

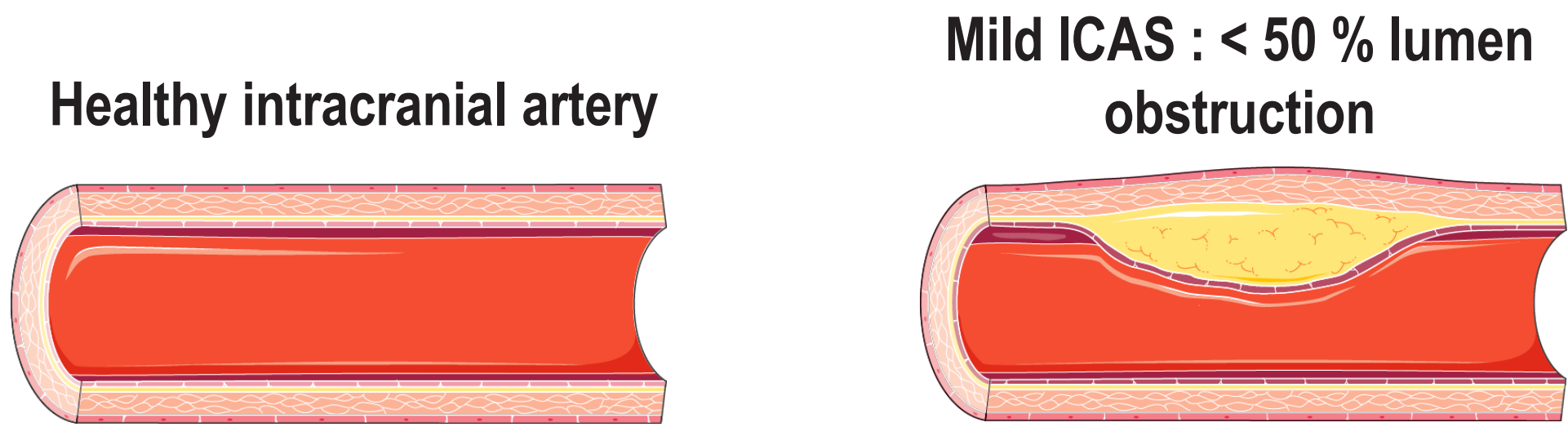
MILD INTRACRANIAL ARTERIAL STENOSIS IS ASSOCIATED WITH COGNITIVE DECLINE: A CASE-CONTROL STUDY

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INTRODUCTION

The investigation of vascular causes of cognitive decline and dementia have grown popular for providing pathways to dementia that are more preventable. Of these pathways, **severe intracranial arterial stenosis** (ICAS), which is when an atherosclerotic plaque or other vasculopathy obstructs $\geq 50\%$ of the arterial lumen, leads to greater risk of incident dementia (HR = 1.89) (1).



However, **mild ICAS** (< 50 % obstruction) remains less studied and has therefore less clear clinical guidelines. Furthermore, no studies have demonstrated any impact of increasing ICAS burden (ie : number of stenoses, number of arteries affected, etc.) on cognitive risk. We hypothesize that mild ICAS is associated with cognitive decline and that ICAS burden markers could reveal increased cognitive risk beyond mere ICAS presence.

OBJECTIVES

1. Determine if mild ICAS of the internal carotid arteries and the basilar artery is associated with cognitive decline.
2. Investigate the differences in ICAS-cognitive decline association in between sex.
3. Within population of patients with ≥ 1 stenosis, investigate separate markers of ICAS burden on cognitive decline.

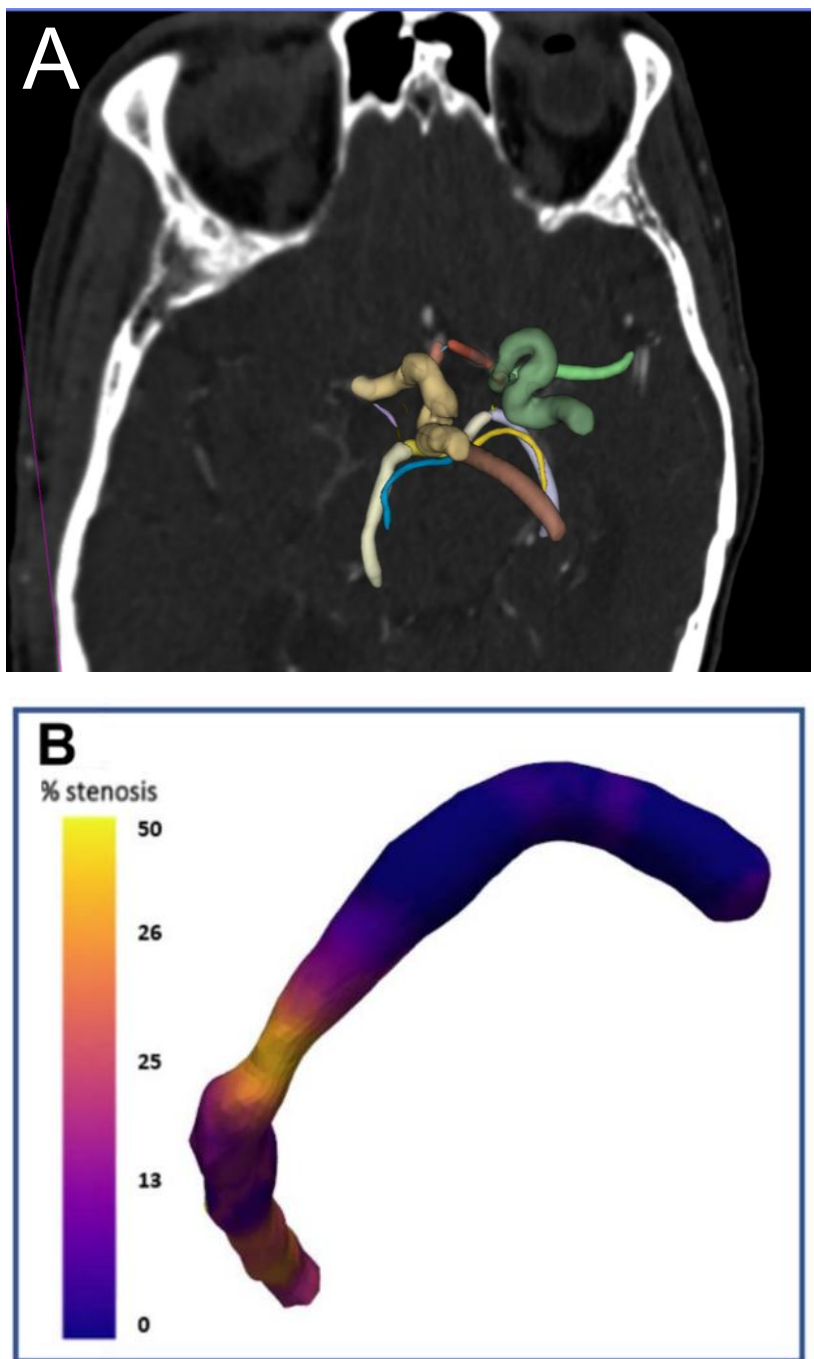
DESIGN AND METHODS

Design : Retrospective case-control

	Case group	Control group
Cerebral CTA	✓	✓
Outcome	Cognitive decline	No cognitive decline
N	270	449
N Male (%)	130 (48.1)	202 (45.0)
Mean age (sd)	76.3 (9.06)	66.8 (9.42)
Mean time to diagnosis/follow up, y (sd)	3.99 (2.11)	4.16 (1.22)

Methods

- Automatic segmentation of intracranial arteries by AISSIA using CTA (2)
- Stenosis detection by validated in-house algorithm (3)
 - Stenosis percent = $(1 - (D(\text{stenosis})/D(\text{normal}))) \times 100$
 - Artery specific stenosis count
- Logistic regression models. Covariates:
 - Age
 - Sex
 - Brain parenchymal fraction (cerebral volume/intracranial volume)



RESULTS

Table 1. Odds ratios (95% CI) for cognitive decline associated with ICAS (ref. group: absence of ICAS in respective artery group).

	Any ICAS	Only mild ICAS	Any severe ICAS
Internal carotid arteries	3.01 (1.82 – 5.17)	2.84 (1.69 – 4.92)	3.54 (1.97 – 6.55)
Basilar artery	1.57 (0.97 – 2.55)	1.70 (1.02 – 2.82)	0.86 (0.20 – 3.32)

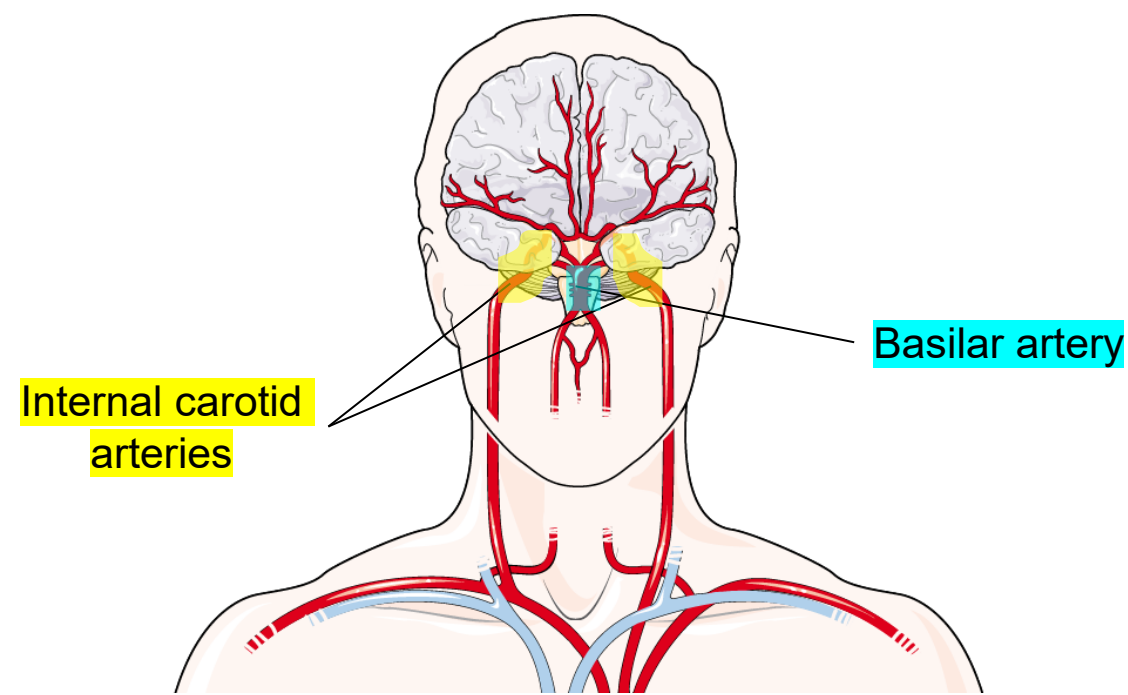


Table 2 and Figure 1. Odds ratios (95% CI) for cognitive decline associated with ICAS in the internal carotid arteries, stratifying for sex (ref group: absence of ICAS in internal carotid arteries). Y axis represents predicted probability of cognitive decline by logistic regression.

	Any ICAS	Only mild ICAS	Any severe ICAS
Internal carotid, male	4.15 (1.89 – 10.21)	3.77 (1.75 – 8.96)	6.93 (2.92 – 17.84)
Internal carotid, female	2.02 (1.04 – 4.17)	2.13 (1.07 – 4.45)	1.75 (0.78 – 4.05)

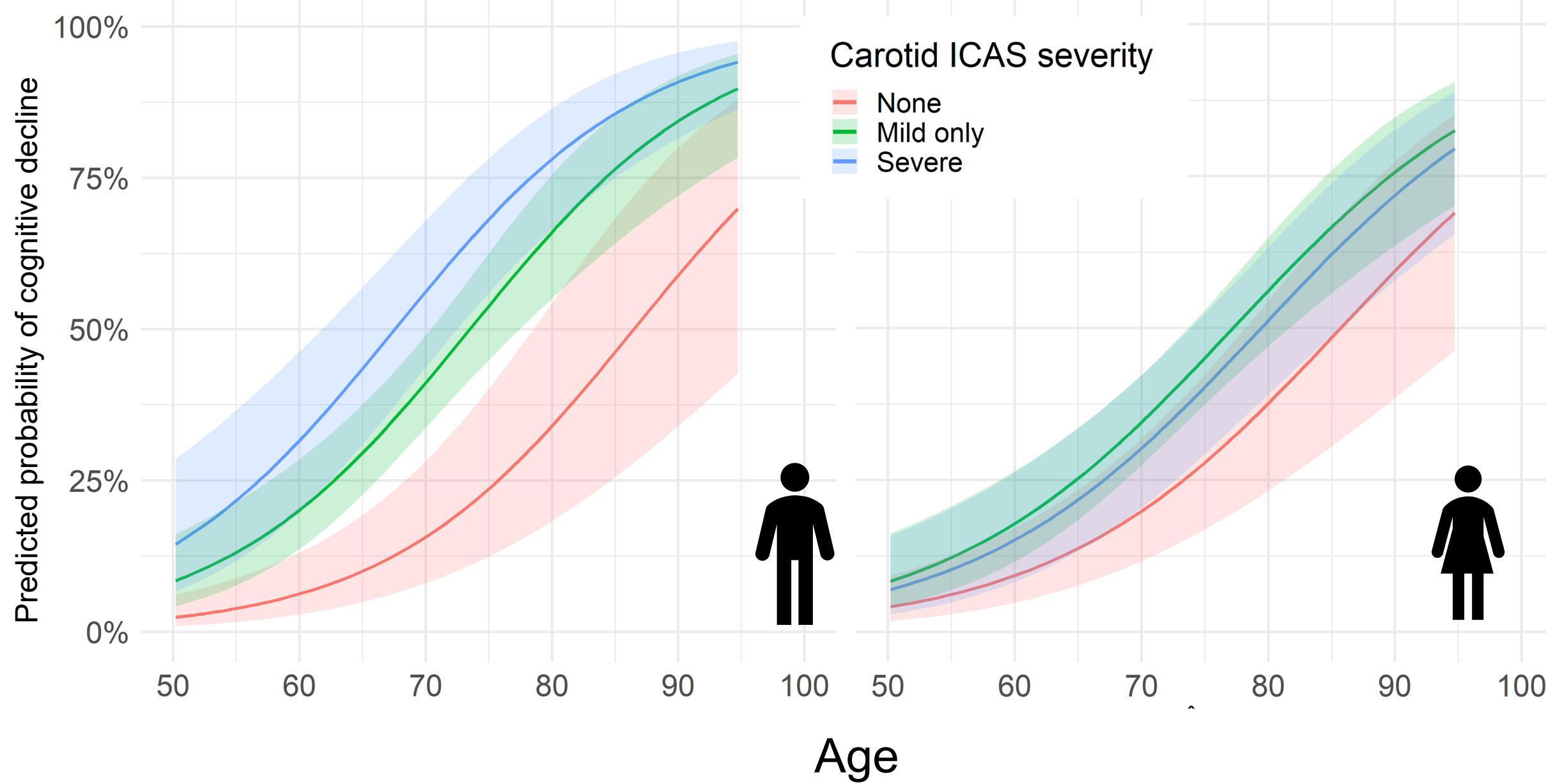
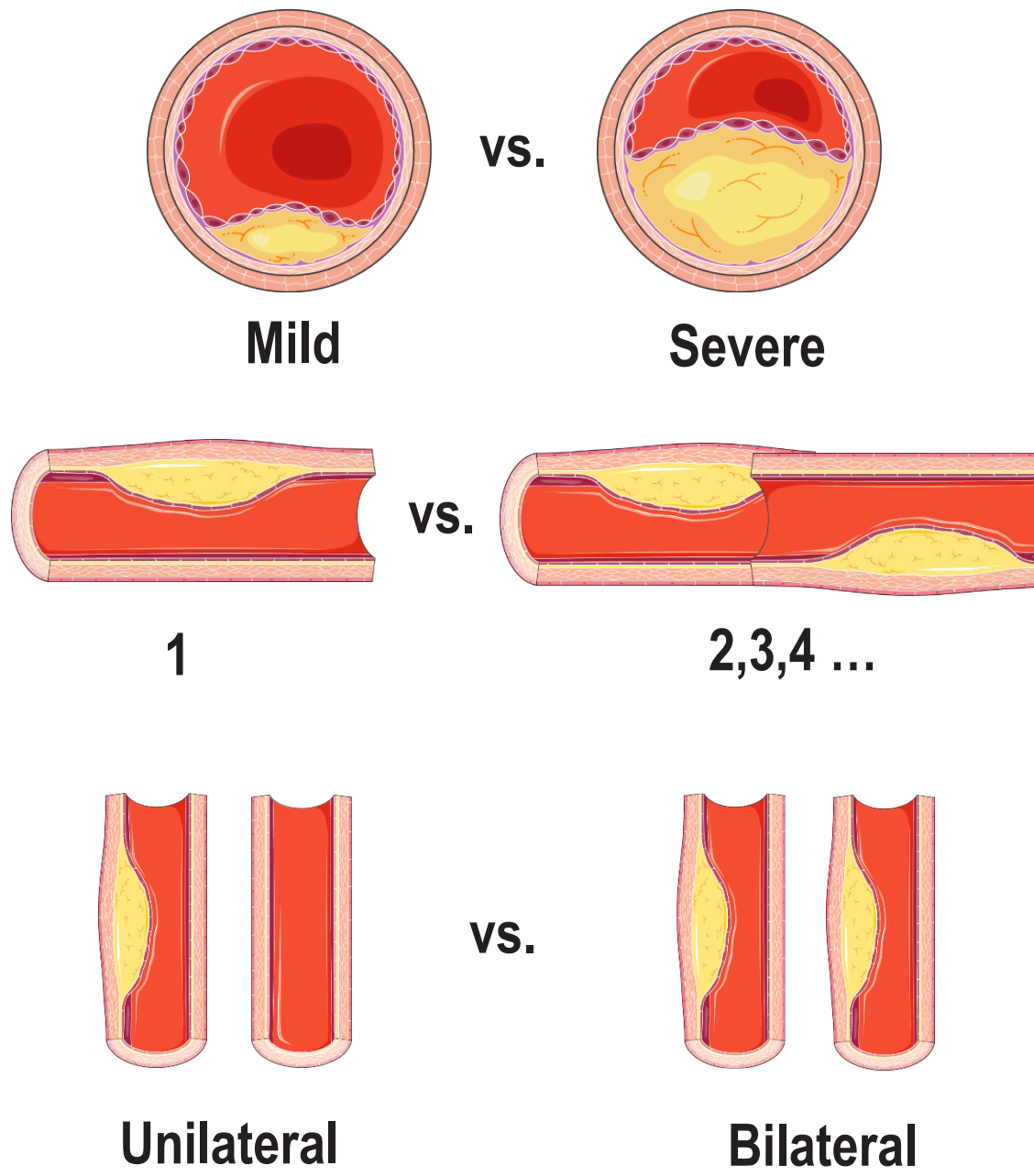


Table 3. Odds ratios (95% CI) for cognitive decline associated with ICAS burden markers. Separate logistic regression models were used to evaluate each marker and population was restricted to patients presenting ≥ 1 carotid ICAS stenosis.

	Internal carotid	Internal carotid, male	Internal carotid, female
Severe ICAS (ref. group: mild ICAS)	1.26 (0.84 – 1.90)	1.84 (1.03 – 3.30)	0.83 (0.46 – 1.49)
Stenosis count (ref. group: 1 stenosis)	1.09 (0.98 – 1.20)	1.09 (0.96 – 1.25)	1.05 (0.91 – 1.23)
Bilateral disease (ref. group: unilateral disease)	1.07 (0.73 – 1.58)	1.01 (0.59 – 1.74)	1.09 (0.63 – 1.90)



DISCUSSION

- Mild ICAS = **significantly associated** with cognitive decline for the internal carotid arteries.
- Basilar artery: **no dose-response effect**, possibly due to low number of basilar stenoses or to greater importance of anterior circulation in cognitive health.
- Sex differences: ICAS had a **weaker and non dose-response effect in women** as opposed to men. This could imply vascular cognitive protection in women.
- ICAS burden: only severity of stenosis in men had a meaningful impact on cognitive outcome, once again suggesting stronger effect in men. Also suggests that largest leap in risk = **mere presence of ICAS** rather than more widespread and severe ICAS.
- All results were independant of baseline brain volume, suggesting a **pure vascular pathway** towards cognitive decline.

LIMITATIONS

- Awaiting data on cardiovascular comorbidities needed to properly control regression models (history of diabetes, hypertension, stroke, etc.)
- Selection bias: population selected needed to have undergone cerebral CTA, therefore population isn't fully representative of real-world risk.

CONCLUSION

- Mild ICAS of the internal carotid arteries was found to have significant association with cognitive decline, independant of baseline brain volume.
- Effects in men and women differed, suggesting potential vascular protection in women.
- Further studies of mild ICAS are warranted to investigate other cerebro-cognitive consequences and the relevance of preventative treatment



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