

Prognostic Significance of Age and Gender in Aneurysmal Subarachnoid Hemorrhage: Pooled Analysis of Individual Patient Data from the SAHIT Repository

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Introduction

Age and gender are important constitutive factors influencing the etiopathogenesis and outcomes of aneurysmal subarachnoid hemorrhage (aSAH). We explored the prognostic value of age and gender in patients whose clinical records are archived in the Subarachnoid Hemorrhage International Trialists (SAHIT) repository. The purposes of the study were to (1) investigate the change point in the prognostic effect of age (2) more accurately estimate the prognostic strength of age and gender for 3-month functional outcomes on the GOS (3) examine whether the effects of age and gender differ between trial and non-trial patients.

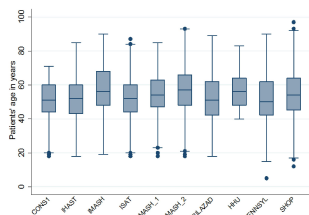
Methods 1:

We abstracted individual patient data (N=10,951) on age and gender from 8 RCT and 2 prospective hospital datasets in the SAHIT repository and analyzed the strength of prognostic associations using binary and proportional odds logistic regression, and random effects meta-analysis.

Methods 2:

We analyzed age as a continuous predictor using spline functions, scaling the effect as the odds ratio over the difference between the 75th and 25th percentiles. Multivariable analysis sequentially accounted for the effect of clinical, neuroimaging and treatment covariates.

Box plot of age distribution across included studies

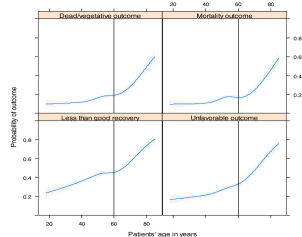


Average age of patients was comparable across studies

Results 1:

Age has a monotone relationship to GOS outcomes, which is adequately approximated as a linear function. Optimal change point in age effect is related to dichotomization point. Prognosis worsen markedly only after age 60 years.

Spline analysis of relationship between age and 3-month GOS



Shape of age effect on GOS outcomes vary with dichotomization points

Results 2:

The univariate common odds ratio associated with the effect of age was 1.78 (95% CI, 1.61 – 1.98); and the effect of gender was OR 1.20 (95% CI, 1.04 – 1.39).

Random effects IPD meta-analysis of the effect of age and gender

Study	OR	95% CI	%	Study	OR	95% CI	%
CINDICORE-1	1.02	(0.71, 1.48)	100%	CINDICORE-1	1.02	(0.71, 1.48)	100%
MASH	1.70	(1.41, 2.03)	100%	MASH	1.70	(1.41, 2.03)	100%
MASH-1	1.80	(1.58, 2.06)	100%	MASH-1	1.80	(1.58, 2.06)	100%
ISAT	1.40	(1.24, 1.58)	100%	ISAT	1.40	(1.24, 1.58)	100%
MASH-2	1.80	(1.58, 2.06)	100%	MASH-2	1.80	(1.58, 2.06)	100%
MASH-2	2.30	(1.94, 2.76)	100%	MASH-2	2.30	(1.94, 2.76)	100%
TRIS-2/3	1.80	(1.58, 2.06)	100%	TRIS-2/3	1.80	(1.58, 2.06)	100%
PHO	1.20	(1.04, 1.39)	100%	PHO	1.20	(1.04, 1.39)	100%
PHO-2	1.20	(1.04, 1.39)	100%	PHO-2	1.20	(1.04, 1.39)	100%
Total	1.78	(1.61, 1.98)	100%	Total	1.20	(1.04, 1.39)	100%

Age effect is consistent across studies; gender effect is not consistent across studies

Results 3:

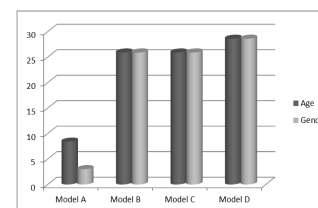
In adjusted analysis, the effect of age was reduced to OR, 1.69 (1.59-1.81); and the effect of gender became insignificant, OR, 1.04 (0.84-1.29).

Multivariate ordinal analysis of effects of age and gender

	Model A	Model B	Model C	Model D
Age	1.86 (1.75-1.94)	1.80 (1.70-1.90)	1.71 (1.60-1.82)	1.69 (1.59-1.81)
Female	1.21 (1.05-1.40)	1.10 (0.91-1.33)	1.03 (0.84-1.28)	1.04 (0.84-1.29)

Model A: Predictor + Study
Model B: Model A + WINS + Age
Model C: Model B + Neuroimaging data (Fisher grade+ Artery + Ruptured aneurysm size)
Model D: Model C + Repair (clipping vs. coiling vs. conservative)

Relative prognostic value of age and gender expressed as Nagelkerke's R2 values



Age accounted for only 8.4% of the explained variance in 3-month GOS

Acknowledgement:

Members of the SAHIT collaboration are gratefully acknowledged for data provision.

Conclusion:

The age of 60 years adequately describes the change point in prognostic effect of age. Age has independent but moderate effect on short term prognosis of aSAH. Gender is not independently associated with short term outcome.