Advancing the detection of early Alzheimer's via clinical biomarkers

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Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative condition marked by cognitive decline and memory loss [1]. The prevalence of dementia, primarily linked to AD, is on the rise globally, including in the United States. Initial symptoms are often nonspecific and can easily be overlooked. Diagnosis traditionally relies on subjective clinical and cognitive assessments, lacking precision [2]. Presently, there are no established objective biomarkers for early AD detection. Our research addresses this gap by proposing laboratory-based biomarkers, utilizing retrospective critical care medical data from the MIMIC-IV database, offering potential advancements in AD diagnosis and management [3].

Objectives: Our objective is to determine lab-based biomarkers for early AD detection based on retrospectively collected critical care medical data from the MIMIC-IV database.

Methods: The MIMIC-IV database that includes critical care data from 40,000 patients admitted to intensive care units at the Beth Israel Deaconess Medical Center was utilized. For each lab (n=1,600+), MIMIC-IV was filtered for patients with a primary diagnosis of AD and each case was age- and sex-matched to four control patients. Welch's two sample t-test was used to compare derived means and standard deviations in AD vs. control groups. Effect sizes (ES) were calculated to assess the practical significance of our results.

Results: Of 477 labs, 51 were significantly different between AD and CTL groups ($p<0.05$). Of these, 22 had a moderate-large ES (range 0.27-1.16). Of 227 labs exclusive to females, 22 were significantly different between female AD and CTL groups ($p<0.05$). Of these, 6 had a moderate ES (0.35-0.48). Lastly, of 210 labs exclusive to males, 22 were significantly different between male AD and CTL groups ($p<0.05$). Of these, 9 had a moderate ES (0.26-0.49).

Conclusion: Potential lab-based biomarkers for AD fell in the following broader diagnostic categories: kidney function (urea nitrogen), cardiovascular (cholesterol), and electrolyte/metabolic balance (chloride, urine glucose). Although females and males had overlapping labs, males were distinguished by hematological labs, indicating the importance of considering sex in biomarker discovery for AD.

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