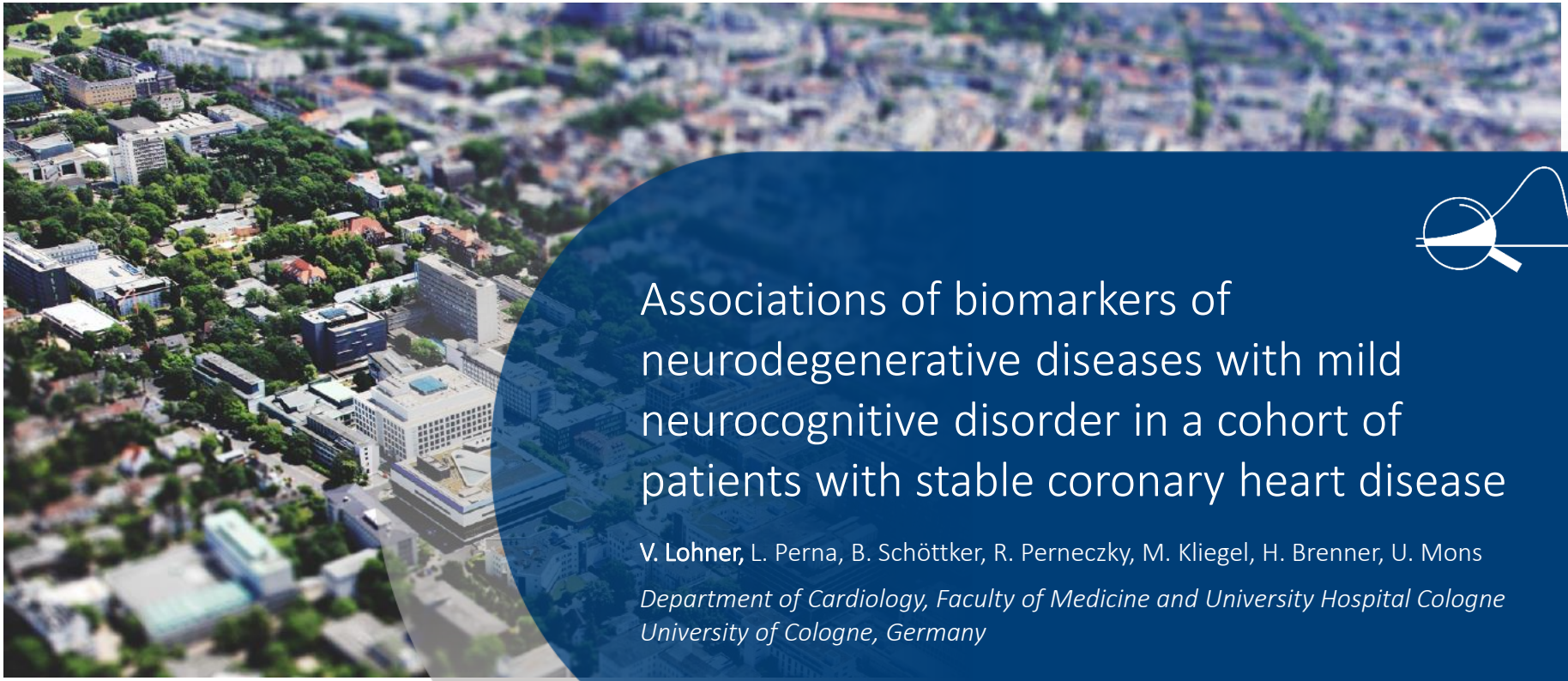
UNIKLINIK KÖLN



Associations of biomarkers of neurodegenerative diseases with mild neurocognitive disorder in a cohort of patients with stable coronary heart disease

V. Lohner, L. Perna, B. Schöttker, R. Perneczky, M. Kliegel, H. Brenner, U. Mons

Department of Cardiology, Faculty of Medicine and University Hospital Cologne University of Cologne, Germany

Blood-based biomarkers of neurodegenerative diseases

Glial fibrillary acidic protein (GFAP):

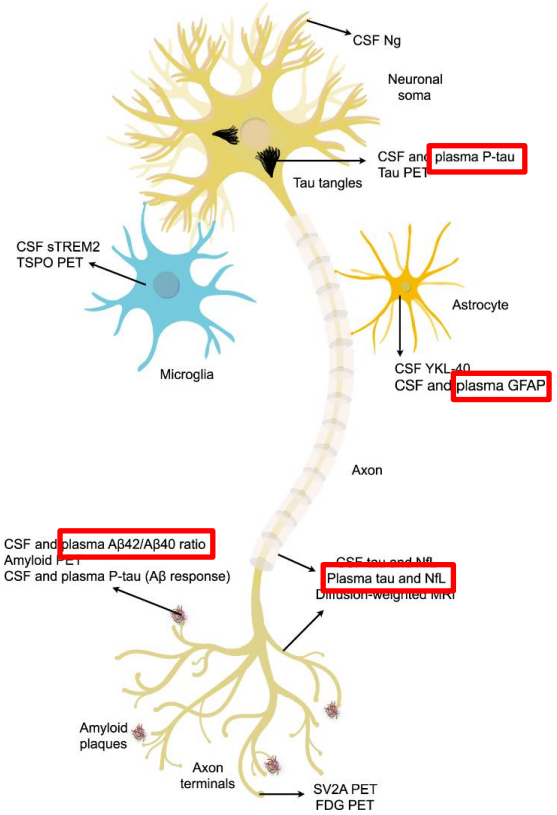
- Marker of astrocytic activation/degeneration
- Reflects neuronal damage
- Irrespective of cause

Neurofilament light chain (NfL):

- Reflects neuroaxonal degeneration and injury
- Irrespective of cause

Phosphorylated tau181 (p-tau181):

- Reflects pathophysiology related to Alzheimer's disease across different types of dementia



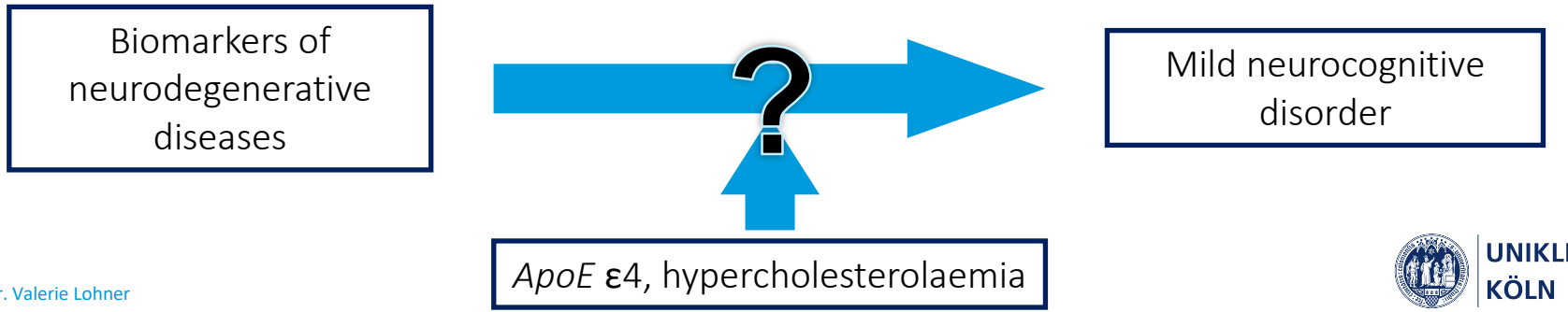
UNIKLINIK KÖLN

Blood-based biomarkers of neurodegenerative diseases

- Associated with cognitive function and risk of developing dementia in several populations
- Predictive utility for cognitive performance in patients with cardiovascular disease unexplored
- Potential interactions of total cholesterol (TC) levels and E (*ApoE*) genotype with these biomarkers

Aim

- To explore prognostic value of blood-based biomarkers of neurodegenerative diseases for mild neurocognitive disorder (MiND) after ten years in patients with chronic coronary syndrome



UNIKLINIK KÖLN

Methods

Study population
- Persons with chronic coronary syndrome who participated in 10-year follow-up cognitive assessment (KAROLA study)
- Age range: 30 – 70 years

Outcome: mild neurocognitive disorder
- Cognitive Telephone Screening Instrument (COGTEL)
- Assessed after ten years
- Cut-off for MiND: ≤21.8 points on COGTEL

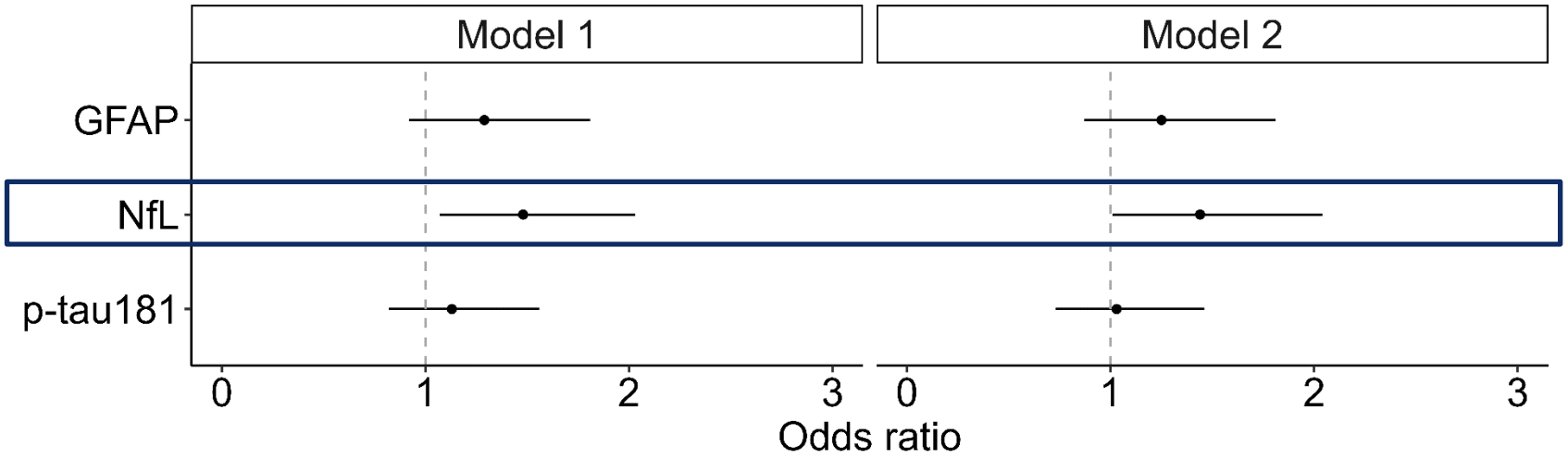
Biomarkers of neurodegenerative diseases
- Measured in serum at baseline: GFAP, NfL, and p-tau181
- Single-Molecule Array (Simoa) Technology (Quanterix, USA)

Statistical data analysis
- Multivariable logistic regression models
- Adjusted for risk factors and comorbidities
- Test of interaction for biomarker with hypercholesterolaemia and *ApoE* ε4

Characteristics of the study population

		Sample (n=363)
Age groups, n (%)	30-49 years	51 (14.0)
	50-59 years	127 (35.0)
	60+ years	185 (51.0)
Men, n (%)		307 (84.6)
APOE ε4 carriers, n (%)		106 (30.0)
Hypercholesterolaemia, n (%)	TC < 200 mg/dL without statin use	60 (16.5)
	TC < 200 mg/dL with statin use	248 (68.3)
	TC ≥ 200 mg/dL with(out) statin use	49 (13.5)
Biomarker of neurodegenerative diseases	p-tau181 (pg/mL), median [IQR]	1.1 [0.8, 1.6]
	NfL (pg/mL), mean (SD)	23.9 (30.2)
	GFAP (pg/mL), median [IQR]	97.7 [70.8, 133.4]
Mild neurocognitive disorder at follow-up, n (%)		55 (15.2)

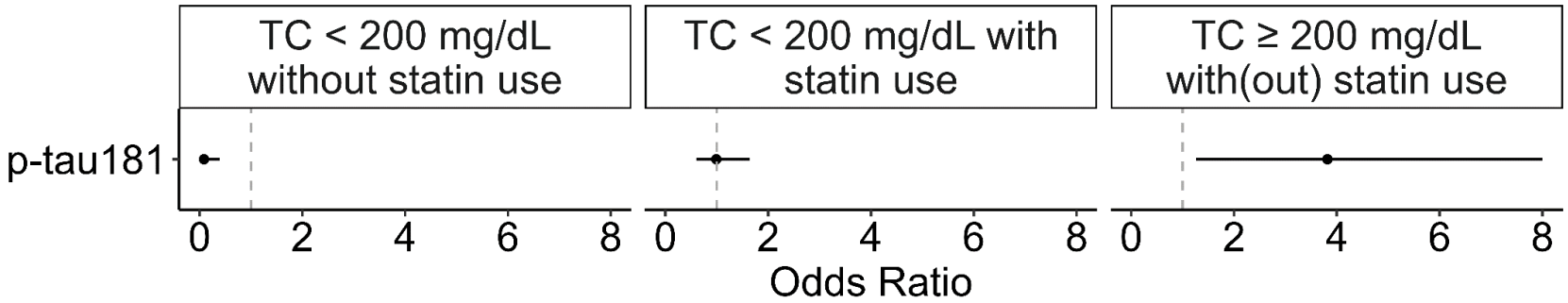
Association of biomarkers of neurodegenerative diseases with MiND



Model 1 was adjusted for age, sex, study centre, estimated glomerular filtration rate, and hearing impairment.
Model 2 was additionally adjusted for *ApoE* ε4, hypercholesterolaemia, and risk factors (depression, alcohol intake, body mass index, smoking, history of myocardial infarction, history of stroke, diabetes mellitus, and hypertension).

UNIKLINIK KÖLN

Association of p-tau181 with MiND – stratified by hypercholesterolaemia



Models were fully adjusted (age, sex, study centre, estimated glomerular filtration rate, hearing impairment, *ApoE* ε4, and risk factors (depression, alcohol intake, body mass index, smoking, history of myocardial infarction, history of stroke, diabetes mellitus, and hypertension)), except for the model for patients with TC ≥ 200 mg/dL with(out) statin use, which has only been partly adjusted (age, sex, study centre, estimated glomerular filtration rate, hearing impairment, ApoE ε4) due to low numbers in risk factors.

UNIKLINIK KÖLN

Summary and discussion

- Higher levels of NfL were associated with higher risk of developing MiND after ten years
- Counterintuitive association of p-tau181 with MiND in patients with TC < 200 mg/dL without statin use
- *ApoE* ε4 did not seem to act as effect modifier
- GFAP was not associated with MiND

- Selection bias: inclusion based on participation in 10-year follow-up cognitive assessment
- Limited sample size

Conclusions

- NfL and p-tau181 predict MiND after ten years in patients with chronic coronary syndrome
- Strength of associations for p-tau181 depending on hypercholesterolaemia; strongest association in patients with TC > 200 mg/dL independent of statin use
- Deterioration in cognitive performance in this population might be halted through early management of hypercholesterolaemia
  → more research warranted
- Biomarkers of neurodegenerative diseases may be utilised to identify people at higher risk of MiND
- Pathophysiology of interplay between biomarkers of neurodegenerative diseases and cardiovascular disease remains to be elucidated

Contact:
valerie.lohner@uk-koeln.de

UNIKLINIK KÖLN
Funding: Marga and Walter Boll Foundation, Kerpen, Germany.