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FEATURES OF HEART RATE VARIABILITY (HRV) AND INDICATORS OF DAILY BLOOD PRESSURE MONITORING (ABPM) IN PATIENTS WITH DIABETES MELLITUS WITH DIFFERENT PATHOGENETIC SUBTYPES OF ISCHEMIC STROKE

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Abstract
Heart rate variability (HRV) and daily blood pressure monitoring (ABPM) serve as critical tools in assessing cardiovascular and autonomic regulation in patients with ischemic stroke (IS). In individuals with concomitant type 2 diabetes mellitus (T2DM), these parameters may differ significantly, influenced by the interplay between the systemic metabolic dysregulation of T2DM and cerebrovascular pathology. This study explores HRV and ABPM characteristics in 256 patients with IS, divided into groups based on the presence of T2DM, to delineate the impacts of diabetes on stroke-related cardiovascular dysregulation.

Keywords Ischemic Stroke, Type 2 Diabetes Mellitus, Heart Rate Variability (HRV), Daily Blood Pressure Monitoring (ABPM), Autonomic Dysfunction, Blood Pressure Variability, Nocturnal Hypertension, Pathogenetic Subtypes, Atherothrombotic Stroke, Cardioembolic Stroke, Lacunar Stroke, Diabetic Neuropathy.

INTRODUCTION

Ischemic stroke (IS) is a leading cause of morbidity and mortality worldwide, with type 2 diabetes mellitus (T2DM) acting as a major risk factor for its occurrence and severity. T2DM exacerbates vascular damage through mechanisms such as endothelial dysfunction, chronic inflammation, and oxidative stress, which may influence autonomic regulation and cardiovascular function [1] HRV and ABPM are invaluable tools for evaluating these changes. This study aims to investigate the HRV and ABPM profiles in IS patients with and without T2DM, focusing on their distinct pathogenetic subtypes.

METHODS

The study included 256 patients diagnosed with IS

in the acute and pre-acute periods. Participants were categorized into two groups: 1) main mroup (MG) comprised 124 patients (67 women and 57 men; mean age 51–79 years) with IS and concomitant T2DM. 2) Comparison Group (CG) Consisted of 132 patients (67 women and 70 men; mean age 54–76 years) with IS but without T2DM. Diagnostic criteria - IS was confirmed via clinical assessment and neuroimaging (MRI or CT). T2DM diagnosis adhered to ADA guidelines, including fasting glucose and HbA1c levels.

RESULTS

T2DM in MG was associated with poorly controlled glycemic status, with an average fasting glucose level of 9.8 ± 2.4 mmol/L and mean HbA1c of 8.1 ± 1.2%. These metrics significantly differed from CG (fasting glucose: 5.6 ± 0.7 mmol/L, HbA1c: 5.4 ± 0.8%, both $p < 0.001$). Additionally, MG patients presented higher baseline levels of total cholesterol (6.1 ± 1.4 mmol/L vs. 5.3 ± 1.2 mmol/L, $p < 0.01$) and triglycerides (2.3 ± 0.6 mmol/L vs. 1.7 ± 0.5 mmol/L, $p < 0.01$).

HRV analysis revealed distinct differences between MG and CG, reflecting significant autonomic dysregulation in diabetic patients. Time-Domain Indices SDNN (Standard Deviation of NN intervals): MG patients showed reduced values (92 ± 15 ms) compared to CG (108 ± 17 ms, $p < 0.01$). This reduction indicates diminished overall heart rate variability, a marker of compromised autonomic regulation. RMSSD (Root Mean Square of Successive Differences): MG patients had lower RMSSD values (28 ± 6 ms) compared to CG (36 ± 8 ms, $p < 0.01$), highlighting reduced parasympathetic activity.

Frequency-Domain Indices: LF (Low-Frequency Power): Both groups exhibited increased LF values during the acute stroke phase, but MG patients showed significantly higher values (725 ± 98 ms^2 vs. 640 ± 86 ms^2, $p < 0.01$), indicating heightened sympathetic activation. HF (High-Frequency Power): MG demonstrated reduced HF power (180 ± 34 ms^2 vs. 250 ± 42 ms^2, $p < 0.01$), reflecting blunted parasympathetic activity. LF/HF Ratio: MG patients exhibited a higher LF/HF ratio (2.1 ± 0.5) compared to CG (1.6 ± 0.4, $p < 0.01$), suggesting a pronounced autonomic imbalance with sympathetic dominance.

ABPM findings indicated notable differences between MG and CG, with MG patients showing more pronounced blood pressure dysregulation: Daytime Systolic BP (SBP): MG (143 ± 12 mmHg) was significantly higher than CG (135 ± 10 mmHg, $p < 0.001$). Daytime Diastolic BP (DBP): MG patients also showed elevated DBP levels (89 ± 7 mmHg vs. 82 ± 6 mmHg, $p < 0.001$). Nighttime BP: Both SBP and DBP were elevated in MG (mean SBP: 137 ± 11 mmHg, DBP: 85 ± 6 mmHg) compared to CG (SBP: 128 ± 9 mmHg, DBP: 78 ± 5 mmHg, $p < 0.001$).

BP variability was significantly greater in MG, with a standard deviation of SBP at 15 ± 3 mmHg compared to 12 ± 2 mmHg in CG ($p < 0.01$). MG patients had increased diurnal BP variability, with 68% exceeding normal thresholds compared to 45% in CG ($p < 0.01$).

Nocturnal Dipping Status the "non-dipper" pattern, characterized by <10% nocturnal BP reduction, was observed in 65% of MG patients compared to 38% of CG patients ($p < 0.01$). A "reverse dipper" pattern, where nighttime BP exceeds daytime BP, was more prevalent in MG (18%) than in CG (5%, $p < 0.05$).

- MG patients exhibited significantly higher pulse pressure (56 ± 8 mmHg) compared to CG (48 ± 6 mmHg, $p < 0.01$), indicating increased arterial stiffness and a greater cardiovascular risk burden.

Differences in HRV and ABPM parameters were further analyzed across the three major pathogenetic subtypes of IS: Atherothrombotic

Stroke - Predominant in both groups (MG: 52%, CG: 47%). MG patients demonstrated greater BP variability (mean SBP SD: 16 ± 3 mmHg vs. 13 ± 2 mmHg, $p < 0.01$) and higher LF/HF ratios (2.3 ± 0.4 vs. 1.8 ± 0.3, $p < 0.01$). Cardioembolic Stroke - More common in MG (26%) than CG (21%). MG patients exhibited pronounced HRV reductions, particularly in HF power (160 ± 30 ms^2 vs. 230 ± 35 ms^2, $p < 0.01$), indicating severe parasympathetic dysfunction. Lacunar subtype was associated with the highest BP variability among MG patients (mean SBP SD: 17 ± 4 mmHg) and a "reverse dipper" pattern in 25% of cases (vs. 8% in CG, $p < 0.01$).

Parameter	**(MG) (IS without T2DM)**	**Group (CG) (IS without T2DM)**	**p-value**	**Remarks**
Number of Patients	124	132	-	Comparable group sizes.
Mean Age (years)	63.5 ± 6.4	64.2 ± 5.8	0.42	No significant age difference.
Gender (Female)	67 (54.0%)	67 (47.0%)	0.21	Similar gender distribution.
Fasting Glucose (mmol/L)	9.8 ± 2.4	5.6 ± 0.7	<0.001	Higher in MG, indicating poor glycemic control.
HbA1c (%)	8.1 ± 1.2	5.4 ± 0.8	<0.001	Significantly elevated in MG.
SDNN (ms)	92 ± 15	108 ± 17	<0.01	Lower in MG, indicating reduced overall HRV.
RMSSD (ms)	28 ± 6	36 ± 8	<0.01	Reduced parasympathetic activity in MG.
LF/HF Ratio	2.1 ± 0.5	1.6 ± 0.4	<0.01	Higher in MG, suggesting sympathetic dominance.

Daytime SBP (mmHg)	143 ± 12	135 ± 10	<0.001	Elevated in MG, reflecting poor BP control.
Daytime DBP (mmHg)	89 ± 7	82 ± 6	<0.001	Higher diastolic pressure in MG.
Nighttime SBP (mmHg)	137 ± 11	128 ± 9	<0.001	Increased nocturnal BP in MG.
Nighttime DBP (mmHg)	85 ± 6	78 ± 5	<0.001	Elevated nighttime DBP in MG.
BP Variability (SBP SD)	15 ± 3	12 ± 2	<0.01	Greater BP variability in MG.
Non-Dipper Pattern (%)	65 %	38%	<0.01	More prevalent in MG.
Reverse Dipper Pattern (%)	18%	5%	<0.05	Significant increase in reverse dipper status in MG.
Pulse Pressure (mmHg)	56 ± 8	48 ± 6	<0.01	Higher PP in MG, indicating greater arterial stiffness.
Atherothrombotic Stroke (%)	52%	47%	NS	Slightly more frequent in MG, though not statistically significant.
Cardioembolic Stroke (%)	26%	21%	NS	More prevalent in MG but without significance in the general analysis.
Lacunar Stroke (%)	22%	32%	NS	Less frequent in MG, yet showed

				distinct BP and HRV patterns in subgroup.

Patients with IS and concomitant T2DM exhibited significant impairments in HRV, with higher LF/HF ratios and lower SDNN and RMSSD values, suggesting greater autonomic dysfunction compared to non-diabetic IS patients. ABPM profiles revealed heightened BP variability, a higher prevalence of non-dipper and reverse dipper patterns, and elevated pulse pressure in the diabetic cohort. These findings underscore the compounded cardiovascular and autonomic burden faced by IS patients with T2DM, particularly in certain pathogenetic subtypes such as lacunar stroke.

DISCUSSION

This study highlights the significant differences in heart rate variability (HRV) and daily blood pressure monitoring (ABPM) parameters between ischemic stroke (IS) patients with and without type 2 diabetes mellitus (T2DM). These findings underscore the compounded cardiovascular and autonomic dysregulation faced by IS patients with T2DM and provide valuable insights for targeted management strategies [2].

Reduced HRV in the main group (MG) reflects a significant impairment in autonomic function. Specifically, lower time-domain indices such as SDNN and RMSSD suggest reduced overall variability and parasympathetic activity, respectively [3]. Frequency-domain analysis further corroborates these findings, with higher LF/HF ratios indicating a shift toward sympathetic dominance.

The interplay between T2DM and stroke pathophysiology likely exacerbates autonomic dysfunction. Chronic hyperglycemia in T2DM is associated with advanced glycation end-product (AGE) formation, oxidative stress, and microvascular damage, which impair autonomic nerve fibers. Furthermore, IS itself disrupts the autonomic nervous system by damaging brain areas responsible for cardiovascular regulation, such as the insular cortex. The combination of these factors in MG results in heightened sympathetic activity and reduced parasympathetic modulation, increasing cardiovascular risk [4].

ABPM findings demonstrate significantly greater blood pressure variability (BPV), higher mean daytime and nighttime BP levels, and abnormal nocturnal BP patterns in MG. These abnormalities are of particular concern as they are strongly associated with poor stroke outcomes, including recurrent events, larger infarct size, and higher mortality.

Elevated BPV, as seen in MG, reflects greater fluctuations in BP over 24 hours. This variability is linked to vascular stiffness and impaired baroreceptor sensitivity, both of which are common in T2DM due to endothelial dysfunction and atherosclerosis. Increased BPV places additional strain on the cerebrovascular system, increasing the risk of further ischemic damage [5].

The high prevalence of non-dipper and reverse dipper patterns in MG patients indicates inadequate nocturnal BP reduction, which may be attributed to autonomic neuropathy, increased sympathetic activity, and altered renal sodium handling in T2DM. These patterns are particularly detrimental as they reduce the heart and vasculature's recovery time during sleep, leading to higher cardiovascular stress.

Pulse pressure, a surrogate marker of arterial stiffness, was significantly higher in MG. Arterial stiffness is a hallmark of vascular aging and is accelerated in T2DM due to chronic inflammation, vascular calcification, and collagen cross-linking. Elevated PP contributes to end-organ damage, including the brain, and may explain the more severe stroke presentations observed in diabetic patients.

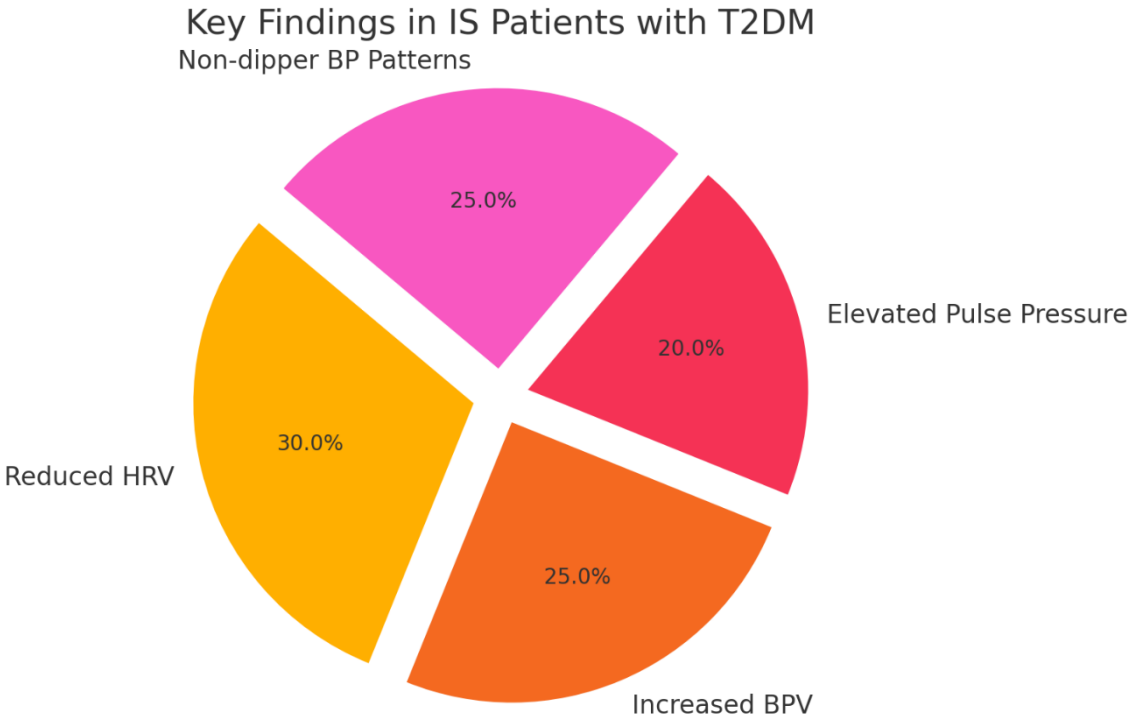
Analysis of IS pathogenetic subtypes revealed distinct HRV and ABPM profiles in MG patients: 1) Atherothrombotic Stroke - MG patients with this subtype exhibited the most significant BP variability and autonomic imbalance. This is consistent with the role of T2DM in accelerating atherosclerosis and its associated vascular instability [6]. 2) Cardioembolic Stroke - Although less frequent, cardioembolic stroke in MG patients was associated with pronounced parasympathetic dysfunction, as evidenced by reduced HF power. This could be related to the systemic nature of embolic sources, often compounded by T2DM-related cardiomyopathy or atrial fibrillation. 3) Lacunar infarcts, associated with small-vessel disease, showed the highest BP variability among MG patients. The involvement of microangiopathy in T2DM likely exacerbates these fluctuations, contributing to the development and progression of lacunar infarcts [6].

The results of this study have important clinical implications for the management of IS patients with T2DM: HRV and ABPM provide valuable insights into the cardiovascular and autonomic state of stroke patients, particularly those with T2DM. Routine use of these tools could help identify high-risk patients, guide individualized treatment plans, and monitor therapeutic efficacy [7].

Strategies to restore autonomic balance, such as biofeedback training, aerobic exercise, and pharmacological modulation of sympathetic overactivity, may benefit IS patients with T2DM [8]. Given the significant BP dysregulation observed in MG, aggressive management of BP, including reducing variability and addressing nocturnal hypertension, should be prioritized. Long-acting antihypertensive agents and chronotherapy (timed medication administration) may be particularly effective in achieving these goals. Treatment strategies targeting T2DM-specific mechanisms, such as glycemic control, endothelial protection, and reduction of vascular stiffness, are critical. Novel agents such as SGLT2 inhibitors and GLP-1 receptor agonists may offer dual benefits for glucose regulation and cardiovascular protection.

While this study provides valuable insights, certain limitations warrant consideration. The cross-sectional design precludes causal inferences, and longer-term studies are needed to establish the prognostic significance of HRV and ABPM abnormalities in this population. Additionally, subgroup analysis by pathogenetic subtype would benefit from larger sample sizes to enhance statistical power.

Pie Chart of Key Findings in IS Patients with T2DM



CONCLUSION

This study demonstrates the profound impact of type 2 diabetes mellitus (T2DM) on the cardiovascular and autonomic profiles of patients with ischemic stroke (IS). The results highlight that IS patients with T2DM experience significantly greater autonomic dysfunction, as evidenced by reduced heart rate variability (HRV) parameters, and more pronounced blood pressure (BP) dysregulation, including increased BP variability, nocturnal hypertension, and non-dipping patterns. These abnormalities are closely linked to the pathophysiological mechanisms of T2DM, including endothelial dysfunction, arterial stiffness, and autonomic neuropathy, all of which exacerbate the severity and complexity of IS.

The findings also reveal subtype-specific differences in pathogenetic mechanisms, with atherothrombotic and lacunar strokes showing the greatest BP variability and autonomic imbalance. Such insights underscore the need for tailored management strategies that address the dual challenges of stroke and diabetes. Incorporating HRV and ABPM into routine clinical care could facilitate early detection of high-risk patients, allowing for the implementation of targeted therapies to optimize autonomic function and BP control.

Future research should focus on the longitudinal impact of these abnormalities on stroke outcomes and explore the efficacy of personalized interventions. By addressing the interconnected pathophysiological pathways of IS and T2DM, clinicians can improve survival and reduce complications, ultimately enhancing the quality of life for this vulnerable patient population.

REFERENCES

1. Chen Y. K. et al. Diurnal blood pressure and heart rate variability in hypertensive patients with cerebral small vessel disease: a case-control study //Journal of Stroke and Cerebrovascular Diseases. – 2021. – Т. 30. – №. 5. – С. 105673.
2. Matei D. V. ASSESSMENT OF CARDIAC AUTONOMIC CONTROL BY LINEAR AND NONLINEAR ANALYSES OF THE HEART RATE.
3. Sgoifo A. et al. Autonomic dysfunction and heart rate variability in depression //Stress. – 2015. – Т. 18. – №. 3. – С. 343-352.
4. Elia A., Fossati S. Autonomic nervous system and cardiac neuro-signaling pathway modulation in cardiovascular disorders and Alzheimer's disease //Frontiers in Physiology. – 2023. – Т. 14. – С. 1060666.
5. Mena L. J. et al. 24-hour blood pressure variability assessed by average real variability: a systematic review and meta-analysis //Journal of the American Heart Association. – 2017. – Т. 6. – №. 10. – С. e006895.
6. Alsharari R. Cardiovascular haemodynamics and autonomic function in resistant hypertension: relation to blood pressure control : дис. – University of Birmingham, 2023.
7. Vaidya A. et al. Primary aldosteronism: state-of-the-art review //American Journal of Hypertension. – 2022. – Т. 35. – №. 12. – С. 967-988.
8. Besnier F. et al. Exercise training-induced modification in autonomic nervous system: An update for cardiac patients //Annals of physical and rehabilitation medicine. – 2017. – Т. 60. – №. 1. – С. 27-35.