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MRI carotid plaque imaging predicts future stroke in patients with mild to moderate stenosis – ICAD study

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Stroke association

Introduction

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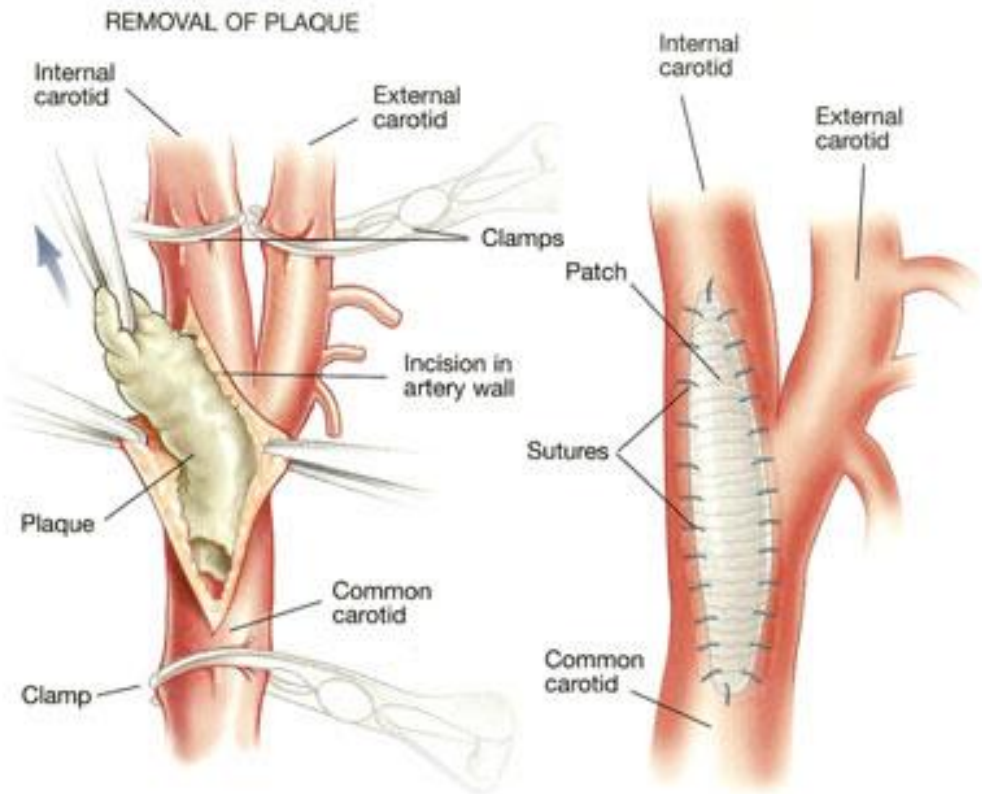
- Carotid Endarterectomy reduces risk of recurrent stroke in patients with symptomatic carotid artery stenosis



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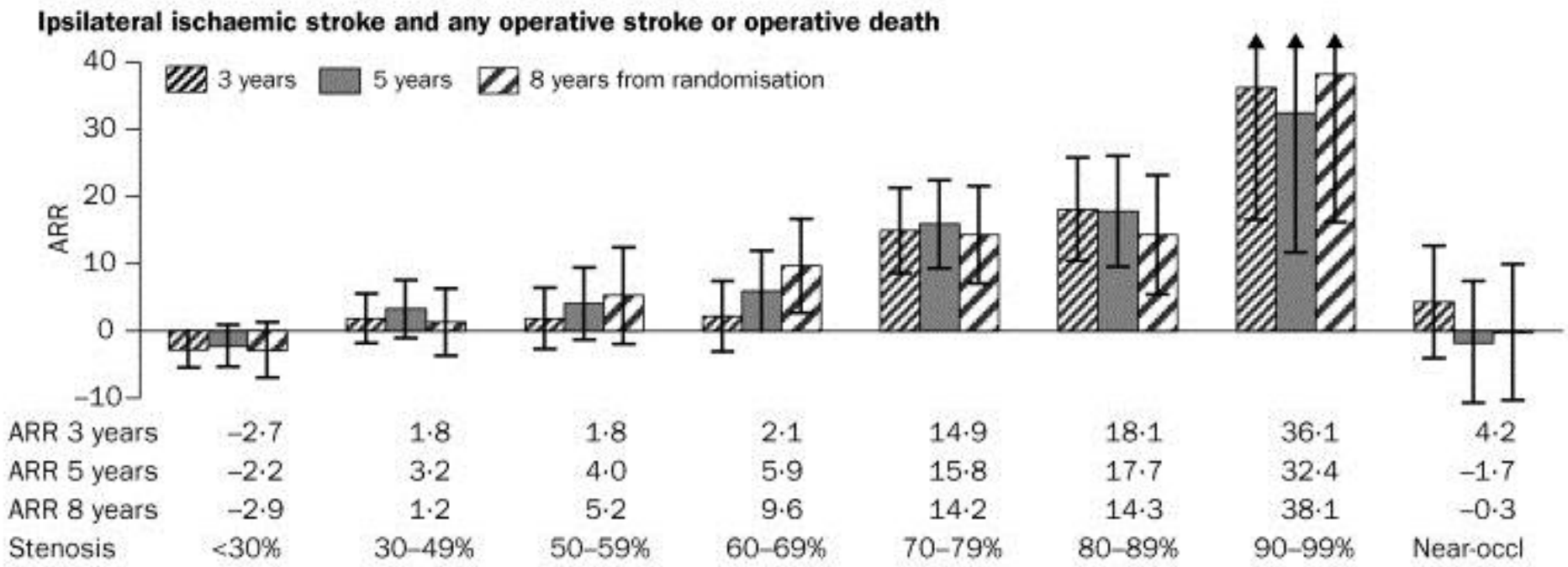
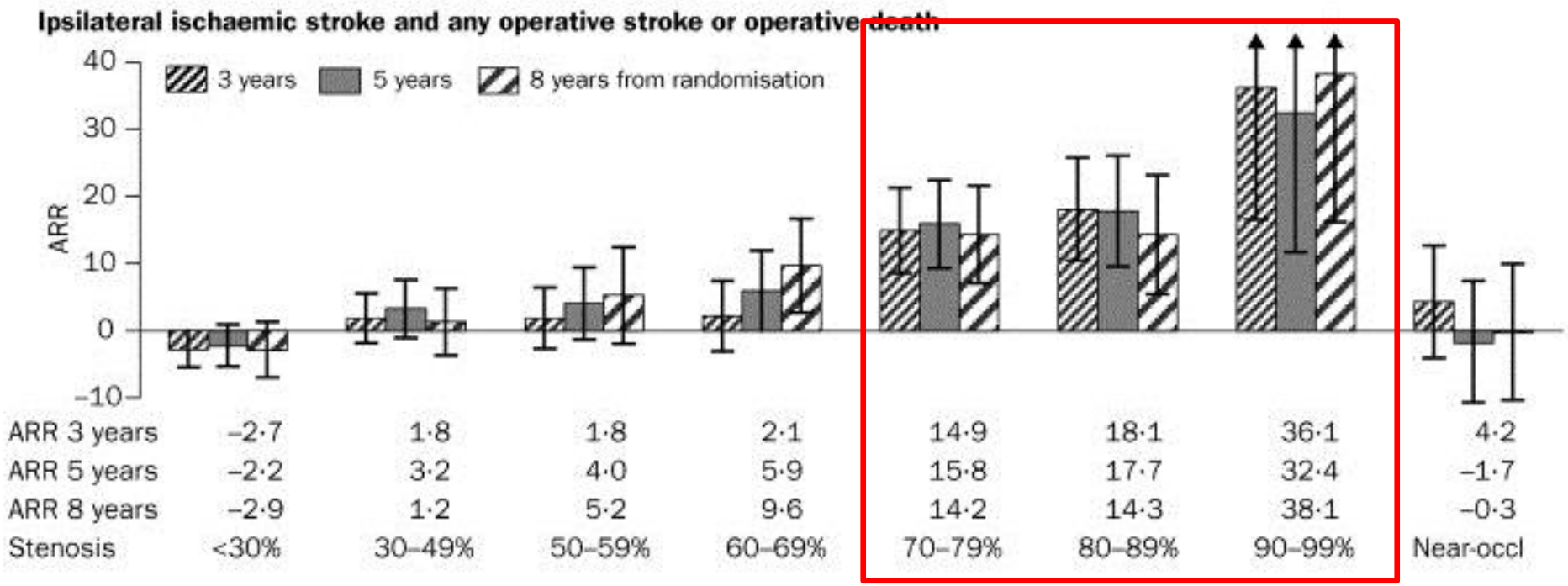


Pooled analysis of NASCET, ECST and VA trials: n = 6092 patients
Rothwell *et al*, Lancet 2003; 361: 107-116

Introduction



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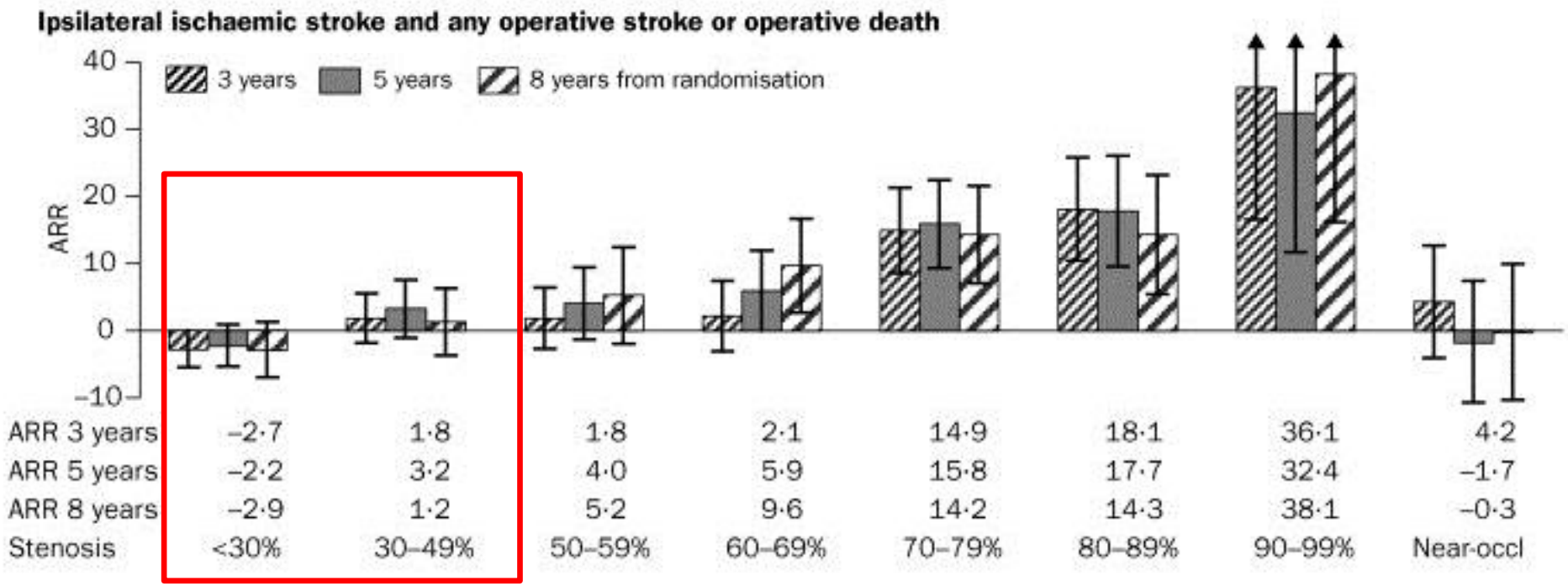

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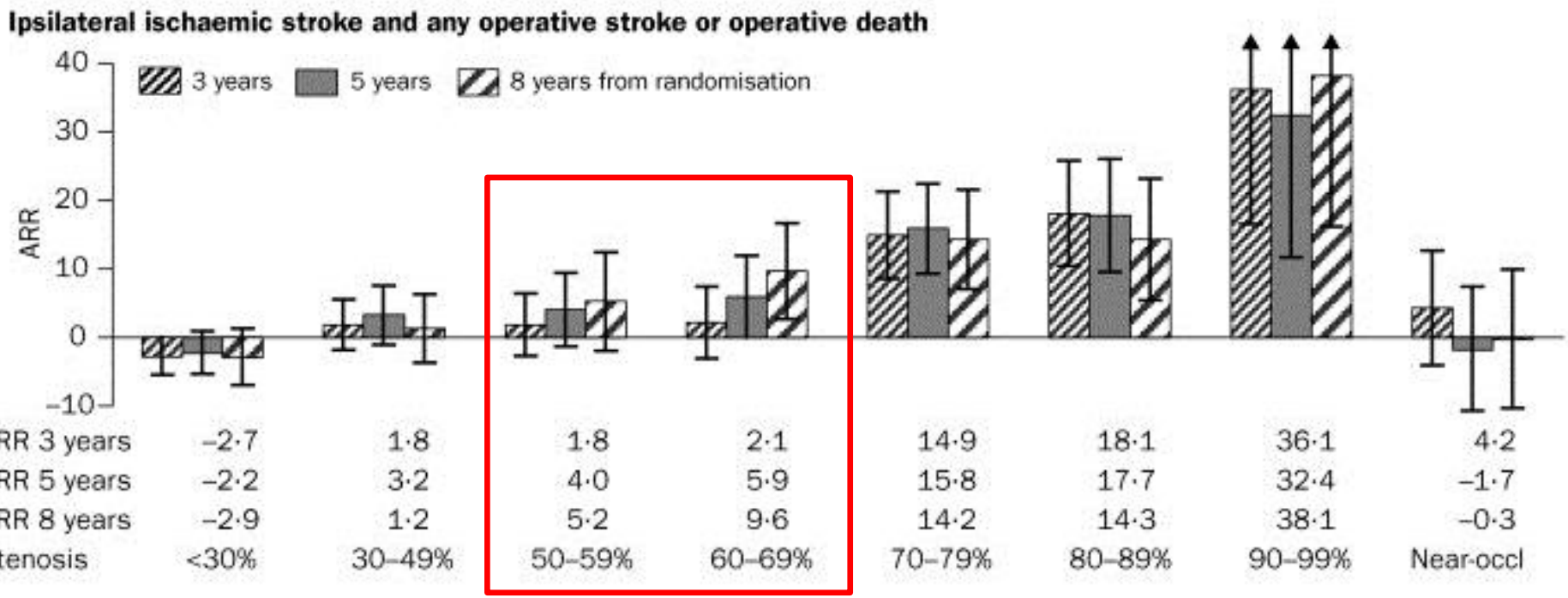

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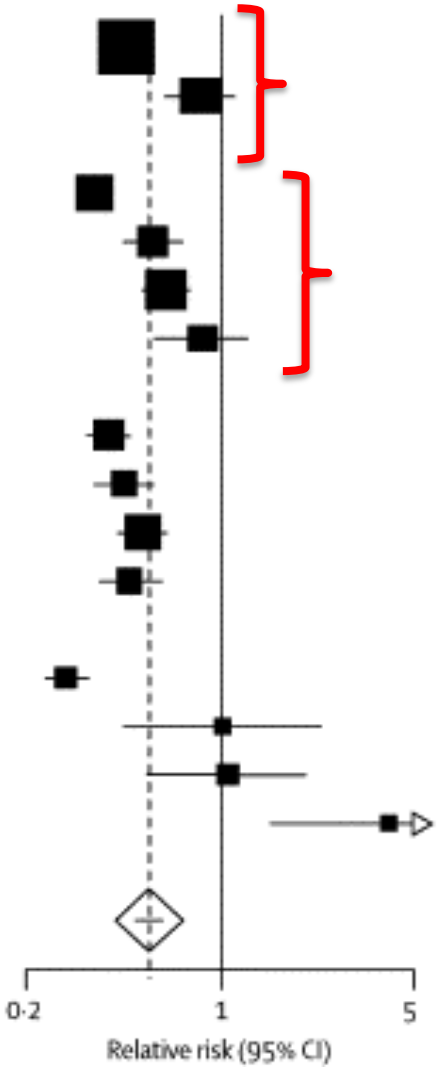
Subgroup	Events/patients Surgical	Events/patients Medical	RR	95% CI
Sex				
Male	92/890	172/784	0·46	0·41–0·51
Female	59/436	55/346	0·84	0·63–1·12
Time since last event				
<2 weeks	30/284	80/269	0·35	0·31–0·40
2–4 weeks	29/233	41/193	0·57	0·45–0·73
4–12 weeks	56/512	76/450	0·63	0·52–0·78
>12 weeks	36/297	30/218	0·85	0·58–1·26
Time since last event: males				
<2 weeks	20/178	52/185	0·39	0·33–0·47
2–4 weeks	16/139	33/136	0·45	0·35–0·58
4–12 weeks	37/365	60/317	0·52	0·43–0·64
>12 weeks	19/208	27/146	0·47	0·36–0·61
Time since last event: females				
<2 weeks	10/106	28/84	0·28	0·23–0·33
2–4 weeks	13/94	8/57	1·00	0·44–2·26
4–12 weeks	19/147	16/133	1·04	0·54–1·99
>12 weeks	17/89	3/72	4·30	1·48–12·46
Total	151/1326	227/1130	0·55	0·50–0·62



Rothwell *et al*, Lancet 2005; 365: 256-265

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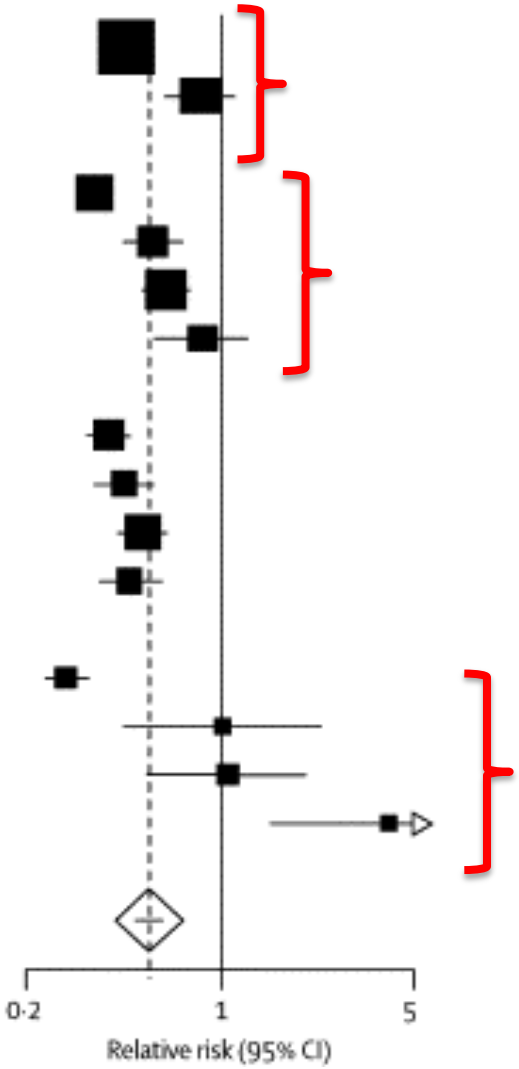

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Introduction

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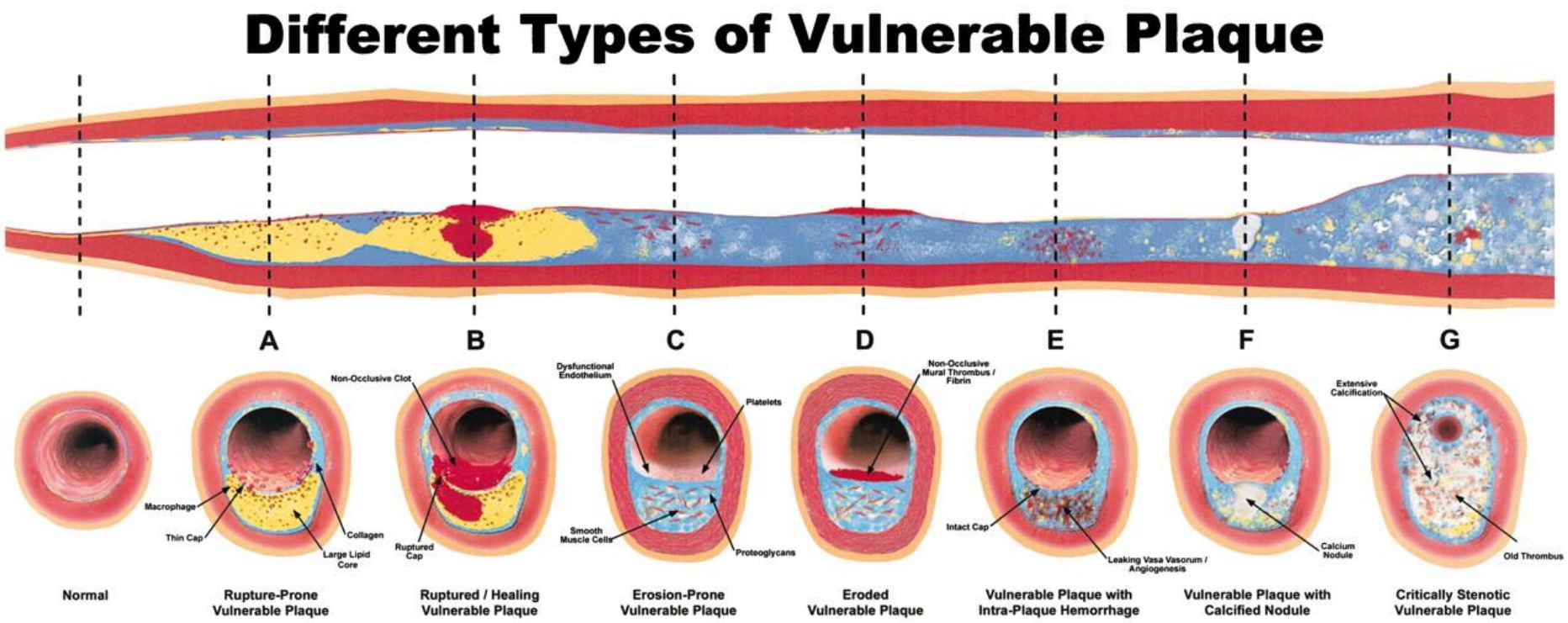
- Unstable/vulnerable carotid plaque
- Beyond the luminal stenosis ➔ Plaque imaging



Naghavi *et al*, Circulation, 2003; 108: 1664-1672.

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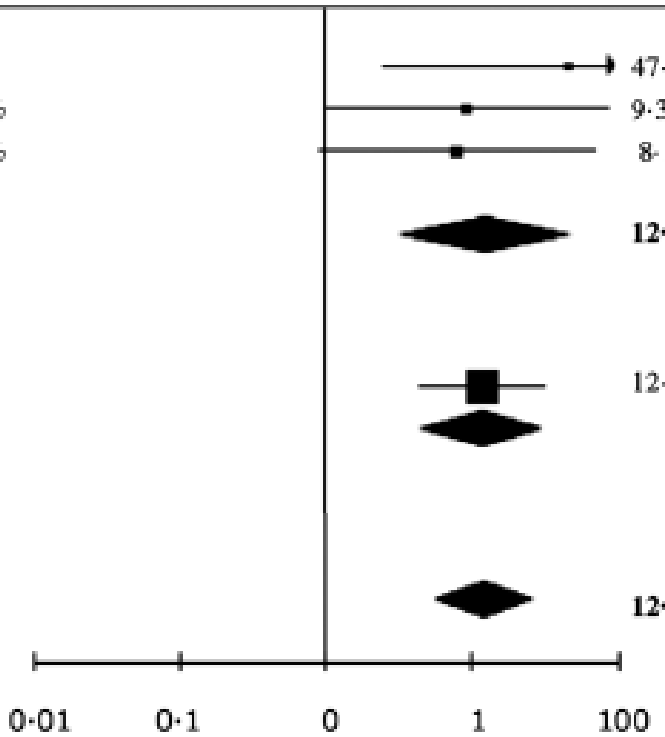
Study	DoS%	MRIPH+ Event/total	MRIPH- Event/total	Weight (%)	Odds ratio (95% CI)
Studies on Symptomatic Carotid stenosis					
Teng, et al. 2011[28]	30-69	11/21	0/21	7·5%	47·10 (2·52 – 878·46)
Lin, et al. 2006[24]	ND	5/21†	1/31	12·8%	9·38 (1·01 – 87·28)
Kurosaki, et al. 2011[33]	70-99	7/32	1/30	13·7%	8·12 (0·93 – 70·59)
Subtotal (95% CI)		**23/74**	**2/82**	**34%**	**12·62 (3·20 – 49·73)**
Heterogeneity: $Tau^2 = 0·00$, $Chi^2 = 1·03$, df = 3 (P = 0·60); $I^2 = 0\%$					
Test for overall effect: Z = 3·62 (P = 0·0003)					
Present study incl. Altaf et al.[30,31]	50-99	57/114	5/65	66%	12·00 (4·49 – 32·08)
Total Symptomatic Carotid stenosis (95% CI)		**80/188**	**7/147**	**100%**	**12·21 (5·49 – 27·14)**



Hosseini et al, Ann Neurol, 2013; 73(6): 774–784.

Aim & outcomes

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- To determine whether MRI-PH can predict future stroke in patients with symptomatic mild-moderate carotid stenosis

- 1° outcome
  - Ipsilateral ischaemic stroke or DWI+TIA
- 2° outcomes
  - Stroke only
  - All recurrent ipsilateral cerebrovascular event

Methods

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- Prospective observational study
  - Adults with a recent TIA, stroke or AmFx
  - Symptomatic 30-99% carotid stenosis
  - No planned carotid intervention
  - Excluded if contraindication to MRI, unable to consent, planned CEA

  - Cerebrovascular events, vascular risk factors, comorbidities and medications
  - 6 monthly clinical/telephone follow-up

Methods

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- Brain and carotid imaging
  - DTI, FLAIR, DWI, fMRI
  - Time of Flight MRA ± CE-MRA

- MRI carotid wall imaging
  - Coronal T_1-weighted 3D MPRAGE (Black-blood and fat-saturation)
- Signal Intensity Ratio = SI_{plaque}/SI_{muscle}
  - MRIPH+ve if > 1.5
  - MRIPH-ve if < 1.5

Results

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Over 4000 were patients screened

190 agreed to participate

38 excluded:
- 10 did not have MRI
- 1 poor quality MRI
- 2 <30% carotid stenosis
- 5 occluded ipsilateral carotid artery
- 12 asymptomatic carotid disease
- 6 contralateral carotid stenosis
- 2 posterior circulation stroke

152 recruited (92M, 60F)

1 lost to follow-up

17 70-99% stenosis

134 patients in 30-69% analysis
79 males, 55 females. Median age: 76

Results

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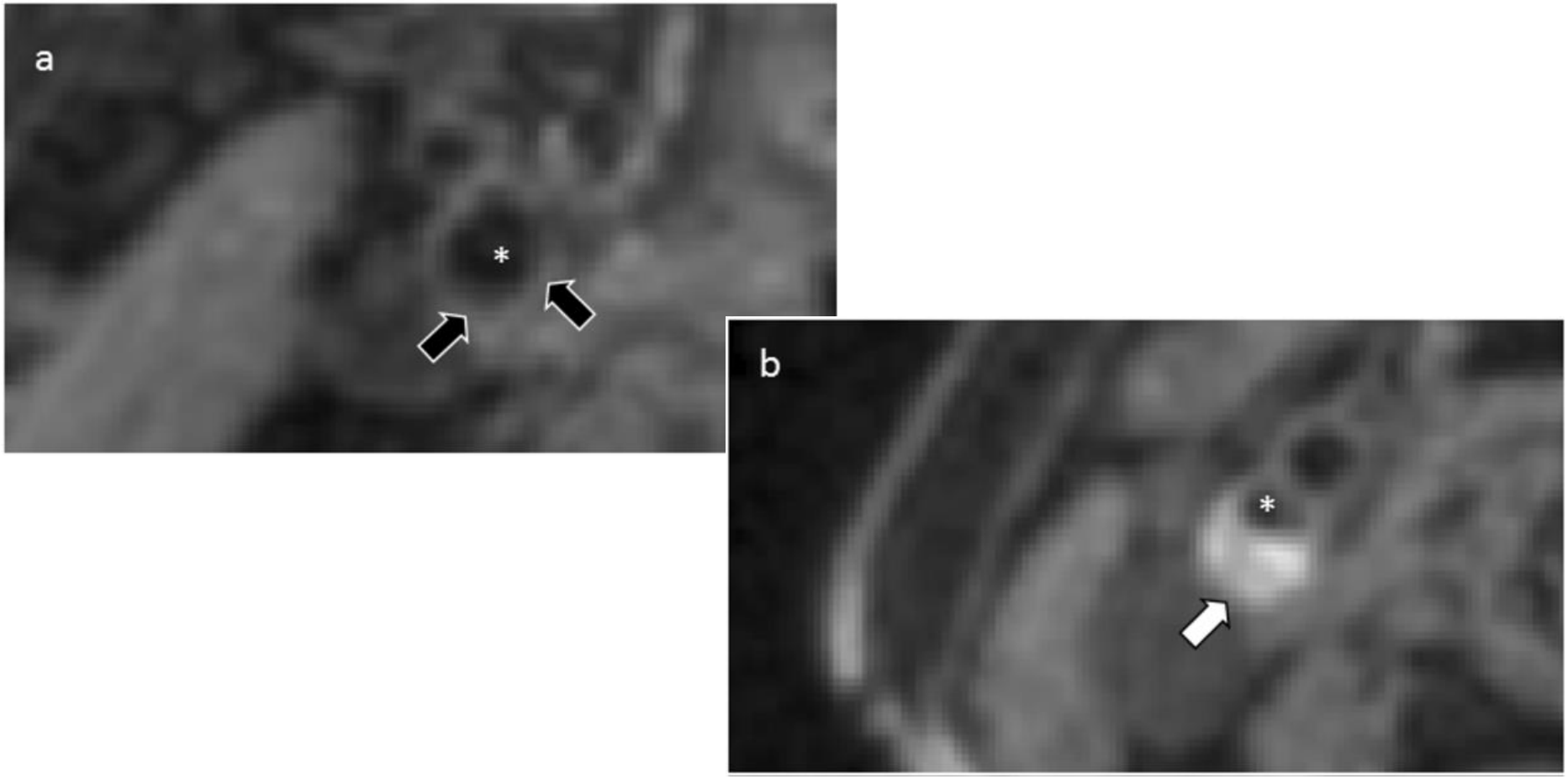
- MRIPH in ICAD study



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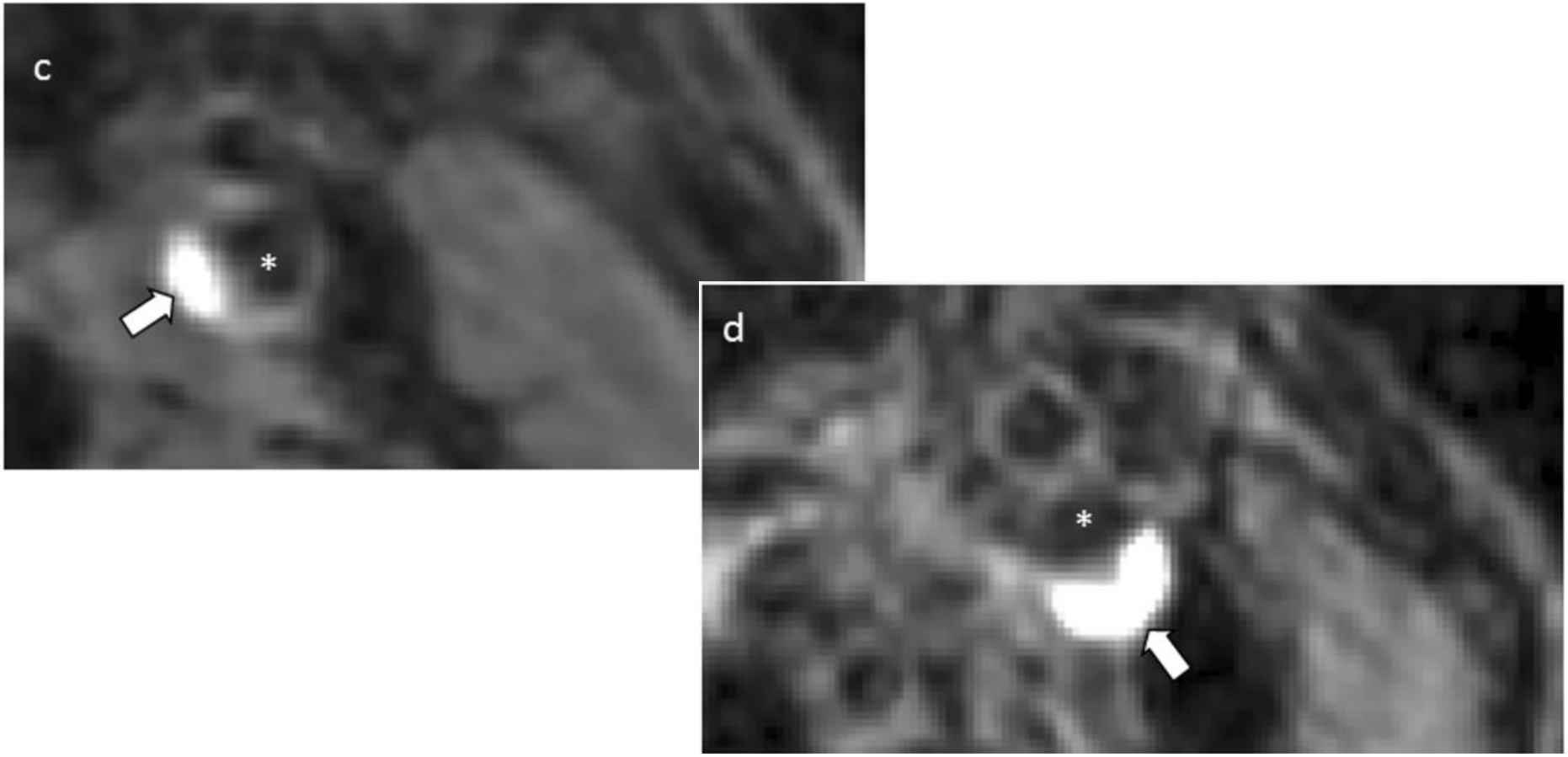

Results

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- 47 (35.1%) patients showed ipsilateral MRI-PH
  - Of which 36 were male; $\chi^2 = 9.3$, P=0.002

Ipsilateral carotid stenosis (P=0.97)	MRIPH positive	MRIPH negative
30-49%	22	40
50-59%	17	33
60-69%	8	14

- No other demographic or risk factor was significantly associated with MRIPH presence.

Results

- Follow-up period
  - Median = 656 days, IQR = 349-994
  - For 30-69% stenosis

Event	MRIPH positive	MRIPH negative	Total
Stroke	8	4	12
DWI+ TIA	1	0	1
TIA	1	2	3
AmFx	0	1	1
CEA	3	2	5
Death	7	12	19

Results

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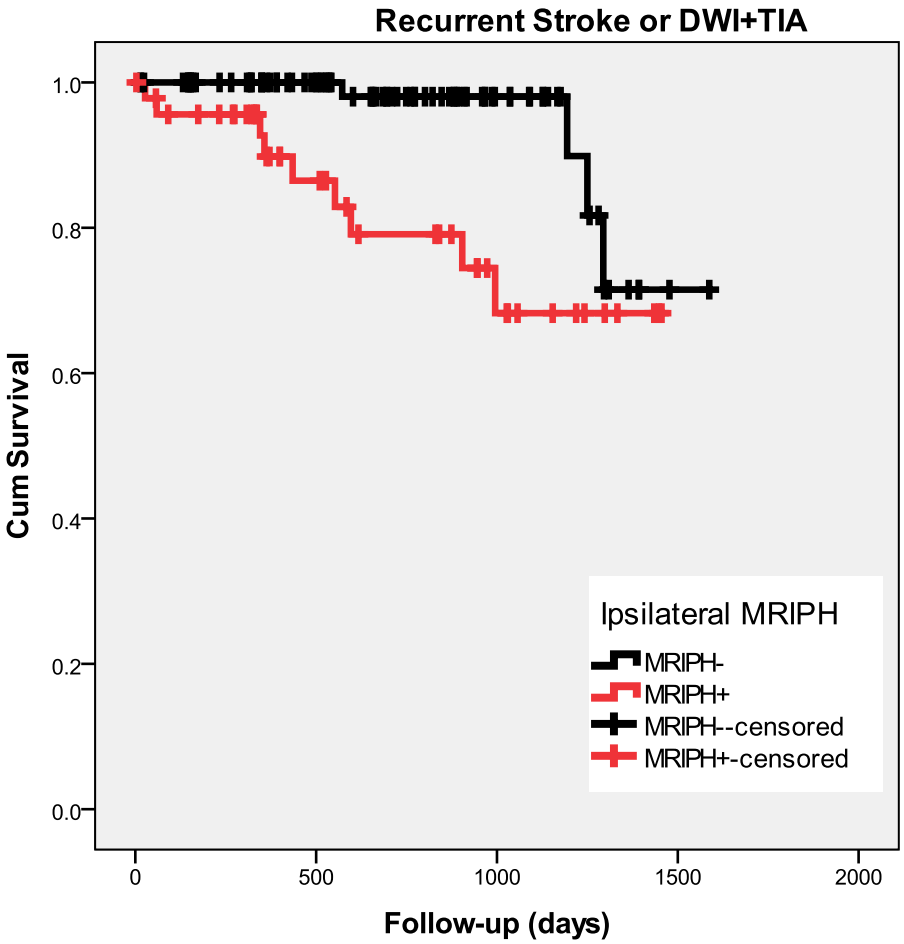
- Presence of MRIPH
  - Infarction: **HR = 4.4** (95%CI 1.36 – 14.43, P=0.013)
  - Stroke only: **HR = 4.08** (95% CI 1.23 – 13.58, P=0.02)

- Controlling for stenosis
  - HR for stroke was **4.69** (95%CI 1.40–15.74, P=0.012)



Results

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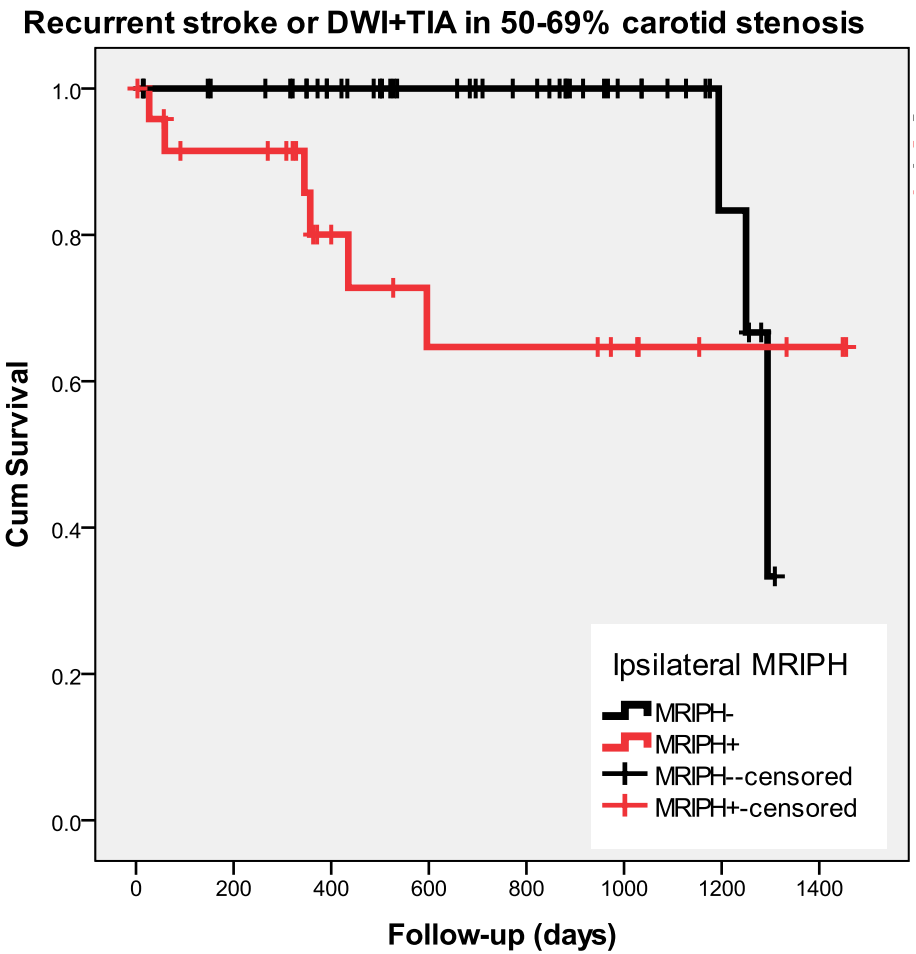
- For 50-69% stenosis
  - 72 participants
  - 9 strokes
  - HR = **4.1**
    95%CI 1.01 – 16.81, P=0.049
  - Risk difference **35% at 3 years**

50-69%



Results

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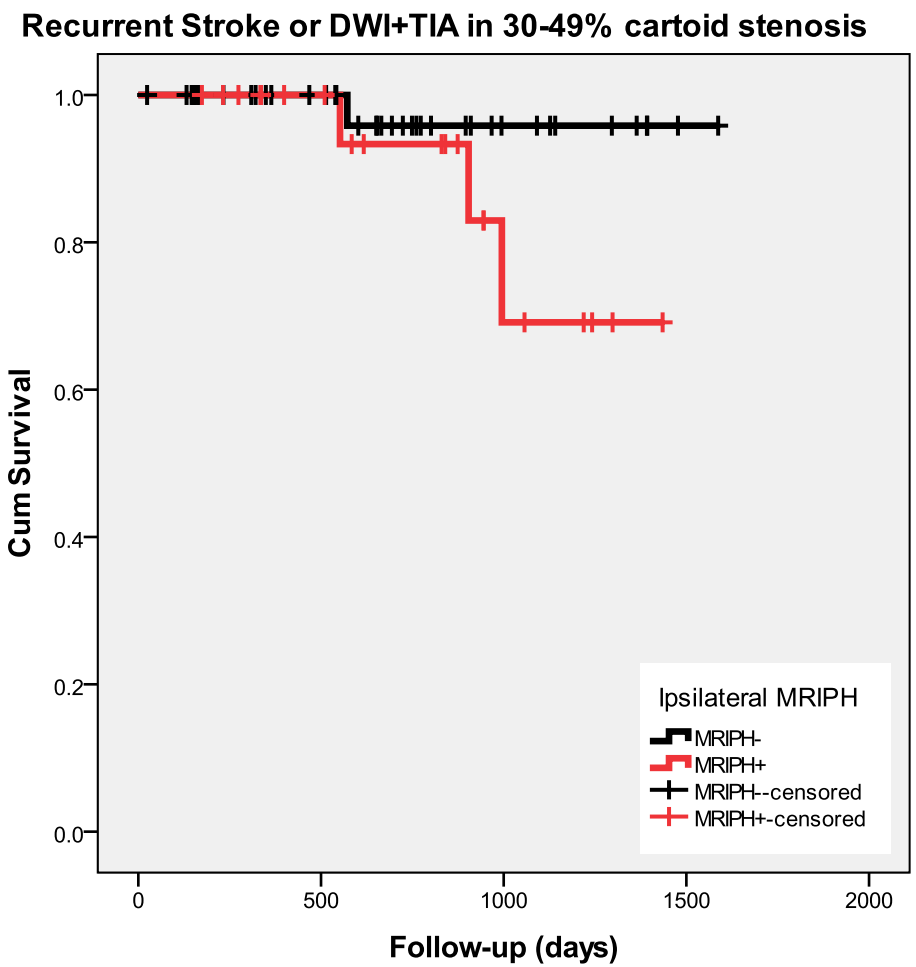
- For 30-49% stenosis
  - 62 participants
  - 4 infarctions
  - HR = 4.6
    95%CI 0.47 – 44.3, **P=0.19**
  - Low power due to number of events

30-49%



Conclusions

- In symptomatic patients with moderate carotid stenosis, MRI-PH is a significant predictor of future cerebral infarction and stroke.

- This study builds on previous evidence for MRIPH in moderate stenosis*

*Hosseini et al, Ann Neurol, 2013; 73(6): 774–784.

Conclusions

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- MRI-PH status can thus offer decision support when there is clinical uncertainty regarding the benefit of carotid intervention.
  - MRIPH is stable for up to 2 years*

- Inclusion of MRIPH into clinical risk tools.

- Easily accessible and quick technique, MRIPH should be implemented into clinical practice as standard care.

*Simpson et al, AJNR, 2015;

Acknowledgements

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- Dr Akram Hosseini
- Mr Nishath Altaf
- Professor Philip Bath
- Mr Shane MacSweeney
- Professor Dorothee Auer
- Dr Robert Dineen
- Anita French
- Dr Daniel Rodriguez
- Dr Solomon Akwei
- Dr Tim England
- Dr Mohana Maddula

- Funders
  - Stroke Association Junior Research Training Fellowship
  - Rosetrees Trust
  - Nottingham Vascular Research Fund
  - NIHR Research for Patient Benefit programme

Declaration: This presentation presents independent research funded by the NIHR under its RfPB Programme (Ref: PB-PG-0107-11438). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. None of the sponsors had any role in study design, data collection, data analysis, data interpretation, writing the report, or in decision making to submit for publication.