



Novel Serum Metabolic Indices as Predictors of Alzheimer's Disease in Taiwanese Population

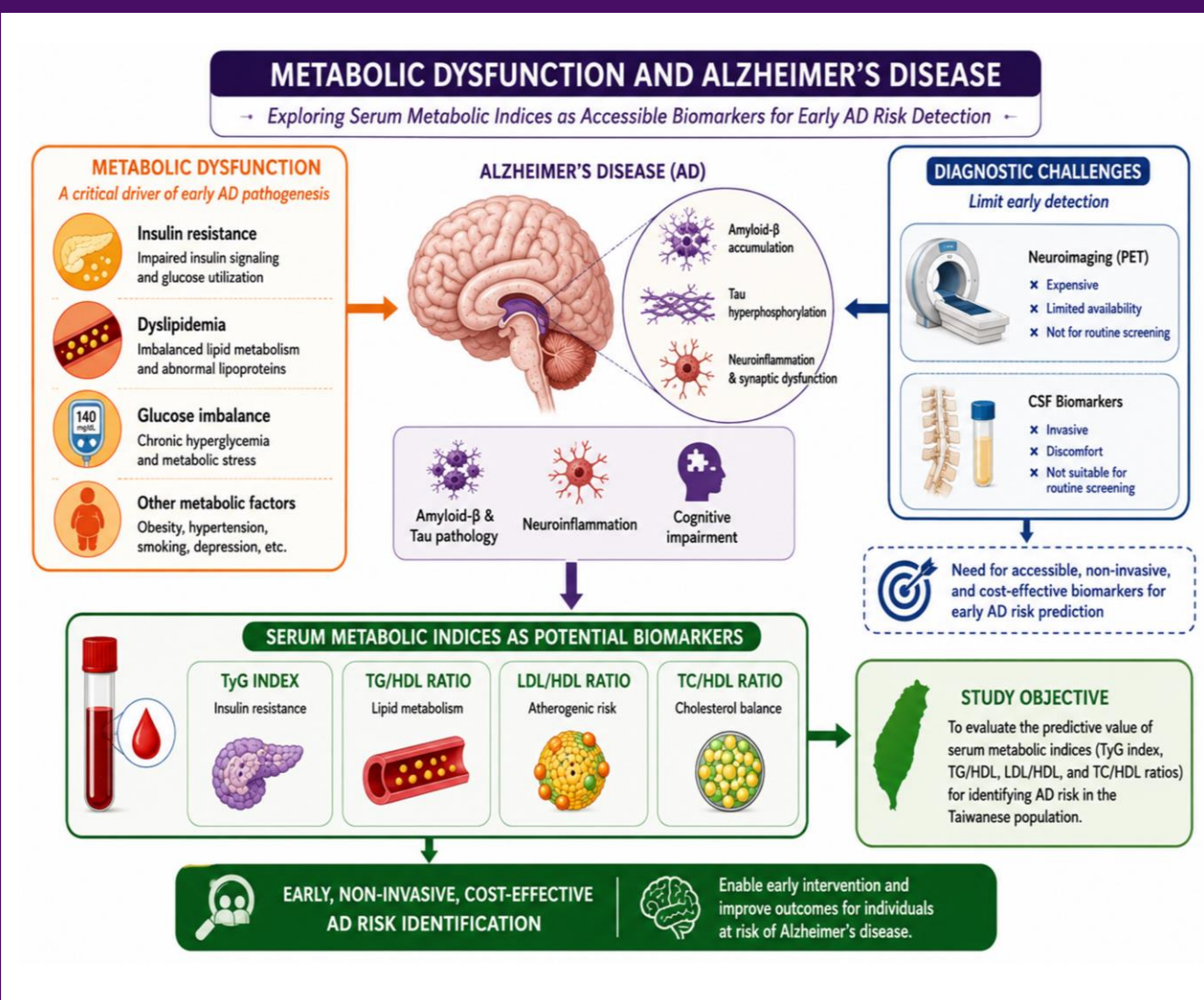


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Routine blood lipid ratios (TC/HDL and LDL/HDL) showed the best predictive performance for Alzheimer's disease risk, supporting their potential as simple, non-invasive, and cost-effective biomarkers for early AD screening.

INTRODUCTION



B DEFINITION OF METABOLIC INDICES (MI)

Metabolic indices were calculated based on previous studies as follows:

Metabolic Index	Formula	Description
1. TyG-index	$\ln \left(\frac{\text{Triglycerides} \times \text{Fasting glucose}}{2} \right)$	Natural logarithm of triglycerides and fasting glucose
2. TG/HDL ratio	$\frac{\text{Triglycerides}}{\text{HDL-C}}$	Ratio of triglycerides to high-density lipoprotein cholesterol
3. TC/HDL ratio	$\frac{\text{Total cholesterol}}{\text{HDL-C}}$	Ratio of total cholesterol to high-density lipoprotein cholesterol
4. LDL/HDL ratio	$\frac{\text{LDL-C}}{\text{HDL-C}}$	Ratio of low-density lipoprotein cholesterol to high-density lipoprotein cholesterol

Legend

TG : Triglycerides	TC : Total cholesterol
HDL-C : High-density lipoprotein cholesterol	In : Natural logarithm
LDL-C : Low-density lipoprotein cholesterol	Fasting glucose : Fasting plasma glucose

Note: All lipid parameters are measured in mg/dL.

RESULTS

Table 1. Demographic characteristics

Variable	HC (n=60)	AD (n=73)	p-Value
Age, years	78 (IQR,10)	76 (IQR,12)	0.399
Sex			0.861
Male %	41.67 (25)	43.84 (32)	
Female %	58.33 (35)	56.16 (41)	
Total protein (g/L)	72.49 (IQR, 43.95)	71.4 (IQR, 28.03)	0.38
Fasting glucose (mg/dL)	104.5 (IQR, 24)	105 (IQR, 32)	0.468
HbA1c %	5.975 (IQR, 1.14)	5.9 (IQR, 1.04)	0.845
TG (mg/dL)	115 (IQR, 70.9)	102.2 (IQR, 71)	0.226
TC (mg/dL)	178 (IQR, 54)	186.29 (IQR, 54)	0.215
HDL (mg/dL)	48 (IQR, 21.33)	53.5 (IQR, 20.5)	0.184
LDL (mg/dL)	103.5 (IQR, 54)	108 (IQR, 46)	0.296
ALT((IU/L))	21 (IQR, 16.7)	19 (IQR, 9)	0.224
Creatinine (mg/dL)	0.94 (IQR, 0.41)	1.0 (IQR, 0.43)	0.72
TyG index	4.68 (IQR, 0.33)	4.71 (IQR, 0.4)	0.474
TG/HDL ratio	1.86 (IQR, 1.8)	2.59 (IQR, 2.87)	0.008
LDL/HDL ratio	1.55 (IQR, 2.21)	2.31 (IQR, 0.89)	<0.001
TC/HDL ratio	3.14 (IQR, 1.4)	4.15 (IQR, 1.51)	<0.001

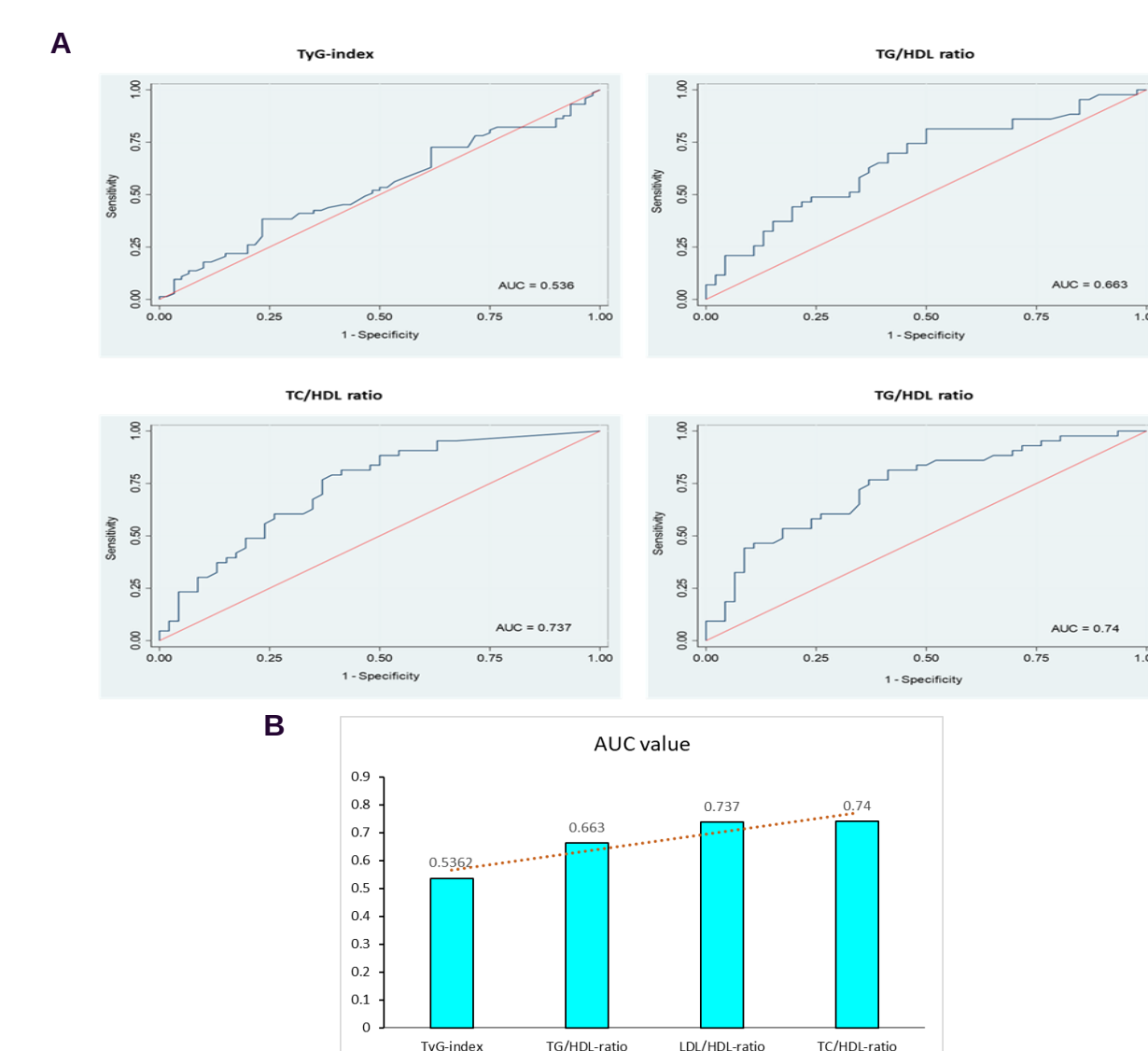
Categorical values are n (%), continuous values are median (interquartile range; IQR). ALT, alanine aminotransferase; HbA1c, glycohemoglobin A1c; HDL, high-density lipoprotein-cholesterol; LDL, low-density lipoprotein-cholesterol; TC, total cholesterol; TG, triglycerides; TyG-index, triglyceride-glucose index.

Table 2. Association between metabolic indices and AD

Variables	Odd ratio (95% CI)	p-value
TyG-index	1.6 (0.51-5.03)	0.423
TG/HDL-ratio	1.28 (1.03-1.59)	0.024
TC/HDL-ratio	2.01 (1.32-3.06)	0.001
LDL/HDL-ratio	2.43 (1.5-3.93)	<0.001

TyG-index, triglyceride glucose index; TG/HDL, triglyceride- to-high density lipoprotein ratio; LDL/HDL ratio, low density lipoprotein-to-high density lipoprotein ratio; TC/HDL, total cholesterol - to-high density lipoprotein ratio.

Figure 1. Predictive value of metabolic indices in AD



Discriminatory ability of the metabolic indices. (A) ROC curve of metabolic indices for Alzheimer's disease prediction. (B) Bar chart showing the predictive value of metabolic indices.

DISCUSSION

A. Clinical Significance

- Lipid-based metabolic indices derived from routine blood tests may provide simple, cost-effective, and non-invasive biomarkers for AD risk assessment.
- TC/HDL and LDL/HDL ratios demonstrated the best predictive performance and may improve early risk stratification when combined with existing clinical assessments.
- These biomarkers have potential utility for identifying individuals who may benefit from early preventive interventions.

B. Limitations

- Cross-sectional design precludes causal inference.
- Moderate sample size from a single Taiwanese cohort may limit generalizability.
- Potential confounding factors (e.g., APOE genotype, diet, physical activity, and lipid-lowering medications) were not fully evaluated.
- Larger, multi-center longitudinal studies are needed to validate these findings.

CONCLUSIONS

- TG/HDL, LDL/HDL, and TC/HDL ratios were significantly associated with AD risk.
- The TC/HDL ratio demonstrated the highest predictive performance (AUC = 0.740), closely followed by the LDL/HDL ratio (AUC = 0.737).

- The TC/HDL ratio showed the highest predictive performance (AUC = 0.740), closely followed by the LDL/HDL ratio (AUC = 0.737), while the TG/HDL ratio showed moderate predictive ability (AUC = 0.663).
- The TyG index demonstrated poor discriminatory performance (AUC = 0.536) and was not significantly associated with AD risk.
- These findings support TC/HDL and LDL/HDL ratios as promising, accessible, and cost-effective blood-based biomarkers for early AD risk assessment.

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METHODS

