobasilar system (other than basilar tip)	87 (5·1%)	72 (3·8%)	40 (8·9%)		
Tip of basilar artery	112 (6·6%)	105 (5·5%)	67 (14·9%)		

ISUIA : motivo dell'angiografia diagnostica

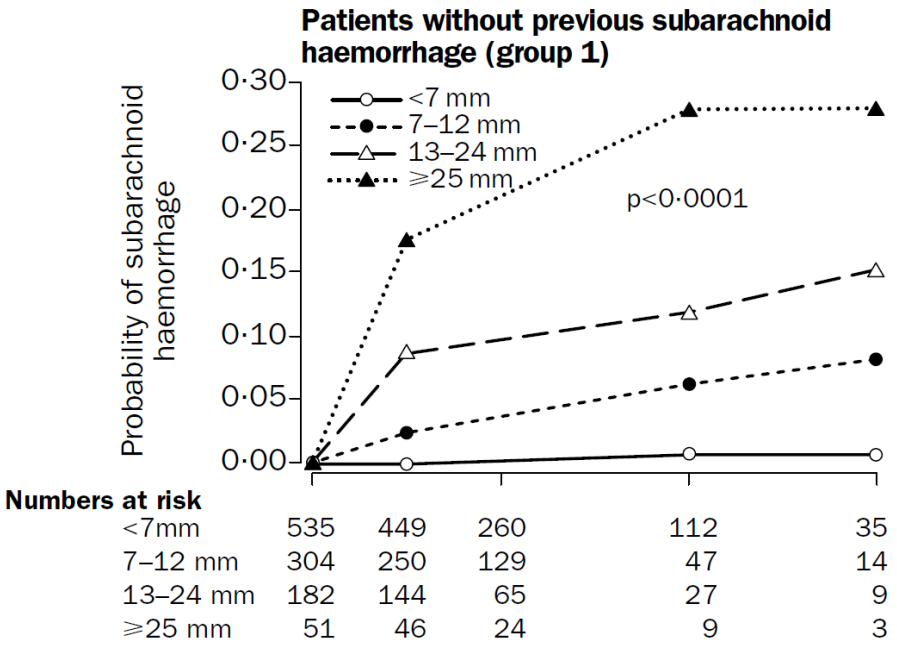
	No surgery	Surgery		p*	p†
		Open surgical	Endovascular		
Subarachnoid haemorrhage	514 (30·4%)	263 (13·7%)	38 (8·5%)	<0·0001	0·003
Cranial nerve deficit	135 (8·0%)	197 (10·3%)	113 (25·2%)	<0·0001	<0·0001
Other aneurysm mass effect	45 (2·7%)	103 (5·4%)	38 (8·5%)	<0·0001	0·012
Ischaemic cerebrovascular disease	178 (10·5%)	102 (5·3%)	22 (4·9%)	<0·0001	0·746
Subdural or intracerebral haematoma	21 (1·2%)	6 (0·3%)	2 (0·4%)	0·003	0·662
Brain tumour	13 (0·8%)	6 (0·3%)	3 (0·7%)	0·165	0·270
Central nervous system degenerative condition	7 (0·4%)	4 (0·2%)	3 (0·7%)	0·267	0·147
Convulsive disorder	49 (2·9%)	85 (4·4%)	18 (4·0%)	0·049	0·696
Headaches	401 (23·7%)	643 (33·6%)	166 (37·0%)	<0·0001	0·161
Transient ischaemic attack	180 (10·6%)	133 (6·9%)	26 (5·8%)	<0·0001	0·387
Undefined spells	121 (7·1%)	200 (10·4%)	46 (10·3%)	0·002	0·915
CT	510 (30·1%)	748 (39·0%)	190 (42·4%)	<0·0001	0·189
MRI	434 (25·6%)	826 (43·1%)	235 (52·5%)	<0·0001	<0·0001
Other	502 (29·7%)	565 (29·5%)	116 (25·9%)	0·130	0·130

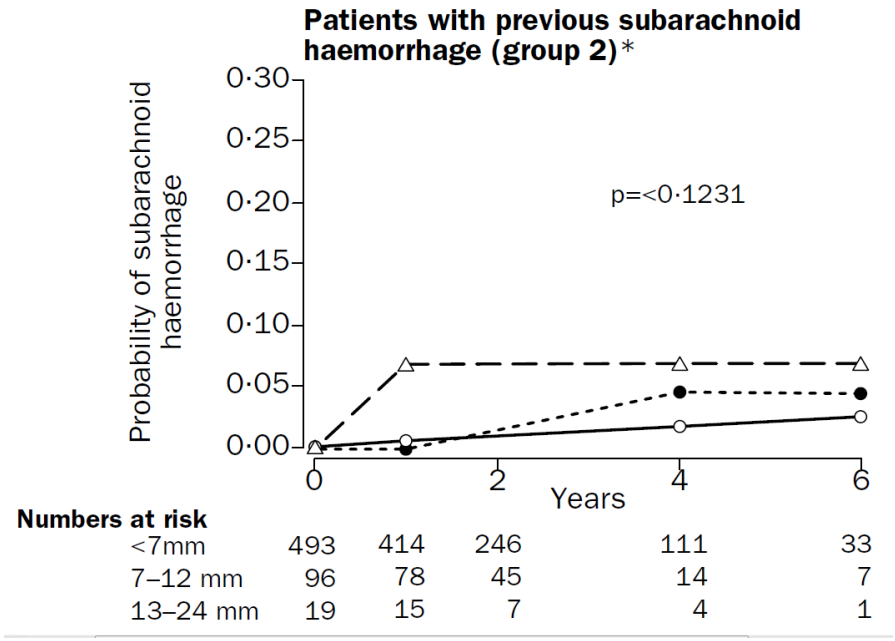
ISUIA: caratteristiche cliniche dei pazienti

	No surgery	Surgery		p*	p†
		Open surgical	Endovascular		
Medical history					
Hypertension	732 (43·6%)	730 (38·3%)	188 (42·1%)	0·004	0·143
Hypertension therapy	637 (37·8%)	640 (33·5%)	162 (36·1%)	0·002	0·294
Atrial fibrillation	57 (3·4%)	44 (2·3%)	12 (2·7%)	0·133	0·636
Cardiac arrhythmias	78 (4·7%)	95 (5·0%)	21 (4·7%)	0·916	0·822
Congestive heart failure	18 (1·1%)	8 (0·4%)	5 (1·1%)	0·054	0·102
Myocardial infarction	109 (6·5%)	77 (4·0%)	23 (5·2%)	0·004	0·299
Valvular disease	37 (2·2%)	40 (2·1%)	12 (2·7%)	0·740	0·450
Family history					
Aneurysms	276 (18·4%)	400 (22·9%)	65 (16·2%)	0·001	0·003
Subarachnoid haemorrhage	271 (18·0%)	350 (20·2%)	64 (15·8%)	0·070	0·042
Indeterminate haemorrhage	147 (10·0%)	209 (12·2%)	38 (9·4%)	0·075	0·118
Indeterminate stroke	553 (36·2%)	631 (32·7%)	144 (35·0%)	0·895	0·766
Coronary artery disease	662 (43·0%)	793 (45·0%)	174 (41·6%)	0·326	0·215
Intermittent claudication	107 (8·0%)	111 (7·0%)	26 (6·8%)	0·521	0·902
Focal cerebral ischaemic episodes‡	143 (10·5%)	180 (11·5%)	42 (11·0%)	0·702	0·768
Behavioural history					
Alcohol (>5 drinks per 24 h)	502 (30·2%)	498 (26·3%)	97 (21·7%)	0·001	0·045
Current smoker	693 (41·1%)	900 (47·2%)	174 (38·6%)	<0·0001	<0·0001
Former smoker	602 (35·7%)	608 (31·9%)	145 (32·2%)		
Use of stimulants	79 (4·7%)	145 (7·6%)	22 (4·9%)	0·001	0·042
Use of oral contraceptives	542 (44·7%)	753 (52·8%)	167 (48·7%)	<0·0001	0·174
Associated disorders					
Coarctation of aorta	9 (0·5%)	2 (0·1%)	0 (0·0%)	0·023	0·493
Polycystic kidney disease	25 (1·6%)	39 (2·1%)	7 (1·6%)	0·531	0·487
Arteriovenous malformation	34 (2·0%)	38 (2·0%)	13 (2·9%)	0·465	0·235
Ehlers-Danlos syndrome	0 (0%)	0 (0·0%)	0 (0·0%)		
Neurofibromatosis	0 (0%)	2 (0·1%)	2 (0·5%)	0·044	0·162
Tuberous sclerosis	0 (0%)	2 (0·1%)	0 (0·0%)	0·225	0·494
Moyamoya disease	0 (0%)	0 (0·0%)	0 (0·0%)		
Hypocoagulable state	6 (0·4%)	4 (0·2%)	1 (0·2%)	0·672	0·952
Fibromuscular disease	14 (0·9%)	22 (1·1%)	7 (1·6%)	0·453	0·482

ISUIA: Storia naturale

1692 pazienti con (1077 pazienti nel gruppo 1 e 615 nel gruppo 2) sono stati trattati conservativamente.
Tempo medio di follow up 4.1 anni
193 pazienti morti per alter cause





41 emorragie subaracnoidee
2 in pazienti con aneurismi < 7 mm
5 in pazienti con aneurismi 7–9 mm

8 emorragie subaracnoidee
per aneurismi inferiori ai 7 mm

SEDE DELL'ANEURISMA E ROTTURA

	<7 mm		7–12 mm	13–24 mm	⩾25 mm
	Group 1	Group 2			
Cavernous carotid artery (n=210)	0	0	0	3·0%	6·4%
AC/MC/IC (n=1037)	0	1·5%	2·6%	14·5%	40%
Post-P comm (n=445)	2·5%	3·4%	14·5%	18·4%	50%

AC=anterior communicating or anterior cerebral artery. IC=internal carotid artery (not cavernous carotid artery). MC=middle cerebral artery. Post-P comm=vertebrobasilar, posterior cerebral arterial system, or the posterior communicating artery.

Table 4: **5-year cumulative rupture rates according to size and location of unruptured aneurysm**

PAZIENTI TRATTATI

	Open surgical		Endovascular	
	Group 1 (n=1591)	Group 2 (n=326)	Group 1 (n=409)	Group 2 (n=42)
At 30 days				
Surgery-related death	28 (1·8%)	1 (0·3%)	8 (2·0%)	0
Disability				
Rankin score of 3–5 only	48 (3·0%)	7 (2·1%)	9 (2·2%)	1 (2·4%)
Impaired cognitive status only	68 (4·3%)	21 (6·4%)	13 (3·2%)	2 (4·8%)
Rankin score of 3–5 and impaired cognitive status	74 (4·7%)	7 (2·1%)	8 (2·0%)	0 (0·0%)
Overall morbidity and mortality for all patients	218 (13·7%)	36 (11·0%)	38 (9·3%)	3 (7·1%)
At 1 year				
Surgery-related death	43 (2·7%)	2 (0·6%)	14 (3·4%)	0
Disability				
Rankin score of 3–5 only	22 (1·4%)	3 (0·9%)	4 (1·0%)	0
Impaired cognitive status only	87 (5·5%)	23 (7·1%)	13 (3·2%)	3 (7·1%)
Both Rankin score of 3–5 and impaired cognitive status	48 (3·0%)	5 (1·5%)	9 (2·2%)	0 (0·0%)
Overall morbidity and mortality* for all patients	200 (12·6%)	33 (10·1%)	40 9·8%)	3 (7·1%)

*Overall morbidity and mortality includes death, and one of both Rankin score 3–5 and impaired cognitive status.

Table 5: **Outcome 30 days and 1 year after surgery**

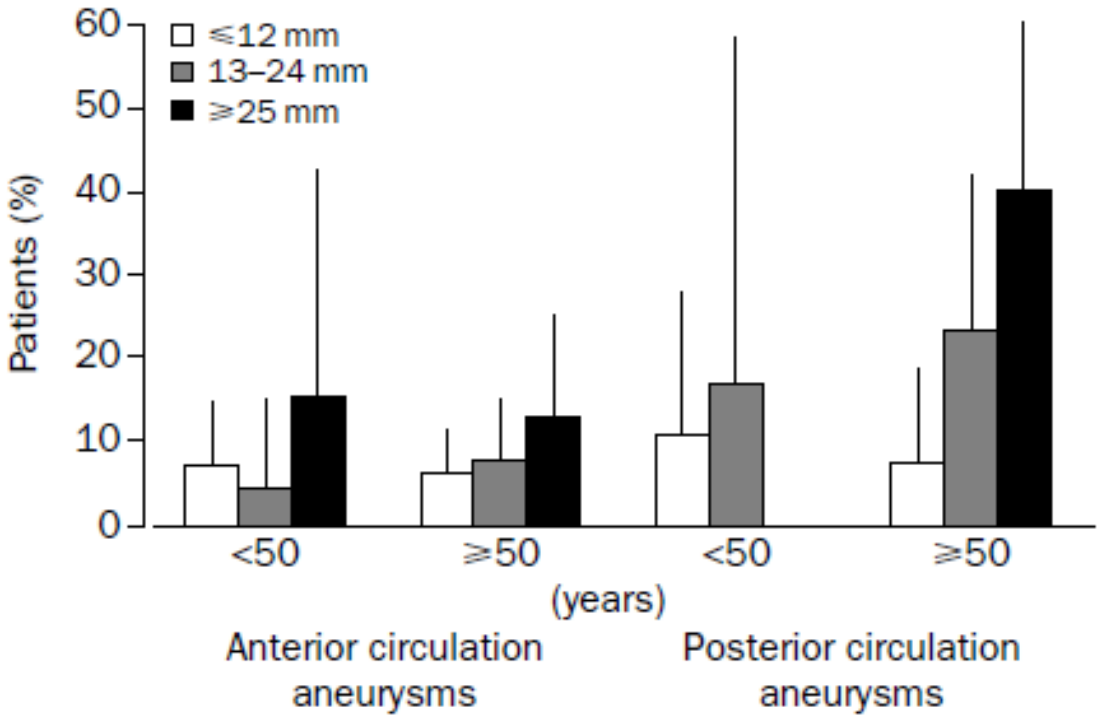


Figure 4: **Poor endovascular outcomes at 1 year by age, site, and size of aneurysm**

Poor outcome is death, a Rankin score between 3 and 5, or impaired cognitive status. Bars show 95% CI.

Patients' age is an important factor in overall surgical outcome, with a substantial increase in risk for those about 50 years and older, which rises substantially after age 60–70 years.

Nei pazienti > 65 anni il rischio chirurgico è stato il 30%

Neurosurgery ottobre 2016
Rahme RJ, Pines AR, Krishna C, Bendok BR

Understanding Rupture Risk Factors for Intracranial Aneurysms: Which Ticking Time Bomb Needs to be Defused?

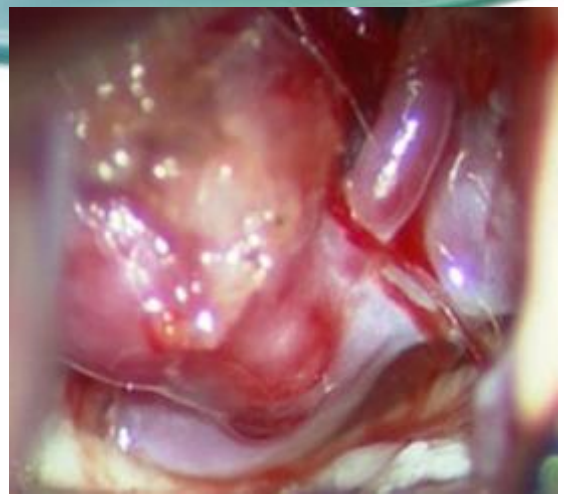
Understanding the natural history of a disease is paramount to defining treatment strategies and algorithms. Intracranial aneurysms are no exception to this rule. Over the past decade, an extensive body of literature has been generated with the goal of improving our understanding of intracranial aneurysms and the factors that govern their rupture risk.[1-5] However, most large-scale trials have been marred with controversy, including the International Study of Unruptured Intracranial Aneurysms (ISUIA),[6] the shortcomings of which are well documented.[7-9] Although certain intrinsic and extrinsic factors have consistently been found to be associated with a higher risk of rupture in various studies, there is still a lack of a complete understanding of the natural history of intracranial aneurysms. In addition, in further analysis of the known risk factors, some discrepancies start to emerge. For example, although aneurysm size is a well-documented risk factor, the optimal cutoff size is yet to be defined. Aneurysm location can also affect rupture risk independently of size. In addition, with the increasing number of population-based studies, certain reports of interracial differences have emerged, further adding to the complexity of the matter.[5,10]

In the face of all this uncertainty, Murayama et al[11] conservatively followed up a cohort of

Table. Annual Rate of Rupture According to Size and Location of Aneurysm[a]

Location	2-4 mm	5-6 mm	7-9 mm	10-24 mm	≥25 mm	Total
ACA	0.45 (0.19-1.07)	4.01 (1.5-10.68)	0	0	N/A	0.72 (0.37-1.38)
ICA without Pcom	0.11 (0.28-0.45)	0	4.7 (0.66-33.2)	2.6 (0.37-18.6)	0	0.2 (0.08-0.55)
ICA-Pcom	0.29 (0.11-0.77)	3.78 (1.22-11.73)	8.38 (2.70-25.97)	31.98 (13.27-76.60)	220.03 (30.99-1562.81)	1.6 (0.65-1.72)
MCA	0.44 (0.22-0.87)	3.0 (1.20-7.20)	0	20.34 (6.46-62.12)	N/A	0.79 (0.48-1.28)
VABA	0.62 (0.20-1.91)	6.43 (2.67-15.44)	0	5.88 (1.47-23.52)	2435 (343-17286.24)	1.74 (0.96-3.15)
Overall aneurysm-years	0.33 (0.22-0.51)	3.07 (1.91-4.93)	2.9 (1.09-7.72)	10.24 (5.67-18.49)	33.05 (8.27-132.17)	0.76 (0.58-0.98)

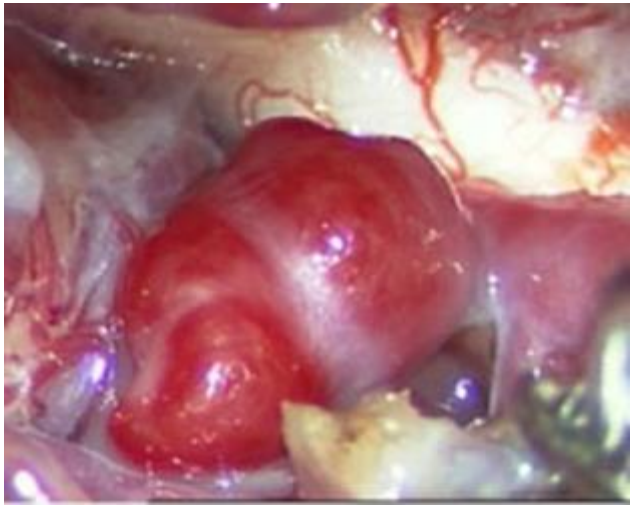
[a]ACA, anterior cerebral artery; ICA, internal carotid artery; MCA, middle cerebral artery; Pcom, posterior communicating artery; VABA, vertebral artery–basilar artery. Results reported as rate of rupture per aneurysm per year (%) (95% confidence interval). Modified with permission from Murayama Y, Takao H, Ishibashi T, et al. Risk analysis of unruptured intracranial aneurysms: prospective 10-year cohort study. *Stroke*. 2016;47(2):365-371.



Aneurismi non rotti

J Neurosurg. 2014 Aug 29:1-15.

Age-related differences in unruptured intracranial aneurysms: 1-year outcomes.

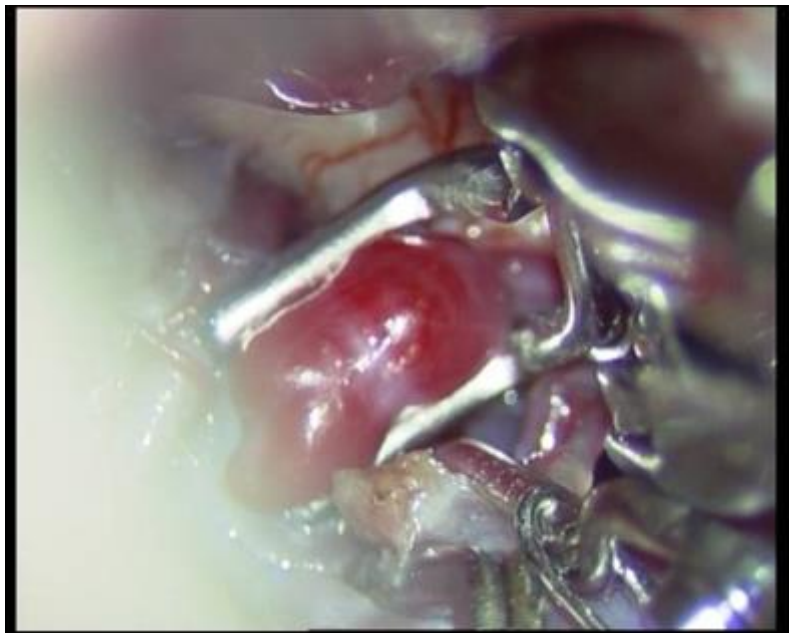


Mahaney KB1, Brown RD Jr, Meissner I, Piepgras DG, Huston J 3rd, Zhang J, Torner JC; for the ISUIA Investigators.

559 pazienti

3 gruppi: < 50, 50-65, > 65 anni

Valutazione di Outcome ad 1 anno considerando:
tasso di sanguinamento,
morbilità e mortalità da emorragia o da procedura e
mortalità globale



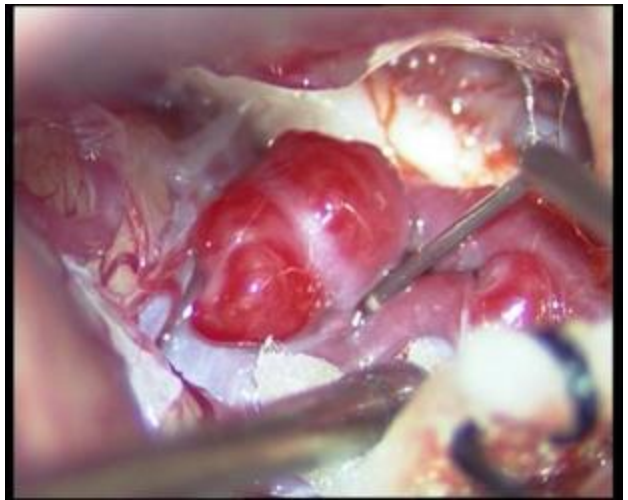
RISULTATI

La mortalità per sanguinamento non aumenta con l'età

La mortalità e la morbilità aumentano con l'aumentare dell'età con la chirurgia, ma non con il trattamento endovascolare

La morbilità neurologica è del 19% nei pazienti chirurgici anziani e dell'8% nei pazienti trattati per via endovascolare

Il trattamento chirurgico ha migliori risultati dell'endoscolare nei pazienti giovani (<50 aa)



Antiaggreganti? SI

- Aspirin as a promising agent for decreasing incidence of cerebral aneurysm rupture.

- Hasan DM, Mahaney KB, Brown RD Jr, Meissner I, Piepgras DG, Huston J, Capuano AW, Torner JC; International Study of Unruptured Intracranial Aneurysms Investigators.

- Stroke. 2011 Nov;42(11):3156-62.

Antiaggreganti

- Aspirin for prevention of subarachnoid hemorrhage: the stage is set for a randomized controlled trial.

- Chalouhi N, Jabbour P, Hasan D, Starke RM.

- Neurosurgery. 2014 Jan;74(1):E147-8

Anticoagulanti? Probabilmente si

- The safety of anticoagulation in patients with intracranial aneurysms.
- Tarlov N1, Norbash AM, Nguyen TN.
- J Neurointerv Surg. 2013 Sep 1;5(5):405-9.

- 42 pazienti
- INR>2
- Diametro aneurisma 5.1±3.6 mm
- Follow up medio 495±749 giorni per paziente
- Nessun sanguinamento