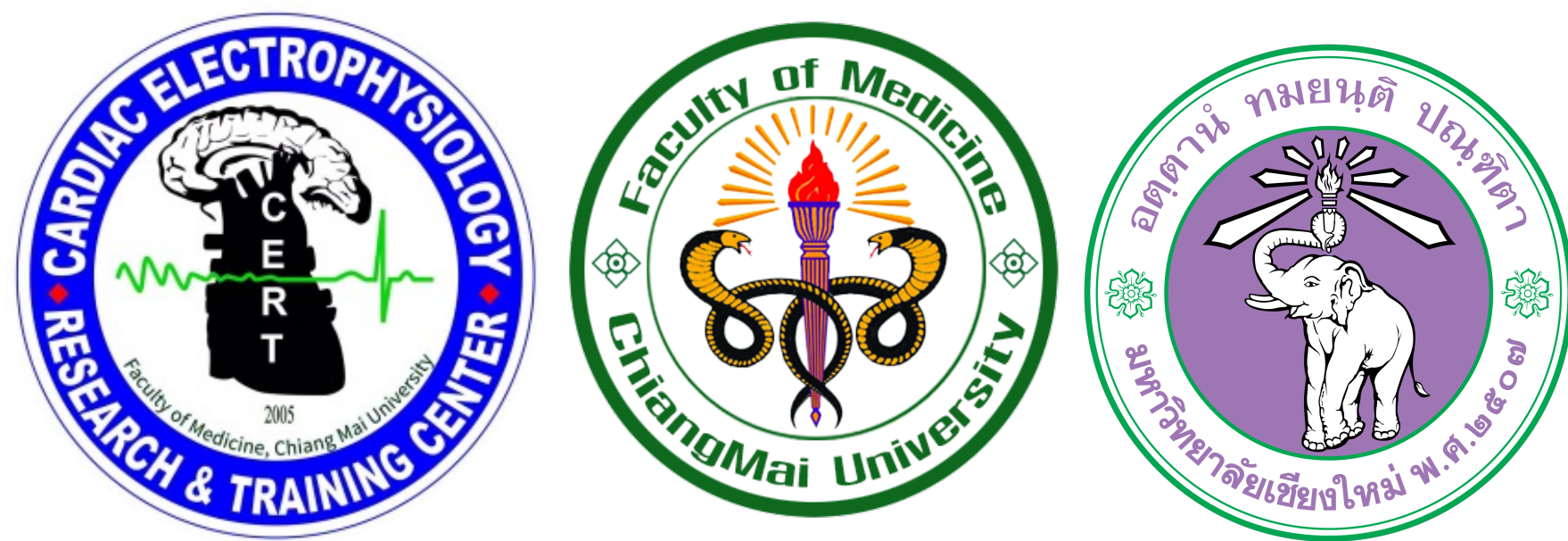


Inflammatory Cytokines and Mitochondrial Dysfunction Are Associated With Cognitive Impairment After Traumatic Brain Injury



P3-06

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These findings suggest that circulating biomarkers may reflect secondary injury mechanisms and could support early cognitive risk stratification after TBI.

BACKGROUND

- Traumatic brain injury (TBI) is a major cause of long-term neurological disability, and cognitive impairment may occur even after relatively mild injury.
- Secondary injury mechanisms, including inflammation, oxidative stress, mitochondrial dysfunction, and apoptosis, may exacerbate neuronal damage and contribute to early cognitive decline.
- Circulating biomarkers may reflect these ongoing biological responses and provide information beyond conventional clinical assessment and neuroimaging.
- However, the associations between peripheral inflammatory, oxidative stress, mitochondrial, apoptosis-related, and glial biomarkers and early cognitive performance after TBI remain incompletely understood.

AIM

Aim: to determine whether circulating inflammatory, oxidative stress, mitochondrial, apoptotic, and glial-associated biomarkers, as well as imaging-based bleeding parameters are associated with early cognitive impairment in patients with TBI.

METHODS

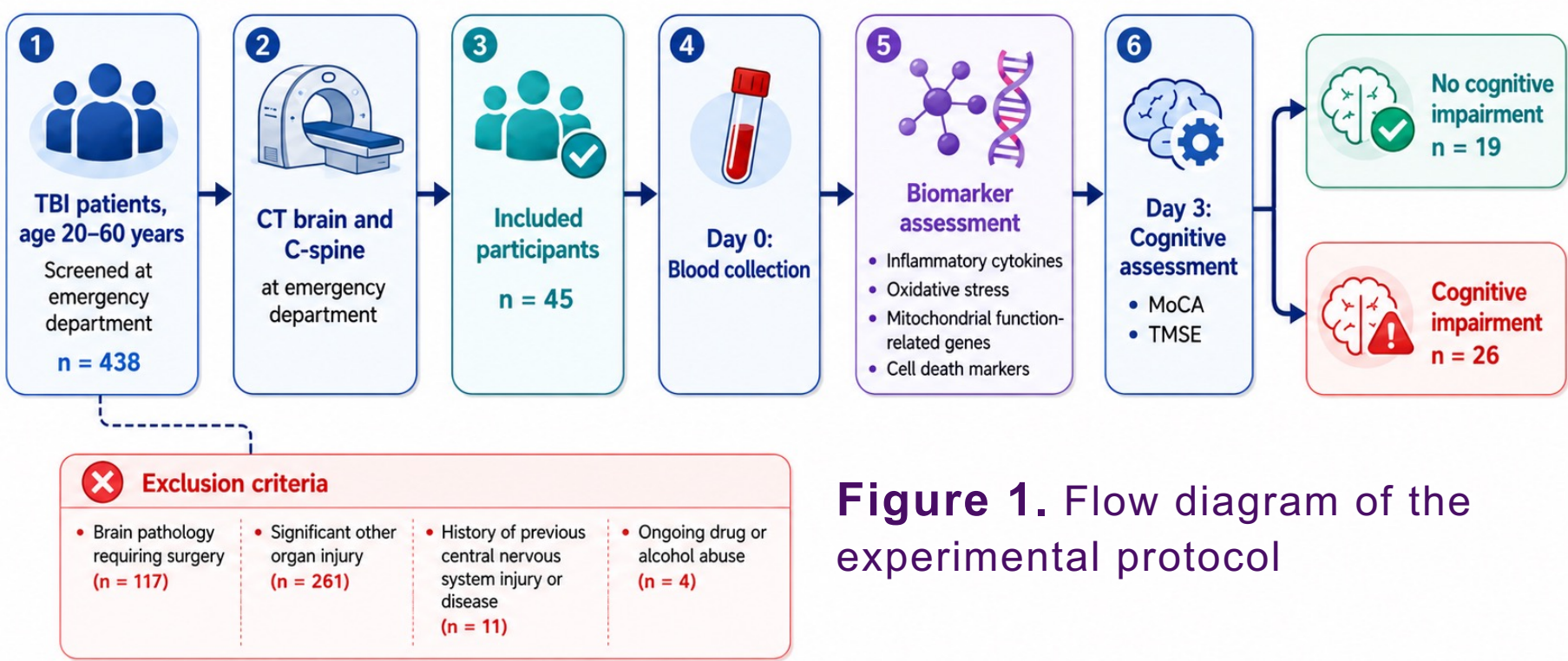


Figure 1. Flow diagram of the experimental protocol

Forty-five patients with traumatic brain injury were enrolled after emergency department screening. Admission blood samples were analyzed for inflammatory, oxidative stress, mitochondrial function-related, and cell death biomarkers. Cognitive function was assessed on day 3 using the MoCA and TMSE, followed by classification into cognitive impairment and no cognitive impairment groups.

RESULTS

1 Cognitive impairment following TBI is associated with inflammation, oxidative stress, mitochondrial dysfunction, and apoptosis.

- 58% of TBI patients developed cognitive impairment.
- Median MoCA and TMSE scores of 23 and 27.5, respectively.
- Lower MoCA and TMSE scores were associated with greater mRNA expression of inflammatory, antioxidant, mitochondrial respiration, mitochondrial dynamics, and apoptosis.
- Both cognitive scores were also negatively correlated with temporal lobe bleeding volume, whereas circulating S100B and GFAP levels showed no significant association with cognitive performance (Figure 2).

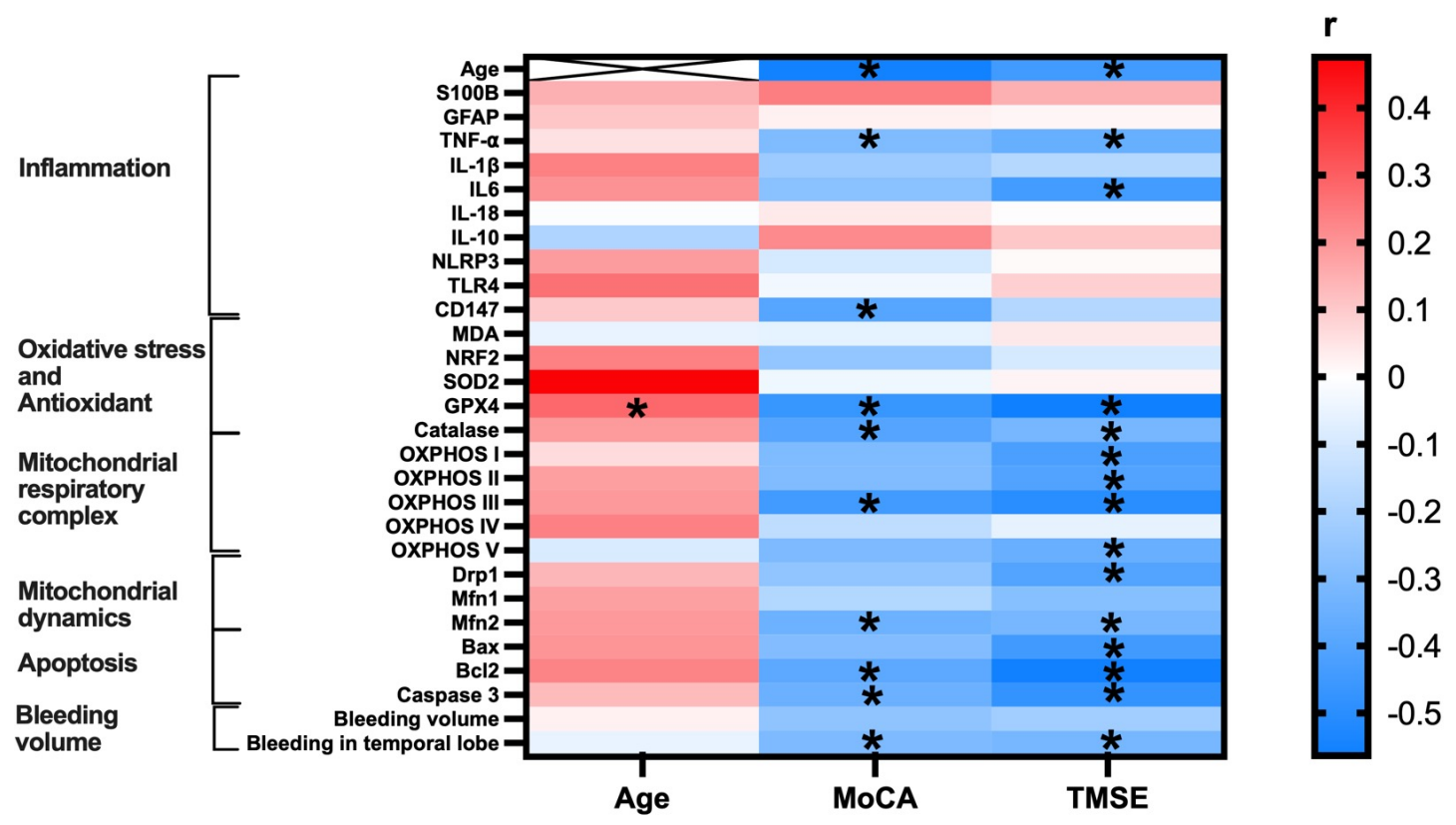


Figure 2. Correlation analysis with spearman rho between age, MoCA and TMSE scores vs. circulating biomarkers in patients with TBI. *p < 0.05.

2 MCI patients had higher inflammation, anti-oxidant levels, and mitochondrial impairment.

- Compared with patients without cognitive impairment, those who developed cognitive impairment showed lower performance across all MoCA domains, particularly orientation, delayed recall, abstraction, and language (Figure 3A).
- MCI patients were older (Figure 3B).
- MCI had higher expression of CD147, GPX4, catalase, mitochondrial respiratory complex III, Mfn2, and Bcl-2 (Figure 3D-I).
- In contrast, TNF-α, caspase-3, and temporal lobe bleeding volume did not differ significantly between the two groups (Figure 3C,J-K).

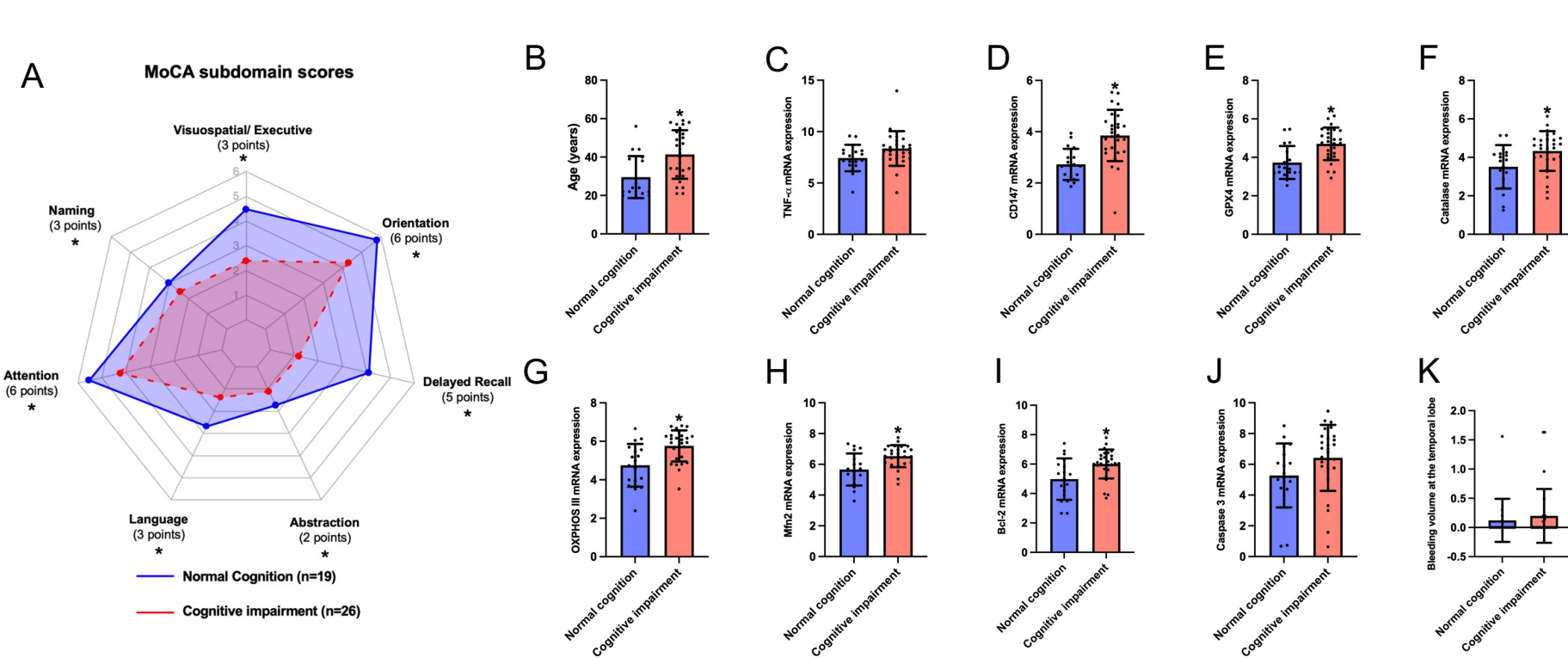


Figure 3. Radar plot illustrating Montreal Cognitive Assessment (MoCA) subdomain scores in patients with normal cognition (blue) and cognitive impairment (red) at day 3 post-admission. (A), Patients with cognitive impairment exhibited significantly higher age (B) and increased expression of CD147 (D), GPX4 (E), catalase (F), OXPHOS Complex III (G), Mfn2 (H), and Bcl-2 (I) mRNA. No significant difference was observed in TNF-α (C), caspase-3 (J) mRNA expression, and bleeding volume at the temporal lobe (K). Data are presented as mean ± SEM with individual data points. *p < 0.05 versus normal cognition group.

CONCLUSION

Early cognitive impairment was common after TBI and was associated with systemic inflammatory activation, oxidative stress, mitochondrial dysfunction, and apoptosis-related changes. Higher expression of CD147, GPX4, catalase, mitochondrial respiratory complex III, Mfn2, and Bcl-2 was observed in patients with cognitive impairment, whereas S100B and GFAP were not significantly related to cognitive performance. These findings suggest that circulating biomarkers may reflect secondary injury mechanisms and could support early cognitive risk stratification after TBI.

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