Natural History of Unruptured Intracranial Aneurysms: A Meta-Analysis of Prospective Studies

Robert F. Rudy BS; Hormuzdiyar H. Dasenbrock MD; Rose Du MD, PhD

Brigham and Women's Hospital Department of Neurosurgery and Harvard Medical School
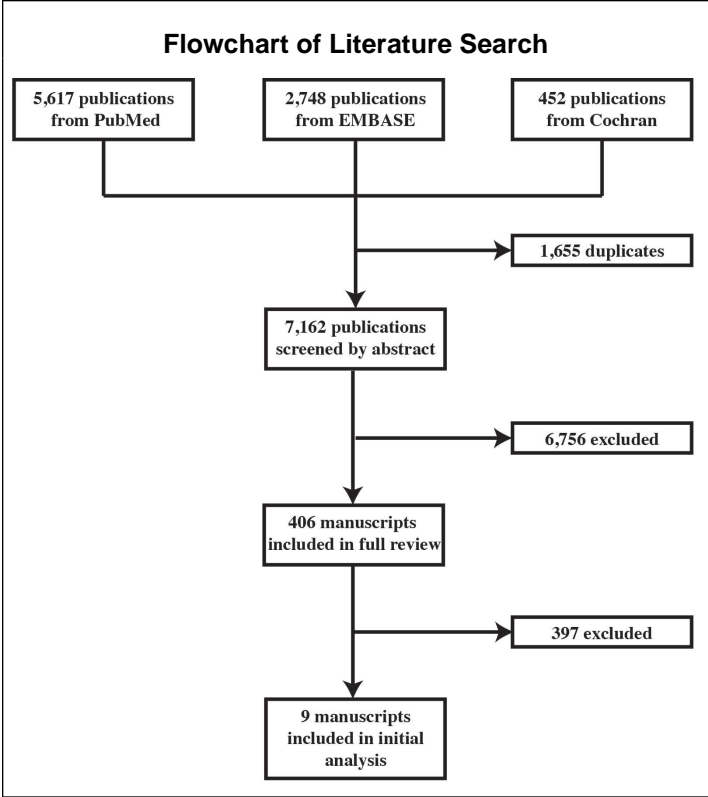
Introduction

The predictors of the rupture of cerebral aneurysms remain only partially understood. Further assessment of the hemorrhage risk of cerebral aneurysms may aid cerebrovascular surgeons when comparing the risk of subarachnoid hemorrhage with the periprocedural risk from aneurysm obliteration. The goal of this study was to perform a study-level meta-analysis of prospective, longitudinal studies to estimate the annual subarachnoid hemorrhage rate and predictors of aneurysm rupture.

Methods

The Medline, EMBASE, and Cochran databases were queried for studies evaluating the hemorrhage risk of unruptured intracranial aneurysms that were published through May 5th, 2015. Records identified in the search were screened by abstract and relevant articles were obtained and read in full to determine eligibility.

Flowchart of Literature Search

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5,617 publications    2,748 publications    452 publications
from PubMed           from EMBASE           from Cochran

                                    → 1,655 duplicates

7,162 publications
screened by abstract
                                    → 6,756 excluded

406 manuscripts
included in full review
                                    → 397 excluded

9 manuscripts
included in initial
analysis
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Methods

Longitudinal, prospective studies with data on the risk of rupture of untreated cerebral aneurysms were included. Two investigators extracted data on patient age, sex, hypertension, smoking, family history of subarachnoid hemorrhage, aneurysm size, and arterial location.

Results

From the 7,162 studies identified in the initial search, 406 studies were obtained in full and 9 met inclusion criteria. A total of 9,111 patients with 11,543 aneurysms were included, who were followed for 25,642 patient years. Study populations were from North America, Europe and Japan. The mean age of patients enrolled was 60.4 years and 68.4% were female. The overall annual rupture rate was 0.8%. Univariable meta-regression analysis identified aneurysm size greater than 7mm, male sex, and Finnish or Japanese study population as significantly associated with increased risk of rupture (p=0.04). However, in multivariable meta-regression, only size larger than 7mm remained independently associated with aneurysm rupture (p=0.002).
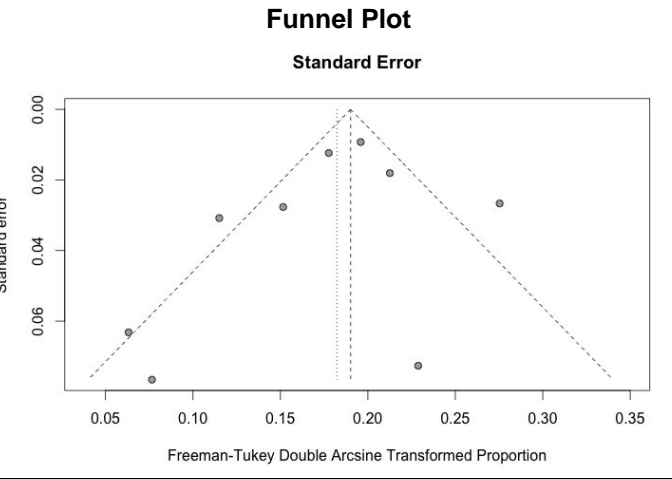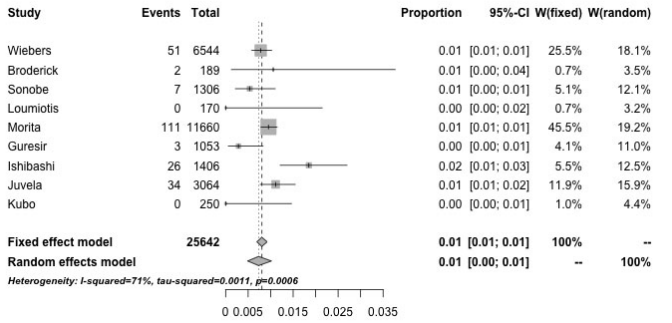
Studies Included in Analysis

First Author	Year	Number Subjects	Number Aneurysms	Number SAH (subjects)	Mean Age	Percent Female	Percent Ever Smoker	Percent HTN	Percent Family Hx of SAH
Wiebers	2003	1692	2686	51	55.2	74.5	76.8	43.6	18
Broderick	2009	113	148	2	51.4	66	83	50	-
Sonobe	2010	374	448	7	61.9	63.6	-	24.9	8.3
Loumiotis	2011	125	160	0	64.4	73.6	-	-	-
Morita	2012	5720	6697	111	62.5	66.5	16.8	43.4	12.9
Guresir	2013	263	384	3	55	77.6	57.4	42.6	3
Ishibashi	2013	603	741	26	59.2	71.1	-	-	-
Juvela	2013	142	181	34	41.8	53.5	70	36	10
Kubo	2014	79	98	0	73.9	73.4	-	68.4	3.8

Variables Associated with Aneurysm Rupture Achieving Statistical Significance

Univariate	p≤0.04
Aneurysm Size > 7mm	
Male Sex	
Finish or Japanese Study Population	
Multivariate	p=0.002
Aneurysm Size >7mm	

Support

Forest Plot of Incidence Rates from Included Studies

Study	Events	Total	Proportion	95%-CI	W(fixed)	W(random)
Wiebers	51	6544	0.01	[0.01; 0.01]	25.5%	18.1%
Broderick	2	189	0.01	[0.00; 0.04]	0.7%	3.5%
Sonobe	7	1306	0.01	[0.00; 0.01]	5.1%	12.1%
Loumiotis	0	170	0.00	[0.00; 0.02]	0.7%	3.2%
Morita	111	11660	0.01	[0.01; 0.01]	45.5%	19.2%
Guresir	3	1053	0.00	[0.00; 0.01]	4.1%	11.0%
Ishibashi	26	1406	0.02	[0.01; 0.03]	5.5%	12.5%
Juvela	34	3064	0.01	[0.01; 0.02]	11.9%	15.9%
Kubo	0	250	0.00	[0.00; 0.01]	1.0%	4.4%
Fixed effect model		25642	0.01	[0.01; 0.01]	100%	--
Random effects model			0.01	[0.00; 0.01]	--	100%

Heterogeneity: I-squared=71%, tau-squared=0.0011, p=0.0006

Funnel Plot

Standard Error

Conclusions

In this study-level meta-analysis of prospective, longitudinal studies, the annual rupture rate of cerebral aneurysms was 0.8%. However, the only independent predictor of subarachnoid hemorrhage was aneurysm size greater than 7 mm.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) describe the importance of characterizing the natural history of intracranial aneurysms, 2) discuss putative risk factors for the rupture of intracranial aneurysms, and 3) identify factors that particularly worrisome for aneurysm rupture.