The risk of MR-detected carotid plaque hemorrhage on recurrent or first-time stroke: a meta-analysis of individual patient data

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DISCLOSURE

Speaker name:

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I have the following potential conflicts of interest to report:

- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)
- ☑ I do not have any potential conflict of interest

CLINICAL BACKGROUND

- Carotid intraplaque Hemorrhage (IPH): association with first-time and recurrent cerebrovascular symptoms

- MRI is ideally suited to visualize intraplaque hemorrhage with high correlation to histology[1]

- Cohort based meta-analyses[2,3,4]: ~5–12 fold increased risk for ipsilateral cerebrovascular events (stroke, TIA, amaurosis fugax) in vessels with IPH

  → Limitations: Heterogeneity, combined study endpoints, lack of individual patient information (e.g. risk factors, degree of stenosis)

Carotid Plaque MRI and Stroke Risk
A Systematic Review and Meta-analysis

Carotid Plaque Hemorrhage on Magnetic Resonance Imaging Strongly Predicts Recurrent Ischemia and Stroke

Meta-Analysis and Systematic Review of the Predictive Value of Carotid Plaque Hemorrhage on Cerebrovascular Events by Magnetic Resonance Imaging

[2] Gupta A et al., Stroke 2013

[3] Hosseini AA, et al., Ann Neurol 2013

[4] Saam T et al., JACC 2013

[1] Cai JM et al., Circulation 2002

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CLINICAL BACKGROUND

- Current consensus[1]: use of ischemic stroke as sole outcome event in clinical / therapeutic studies

- Low number of stroke in individual MR-IPH based studies impedes precise risk estimates

- Pooling of individual patient data[2]

  → Reasonable case numbers

  → Adjustment for risk factors and degree of stenosis

[1] Sacco RL et al., Stroke 2013
[2] Drazen JM, N Engl J Med 2015

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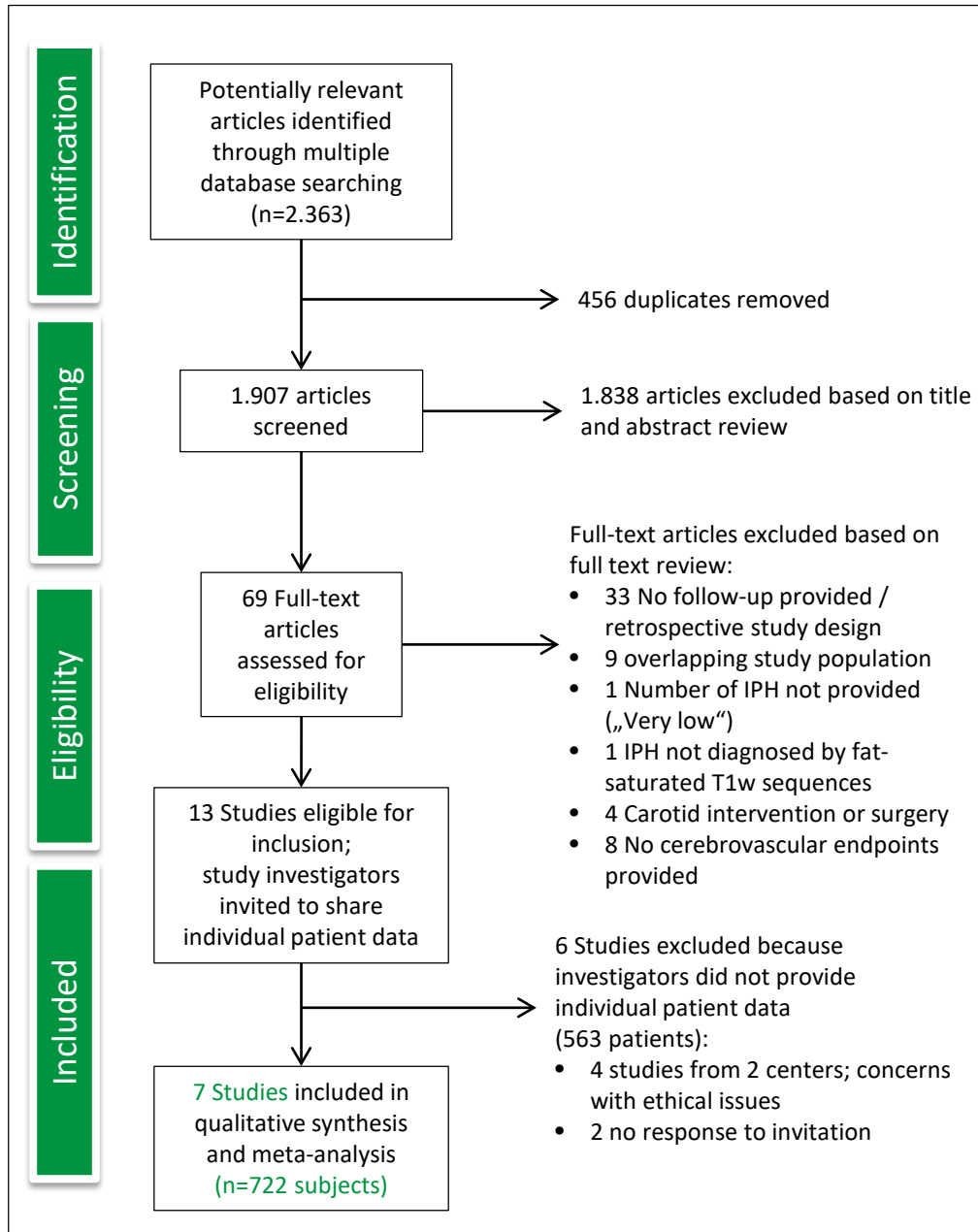
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STUDY AIM

- To estimate the precise risk of MR-detected carotid plaque hemorrhage on recurrent or first-time stroke during follow-up in previously symptomatic and asymptomatic patients in an individual patient based meta-analysis
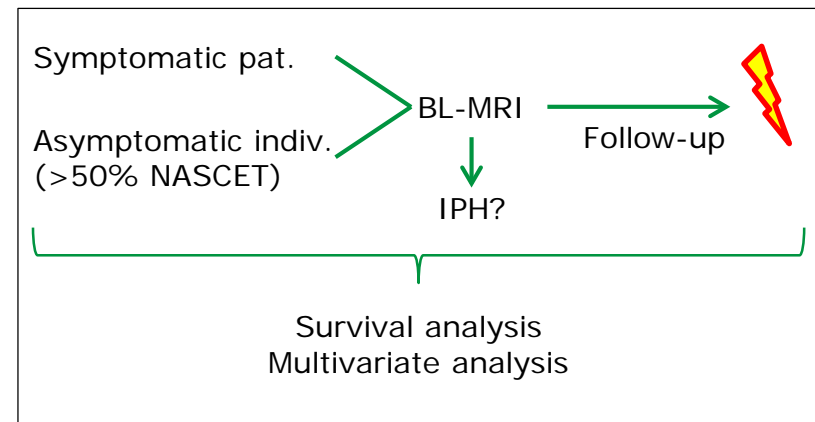
LITERATURE RESEARCH / INCLUSION CRITERIA

Identification

Potentially relevant articles identified through multiple database searching (n=2.363)

456 duplicates removed

Screening

1.907 articles screened

1.838 articles excluded based on title and abstract review

Eligibility

69 Full-text articles assessed for eligibility

Full-text articles excluded based on full text review:
- 33 No follow-up provided / retrospective study design
- 9 overlapping study population
- 1 Number of IPH not provided („Very low")
- 1 IPH not diagnosed by fat-saturated T1w sequences
- 4 Carotid intervention or surgery
- 8 No cerebrovascular endpoints provided

13 Studies eligible for inclusion; study investigators invited to share individual patient data

6 Studies excluded because investigators did not provide individual patient data (563 patients):
- 4 studies from 2 centers; concerns with ethical issues
- 2 no response to invitation

Included

7 Studies included in qualitative synthesis and meta-analysis (n=722 subjects)

Inclusion criteria

- Studies containing ≥20 subjects
- Detailed assessment of IPH in the carotid arteries at baseline on a MRI scanner ≥1.5T
- Evaluation of carotid stenosis degree
- Clinical follow-up after carotid MRI

Symptomatic pat.

Asymptomatic indiv. (>50% NASCET)

BL-MRI

Follow-up

IPH?

Survival analysis
Multivariate analysis

	Symptomatic (n=560)	Asymptomatic with >50% stenosis (n=136)
Age at baseline (years)	72.8 ± 9.7	73.4 ± 8.9
Male	386 (68.9%)	115 (84.6%)
Diabetes mellitus	125 (22.3%)	31 (22.8%)
Hypertension	370 (66.1%)	105 (77.2%)
Any smoking (former or current)	270 (48.2%)	90 (66.2%)
Type of Symptoms at time of inclusion		
stroke	285 (50.9%)	-
TIA	201 (35.9%)	-
retinal ischemia	74 (13.2%)	-
asymptomatic	-	136 (100%)
IPH in the baseline carotid MRI	289 (51.6%)	40 (29.4%)
Stenosis		
< 50%	187 (33.4%)	-
50 – 69%	192 (34.3%)	128 (94.1%)
70 – 99%	181 (32.3%)	8 (5.9%)
Type of symptoms at event during follow-up		
stroke	60 (10.7%)	6 (4.4%)
TIA	42 (7.5%)	4 (2.9%)
retinal ischemia	15 (2.7%)	0 (0%)
no event	443 (79.1%)	126 (92.6%)
Time between qualifying event and MRI (days)	24.0 (8.0 – 47.0)	-
Duration of follow-up (months)	12.0 (2.9 – 21.2)	30.9 (18.9 – 40.5)
	Total: 1.121 patient years	
Time between inclusion and outcome event (months)	5.2 (1.1 – 17.7)	12.0 (4.8 – 17.5)

Data are mean±SD, median (IQR) or number (%). IPH=intra-plaque hemorrhage.

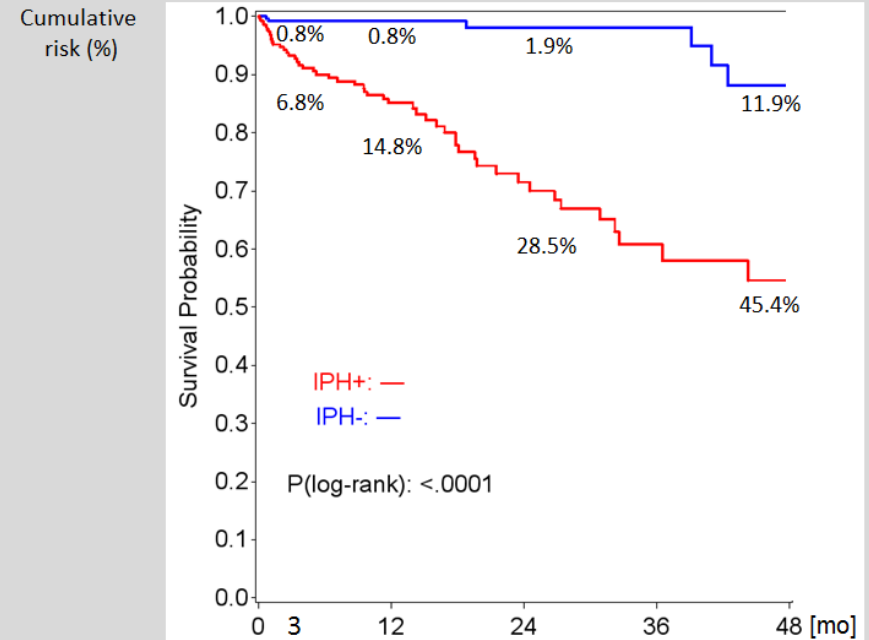# KAPLAN-MEIER PLOTS & CUMULATIVE RISK OF FUTURE STROKE EVENT

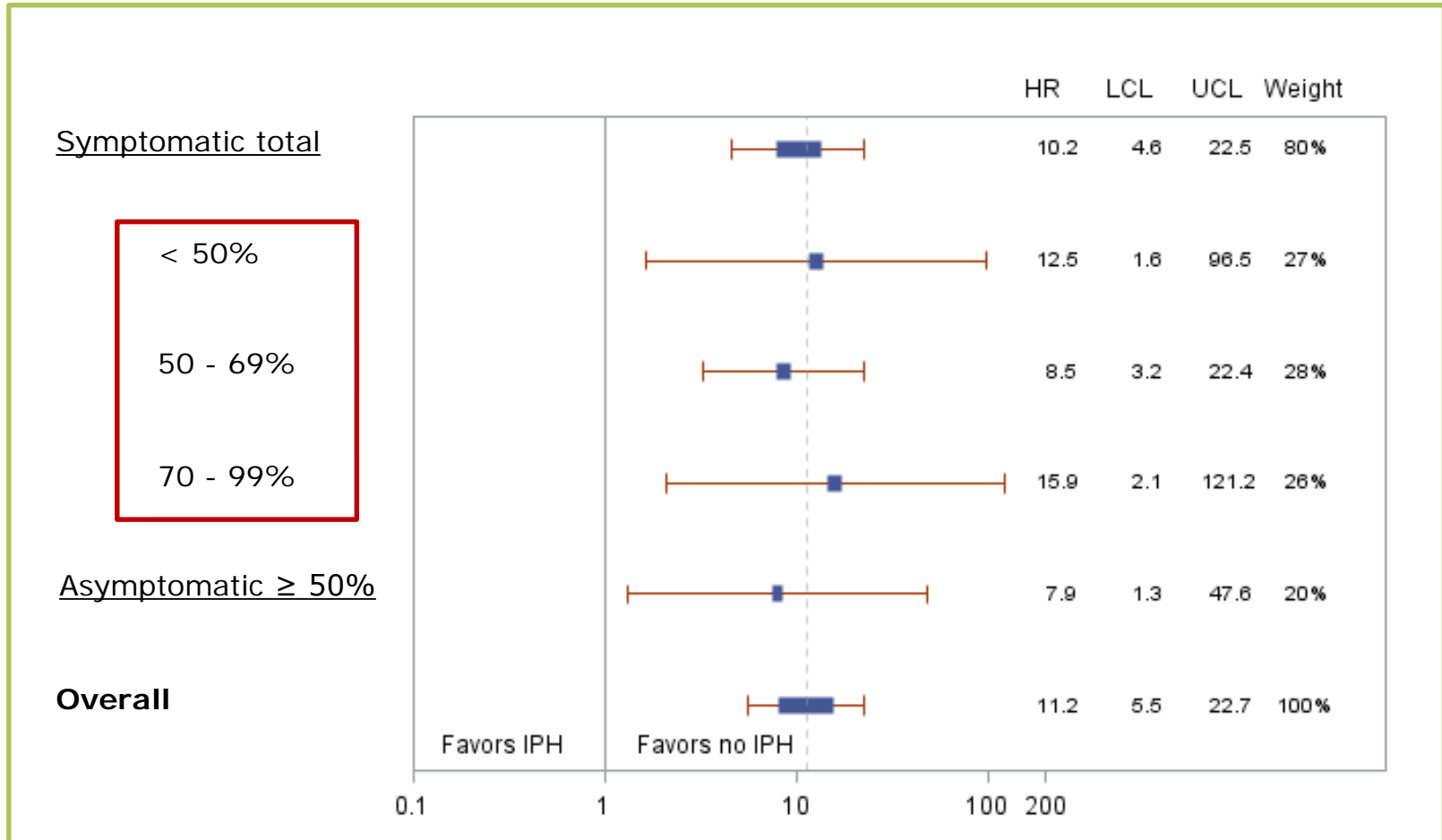## Asymptomatic individuals (>50% stenosis)
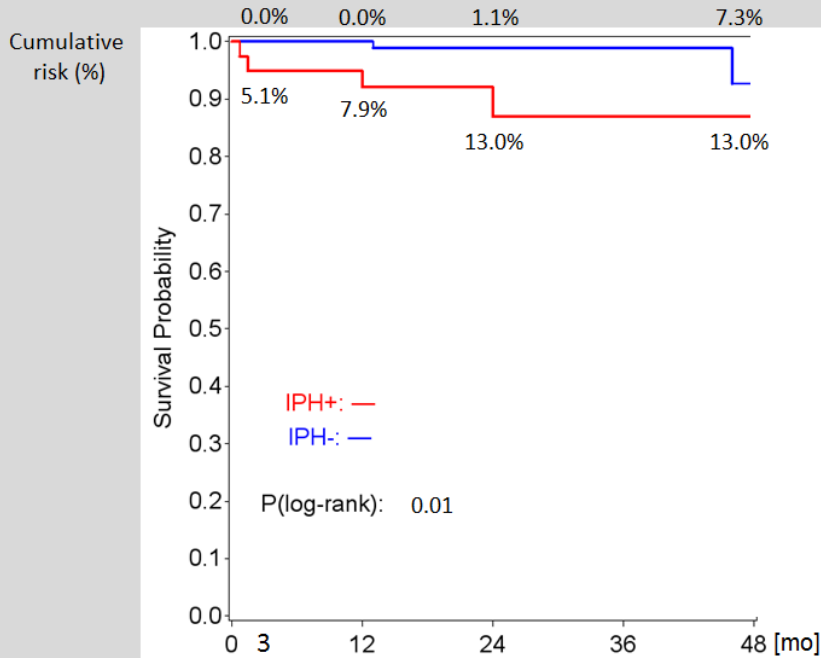
Symptomatic patients (all stenoses)

7.9 (95% CI 1.3 – 47.6)   Hazard Ratio (unadjusted)   10.2 (4.6 – 22.5)

ASSOCIATION OF IPH WITH FUTURE IPSILATERAL STROKE

	HR	LCL	UCL	Weight
Symptomatic total	10.2	4.6	22.5	80%
< 50%	12.5	1.6	96.5	27%
50 - 69%	8.5	3.2	22.4	28%
70 - 99%	15.9	2.1	121.2	26%
Asymptomatic ≥ 50%	7.9	1.3	47.6	20%
Overall	11.2	5.5	22.7	100%

Favors IPH   Favors no IPH

0.1   1   10   100 200

INFLUENCE OF CARDIOVSCULAR RISK-FACTOS ON THE OCCURENCE OF STROKE EVENTS

Frailty model comparing stroke risk depending on baseline characteristics in all symptomatic patients.

	Participants (N)	Hazard Ratio (95% CI)	P-Value
Age			
< 65 yrs*	105	1.00	
65-74 yrs	150	0.88 (0.37 – 2.07)	0.76
> 74 yrs	303	0.74 (0.33 – 1.66)	0.46
Sex			
Male*	384		
Female	174	1.05 (0.52 – 2.13)	0.89
Diabetes mellitus			
no*	125		
yes	189	1.73 (0.95 – 3.17)	0.07
Hypertension			
no*	189		
yes	369	1.09 (0.55 – 2.18)	0.8
Degree of stenosis			
< 50%*	186	1.00	
50 – 69%	191	2.00 (0.96 – 4.20)	0.066
70 – 99%	181	3.37 (1.46 – 7.79)	0.004
Type of qualifying event			
Stroke*	284	1.00	
TIA	200	1.1 (0.62 – 1.95)	0.75
Retinal ischaemia	74	0.36 (0.10 – 1.23)	0.10
(incl. Retinal infarction and AmF)			
IPH at inclusion			
no*	271		
yes	287	10.81 (4.72 – 24.76)	< 0.001

* reference category

CONCLUSION

- Presence of IPH increases the risk for future stroke ~8-fold in asymptomatic (>50% carotid stenosis) individuals, and ~10-fold in symptomatic patients among all stenosis categories.

- Among classical risk factors only the degree of stenosis significantly increases stroke risk, however, with clearly lower hazard ratios.

- Study results provide needed risk estimates for the planning of interventional / therapeutic studies.

- IPH-status should be recognized as additional criterion in future risk scores.

➡ Improve the selection of patients for the best treatment option

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THANK YOU