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RESEARCH ARTICLE OPEN ACCESS

Brain–Heart axis dysfunction in hypertensive patients: A clinical correlation study

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Abstract
Objective: To investigate the clinical correlates of brain–heart axis dysfunction in hypertensive patients by evaluating cardiovascular, neurological, autonomic, and inflammatory profiles.
Methods: A prospective clinical correlation study was conducted from October 2024 to September 2025 at Tikrit Teaching Hospital. A total of 350 hypertensive adults (aged 40–75 years) were classified into two groups: 200 with brain–heart axis dysfunction and 150 without. Assessments included cardiovascular (blood pressure, ECG, echocardiography, ambulatory blood pressure monitoring, pulse wave velocity), neurological (MRI, Montreal parameters (cardiac biomarkers, inflammatory markers, oxidative stress markers).
Results: The study group demonstrated significantly higher systolic and diastolic blood pressure, left ventricular mass index, arterial stiffness, and ECG abnormalities (all $p < 0.001$). Neurological assessment revealed lower cognitive scores, higher white matter lesion burden, reduced heart rate variability, and impaired baroreflex sensitivity (all $p < 0.001$). Laboratory findings indicated elevated troponin, NT-proBNP, hs-CRP, IL-6, and malondialdehyde, alongside reduced superoxide dismutase activity (all $p < 0.001$).
Conclusion: Brain–heart axis dysfunction is associated with more severe cardiovascular, neurological, and inflammatory derangements in hypertensive patients. Integrated assessment of autonomic, cognitive, and inflammatory markers may improve risk stratification and guide targeted interventions.

Keywords: Brain–heart axis, Hypertension, Heart rate variability, Cognitive dysfunction, Cardiovascular risk

Plain English Summary

This study looked at how the connection between the brain and the heart, called the brain–heart axis, affects people with high blood pressure. We compared two groups of hypertensive patients: one with evidence of brain–heart axis problems and one without. We found that those with brain–heart axis dysfunction had higher blood pressure, stiffer arteries, more heart abnormalities, poorer memory and thinking skills, and higher levels of inflammation and stress markers in the blood. These findings suggest that checking for brain–heart axis problems in people with high blood pressure could help identify those at greater risk of heart and brain complications, allowing for earlier and more personalised treatment.

Introduction

Hypertension remains a leading global cause of cardiovascular morbidity and mortality, affecting over 1.28 billion adults worldwide and contributing to premature death (1). Traditionally viewed as a vascular disorder, emerging evidence implicates central neural mechanisms and bidirectional brain–heart interactions in its pathophysiology (2). The brain–heart axis encompasses autonomic, neurohormonal, inflammatory, and immune-mediated pathways that integrate central nervous system activity with cardiovascular function (3).

Dysregulation of the autonomic nervous system (ANS), characterised by sympathetic overactivity and parasympathetic withdrawal, is a key feature of hypertension (4). Markers like heart rate variability (HRV) and baroreflex sensitivity (BRS) are critical for evaluating this autonomic function, with low HRV indicating poor adaptive control (5). Furthermore, hypertension is increasingly linked to cognitive impairment through mechanisms

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such as cerebral hypoperfusion and neuroinflammation (6). Inflammatory cytokines and oxidative stress are also elevated in hypertensive patients, contributing to endothelial dysfunction and end-organ damage (7, 8).
Novel cardiovascular evaluations and neuroimaging now allow for a more integrative assessment of the brain–heart axis (9, 10). This study aimed to evaluate the association between brain–heart axis dysfunction and comprehensive cardiovascular, neurological, autonomic, and laboratory profiles in adults with hypertension.

Methods

Study Design and Setting

This was a prospective clinical correlation study conducted at Tikrit Teaching Hospital and its outpatient clinics from October 2024 to September 2025.

Study Population

A total of 350 hypertensive adults aged 40–75 years were enrolled. Participants were classified into two groups:
Study group (n=200): Hypertensive patients with brain–heart axis dysfunction.
Control group (n=150): Hypertensive patients without brain–heart axis dysfunction.

Operational Definition of Brain–Heart Axis Dysfunction

Dysfunction was defined by the presence of at least two of the following criteria:
1. HRV (SDNN) < 40 ms
2. MoCA score < 26
3. White matter lesion burden ≥ Fazekas grade 2 on MRI
4. Baroreflex sensitivity < 7 ms/mmHg

Inclusion and Exclusion Criteria

Inclusion: diagnosis of essential hypertension. Exclusion: secondary hypertension, history of stroke, Parkinson's disease, severe renal or hepatic impairment, or active malignancy.

Cardiovascular Assessment

1. Blood pressure was measured using automated oscillometric devices.
2. A 12-lead ECG was performed and interpreted by a cardiologist.
3. Echocardiography was conducted to assess left ventricular mass index (LVMI) using the Devereux formula, a standard method in clinical hypertension assessment (11).
4. Ambulatory blood pressure monitoring (ABPM) was performed over 24 hours.
5. Pulse wave velocity (PWV) was measured using a validated tonometry system; studies show its correlation with left ventricular mass (12).

Neurological and Autonomic Assessment

1. Brain MRI (1.5T) included T1, T2, and FLAIR sequences. White matter lesions were graded using the Fazekas scale.
2. 3Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE).
3. HRV and BRS were derived from 10-minute resting ECG recordings analysed with dedicated software (Kubios HRV Premium).

Laboratory Investigations

Fasting blood samples were analysed for:
1. Cardiac biomarkers: troponin I, NT-proBNP
2. Inflammatory markers: hs-CRP, IL-6
3. Oxidative stress markers: malondialdehyde (MDA), superoxide dismutase (SOD)
4. Metabolic parameters: HbA1c, lipid profile. Biomarker assessment is crucial for understanding the matrix of hypertensive heart disease (13).

Statistical Analysis

Data were analysed using SPSS version 23. Continuous variables were expressed as mean ± standard deviation and compared using independent t-tests or Mann–Whitney U tests. Categorical variables were compared using chi-square tests. Pearson's correlation was used to assess associations. Multivariable linear regression models were applied to adjust for age, sex, hypertension duration, and medication use. A two-tailed p-value < 0.05 was considered significant.

Results

Demographic and Clinical Characteristics

The groups were comparable in age, sex distribution, and duration of hypertension (Table 1).

Table 1: Demographic Characteristics

Characteristic	Study Group (n=200)	Control Group (n=150)	p-value
Age (years)	62.3 ± 8.5	61.1 ± 9.2	0.28
Male, n (%)	112 (56)	84 (56)	0.99
Hypertension duration (years)	8.7 ± 4.3	7.9 ± 3.9	0.15

Cardiovascular Parameters

The study group had significantly higher systolic and diastolic blood pressure, LVMI, PWV, and

prevalence of ECG abnormalities (all p < 0.001) (Table 2), aligning with known associations between arterial stiffness and target organ damage (14).

Table 2: Cardiovascular Parameters

Parameter	Study Group	Control Group	p-value
Systolic BP (mmHg)	152.8 ± 12.4	139.5 ± 10.8	<0.001
Diastolic BP (mmHg)	94.7 ± 8.1	87.3 ± 7.5	<0.001
LVMI (g/m²)	128.5 ± 18.3	112.7 ± 16.9	<0.001
PWV (m/s)	11.2 ± 1.6	9.6 ± 1.3	<0.001
ECG abnormalities, n (%)	48 (24)	21 (14)	0.02

Neurological and Autonomic Parameters
The study group exhibited lower MoCA and MMSE scores, a higher white matter lesion burden, reduced HRV, and a lower BRS (all p < 0.001) (Table 3).

Table 3: Neurological and Autonomic Parameters

Parameter	Study Group	Control Group	p-value
MoCA score	24.2 ± 3.1	27.1 ± 2.5	<0.001
MMSE score	26.8 ± 2.9	28.5 ± 1.7	<0.001
White matter lesions, n (%)	70 (35)	22 (15)	<0.001
HRV (SDNN, ms)	32.4 ± 8.5	45.6 ± 9.1	<0.001
Baroreflex sensitivity (ms/mmHg)	6.2 ± 1.4	8.1 ± 1.2	<0.001

Laboratory Parameters
The study group exhibited higher levels of cardiac biomarkers, inflammatory markers, and oxidative stress markers, alongside lower SOD activity and higher HbA1c (all p < 0.001) (Table 4).

Table 4: Laboratory Parameters

Parameter	Study Group	Control Group	p-value
Troponin (ng/L)	18.5 ± 5.3	11.2 ± 4.1	<0.001
NT-proBNP (pg/mL)	320 ± 85	210 ± 70	<0.001
hs-CRP (mg/L)	4.2 ± 1.1	2.7 ± 0.9	<0.001
IL-6 (pg/mL)	6.5 ± 2.0	4.1 ± 1.3	<0.001
MDA (µmol/L)	3.8 ± 1.0	2.4 ± 0.8	<0.001
SOD (U/mL)	112 ± 25	145 ± 28	<0.001
HbA1c (%)	6.8 ± 0.9	6.2 ± 0.8	<0.001

Correlation Analysis
Significant correlations were observed between HRV and systolic BP (r = -0.48, p < 0.001), MoCA score and PWV (r = -0.35, p < 0.001), hs-CRP and LVMI (r = 0.42, p < 0.001), and IL-6 and NT-proBNP (r = 0.37, p < 0.001).

Multivariable Regression
After adjusting for covariates, brain–heart axis dysfunction remained independently associated with higher LVMI, PWV, and lower MoCA scores (all p < 0.01).

Discussion

This study demonstrates that hypertensive patients with brain–heart axis dysfunction exhibit more severe cardiovascular, neurological, and inflammatory derangements compared to those without such dysfunction. Our findings align with growing evidence implicating autonomic dysregulation, neuroinflammation, and oxidative stress in hypertension-related end-organ damage (8, 15).

The observed associations between reduced HRV, elevated arterial stiffness, and cognitive decline suggest shared pathways of neural–vascular deterioration. The strong correlation between inflammatory markers (hs-CRP, IL-6) and cardiac remodelling supports a role for systemic inflammation in hypertensive heart disease, consistent with the concept of neuroinflammatory interactions along the brain-heart axis (16). These integrative pathways connecting vascular, neural, and inflammatory systems are increasingly recognised in clinical settings (17).

The positive correlation between IL-6 and NT-proBNP further advocates for a relationship between systemic inflammation and myocardial strain. These interconnected findings suggest that hypertension, autonomic dysregulation, inflammation, and vascular stiffness operate as a

network rather than independent entities (18). Insights from cardiovascular imaging support models, such as the "selfish brain" hypothesis, which links brainstem perfusion demands to systemic hypertension and cardiac sequelae (19).

Furthermore, the broader context of neuro-cardiac communication may extend to systems like the gut-brain-bone marrow axis, highlighting complex neuroimmune networks in hypertension (20). Genetic studies also suggest shared aetiology between cardiovascular and neuropsychiatric disorders via the brain–heart axis (21). Our observation of elevated oxidative stress (MDA, SOD) aligns with molecular pathways implicated in neurovascular damage along this axis (22). The relationship between arterial stiffness, high blood pressure, and hypertensive phenotypes further contextualises our vascular findings (23). Finally, the cross-talk between the microbiota–gut–brain axis and blood pressure regulation represents an expanding frontier in understanding the systemic nature of hypertension (24).

Study limitations

This study has several limitations. Its cross-sectional design precludes causal inference. The single-centre setting may limit generalisability. Residual confounding from unmeasured variables (e.g., diet, stress) is possible. Medication effects on autonomic and inflammatory markers were not fully controlled. Future longitudinal studies are needed to validate these associations and explore therapeutic implications.

Conclusion

Brain–heart axis dysfunction is associated with more severe cardiovascular, cognitive, and inflammatory abnormalities in hypertensive patients. Comprehensive assessment of autonomic, neurological, and inflammatory markers may enhance risk stratification and inform personalised management strategies. Further research is warranted to elucidate underlying mechanisms and evaluate targeted interventions.

List of Abbreviations

ABPM: Ambulatory Blood Pressure Monitoring
BRS: Baroreflex Sensitivity
CVD: Cardiovascular Disease
HRV: Heart Rate Variability
LVMI: Left Ventricular Mass Index
MoCA: Montreal Cognitive Assessment
MMSE: Mini-Mental State Examination
MRI: Magnetic Resonance Imaging
PWV: Pulse Wave Velocity

Declarations

Ethics Approval and Consent to Participate

This study was approved by the Institutional Review Board of Tikrit University (Approval No: TU-2024-087). Written informed consent was obtained from all participants.

Consent for Publication

All the authors gave consent for the publication of the work under the Creative Commons Attribution Non-Commercial 4.0 license.

Data Availability

The datasets used and analysed during this study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare no competing interests.

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Author Contributions

SBT: Conceptualisation, methodology, writing – original draft.
AAH: Data curation, formal analysis.
ZMG: Investigation, validation. All authors reviewed and approved the final manuscript.

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