

Association Of Body Mass Index With ADRD Cerebrospinal Fluid Biomarkers: A Nationwide Cohort Study

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INTRODUCTION

Midlife obesity, measured by body mass index (BMI), is associated with an increased risk of dementia, whereas low BMI in late life is linked to late-onset Alzheimer's disease and vascular complications. However, the relationship between BMI and cerebrospinal fluid (CSF) biomarkers of Alzheimer's disease and related dementias (ADRD) remains unclear [1,2].

AIM

This study aimed to examine the association between BMI and CSF biomarkers of ADRD.

METHOD

We used data from the Swedish Registry for Cognitive/Dementia Disorders (SveDem, 2007-2020) and included all individuals with dementia who had complete CSF biomarker data. BMI (kg/m^2) was categorized as underweight (<18.5), normal weight ($18.5 \leq \text{BMI} < 25$), overweight ($25 \leq \text{BMI} < 30$), and obese (≥ 30). Outcomes included CSF biomarkers ($\text{A}\beta_{40}$, $\text{A}\beta_{42}$, $\text{A}\beta_{42}/40$, $\text{A}\beta_{42}/\text{phosphorylated tau}$, total tau, and phosphorylated tau), the albumin quotient (QAlb), glial fibrillary acidic protein (GFAP), neurofilament light chain (NfL), and Alzheimer's disease (AD) pathology. AD pathology was assessed as a binary outcome defined by a positive $\text{A}\beta_{42}/40$ or $\text{A}\beta_{42}/\text{phosphorylated tau}$ ratio. Linear regression models were used for continuous biomarkers, and logistic regression models were used for AD pathology, adjusting for age, sex, Mini-Mental State Examination (MMSE) score, comorbidities, and dementia subtype.

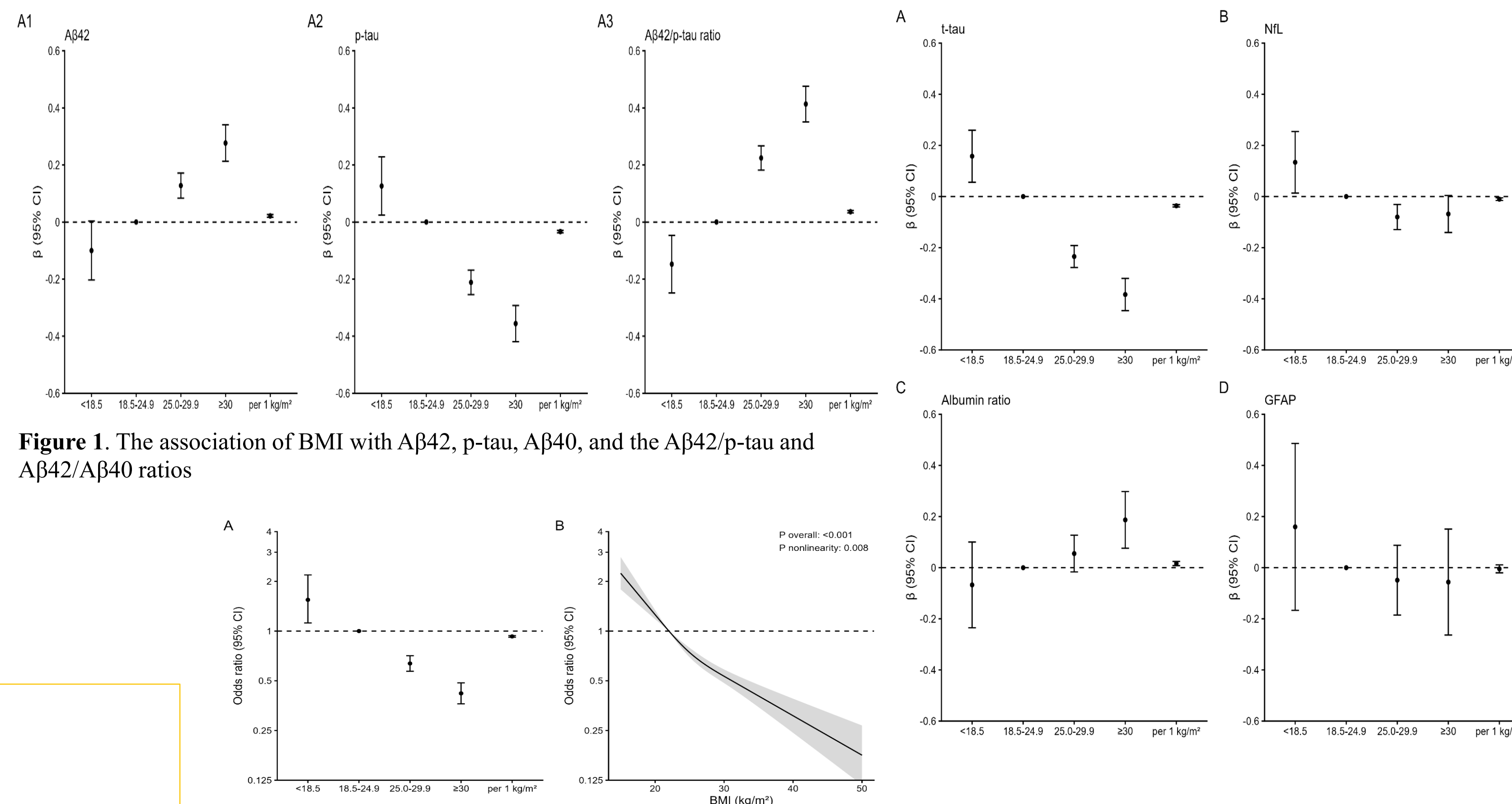


Figure 2. Associations between BMI and AD pathology

RESULTS

A total of 10,242 participants were included (53% female; mean age 73 ± 8 years; mean $\text{BMI} 25 \pm 4 \text{ kg}/\text{m}^2$). Overall, 33% were overweight, 12% obese, and 4% underweight. Compared with normal weight, underweight was associated with higher odds of AD pathology (OR, 1.55; 95% CI, 1.12–2.19), whereas overweight (OR, 0.64; 95% CI, 0.57–0.71) and obesity (OR, 0.42; 95% CI, 0.36–0.49) were associated with lower odds. Obesity was also associated with impaired blood-brain barrier (BBB) integrity, reflected by a higher QAlb ($\beta = 0.59 [0.19-0.99]$). In contrast, underweight was associated with higher NfL levels (adjusted $\beta = 511.28 [185.19-827.36]$ ng/L). Compared with normal-weight individuals, overweight (odds ratio [OR] = 0.96 [95% CI: 0.94-0.97]) and obese participants (OR = 0.90 [0.88-0.92]) had lower odds of Alzheimer's disease pathology.

CONCLUSIONS

These findings indicate a complex relationship between BMI and neurodegeneration, with obesity associated with lower AD pathology but impaired BBB integrity (QAlb), and under weight associated with greater neuronal death, as reflected by higher NfL levels.

REFERENCES

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