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Chinese Hypertension Meeting (CHM 2025)

Abstracts

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Identification and Validation of Immune-Related Genes in Acute Myocardial Infarction Using Machine Learning and Weighted Gene Co-expression Network Analysis

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Objective: This study aimed to identify key immune-related regulatory genes in acute myocardial infarction (AMI) to elucidate novel molecular mechanisms and potential therapeutic targets.

Methods: We analyzed AMI gene expression datasets (GSE183272) using differentially expressed gene (DEG), support Vector Machine Recursive Feature Elimination (SVM-RFE), Weighted Gene Co-expression Network Analysis (WGCNA), and Random Forest models to identify candidate genes. Validation used a single-cell sequencing (scRNA-seq) dataset (GSE163465) and CIBERSORT for immune infiltration analysis. Single-gene Gene Set Enrichment Analysis (GSEA) explored the molecular mechanisms.Finally, we established 3-day, 7-day, and 21-day AMI mouse models and quantitatively assessed the differential expression of key genes at various time points using techniques such as RT-qPCR, IHC, and Western blot. The cellular localization of target genes in myocardial tissue was determined using immunofluorescence double staining.

Results: Differential analysis found 59 genes enriched in pathways like cell chemotaxis, leukocyte migration, and IL-17 signaling. Machine learning identified 13 significant genes. WGCNA identified 39 modules; the Lightcyan module correlated most with AMI. Key genes Chil3, Cxcr6, Ccl7, and Clec4d were identified. Single-cell analysis revealed significant gene expression differences across cell subpopulations. Immune infiltration analysis showed a strong association between key genes and immune responses.Experimental results demonstrated that the expression of the four key genes increased significantly in AMI models compared to the control group, with gene expression levels progressively rising with a prolonged duration of infarction. Immunofluorescence double staining results indicated that Clec4d is predominantly expressed in Vimentin-positive fibroblasts.

Conclusions: Chil3, Cxcr6, Ccl7, and Clec4d were identified as key immune-related genes in AMI, validated in animal models. These findings provide new insights into AMI diagnosis and treatment strategies, enhancing our understanding of underlying mechanisms.

Key words: Acute myocardial infarction; WGCNA; machine learning; single-cell sequencing; immune-related gene

论文 ID：5

Association between the triglyceride-glucose-body mass index and Cardiometabolic Multimorbidity risk in middle-aged and elderly chinese: a nationwide prospective cohort study

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Objective: To investigate the association between the triglyceride glucose-body mass index (TyG-BMI) and the risk of cardiometabolic multimorbidity (CMM) in middle-aged and elderly populations, providing a scientific basis for the early prevention of CMM.

Methods: This study utilized data from the China Health and Retirement Longitudinal Study (CHARLS) cohort, including 8,020 participants aged ≥45 years without baseline CMM, with a median follow-up of 9 years. Kaplan-Meier analysis was applied to assess the cumulative incidence of CMM. The association between TyG-BMI and CMM was evaluated using multivariable Cox proportional hazards regression models, and restricted cubic spline (RCS) regression was employed to explore nonlinear relationships. Subgroup and sensitivity analyses were conducted to validate the robustness of the findings.

Results: During follow-up, 409 new CMM cases were identified. Multivariable Cox regression revealed that each 1-standard deviation (SD) increase in TyG-BMI was associated with a 43% higher risk of CMM (HR = 1.43, 95% CI: 1.30 - 1.58). When categorized by quartiles, the highest quartile group (Q4) exhibited a 266% increased risk of CMM compared

to the lowest quartile (Q1) (HR = 3.66, 95% CI: 2.40 - 5.59). RCS analysis identified a nonlinear relationship between TyG-BMI and CMM, with an inflection point at 229.35. Below this threshold, each unit increase in TyG-BMI raised the risk by 1.1% (HR = 1.011), while no significant association was observed above the inflection point. Subgroup analyses confirmed consistent predictive effects across age, sex, and residential subgroups, and sensitivity analyses further supported the robustness of the results.

Conclusions: In the middle-aged and elderly Chinese population, elevated TyG-BMI is significantly associated with an increased risk of CMM. TyG-BMI may serve as a potential predictive marker for CMM, and its monitoring could provide valuable insights for the early prevention and management of CMM.

Key words: triglyceride glucose-body mass index; cardiometabolic multimorbidity; BMI; TyG

论文 ID：8

Platelet PAR4 Overexpression Exacerbates Thrombotic Risk in Hypertension via TGF-β/Smad2/AT1R Axis

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Background: Hypertensive patients are highly susceptible to developing a pro-thrombotic state, which substantially elevates their cardiovascular risk. Although platelet activation is pivotal in thrombosis, its precise contribution to thrombotic events in hypertension remains largely unclear.

Objectives: This study aims to elucidate the underlying mechanisms of platelet hyperactivation for the higher prevalence of thrombotic complications in hypertension.

Methods: Platelets from healthy volunteers, hypertensive patients, Wistar-Kyoto (WKY) rats, spontaneously hypertensive rats (SHRs), as well as wild-type and L-NAME induced hypertensive mice were utilized. We employed RNA-seq, RT-PCR, flow cytometry, Western blot, immunofluorescence, in vitro platelet functional studies, in vivo FeCl3-induced thrombosis models, and ex vivo microfluidic whole - blood perfusion assays to evaluate the changes in platelet and PAR4 expression. Moreover, megakaryocyte cultures and platelet-specific TGF-β knockout mouse models were used to systematically investigate the regulatory role of the TGF-β/smad2 pathway in PAR4 receptor expression.

Results: Comparative analysis of platelets from 50 hypertensive patients versus normotensive controls demonstrated 2.3-fold elevated PAR4 expression (Western blot, $p<0.01$), corroborated in spontaneous hypertensive rats (SHRs) and L-NAME-induced hypertensive mice. Functional characterization revealed PAR4 hyperactivation potentiates thrombin signaling via amplified Gq/G12/13 pathways, driving exacerbated aggregation responses (AUC +58%, $p<0.001$), αIIbβ3 activation (PAC-1 binding +142%), and accelerated thrombus formation under arterial shear (-44% adhesion area, microfluidic assay). Mechanistic interrogation through megakaryocyte cultures and platelet-specific TGF-β knockout models identified TGF-β/Smad2 signaling as the transcriptional regulator of PAR4 upregulation. Angiotensin II was shown to activate platelet AT1Rs, initiating a signaling cascade that amplifies TGF-β/Smad2 activity and subsequent PAR4 overexpression. Valsartan, an AT1 receptor blocker, effectively suppresses PAR4 expression, thereby inhibiting platelet activation and thrombus formation in hypertensive patients

Conclusions: These findings highlight that hypertensive patients have significantly elevated platelet PAR4 expression which leads to platelet hyperactivity, while providing mechanistic justification for repurposing AT1R antagonists to concurrently address thrombotic risk. The identified AT1R/TGF-β/Smad2 axis offers a precision therapeutic target, enabling antiplatelets without exacerbating bleeding risks inherent to conventional antiplatelet regimens.

Key words: Platelet; PAR4; Thrombotic Risk; Hypertension

论文 ID：9

H3K18la Lactylation Promotes Cardiac Hypertrophy through Activating GATA4 Signaling

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Background： Elevated lactate levels have been implicated in heart failure, with histone lactylation, particularly lactylation of histone 3 on lysine residue 18 (H3K18la), emerging as a critical factor in cardiovascular disease pathogenesis. However, its specific role in cardiac hypertrophy remains unclear.Purpose: This study investigates the role of H3K18la in promoting cardiac hypertrophy through the activation of GATA Binding Protein 4 (GATA4) pathways.

Methods： A transverse aortic constriction-induced mice model and a phenylephrine-induced hypertrophic cardiomyocyte model were utilized to simulate cardiac hypertrophy. Serum lactate levels were measured in patients with colorimetric assay kit. Pan-Kla and H3K18la levels were quantified using Western Blotting and Immunohistochemistry. Morphological changes associated with hypertrophy were assessed by measuring heart and left ventricle weights, as well as cardiomyocyte cross-sectional areas. Expression levels of hypertrophic markers (ANP, BNP, β-MHC) were measured to evaluate hypertrophy severity. Immunoprecipitation and LC-MS/MS were utilized to identify interacting proteins. Luciferase reporter assay was employed to assess transcriptional activity.

Results： Clinical observations revealed a positive correlation between serum lactate levels and hypertrophic cardiomyopathy in patients. Elevated levels of Pan-Kla and H3K18la were detected in hypertrophic left ventricular tissues and cardiomyocytes, accompanied by increased heart and left ventricle weights, enlarged cardiomyocyte cross-sectional areas, and heightened expression of ANP, BNP, and β-MHC. Inhibition of lactylation reversed these effects, suggesting a direct role of H3K18la in hypertrophic gene expression. Mechanistically, H3K18la was found to interact with GATA4, enhancing its transcriptional activity as demonstrated by increased ANP promoter activity. Furthermore, suppression of

GATA4 mitigated the hypertrophic response, highlighting its crucial role downstream of H3K18la.

Conclusions: Our findings identify H3K18la lactylation as a novel epigenetic mechanism driving cardiac hypertrophy through GATA4 activation. This implicates potential therapeutic targets for hypertrophic heart diseases.

Key words: Histone lactylation; H3K18la; Cardiac hypertrophy; GATA4

论文 ID：11

From Genes to Disease: The Unidirectional Impact of Immune Cells on Pulmonary Arterial Hypertension

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Purpose: Pulmonary arterial hypertension (PAH) is a severe cardiopulmonary disorder characterized by high mortality and significant morbidity. Immune cells have been implicated in the pathogenesis of PAH, yet the precise causal relationships remain unclear. This study aims to investigate the causal relationships between 731 immune cell phenotypes and PAH using bidirectional Mendelian randomization (MR) analysis.

Methods: We conducted a bidirectional two-sample MR study utilizing data from the Finngen and OPEN GWAS databases. Genetic variants significantly associated with 731 immune cell phenotypes were used as instrumental variables (IVs) to assess their causal effect on PAH. The inverse variance weighted (IVW) method was the primary analysis approach, supplemented by MR-Egger regression and sensitivity analyses to test for pleiotropy and heterogeneity.

Results: Forward MR analysis revealed that six immune cell phenotypes, including subsets of B cells, T cells, and regulatory T cells (Tregs), were positively associated with PAH development, while three phenotypes showed a protective effect. Conversely,

reverse MR analysis indicated that PAH could influence specific immune cell phenotypes, though no bidirectional causal relationships were identified. Sensitivity analyses confirmed the robustness of these findings, showing no evidence of horizontal pleiotropy or heterogeneity.

Conclusions: This study elucidates the complex and unidirectional causal relationships between immune cell phenotypes and PAH, highlighting the role of immune dysregulation in PAH pathogenesis. These findings provide novel insights into the immunopathology of PAH and suggest potential therapeutic targets for further exploration in clinical research.

Key words: Pulmonary arterial hypertension, Mendelian randomization, immune cells, genetic epidemiology, causal inference.

论文 ID：19

Non-High Density Lipoprotein to High Density Lipoprotein Cholesterol Ratio and Its Association with Hypertension in Chinese Adults:

A Cross-Sectional Study from CHARLS

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Background: The non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) is a potential prognostic indicator for cardiovascular risk. However, the association between hypertension (HTN) and NHHR is still unclear. Thus, this study examined their association with the Chinese population.

Methods: This study enrolled approximately 11084 Chinese participants (>18 years). The participants were assigned to 4 groups as per the NHHR quartile, ranging from Q1 to Q4. Multivariate logistic regression was employed to evaluate the correlation between HTN and NHHR by progressively adjusting the model.

Results: The overall incidence of HTN among the selected participants was 41.2%, and among them, 54.3% were female. Compared to participants with lower NHHR levels (Q1(< 2.08)), those with elevated NHHR levels (Q2 (2.08-2.61); Q3 (2.62-3.21); Q4 (> 3.21)) had substantially higher risks of HTN (OR of Q2 1.26; 95% CI 1.12, 1.43; OR of Q3 1.43; 95% CI 1.26, 1.63; OR of Q4 1.63; 95% CI 1.43, 1.87)). Females also showed a more significant correlation between HTN and NHHR.

Conclusions: The study concluded that the HTN risk in Chinese adults is strongly associated with a higher NHHR level.

Key words: NHHR, Hypertension,Cross-Sectional Study, CHARLS

论文 ID：24

Association of Perirenal Fat Thickness and the Risk of Development for Hypertension in High-normal Blood Pressure Population

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Objectives: To investigate the relationship between perirenal fat thickness (PRFT) and the occurrence of hypertension in individuals with high-normal blood pressure.

Methods: A total of 166 participants with high-normal blood pressure were enrolled from the Department of Cardiology of First Affiliated Hospital of Xi’an Jiaotong University from May 2023 to March 2024. Demographic characteristics, anthropometric measurements, and biochemical assays were obtained. Perirenal ultrasonographic fat thickness was measured.The cumulative incidence of hypertension was calculated via one year follow-up after enrollment. Univariate and multivariate logistic regression models were performed to assess the association of PRFT and the incidence of hypertension from high-normal blood pressure.

Results: The average age of participants was 50.05±9.59 years old. The mean systolic blood pressure and mean diastolic blood pressure at inclusion were 136 (133, 138) mmHg and 87 (84, 89) mmHg, respectively. The median of PRFT was 30 (25, 38) mm. It was divided into low PRFT group (PRFT≤30 mm, n=90) and high PRFT group (PRFT>30 mm, n=76) . Compared with low PRFT group, individuals in high PRFT group were generally males with higher obesity indicators of body mass index (BMI), waist circumference, hip circumference, waist-to-hip ratio and higher levels of serum uric acid, fasting plasma glucose, urinary albumin creatinine ratio (ACR) and triglyceride glucose index (P<0.05). At one year follow-up, there were 29 participants (17.5%) with high-normal blood pressure developed hypertension, higher PRFT was correlated with an increased cumulative incidence of hypertension (28.9% vs. 7.8%, P < 0.001). After adjusting age, gender, BMI, systolic blood pressure, diastolic blood pressure, diabetes, dyslipidemia, smoking, drinking, salt intake, uric acid and eGFR, the risk factors contributing to the risk for hypertension were PRFT (OR 1.15, 95%CI: 1.08~1.24, P<0.001) and urinary ACR (OR 1.03, 95%CI: 1.01~1.04, P=0.007). After adjusting for covariates in linear regression analysis, ACR increased by 0.61 mg/g for per 1cm PRFT increment. Mediation analysis showed ACR mediated 6.08% of PRFT for the incidence of hypertension from high-normal blood pressure. The area under curve was 0.80 (95%CI: 0.71~0.89) in receiver operating characteristic analysis, indicating PRFT demonstrated a significant capacity for identifying the occurrence of hypertension.

Conclusion: Increased PRFT was associated with the risk of development for hypertension from high-normal blood pressure, which urinary ACR partially plays a mediation.

Key words: high-normal blood pressure, perirenal fat thickness, urinary albumin creatinine ratio

论文 ID：35

Increasing S1P Promotes M1 Macrophage in Chronic Obstructive Pulmonary Disease and Chronic Obstructive Pulmonary Disease-obstructive Sleep Apnea Overlap Syndrome via S1PR1/HDAC1 Signaling

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Background: Chronic obstructive pulmonary disease (COPD) is characterized by irreversible airflow limitation and chronic airway inflammation. Obstructive sleep apnea (OSA) is a common clinical condition with partial or complete pharyngeal collapses occurring repeatedly during sleep. COPD-OSA is the coexistence of COPD and OSA. Abnormal macrophages play important roles in COPD progression. Sphingosine-1-phosphate (S1P) has emerged as an important molecule in COPD. This study aimed to explore the change and potential functional mechanism of S1P in COPD and COPD-OSA.

Methods: Flow cytometry (FCM) was used to detect the M1 and M2 macrophage cell ratio. Enzyme linked immunosorbent assay (ELISA) was used to detect the S1P levels. Quantitative real-time polymerase chain reaction (qRT-PCR) and western blot were used to detect the expression levels of S1P receptor 1 (S1PR1). Cytokine levels were detected by multiple microsphere flow immunofluorescence assay. The THP-1 cells of in vitro models were exposed to cigarette smoke extract (CSE).

Results: Firstly, we found that the ratio of pro-inflammatory M1 macrophage was increased in COPD and COPD-OSA patients [vs. healthy controls (HCs)], whereas that of anti-inflammatory M2 macrophage was decreased. Notably, compared with COPD alone, COPD-OSA showed more M1 macrophage and less M2 macrophage. Secondly, we observed significantly increased plasma S1P levels in COPD and COPD-OSA (level: COPD-OSA > COPD > HC). Furthermore, the effect of S1P on macrophage polarization was investigated. The results showed that S1P treatment could enhance the efficiency of M1 polarization of THP-1 in response to lipopolysaccharide (LPS)/interferon-γ (IFN-γ) stimulation. Correspondingly, in peripheral

blood mononuclear cells (PBMCs) and monocyte derived macrophages (MDMs) from COPD and COPD-OSA, the S1PR1 expression levels were higher than that from HC.

Conclusions: This study suggested that increasing S1P levels could facilitate macrophage polarization toward M1 subtype in COPD and COPD-OSA.

Key words Obstructive sleep apnea (OSA); chronic obstructive pulmonary disease (COPD); macrophage polarization; sphingosine-1-phosphate (S1P); S1P receptor 1 (S1PR1)

论文 ID：41

A comparative study of sackubactril valsartan sodium and amlodipine besylate on vascular remodeling in patients with hypertension

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Objective: To evaluate the comparative study of sackubactrivalsartan and amlodipine besylate on vascular remodeling in patients with hypertension.

Method: A total of 200 hypertensive patients admitted to the Department of Cardiology of our hospital from April 2022 to April 2024 were selected and divided into treatment group (n=100) and control group (n=100) by random number table method. The case group was treated with sakubactril valsartan sodium tablets, the initial dose was 100mg, once a day, after 2 weeks, the blood pressure was not up to the standard can be increased to 200mg, once a day, the maximum dose is not more than 400mg, once a day. The control group was treated with amlodipine besylate, the initial dose was 5mg once a day, the dose was adjusted according to the control of blood pressure, the maximum dose was not more than 10mg once a day. Both groups can be combined with other antihypertensive drugs when necessary. Blood pressure (systolic blood pressure, diastolic blood pressure, pulse pressure difference), pulse wave conduction velocity (PWV), ankle-brachial index (ABI),

arteriosclerosis index and pulse pressure index were observed before treatment, 2 weeks, 4 weeks, 12 weeks and 24 weeks after treatment.

Result: After 2 weeks of treatment, the blood pressure indexes of both groups decreased from the baseline level, but the difference was not statistically significant (P>0.05). After 4 and 12 weeks of treatment, the diastolic blood pressure in the case group was significantly lower than that in the control group (P<0.05), but there was no statistical significance in systolic blood pressure and pulse pressure difference (P>0.05). After 24 weeks of treatment, the systolic blood pressure, diastolic blood pressure and pulse pressure difference in the case group were significantly lower than those in the control group (P<0.05).Compared with baseline, PWV values in the case group decreased by 0.63 m/s, 0.92 m/s, 1.66 m/s, and 2.24 m/s at 2, 4, 12, and 24 weeks, respectively. After 4, 12 and 24 weeks of treatment, PWV was significantly lower than that of control group, and the difference was statistically significant (P<0.05).After 12 weeks of treatment, ABI in case group (1.01±0.09) was significantly higher than that in control group (0.91±0.06), and the difference was statistically significant (P<0.05). After 24 weeks of treatment, ABI of the case group was further increased to 1.12±0.08, while that of the control group was 0.95±0.05, and the difference between the two groups was more significant (P<0.05).After 4 weeks of treatment, the arteriosclerosis index in the case group decreased significantly to 0.61±0.13, significantly lower than that in the control group (0.77±0.18, P=0.022), and decreased to 0.55±0.25 and 0.49±0.33 at 12 and 24 weeks of treatment, respectively. Compared with the control group, the differences were statistically significant (P=0.215 and P=0.110). After 24 weeks of treatment, the pulse pressure index of the two groups continued to decrease, and the case group (0.46±0.14) was significantly lower than the control group (0.56±0.11), the difference was statistically significant (P<0.001).Univariate Logistic regression analysis showed that the oral administration of Sakubactril valsartan sodium tablets was significantly associated with the decrease of PWV, arteriosclerosis index, pulse pressure index and the increase of ABI (P<0.05).

Conclusion: Compared with amlodipine, sacubatrotrivalsartan can effectively improve vascular endothelial function and arterial stiffness in hypertensive patients and delay the progression of atherosclerosis.

Key words: sackubactril valsartan sodium ; amlodipine besylate ; vascular remodeling; hypertension

论文 ID：42

High Dosage Sacubitril/Valsartan on Blood Pressure Variability in Hypertension

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Objective: This study aimed to compare the effects of high doseage Sacubitril/Valsartan BPV in hypertension.

Method: 68 patients diagnosed with hypertension were randomly assigned, according to random numbers generated by SPSS 22.0. All patients underwent 24-hour ambulatory blood pressure monitoring(ABPM) using a cuff-based device, And following-up visit and re-examination of ABPM after a month.

Result: 34 patients were enrolled in the 200 mg QD group and 34 patients in the 100 mg BID group. the 200 mg QD group, showed more pronounced effects in controlling nighttime BP (SBP: 118.1±18.6 mmHg vs. 125.7±15.8 mmHg; P = 0.01; DBP: 75.1±17.4 mmHg vs. 81.4±18.8 mmHg; P=0.05; reducing the standard deviation of nighttime SBP (10.8 ± 6.4 mmHg vs. 12.8 ± 6.0mmHg; P=0.05; increasing reduction the rate of nighttime BP (SBP: 9.6 ± 5.8% vs. 9.8 ± 9.8%; P = 0.016; DBP: 12.3 ± 9.1% vs. 11.8±1.2%; P=0.01, improving the time in target range(TTR) of SBP (22.1±16.7% vs. 10.9±12.6%; P=0.01; and lowering the average real variability(ARV) of nighttime SBP (10.3±2.6mmHg vs. 12.0±3.2mmHg; P=0.01.

Conclusion: 200 mg once daily administration of Sacubitril/Valsartan led to greater improvements in nighttime BP control, decreases in nighttime BP variability, higher nighttime BP reduction rates

Key words: Sacubitril/Valsartan, Hypertension, Blood Pressure Variability

论文 ID：46

Association of Regular Health Check-ups with a Reduction in Mortality in 625,279 Elderly Subjects with Hypertension: A Population-based Cohort Study

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Objectives: Health check-ups constitute an essential part of China's primary health care policy and a key measure for health screening and risk assessment for elderly people with hypertension and chronic diseases. The role of health check-ups in reducing the incidence of cardiovascular or all-cause mortality remains controversial. Little is known about the relationship between health check-ups and cardiovascular or all-cause mortality in elderly individuals with hypertension.

Methods: This retrospective cohort study included 625,279 elderly participants with hypertension. We tested the associations of regular and irregular health check-ups with CVD-related mortality, all-cause mortality and non-CVD-related mortality via IPTW matching and Cox proportional hazard models.

Results: A total of 625,279 participants completed health assessments. During a median follow-up of 5.43 years, 45,927 CVD-related deaths and 25,519 non-CVD-related deaths were recorded. After IPTW, the habit of regular health check-ups was significantly associated with CVD-related mortality and all-cause mortality (HR: 0.442, 0.434 - 0.450; HR: 0.441, 0.435 - 0.448). An even stronger association between the habit of regular healthy check-ups and CVD-related mortality was observed in subjects with diabetes (HR: 0.40, 0.39 - 0.42, 0.42 p for interaction <0.001), dyslipidaemia (HR: 0.43, 0.42 - 0.44, p for interaction <0.001) and a high risk or very high risk of hypertension (HR: 0.41, 0.40 - 0.42, p for interaction <0.001).

Conclusions: Habitual healthy check-ups may be associated with reductions in CVD mortality and all-cause mortality in the elderly population with hypertension, especially in individuals with diabetes, dyslipidaemia, and a high risk or very high risk of hypertension.

Key words: Elderly, hypertension, health check-up, primary health care, mortality.

论文 ID：54

Initial Treatment with A Single Capsule Containing Half-dose Quadruple Therapy vs Standard-dose Dual Therapy in Hypertensive Patients (QUADUAL): A Randomized, Blinded, Crossover Trial

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Background: Guidelines recognized dual combination in initial antihypertensive therapy. Studies found that low-dose quadruple combination were superior to monotherapy. However, whether low-dose quadruple therapy is better than dual combination is unknown.

Methods: A randomized blinded crossover trial was conducted to compare the efficacy and safety of low-dose quadruple antihypertensives (irbesartan 75 mg + metoprolol 23.75 mg + amlodipine 2.5 mg + indapamide 1.25 mg) with standard-dose dual antihypertensives (irbesartan 150 mg + amlodipine 5 mg), both in a single pill, in the initial treatment of patients with mild to moderate hypertension. Patients were randomly assigned in a 1:1 ratio to two crossover sequences. Each sequence received four-weeks of either half-dose quadruple antihypertensives or standard-dose dual antihypertensives, followed by a two-week washout and crossover for four-weeks. Participants and researchers were blinded. The main outcomes were the reduction of blood pressure and safety outcomes. Analyses were per intention to treat.

Results: A total of 90 eligible participants were randomized between July 13, 2022, and April 20, 2023. The mean age was 43.88 years (SD 10.31), and 25.6% were women. The mean

baseline 24-h blood pressure was 145.59/93.84 mm Hg. Compared to the standard-dose dual treatment, the half-dose quadruple treatment resulted in a further reduction in mean 24-hour blood pressure by 4.72/4.17 mm Hg (P < 0.001 for both systolic and diastolic blood pressure), mean daytime blood pressure by 5.52/4.73 mm Hg (P < 0.001 for both), mean nighttime blood pressure by 2.37/2.25 mm Hg (P = 0.034 and 0.014, respectively), and mean office blood pressure by 2.91/1.73 mm Hg (P < 0.001 and 0.014, respectively). Apart from significant increases of fasting blood glucose (P = 0.029) and blood uric acid (P < 0.001) in the half-dose quadruple group, no other adverse events or changes in laboratory values differed significantly between the two treatments.

Conclusions: Initiating treatment with half-dose quadruple combination therapy was more effective in lowering blood pressure than standard-dose dual therapy. The safety of half-dose quadruple therapy was comparable.

Trial Registration

ClinicalTrials.gov Identifier: NCT05377203.

Key words: hypertension, antihypertensive, low-dose combination, randomized controlled trial

论文 ID：71

Association between A Body Shape Index (ABSI) and Adult Hypertension Prevalence: A US Population Study

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Background: A Body Shape Index (ABSI) is a novel metric that reflects visceral adiposity and has demonstrated potential advantages over traditional obesity indices. We examined the link between ABSI and the prevalence of US adult hypertension.

Methods: Data from 25,368 National Health and Nutrition Examination Survey (NHANES, 2007–2016) participants were used to determine the ABSI [circumference of the waist

divided by (BMI2/3 × height1/2)]. Non-linear relationships were examined using multivariable logistic regression and smoothed curve fitting. Subgroup analyses were stratified by demographic and metabolic factors.

Results: ABSI and risk of hypertension shared a W-shaped link. Below the inflection point (ABSI = 8.47), each ABSI unit increase was linked to a 38% increased risk of hypertension (odds ratio [OR] = 1.38, 95% confidence interval [CI]: 1.25 - 1.52). Above 8.47, a weaker inverse link emerged (OR = 0.84, 95% CI: 0.70 - 1.00). The subgroup analyses revealed effect modification by gender, age, and diabetes status (P < 0.0001).

Conclusion: ABSI demonstrates a non-linear association with hypertension prevalence, suggesting its potential utility in visceral obesity-related cardiovascular risk stratification.

Key words: A Body Shape Index, hypertension, cross-sectional study, NHANES

论文 ID：86

Outcomes of Hyperbaric Oxygen Therapy Patients with Acute Coronary Syndrome Followingperfusion: A Meta-Analysis

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Objective: Acute coronary syndrome (ACS) represents a significant burden on cardiovascular health worldwide, with coronary reperfusion therapy—including thrombolysis and primary percutaneous coronary intervention (PCI)—being one of its primary treatment methods. Despite the efficacy of reperfusion therapy, patients remain at high risk for major adverse cardiovascular events (MACEs). Hyperbaric oxygen therapy (HBOT) has been proposed as an adjuvant treatment that may enhance the prognosis of ACS patients following reperfusion therapy. This meta-analysis aims to systematically assess the impact of HBOT on the incidence of MACE, all-cause mortality, and recurrent myocardial infarction in ACS patients post-reperfusion treatment

Methods: We conducted a comprehensive literature search using keywords such as 'Hyperbaric oxygen,' 'HBO,' 'HPO,' 'myocardial infarction,' 'MI,' 'ACS,' and 'acute coronary syndrome.' The search spanned databases including PubMed, Embase, and the Cochrane Library to identify relevant randomized controlled trials (RCTs) published up to December 2024. Studies meeting the inclusion criteria were selected and included. The aggregated data was analyzed using relative risk (RR) and a 95% confidence interval (CI). Heterogeneity was assessed using the I^2 statistic.

Results: Our study included 3 randomized controlled trials with a total of 234 patients. The meta-analysis results demonstrated that hyperbaric oxygen therapy (HBOT) significantly reduced the incidence of major adverse cardiovascular events (MACE) in patients with acute coronary syndrome following reperfusion therapy, showing statistical significance (OR=0.75, 95% CI: 0.60-0.92, p=0.001). HBOT also significantly decreased the incidence of recurrent myocardial infarction in these patients, with statistical significance (OR=0.21, 95% CI: 0.04-1.01, p=0.05). However, HBOT did not have a significant effect on all-cause mortality (RR=0.44, 95% CI: 0.11-1.71, p=0.24).

Conclusion: Hyperbaric oxygen therapy (HBOT) has statistically significant effects in reducing the incidence of major adverse cardiovascular events (MACE) and reinfarction in patients with acute coronary syndrome (ACS) following reperfusion treatment, suggesting that HBOT may serve as an effective adjunctive measure in this context. However, HBOT did not demonstrate a significant impact on all-cause mortality, indicating that further research is necessary to comprehensively evaluate its clinical benefits and potential risks. Large-scale, long-term follow-up randomized controlled trials (RCTs) in the future will be essential to better elucidate the role of HBOT in the management of ACS patients.

Key words: acute coronary syndrome, hyperbaric oxygen therapy, reperfused therapy, meta analysis.

论文 ID：88

Propensity Score Analysis of Triglyceride-Glucose (TyG) Index in Newly Diagnosed Patients with Essential Hypertension as a Predictor of Microalbuminuria

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Background: The Triglyceride-Glucose (TyG) index has emerged as a potential predictor for microalbuminuria (MAU) in patients with essential hypertension. This study aims to assess the TyG index as a predictor of MAU in newly diagnosed hypertensive patients, using propensity score matching (PSM) to control for confounding factors.

Methods: A cohort of 2,052 newly diagnosed hypertensive patients from Changde Hospital, China (January 2020 to December 2024), was analyzed. The TyG index cutoff value was determined by ROC analysis, with a value of 9.125. PSM was employed to balance baseline differences between low and high TyG groups, and logistic regression models were used to analyze the association between TyG and MAU. Subgroup analyses and sensitivity analyses were conducted to evaluate the robustness of the findings.

Results: In the final cohort, 2,052 patients were divided into two groups based on the optimal TyG cutoff value of 9.125. After propensity score matching (PSM), the high TyG group (≥9.125) exhibited significantly higher rates of MAU compared to the low TyG group (<9.125). In the adjusted models, the odds ratio (OR) for MAU in the high TyG group was 2.37 (95% CI: 1.73 - 3.26). The analysis revealed a non-linear, L-shaped association between TyG and MAU, with a marked increase in the prevalence of MAU in the high TyG group. Sensitivity analyses, including inverse probability treatment weighting (IPTW), reinforced these findings, with the high TyG group consistently showing a higher risk of MAU across both original and matched cohorts. The TyG index also demonstrated moderate predictive ability for MAU, with an area under the curve (AUC) of 0.572 in the original cohort and 0.582 in the matched cohort.

Conclusion: The TyG index is an effective and accessible biomarker for predicting MAU in newly diagnosed hypertensive patients, providing valuable insight for early detection of kidney damage in this population.

Key words: Propensity Score Analysis; the Triglyceride-Glucose; microalbuminuria

论文 ID：89

The Utility of 68Ga-Pentixafor PET/CT in Superselective Adrenal Artery Embolization (SAAE) for Treating Aldosterone Adenomas

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Objective: The expression of CXC chemokine receptor 4 (CXCR4) has been proved to be a valuable tool to guide the diagnosis and treatment of Aldosterone-producing Adenoma (APA). In this study, our aim is to evaluate whether CXCR4 imaging with 68Ga-pentixafor PET/CT has significantly changed before and after superselective adrenal artery embolization (SAAE).

Methods: We prospectively recruited 25 patients with clinically diagnosed APA. All patients were examined by 68Ga-pentixafor PET/CT and adrenal venous blood sampling (AVS). PET/CT showed that the tracer uptake of unilateral nodular adrenal gland was higher than that of normal adrenal tissue. AVS showed that the dominant secretory side was consistent with PET/CT. Patients were successfully treated with SAAE. Clinical follow-up was carried out according to PASO criteria, such as drug type, blood pressure, serum potassium and aldosterone/renin ratio, to evaluate the surgical effect. After operation, 68Ga-pentixafor was performed again, and the maximum standardized uptake value (SUVmax) was used to observe the uptake of adrenal lesions after SAAE.

Result: Among the 25 APA patients who successfully underwent SAAE, 14 were male, with an average age of 51.88± 8.89 years. The coincidence rate between 68Ga-pentixafor PET/CT and AVS was 100%. Before operation, the SUVmax of the diseased side (16.79 ±2.51, n = 25) was significantly higher than that of the non-diseased side (4.56± 0.57, $P < 0.01$).

According to PASO criteria, 13 of 25 patients achieved clinical complete remission, nine achieved partial remission and three were ineffective. At the same time, 19 cases achieved biochemical complete remission and 3 cases achieved partial remission. For 22 patients with complete remission and partial patients, 68Ga-pentixafor PET/CT showed that the SUVmax of the diseased side decreased significantly (16.75±2.54 vs 4.37±1.52,n =22, P< 0.001). For the invalid patients, the SUVmax did not change (17.07±2.72 vs 16.17±2.72,n =3, p=0.842). According to the average value (65%) of the decrease of SUVmax, 25 patients were divided into two groups: the decrease of SUVmax was ≥65% and < 65%. The decrease of SUVmax was correlated with the good prognosis of patients under PASO standard (P = 0.009).

Conclusion: The decrease of SUVmax is related to the prognosis. CXCR4 imaging with 68Ga-pentixafor can be used for evaluation before and after SAAE in APA patients.

Key words: 68Ga-Pentixafor, CXC chemokine receptor 4, superselective adrenal artery embolization,aldosterone-producing adenoma.

论文 ID：106

Correlation Between Thyroid Function Parameters and Aldosterone-Renin Ratio in Patients with Primary Aldosteronism and Its Impact on Target Organ Damage

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Background: Primary aldosteronism (PA) is one of the most common causes of secondary hypertension. The relationship between thyroid function parameters and the aldosterone-renin ratio (ARR) in PA patients, as well as their combined impact on target organ damage, remains incompletely understood.

Methods: We conducted a retrospective analysis of 317 patients diagnosed with or suspected of PA. Demographic data, thyroid function parameters (TSH, FT3, FT4, TT3, TT4, TPO-Ab, TG-Ab), aldosterone, plasma renin activity (PRA), ARR, and markers of target organ damage were analyzed. The relationship between thyroid function parameters and ARR was

evaluated, and their association with cardiovascular, cerebrovascular, and renal damage was assessed.

Results: Among 317 patients (54.9% male, 45.1% female), 229 (72.24%) were diagnosed with PA. Hypertension was present in 248 patients (78.23%), with 239 (75.39%) classified as grade 3 (very high risk). Mean TSH was 16.113 ± 2.408 μIU/mL, mean ARR was 48.058 ± 3.161. Significant correlations were found between TSH and ARR ($r=0.35$, $p<0.01$). Patients with higher ARR values showed higher prevalence of target organ damage, including coronary artery atherosclerosis (24.92%), carotid artery atherosclerosis (21.45%), and lacunar cerebral infarction (31.86%). Multiple regression analysis revealed that both thyroid function abnormalities and elevated ARR were independently associated with increased risk of target organ damage.

Conclusion: Thyroid function parameters, particularly TSH, correlate significantly with ARR in PA patients. Both thyroid dysfunction and elevated ARR contribute independently to target organ damage. Comprehensive evaluation of both endocrine systems may improve risk stratification and management of PA patients.

Key words: Primary aldosteronism, thyroid function, aldosterone-renin ratio, target organ damage, hypertension

论文 ID：117

The Relationship between Surgical Outcomes and KCNJ5 Mutations and Pathological Classification in Patients with Unilateral Primary Aldosteronism

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Objective: To investigate the correlations of KCNJ5 gene mutations and CYP11B1/CYP11B2 immunohistochemical (IHC) pathological subtypes with clinical characteristics and postoperative outcomes in patients with unilateral primary aldosteronism undergoing adrenalectomy.

Methods: A retrospective analysis was conducted on 100 primary aldosteronism patients who underwent unilateral adrenalectomy. Sanger sequencing was performed to detect KCNJ5 mutations, and postoperative tissues were subtyped via CYP11B1/CYP11B2 IHC. Associations between these molecular markers and baseline clinical parameters, biochemical profiles, and surgical outcomes were analyzed.

Results: Among the 100 patients, the somatic mutation rate of KCNJ5 was 69%. Compared to the wild-type group, patients with KCNJ5 mutations were younger at onset, predominantly female, and exhibited lower preoperative plasma renin concentrations (all $P<0.05$). In the KCNJ5-mutated subgroup, those achieving complete clinical remission had younger age, shorter duration of hypertension, higher preoperative serum/urinary aldosterone levels, higher lateralization indices, fewer defined daily doses of preoperative antihypertensive medications, and larger tumor diameters. Patients with KCNJ5 mutations and $CYP11B2^{+}$ single-positive staining demonstrated stronger CYP11B2 expression intensity compared to those with $CYP11B1^{+}/CYP11B2^{+}$ co-expression, along with a significant postoperative reduction in antihypertensive medication use, though clinical remission rates were similar.

Conclusion: Unilateral primary aldosteronism patients harboring KCNJ5 somatic mutations and high CYP11B2 expression exhibit favorable prognoses. KCNJ5 mutation was significantly associated with pathological subtype (high expression), and their combination may serve as a predictive marker for postoperative clinical remission. This study provides molecular and pathological insights for individualized prognostic evaluation and therapeutic decision-making in primary aldosteronism.

Key words Primary aldosteronism; Unilateral adrenalectomy; Adrenal venous sampling; KCNJ5; CYP11B1/CYP11B2

论文 ID：119

The Modifying Effects of HS-CRP on the Association Between Blood Pressure and Stroke Risk in a Non-Hypertensive Population: A Prospective Cohort Study

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Introduction: Stroke persists as the second leading etiology of death worldwide and the predominant cause of disability. High blood pressure (BP) is the most critical modifiable risk factor for stroke events. However, the risk of stroke with systolic/diastolic BP (SBP/DBP) below 140/90 mm Hg is easily overlooked. On the other hand, high-sensitivity C-reactive protein (HS-CRP) is an important inflammatory biomarker and is now recognized to play a fundamental role in atherogenesis and is an important independent risk factor for strokes. Both BP and inflammation are considered important factors in stroke risk assessment. Nevertheless, the relationship between inflammation, BP, and risk for future stroke events and the potential modified effect of HS-CRP on the associations between BP and stroke events remain unclear in people without hypertension.

To address this issue, we sought to determine the relationship between normal BP and stroke events stratified by HS-CRP levels in a large cohort of the population without hypertension, using data from the China Health and Retirement Longitudinal Study (CHARLS).

Methods: The CHARLS was a prospective and nationally representative cohort conducted in China. For this analysis, we utilized data from the initial wave of the study in 2011 as the baseline. Subsequent waves, including wave 2 in 2013, wave 3 in 2015, wave 4 in 2018,

and wave 5 in 2020, were considered follow-up surveys. We used data from the baseline to evaluate the exposure and the follow-up survey to evaluate the outcome. The CHARLS protocol was approved by the Ethics Review Committees of Peking University, and written informed consent was obtained from all participants involved in the cohort study. All participants followed at 2-year, occasionally 3-year, intervals.

Cox proportional hazard models assessed the relationship between BP and stroke events. The Schoenfeld residuals test was used to assess the Cox proportional hazards assumption, and results showing the models meet the proportional hazards assumption. The model was adjusted for age, sex, residential area, education levels, current cigarette smoking, current alcohol drinking, BMI, LDL-C levels, HbA1c levels, disease history of diabetes mellitus, and Cardiac events. Using the likelihood ratio test within models that incorporated multiplicative interaction terms evaluated the impact of the interaction between HS-CRP levels and BP on stroke events. Additionally, nonparametric restricted cubic splines, with four knots positioned at the 5th, 35th, 65th, and 95th percentiles of the BP distribution specific to each subgroup, were employed to investigate the relationship pattern between BP and the occurrence of stroke events.

Results: According to inclusion and exclusion criteria, 4509 participants from CHARLS (male: 45.2%, media age:56 years) were included in this study.

During up to 9 years of follow-up in the CHARLS, a total of 316 patients had stroke events. In the total study population, SBP, DBP, and MAP were significantly associated with stroke events. Moreover, we assessed increasing per unit SD of SBP (hazard ratio [HR] 1.19; (95% confidence interval [CI] 1.07-1.34); Model 2), DBP (HR 1.22; (95% CI 1.09-1.37); Model 2), and MAP (HR 1.23; (95% CI 1.10-1.38); Model 2) on the risk of stroke events.

Table 2 displays the association between BP, assessed both as a categorial and continuous variable, with the respective risks of incident stroke events. A significant interaction was observed between SBP and HS-CRP on stroke events (P for interaction <0.05 in Model 3 in Table 2). After fully adjusting for potential confounders, in the high HS-CRP levels group, patients in the highest group of SBP had significantly higher risks of incident stroke than those in the lowest group (HR 1.98 (95% CI 1.35 - 2.92), P < 0.001). Additionally, we found that per 1-SD SBP levels increased a 1.40-fold risk of stroke events. However, in the low HS-CRP levels group, there was no significant association between the risk of stroke events and SBP (HR, 0.98; (95%CI, 0.83 - 1.16), P =0.434). On the other hand, in the high HS-CRP levels group, patients in the highest group of DBP and MAP had

significantly higher risks of incident stroke than those in the lowest group after fully adjusting for potential confounders (DBP: HR 1.60 (95% CI 1.03 - 2.49), MAP: HR 2.02 (95% CI 1.34 - 3.06), respectively). And per 1-SD DBP/MAP levels increased a 1.32-fold/1.39-fold risk of stroke events. However, after adjusting multiple potential confounders, we observed no significant interaction between DBP/MAP and HS-CRP on stroke events.

In the restricted cubic spline, linear dose-response associations were found between SBP, DBP, MAP, and stroke risk at high HS-CRP levels (P linear<0.001) but not at low HS-CRP levels.

Conclusion: Our study found that high BP within the normal range was an independent risk factor for future stroke events at high HS-CRP levels, but not at low HS-CRP levels, in middle-aged and elderly Chinese without hypertension. In addition, there was an interaction between HS-CRP and the high value of normal SBP on future risk of stroke events.

Key words: Blood pressure; HS-CRP; Stroke; CHARLS

论文 ID：123

Association of the Urban Environments with Atherosclerotic Cardiovascular Disease

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Background and Aims

Urban environments affect cardiovascular health, yet only a few specific exposures have been explored in isolation and mostly adopting cross-sectional design. The influence of socioeconomic status and genetic predisposition also remains unclear.

Methods

This study was based on 206,681 participants free of atherosclerotic cardiovascular disease (ASCVD) at baseline from UK Biobank. A total of 213 urban environment variables were collected. Cox models and regularized Cox models were employed to analyze the

association between urban environment exposures and the risk of developing ASCVD. Further, pathways of environmental effects on ASCVD were identified through sparse canonical correlation and mediation analyses. The roles of socioeconomic status and genetic predisposition were assessed by evaluating potential interactions.

Results

The multi-approach analyses highlighted air pollution, industrial sites, and complex street networks as primary environmental risk factors. Instead, land-use density of leisure, public services, infrastructure and residential, and drinking water hardness showed a negative association with ASCVD risk. Distinct urban environment patterns through diverse pathways influence ASCVD. The environment characterized by pollution and complex streets impact ASCVD through adverse mental health (mediation proportion:30.7%, 95% CI:22.4%-44.0%), while highly-developed community and high-water hardness environment via cardiometabolic status (22.6%, 95% CI:19.7%-26.0%). Further, there were significant interactions effect of socioeconomic status and urban environment on ASCVD, yet there were no similar findings for ASCVD genetic predisposition.

Conclusions

A wide range of urban environmental exposures were associated with the risk of developing ASCVD. These effects were mediated by different individual modifiable factors, with low socioeconomic status amplifying disadvantaged urban environment effects on ASCVD. This research deepened our understanding of city-cardiovascular health links.

Key words: Urban environment, City, Atherosclerotic cardiovascular disease, Exposome

论文 ID：128

Advancing Urban-rural Equity in Hypertension Care Cascades to Reduce Cardiovascular Disease Burden in China: A Microsimulation Study

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Background

Although hypertension remains the leading modifiable contributor to CVD-related deaths and disability, improving hypertension management performance in China has uncertain implications across different socioeconomic and demographic groups. In this study, we developed a microsimulation model to estimate how scale-up in hypertension care cascade performance could prevent CVD cases and advance health equity in the Chinese adult population.

Methods

Using 86,071 individual-level data from nationally and provincially representative survey in China, we simulated two scenarios for the hypertension care cascades (diagnosis scenario and treatment scenario) based on a microsimulation model. Diagnosis (diagnosis scenario) and treatment (treatment scenario) levels for all urban and rural areas to match the best-performing province's urban or rural rates. We then estimated the effects of intervention scenarios on CVD risk and prevented occurrences of CVD cases per 1,000 people with hypertension, stratified by demographic and regional subgroups. Key outcomes were computed as the difference between CVD risk levels in the baseline and intervention scenarios (diagnosis or treatment). We also calculated the percentage point gap in CVD risk between urban and rural populations within each province and scenario to examine the intervention's effect on urban-rural disparities in CVD risk. Results were further disaggregated by human development index (HDI) categories and seven geographic regions. All analyses were conducted independently by urban-rural residence and sex.

Results

The total number of individual respondents included in the simulated population was 86,071 adults aged 20-85 years with hypertension. The median age was 56.3 years (IQR 45.4-68.1), with 46.3% (39,817) of female. HDI regions exhibited non-linear disparities in hypertension care cascade performance. Transitioning from baseline to diagnosis and treatment scenarios substantially reduced mean 10-year CVD risk across all provinces, with rural populations and males experiencing the most pronounced improvements. Most provinces saw narrowed urban-rural CVD risk gaps and national inequalities in CVD burden would be reduced, particularly under treatment scenarios. Nationally, the number of CVD occurrences prevented during the 10-year period for diagnosis and treatment scenarios were 1.75 million

and 2.41 million, respectively. Under treatment scenarios, rural areas in Northwest China demonstrated the highest CVD case averted (11.3 per 1,000 individuals with hypertension), followed by urban Northeast China (9.6 per 1,000) and rural Northeast China (9.5 per 1,000). For different HDI regions, rural areas in upper-middle HDI regions averted the most CVD cases (9.7 per 1,000 individuals with hypertension) under treatment scenario, surpassing urban counterparts (6.9 per 1,000), while lower-middle HDI regions showed narrower urban-rural differences (7.3 vs. 7.0 per 1,000) under treatment scenarios. Provincial-level analyses highlighted rural Shaanxi as the top performer in CVD cases prevention under treatment scenario (15.3 per 1,000), followed by rural areas in Shandong (12.2 per 1,000) in the treatment scenario and rural areas in Shaanxi in the diagnosis scenario (12.0 per 1,000). Sex-specific analyses revealed consistent male-favoring disparities, with upper-middle HDI regions achieving the highest male-specific CVD reduction (11.1 per 1,000). Males in Shaanxi, Shandong, and Liaoning showed the largest improvements in CVD cases preventions in the treatment scenarios. The health gains of hypertension management strategies varied significantly depending on the target definition in the simulated intervention scenarios.

Conclusions

Strengthening hypertension care cascade performance across China could substantially prevent CVD burden, particularly among rural population and among males in upper-middle HDI regions. Prioritizing targeted enhancements in hypertension diagnosis and treatment adherence would not only reduce preventable CVD outcomes but also address persistent residence- and sex-based disparities in healthcare equity.

Key words： hypertension; management; disparity; health equity; microsimulation

论文 ID：139

C3aRA Disrupts the IgG/IL-6 Positive Feedback Loop to Ameliorate Adipose Tissue Senescence and Metabolic Dysfunction

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Objective: Adipose senescence and metabolic dysfunction are fundamental to metabolic diseases. Complement C3a plays a critical role in regulating immunity and metabolism. This study investigates the mechanism by which the C3a receptor antagonist (C3aRA) improves adipose senescence and metabolic disorders.

Methods: A high-fat diet (HFD)-induced obesity (DIO) mouse model was established. C3aRA was administered intraperitoneally to evaluate its effects on senescence and metabolic parameters. Transcriptomic analysis revealed C3aRA-mediated modulation of B cell activation. μMT (B cell-deficient) DIO mice and IgG-injected DIO mouse models were established, alongside in vitro, B cell-adipocyte co-culture experiments and IgG-treated adipocyte assays were performed to evaluate the roles of B cells/IgG in adipose senescence and metabolism. DIO mice were established with intraperitoneal injections of C3aRA and IgG, separately, B cells pretreated with C3aRA were co-cultured with adipocytes in vitro to evaluate the role of B cell/IgG in mediating C3aRA's effects on adipose senescence and metabolism. Transcriptomics identified IgG-induced IL-6 synthesis in adipocytes. Clazakizumab (an anti-IL-6 monoclonal antibody) was administered to DIO mice, and IL-6/C3aRA-pretreated B cells were co-cultured with adipocytes to explore IL-6's role in C3aRA-regulated B cell activation and adipose senescence.

Results: Serum C3a levels were elevated in DIO mice, while C3aRA suppressed epididymal white adipose tissue (eWAT) senescence and improved metabolic profiles. Transcriptomics indicated C3aRA inhibited B cell activation in WAT. Notably, C3aR was absent in adipocytes but expressed on B cells, suggesting that C3aRA could exert its effects via B cell C3aR signaling. IgG deposition in eWAT increased in DIO mice, which C3aRA attenuated. μMT mice exhibited improved metabolism versus wild-type, but IgG injection reversed this benefit. In vitro, both B cell co-culture and IgG treatment induced adipocyte senescence. Critically, IgG injection antagonized the ability of C3aRA to suppress eWAT senescence and improve metabolism in DIO mice, further confirming C3aRA ameliorates metabolic dysfunction by modulating B cell-derived IgG production. Transcriptomics revealed IgG upregulated adipocyte IL-6. IL-6 blockade via Clazakizumab attenuated eWAT senescence, improved metabolic function, and reduced IgG accumulation in eWAT. In parallel, in vitro experiments demonstrated that IL-6 activates B cells to enhance IgG production, suggesting that IL-6 promotes B cell activation and IgG generation, thereby establishing a positive feedback loop. Further co-culture of IL-6-pretreated B cells with adipocytes

exacerbated adipocyte senescence, which was antagonized by C3aRA, demonstrating that C3aRA effectively disrupts this pathogenic loop.

Conclusion: C3aRA disrupts the IgG/IL-6 positive feedback loop, ameliorating metabolic dysfunction and adipose senescence, offering a novel therapeutic strategy for obesity-related metabolic disorders.

Key words: C3a receptor antagonist,IgG/IL-6 axis,Adipose tissue senescence,Metabolic dysfunction,Inflammatory feedback loop

论文 ID：144

Association between Changes in the C-Reactive Protein-Triglyceride Glucose Index and Incident Stroke: A National Prospective Cohort Study

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Introduction

Stroke is characterized by high incidence, mortality, and disability rates. According to the Global Burden of Disease data, the contribution of stroke to the global disease burden has risen from the fifth leading cause in 1990 to the second leading cause in 2019. Recently, a novel biomarker, the C-reactive protein-triglyceride glucose index (CTI), has been proposed as a composite measure reflecting both inflammatory status and insulin resistance levels. Accumulating evidence suggests that the CTI may emerge as a novel risk factor for cardiovascular diseases, cancer, diabetes, and other conditions, or be associated with their early development. Notably, these findings are primarily derived from studies utilizing single measurements, which are insufficient to reflect long-term status. It is postulated that, beyond a single measurement value, long-term cumulative exposure or sustained high levels may also be significant factors influencing disease risk. However, to date, no studies have investigated the relationship between long-term changes in CTI and stroke incidence in the general population.

This study aims to utilize data from the China Health and Retirement Longitudinal Study (CHARLS) to investigate the association between long-term changes in CTI and the risk of future stroke incidence in the general Chinese population.

Methods

Study Population

The CHARLS is a nationally representative prospective cohort study conducted in China. Participants were selected using a multi-stage clustered sampling method from 28 provinces across China. For this study, we utilized data from Wave 2 (2011) and Wave 3 (2015) of CHARLS as the baseline period. Subsequent waves, including Wave 4 (2018) and Wave 5 (2020), were considered follow-up surveys.

Assessment of Long-term CTI Changes

In CHARLS, trained technicians collected blood samples during the 2011 and 2015 waves and measured levels of high-sensitivity C-reactive protein (hsCRP), fasting blood glucose (FBG), and triglycerides (TG). The CTI was calculated using the following formula:

$$CTI = 0.412 \times \mathrm{Ln}(\text{hsCRP [mg/dL]}) + \mathrm{Ln}(\text{TG [mg/dL]} \times \text{FBG [mg/dL]}) / 2$$

To characterize long-term changes in CTI between the 2011 and 2015 assessments, we performed K-means cluster analysis using the "cluster" and "factoextra" packages in R

software. This process was iterated until the cluster centroids stabilized or a predetermined number of iterations was reached.

Additionally, we calculated cumulative CTI based on previous studies, defined as:

Cumulative CTI = [First CTI assessment + Second CTI assessment) / 2] × Time Interval (years between assessments).

Statistical analysis

Through cluster analysis, the long-term changes of CTI were divided into four groups: cluster 1 (continuously low), cluster 2 (from high to low), cluster 3 (from low to high), and cluster 4 (continuously high).

Cox proportional hazard models assessed the relationship between CTI and stroke incidents. Model was adjusted age, sex, region, education levels, current cigarette smoking, current alcohol drinking, BMI, LDL-C levels, HbA1c levels, systolic blood pressure, disease history of diabetes mellitus, and use of diabetes medications. The multiplicative interaction terms were fitted to examine the potential effects of subgroups.

Additionally, nonparametric restricted cubic splines were employed to investigate the relationship pattern between cumulative CTI and the risk of stroke incident.

All analyses were done with SAS software (version 9.4) and R software (version 4.42). Two tailed $P<0.05$ all were considered a significant level.

Results

The study included 6361 participants (45.02% male, 54.98% female), with a mean age of 58.23±8.53 years. During the 5-year follow-up period, a total of 556 (8.74%) stroke events occurred. The association between long-term CTI changes and stroke incidence risk was explored using three established Cox proportional hazards models.

As presented in Table 1, in the fully adjusted multivariable model (Model 3), compared to Cluster 1, the risk of stroke incidence was significantly elevated in Cluster 3 (HR: 1.72, 95% CI: 1.36－2.17) and Cluster 4 (HR: 1.86, 95% CI: 1.44－2.40). Furthermore, a significant trend was observed, indicating an increased risk of stroke incidence with rising CTI levels (P for trend < 0.001).

The relationship between cumulative CTI and stroke risk was further analyzed. In Model 3, compared to the lowest quartile (Q1) of cumulative CTI, the highest quartile (Q4) was

associated with a significantly higher stroke risk (HR: 1.68, 95% CI: 1.30 - 2.18). A significant increasing trend in stroke risk was also observed with higher cumulative CTI levels (P for trend < 0.001). Additionally, for each 1-standard deviation (SD) increase in cumulative CTI, the risk of stroke incidence increased by 26%. In the subgroup analysis, Cluster 3 and Cluster 4 were significantly associated with stroke incidents in all subgroups. The multiplicative interaction terms were not found.

Moreover, multivariable-adjusted restricted cubic spline curve analysis revealed a linear dose-response relationship between cumulative CTI and the risk of stroke incidence.

Conclusion

Our findings demonstrate that long-term changes in the CTI are independently associated with the risk of stroke incidence. Individuals exhibiting persistently high or increasing CTI levels (from low to high) during follow-up faced an elevated risk of stroke. Therefore, long-term monitoring of CTI trajectories may serve as a critical factor for stroke prevention strategies.

Key words: long-term, CTI, stroke, CHARLS

论文 ID：146

Ambulatory Blood Pressure Characteristics and Target Organ Damage in Primary Aldosteronism: Associations with Cardiac Hypertrophy, Proteinuria, and Renal Function

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Objective: To investigate the 24-hour ambulatory blood pressure (ABPM) characteristics and their associations with target organ damage in patients with primary aldosteronism (PA).

Methods: This study enrolled 208 PA patients in the Fuwai Hospital between June 2023 and December 2024 (122 unilateral [UPA] and 86 bilateral [BPA], confirmed by adrenal venous sampling and 200 essential hypertension (EH) controls. ABPM metrics, biochemical parameters,

and target organ damage markers (left ventricular mass index [LVMI], urinary albumin-to-creatinine ratio [UACR], estimated glomerular filtration rate [eGFR]) were analyzed. Statistical comparisons included t-tests/Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables. Spearman correlation analysis and multivariate regression assessed ABPM- target organ damage relationships.

Results: Patients with PA demonstrated significantly higher 24-hour systolic and diastolic blood pressure and elevated nighttime blood pressure compared to EH controls. A reversed-dipper circadian pattern was more prevalent in PA than EH controls (41.8% vs. 15.0%, $P < 0.01$). However, no significant differences in ABPM metrics were observed between UPA and BPA subgroups. PA patients with high aldosterone level demonstrated significantly elevated nighttime systolic BP (145.7±17.1 vs. 140.8±16.9 mmHg, $P=0.038$) and higher 24-hour BP load ($P<0.01$) compared to those below the median. Correlation analyses revealed that 24-hour systolic blood pressure (SBP) was positively associated with UACR ($r = 0.440$, $P < 0.01$) and LVMI ($r = 0.283$, $P < 0.01$), and inversely correlated with eGFR ($r = -0.164$, $P = 0.016$). Notably, nighttime SBP showed the strongest association with UACR ($r = 0.411$, $P < 0.01$). In multivariate regression, elevated upright aldosterone (OR 1.022, $p = 0.046$), lower serum potassium (OR=0.319, P=0.020), higher 24-hour SBP (OR=1.029, P=0.019) and higher BMI (OR=1.094, P=0.041) independently predicted target organ damage.

Conclusions: PA is characterized by disrupted 24-hour blood pressure regulation, particularly elevated nighttime systolic pressure and non-dipping patterns, which are associated with renal and cardiac damage. These findings underscore the importance of ABPM in risk stratification and tailored management of PA.

Key words Primary aldosteronism, Ambulatory blood pressure monitoring, Target organ damage, Secondary hypertension

论文 ID：147

Life's Essential 8 Cardiovascular Health and Cardiovascular Disease Risk in Hypertension: Effect Modification by Age at Diagnosis

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Background: The evidence on the association between cardiovascular health (CVH) as measured by the American Heart Association's Life Essential 8 (LE8) and cardiovascular disease (CVD) in hypertensive patients is lacking and whether this association differs across the hypertension onset age remains unknown.

Methods: This study included 78,822 participants free of prevalent hypertension and CVD at baseline from Kailuan study. During follow-up, 22,217 participants were diagnosed as having hypertension. For each case subject, control subjects were selected from the participants who attended the examination in the same year and without hypertension during follow-up. Changes in CVH status were evaluated between the first survey and the second survey. Cox proportional hazards regression models with age as the time scale were used.

Results: Overall, 1,887 CVD cases occurred during a median follow-up of 9.62 years. Having better CVH status significantly reduced the risk of CVD events in hypertension, and the association was more evident in participants with hypertension diagnosed <45 years (HR, 0.53 [95%CI: 0.36-0.79]). Compared with participants without hypertension, participants maintaining moderate/high CVH status were still at higher risk of CVD in hypertension, and the hazards of outcomes were gradually attenuated with the increase in hypertension onset age. The magnitude of the decremental risk for CVD associated with per 10-point increment in CVH score was greatest among participants with hypertension onset < 45 years (HR,0.71 [95%CI, 0.56-0.89]).

Conclusions: These data support the beneficial effect of attaining preferable CVH status, as defined by LE8, on CVD among hypertensive patients, and this association was more evident in patients diagnosed at younger ages.

Key words: cardiovascular health, hypertension, cardiovascular disease, onset age, prevention, life's essential 8

论文 ID：157

A Predictive Model of Adverse Pregnancy Outcomes in Advanced Maternal Age Women with Preeclampsia was Constructed Based on Machine Learning

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Objective: The objective of this study is to apply machine learning techniques to develop a prediction model for the risk of hypertensive disorders in pregnancy and adverse pregnancy outcomes among elderly pregnant women. The ultimate aim is to more accurately predict the risk of such conditions and reduce the occurrence of adverse pregnancy outcomes. Hypertensive disorders in pregnancy, especially preeclampsia, are one of the leading causes of maternal and fetal morbidity and mortality. Elderly pregnant women, defined as those aged 35 or older, face higher risks of complications, making the development of an effective prediction model critical for improving maternal and fetal health.

Methods: This study focused on elderly pregnant women diagnosed with preeclampsia, and patients were followed up until 3 months postpartum. The primary goal was to identify and evaluate potential risk factors for adverse pregnancy outcomes in this population. To construct prediction models, we employed several machine learning classification algorithms, including logistic regression (LR), adaptive boosting (AdaBoost), complement naive Bayes (CNB), multi-layer perceptron (MLP), support vector machine (SVM), and K-nearest neighbors (KNN). These algorithms were selected for their established success in classification tasks across various fields, including healthcare. The dataset used for model development consisted of clinical data collected from elderly women diagnosed with preeclampsia. The features included medical history, blood pressure readings, laboratory results, and other clinical indicators.The models were first trained on a subset of the dataset, and then evaluated using a separate validation set to assess their predictive performance. The

performance of each model was evaluated using area under the curve (AUC) and accuracy metrics, which are commonly used to determine the effectiveness of classification models in binary prediction tasks. In addition to training and evaluating the models, the study also performed a model fusion analysis to combine the results of multiple algorithms, potentially improving the overall predictive power.

Results: A total of 860 elderly preeclamptic patients were included in this study, of which 322 patients experienced adverse pregnancy outcomes, such as preterm birth, fetal growth restriction, and other complications. The data were analyzed using the selected features, and prediction models were developed based on the six machine learning algorithms. The models were tested on a validation set, and the results showed varying performance across the different algorithms. The AUC values and accuracy for each model were as follows:

Logistic Regression (LR): AUC = 0.772 (95% CI: 0.692-0.853)

AdaBoost: AUC = 0.927 (95% CI: 0.884-0.970)

Complement Naive Bayes (CNB): AUC = 0.770 (95% CI: 0.690-0.850)

Multi-Layer Perceptron (MLP): AUC = 0.653 (95% CI: 0.561-0.746)

Support Vector Machine (SVM): AUC = 0.760 (95% CI: 0.678-0.842)

K-Nearest Neighbors (KNN): AUC = 0.861 (95% CI: 0.803-0.919)

The AdaBoost model demonstrated the highest predictive power with an AUC of 0.927, which suggests that it was the most effective model for predicting adverse pregnancy outcomes in this population. Other models, such as KNN, also performed well, with an AUC of 0.861. Conversely, the MLP model had the lowest AUC (0.653), indicating that it was less effective in predicting the outcomes compared to other models.

Further analysis using SHAP (Shapley Additive Explanations) values highlighted the most important features in predicting adverse pregnancy outcomes. These included systolic blood pressure, gestational age, blood urea nitrogen, and white blood cell count. These factors showed the greatest predictive value for identifying patients at risk of complications during pregnancy. Additionally, the external validation group, which was composed of a separate set of patients, yielded an AUC of 0.916 (95% CI: 0.865-0.967), confirming the robustness of the AdaBoost model.

Conclusion

In conclusion, systolic blood pressure, gestational age, blood urea nitrogen, and white blood cell count were identified as the most significant predictors for adverse pregnancy outcomes in elderly preeclamptic patients. The AdaBoost model, with its superior performance in terms of AUC and accuracy, proved to be the most reliable tool for predicting adverse outcomes. This model can potentially be used in clinical settings to identify high-risk elderly pregnant women early and allow for targeted interventions, which may help reduce maternal and fetal morbidity and mortality.

This study highlights the potential of machine learning models, specifically AdaBoost, in improving the prediction of adverse pregnancy outcomes among elderly women with preeclampsia. The findings suggest that integrating these predictive models into clinical practice could improve the management and monitoring of high-risk pregnancies.

Key words: Machine Learning; Elderly Pregnant Women; Adverse Pregnancy Outcomes; Prediction Model; Preeclampsia

论文 ID：159

CEMIP Maintains Vascular Contractility by Controlling PP1c-MLC20 Cascade in SMCs

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Hypertension is the main independent risk factor for many cardiovascular diseases, and the increase of vascular resistance is one of the key pathophysiological mechanisms leading to the development of hypertension, and long-term smooth muscle cell hyperresponsiveness leads to vascular remodeling and extensive extracellular matrix synthesis leading to increased vascular wall rigidity, and impaired vascular elasticity, which in turn leads to hypertension. Dynamic changes in vascular diameter are largely dependent on contractile activation and inactivation of contractile proteins in vascular smooth muscle cells. As newly discovered macromolecular proteins, cell migration induction and hyaluronic acid

binding proteins (CEMIP)have rarely been reported in regulating the function of smooth muscle contraction.The mice lacking CEMIP in SMCs showed significantly reduced contractility and blood pressure compared with their counterparts of age-matched wild-type littermates ($Cemip^{flox/flox}$). Mechanistically, we demonstrated that CEMIP directly interacted with MLC20 to maintain its phosphorylation. In addition, CEMIP sequestered MLC20myosin light chain 20 from its phosphatase, PP1c, without affecting the kinase MLCK (myosin light chain kinase). Moreover, CEMIP contains 3 critical RVxF motifs that are responsible for binding to PP1c. Mutations in these motifs restored the interaction between PP1c and MLC20.

Key words Blood pressure; Cell contractility; Vascular smooth muscle; Mutation;Myosin light chains

论文 ID：161

Single-cell RNA Sequencing Reveals Critical Role of GZMK+ CD8+ T Cells in Primary Hypertension

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Background: Hypertension remains the leading manageable risk factor for global cardiovascular mortality. In China in particular, the aging population has seen a significant rise in hypertension incidence, escalating from 5.1% (1958–1959) to 23.2% (2012–2015). This epidemiological shift underscores the growing public health burden and the demand to understand its pathogenesis better and to develop more effective therapeutics. Recent emerging studies have implicated the role of the immune system in hypertension, but a comprehensive atlas of the immune cells in the peripheral circulation in primary hypertension is yet to be established, and key immune cell types and their mechanisms remain to be identified.

Methods: Six hypertensive patients were enrolled for single-cell RNA sequencing of peripheral blood samples, and 4 healthy subjects from were used as controls. For flow

cytometry experiments, 23 control subjects and 27 hypertensive patients were enrolled. Animal experiment on mouse models of AngII-induced hypertension are currently being conducted.

Results: Our results show that hypertension alters peripheral immune cell atlas in patients, producing significant changes in T cells and monocytes. Further analysis of the T cell landscape shows Granzyme K-positive (GZMK+) CD8+ T cells are the only distinctly T cell subset that is significantly altered in hypertensive patients conpared with controls, which is significantly upregulated in hypertensive patients. Pathway enrichment in GZMK+ CD8+T-cell clusters shows hypertension alters critical biological pathways in patients. GZMK+ CD8+T-cell upregulation in hypertensive patients is further confirmed by flow cytometry, and that hypertension-associated GZMK+ CD8+T-cell upregulation is aggravated by aging.

Conclusion: Our results suggest GZMK+ CD8+T-cells are the key impacting immune cell type in hypertension. Further investigation of GZMK+ CD8+T-cell accumulation in target organs, crosstalk with local cell types, effect on angiogenesis or complement secretion, and potential inhibitors are potential future directions.

Key words Single-cell RNA sequencing, hypertension, immune system, T Cells

论文 ID：167

Associations of extreme temperatures with hypertensive diseases mortality: findings from the vital registration in Shanghai, China

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Objective: This study aims to investigate the relationship between extreme temperatures and hypertensive disease (HD) mortality in Shanghai and to explore the time-lagged effects of extreme temperatures,

Methods: Daily HD mortality data in Shanghai were collected from the Shanghai Death Registration System from 2015-2020. According to the International Classification of Diseases-10th Revision (ICD-10), HD mortality was defined as deaths with an underlying cause of I10–I15. We defined the 2.5th and 97.5th percentiles of daily temperatures as extreme cold and extreme heat, respectively, with the minimum mortality temperature as the reference. The distributed lag non-linear model was utilized with a 0–14-day lag period.

Results: A total of 2,192 HD deaths were reported during the study period. The effects of extreme cold on HD mortality in the total population, males, and females were observed on the 4th, 3rd, and 7th days after exposure, respectively, with the maximum cumulative lagged effects at 14 days being [relative risk (RR) = 2.23, 95% confidence interval (CI): 1.82-2.72], [2.40, (1.80-3.20)] and [2.09, (1.57-2.78)], respectively. The effects of extreme heat on HD mortality in the total population and females were observed on the day of exposure, with the maximum cumulative lagged effects at 7 days being [1.18, (1.00-1.18)] and [1.24, (1.09-1.43)], respectively. For males, the effect of extreme heat was observed on the 13th day after exposure, with the maximum cumulative lagged effect at 14 days being [1.13, (1.01-1.26)].

Conclusion: Targeted protective measures should be implemented for different gender groups of hypertension patients to mitigate the adverse effects of extreme temperatures.

Key words: extreme temperature; hypertensive disease; climate change; mortality.

论文 ID：182

NOL6 Regulates the Development of Hypertension Through Ribosome Biogenesis and Endothelial Dysfunction

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Objective: This study aimed to investigate the role of nucleolar protein 6 (NOL6) in the pathogenesis of hypertension and to elucidate its molecular mechanism in regulating vascular endothelial function through modulation of ribosome biogenesis.

Methods: Differential gene expression analysis was performed using the GEO hypertension-related microarray dataset (GSE212338), in combination with a ribosome biogenesis-related gene set, to identify key genes involved in both processes. In vivo, a rat model of hypertension was established using Nω-nitro-L-arginine methyl ester (L-NAME). Animals were divided into control and L-NAME groups. Aortic structural changes were assessed by hematoxylin and eosin (HE) staining. Quantitative PCR (qPCR) was used to measure ribosomal RNA (rRNA) levels in the aorta, while Western blotting evaluated NOL6 protein expression. In vitro, human umbilical vein endothelial cells (HUVECs) were treated under five conditions: Control, Angiotensin II (Ang II), Ang II + si-NC, Ang II + si-NOL6, and Ang II + CX-5461 (a ribosome biogenesis inhibitor). EU incorporation assays assessed nascent RNA synthesis. qPCR and Western blotting were employed to analyze the expression of NOL6, rRNA, and endothelial nitric oxide synthase (eNOS)/phosphorylated eNOS (p-eNOS).

Results: Six genes were identified to be closely associated with both hypertension and ribosome biogenesis, with NOL6 showing the most significant differential expression. In hypertensive rats, aortic wall thickness increased significantly, accompanied by elevated rRNA and NOL6 expression. In vitro, Ang II stimulation upregulated NOL6 expression, enhanced rRNA synthesis, and increased nascent RNA production in HUVECs. Knockdown of NOL6 or treatment with CX-5461 significantly suppressed rRNA and nascent RNA synthesis while markedly increasing eNOS and p-eNOS expression. These results suggest that NOL6 plays a crucial role in promoting ribosome biogenesis and repressing endothelial NO signaling.

Conclusion: NOL6 contributes to the development and progression of hypertension by enhancing ribosome biogenesis and inhibiting eNOS expression. This study reveals, for the first time, a novel regulatory mechanism of NOL6 in hypertension and provides a potential therapeutic target for intervention.

Key words: nucleolin 6 (NOL6); ribosome biogenesis; hypertension; endothelial cell; eNOS

论文 ID：191

How does Biological Age Acceleration Mediate the Associations of Obesity with Cardiovascular Disease? Evidence from International Multi-cohort Studies

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Background: Recent basic biological research found that obesity accelerates biological aging and increases cardiovascular disease (CVD) risk. However, there is still a lack of real-world population evidence. This study aimed to explore the potential mediation roles of biological age acceleration in the associations between different dimensions of obesity characterization and incident CVD.

Methods: This international multi-cohort study included participants aged over 45 years with 3 waves longitudinal data from China Health and Retirement Longitudinal Study (CHARLS). China Health and Nutrition Survey (CHNS) was used to develop Klemera-Doubal method-biological age (KDM-BA), and the validation analysis was performed in UK Biobank (UKB) and Hongguang Elderly Health Examination Cohort (HEHEC). Obesity indices including body mass index (BMI), waist circumference (WC), waist height ratio (WtHR), body roundness index (BRI) for body shape; Chinese visceral adiposity index (CVAI), lipid accumulation product (LAP) for visceral fat accumulation; triglyceride-glucose index (TyG) and its derivatives (TyG-BMI, TyG-WC, TyG-WtHR) for metabolic function were used to measure obesity across different dimensions. Biological age acceleration was evaluated by the classic KDM-BA acceleration (KDM-BAacc). Causal mediation analyses assessed the role of biological age acceleration in mediating obesity and incident CVD.

Results: In CHARLS, the median follow-up period was 9.00 years, with a baseline age of 58(52, 65) years. Obesity, KDM-BAacc, and CVD were all significantly associated with each other. For each 1-year increase in KDM-BAacc, the risk of incident stroke, heart disease and CVD increased by 68% (OR: 1.68, 95%CI: 1.35 - 2.09), 35% (OR: 1.35, 95%CI: 1.15 - 1.59), and 44% (OR: 1.44, 95%CI: 1.25 - 1.65), respectively. KDM-BAacc mediated the associations between BMI, WC, WtHR, BRI, CVAI, LAP, TyG-BMI, TyG-WC, TyG-WtHR, with CVD, with the

mediation proportions ranging from 10.03% to 25.46%. However, the mediating effect was significant mostly in middle-aged individuals aged 45-65 years. Furthermore, sex differences existed in the mediation mechanisms. Biological age acceleration strongly mediated body shape indices and incident CVD in males, whereas in females, it predominantly mediated visceral fat accumulation and metabolic function dimensions with incident CVD. Similar main results were found in UKB and HEHEC.

Conclusions: Biological age acceleration partially mediates the relationship between obesity and incident CVD. This temporal evidence firstly validated the mediation pathway based on international cohorts, emphasizing the importance of addressing biological aging processes in population aged 45-65 years while providing sex-specific obesity intervention strategies to prevent CVD.

Key words: Biological age acceleration; Obesity; Cardiovascular disease; Cohort

论文 ID：213

Association of Muscle Strength with Cardiovascular Disease by Life's Essential 8: A Prospective Cohort Study of 238,592 UK Biobank Participants

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Background: Muscle strength is a recognized CVD risk factor, but its impact across varying Life's Essential 8 (LE8) levels (American Heart Association's [AHA's] cardiovascular health metric) is unclear. This study aims to investigate the joint and interactive association of the muscle strength and LE8 with CVD risk.

Methods: We analyzed 238,592 UK Biobank participants (mean age 55.65±8.06 years). Muscle strength was assessed by grip strength and categorized into high/medium/low (gender-

age tertiles). LE8, determined by eight elements (nicotine, physical activity, diet, sleep, BMI, blood pressure, glucose, and lipids), was categorized into ideal, medium, and low groups based on AHA recommendation. Cox regression examined joint associations with incident CVD, adjusted for age, sex, race, education, income, alcohol, hyperthyroidism, depression, chronic kidney failure. Multiplicative/additive interactions assessed.

Results: Over 14.9-year median follow-up, 26,281 CVD cases occurred. Among individuals with ideal LE8, reduced muscle strength did not increase CVD risk (medium vs high: HR=0.91, 95%CI 0.79-1.05; low vs high: HR=1.04, 0.91-1.18). However, low muscle strength synergized with non-ideal LE8, and the highest risk was in low LE8/low muscle strength (HR=3.06, 2.75-3.41 vs ideal/high). Additive interaction existed between low LE8 and low muscle strength (RERI=0.47, 0.26-0.68; AP=15%, 8%-22%), indicating 15% of excess risk attributable to synergy.

Conclusion: Muscle strength decline alone does not elevate CVD risk in individuals with ideal LE8. However, low muscle strength significantly amplifies CVD risk in those with non-ideal LE8 due to synergistic interaction. Interventions targeting muscle strength in populations with lower LE8 may effectively reduce CVD burden.Keywords: Grip strength, LE8, CVD, Interaction, Precision prevention.

Key words： Grip strength, LE8, CVD, Interaction, Precision prevention.

论文 ID：220

Isolated Renin-Mediated Hypertension in a Middle-Aged Woman with Unilateral Renal Artery Stenosis: An Unusual Presentation of Takayasu Arteritis

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Background: Takayasu arteritis (TA) is a rare, chronic large-vessel vasculitis that primarily affects young women and typically presents with systemic symptoms or vascular complications. Renin-mediated hypertension due to renal artery stenosis is a known but uncommonly recognized manifestation of TA as a primary disease manifestation.

Case Presentation: A 42-year-old Sri Lankan woman was diagnosed with hypertension on 8 November 2024, after presenting to the Emergency Department with right-sided headache. She had no systemic symptoms. She was initially treated with amlodipine, which was later switched to enalapril due to persistent headache. Her first clinic follow-up with General Medicine was on 2nd January 2025, and she was subsequently evaluated in both Sri Lanka and Singapore.

On examination, her left carotid and left dorsalis pedis pulsations were reduced, while other peripheral pulses were normal. Blood pressure was higher in the lower limbs (189/90 mmHg right leg, 187/76 mmHg left leg) compared to the upper limbs (135/75 mmHg right arm, 131/75 mmHg left arm). There was no radio-radial delay or radio-femoral delay. Cardiovascular and respiratory examinations were unremarkable.

Investigations showed hypokalaemia (K+ 3.2mmo/L), likely secondary to hyperreninemia, and sinus tachycardia confirmed on ECG and 24-hour Holter monitor. Plasma renin was markedly elevated (2,563 uIU/mL; normal upper limit 46.1 uIU/mL). Serum aldosterone was 17.90 ng/dL, with a low aldosterone renin ratio (ARR 0.01).

Renal artery doppler ultrasound showed left renal artery stenosis. CT angiography confirmed this finding and revealed mural thickening of the infra-renal abdominal aorta, and multifocal thickening of left internal iliac artery, consistent with Takayasu arteritis. ESR was elevated at 63 mm/hr, supporting an underlying inflammatory process. She was started on prednisolone and azathioprine.

Conclusion: This case highlights the importance of considering TA as a differential diagnosis to fibromuscular dysplasia (FMD) in young or middle-aged women presenting with unexplained hypertension with renal artery stenosis. The presence of diminished peripheral pulses and markedly elevated serum renin, in the context of renal artery stenosis, should raise the clinical suspicion for this uncommon etiology. Vascular imaging, such as CT angiography, may be helpful in distinguishing between TA and FMD.

Key words: Renin-Mediated Hypertension; Unilateral Renal Artery Stenosis and Takayasu Arteritis

论文 ID：222

Long-term Exposure to Particulate Matter and The Incidence of Metabolic Syndrome and Its Components: A Prospective Cohort Study in Eastern China

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Background: Although epidemiological studies have suggested that particulate matter (PM) may contribute to an increased risk of metabolic syndrome (MetS), evidence on the long-term associations of PM exposure on the incidence of components of MetS are currently scarce and inconsistent. We conducted this prospective cohort study to investigate the associations of long-term exposure to particulate matter (PM) including of PM2.5 and PM10 with the incidence of metabolic syndrome (MetS) and its components, and explore the associations of exposure to PM2.5 and PM10 with the continuous metabolic indicators of MetS.

Methods: We utilized follow-up data collected from a cohort in Eastern China, encompassing 44,720 individuals between 2014 and 2021. Residential exposures to fine particles (PM2.5) and inhalable particles (PM10) for each participant were predicted using a satellite-based model with a spatial resolution of 1×1 km. We employed generalized estimation equations model to assess the associations of long-term PM exposures with incident MetS and its components, as well as the continuous metabolic indicators related to MetS. We also depicted the exposure-response (E-R) relationship curve to illustrate the relationship.

Results: For each 10 μg/m³ increase in annual average concentration of PM2.5, there was significant increases in the incidence of MetS (Relative risk: 1.173, 1.1-1.3), elevated triglycerides (TG) (1.170, 1.100-1.244), decreased high-density lipoprotein cholesterol (HDL-C) (1.182, 1.105-1.265), elevated fasting blood glucose (FBG) (2.046, 1.941-2.156), and elevated blood pressure (BP) (1.296, 1.169-1.437). The RR associated with PM10 were smaller compared to PM2.5 but still statistically significant. The analyses of continuous metabolic indicators indicated that long-term exposure to PM was positively associated with FBG and systolic BP, and inversely associated with HDL-C. In subgroup

analyses, we observed that the association between PM and MetS was significant only among non-smokers in the two smoking status subgroups, which is consistent with findings reported in previous cohort studies. Further stratified analyses indicated that association between PM and MetS was observed exclusively among individuals with lower educational attainment, a reasonable explanation is that individuals with lower education levels may be exposed to higher environmental PM concentrations. They may also have lower socioeconomic status, limited access to air conditioning, and fewer opportunities to obtain high-quality healthcare

Conclusions: This cohort study provides valuable evidence of the increased risk of MetS and its components associated with long-term exposure to PM in areas with high pollution levels. Furthermore, the effect of PM on elevated FBG, one of the components of MetS, is the most pronounced. Additionally, non-smokers and those with lower educational attainment demonstrated higher vulnerability to PM exposure. These associations were robust to the adjustment for gaseous pollutants. We also found significant positive associations between long-term exposure to PM2.5 and PM10 with FBG and SBP, along with a significant inversely association between long-term exposure to PM2.5 with HDL-C. These findings are valuable for revising air quality guidelines/standards and for targeted prevention in high-risk populations for MetS.

Key words Particulate matter; air pollution; long-term exposure; metabolic syndrome; cohort study.

论文 ID：223

Interplay Between Triglyceride-Glucose Index and Cardiovascular Events in Hypertensive Patients with Controlled Blood Pressure (SBP<140 mmHg): Insights from the SPRINT Trial

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Introduction: Hypertension significantly contributes to cardiovascular events and global all-cause mortality. The triglyceride-glucose (TyG) index, amarker of insulin resistance (IR), is an established risk factor for cardiovascular disease (CVD) events. This study examined the relationship between the TyG index and cardiovascular events in patients with controlled hypertension (SBP <140 mmHg).

Methods: We performed a post-hoc analysis of data from the Systolic Blood Pressure Intervention Trial (SPRINT), involving 9,323 participants with controlled hypertension. The triglyceride-glucose (TyG) index served as a surrogate marker for IR. Cox restricted cubic regression analysis and multivariate Cox regression models were employed to investigate the association between the TyG index and CVD outcomes, adjusting for established cardiovascular risk factors. The impact of intensive versus standard BP control on CVD risk associated with high IR levels were also analyzed.

Results: Over a median follow-up of 3.33 years, 725 CVD events were recorded. The TyG index was independently linked to a heightened risk of CVD events, with the highest quartile (Q4:8.93≤TyG<12.47) exhibiting a significantly greater risk (HR = 1.57, 95% CI: 1.18 - 2.08) compared to the lowest quartile (Q1: 6.74 ≤ TyG < 8.21). The significantly trend was seen only in the standard treatment group (p for trend = 0.001).

Conclusions: The TyG index is a robust predictor of CVD events in patients with controlled hypertension, and a stronger association between the TyG index and CVD risk was seen in the standard treatment group, but not in the intensive treatment group.

Key words Hypertension, Insulin Resistance, TyG Index, Cardiovascular Disease, Blood Pressure Control

论文 ID：225

Breaking the Mitochondrial Balance: How Testosterone Rewires the Heart via mTORC2/ATG9A

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Objectives: The role of sex hormones in postmenopausal hypertension has gained growing interest. This study investigates the mechanisms underlying testosterone-induced cardiomyocyte hypertrophy.

Methods: The H9C2 cardiomyocyte cell line was treated with 1 μM testosterone for 48 hours to establish an in vitro model of cardiomyocyte hypertrophy. Western Blot and immunofluorescence staining were performed to evaluate the expression of proteins and assess mitochondrial function. P-value < 0.05 was considered statistically significant.

Results:

1.mTORC2 Activation: Testosterone significantly increased ANP ($P<0.05$), p-Rictor ($P<0.05$), and mTORC2 ($P<0.0001$) levels, indicating mTORC2 pathway activation.

2.Autophagy Induction: LC3-II and ATG9A were upregulated ($P<0.05$), while P62/SQSTM1 was downregulated ($P<0.001$), suggesting enhanced autophagy.

3.Mitochondrial Remodeling: Expression of Fundc1 ($P<0.0001$), MFN2 ($P<0.01$), Drp1 ($P<0.05$), and Beclin-1 ($P<0.0001$) increased, indicating active mitophagy and mitochondrial dynamics. Moreover, TEM showed swollen mitochondria and increased autophagosomes after testosterone treatment.

4.ROS Accumulation: Testosterone significantly elevated ROS levels ($P<0.0001$), as shown by DCFH-DA staining and flow cytometry. Furthermore, JC-1 assay revealed decreased mitochondrial membrane potential ($P<0.001$), reflecting impaired mitochondrial integrity.

5. Mito-Tracker Red staining was used to observe mitochondrial morphology in H9C2 cells. The results showed that, compared with the control group, cells in the testosterone-treated group exhibited significantly reduced mitochondrial fluorescence intensity, along with abnormal morphological features such as punctate, fragmented, and aggregated mitochondria. These findings suggest disruption of the mitochondrial network, a decline in membrane potential, and impaired mitochondrial function.

Conclusion: Testosterone promotes cardiomyocyte hypertrophy by activating the mTORC2/ATG9A signaling pathway, leading to enhanced autophagy and mitophagy.

Key words: Testosterone, Cardiac hypertrophy, mitophagy, mTORC2, and Atga9.

论文 ID：236

Prevalence of High Blood Pressure and Its Association with Types of Obesity among School-Aged Children and Adolescents in Hainan Province

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Introduction: Childhood and adolescent hypertension is an increasingly significant public health issue worldwide. However, limited data are available on blood pressure (BP) status among youth in Hainan Province. This study aimed to assess the prevalence of high BP and its association with various types of obesity among school-aged children and adolescents in Hainan.

Methods: A multi-stage stratified random sample of 16 048 students aged 7-18 years was drawn from seven cities or counties in Hainan as part of the 2019 Hainan Student Physique and Health Survey. Participants were categorized into four obesity types: non-obese, general, central, and compound, which based on BMI and waist-to-height ratio. High BP was defined using national pediatric BP percentiles and hypertension guidelines. Descriptive statistics, ANOVA, and multivariate logistic regression (stratified by gender and adjusted for age, residence, and ethnicity) were used to assess associations.

Results: The overall prevalence of high BP was 9.7%. The prevalence rates of general obesity, central obesity, and compound obesity were 1.2%, 7.0%, and 6.3%, respectively. Logistic regression analysis demonstrated strong associations between central and compound obesity and high BP in males (OR = 2.07 and 2.94, respectively; $p < 0.001$) and females (OR = 1.60 and 2.59, respectively; $p < 0.001$). General obesity was significantly associated with high BP only in females (OR = 2.53; 95% CI: 1.39-4.35), but not in males.

Conclusion: This first province-wide study of pediatric BP in Hainan shows a notable prevalence of high BP and obesity, especially central and compound types. Despite being based on 2019 data, the findings remain relevant and highlight the need for ongoing monitoring and targeted interventions in tropical regions.

Key words high blood pressure, obesity, child, adolescent, Hainan province

论文 ID：237

Subclinical Cardiac Changes, Systolic Blood Pressure, and Cardiovascular Risk in Adults Without Cardiovascular Disease

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Background: Subclinical cardiac changes detected by echocardiography, such as left ventricular hypertrophy (LVH), left atrial enlargement, left ventricular dilation, and reduced ejection fraction, are associated with increased cardiovascular risk. However, it remains uncertain whether integrating such changes into risk assessment can inform blood pressure (BP)-lowering strategies, particularly in individuals without established cardiovascular disease (CVD).

Methods: We analyzed data from 15,825 adults free of CVD who underwent echocardiography as part of the China PEACE Million Persons Project in Guangdong Province (2016-2020). Participants were categorized based on the number of subclinical cardiac changes (0, 1, or 2-4) and stratified by baseline systolic BP (<130, 130-139, or ≥140 mm Hg). The primary outcome was total CVD, including coronary heart disease, myocardial infarction, stroke, heart failure, and cardiovascular death. Multivariable Cox regression was used to estimate hazard ratios (HRs), and model performance was assessed using C-statistics, net reclassification improvement (NRI), and integrated discrimination improvement (IDI).

Results: Over a median follow-up of 3.6 years, 1,472 participants experienced CVD events. A stepwise increase in CVD risk was observed with a higher number of subclinical cardiac changes, independent of BP levels. For instance, individuals with SBP 130-139 mm Hg and one subclinical change (HR 1.63, 95% CI 1.19-2.25) and those with SBP <130 mm Hg and 2-4 subclinical changes (HR 2.09, 95% CI 1.47-2.99) had significantly higher CVD risk compared to those with SBP ≥140 mm Hg but no subclinical changes. Incorporating

echocardiographic findings into the base risk model significantly improved discrimination (C-statistic from 0.737 to 0.740, P=0.001), NRI (0.232, P<0.001), and IDI (0.001, P<0.001). The estimated number needed to treat (NNT) over 3 years to prevent one CVD event was substantially lower among participants with mildly elevated BP and multiple subclinical cardiac changes (e.g., NNT=8 for SBP 120–139 mm Hg with ≥2 changes).

Conclusions: Echocardiographically detected subclinical cardiac changes provide incremental prognostic value beyond BP levels and may refine risk stratification for guiding antihypertensive treatment, especially among individuals with borderline or mildly elevated BP. Prospective trials are warranted to validate these findings and support the use of echocardiography in primary prevention.

Key words Blood pressure; Cardiovascular disease; Echocardiography

论文 ID：242

Bone Morphogenetic Protein 9 as a Novel Regulator of Hypertension: Targeting VSMC Phenotypic Switching for Vascular Remodeling

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Background: Hypertension is the most important risk factor for cardiovascular disease and death. However, the mechanism of hypertension has not been fully clarified. Bone morphogenetic protein 9 (BMP9) is known as an important regulator of vascular homeostasis. Recent studies have found that mutations in the gene encoding BMP9 are associated with elevated systolic blood pressure. Therefore, we studied the role of BMP9 in promoting hypertension.

Methods: The expressional profiles of BMP9 in plasma samples of hypertensive subjects and controls were determined by enzyme-linked immunosorbent assay.BMP9 transgenic rats (Tg) were constructed to analyze the function of BMP9. The blood pressure levels were measured

using the tail-cuff system and radiotelemetry methods. The role of BMP9 in vascular remodeling was determined by vascular relaxation studies.

Results: Circulating BMP9 concentrations, as determined by enzyme-linked immunosorbent assay, were significantly higher in hypertensive patients than in controls (251.07 ± 54.66 vs. 226.08 ± 56.70 pg/mL; $P < 0.01$). We found that the blood pressure levels of Tg rats were significantly higher than those littermates wild-type rats (WT). Besides, BMP9 overexpression caused dysfunctional vasoconstriction and vasodilation, remodeling of arterial walls, and increased vascular superoxide stress, inflammation, and collagen deposition. These findings indicate that BMP9 is a prohypertensive factor that directly promotes vascular remodeling. In order to explore the possible mechanism of the increase of blood pressure caused by BMP9, immunofluorescence staining method was used to detect the expression of BMP9 in vascular tissues. The results showed that BMP9 expression was increased and predominantly located in vascular smooth muscle cells (VSMC). In vitro, BMP9 improves contraction, proliferation, and migration in human artery smooth muscle cells (HASMC).

Conclusions: BMP9 acts on vascular smooth muscle, promoting vascular oxidative stress, inflammation and collagen deposition, leading to vascular remodeling and dysfunction, resulting in increased blood pressure. BMP9 may be a novel therapeutic target against pathological hypertension.

Key words: Hypertension, BMP9, Vascular smooth muscle, Vascular remodeling

论文 ID：243

Mitochondrial VDAC1-MCU Crosstalk Drives Pathological Cardiac Remodeling and Defective Mitophagy in Human iPSC-cardiomyocytes

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Hypertension-induced left ventricular hypertrophy (LVH) poses a significant global health burden, yet the underlying mechanisms linking mitochondrial dysfunction to disease progression remain poorly understood. Voltage-dependent anion channel 1 (VDAC1) and the mitochondrial calcium uniporter (MCU) are central regulators of calcium homeostasis and mitochondrial bioenergetics, but their pathogenic roles in hypertensive cardiomyopathy are undefined.

Here, we established a patient-specific disease model by differentiating induced pluripotent stem cells (iPSCs) from hypertensive LVH patients into cardiomyocytes (iPSC-CMs). Transcriptomic and functional analyses revealed profound mitochondrial perturbations, including reactive oxygen species (ROS) overproduction, impaired oxidative phosphorylation, and mitochondrial calcium overload, accompanied by upregulated VDAC1 and MCU expression. Mechanistically, co-immunoprecipitation demonstrated enhanced VDAC1-MCU interaction, driving pathological mitochondrial calcium influx. Genetic silencing of MCU (siMCU) or pharmacological inhibition of VDAC1 oligomerization (VBIT4) attenuated calcium overload, restored redox balance, and improved mitochondrial respiration. These interventions further mitigated maladaptive mitophagy (LC3II/I and p62 modulation) and cellular damage (reduced nuclear pyknosis and fibrosis).

Our findings identify the VDAC1-MCU axis as a critical mediator of mitochondrial dysfunction in hypertensive LVH, bridging organelle crosstalk to disease pathogenesis. By delineating this mechanistic nexus, we provide a translation framework for targeted therapy, including drug exploration, biomarker development, and precision medicine strategies, to counteract hypertensive cardiac remodeling.

Key words: hypertension, left ventricular hypertrophy, induced pluripotent stem cells, voltage-dependent anion channels, mitochondrial calcium uniporter

论文 ID：246

Prediction of Cardiometabolic Multimorbidity Risk in Middle-Aged and Older Chinese Adults: Longitudinal Analysis of Triglyceride Glucose-Body Mass Index (TyG-BMI) and Its Dynamic Trajectories

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Background: Current evidence lacks robust longitudinal studies examining the association between triglyceride glucose-body mass index (TyG-BMI) and cardiometabolic multimorbidity (CMM), despite the growing clinical significance of concurrent cardiometabolic diseases. This study aims to establish the predictive value of TyG-BMI for CMM development, characterize its dose-response relationship, and identify high-risk trajectory patterns in middle-aged and elderly Chinese adults.

Methods: We analyzed four waves of data (2011-2018) from the China Health and Retirement Longitudinal Study (CHARLS), involving 8,020 participants aged ≥45 years without baseline CMM (defined as ≥2 concurrent conditions: diabetes, stroke, or heart

disease). The nationally representative CHARLS cohort was established through multistage probability sampling. Cox regression and restricted cubic splines (RCS) evaluated hazard ratios and nonlinearity, while Longitudinal Targeted Maximum Likelihood Estimation (LTMLE) assessed dynamic TyG-BMI trajectories. Sensitivity analyses and subgroup stratifications were performed to ensure robustness.

Results: Over 9 years of follow-up, 409 participants developed CMM. Higher TyG-BMI quartiles were associated with progressively higher CMM incidence (Kaplan-Meier $P < 0.05$). A 1-SD increase in TyG-BMI was linked to a 43% higher CMM risk (adjusted HR = 1.43, 95% CI: 1.30 – 1.58). RCS analysis identified a nonlinear association ($P < 0.05$). Four TyG-BMI trajectories emerged: low stable, increasing, decreasing, and high stable. LTMLE analysis revealed that the high stable and increasing trajectories had significantly higher CMM risks (HR = 1.11, 95% CI: 1.09 – 1.14, and HR = 1.07, 95% CI: 1.04 – 1.10, respectively) compared to the low stable trajectory, while the decreasing trajectory showed a potential risk reduction. Subgroup and sensitivity analyses confirmed the consistency of these findings.

Conclusions: This study provides novel evidence that TyG-BMI is a strong, independent predictor of CMM development, with distinct nonlinear patterns and trajectory-dependent effects. The high-stable TyG-BMI pattern, reflecting sustained insulin resistance and obesity, conferred the greatest risk. These findings highlight TyG-BMI's potential as a clinical tool for early CMM risk stratification and personalized prevention strategies in aging populations.

Key words: cardiometabolic multimorbidity, CHARLS, TyG-BMI, insulin resistance, dynamic trajectory pattern

论文 ID：252

Endothelial Dysfunction Was Associated with Over 10-year Prognosis in Southern Chinese: A Retrospective Cohort Study

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Objective: To explore the relationship between endothelial dysfunction (ED) evaluated by brachial artery flow-mediated dilation (FMD) and long-term prognosis in southern Chinese.

Methods: This was a retrospective cohort study, including 1615 patients from the "Fuzhou Study" enrolled from 2000 to 2016. A cutpoint of brachial artery FMD < 8% was used to distinguish normal or abnormal vasodilation. Primary endpoint: all-cause death, secondary endpoints: non-fatal myocardial infarction and non-fatal stroke. Composite events included primary endpoint and secondary endpoints.

Results: After a median of 10 years, a total of 1229 participants were ultimately followed up, whom were then divided into normal endothelial function group (n=561) and ED group (n=668). Compared with subjects with normal endothelial function, patients with ED had higher rate of mortality (13.3% vs 5.2%, $p < 0.001$) and incidence of composite events (18.7%vs 8.6%, $p < 0.001$). After adjustment of age, gender, body mass index, blood pressure, heart rate, smoking, drinking, biochemical indicators and medication (antihypertensive medication, statin and antiplatelet drugs), the risk of all-cause death in ED patients was twice as those with normal endothelial function (HR 2.043, $p = 0.007$) and the risk of composite endpoint events was nearly twice (HR 1.788, $p = 0.005$). Moreover, ROC analysis conducted in elderly individuals (n=439) showed FMD combined with creatinine had a better discrimination for all-cause death than age.

Conclusions: FMD of brachial artery was associated with over 10-year prognosis in southern Chinese, ED increased the risk for all-cause mortality and composite events. In clinical practice, brachial artery FMD combined with creatinine may be used to predict all-cause death in elderly.

Key words：Keywords: Endothelial dysfunction, FMD, Long-term prognosis, Elderly.

论文 ID：255

Sex- and Age-Specific Associations Between Vitamin D Levels and Serum Uric Acid in Chinese Adults: A Nationwide Cross-Sectional Study

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Background: Vitamin D is essential for calcium homeostasis, bone health, and immune function, yet its association with serum uric acid (UA) remains uncertain. This study evaluates vitamin D status in Chinese adults and explores its sex- and age-specific relationships with UA and hyperuricemia (HUA).

Methods: We conducted a cross-sectional analysis of 15,116 males and 25,895 females from The China Precision Nutrition and Health KAP Real World Study (CPNAS). Smooth curve fitting visualized dose-response relationships, while multivariate regression assessed associations between vitamin D and UA/HUA. Subgroup analyses (age <70 vs. ≥70, male vs. female) explored potential variations.

Results: The study revealed a high prevalence of vitamin D deficiency (33.5%) and insufficiency (53%) in Chinese adults. Among males under 70 years, we observed an inverse J-shaped relationship between vitamin D and serum UA levels (p-nonlinear =0.046). Compared to those with vitamin D <22 ng/mL, participants with moderate levels (22-30 ng/mL) showed significantly lower UA (β=-5.40 to -4.36, all p <0.05), while no significant reduction occurred at higher concentrations (≥25.8-30 ng/mL, p>0.05). Notably, this association was absent in males ≥70 years. In contrast, females exhibited a consistent positive linear relationship between vitamin D and UA. These patterns were similarly observed for hyperuricemia risk in both sexes.

Conclusion: Vitamin D levels are differentially associated with UA and HUA based on sex and age, highlighting the need for personalized approaches in managing vitamin D and UA metabolism.

Key words: vitamin D, vitamin D deficiency, serum uric acid, hyperuricemia, Chinese cohort

论文 ID：257

Maternal Morning Hypertension and Adverse Pregnancy Outcomes

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Background: The prognostic significance of morning hypertension, including its quantitative magnitude and qualitative phenotypes, for adverse pregnancy outcomes (APOs) remains unclear. This study investigated associations between morning blood pressure (BP) parameters and APO risk.

Methods: This retrospective cohort study (Guangdong Women and Children Hospital, 2017–2022) included singleton pregnancies with ≥ 1 risk factor for hypertensive disorders of pregnancy (HDP) or HDP diagnosis. Morning systolic/diastolic BP, morning BP surge, and morning hypertension phenotypes were defined based on ambulatory blood pressure monitoring (ABPM). Multivariable logistic regression analyzed associations with APOs, adjusted for maternal age, pre-pregnancy body mass index, gravidity, parity, gestational week at ABPM,

and use of antihypertensive medications prior to monitoring. The morning surge model was additionally adjusted for 24h average SBP. Restricted cubic splines were employed to examine potential nonlinear relationships.

Results: Among 1,833 participants, 26.7% (n = 490) exhibited morning hypertension. Morning BP correlated strongly with nighttime BP (r = 0.78), but moderately with office BP (r = 0.41). Morning BP showed a nonlinear J-shaped association with APOs. Concurrent morning and nighttime hypertension posed the greatest risk (composite APOs aOR 3.16, 95% CI: 2.34–4.27). Isolated morning hypertension (composite APOs aOR 1.80) showed higher risk than isolated office hypertension (non-significant).

Conclusions: The association between elevated morning BP and increased risk of APOs is more pronounced in the presence of nighttime hypertension or non-dipping patterns, suggesting that circadian BP monitoring may play a role in risk stratification.

Key words: pregnancy, ambulatory blood pressure measurement, morning blood pressure, morning blood pressure surge, nighttime hypertension

论文 ID：264

Targeting the Endothelin-Notch1 Axis: Ambrisentan Attenuates Apatinib-Induced Hypertension in Hepatocellular Carcinoma Mice

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Background & Purpose:

Apatinib, an anti-angiogenic tyrosine kinase inhibitor (TKI), improves hepatocellular carcinoma (HCC) outcomes but causes dose-limiting hypertension via endothelinsystem activation. The downstream mechanisms remain unclear. Notch1 signaling regulates vascular tone and crosstalks with endothelin. This studyinvestigates whether the endothelin receptor

antagonist (ERA) ambrisentan ameliorates apatinib-induced hypertension by modulating the Notch1 pathway.

Research Methods:

1. Animal Model & Groups: HepG2 xenograft mice (BALB/c nude, n=10/group) were randomized into: ①Control: saline (0.2 mL/day, oral gavage); ②Apatinib: apatinib (100 mg/kg/day); ③Combination: apatinib (50 mg/kg/day) + ambrisentan (10 mg/kg/day) .Treatment duration: 28days.

2. Blood Pressure Monitoring:

（1）Non-invasive tail-cuff system (BP-2000)

（2）Measurements: 4×/week (9:00–11:00 AM)

3. Sample Analysis:

（1）Serum: ELISA for endothelin-1 (ET-1) and angiotensin II (Ang II).

（2）Tissue:①Western blot for NICD1 (Notch1 intracellular domain) and Hes1 in tumors/aortas. ②Dual immunofluorescence: ETAR/Notch1 co-localization in aortic endothelium.

4. Vascular Function: ①Ex vivo aortic ring assay: Cumulative ET-1 stimulation (10^{-10} to 10^{-7} M); ②Calculation of Emax (maximal contraction) and EC_{50}.

5. Statistical Analysis:ANOVA with Tukey's post-hoc test (GraphPad Prism 9.0). Significance: *p* < 0.05.

Research Results:

1. Hypertension Attenuation:

（1）Apatinib increased systolic blood pressure (SBP) by 28.4 ± 3.2 mmHg vs. control (*p* < 0.001).

（2）Combination therapy normalized SBP (ΔSBP: +5.1 ± 2.1 mmHg vs. apatinib; *p* < 0.001).

2. Endothelin-Notch1 Pathway Activation:

Target	Apatinib vs. Control	Combination vs. Apatinib

Target	Apatinib vs. Control	Combination vs. Apatinib
Serum ET-1	↑2.8-fold (*p* < 0.001)	↓50% (*p* = 0.002)
Aortic NICD1	↑3.5-fold (*p* < 0.001)	↓58% (*p* < 0.001)
Tumor Hes1	↑2.1-fold (*p* = 0.004)	↓52% (*p* = 0.006)
ETAR/Notch1 co-localization	↑2.7-fold (*p* < 0.001)	↓65% (*p* < 0.001)

3. Vascular Hyperreactivity:

Apatinib enhanced aortic sensitivity to ET-1: Emax ↑35% (*p* = 0.007) EC_{50} ↓3.2-fold (*p* = 0.003); Ambrisentan restored normal vascular reactivity.

4. Preserved Antitumor Efficacy:

Tumor growth inhibition: Apatinib: 71.5 ± 6.2%; Combination: 68.3 ± 7.1% (*p* = 0.28 vs. apatinib).

Research Conclusion:

1. Ambrisentan effectively reverses apatinib-induced hypertension by blocking ETAR-Notch1 crosstalk, evidenced by: Suppression of NICD1 cleavage and Hes1 expression. Normalization of vascular hyperreactivity.

2. First demonstration that Notch1 signaling is a key downstream effector in TKI-induced hypertension.

3. Ambrisentan does not compromise apatinib's antitumor efficacy in HCC models.

4. These findings support clinical translation of ERAs for managing TKI-related cardiovascular toxicity and validate Notch1 as a predictive biomarker.

Key words: Notch1 signaling; Endothelin receptor antagonist; Apatinib; Hypertension; Treatment-related toxicity; Hepatocellular carcinoma

论文 ID：274

Investigation of Therapeutic Inertia and Influencing Factors in Primary Care Physicians during Hypertension Diagnosis and Treatment Process

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Background: Hypertension is a common chronic disease that seriously endangers the health of the population. The primary-care doctors are the main force in the management of hypertension. However, the doctor-induced therapeutic of inertia greatly affects the achievement of primary-care hypertension control. Objective The aim of this study is to investigate the current status of therapeutic inertia among primary healthcare providers in the diagnosis and treatment process of hypertension, and analyze the causes of therapeutic inertia, providing a reference basis for improving hypertension control rates in China.

Methods: A simple random sampling method was used to distribute questionnaires to primary healthcare providers in 32 primary healthcare institutions in Tianjin from July to August 2023. The therapeutic inertia in the diagnosis and treatment process of hypertension was evaluated from three dimensions: "soft reasons" and "overestimation of treatment efficacy" as well as "medical insurance policies". Binary Logistic regression analysis was employed to explore the influencing factors of therapeutic inertia.

Results: A total of 407 questionnaires were distributed in this study, and 386 valid questionnaires were collected, yielding an effective response rate of 94.84%. The average score for primary healthcare providers' knowledge of hypertension diagnosis and treatment was 6（0.5）, with a scoring rate of 61.11%（5.50/9.00）. The total score for therapeutic inertia in hypertension management was 48（7.0）, with a scoring rate of 56.55%（45.24/80.00）. The scores for the "soft reasons" dimension, "overestimation of treatment efficacy" dimension, and "medical insurance policies" dimension were 26（4.8）, 10（2.0）, and 6（2.5） respectively, with scoring rates of 51.92%（25.96/50.00）, 65.40%（9.81/15.00）, and 46.40%（6.96/15.00） respectively. When comparing the average scores

of the three dimensions of therapeutic inertia, the "overestimation of treatment efficacy" dimension had the highest score compared to the other two groups (P<0.05). Multivariate analysis indicated that gender, region, mastery of hypertension diagnosis and treatment, and a daily voulme of hypertensive individuals treated are the main factors influencing Therapeutic inertia among primary care physicians (P<0.05).

Conclusion: Therapeutic inertia is prevalent among primary healthcare providers in the diagnosis and treatment process of hypertension. Low levels of hypertension treatment cognition, "overestimation of treatment efficacy", and "soft reasons" are the primary factors contributing to therapeutic inertia among primary healthcare providers. It is recommended to strengthen education on therapeutic inertia in hypertension, conduct diversified training on diagnostic and management knowledge, and promote clinical informatization and artificial intelligence decision-making systems to effectively improve the therapeutic inertia of primary healthcare providers in hypertension management.

Key words: Hypertension; Community management; Primary care doctors; Physician cognition; Therapeutic inertia; Tianjin

论文 ID：279

Impact of Early Intensive Lipid-Lowering Therapy on Lipid Goal Attainment in Chinese ACS Patients: Preliminary Results from a Prospective Multicenter Study (ELITE-ACS)

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Background: In China, acute coronary syndrome (ACS) patients exhibit suboptimal lipid goal attainment and high recurrent event rates. While PCSK9 inhibitors offer potent lipid-

lowering effects, real-world evidence supporting their early initiation in Chinese ACS populations is limited. This study assessed the impact of early in-hospital intensive lipid-lowering therapy (LLT) on achieving lipid targets.

Methods: This preliminary analysis of the prospective, multicenter, real-world study (ELITE-ACS), which planned enroll 6,000 ACS patients across 30 hospitals. Participants were categorized by initial in-hospital LLT: statin, statin+ezetimibe, PCSK9 inhibitor±statin. Primary endpoint was the LDL-C goal attainment (<1.4 mmol/L) rates across treatment arms at discharge and 1, 3, 6, and 12 months. Secondary endpoints included time to LDL-C goal attainment, magnitude of LDL-C reduction, and major adverse cardiovascular events.

Results: Among 1611 enrolled patients analyzed (November 2022-January 2025, statin: statin+ezetimibe: PCSK9 inhibitor±statin=784:331:496), PCSK9 inhibitor therapy achieved significantly greater LDL-C reductions (discharge: -34.11% vs. -20.96%/-15.91%; 6 months: -52.87% vs. -40.55%/-37.95%; all P<0.001) and higher LDL-C goal attainment rates (discharge: 27.6% vs. 8.7%/4.5%; 6 months: 42.7% vs. 33.9%/22.4%; all P<0.001). Furthermore, PCSK9 inhibitors significantly reduced lipoprotein(a) levels by 24.01% and 37.29% at 1 and 3 months post-discharge, respectively. A numerically lower MACE incidence was observed with PCSK9 inhibitors (2.6% vs. 6.1%/5.4%; P=0.037), though Kaplan-Meier analysis showed no statistical difference (P=0.204).

Conclusion: Early in-hospital PCSK9 inhibitor initiation significantly improves LDL-C goal attainment in Chinese ACS patients, demonstrating its potential for optimizing real-world management and providing crucial evidence for intensive lipid-lowering strategies, though longer follow-up is warranted to assess its impact on cardiovascular outcomes.

Key words：Acute Coronary Syndrome; PCSK9 Inhibitors; Early Intensive Lipid-Lowering Therapy; Real-World Evidence; Lipid Goal Attainment

论文 ID：280

Association Between Post-Saline Infusion Test Plasma Aldosterone Concentration levels and Nocturnal Hypertension

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Purpose: Nocturnal hypertension (NH) is recognized as a risk factor for target organ damage and all-cause mortality. The plasma aldosterone concentration (PAC) is associated with NH in primary aldosteronism (PA) patients. The post-saline infusion test plasma aldosterone concentration (post-SIT PAC) shows autonomous aldosterone secretion levels. However, the association between post-SIT PAC and NH is undefined. Thus, we aim to assess the association between post-SIT PAC levels and NH.

Methods: Based on the aldosterone-to-renin ratio, and current guideline-recommended results of the saline suppression test, patients who underwent a saline infusion test (SIT), were categorized into three groups: negative (post-SIT PAC < 50 pg/mL, n=86), borderline (post-SIT PAC 50 - 100 pg/mL, n=180), and positive (post-SIT PAC > 100 pg/mL, n=75). Restricted cubic spline plots (RCS) were employed to investigate the dose-response relationship between post-SIT PAC and NH. Multivariable logistic regression models were used to adjust for confounders.

Results: In this cross-sectional study, the post-SIT PAC was positively associate with NH and shows a significant nonlinear trend (P-nonlinear < 0.05). After multivariable adjustment, post-SIT PAC was significantly positively correlated with NH (OR = 1.007; 95% CI:1.000-1.013; P < 0.05). However, the basal PAC itself was not significantly correlated with NH. In addition, the guideline-defined subgroups with higher post-SIT PAC show higher prevalence of NH (P < 0.05).

Conclusion: The autonomous aldosterone secretion level, not the basal aldosterone level itself, is relevant to NH in all patients undergoing SIT. In addition, the prevalence of NH increases nonlinearly with higher post-SIT PAC levels.

Key words: Ambulatory blood pressure monitoring, autonomous aldosterone secretion, primary aldosteronism, saline infusion test, hypertension.

论文 ID：284

Study on Hypertension Intervention Based on Dual-Channel Integration Model: Synergistic Effects of Narrative Resonance and Cognitive Closed-Loop

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Objective: The purpose of this article is to investigate the mechanism by which a dual-channel integration model of narrative resonance and cognitive closed-loop enhances hypertension-related health literacy, thereby effectively improving blood pressure control, metabolic parameters, and quality of life in patients with hypertension.

Methods: A total of 103 patients with essential hypertension who met the diagnostic criteria specified in the Chinese Guidelines for the Prevention and Treatment of Hypertension (2023) were enrolled and randomly divided into an intervention group (n=52) and a control group (n=51). The intervention group received a 12-week dual-channel intervention, consisting of emotional intervention (WeChat-based delivery of three types of scenario-based cases based on narrative medicine) and cognitive intervention (Teach-back closed-loop pathway combined with real-time feedback).The control group received routine community management (once-monthly outpatient follow-up + paper manuals). Differences in systolic blood pressure (SBP), diastolic blood pressure (DBP), metabolic indicators, medication adherence, hypertension knowledge scores, and quality of life scores were compared between the two groups before and after intervention.

Results: There were no significant differences in baseline demographic characteristics between the two groups (all $P>0.05$). After 3 months of intervention, the intervention group showed a reduction in SBP of 15.22±6.4 mmHg and a reduction in DBP of 9.02±3.6 mmHg compared with baseline, which were significantly better than those in the control group

(P<0.001). In the intervention group, body weight, BMI, total cholesterol, and low-density lipoprotein cholesterol (LDL-C) improved significantly (P<0.05), and the uric acid level decreased significantly within the group (P<0.001). The hypertension knowledge score in the intervention group increased by 4.93±2.40 points, and the quality of life score increased by 15.34±7.68 points, both of which were significantly higher than those in the control group (P<0.01). There was no significant difference in the number of medications taken between the two groups, but the intervention group had more medical visits (3.13±0.91 vs 2.11±0.78, P=0.001).

Conclusion: The dual-channel integration model can effectively improve blood pressure and metabolic indicators in hypertensive patients, enhance disease cognition and quality of life, and provide a new strategy for chronic disease management.

Key words: Hypertension, Narrative medicine,Teach-back, Blood pressure control, Randomized controlled trial

论文 ID：285

The Effect Modification of Systolic Blood Pressure on the Association of Frailty and Cardiovascular Disease in Community-dwelling Adults

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Background: Frailty has been increasingly recognized as an important predictor of cardiovascular disease (CVD) risk; however, the modifying role of systolic blood pressure (SBP) in this association remains unclear. This study aimed to investigate the impact of SBP on the relationship between frailty and CVD risk.

Method: This study utilized data from the China Health and Retirement Longitudinal Study (CHARLS), including 7,210 community-dwelling adults aged ≥45 years. Frailty status was assessed using a constructed frailty index, and participants were stratified based on SBP levels. The primary outcome was incident CVD events during follow-up. Cox proportional

hazards models were employed to examine the association between frailty and CVD risk, with SBP evaluated as an effect modifier.

Results: During 53,531 person-years of follow-up, 1,663 CVD events occurred, with an overall incidence of 31.1 per 1,000 person-years. Frailty was associated with a higher CVD incidence, particularly among those with SBP 120–129 mmHg (HR 3.13, 95% CI 2.22–4.42). The risk increase was 28% (SBP < 120 mmHg), 54% (120–129 mmHg), and 25% (≥130 mmHg) per SD frailty index increment. Restricted cubic spline analysis showed a nonlinear trend, with risk leveling off in low and high SBP groups but rising steadily in the 120–129 mmHg category. Frailty consistently increased CVD risk across all SBP strata.

Conclusions: Frailty is a significant risk factor for CVD, and SBP modulates this relationship.

Key words: Effect Modification, Frailty, Cardiovascular Disease

论文 ID：292

Sudden Cardiac Death in Chronic Kidney Disease

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Background: Patients with chronic kidney disease (CKD) are recognized as a higher risk group for cardiovascular disease (CVD) due to various traditional risk factors, kidney-specific factors, and comorbidities, which has recently attracted significant attention. However, the long-term risk of acute CVD events such as sudden cardiac death (SCD) in CKD patients is unclear. Using data from two large-scale cohorts of >450,000 participants, this study aimed to assess the long-term association of CKD and SCD risk, as well as combined with circulating proteins to identify candidate proteins to predict SCD risk.

Methods: In the exploration cohort, a total of 349,648 participants from the UK Biobank were included. In the validation cohort, 111,119 population with available data from

Changsha cohort were enrolled. The exposure was CKD diagnosis and the endpoint was incident SCD in the present study. Associations of CKD and SCD were estimated using Cox proportional hazard models. Key proteins were analyzed using t-test, multiple linear regression, Cox proportional hazard models, and LASSO regression.

Results: During the median follow-up of 13.63 years in exploration cohort and 8.00 years in valiadtion cohort, CKD was associated with the increased risk of SCD (Exploration cohort: HR: 1.33; 95% CI: 1.22-1.45; P<0.001; Validation cohort: HR: 1.87; 95% CI: 1.05-3.33; P=0.037) in final adjusted model. The results remained robust in the series of sensitivity analyses. Further stratified analyses by CKD stage revealed that individuals with both early-stage and advanced-stage kidney disease exhibited a significantly higher risk of SCD compared to those without renal disease. After the 3-step analysis in circulating proteins, five key CKD-associated proteins were shown to be involved in SCD risk. Notably, in the proteomic analysis replication cohort from Framingham Offspring Cohort, both NT-proBNP (N-terminal pro-brain natriuretic peptide) and FGF23 (Fibroblast growth factor 23) retained significant predictive value for SCD risk among individuals with CKD.

Conclusions: Patients with CKD have an increased risk of SCD in the long term, underscoring the imperative for strategies that address both cardiovascular risk and renal function in this population. FGF23 and NT-proBNP show potential as valuable candidate proteins for predicting and managing SCD risk among CKD patients.

Key words: Sudden cardiac death; Chronic kidney disease; Cardiovascular disease; Circulating protein

论文 ID：295

Association between Obesity Status and Hypertension Phenotypes: Are Inflammatory Indicators the Missing Link? Evidence from A Large Population Study

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Background: Hypertension exhibits variability in diagnosis and treatment across phenotypes. Obesity and metabolic disorders are key risk factors, interacting with inflammatory states. This study explores their associations with hypertension phenotypes and the mediating role of inflammation.

Methods: This study analyzed 17,158 participants from NHANES (2007–2018). Associations were evaluated using weighted generalized linear models, with the ROC curves identifying optimal obesity indices. Stratified analyses were conducted by gender, lifestyle, and diet. Mediation analysis assessed inflammation's role, with effect sizes calculated via the Sobel test.

Results: Among six obesity indicators, Weight-Waist Index (WWI) was better for Isolated Systolic Hypertension (ISH) (area under curve[AUC]:0.64, 95%confidence interval[CI]:0.62-0.67), Waist Circumference (WC) was better for Isolated Diastolic Hypertension (IDH) (AUC:0.68, 95%CI:0.67-0.69). High WC/WWI without metabolic disorders linked to IDH (odds ratio[OR] 3.02, 95% CI 1.57–5.82), not ISH or Systolic-Diastolic Hypertension (SDH) ($P > 0.05$). High WC/WWI with metabolic disorders associated with all phenotypes (IDH: OR 3.62, 95% CI 2.19–5.97; ISH: OR 1.76, 95% CI 1.09–2.84; SDH: OR 2.04, 95% CI 1.25–3.34). Inflammation mediated partially: 6.44% via RBC in IDH (non-obese metabolic disorders, $P<0.001$), 18.4% via LBDMONO in ISH (obese without metabolic disorders, $P<0.05$). Stratified analyses showed phenotype-specific differences: IDH non-significant, ISH by smoking, SDH by age.

Conclusion: High WC without metabolic disorders is linked to IDH, while metabolically disordered obesity correlates with all phenotypes. These effects are mediated by distinct variables, aiding phenotype-specific diagnosis and treatment.

Key words: Obesity; Metabolic Disorders; Hypertension Phenotypes; Inflammation; Mediation Analysis; NHANES

论文 ID：297

Association between Control of Cardiovascular Risk Factors and All-cause Mortality in Population with Stage 4 of Cardiovascular-Kidney-Metabolic Syndrome

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Objective: The American Heart Association (AHA) proposed the concept of Cardiovascular-Kidney-Metabolic (CKM) syndrome in 2023, reflecting the growing emphasis within the medical community on the interrelated nature of cardiovascular diseases, kidney diseases, and metabolic disorders. Although existing evidence has demonstrated that intensive single-factor interventions significantly improve prognosis in different populations, it remains unclear whether intensive multifactorial intervention can reduce all-cause mortality risk among the population with stage 4 of CKM syndrome compared with earlier stages such as stage 3.

Methods: This study is based on the Kailuan cohort, which included 4,991 participants with stage 4 of CKM syndrome and matched them with 9,980 control individuals with stage 3 based on age(±1 years) and sex. We determined the stages of CKM syndrome according to the definition by the AHA. Intensive control targets included: (1) blood pressure (SBP <130 mmHg); (2) lipid-lowering (LDL-C) targets instructed by current AACE guidelines, stratified according to subtypes of stage 4 of CKM syndrome; (3) glucose (FPG <6.1 mmol/L); and (4) weight management (BMI <23 kg/m²). The primary outcome was all-cause mortality. Analyses were conducted using multivariable-adjusted Cox proportional hazards regression models, supplemented by subgroup and sensitivity analyses.

Results: In population with stage 4 of CKM syndrome, those with 0 controlled risk factors showed significantly increased risk of all-cause mortality (fully adjusted HR 1.63, 95%CI 1.43-1.86) compared with control group. Conversely, patients with all 4 risk factors controlled exhibited non-significant risk of outcome (fully adjusted HR 1.09, 95%CI 0.83-1.43) (Table 1). Subgroup and sensitivity analyses yielded consistent results (Table 2-3).

Conclusions: Population with stage 4 of CKM syndrome who had controlled blood pressure, lipids, glucose and BMI attain comparable all-cause mortality risk to Stage 3 counterparts related with 10-year ASCVD high-risk status. This evidence establishes comprehensive management of cardiovascular risk factors as a pivotal strategy for ameliorating prognosis in advanced-stage CKM syndrome, providing a theoretical foundation for optimizing therapeutic interventions.

Key words: Cardiovascular risk factors; Cardiovascular-Kidney-Metabolic Syndrome

论文 ID：302

LncRNA CoroMaker Promotes Atherosclerotic Plaque Instability by Enhancing N6-methyladenosine Reader IGF2BP2 Dependent Stabilization of RIPK1: Implication in Atherosclerosis

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Background: We previously identified lncRNA CoroMarker as a novel diagnostic biomarker for coronary artery disease (CAD), but its specific molecular mechanism remains unclear. Atherosclerosis is the common pathogenetic basis of CAD, and this study aimed to explore the role and mechanism of CoroMarker on the atherosclerotic plaque instability.

Methods: The full-length sequence and intracellular location of CoroMarker were determined in endothelial cells (ECs), and qRT-PCR and FISH assays identified CoroMarker expressed in the atherosclerotic plaques of CAD patients. ApoE-/- mice were administrated with adeno-associated virus (AAV) carrying human CoroMarker vector and

followed by 14-week high fat feeding. Interaction of CoroMarker binding to IGF2BP2 and recognizing RIPK1 through m6A methylation were revealed by bioinformatic prediction, mass spectrometry and RIP-sequencing analyses, and further confirmed by gain- and loss-function assays. The plaque instability was assessed by detecting angiogenesis, and the expression levels of adhesion molecules and inflammatory cytokines.

Results: CoroMarker was abundantly expressed in the cytoplasm of ECs, and was upregulated in the circulating ECs and plaques of CAD patients. AAV-mediated overexpression of CoroMarker exacerbated atherosclerotic plaques instability in ApoE-/- mice. Adding ox-LDL promoted angiogenesis, and enhanced the expression levels of adhesion molecules and inflammatory cytokines in HUVECs, which were exacerbated by CoroMarker overexpression while inhibited by CoroMarker knock-down. RNA pull-down and RNA Immunoprecipitation (RIP) found CoroMarker bond to IGF2BP2 and increased m6A methylation-dependent RIPK1 stability to activate IKK signaling. Mutations of CoroMarker binding to IGF2BP2, m6A methylation inhibition and knock-down of IGF2BP2 or RIPK1, all abolished the pro-atherosclerosis effect of CoroMarker in HUVECs.

Conclusion: CoroMarker promotes atherosclerotic plaque instability through binding to IGF2BP2 and increased m6A methylation-dependent RIPK1 stability in ECs, which may help understanding the AS pathogenesis and find novel therapeutic targets for preventing plaques rupture.

Key words： LncRNA CoroMaker, IGF2BP2, m6A methylation, RIPK1, atherosclerosis, plaque instability

论文 ID：304

Effect of Amlodipine-based Therapy on TTR and Long-term BPV in Chinese Primary Hypertension Patients across Age Groups: A Retrospective Study

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Background: To compare the systolic blood pressure (SBP) time in target range (TTR), long-term blood pressure variability (BPV) and BP control among the different age groups (18-45, 46-64, 65-79, ≥80 years old) in primary hypertension patients treated with amlodipine-based antihypertensive therapy (≥12 months).

Methods: Data comes from adult patients treated with amlodipine-based antihypertensive therapy at the time of enrollment from the China Hypertension Center. We extracted demographic information, BP measurements, and laboratory tests and discussed the differences between baseline characteristics, SBP TTR, long-term BPV and BP control among the different age groups.

Results: A total of 36,153 patients were involved, including 2,681, 14,300, 15,595, 3,577 patients in each group. Young and middle-aged groups demonstrated better indictors improvement. The SBP TTR declined with age, 82.52±19.68%, 81.98±20.69%, 79.10±22.96%, 78.33±23.50%, with significant difference (p value < 0.001). The BP control decreased with age, 84.04%, 83.20%, 80.44%, and 79.59%, with significant difference (p value < 0.001). BPV showed an increasing trend with age, although no significant statistical difference (p value = 0.051). During the follow-up period, SBP TTR and BP control increased, while BPV decreased and most of the differences were significant.

Conclusions: In all age groups, SBP TTR remained above 78% throughout the overall follow-up period. Regardless of age, long-term continuous use amlodipine is beneficial to achieve higher and smoothly BP control, further improving the long-term prognosis of hypertensive patients.

Key words: amlodipine, age-specific, blood pressure variability, time in target range, blood pressure control rate

论文 ID：314

“U”-Shaped Association Between Plasma Vitamin D Levels and Serum Homocysteine in a Large Chinese Adult Population: Implications for Precision Vitamin D Nutrition

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Background: Vitamin D (VD) deficiency and elevated homocysteine (Hcy) levels are both well-established risk factors for cardiovascular disease (CVD). However, the relationship between VD and Hcy remains unclear. This study aimed to explore the association between plasma VD levels and serum Hcy concentrations, as well as the risk of hyperhomocysteinemia (HHcy), in a large Chinese population.

Methods: This study analyzed baseline data of 40,906 individuals from the China Precision Nutrition and Health-KAP (Knowledge, Attitude, and Practice) Real-World Study (CPNAS), with a median age of 65.4 years (IQR: 58.1 – 71.4), and 63.2% females. Multivariable linear regression was performed to evaluate the association between baseline plasma VD and serum Hcy. Logistic regression was used to assess the relationship between VD and HHcy. To investigate potential nonlinear associations, smooth curve fitting was applied. Additionally, subgroup analyses were conducted to explore potential effect modification by factors such as age, sex,BMI, smoking, and key nutritional or genetic markers.

Results: VD levels were positively associated with both Hcy and HHcy before accounting for covariables. After adjusting for age and sex, U-shaped relationships emerged between VD-Hcy and VD-HHcy, which remained significant following further multivariable adjustments. When plasma VD levels were categorized into quintiles, individuals in quintiles Q1 – Q3 (VD < 24.3 ng/mL) and Q5 (VD ≥ 28.2 ng/mL) had significantly elevated Hcy concentrations (by 0.16 μmol/L) and increased risks of HHcy (by 11% and 10%, respectively)

compared with those in Q4 (24.3–28.2 ng/mL). Subgroup analyses revealed that the U-shaped relationship was more pronounced among males.

Conclusions: In this large sample of Chinese adults, plasma VD levels demonstrated a U-shaped association with serum Hcy and the risk of HHcy, and more pronounced among males. If confirmed by further research, these findings may have important implications for precision vitamin D supplementation and CVD prevention.

Key words: Vitamin D, Homocysteine, Hyperhomocysteinemia, Cardiovascular Disease, Cross-sectional study

论文 ID：330

A Self-amplifying Loop Linking mtDNA Release to Vascular Endothelial Inflammation via TBK1-mediated VDAC1 Phosphorylation in Hypertension

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Aims: Inflammatory injury of vascular endothelium serves as a critical pathophysiological basis for hypertension-associated vascular diseases. Mitochondrial DNA (mtDNA), acting as a damage-associated molecular pattern, can potently activate inflammatory responses. However, the regulatory mechanisms governing mtDNA release and its specific role in hypertension remain to be fully elucidated.

Methods and results: Here we report that hypertensive patients exhibited significantly elevated levels of cell-free mitochondrial DNA (cf-mtDNA) in plasma, which strongly correlated with blood pressure and vascular dysfunction. Notably, antihypertensive treatment effectively reduced cf-mtDNA levels in these patients. Parallel observations were made in hypertensive mouse models. Through systematic screening of mtDNA downstream pathways, we demonstrated that mtDNA triggered vascular endothelial inflammation via activation of the cGAS-STING-TBK1 signaling axis. Genetic ablation of STING, either globally or specifically in endothelium, markedly attenuated hypertensive vascular

inflammation and improved endothelial function. Mechanistically, integrated multi-omics analyses and functional studies revealed that TBK1 phosphorylated VDAC1 at Ser104, promoting its oligomerization and subsequent mtDNA release. Both VDAC1-S104A mutation and pharmacological inhibition of VDAC1 oligomerization reduced endothelial mtDNA release, suppressed cGAS-STING pathway activation and restored endothelial function.

Conclusion: Collectively, these findings elucidate a self-amplifying cycle of "mtDNA release-cGAS-STING activation-TBK1-mediated VDAC1 phosphorylation and oligomerization-further mtDNA liberation" in hypertensive endothelium. Our work not only advances the "mitochondria-inflammation" paradigm in hypertensive vascular injury but also opens new avenues for developing mechanism-based interventions against vascular complications in hypertension.

Key words: Hypertension; Endothelial dysfunction; Inflammation; mitochondrial DNA; VDAC1

论文 ID：335

The Cross-sectional Association between Multimorbidity and Sleep Quality and Duration among the Elderly Community Dwellers in Northwest China

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Background: Multimorbidity, defined as the coexistence of two or more chronic diseases, is highly prevalent among the elderly population and is associated with adverse outcomes. However, little is known about its relationship with sleep issues, particularly in this

demographic. Therefore, this study aimed to investigate its association with sleep quality and duration among the elderly.

Methods: This cross-sectional study conducted in Emin County, Xinjiang, China, which included a population aged 60 years and above. We employed the Pittsburgh Sleep Quality Index (PSQI) score to assess sleep quality and duration. Multimorbidity was determined through self-reports, physical examination, blood tests, and imaging. Logistic regression analyses were used to explore the association between multimorbidity and sleep patterns, adjusting for confounders.

Results: A total of 8205 elderly participants were included of whom 66.8% suffered from multimorbidity. Participants with multimorbidity exhibited higher total PSQI scores [6 (3,9)], and a higher percentage of poor sleep quality (50.6%), compared to those without multimorbidity. Multimorbidity was significantly associated with the presence of poor sleep quality (OR=1.27, 95% CI: 1.14-1.41, P<0.001) before and after adjusting for confounders, The risk of having poor sleep quality significantly increased as the number of multimorbidity increased. The OR (95% CI) values were 1.16 (1.02,1.32) for two diseases, 1.54 (1.26,1.90) for ≥5 diseases. In the adjusted model for total participants, having four diseases (OR=1.26, 95% CI: 1.05-1.51, p=0.013) and five or more diseases (OR=1.29, 95% CI: 1.03-1.61, p=0.029) were associated with shorter sleep duration. Furthermore, those with five or more diseases associated with longer sleep duration (OR=1.40, 95% CI: 1.00-1.95, p=0.057).

Conclusion: There is a significant association between multimorbidity and poor sleep quality in older community dwellers, which may provide clues for disease prevention.

Key words：multimorbidity, sleep quality, sleep duration, elderly

论文 ID：343

Unveiling Geographical Correlations, Gender - Specific Traits, and Global Health Burden Gaps of Pulmonary Arterial Hypertension in Women of Reproductive Age: Insights from GBD 2011 - 2021 Data

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Aim: To evaluate the impact of geographical factors on pulmonary arterial hypertension (PAH) among women of reproductive age (WRA).

Methods: This investigation analyzed data from the Global Burden of Disease (GBD) database for 2011 - 2021, combining Geographic Information Systems (GIS) with pulmonary hypertension incidence and case fatality rates. Disease records were geocoded to establish precise location linkages. GIS integrated geospatial data across global administrative divisions, establishing location as a primary analytical variable. All point estimates incorporated 95% uncertainty intervals (UIs). Joinpoint regression models examined global and regional trends in incidence and mortality rates from 2011 - 2021, calculating the annual percentage change (APC), average annual percentage change (AAPC), and 95% confidence intervals (CIs).

Results: In 2021, PAH incidence and mortality rates were most pronounced in Asia and Africa compared to Europe and the Americas. Among women of reproductive age, the 45 - 49 age group demonstrated the highest incidence, while the 40 - 44 age group exhibited the highest mortality. PAH accounted for 103,151 disability-adjusted life years (DALYs) and 8,690 years of life lost (YLLs). Globally, from 2011 to 2021, PAH incidence increased significantly (AAPC = 0.33%, 95% CI: 0.30 - 0.41; $P < 0.001$), while mortality decreased (AAPC = -1.66%, 95% CI: -1.77 to -1.54; $P < 0.001$). Incidence correlations revealed strong associations between male cases and the overall population ($r = 0.97$), moderate correlations for female cases with the overall population ($r = 0.42$) and male cases ($r = 0.41$), and weak female-altitude correlation ($r = 0.15$) compared to males and the overall population ($r = 0.01$). For case fatality rates, male, female, and overall rates demonstrated high correlation ($r = 0.94$),

with moderate male-female correlation (r = 0.78). Altitude showed weak associations with male (r = 0.22), overall (r = 0.18), and female (r = 0.10) mortality, indicating limited influence.

Conclusions: Recent evidence indicates a weak but significant relationship between altitude and PAH among WRA in high-altitude regions, highlighting the importance of targeted surveillance. Similarly, altitude shows comparable associations with male PAH outcomes.

Key words：ulmonary arterial hypertension,women of reproductive age, DALYs, Global Burden of Disease 2021,Multi-modal Perspective insights

论文 ID：344

Baseline LDL-C Levels Modify Neutrophil to High-density Lipoprotein Cholesterol Ratio-related Risk for Coronary Heart Disease: Insights From BRIC Study

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Background: While recent studies have identified the neutrophil to high-density lipoprotein cholesterol ratio (NHR) as a significant risk factor for major adverse cardiovascular events (MACE) in patients with acute coronary syndrome (ACS), whether baseline low-density lipoprotein cholesterol (LDL-C) levels modulate the prognostic value of NHR still remains unclear. The study aimed to investigate the association between NHR and MACE across different baseline LDL-C strata in ACS patients.

Methods: This study is a post-hoc analysis of a prospective cohort study (BRIC study), including 1,736 ACS patients who underwent percutaneous coronary intervention (PCI) and were followed for one year across 30 Chinese hospitals. Patients were stratified into tertiles based on the NHR values measured at baseline upon admission. Additionally, they were categorized into high- and low-LDL-C subgroups using the median LDL-C level as the

cutoff. Kaplan-Meier curves and log-rank test were used to investigate the differences of survival among NHR tertile groups. Multivariate Cox regression analysis, restricted cubic spline analysis, and subgroup analysis were applied to explore the relationship of NHR with MACE among LDL-C subgroups.

Results: During one year of follow-up, 42 (2.4%) MACEs occurred among 1,736 patients with ACS. No significant correlation was observed between NHR and LDL-C (Spearman's rho=0.082), however, a significant interaction effect on MACE was detected (P for interaction=0.017). Significant associations between NHR and MACE were observed both in the overall population and the high LDL-C subgroup, but no significant association was detected in the low LDL-C subgroup. Specifically, in the overall population, when analyzed as a continuous variable, NHR was associated with significantly increased MACE risk (HR=1.094, 95% CI: 1.005-1.190, P=0.038), though no significant difference was found for Tertile 1 versus Tertile 3 (HR=1.965, 95% CI: 0.871-4.434, P=0.104). In the high LDL-C subgroup, as a continuous variable, NHR remained significantly associated with MACE (HR=1.187, 95% CI: 1.085-1.300, P<0.001). Notably, for Tertile 3 versus Tertile 1, increased MACE risk was still observed (HR=5.098, 95% CI: 1.318-19.524, P=0.021). In contrast, in the low LDL-C subgroup, no significant association between NHR and MACE was observed, whether analyzed as a continuous variable or categorical tertile groups. Restricted cubic spline analysis revealed linear dose-response relationships between NHR and MACE in the overall population (P for overall=0.0494) and high LDL-C subgroup (P for overall=0.0022). Furthermore, linear relationships were observed between NHR and MACE in the overall population (P for nonlinear=0.3799) and high LDL-C subgroup (P for nonlinear=0.5732). No significant dose-response relationship was observed between NHR and MACE in the low LDL-C subgroup (P for overall=0.2926).

Conclusion: In individuals with ACS, under low LDL-C levels, the pathogenic role of NHR—a composite marker of systemic inflammation and lipid metabolism dysregulation—diminishes, showing no significant association with MACE. Conversely, under high baseline LDL-C conditions, NHR exhibits enhanced pathogenicity. These findings suggest that heightened cardiovascular risk stratification, including anti-inflammatory interventions, should be prioritized in patients with elevated LDL-C conditions to mitigate overall cardiovascular morbidity and mortality.

Key words: Acute Coronary Syndrome; Neutrophil to High-density Lipoprotein Cholesterol Ratio; Baseline LDL-C Levels; Main Adverse Cardiovascular Events

论文 ID：345

GSDMD-mediated Pyroptosis Promotes Cardiac Remodeling in Pressure Overload

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Background: Gasdermin D (GSDMD) forms membrane pores to execute pyroptosis. But the mechanism of how cardiomyocyte pyroptosis induces cardiac remodeling in pressure overload remains unclear. We investigated the role of GSDMD-mediated pyroptosis in the pathogenesis of cardiac remodeling in pressure overload.

Methods: Wild-type (WT) and cardiomyocyte-specific GSDMD-deficient (GSDMD-CKO) mice were subjected to transverse aortic constriction (TAC) to induce pressure overload. Four weeks after surgery, left ventricular structure and function were evaluated by echocardiographic, invasive hemodynamic and histological analysis. Pertinent signaling pathways related to pyroptosis, hypertrophy and fibrosis were investigated by histochemistry, RT-PCR and western blotting. The serum levels of GSDMD and IL-18 collected from healthy volunteers or hypertensive patients were measured by ELISA.

Results: We found TAC induced cardiomyocyte pyroptosis and release of pro-inflammatory cytokines IL-18. The serum GSDMD level was significantly higher in hypertensive patients than in healthy volunteers, and induced more dramatic release of mature IL-18. GSDMD deletion remarkably mitigated TAC-induced cardiomyocyte pyroptosis. Furthermore, GSDMD deficiency in cardiomyocytes significantly reduced myocardial hypertrophy and fibrosis. The deterioration of cardiac remodeling by GSDMD-mediated pyroptosis was associated with activating JNK and p38 signaling pathways, but not ERK or Akt signaling pathway.

Conclusion: In conclusion, our results demonstrate that GSDMD serves as a key executioner of pyroptosis in cardiac remodeling induced by pressure overload. GSDMD-mediated pyroptosis activates JNK and p38 signaling pathways, and this may provide a new therapeutic target for cardiac remodeling induced by pressure overload.

Key words: Gasdermin D (GSDMD); pyroptosis; pressure overload; transverse aortic constriction (TAC); cardiac remodeling

论文 ID：360

Investigation of Screening for Primary Aldosteronism in an Adrenalectomy Population: A Multicenter Cross Sectional Study

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Purpose: Primary aldosteronism (PA) is a common secondary hypertension which is the leading cause of heart failure and chronic kidney disease. However, the screening rate and prevalence of PA are inconsistent across countries. Therefore, we conducted a multiple-center cross-sectional study to investigate the preoperative screening rate and prevalence of PA in patients who already have adrenalectomy based on postoperative immunohistochemically staining in China.

Methods: A total of 1,014 patients who had adrenalectomy and were diagnosed with adrenocortical adenoma or nodular hyperplasia by hematoxylin-eosin (HE) staining were collected. Immunohistochemical staining for specific aldosterone synthase (CYP11B2) monoclonal antibodies was performed on postoperative specimens. Analysis of staining results according to the consensus on the histopathology of PA.

Results: There were 224 patients (22.09%) who were screened and diagnosed with secondary hypertension preoperatively, including 170 (16.77%) patients with PA, 51 (5.03%) patients with adrenocorticotropic hormone (ACTH) independent Cushing's syndrome (CS) or subclinical CS, and 3 patients with aldosterone and cortisol co-secretion. The positive

rate of CYP11B2 was 94.23% in PA patients. Of the remaining 790 (77.91%) patients, based on CYP11B2 immunohistochemical staining results, histopathology identified 129 patients (12.72%) with classical lesions and 415 (40.93%) with non-classical lesions of unilateral PA. There were still 24.26% of patients who underwent adrenalectomy without pathological staining of the aldosterone autonomic secretory function. The proportion of patients with aldosterone autonomic secretion lesions decreases with age, and the proportion of APM and MAPM in aldosterone autonomic secretion lesions increases with age.

Conclusions: The screening for PA was inadequate, so improving preoperative screening for PA was crucial. CYP11B2 as the powerful tool for diagnosing aldosterone autonomic secretion function in adrenocortical lesions, which should be routinely used for postoperative pathological examination.

Key words:primary aldosteronism, screening, aldosterone synthase, immunohistochemical staining

论文 ID：369

Impairment of Renal Sodium Handling Contributes to Obesity-associated Salt-sensitive Hypertension:

Role of Na/K-ATPase/Src/ROS Signaling and IL-6/STAT3 Pathway

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Objective: Impaired renal sodium handling is a critical contributor to obesity-associated salt-sensitive hypertension (ssHTN). This study aims to elucidate the

mechanistic role of Na^+/K^+-ATPase (NKA)/Src/ROS signaling and the downstream IL-6/STAT3 inflammatory pathway in mediating renal sodium dysregulation and hypertension.

Methods: C57BL/6J mice, both lean and high-fat diet induced obese, were fed high-salt diets and treated with Co(III) protoporphyrin IX chloride (CoPP) to induce heme oxygenase-1 (HO-1). Renal oxidative stress and inflammation were assessed by ROS, MDA, protein carbonylation, and IL-6/STAT3 activity. Western blot and histology were used to evaluate NKA/Src activation and renal injury. Urinary sodium excretion and metabolomic profiling were also analyzed.

Results: Obese mice exhibited elevated oxidative stress, enhanced NKA/Src signaling, IL-6/STAT3 activation, and sodium retention. CoPP-induced HO-1 expression significantly reduced ROS levels, suppressed IL-6 and STAT3 phosphorylation, and improved sodium excretion. HO-1 induction also disrupted NKA-Src interaction and attenuated renal damage. Urinary metabolomics confirmed restoration of redox and sodium handling pathways.

Conclusion: The NKA/Src/ROS axis and IL-6/STAT3 signaling are key mediators of renal sodium handling impairment in obesity-related SSHTN. HO-1 upregulation mitigates this process by targeting both oxidative and inflammatory responses. These findings highlight new therapeutic avenues targeting redox-sensitive NKA signaling and inflammatory pathways in SSHTN.

Key words: Renal sodium metabolism; HO-1; Na/K-ATPase; Salt-sensitive hypertension; Obesity.

论文 ID：373

Types, Influencing Factors, Retest Diagnostic Value and Rhythm Analysis of Supine Hypertension Complicated with Orthostatic Hypotension

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Objectives: Orthostatic hypotension (OH) is a common disabling complication in patients with hypertension and chronic diseases, which can increase the risk of all-cause mortality, myocardial infarction, stroke, heart failure and atrial fibrillation. However, there is still a lack of research at home and abroad on the accuracy of diagnostic methods of orthostatic hypotension, different types of influencing factors and the rhythmicity of multiple measurements on different days.

This study explore the influencing factors of different types of orthostatic hypotension, and to explore the diagnostic accuracy of single measurement, risk differences in different time periods and rhythmicity of supine hypertension patients with orthostatic hypotension through multiple measurements on different days.

Methods: According to the diagnostic criteria of 20mmhg decrease in systolic blood pressure or 10mmhg decrease in diastolic blood pressure within 1/3/5 minutes after body position change (lying upright position), 192 patients with supine hypertension and orthostatic hypotension were included. According to the body position blood pressure measurement data at admission, they were divided into non neurogenic group (n=94) and neurogenic group (n=98). These patients were retested in four different time periods on the same day (7-8 o'clock pre-breakfast, 9-11 o'clock two hours after breakfast, 16-18 o'clock in the afternoon and 21-22 o'clock pre-sleep), and 24-hour ambulatory blood pressure monitoring (ambulatory ory blood pressure monitoring (ABPM) records and admission examination results were used as baseline data for correlation, risk prediction model and rhythm analysis.

Result: 1. 116 patients (60.4%) were confirmed to be orthostatic hypotension (positive) after multiple retests on a different day, of which 79 (42.7%) were confirmed to be positive in the morning during the four time periods. 2. for patients with different types of orthostatic hypotension (non neurogenic n=94, neurogenic n=98), the average age of patients with neurogenic hypotension was higher (56.5 ± 14.6 years, p=0.006), the weight was lower (73.2 ± 15.3kg, p=0.03), more sleep disorders (30.6%, p=0.005), the daytime diastolic pressure (87.2 ± 11.5mmhg, p=0.015) and the whole day diastolic pressure (86.0mmhg, p=0.048) were lower. 3. rhythmicity analysis found that the average decline and fluctuation amplitude of systolic blood pressure and diastolic blood pressure decline were significant, supporting the overall rhythmicity. According to the model, the decline of systolic and diastolic blood pressure reached the peak around 8 am, and the decline of systolic and diastolic blood pressure reached the trough around 21 PM.

Conclusion: 1.Diagnostic implications: Morning measurements yield highest sensitivity. Single-timepoint screening misses >40% of cases; 2. nOH: Prioritize sleep disorder management and glycemic/renal protection. Non-nOH: Address proteinuria, renal artery stenosis, and BMI control; 3. OH management requires circadian alignment: Prevent morning drops, maintain evening stability.

Key words: Orthostatic hypotension、ABPM、rhythm

论文 ID：381

Arm and Thigh to Waist Circumference Ratio (ATC/WC) and All-Cause Mortality, Cardiovascular Mortality, Hypertension, and Diabetes

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Background: Larger upper or lower limb circumferences have been validated as excellent protective indicators for mortality prediction. However, researchers have observed a higher prevalence of obesity, hypertension, and diabetes in some populations with larger limb circumferences. This study aims to evaluate the relationship between ATC/WC ratio, ATC and all-cause and cardiovascular mortality, hypertension, and diabetes.

Methods: Using data from the 1999–2006 National Health and Nutrition Examination Survey (NHANES), we included 17,276 participants. We calculated the sum of arm and thigh circumferences (ATC) and the ATC/WC ratio. Cox proportional hazards models were utilized to assess the association of ATC/WC with all-cause mortality and cardiovascular mortality in cohort analyses. Generalized linear models were utilized to evaluate the relationship between ATC/WC and hypertension and diabetes in cross-sectional analyses. Restricted cubic spline models were employed to analyze dose-response relationships.

Findings: Over a median follow-up of 18.04 years, there were 3,927 deaths, including 1,047 cardiovascular-related deaths. Compared to Q1, participants in Q4 of ATC/WC

experienced significantly lower all-cause mortality (HR=0.48, 95% CI: 0.39 - 0.59) and cardiovascular mortality (HR=0.32, 95% CI: 0.21 - 0.49). Additionally, the risks of hypertension (OR=0.50; 95% CI: 0.42 - 0.60) and diabetes (OR=0.28; 95% CI: 0.20 - 0.40) were markedly reduced. There was a significant linear association between ATC/WC and all outcomes ($p < 0.001$). Conversely, ATC alone was positively associated with cardiovascular risk factors prior to adjusting for BMI or WC, with these associations reversing post-adjustment.

Interpretation: The ATC/WC ratio showed significant inverse associations with all-cause mortality, cardiovascular mortality, and risks of hypertension and diabetes. ATC alone showed significant inverse associations with mortality, significant positive associations with risks of hypertension and diabetes prior to adjusting for BMI or WC, with these associations reversing post-adjustment. These findings emphasize the importance of assessing ATC/WC, rather than limb circumference alone, when simultaneously considering both mortality and risk factors.

Key words: limb circumference; arm circumference; thigh circumference; all-cause mortality; cardiovascular mortality; cardiovascular risk factors; hypertension; diabetes.

论文 ID：385

Doppler Ultrasound Evaluation Reveal High Rate of the Underdiagnosis of Renal Artery Fibromuscular Dysplasia with Isolated Renal Branch Artery Stenosis

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Fibromuscular dysplasia (FMD) is a nonatherosclerotic, noninflammatory vascular disease that most commonly affects renal arteries. According to the international consensus, it has been proposed that computed tomography angiography (CTA) is the initial test of choice for suspected FMD. However, CTA might underestimate the isolated renal branch artery FMD. Within the prospective RA-FMD study (Renal Artery Fibromuscular Dysplasia Registry,

NCT05363748), we evaluated 179 patients with renal FMD lesions confirmed by renal artery angiography, of out of 350 patients included in the registry. All patients underwent ultrasound and CTA to evaluate renal arteries. Of 179 study participants, with a mean diagnosed age of 26.5±10.7 years, 115 (64.2%) were female, 31 (17.3%) were children. All patients had diagnosed hypertension at a mean age of 21.3±8.4 years. 69.2% were focal and 25.1% were multivessel. Patients with Isolated renal branch artery FMD, compared to those without, were younger (20.3 vs. 27.6 years, P = 0.015) and more often male (61.9% vs. 32.2%, P = 0.007), had a higher proportion of focal FMD (90.5% vs. 69.5%, P = 0.044) and had higher level of direct renin concentration (127.1 vs. 72.1 pg/ml, P = 0.14). 9 (42.8%) patients with Isolated renal branch artery FMD was missed by CTA. After a median of 7 years follow-up, Isolated renal branch artery FMD, had a similar cure rate of hypertension than those without after revascularization (47.4% vs. 57.1%, P = 0.42). It is recommended that every hypertensive patient with secondary hyperaldosteronism should undergo renal artery ultrasound to screen isolated renal branch artery FMD, which was easily underestimated by CTA.

Key words: fibromuscular dysplasia, hypertension, isolated renal branch artery, ultrasound, stenosis

论文 ID：403

Aldosterone Promotes Aortic Dissection through Lactate/Lactylation-mediated Phenotypic Switching of Vascular Smooth Muscle Cell

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Objective: Aortic dissection (AD), a life-threatening vascular condition with limited therapeutic options, is closely associated with vascular smooth muscle cell (VSMC) phenotypic switching. While elevated plasma aldosterone levels have been observed in AD patients, the role of aldosterone in VSMC differentiation and the occurrence of TAD remains

elusive. The purpose of this study is to explore the molecular mechanism of aldosterone-induced aortic dissection.

Methods and Results: Utilizing an aldosterone-infused C57BL/6 mouse model and human aortic VSMC with multi-omics approaches and a variety of experimental methods, we reveal that aldosterone significantly elevates lactate levels via MR activation. This lactate surge induces extensive protein lactylation modifications, particularly targeting inflammatory regulators and vascular structural proteins. Especially, the lactylation of myosin heavy chain (Myh11) is significantly upregulated in aldosterone group,which affects its binding to actin, influences the vasoconstriction function, and damages the cellular structure. The lactylation-driven molecular changes accelerate VSMC phenotypic switching, disrupt vascular integrity, and ultimately trigger AD development. Importantly, both MR antagonist (spironolactone) and lactate dehydrogenase A inhibitor (GNE-140) effectively mitigated aldosterone-induced pathological changes in vitro.

Conclusions: Our findings provide the first proteomic evidence of lactate-mediated lactylation as a key mechanism in aldosterone-induced AD pathogenesis, providing a new insight into the pathological mechanism of AD and identifying MR signaling and lactate metabolism as promising therapeutic targets for AD prevention and treatment.

Key words: Aldosterone; Lactate; Lactylation Modification;Vascular Smooth Muscle Cell; Phenotypic Switch; Aortic Dissection

论文 ID：405

Relationship between Serum Ferritin and The Risk of All-cause Death in Patients with Coronary Artery Disease

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Objective: Ferritin is independently associated with oxidized low-density lipoprotein (LDL). While high LDL levels are known independent risk factors for cardiovascular diseases, few studies have investigated the relationship between serum ferritin levels and long-term outcomes in CAD patients.

Methods: A prospective cohort study of CAD participants was performed in Xinjiang Medical University Affiliated First Hospital from December 2016 to October 2021. 1,089 CAD patients were divided into two groups according to baseline serum ferritin concentration (ferritin <160, n = 715 and ferritin ⩾160, n = 374). We investigated long-term mortality as the primary endpoint, including all-cause mortality (ACM) and cardiac mortality (CM). The longest follow-up duration was 60 months.

Results: In this study, a total of 17 ACMs, 12 CMs, 34 MACEs, and 41 MACCEs were recorded. There were significant differences between the two groups in the incidence of ACM (P = 0.002) and CM (P = 0.019). After controlling for covariates, multivariate Cox regression analysis showed that ferritin was an independent predictor for ACM (hazard ratio [HR]: 2.674, 95% confidence interval [CI]: 1.197-5.971, P = 0.016) in CAD patients.

Conclusions: High ferritin levels are strongly associated with the higher risk of ACM in CAD patients.

Key words Ferritin; Mortality; Coronary artery disease, Predictor

论文 ID：406

Joint Effect of Blood Pressure Variability and Glycemic Variability on CVD Mortality Risk in Elderly with Hypertension and Diabetes

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Background: The role of blood pressure variability and glycemic variability in association with reduction of the incidence for cardiovascular or all-cause mortality

remains controversial, especially in in elderly with hypertension and diabetes. This study aims to investigates the joint effect of blood pressure and glycemic variability on the risk of all-cause death in elderly with hypertension and diabetes

Methods: The study was conducted using the data based on the health examination data of elderly patients with hypertension combined with diabetes in China from 2012 to 2016. Age, gender, blood pressure and fasting blood sugar (FBG) of the study subjects were collected, and the death outcomes from 2017 to 2021 were followed up. Blood pressure and Glycemic variability was calculated based on standard deviation (SD) and coefficient of variation (CV), and cumulative event incidence was estimated using Kaplan-Meier survival curve and Log-rank test using quartile stratification. multivariable-adjusted time-dependent Cox proportional hazards analyses were performed to examine the joint effects of blood pressure and Glycemic variability on mortality risk.

Results: A total of 330,988 elderly participants with hypertension and diabetes (34.41% males, the median age was 68 [IQR: 63, 74] years), had complete health assessments. At a mean follow-up of 5.61 years, 35,073 all-cause deaths (10.60%) and 20,109 CVD related deaths(6.08%) were recorded . In the fully adjusted models, an increased SBP CV and FBG CV was significantly associated with an increased CVD morality (P for trend <0.001), reflecting a 4.3% or 33% increased risk comparing participants with an increase in SBP CV or FBG CV above Q4 with those below Q1. Finally, the hazard ratio (P < 0.001) for CVD-related death for high SBP CV was 1.04 (1.02-1.06) and for high FBG CV was 1.34 (1.32-1.37).

Conclusions: Our findings suggest that variability in Glycemic and systolic blood pressure is significantly associated with mortality in elderly with hypertension and diabetes, especially in groups younger than 75 years of age (P for interaction < 0.05). The variability of these two parameters may be a potential target for chronic disease management in the future.

Key words: Blood pressure, Glycosylated hemoglobin, variability, hypertension, diabetes, mortality

论文 ID：411

Rate Pressure Product as A Novel Predictor of Long-term Adverse Outcomes in Patients after Percutaneous Coronary Intervention: A Retrospective Cohort Study

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Objectives: Previous studies have suggested that heart rate (HR) and blood pressure (BP) play important roles in the development of adverse outcomes in patients with coronary artery disease (CAD) who underwent percutaneous coronary intervention (PCI). However, the relationship between the rate pressure product (RPP) and long-term outcomes has rarely been investigated. This study investigated the effects of RPP on the clinical outcomes of CAD patients who underwent PCI.

Methods: In this study, a total of 6,015 CAD patients were enrolled. All patients were from the CORFCHD-PCI study. They were divided into two groups according to RPP (RPP<10,269, n=4,018 and RPP≥10,269, n=1,997). In addition, the median follow-up time was 32 months. The primary endpoint was long-term mortality, including all-cause mortality (ACM) and cardiac mortality (CM). The secondary endpoints were major adverse cardiovascular events (MACEs) and major adverse cardiovascular and cerebrovascular events (MACCEs).

Results: We found that there were significant differences between the two groups in the incidences of ACM, CM, MACCEs and MACEs (all P<0.05). Among the CAD patients with ACM, CM, MACCEs and MACEs, the mean survival time of the low-value group was significantly higher than that of the high-value group. Multivariate Cox regression analyses showed that RPP was an independent predictor for ACM (hazard ratio (HR)=1.605, 95% confidence interval (CI): 1.215-2.120, P=0.001), CM (HR=1.733, 95% CI: 1.267-2.369, P=0.001), MACCEs (HR=1.271, 95% CI: 1.063-1.518, P=0.008) and MACEs (HR=1.315, 95% CI: 1.092-1.584, P=0.004) in stable CAD patients. While there was no significant correlation between the RPP and the adverse outcomes in acute coronary syndrome (ACS) patients.

Conclusion: In summary, RPP is an independent predictor of long-term prognosis in CAD patients who underwent PCI. A higher baseline RPP before PCI increased the risk of adverse

outcomes. Compared with heart rate and blood pressure alone, RPP has a higher predictive value for adverse clinical outcomes.

Key words: Keywords: Coronary artery disease, Rate pressure product, Mortality, Outcomes, Percutaneous coronary intervention

论文 ID：413

Efficacy, Quality of Life, and Cost-Effectiveness of Superselective Adrenal Arterial Embolization in Idiopathic Hyperaldosteronism: A Comparative Study

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Objectives: Idiopathic hyperaldosteronism (IHA) is the most common subtype of primary aldosteronism, typically managed with mineralocorticoid receptor antagonists (MRAs). However, long-term MRA therapy is associated with suboptimal cardiovascular outcomes and adverse effects. Superselective adrenal arterial embolization (SAAE) is a novel minimally invasive alternative, but its long-term efficacy, particularly regarding quality of life and cost-effectiveness, remains underexplored.

Methods and Results: In this study, 82 patients with bilateral IHA were prospectively enrolled and assigned to three groups: SAAE (n = 42), MRA therapy (n = 20), and a control cohort (n = 20). Outcomes, including blood pressure, serum potassium, aldosterone-renin ratio normalization, and quality of life (measured by SF-36 and EQ-5D), were assessed at 12 months. A supervised Random Forest model was developed to predict treatment success. A five-year cost-utility analysis compared SAAE and MRA therapy from a healthcare system perspective. Results showed that SAAE led to greater reductions in blood pressure (mean −27.4 ± 21.3 mmHg systolic, −23.1 ± 17.4 mmHg diastolic) compared to MRA therapy (−15.6 ± 11.4 mmHg systolic, −12.4 ± 10.1 mmHg diastolic, $p < 0.001$). Clinical success was achieved in 63.2% of the SAAE group, with biochemical remission in 39.6%.

SAAE also led to greater improvements in quality of life and demonstrated lower costs and higher quality-adjusted life years (QALYs) compared to MRA therapy. SAAE is a safe, effective, and cost-effective treatment for IHA, offering superior blood pressure control, hormonal normalization, and improved quality of life compared to MRAs.

Key words: Idiopathic Hyperaldosteronism; Superselective Adrenal Arterial Embolization (SAAE); AI Predictive Modeling; Clinical and Biochemical Success; Quality of Life (QoL); Cost-Effectiveness Analysis

论文 ID：420

Impact of Obesity on Blood Pressure Variability and Early Cardiovascular Risk in Hypertensive Children: A Retrospective Study Based on Ambulatory Monitoring and Echocardiography

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Objective: To investigate the association between obesity and 24-hour blood pressure variability (BPV) in children with primary hypertension, and to assess its relationship with early cardiac structural changes and metabolic risk factors.

Methods: This retrospective observational study included 60 children aged 6 to 17 years diagnosed with primary hypertension between 2018 and 2023. Participants were categorized as obese or non-obese based on BMI ≥95th percentile.All patients underwent 24-hour ambulatory blood pressure monitoring (ABPM), and BPV was assessed using standard deviation (SD), coefficient of variation (CV), and average real variability (ARV) for both systolic and diastolic blood pressure.Echocardiographic evaluations included measurements of left atrial diameter (LAD) and identification of left ventricular hypertrophy (LVH) based on pediatric normative references.

Fasting blood tests were performed to determine levels of triglycerides, HDL-C, LDL-C, total cholesterol, and C-reactive protein (CRP).Statistical comparisons between groups were

conducted using t-tests or non-parametric equivalents for continuous variables and chi-square tests for categorical variables. Correlation and multivariate regression analyses were used to examine the relationship between BPV, obesity status, cardiac structure, and metabolic markers, adjusting for age, sex, and mean BP.

Results: Obese hypertensive children exhibited significantly greater BPV compared to their non-obese peers ($p < 0.001$). They also showed a higher prevalence of LVH and increased indexed LAD ($p < 0.01$). Metabolic profiles were more unfavorable in the obese group, with higher CRP levels, elevated triglycerides, and reduced HDL-C ($p < 0.01$). BPV was positively associated with LAD size, CRP concentration, and dyslipidemia patterns. Obesity and CRP emerged as independent predictors of BPV and cardiac structural changes in multivariate models.

Conclusion Obesity in hypertensive children is associated with elevated blood pressure variability, early cardiac structural alterations such as left atrial enlargement and left ventricular hypertrophy, and pro-inflammatory metabolic risk profiles. These associations appear to be independent of mean blood pressure values. the integration of BPV analysis, echocardiographic assessment of cardiac structure (such as LAD and LVH), and metabolic screening in the risk stratification of pediatric hypertension, especially in the context of obesity. Early identification of these high-risk features may inform more targeted interventions and prevent future cardiovascular complications.

Key words: Obesity; Blood Pressure Variability; Pediatric Hypertension; Ambulatory Blood Pressure Monitoring; Left Ventricular Hypertrophy

论文 ID：426

Automated Machine Learning for Predicting Left Ventricular Hypertrophy from Ambulatory Blood Pressure in Children: A Multi-Feature Retrospective Study

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Objective: To investigate whether automated machine learning (**AutoML**) can effectively predict left ventricular hypertrophy (LVH) in children with hypertension using ambulatory blood pressure monitoring (ABPM) data.

Methods: We retrospectively analyzed data from 160 hypertensive children aged 8 to 16 years, including 24-hour ABPM (up to 48 time points per patient), echocardiographic assessment of LVH, and clinical variables. A comprehensive set of features—such as systolic/diastolic blood pressure variability, nocturnal dipping status, and pulse pressure—was derived from ABPM recordings.Model development and evaluation were conducted using **AutoGluon**, a AutoML framework that automatically performs feature selection, model selection, and hyperparameter optimization. AutoGluon ensembles various algorithms including gradient boosting machines (LightGBM, CatBoost), random forests, and tabular neural networks. Model performance was evaluated via 5-fold cross-validation using AUC, accuracy, and F1-score as metrics.

Results: The AutoGluon-generated ensemble achieved an AUC of 0.87 (95% CI: 0.82–0.91), with an accuracy of 81.2% and an F1-score of 0.78. Nocturnal systolic BP, high blood pressure variability, and reduced nighttime dipping were key predictive features. SHAP value analysis highlighted their clinical importance. Compared to baseline logistic regression (AUC 0.69), the AutoML approach demonstrated superior performance ($p < 0.001$).

Conclusion: AutoML applied to pediatric ABPM data enables accurate and interpretable prediction of early target organ damage. Our findings support the integration of AutoML tools such as AutoGluon in pediatric hypertension care for personalized risk assessment.

Key words: Pediatric Hypertension, Ambulatory Blood Pressure, Machine Learning, AutoML, Left Ventricular Hypertrophy

论文 ID：446

Exploration of Risk Factors for Abnormal Circadian Blood Pressure Rhythm in Hypertensive Patients with Chronic Kidney Disease

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Background: Abnormal circadian blood pressure (BP) rhythm is a significant predictor of cardiovascular events in hypertension patients. Among those with chronic kidney disease (CKD), the prevalence of non-dipper and reverse-dipper BP patterns is elevated. However, the risk factors remain incompletely elucidated. This study aimed to investigate risk factors of abnormal circadian BP rhythm in hypertensive patients with CKD through a single-center retrospective cohort analysis.

Methods: The retrospective cohort included 1,041 hypertensive patients hospitalized at the Sixth Medical Center of PLA General Hospital between Oct, 2022 and Mar, 2024. Participants were stratified into two groups according to CKD comorbidity status. Baseline characteristics and distribution of four BP rhythm phenotypes were analyzed. Univariate and multivariate logistic regression models were employed to identify related factors of abnormal BP rhythm in the CKD-hypertension (HT) group.

Results: The mean age of the cohort was 54.63 ± 15.08 years, with 57.25% (n=596) being male. Compared to the HT group, CKD+HT patients exhibited significantly higher age, admission systolic BP (SBP), and C-reactive protein levels (all $p<0.05$). Ambulatory BP monitoring revealed higher 24-hour mean SBP, daytime mean SBP, nighttime mean SBP, and 24-hour SBP standard deviation in the CKD+HT group ($p<0.05$). Phenotypic analysis demonstrated a lower prevalence of dipper rhythm and a higher proportion of reverse-dipper rhythm among CKD+HT patients. Logistic regression showed CKD as an independent correlate of reverse-dipper rhythm (OR: 1.492; 95% CI: 1.031 - 2.160). In CKD+HT patients, BMI(OR:0.756,95%CI:0.605-0.945) was negatively correlated with abnormal circadian BP rhythm, while the 24h-average systolic blood pressure(OR:1.061,95%CI:1.004-1.122) had a positive correlation.

Conclusion: Hypertensive patients with CKD display a higher prevalence of abnormal circadian BP rhythm patterns, with BMI may be a protective factor of abnormal rhythm.

Key words: abnormal circadian blood pressure rhythm, hypertension, chronic kidney disease

论文 ID：448

Development and Implementation of an Artificial Intelligence-Based Interpretation System for Adrenal Vein Sampling

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Objective: Primary aldosteronism (PA) is a significant cause of secondary hypertension. Compared to essential hypertension at similar blood pressure levels, PA substantially increases cardiovascular risk, and pharmacological treatment of PA faces significant challenges. Therefore, developing rational diagnostic and therapeutic strategies is a clinical priority, with determining bilateral adrenal involvement being a critical factor in selecting treatment approaches. Recent domestic and international guidelines and consensus statements emphasize the importance of adrenal vein sampling (AVS), widely recognized as the gold standard for identifying lateralized aldosterone excess and guiding treatment decisions. However, this technique remains underutilized in China, and the interpretation of results varies significantly across institutions, necessitating standardization. Advances in artificial intelligence (AI) and hospital information systems now enable automated collation and interpretation of AVS results. This study employs a locally deployed multimodal AI model within hospital intranets to automatically extract and summarize AVS results from the Laboratory Information System (LIS), providing one-click interpretation of sampling success and lateralization. This approach aims to support standardized adoption of AVS.

Methods: To accommodate institutional variations, an AI agent based on the Fast Healthcare Interoperability Resources (FHIR) standard was developed. The agent retrieves—via standard intranet interfaces and using patient IDs and AVS dates—aldosterone and cortisol values, units, reference ranges, and physician-annotated sampling sites from the LIS within one-week post-AVS. Data is converted into standardized FHIR resources using a locally deployed DeepSeek large language model (LLM). A Retrieval-Augmented Generation (RAG) system, integrating PA management guidelines and historical consultation records from Peking University First Hospital, then organizes AVS results into structured tables, evaluates sampling success for each site, and identifies lateralization (Figure 1). Furthermore, the performance of different LLM models including DeepSeek, ChatGPT, Claude, Gemini were compared on the same AVS patients with de-identification.

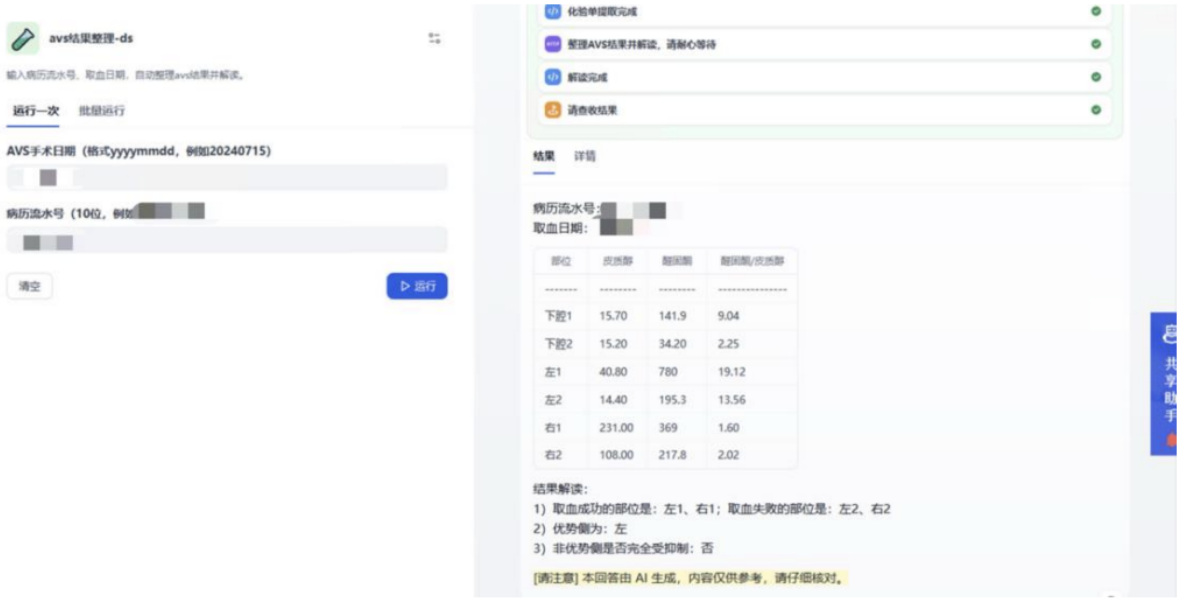

Figure 1: System demonstration of automated collation and interpretation of real-world AVS results

Results: Since deployment, the system has provided efficient services to physicians in cardiology, endocrinology, and other departments at Peking University First Hospital. Average processing times were 74.93 ms for LIS data extraction and FHIR conversion, and 12.51 s for AVS interpretation, consuming 8.18k tokens. This has significantly improved workflow efficiency and standardized AVS reporting and interpretation. For AVS results interpretation, only DeepSeek could accurately identify the success or failure for different sites.

Conclusion: Locally deployed AI in healthcare settings enhances the efficiency of AVS result collation and interpretation. However, the accuracy of different large language models for this task and the system's impact on subsequent PA management decisions require validation through large-scale prospective clinical studies.

Key words: Primary aldosteronism; adrenal vein sampling; artificial intelligence; large language model; FHIR;

论文 ID：452

The Association of Rs1104739 Polymorphism of NDUFS8 Gene and Essential Hypertension and Hypertension-induced Left Ventricular Hypertrophy

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Objective: To investigate the association between rs1104739 polymorphism of NDUFS8 gene and essential hypertension and hypertension-induced left ventricular hypertrophy.

Methods: This is a cross-sectional, case-control trial. The subjects were selected from the Department of Cardiology and Health Examination Center of the First Affiliated Hospital of Kunming Medical University. Among them, there were 829 patients with essential hypertension(EH) diagnosed by 2018 Chinese guidelines for the management of hypertension and 619 healthy controls without EH. The general clinical data collected included gender, age, height, weight, smoking status, drinking status, blood pressure, heart rate, etc. Echocardiography datas were collected in the EH group, and the EH patients were divided into left ventricular hypertrophy (LVH) group and non-left ventricular hypertrophy(NLVH) group depend on whether or not LVH is induced. TagSNP rs1104739 of NDUFS8 gene was selected following the linkage disequilibrium principle, then its correlation with genetic susceptibility to EH and EH-induced LVH was studied. T test, one-way anova, analysis of covariance, Mann-Whitney U test and Kruskal-Wallis test were used for numerical variables.

chi-square test was used for classification variables. Logistic regression analysis was adopted to investigate the association between rs1104739 of NDUFS8 gene and EH and EH-induced LVH in Yunnan Han population under five genetic models of addictive, allele, dominant, recessive and overdominant.

Results

1. For NDUFS8 gene rs1104739 polymorphism in EH group, the frequencies of AA, AC and CC genotypes were 52.7%, 39.5% and 7.8%, the frequencies of A and C alleles were 72.4% and 27.6%, respectively. In CT group, the genotype frequencies of AA, AC and CC were 53%, 39.5% and 7.5%, the frequencies of A and C alleles were 72.7% and 27.3%, respectively. The genotype distribution of rs1104739 of NDUFS8 gene were not deviated from Hardy-Weinberg equilibrium in EH group, CT group and EH+CT group.

2. Chi-square test results showed no significant difference between the EH group and the CT group in the five genetic models (addictive model, allele model, dominant model, recessive model and overdominant model) of NDUFS8 gene rs1104739 ($P>0.05$). Logistic regression analysis was adopted to adjust for gender, age and BMI, and there was no significant association between five genetic models of rs1104739 and EH ($P>0.05$).

3. In the EH group, there were significant difference between rs1104739 of NDUFS8 gene genotype model in diastolic blood pressure(DBP) and mean arterial blood pressure(MAP)($P=0.018$, $P=0.019$). Comparison among groups analysis discovered that DBP and MAP were lower in AA genotype carriers than in AC genotype carriers($P<0.01$, $P<0.01$). In overdominant model [AC vs (AA+CC))], DBP and MAP were significantly higher in AC genotypes carriers than in (AA+CC) genotypes carriers($P=0.011$, $P=0.010$). In allele model (A vs C), DBP and MAP were significantly higher in C allele carriers than in A allele carriers($P=0.012$, $P=0.014$).

4. Chi-square test results showed no significant difference between LVH group and NLVH group among five genetic models (genotype model, allele model, dominant model, recessive model, and superdominant model) of rs1104739 ($P>0.05$). Logistic regression analysis was adopted to adjust for gender, age, smoking status, alcohol consumption status and MAP. There was no significant association between the five genetic models of rs1104739 and EH-induced LVH ($P>0.05$).

5. In the EH group, The carriers with C allele had significantly higher level of LVMI than that counterpart of with A allele($P=0.034$), and the carriers of the C allele had

significantly lower level of E peak than that counterpart of A allele(P=0.044). The carriers with CC genotype had significantly higher level of LVMI than that that counterpart of with (AA+AC) genotype(P=0.042), and the carriers of the CC genotype had significantly lower level of E than that counterpart of (AA+AC) genotype(P=0.044).

Conclusion: This study didn't provide evidence for NDUFS8 gene rs1104739 polymorphism conferring susceptibility to EH and EH-induced LVH in the Han population in Yunnan, China. On the other hand, rs1104739 were associated with blood pressure phenotype (DBP and MAP) and Echocardiography datas(LVMI and E peak).

Key words: Essential hypertension; NDUFS8 gene; Rs1104739; Left ventricular hypertrophy

论文 ID：456

An Evaluation of the Precision of Personal Blood Pressure Monitors among Device Owners

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Objective: Applying a stethoscope-based calibration device to verify the accuracy of home oscillometric blood pressure monitors synchronously.

Methods: This study enrolled 448 participants who possessed home oscillometric blood pressure monitors (upper arm type). The accuracy of these home oscillometric devices was verified using an auscultatory method calibrator, with the calibration results being valid only for the individual participants themselves. Descriptive statistics were used to summarize the study findings, including mean and standard deviation. The accuracy of blood pressure measurements was assessed across different brands of monitors. The proportion of patients with differences in blood pressure readings between the tested device and the calibrator of ≥5 mmHg and ≥10 mmHg was calculated. Linear regression analysis was applied to identify factors influencing the discrepancies in blood pressure measurements. Additionally, the results of survey questionnaires completed by some participants were analyzed.

Results: A total of 448 consecutive patients attending a routine clinical visit with their cardiologist (male 215 and female 233) were eligible to participate in this study. The overall mean age of the participants was 62.35±12.59 years. Most of the blood pressure monitors included in this study are of the Omron brand (79.69%, n=357), followed by yuwell (5.8%, n=26), Andon (2.46%, n=11), and others. 76.32% of SBP measurements and 69.89% of DBP measurements from BPMs exhibited differences of ≤5 mmHg compared to the reference calibrator. 70.89% (n=318) were accurate in measuring SBP, and 60.27% (n=270) were accurate in measuring DBP. For Omron monitors, the accuracy rates were 72.27% (n = 258) for SBP and 59.38% (n = 212) for DBP.

Conclusion: Our study revealed that over 20% of blood pressure monitors exhibited discrepancies of more than 5 mmHg compared to a reference calibrator. Overall, the Omron U30, HEM-7211, and U10 models demonstrated relatively higher accuracy in blood pressure measurements. Regular calibration of blood pressure monitors is crucial to ensure accurate measurements for patients.

Key words: oscillometric blood pressure monitors, home blood pressure, blood pressure

论文 ID：459

The Relationship Between Remnant Cholesterol-Inflammatory Index and Hypertension: A Cross-Sectional and Longitudinal Analysis Based on CHARLS

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Objectives: Remnant cholesterol (RC) and high-sensitivity C-reactive protein (hs-CRP) are well-recognized biomarkers of metabolic and inflammatory risk, respectively. While both have been independently associated with hypertension, their combined effect remains underexplored.This study aimed to assess the predictive utility of the Remnant Cholesterol Inflammatory Index (RCII), a novel composite marker integrating RC and hs-CRP, in determining hypertension risk.

Methods: We analyzed 9307 participants aged ≥45 years without baseline hypertension from the China Health and Retirement Longitudinal Study (CHARLS). RCII was calculated as:RCII=RC (mg/dL)×hs-CRP (mg/L)/10.Multiple logistic regression models assessed the association between baseline RCII and risk of hypertension, adjusting for covariates such as age, sex, place of residence, education, history of smoking, history of alcohol use, diabetes, heart disease, and stroke. Subgroup analyses were performed to explore whether the association between RCII and hypertension varied by covariate status.During the 7-year follow-up, 1444 participants (21.4%) developed hypertension. The prevalence of hypertension increased in the higher median RCII group.

Results: In the cross-sectional analysis, a total of 9309 participants were included, after adjusting for potential confounders, there was a significant association between RCII and increased prevalence of hypertension (OR=1.82 ,95% CI:1.62 ~ 2.04, p<0.001), systolic blood pressure (SBP) above 140 mmHg (OR=1.56, 95% CI: 1.38-1.77, p<0.001) , diastolic blood pressure (DBP) above 90 mmHg (OR=1.52, 95% CI: 1.28-1.80, p<0.0001), and pulse pressure (PP) above 60 mmHg (OR=1.20, 95% CI: 1.05-1.36, p=0.006. The longitudinal analysis included 5696 participants, there was a significant association between higher RCII and increased incidence of hypertension (OR=1.37, 95% CI: 1.21-1.56,p<0.001).

Conclusion: RCII, a combined measure of lipid residual risk and inflammation, is a stronger predictor of hypertension.These findings suggest that joint lipid-inflammatory pathways contribute to hypertension development, supporting RCII as a potential clinical risk stratification tool.

Key words: CHARLS, hypertension, Remnant Cholesterol Inflammatory Index (RCII), elderly

论文 ID：479

Sitting Time and Its Reallocation with Physical Activity and Sleep: Associations with Cardiovascular Disease and all-cause Mortality in PURE-China

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Background: Although prolonged sedentary time is associated with adverse health outcomes, limited evidence exists regarding its dose-response relationship in populations with low average sitting time. This study aimed to investigate the association between daily sitting time and the risk of all-cause mortality and cardiovascular disease (CVD), and to evaluate the health effects of reallocating sedentary time to other behaviors in a Chinese cohort with relatively low sedentary time.

Methods: We analyzed data from 41,733 adults aged 35-70 years from the Prospective Urban Rural Epidemiology (PURE)-China cohort, with a median follow-up of 11.9 years. Sitting time, physical activity, and sleep duration were assessed using validated questionnaires. Associations between sitting time and health outcomes were examined using Cox proportional hazards models and isotemporal substitution analysis. Compositional data analysis with g-computation was employed to simulate 10-year risks under time reallocation scenarios.

Results: Sitting time demonstrated a J-shaped association with adverse outcomes, with the lowest risk observed at 2-4 hours per day. Both low (<2 h/day) and high (≥6 h/day) levels of sitting were associated with increased risks of all-cause mortality and CVD, independent of physical activity and other covariates. Among participants sitting ≥4 h/day, replacing 30 minutes of sitting with moderate-to-vigorous physical activity (MVPA) or work-related activity was associated with a 3-7% reduction in risk. Conversely, among participants sitting <4 h/day, reallocating time from physical activity or sleep to sitting was associated with increased risk. G-computation analyses confirmed that reallocating sitting time to MVPA yielded the most pronounced reductions in 10-year mortality risk, particularly in those with high baseline sedentary time.

Conclusion: In a population with generally low sedentary time, both excessive and insufficient sitting are associated with adverse health outcomes. Among individuals with high sitting time, reallocating sitting time to physical activity reduces mortality risk, while in those with low sitting time, reallocating physical activity or prolonged sleep to sitting also confers protective effects. These findings support a nuanced, context-specific approach to sedentary behavior guidelines.

Key words: Sedentary behavior, physical activity, mortality, cardiovascular disease, isotemporal substitution

论文 ID：480

Traditional Risk Factors and Premature Acute Myocardial Infarction: Insights from China Acute Myocardial Infarction Registry

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Background and aims： The rising trend of premature acute myocardial infarction (AMI) in China is a growing concern. This study aims to clarify the impact of traditional risk factors, including diabetes, hypercholesterolemia, hypertension, and smoking, on premature AMI and related mortality, using data from the China Acute Myocardial Infarction (CAMI) registry.

Methods： Data from the CAMI registry was retrospectively analyzed for adults with their first myocardial infarction. Outcomes included life expectancy free of AMI and mortality at 30 days and 2 years. Associations with risk factors (smoking, hypertension, diabetes, hypercholesterolemia) were examined by sex using inverse probability weighting.

Results： Analysis of 21,710 Chinese patients with first acute myocardial infarction (AMI) from January 2013 to September 2014 revealed that those with all four traditional risk factors—smoking, hypercholesterolemia, hypertension, and diabetes—had a 7-year reduction in life expectancy free of AMI in men (from 64.0 ± 13.0 to 56.6 ± 10.2 years; r = −0.137; P<0.001) and a 2-year reduction in women (from 68.2 ± 12.5 to 66.2 ± 9.5 years; r = −0.022; P=0.1046). Premature AMI in women under 65 and men under 55 was significantly associated with current smoking and hypercholesterolemia, with relative risks of 2.10 (95% CI: 1.95－2.25) and 1.50 (95% CI: 1.40－1.61) in men, and 1.23 (95% CI: 1.02－1.48) and 1.32 (95% CI: 1.18－1.48) in women, respectively. Diabetes was notably linked to a higher risk of 2-year mortality in women (RR: 2.12; 95% CI: 1.55－2.90).

Conclusion： Traditional risk factors markedly reduced life expectancy, especially in men, with smoking, hypercholesterolemia, and diabetes closely associated to premature AMI and higher mortality in women, underscoring the need for targeted public health policies.

Key words： Risk factors; Sex differences; Acute myocardial infarction

论文 ID：482

Association between Hypertensive Disorders of Pregnancy and Cancer Risk in Offspring: A Systematic Review and Meta-analysis

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Purpose: Hypertensive disorders of pregnancy (HDP) lead to adverse health outcomes in offspring, such as neurodevelopmental disorders, congenital heart defects and high blood pressure. However, the role of HDP in the risk of cancer in offspring has not reached a consensus. This study aimed to systematically review and synthesize existing studies to estimate the association between maternal HDP and the risk of cancer in offspring.

Methods: Databases including Embase, Web of Science, and PubMed were searched from their inception to January 15, 2025. Subsequently, two researchers independently screened the studies based on predefined inclusion criteria, extracted relevant data, and assessed the risk of bias using the Newcastle-Ottawa Scale tool. The overall risk estimates with 95% confidence intervals (CIs) were calculated using random-effects models.

Results: Thirty-seven studies involving 48,959 cancer cases among 10,615,811 participants were included in our meta-analysis. Mothers who had HDP exposure were significantly associated with an increased risk of cancer in offspring (OR = 1.09, 95%CI: 1.01-1.17, n = 10,615,811 from 37 studies, I2 = 58.3%, GRADE: Very low), especially hematological malignancy (OR = 1.26, 95%CI: (1.08-1.48), n = 6,203,727 from 9 studies, I2 = 47.5%, GRADE: Very low).

Conclusions: This meta-analysis shows that maternal HDP exposure is associated with an increased risk of cancer in offspring. These findings underscore the imperative for early

prevention, prenatal monitoring, and treatment of HDP to improve health outcomes in offspring.

Key words: Hypertensive Disorders of Pregnancy; Pre-eclampsia; Cancer; Meta-analysis

论文 ID：484

Correlation between Metabolic Score for Insulin Resistance (METS-IR) and Blood Pressure Variability in Patients with Hypertension

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Background: The metabolic score for insulin resistance (METS-IR) is a novel assessment tool for insulin resistance that integrates routine clinical parameters (fasting glucose, lipid profiles, and obesity indices) to comprehensively evaluate metabolic status. Studies have confirmed that elevated blood pressure variability (BPV) is an independent predictor of cardiovascular outcomes. Given this, the timely identification of increased BPV holds significant clinical significance. Therefore, This study aimed to investigate the correlation between METS-IR and BPV in hypertensive patients.

Methods: This study enrolled 1003 patients with essential hypertension who were hospitalized at the First Affiliated Hospital of Xi'an Jiaotong University and underwent 24-hour ambulatory blood pressure monitoring (ABPM). Systolic and diastolic blood pressure variability was evaluated using the standard deviation (SD) of systolic BP and diastolic BP readings during 24-hour, daytime, and nighttime periods. The METS-IR was calculated using the following formula: Ln[2*glycemia (mg/dL)+triglycerides (mg/dL)]*BMI/LnHDL-C (mg/dL). Based on baseline METS-IR quartiles, all patients were divided into four groups: quartile1 (METS-IR <35.33, N=250), quartile2 (35.33≤METS-IR<39.97, N=251), quartile3 (39.97≤METS-IR<44.75, N=252) and quartile4 (METS-IR≥44.75, N=250). Spearman's correlation

analysis was employed to evaluate the simple linear relationship between METS-IR and BPV. Univariate linear regression and multiple linear regression models were constructed to examine the association between METS-IR and BPV (with the METS-IR lowest quartile as the reference). Subgroup analysis was performed according to the presence or absence of diabetes.

Results: The mean age of all enrolled patients was 57.23 (47-68) years old. Among them, 622 were male, accounting for 62.0% of the total population. The mean METS-IR was 40.48 (32.33-44.75). The 24-hour, daytime and nighttime systolic BPV were 14.11 (11.79-15.84), 13.67 (11.23-15.52) and 12.08 (9.25-14.11) mmHg, respectively. The corresponding 24-hour, daytime and nighttime diastolic BPV were 10.46 (8.89-11.71), 10.17 (8.40-11.45) and 8.93 (6.78-10.63) mmHg, respectively. Compared to the lowest METS-IR quartile group, hypertensive patients in the highest METS-IR quartile group exhibited significantly elevated 24-hour systolic BPV, 24-hour diastolic BPV, daytime diastolic BPV, nighttime systolic BPV and nighttime diastolic BPV. Spearman's correlation analysis revealed significant positive correlations between METS-IR and the following measures of blood pressure variability: 24-hour systolic BPV, 24-hour diastolic BPV, daytime systolic BPV, daytime diastolic BPV, nighttime systolic BPV and nighttime diastolic BPV (Spearman's correlation coefficients: 0.132, 0.276, 0.088, 0.226, 0.107, 0.178, respectively; all P values<0.05). Univariate linear regression analysis identified the highest METS-IR quartile as a risk factor for blood pressure variability. Subsequent multiple linear regression analysis further demonstrated that the highest METS-IR quartile remained significantly associated with 24-hour systolic BPV, 24-hour diastolic BPV, daytime diastolic BPV, nighttime systolic BPV and nighttime diastolic BPV, independent of corresponding mean blood pressure and other confounding factors such as age, sex, history of calcium channel blocker use and low-density lipoprotein cholesterol. Using the lowest METS-IR quartile subjects as the reference group, the corresponding regression coefficients β (95% confidence interval) were: 0.933 (0.299-1.566), P=0.004; 0.890 (0.448-1.332), P<0.001; 0.701 (0.219-1.183), P=0.004; 1.291(0.531-2.051), P=0.001; 1.168 (0.565-1.770), P<0.001. Subgroup analysis revealed that the interaction term between the highest METS-IR quartile group and diabetes status was not statistically significant for models where 24-hour systolic BPV, 24-hour diastolic BPV, daytime diastolic BPV and nighttime diastolic BPV served as the dependent variables. A statistically significant interaction term was observed for nighttime systolic BPV as the dependent variable. Further analysis demonstrated that the association between the highest METS-IR quartile and nighttime

systolic BPV was significantly stronger among diabetic patients (β:2.544, 95%CI:0.899-4.188, P=0.003) compared to non-diabetic patients (β:0.872, 95%CI:-0.003-1.746, P=0.051).

Conclusion: METS-IR demonstrated a significant and independent association with ambulatory blood pressure variability in patients with essential hypertension.

Key words: Blood pressure variability; Essential hypertension; Metabolic score for insulin resistance

论文 ID：504

The Role of Lifestyle Behaviors in Reducing Cardiovascular Disease and All-cause Mortality Risks Among Patients with Hypertension:

A Population-Based Prospective Cohort Study in China

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Background: Hypertension remains a global health threat and major contributor to life-threatening diseases. Despite the availability of effective medications significantly improves the clinical prognosis of hypertensive patients, the extent to which lifestyle factors play protective roles remains inadequately explored. This study aims to investigate the associations of healthy lifestyles with the risks of cardiovascular disease (CVD) and all-cause mortality in hypertensive patients, and compare the relative importance of each healthy lifestyle behavior, while their joint associations with antihypertensive medication use were also evaluated.

Methods: This study included 16,314 prevalent hypertensive participants recruited at the baseline of the Prospective Urban Rural Epidemiology (PURE)-China study. A healthy lifestyle score (0–6, higher scores indicating healthier lifestyle behaviors) was calculated based on smoking, alcohol consumption, diet, physical activity, sedentary

behavior and sleep duration. Regular use of antihypertensive medication was defined as taking at least once per week over a month.

Results: Over a median follow-up of 11.9 years, 1,423 deaths and 2,418 CVD events were documented. Participants adhering to fewer healthy lifestyle factors exhibited progressively higher risks of all-cause mortality and CVD. Compared to those with 5–6 healthy lifestyle behaviors, having a lifestyle score of 0-2 was associated with the highest risk of all-cause mortality (hazard ratio[HR], 1.77; 95%CI, 1.42-2.20), and CVD (HR, 1.56; 95%CI, 1.28-1.89). A healthy diet ranked to be a relative stronger predictor of all-cause mortality and CVD than other lifestyle behaviors. Furthermore, maintaining a favorable lifestyle was associated with lower all-cause mortality regardless of antihypertensive medication use, while reduction of CVD risk was observed only among non-users of antihypertensive medication.

Key words: Cardiovascular disease; Healthy lifestyle; All-cause mortality; Hypertension; Prospective study.

论文 ID：508

Knowledge, Attitudes, and Practices Survey on Hypertensive Nephropathy Among Hypertensive Patients .A single-center study in Urumqi, Xinjiang, China

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Background: This study aimed to assess the knowledge, attitudes, and practices (KAP) related to hypertensive nephropathy among patients diagnosed with hypertension in the Xinjiang of China.

Methods: A cross-sectional survey was conducted between April 1 and April 30, 2024, in Xinjiang, China. Data were collected using a structured questionnaire designed to capture demographic characteristics and evaluate patients' KAP toward hypertensive nephropathy. Participants were individuals with a confirmed diagnosis of hypertension.

Results: A total of 687 hypertensive patients were included in the final analysis, yielding a response rate of 97.86%. Among them, 58.08% were male. The majority of respondents (42.79%) had been diagnosed with hypertension for three years or less. Their median [q25, q75] knowledge, attitude, and practice scores were 6 (2,10) (possible range: 0-32), 24 (23,26) (possible range: 6-30), and 25 (18,31) (possible range: 9-45), respectively. The structural equation modeling (SEM) showed that knowledge had direct effects on attitude (β = 0.42, $P < 0.001$) and practice (β = 2.87, $P < 0.001$). Meanwhile, attitude had a direct effect on practice (β = -0.31, $P < 0.001$). Furthermore, knowledge indirectly affected practice through attitude (β = -0.13, $P = 0.005$).

Conclusion: Patients diagnosed with hypertension in Xinjiang exhibited limited knowledge, generally positive attitudes, but suboptimal health practices regarding hypertensive nephropathy. To improve clinical outcomes, educational interventions targeting hypertension-related renal complications should be prioritized, with a focus on enhancing patient knowledge as a means to foster more effective self-care behaviors.

Key words: Hypertension; Hypertensive Nephropathy; Knowledge; Attitude; Health Behavior

论文 ID：511

Prognostic Risk Assessment of HFpEF: A Study on Feature Selection and Prediction Model Optimization Based on Machine Learning

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Background: Heart failure with preserved ejection fraction (HFpEF) is a prevalent but poorly understood condition, with its prognostic factors still not fully elucidated. Identifying key determinants of poor outcomes and understanding the role of treatment adherence are critical for improving patient care and long-term prognosis.

Methods: This study followed 461 HFpEF patients for one year, utilizing LASSO regression for feature selection and developing predictive models using decision trees,

random forests, XGBoost, and a stacking ensemble approach. Structural equation modeling (SEM) was used to assess the impact of treatment adherence on prognosis. Among the cohort, 38.2% (n = 176) experienced adverse outcomes, including death and major adverse cardiovascular events (MACE).

Results: Multivariate analysis identified anemia, atrial fibrillation, and elevated blood urea nitrogen as significant risk factors, while higher BMI, plasma albumin, and good treatment adherence were found to be protective. The XGBoost model demonstrated the highest performance (AUC = 0.861), and the stacked ensemble model further improved prediction accuracy (AUC = 0.864). SEM results revealed that treatment adherence significantly influenced prognosis, with inflammatory status, metabolic disorders, and BMI acting as mediators.

Conclusions: Treatment adherence is a crucial determinant of HFpEF prognosis, influencing long-term outcomes significantly. The use of a stacked ensemble model enhances prediction accuracy, suggesting that interventions targeting treatment adherence and metabolic management can improve patient outcomes. Further studies should explore these associations in larger, diverse cohorts to refine clinical strategies for HFpEF.

Key words: HFpEF; Machine Learning; Structural Equation Modeling; Treatment Adherence; Predictive Models

论文 ID：518

The Role of B1a lymphocytes in Blood Pressure Regulation and Vascular Injury

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B cells play a crucial role in mammalian adaptive immunity via processing antigens and producing antibodies. However, whether B cells and immunoglobulins are involved in regulating blood pressure in hypertension remains unclear. We found that the frequency of B1a cells was reduced in blood and peritoneal cavity after angiotensin II (Ang II) infusion.

Then we showed that B1a-cells-deficient mice largely exacerbated the elevation of both systolic and diastolic blood pressure after Ang II-treatment compared with WT (wild type). Vascular dysfunction and damage, including CD4+ T cells and macrophages accumulation, aortic structure remodeling and fibrosis were worse in KO mice compared with WT mice in response to Ang II. Adoptive transfer of B1a cells protected against Ang II-induced hypertension and vascular damage. Our data demonstrated that B1a cells play a protective role in the development of hypertension.

Key words B1a cell, hypertension, vascular injury

论文 ID：533

Association of Diabetes and Dyslipidemia with Mortality Risk in Elderly with Hypertension: A Population-Based Retrospective Cohort Study

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Objectives: While prior studies have established the adverse effects of cardiometabolic comorbidities in general adult populations, evidence remains limited and inconsistent regarding their synergistic impact on mortality risk in older hypertensive patients. This study aimed to investigate the association of diabetes and dyslipidemia with cardiovascular disease (CVD)-related and all-cause mortality in this high-risk demographic.

Methods: In this retrospective cohort study, 438,094 hypertensive participants aged ≥65 years from Hunan Province (2016 health examination cohort) were followed through 2021. Participants were stratified into four mutually exclusive groups: (1) hypertension alone, (2) hypertension with diabetes, (3) hypertension with dyslipidemia, and (4) hypertension with both diabetes and dyslipidemia. Multivariable Cox proportional hazards and Fine-Gray competing risk models were employed to assess mortality risks.

Results: During a median 5.48-year follow-up, 28,857 CVD-related and 16,363 non-CVD-related deaths occurred. Compared to hypertension alone, coexisting diabetes was associated

with elevated risks of CVD-related mortality (HR: 1.24, 95% CI: 1.19－1.29; P<0.001) and all-cause mortality (HR: 1.40, 1.36－1.45; P<0.001). Participants with the triad of hypertension, diabetes, and dyslipidemia exhibited the highest mortality risks (CVD-related HR: 1.39, 1.32－1.46; all-cause HR: 1.54, 1.49－1.60; both P<0.001). Stratified analyses revealed particularly pronounced associations in females (CVD-related HR: 1.51, 1.41－1.61; P for interaction <0.001) and individuals aged 65－74 years (CVD-related HR: 1.58, 1.46－1.70; P for interaction <0.001).

Conclusion: In Elderly with hypertension, concomitant diabetes and dyslipidemia significantly amplify CVD-related and all-cause mortality risks, with heightened vulnerability observed in women and younger elderly individuals (65－74 years). These findings highlight the prognostic significance of comprehensive cardiometabolic management in this population.

Key words: hypertension; Elderly; diabetes mellitus; dyslipidemia; mortality; cohort study

论文 ID：535

Association of Resting Heart Rate Trajectories with New-onset Chronic Kidney Disease in Patients with Hypertension

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Objective: An elevated resting heart rate (RHR) increases the risk of chronic kidney disease (CKD), but the relationship between longitudinal patterns of RHR and the risk of CKD in hypertensive patients is unclear. We aimed to explore the association between RHR trajectories and new-onset CKD in hypertensive patients.

Methods: A total of 21,509 hypertensive participants from the Kailuan cohort who were free of CKD and cardiovascular disease before 2010 were included. The RHR trajectories were

developed using latent mixture modeling based on examination data in 2006, 2008, and 2010. Cox proportional hazards regression models were established to evaluate the association between RHR trajectories and risk of incident CKD.

Results: We identified 4 RHR trajectories in participants with hypertension between 2006 and 2010: low-stable group (n=2,465[11.46%], mean RHR range, 63.33–65.06 beats/min), moderate low-stable group, (n=15,610 [72.57%], mean RHR range, 73.09–74.32 beats/min), moderate high-stable group (n=3,158 [14.68%], mean RHR range, 84.32–85.43 beats/min,) and elevated-stable group (n=276 [1.28%], mean RHR range, 99.63–100.74 beats/min). During an average follow-up of 7.93 years, 2,769 cases of CKD were identified. Compared with the moderate low-stable group, adjusted hazard ratios (HRs) for CKD were 1.15 (95%CI: 1.03 - 1.29) for the low-stable group, 1.22 (95%CI: 1.10 - 1.37) for the moderate high-stable group, and 1.54 (95%CI: 1.13 - 2.09) for the elevated-stable group.

Conclusion: RHR trajectories were associated with the risks of CKD in patients with hypertension.Keywords: resting heart rate, trajectory, hypertension, chro

Key words：resting heart rate, trajectory, hypertension, chronic kidney disease

论文 ID：538

A Predictive Model for the Onset of Atrial Fibrillation in Patients with Hypertension

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Objectives：Hypertension (HT) is a major risk factor for atrial fibrillation (AF). This study aimed to develop and validate a risk prediction model for incident AF in hypertensive

patients. Model performance was evaluated through comprehensive statistical assessment of discrimination, calibration, and clinical utility.

Methods: A retrospective cohort study enrolled 304 hospitalized hypertensive patients: 150 with comorbid AF and 150 with hypertension only (control group). Potential predictors were screened from clinical data. A multivariable logistic regression model was constructed to predict AF risk. Model performance was rigorously assessed using: 1) Discrimination: Receiver Operating Characteristic (ROC) curve analysis (Area Under the Curve, AUC) and the Kolmogorov-Smirnov(K-S)statistic. 2) Calibration: Bootstrap validation (B=200 repetitions) with calibration curves and calculation of the Mean Absolute Error (MAE). 3) Clinical Utility: Decision Curve Analysis (DCA) quantifying Net Benefit across risk thresholds.A points-based nomogram was constructed for individualized risk estimation.

Results: Multivariable regression identified 13 significant predictors ($p<0.05$), presented as Odds Ratios (ORs) with 95% Confidence Intervals (CIs) via forest plot (e.g., Renal Insufficiency: OR=5.74, 95% CI=2.46-15.71, $p=1.71\times10^{-4}$; Adrenal Nodule: OR=0.08, 95% CI=0.03-0.18, $p=3.73\times10^{-8}$). The model demonstrated excellent discrimination (AUC = 0.9092, K-S statistic = 0.7105). However, the wide AUC confidence interval (95% CI: 0.18-0.89) indicated potential instability, suggesting the need for validation in larger cohorts. Calibration was excellent (MAE=0.019), with the bias-corrected calibration curve closely aligning with the ideal line. Decision Curve Analysis confirmed significant clinical utility, demonstrating a positive Net Benefit for risk thresholds between approximately 25% and 75%. The nomogram provides a practical tool for calculating individualized AF probability.

Conclusion: We developed and internally validated a statistically robust prediction model demonstrating high discrimination and calibration for AF risk in hypertensive patients. While clinical utility via DCA is evident, the wide AUC confidence interval necessitates validation in larger cohorts. The nomogram offers a practical tool for identifying high-risk individuals, potentially enabling targeted monitoring and preventive strategies. The observed low anticoagulation rates in high-risk subgroups underscore the critical need for improved risk stratification and management.

Key words: Atrial fibrillation; hypertension; Risk Prediction Model; Nomogram; Logistic Regre- ssion; Model Validation; Clinical Utility

论文 ID：539

A Predictive Model for the Onset of Cardiac Insufficiency in Patients with Hypertension and Persistent Atrial Fibrillation

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Background: The coexistence of HT and persistent atrial fibrillation (Pe-AF) not only complicates therapeutic management but also significantly heightens the risk of adverse cardiovascular events, profoundly impacting patients' quality of life and long-term prognosis. HT promotes the initiation and perpetuation of AF through fibro-inflammatory remodeling of the left atrium. In turn, Pe-AF itself further influences atrial remodeling and aggravates renal dysfunction, thus establishing a deleterious cycle that ultimately culminates in overt heart failure. Despite the well-established epidemiological link, there remains a lack of convenient and accurate tools for assessing the probability of cardiac dysfunction development specifically in patients with HT and Pe-AF.

Methods: We analyzed 395 hospitalized HT-PeAF patients (2010–2019) from Chinese PLA General Hospital. Multivariate logistic regression identified HF predictors. The total score was calculated using prior catheter ablation, LDL-C, Hb, UA, creatinine, TBIL, FBG, RDW, and CAD. A nomogram integrating nine clinical variables was developed and validated using ROC curves, calibration plots, Hosmer-Lemeshow tests, and decision curve analysis.

Results: Patients with cardiac insufficiency (71.11±9.59 years old) were older than those without cardiac insufficiency (68.62 ± 10.30 years old, P =0.017), and they had higher levels of prior catheter ablation and renal insufficiency, but lower levels of CAD than those without cardiac insufficiency. Hemoglobin in HT-PeAF patients with cardiac insufficiency was lower (P =0.017), but higher levels of red blood cell distribution width (RDW), fasting blood glucose (FBG), creatinine, and uric acid (UA) than in those without

cardiac insufficiency. Before adjusting for confounders, prior catheter ablation, LDL-C, Hb(hemoglobin), UA, creatinine, total bilirubin (TBIL), FBG, RDW, and CAD were associated with the occurrence of cardiac insufficiency in patients with HT-PeAF. After adjustment, CAD was associated with a 2.31-fold increased risk of cardiac insufficiency in patients with HT-PeAF (adjusted OR: 2.31, 95% CI: 1.38-3.96). To create a clinically useful and robust prediction model, we included variables based on both statistical significance and clinical relevance. While the final model primarily used variables significant in multivariable analysis ($P < 0.05$), we also retained specific indicators from univariate analysis. These indicators (prior catheter ablation, Hb, UA, FBG) showed a significant link to cardiac insufficiency in univariate screening ($P < 0.05$). The nomogram achieved an AUC of 0.77 (95% CI: 0.72 - 0.81) for cardiac insufficiency prediction, with good calibration (Hosmer-Lemeshow, $p = 0.44$) and clinical utility (DCA-confirmed).

Conclusion: The nine-variable nomogram provides a clinically accessible tool for individualized cardiac insufficiency risk prediction in HT-PeAF patients, but need requires prospective validation in Asian populations.

Key words Hypertension, Persistent atrial fibrillation, cardiac insufficiency, risk factors , Nomogram

论文 ID：540

Effect of Mitochondrial ND6 T14933C Gene Mutation on Blood Pressure Regulation and High-altitude Adaptation

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Background: Previous studies have reported that ND6 mutations are associated with and hypertension. The mitochondrial ND6 mutation may disrupt Complex I stability and impair cardiovascular adaptation, especially under high-altitude hypoxia. The present study explores its impact on blood pressure regulation, right ventricular function, and hypoxic response.

Methods: Eighty-four healthy Han Chinese males underwent mitochondrial genome sequencing to identify the T14933C mutation. Participants were evaluated at sea level, at 4000 m altitude, and in a hypobaric chamber. Data collection included ambulatory blood pressure, echocardiography, and arterial blood gas analysis. Statistical analysis used SPSS with $P<0.05$ as significance.

Results: Among the 84 volunteers, 15 were found to have the m.14933T>C variant. In the plains, ambulatory blood pressure monitoring revealed statistically significant differences in nighttime diastolic blood pressure (n-DBP) (64.9 ± 8.7 vs. 61.1 ± 6.9, $P = 0.028$), nighttime diastolic blood pressure load (10.7 ± 10.4 vs. 3.9 ± 8.5, $P = 0.003$), nighttime systolic blood pressure load (17.9 ± 16.3 vs. 10.1 ± 15.5, $P = 0.038$), 24-hour average diastolic blood pressure (24h-DBP) (72.7 ± 5.2 vs. 68.6 ± 5.9, $P = 0.014$), and daytime systolic blood pressure (d-SBP) (119.1 ± 5.9 vs. 115.2 ± 7.6, $P = 0.015$). Ultrasound examination of the heart indicated statistically significant differences in tricuspid annular plane systolic excursion (TAPSE) (19.8 ± 5.0 vs. 22.4 ± 4.7, $P = 0.037$) and pulmonary artery systolic pressure (PASP) (16.1 ± 8.3 vs. 22.9 ± 11.1, $P = 0.022$).

Ambulatory blood pressure monitoring conducted on the plateau showed statistically significant differences in daytime diastolic blood pressure load (dDBPL) (23.4 ± 18.9 vs. 14.2 ± 12.6, $P = 0.004$), daytime systolic blood pressure load (dSBPL) (29.3 ± 19.6 vs. 16.1 ± 14.8, $P = 0.049$), and daytime diastolic blood pressure (d-DBP) (83.8 ± 7.9 vs. 78.6 ± 8.9, $P = 0.038$). Ultrasound examination of the heart showed statistically significant differences in TAPSE (20.0 ± 5.0 vs. 22.3 ± 4.7, $P = 0.038$) and PASP (16.5 ± 8.3 vs. 22.8 ± 11.1, $P = 0.041$).

In addition to the aforementioned findings, blood pressure indices such as dDBPL and dSBPL were lower in the plains compared to the plateau, suggesting compensatory mechanisms of the cardiovascular system in response to hypoxia, as previously observed.

Conclusion: The mitochondrial ND6 T14933C gene may be involved in blood pressure regulation and right heart adaptation, particularly under hypoxia. Structural disruption of ND6 may impair electron transfer and elevate ROS, contributing to vascular dysfunction.

These findings highlight the mutation as a potential risk factor for cardiovascular maladaptation in high-altitude environments.

Key words: mitochondrial DNA; mutation; blood pressure; regulation; hypoxia

论文 ID：564

Office and Out-of-office Blood Pressure: Patterns of Association in Heart Failure Patients

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Background: Although hypertension guidelines have defined home blood pressure (HBP) and ambulatory blood pressure (ABP) values that correspond to specific office blood pressure (OBP) thresholds, it remains unclear whether these out-of-office BP correspondences are comparable in patients with heart failure (HF). This study aims to elucidate the relationship between OBP and out-of-office BP in individuals with HF.

Methods: A total of 390 HF patients from the Out-of-Office Blood Pressure Measurements in Patients with Heart Failure Registry Study (OOBPM-HF study) were included. Linear regression models were used to explore the relationships between OBP and both HBP and ABP. The HBP and ABP values corresponding to specific OBP values were calculated. Additionally, the coincident OBP and out-of-office BP values were computed. The white coat effect (WCE) was defined as the difference between office systolic BP and daytime ambulatory systolic BP. Moreover, a multivariate linear regression model was employed to identify the determinants of WCE in HF patients.

Results: OBP showed a significant linear correlation with both HBP and ABP, with stronger Pearson correlation coefficients observed for systolic BP ($r = 0.78$ for OBP－ABP; $r = 0.7$ for OBP－HBP) than for diastolic BP ($r = 0.65$ for OBP－ABP; $r = 0.52$ for OBP－HBP). Notably, the slopes of the relationships between OBP and ABP were steeper than those

between OBP and HBP. The corresponding HBP and ABP values for an OBP of 140/90 mmHg were 123.9/78.7 mmHg and 123.9/78.6 mmHg, respectively. The coincident values for OBP and HBP were 110.2/71.9 mmHg, while those for OBP and ABP were 102.5/64.8 mmHg. The mean WCE in HF patients were 8.7 mmHg. After fully adjustment, WCE was independently associated with systolic BP, waist circumference, estimated glomerular filtration rate, and HF with preserved ejection fraction.

Conclusions: In patients with HF, the relationship between office and out-of-office BP measurements differs from that observed in the general population. Out-of-office BP monitoring is recommended for HF patients to accurately assess their BP profile, which is critical for optimizing guideline-directed medical therapy.

Key words: office blood pressure, out-of-office blood pressure, white coat effect

论文 ID：566

Inverted U-shaped Association between Neutrophil-Percentage-to-Albumin Ratio (NPAR) and Cardiovascular-Kidney-Metabolic Syndrome: A Population-based Study

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Background: Cardiovascular-Kidney-Metabolic (CKM) syndrome represents a critical intersection of metabolic dysfunction, cardiovascular disease, and chronic kidney disease (CKD), with systemic inflammation as a key driver. However, existing biomarkers like the neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII) suffer from inconsistent predictive performance. We introduce the Neutrophil-Percentage-to-Albumin Ratio (NPAR)—a novel, integrative biomarker that simultaneously captures neutrophil-driven inflammation and hypoalbuminemia-linked metabolic dysregulation, offering a more robust tool for CKM risk assessment.

Methods: We analyzed 6,711 U.S. adults from NHANES (2009–2018), stratifying CKM severity (stages 0–4) per American Heart Association guidelines. NPAR was calculated as

(neutrophil % / serum albumin [g/dL]). Using survey-weighted multivariable logistic regression, generalized additive models (GAM) with penalized splines, and two-stage threshold regression, we evaluated NPAR's association with advanced CKM (stages 3–4) and compared its predictive performance against NLR and SII.

Results: NPAR demonstrated a robust inverted U-shaped association with advanced CKM (P for nonlinearity < 0.001), with a statistically significant inflection point identified at NPAR = 11.6. Below this threshold, each 1-unit increase in NPAR was associated with 25% higher odds of advanced CKM (adjusted OR 1.25, 95% CI 1.21-1.28). Notably, this association plateaued above the threshold (OR 0.95, 95% CI 0.87-1.05), suggesting distinct pathophysiological phases in CKM progression. In comprehensive multivariable models adjusting for potential confounders, NPAR emerged as the only independent predictor among inflammatory biomarkers examined (joint OR 1.15, 95% CI 1.10-1.21). The discriminative ability of NPAR (AUC 0.63, 95% CI 0.61-0.65) consistently outperformed both NLR (AUC 0.59) and SII (AUC 0.58) in identifying advanced CKM cases.

Conclusion: NPAR is a first-of-its-kind biomarker that dynamically reflects the transition from chronic inflammation to immune depletion in CKM syndrome. Its nonlinear association, validated threshold (11.6), and superior predictive ability position NPAR as a transformative tool for precision-based CKM management.

Key words: Cardiovascular-Kidney-Metabolic (CKM) syndrome, Neutrophil-Percentage-to-Albumin Ratio (NPAR), Inflammation-Immune Depletion, Risk Stratification and Prediction, National Health and Nutrition Examination Survey (NHANES)

论文 ID：575

Role of Vascular Smooth Muscle Cell-Specific CPT1A Deficiency–Mediated Fatty Acid Oxidation Disruption in Promoting Hypertensive Vascular Remodeling

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Objective: Conventional therapeutic targets for hypertension are often widely expressed across multiple tissues and subject to compensatory mechanisms, resulting in adverse effects, drug resistance, and suboptimal blood pressure control. Therefore, there is an urgent need to identify more precise and safer therapeutic strategies and targets. Carnitine palmitoyltransferase 1A (CPT1A), a rate-limiting enzyme in fatty acid oxidation (FAO) located on the outer mitochondrial membrane, plays a critical role in sustaining the energy metabolism and homeostasis of vascular smooth muscle cells (VSMC). Although metabolic reprogramming and mitochondrial dysfunction in the vascular wall have been documented in hypertensive patients, the role of CPT1A in hypertension-associated vascular remodeling remains unclear. This study aimed to systematically investigate the impact and mechanisms of VSMC-specific CPT1A deficiency on vascular remodeling in hypertension, using animal models, metabolic flux analyses, mechanistic validation, and human translational evidence, and to evaluate the feasibility of CPT1A as a therapeutic target.

Methods: VSMC-specific CPT1A knockout (CPT1AˆSMC-KO) and inducible knockout mice were generated. Hypertension was induced using angiotensin II (Ang II) infusion and deoxycorticosterone acetate‐salt (DOCA-salt) models. Blood pressure and circadian rhythm were continuously monitored via telemetry, and vascular stiffness and cardiac function were assessed by pulse wave velocity (PWV) and echocardiography. Structural changes in the vascular wall were evaluated by hematoxylin‐eosin (HE), Masson’s trichrome, and elastin staining. Functional assays included pressure myography and wire myography to assess aortic compliance and endothelium-dependent relaxation. VSMC metabolic activity was quantified using Seahorse assays for oxidative phosphorylation and glycolysis, targeted LC‐MS measurement of FAO-related metabolites, and [ˆ13C]-fatty acid/[ˆ13C]-glucose isotope tracing with flux modeling to determine FAO and glycolysis contributions to ATP production. Mitochondrial function was assessed by respiratory chain complex activity, mitochondrial DNA copy number, ROS production, Nrf2/HO-1 antioxidant pathway activity, and transmission electron microscopy. VSMC phenotypic switching (α-SMA, SM22α, OPN, MMP9), inflammatory mediators (IL-6, TNF-α, MCP-1), and downstream signaling pathways (AMPK, NF-κB, TGF-β) were analyzed by immunofluorescence, qPCR, and Western blotting. Single-cell RNA sequencing (scRNA-seq) and spatial transcriptomics were employed to characterize cellular heterogeneity and spatial metabolic reprogramming induced by CPT1A deficiency, with scATAC-

seq used to investigate epigenetic regulation. To validate causality, rescue experiments were performed using AAV9-SM22α-mediated CPT1A overexpression and pharmacological interventions (AMPK activator AICAR, mitochondrial antioxidant MitoQ, and medium-chain fatty acid supplementation). Translational studies included assessing CPT1A expression and FAO activity in peripheral arterial tissues from hypertensive patients and matched controls, measuring plasma acylcarnitine profiles, correlating them with PWV and flow-mediated dilation (FMD), and analyzing GWAS and eQTL datasets to evaluate associations between CPT1A genetic variants, blood pressure, and vascular stiffness.

Results: Compared with wild-type controls, CPT1A^SMC-KO mice under hypertensive conditions exhibited pronounced vascular wall thickening, increased collagen deposition, elastin fiber fragmentation, reduced vascular compliance, and elevated PWV. VSMCs from knockout mice demonstrated decreased FAO flux, reduced ATP production, enhanced glycolysis, mitochondrial structural abnormalities, elevated ROS, and impaired Nrf2/HO-1 antioxidant signaling. CPT1A deficiency promoted a phenotypic switch from the contractile to the synthetic phenotype, with increased proliferation and migration, elevated inflammatory cytokines, suppressed AMPK signaling, and activation of NF-κB and TGF-β pathways. scRNA-seq and spatial transcriptomics revealed heightened metabolic heterogeneity among VSMC subpopulations and reorganization of inflammation-metabolism interaction networks. Rescue experiments showed that CPT1A overexpression, AMPK activation, or mitochondrial antioxidant treatment partially restored FAO capacity, inhibited phenotypic switching and inflammation, and improved vascular function. In human samples, CPT1A expression was reduced in peripheral arteries from hypertensive patients, and elevated plasma long-chain acylcarnitine levels were significantly associated with increased PWV and reduced FMD. GWAS data suggested functional CPT1A variants were genetically linked to blood pressure regulation.

Conclusion: This study demonstrates that VSMC-specific CPT1A deficiency exacerbates hypertension-induced vascular remodeling via metabolic reprogramming, mitochondrial dysfunction, inflammatory activation, and phenotypic switching, highlighting the pivotal role of FAO in vascular homeostasis. The integration of animal model data, mechanistic validation, pharmacological rescue, and human translational evidence establishes a causal "CPT1A-FAO-vascular remodeling" axis, from metabolic flux alterations to functional impairment and clinical association, providing a strong theoretical and experimental basis for developing FAO-targeted therapeutic strategies for hypertension.

Key words： Keywords: hypertension, fatty acid oxidation, inflammation, vascular smooth muscle cells, vascular remodeling, mitochondrial dysfunction

论文 ID：582

Isolated and Additive Associations of Carotid-femoral and Brachial-ankle Pulse Wave Velocities with Target Organ Damage in Untreated Outpatients

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Carotid-femoral pulse wave velocity (cfPWV)Brachial-ankle pulse wave velocity (baPWV) and carotid-femoral pulse wave velocity (cfPWV)brachial-ankle pulse wave velocity (baPWV)are both reliable indicators of arterial stiffness, with established associations with target organ damage (TOD). However, it remains unclear whether the associations of TOD with these two PWV measures differ, and those with isolated or combined elevated PWVs might have different TOD. Consecutive untreated outpatients referred for 24-hour ambulatory blood pressure monitoring at Ruijin Hospital were recruited. Measures of TOD included pulsatility index of cerebral arteries by transcranial Doppler ultrasonography, carotid intima-media thickness (IMT), estimated glomerular filtration rate (eGFR), and urinary albumin-to-creatinine ratio (ACR). Among the 1798 participants, 1170 (65.1%) had ambulatory hypertension. CfPWV (7.9 ± 1.3 m/s)BaPWV (14.6 ± 2.2 m/s)and cfPWV (7.9 ± 1.3 m/s)baPWV (14.6 ± 2.2 m/s)were closely intercorrelated (r=0.67, P<0.001). Both baPWVcfPWVand cfPWVbaPWV, as a continuous variable, were significantly (P<0.001) associated with pulsatility index, carotid IMT,eGFRand, urinary ACRand carotid IMTin a similar strength. In categorical analyses, when the cfPWV/baPWV <9/<16 m/s group was set as the reference, participants with elevations in both PWV measures demonstrated the most severe TOD (P<0.001), including increased pulsatility index (91.2 vs 83.0 % for right middle cerebral artery),carotid IMT (700.9 vs 613.3 μm), urinary ACR (0.100 vs -0.408 mg/mmol),pulsatility index (91.2 vs 83.0 % for right middle cerebral artery), and decreased eGFR (98.1 vs 106.2

mL/min/1.73 m²). Multivariate analysis adjusted for common risk factors produced consistent results. Both baPWVcfPWVand cfPWVbaPWVare similarly associated with TOD. However, combined elevations in both PWV measures wasisassociated with the most significant TOD, indicating a potential additive effect of the two arterial stiffness measures.

Key words: brachial-ankle pulse wave velocity, carotid-femoral pulse wave velocity, arterial stiffness, target organ damage, hypertension

论文 ID：583

Alerting Reaction of Blood Pressure and Risk of Mortality in an Elderly Chinese Population

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Hypertension guidelines recommend multiple blood pressure readings due to potential alerting reactions during measurements. This study investigated the prognostic significance of this reaction in elderly individuals. The subjects (aged ≥60 years) were recruited from suburban Shanghai. Blood pressure was measured three times in sitting position using an oscillometric device. An alerting reaction is defined as the first blood pressure reading exceeds the average of the subsequent two readings. In total 4512 participants (44.7% men, average age 66.8 years), those with alerting reaction (n=2,633) were younger than those without (65.8 vs. 68.0 years, P<0.0001). During 5.9-year median follow-up (24,576 person-years), 430 total and 221 cardiovascular deaths occurred. Adjusted Cox regression showed alerting reaction was associated with lower total mortality (hazard ratio [HR] 0.82, 95% confidence interval [CI] 0.67-0.99) and cardiovascular mortality (HR 0.64, 95%CI 0.48-0.89). Compared with those without an alerting reaction, individuals with an alerting reaction had a 18% lower risk of total mortality (HR, 0.82; 95% CI, 0.67-0.99; P=0.04) and 36% lower risk of cardiovascular mortality (HR, 0.64; 95%CI, 0.48-0.89; P=0.002) than those without alerting reaction. Further categorical analyses showed the hazard ratio for an alert

reaction of +5 mmHg versus -5 mmHg was 0.75 (95% CI,0.57-0.99) and 0.57 (95% CI, 0.38-0.85) for total and cardiovascular mortality, respectively. In conclusion, this study first identified that the altering reaction of blood pressure is associated with a notably lower mortality risk in an elderly population. The underlying mechanism should be investigated in future studies.

Key words: altering reaction; blood pressure measurement; elderly

论文 ID：589

Inflammation-Mediated Hypertension from PM2.5 Exposure: Epigenetic Regulation of Renal GRK4/Nedd4L/ENaC Signaling Axis

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Background: Ambient fine particulate matter (PM2.5) is a major environmental risk factor for hypertension, yet the renal sodium-handling mechanisms remain incompletely understood.

Objective: This study investigates the role of G protein-coupled receptor kinase 4 (GRK4) and its downstream signaling axis in PM2.5-induced hypertensive pathogenesis.

Methods: Male Sprague-Dawley rats were exposed to PM2.5 (10 or 40 mg/kg) via intratracheal instillation for 12 weeks. Hemodynamic parameters, renal function, and molecular alterations were analyzed using immunohistochemistry, Western blot, qPCR, and co-immunoprecipitation. GRK4 expression was manipulated via lentiviral vectors to validate its role in blood pressure regulation.

Results: PM2.5 exposure induced dose-dependent hypertension, renal dysfunction, and sodium retention. Mechanistically, PM2.5 upregulated renal GRK4 expression through promoter hypomethylation, enhancing its interaction with Nedd4L (a ubiquitin ligase). Phosphorylated Nedd4L (p-Nedd4L) reduced epithelial sodium channel (ENaC) ubiquitination, leading to ENaC

accumulation and sodium reabsorption. GRK4 overexpression exacerbated hypertension and sodium retention, whereas GRK4 knockdown attenuated these effects.

Conclusion: This study identifies a novel signaling axis—GRK4/Nedd4L/ENaC—in PM2.5-induced hypertension, highlighting epigenetic and post-translational regulatory mechanisms. These findings provide mechanistic insights into environmentally mediated hypertensive pathogenesis and suggest potential therapeutic targets for PM2.5-related cardiovascular diseases.

Key words: PM2.5; Hypertension; GRK4; Nedd4L; ENaC; Sodium retention

论文 ID：611

Effects of Intensive Blood Pressure Control on Glycemic Metabolism Related Clinical Outcomes: Results from the ESPRIT Trial

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Background and Aims: The effect of intensive blood pressure (BP) lowering on the risk of glycemic metabolism is unclear. We aimed to evaluate the effect of intensive BP lowering on glycemic metabolism-related clinical outcomes using data from the Effects of intensive Systolic blood Pressure lowering treatment in reducing Risk of vascular events (ESPRIT) trial.

Methods: In this multicenter randomized controlled trial, participants were divided into diabetic and non-diabetic populations based on history of diabetes, baseline glycosylated hemoglobin ≥6.5%, or self-reported use of antidiabetic drugs. Glycemic metabolism-related clinical outcomes included new-onset diabetes in non-diabetic

participants, and glycemic metabolism-related serious adverse events (hypoglycemia, poor glycemic control or diabetic ketosis and other complications) in diabetic participants.

Results: We included 11255 participants, of whom 6497 were non-diabetic (age 64.7±7.2 years) and 4758 were diabetic (age 64.5±7.1 years). The proportion of various antihypertensive drugs in intensive arm was higher than that in standard arm at 1-year of follow-up. Over a median follow-up of 3.4 years, 104 (3.22%) patients in the intensive arm and 101 (3.09%) in the standard arm developed diabetes (hazard ratio [HR]: 1.04; 95% confidence interval (CI): 0.79-1.37). Among diabetic participants, intensive treatment showed no significant increase in glycemic metabolism-related serious adverse events (HR: 0.89; 95% CI: 0.69-1.16).

Conclusion: Intensive BP lowering strategy did not alter the risk of glycemic metabolism-related clinical outcomes in participants with or without diabetes. These findings support the use of intensive BP lowering strategy in patients across different glycemic metabolic profiles, without concern for the risk of glycemic metabolism.

Key words: Hypertension; Intensive blood pressure lowering; New-onset diabetes; Glycemic metabolism; Type 2 diabetes

论文 ID：612

Association between Age of New Onset of Obese and Cardiovascular Disease

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Objectives: Cardiovascular diseases (CVD) remain the leading cause of death worldwide, indicating the insufficient control of risk factors. Emerging evidence suggests that early-onset hypertension and diabetes is associated with a significantly higher risk of CVD

compared to late-onset. However, the relation of obese onset age with CVD remains inconclusive. This study sought to examine the association of onset age of obese with CVD.

Methods: This prospective study included 78,397 participants free of obese, defining as body mass index (BMI)≥ 28 kg/m2, and CVD in the first survey

(2006-2007) of the Kailuan study, a prospective cohort study in Tangshan, China. All participants were followed biennially until December 31, 2022. A total of 12,462 new-onset hypertension cases were identified during follow-up. Participants with new-onset obese were propensity score matched at a ratio of 1:1 with patients remain normal weight (defining as 18.5 ≤BMI< 25 kg/m2) during all 6 exams from 2008-2018 and 2,481 case-control pairs were included. We used Cox regression models to calculate the hazard ratios (HR) of incident CVD [including myocardial infarction (MI), stroke, atrial fibrillation (AF), and heart failure (HF)] across the age groups

Results: During an average follow-up of 9.26 years, we identified 497 incident CVD cases (including 173 cases of MI, 250 cases of stroke, 50 cases of AF, 78 cases of HF) and 180 deaths. After multivariate adjustment, the hazard ratio (95% confidence interval) were 1.51 (1.13–2.02) for the obese onset age <55 years old group of CVD, and 1.67 (1.02–2.72) of myocardial infarction. This association remains significant after sensitivity analysis.

Conclusions: Participans with obese onset age <55 years old were associated with a higher risk for CVD.

Key words: new-onset, age, obese, cardiovascular disease

论文 ID：613

Life’s Essential 8 and All-cause Mortality among patients with Myocardial Infarction: the Kailuan Cohort Study

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Objectives: Patients with myocardial infarction (MI) had significantly higher risk of all-cause mortality compared to non-MI individuals. Recently, the American Heart Association issued Life’s Essential 8 (LE8) to assess and promote cardiovascular health (CVH). However, data are lacking regarding the level of LE8 and future mortality risk in MI patients. Our study aims to elucidate the association between LE8 and mortality risk among MI patients based on the Kailuan study.

Methods: 6,079 patients with MI (from 2006–2020 surveys) were 1:2 matched with 12,145 non-MI control individuals based on age (±2 years) and sex from the Kailuan study. CVH was assessed using the LE8 score (ranged from 0 to 100) and was categorized into low (0–49), moderate (50–79), and high group (≥80). A higher score indicated better overall cardiovascular health. We followed participants for all-cause mortality until December 2022. Cox proportional hazards regression models were used to compute hazard ratios (HRs) and 95% confidence intervals (CIs).

Results: During a median follow-up of 8.83 years, 1,388 deaths occurred. MI patients with high (HR 0.68, 95% CI:0.46–1.00) and moderate (HR 0.75, 95% CI:0.65–0.86) LE8 score group exhibited a reduced risk of all-cause mortality compared with those with low one. Compared to non-MI participants, MI patients with low (HR 1.55, 95% CI:1.35–1.79) and moderate (HR 1.24, 95% CI:1.14–1.35) LE8 score had a higher risk of all-cause mortality. However, MI patients with high LE8 score had a similar mortality risk compared to non-MI patients (HR 1.18, 95% CI 0.81–1.71).

Conclusions: In MI patients, higher LE8 score was associated with a lower risk of all-cause mortality. Maintaining high LE8 level was associated with a mortality risk comparable to that of non-MI individuals.

Key words: Life’s Essential 8, myocardial infarction, all-cause mortality

论文 ID：618

Seasonal Variation in the Office and Out-of-office Blood Pressure Control in Patients Treated with Two Dual Antihypertensive Therapies

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Background: We investigated seasonal variation in the office and out-of-office blood pressure control in hypertensive patients treated with two single-pill dual combination antihypertensive therapies.

Methods: The study participants were hypertensive patients enrolled in a 24-week therapeutic study. Antihypertensive treatment was initiated with amlodipine/benazepril 5/10 mg/day or benazepril/hydrochlorothiazide 10/12.5 mg/day, with the possible up-titration to amlodipine/benazepril 10/20 mg/day or benazepril/hydrochlorothiazide 20/25 mg/day during follow-up.

Results: The proportion of up-titration to higher dosages at 24 weeks of follow-up was significantly higher in the benazepril/hydrochlorothiazide group (n=84) than in the amlodipine/benazepril group in patients who commenced treatment in winter (n=72, 18.9% vs. 5.0%, P=0.02), but not other seasons of treatment commencement (P>0.05). However, the mean changes from baseline to 24 weeks of follow-up in 24-h (mean between-group difference of -2.8 mmHg, P=0.08) and daytime diastolic blood pressure (mean between-group difference of -

3.2 mmHg, P=0.07) tended to be smaller in the benazepril/hydrochlorothiazide group than in the amlodipine/benazepril group in patients who commenced treatment in winter.

Conclusions: The benazepril/hydrochlorothiazide dual therapy requires a higher dosage of medication than the amlodipine/benazepril dual therapy to achieve blood pressure control in patients who commenced treatment in winter.

Key words: Seasonal variation, ambulatory blood pressure, antihypertensive treatment, winter

论文 ID：651

Associations of Combined Patterns of Sleep Duration, Work Hours, and Exercise Volume with Cardiovascular Health and Depression:

Cohort and Cross-sectional Studies from NHANES

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Background: Sleep, work, and exercise are key factors for cardiovascular and mental health, yet their combined effects of different patterns within a limited time framework remain underexplored. This study assesses the relationship between the combination patterns of these factors and cardiovascular health and depression.

Methods: Using NHANES data from 2005 to 2023 (three cross-sectional and four cohort samples), we evaluated associations between sleep duration, work hours, and exercise volume with health outcomes, including all-cause mortality, cardiovascular mortality, major adverse cardiovascular events (MACE), cardiovascular disease risk factors (CVDRF), and depression, utilizing Cox regression and generalized linear models. Based on single lifestyle analyses, we identified 27 lifestyle combinations and evaluated favorable and unfavorable lifestyle patterns through non-inferiority and non-superiority comparisons.

Finally, we examined the associations of these identified lifestyles with physical and mental health.

Results: In the sleep (cross-sectional: n=42,395; cohort: n=29,698), work (cross-sectional: n=39,940; cohort: n=28,047), and exercise (cross-sectional: n=37,939; cohort: n=25,137) analysis, the optimal lifestyle was identified as 6–7 hours of sleep per night, 35–48 work hours per week, and over 1400 minutes of MET of exercise per week. Within the constrained time framework, the three lifestyle factors were integrated into 27 combinations. Final analysis (n = 23,625) identified six favorable, three unfavorable, and eighteen moderate lifestyle patterns. Compared to moderate lifestyles, favorable lifestyles significantly reduced risks of all-cause mortality (HR=0.52,95%CI:0.40–0.67), depression (OR=0.50,95%CI:0.39–0.64), and other outcomes. In contrast, unfavorable lifestyles significantly increased risks of all-cause mortality (HR=2.06,95%CI:1.83–2.31), depression (OR=2.47,95%CI:2.11–2.89), and other outcomes. The identified lifestyles combinations mediated 44.36% and 44.58% of the bidirectional relationships between depression and MACE, respectively.

Conclusion: From the perspective of multiple time allocation patterns within a limited time framework, the combination of sleep duration, work hours, and exercise volume is associated with different risks of cardiovascular and mental health.

Key words: sleep duration, work hours, exercise, lifestyle, cardiovascular, depression.

论文 ID：652

Exploration on the Screening Value of 24-Hour Urinary Aldosterone Determination for Primary Aldosteronism

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Objective: Explore the screening value of 24-hour urinary aldosterone (UAL) for primary aldosteronism (PA) and establish screening cut-off points; compare the consistency of competitive assay, sandwich assay in chemiluminescence immunoassay (CLIA) and liquid chromatography-tandem mass spectrometry (LC-MS/MS) in detecting UAL.

Methods: Included were patients with essential hypertension (n=315) and patients with PA (n=98) who attended the Second Affiliated Hospital of Nanchang University from May 2025 to July 2026. Plasma aldosterone concentration and renin activity were measured. 24-hour urinary aldosterone was collected and tested by competitive assay, sandwich assay in CLIA, and LC-MS/MS. The receiver operating characteristic (ROC) curve of UAL was constructed to establish screening cut-off points, and the analysis of screening value was performed under different subgroup conditions. UAL was detected by 2 different CLIA methods and LC-MS/MS, and their consistency was compared.

Results:

① UAL measured by competitive CLIA was significantly positively correlated with that measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS) ($r = 0.870$, $P < 0.001$). The results of Passing-Bablok regression analysis for aldosterone concentrations obtained by CLIA and LC-MS/MS are shown in the figure. The slope was 1.51, and the intercept was 116.60. Bland-Altman analysis showed that the mean difference in aldosterone concentration between the two detection methods was -244.53 ng/dl.

② UAL measured by sandwich CLIA was significantly positively correlated with that measured by LC-MS/MS ($r = 0.937$, $P < 0.001$). The results of Passing-Bablok regression analysis for aldosterone concentrations obtained by CLIA and LC-MS/MS are shown in the figure. The slope was 0.79, and the intercept was 60.78. Bland-Altman analysis showed that the mean difference in aldosterone concentration between the two detection methods was 181.92 ng/dl.

③ UEA has certain screening value for PA. The area under the curve (AUC) of UAL was 0.66, with a diagnostic cut-off point of 4.206 μg/d, a sensitivity of 71%, and a specificity of 59%. The screening effect of UEA for PA is more prominent in males, people with hypokalemia, and people aged < 60 years.

Variables	Total (n = 413)	Non-PA(n = 315)	PA(n = 98)	P
Male,n(%)	250 (60.53%)	196 (62.22%)	54 (55.10%)	0.208
AGE,years	45.52 ± 12.88	44.50 ± 13.25	48.82 ± 11.03	0.004
DBP,mmHg	102.00 (90.00, 111.00)	102.00 (93.00, 112.00)	100.00 (88.25, 110.00)	0.099
SBP,mmHg	161.00 (148.00, 177.00)	160.00 (147.50, 176.00)	165.50 (153.00, 178.50)	0.153
BMI,kg/m2	26.22 (23.67, 28.41)	26.30 (23.65, 28.43)	26.03 (23.81, 28.32)	0.613
HbA1c	5.60 (5.30, 5.80)	5.60 (5.30, 5.80)	5.60 (5.20, 5.80)	0.841
AST,U/L	21.30 (18.01, 25.97)	21.52 (18.44, 26.27)	20.36 (16.80, 23.56)	0.041
ALT,U/L	23.70 (15.16, 35.79)	23.95 (15.40, 36.15)	20.74 (15.13, 33.66)	0.344
Cr，μmol/L	75.55 (62.55, 87.57)	75.55 (62.14, 87.03)	75.91 (63.95, 90.45)	0.200
EGFR，ml/min/1.73m2	96.50 (82.37, 108.26)	98.67 (84.04, 111.13)	90.25 (76.85, 102.37)	<.001
TG，mmol/L	1.64 (1.14, 2.57)	1.59 (1.13, 2.51)	1.76 (1.25, 2.75)	0.149
TC，mmol/L	4.77 (4.15, 5.52)	4.77 (4.17, 5.46)	4.71 (4.05, 5.60)	0.886
HDL-C，mmol/L	1.23 (1.01, 1.46)	1.22 (1.00, 1.46)	1.25 (1.09, 1.54)	0.158
LDL-Cmmol/L	2.72 (2.06, 3.32)	2.73 (2.09, 3.30)	2.65 (1.88, 3.41)	0.469
Na，mmol/L	140.89 (139.25, 142.10)	140.40 (139.09, 141.80)	141.64 (140.72, 143.19)	<.001
K，mmol/L	3.84 (3.63, 4.11)	3.87 (3.67, 4.15)	3.74 (3.37, 3.96)	<.001
Urinary Na mmol/L	120.63 (82.44, 146.15)	121.01 (82.19, 149.88)	112.84 (85.25, 135.67)	0.180
Urinary K mmol/L	27.83 (20.13, 35.93)	27.11 (19.96, 36.64)	28.89 (21.60, 32.96)	0.283
Urinary Cl mmol/L	110.27 (79.10, 137.90)	112.88 (78.27, 139.22)	107.48 (81.36, 132.03)	0.446
Urinary Cr，umol/L	15920.40 (10533.05, 21227.66)	16709.84 (11301.42, 21422.40)	13980.62 (7519.17, 18899.73)	0.004
24h urinary Na，mmol/d	138.92 (124.11, 158.53)	138.92 (123.86, 158.95)	139.29 (126.77, 155.24)	0.634
Salt intake，g/d	7.88 (6.73, 9.27)	7.88 (6.73, 9.29)	7.85 (6.70, 9.07)	0.781
ALD，ng/dl	14.70 (10.60, 21.70)	13.20 (9.37, 17.95)	20.95 (15.57, 29.77)	<.001
PRA，ng/ml/h	0.95 (0.27, 2.85)	1.60 (0.49, 3.52)	0.26 (0.14, 0.54)	<.001
ARR ,(ng/dl)/(ng/ml/h)	15.57 (5.56, 46.22)	9.00 (4.52, 19.71)	71.96 (35.92, 178.33)	<.001
UEA，μg/d	3.18 (1.81, 5.39)	3.00 (1.61, 4.70)	4.54 (2.76, 7.95)	<.001
Urine volume，L	1.50 (1.10, 2.00)	1.50 (1.10, 2.00)	1.80 (1.40, 2.40)	<.001
Hyperlipemia, n(%)	216 (52.30%)	160 (50.79%)	56 (57.14%)	0.272
Diabetes, n(%)	37 (8.96%)	28 (8.89%)	9 (9.18%)	0.929

Table 1.Baseline Clinical Characteristics.

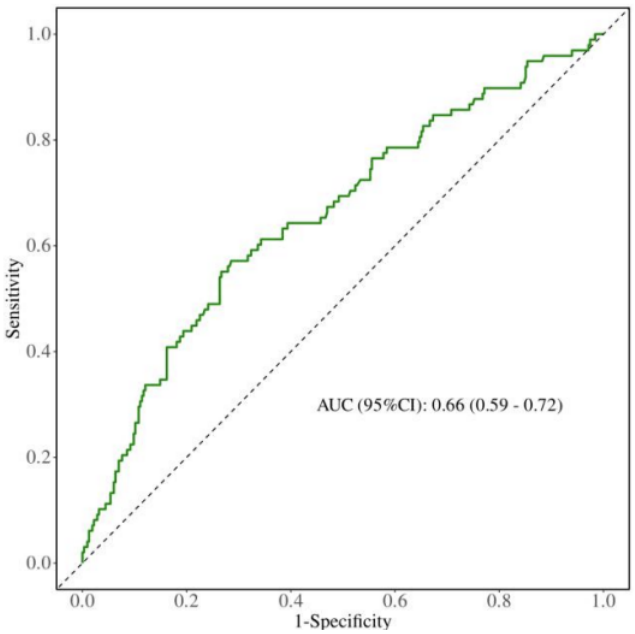

Figure 1. Receiver operating characteristic curve for screening primary aldosteronism using 24-hour urinary aldosterone

Variables	n (%)	OR (95%CI)	*P*	P for interaction
All patients	413 (100.00)	1.15 (1.08 ~ 1.22)	<.001	
Sex				0.055
famale	163 (39.47)	1.08 (0.98 ~ 1.18)	0.127	
male	250 (60.53)	1.22 (1.12 ~ 1.32)	<.001	
Hyperlipemia				0.862
No	197 (47.70)	1.16 (1.07 ~ 1.26)	<.001	
Yes	216 (52.30)	1.15 (1.04 ~ 1.26)	0.004	
Diabetes				0.276
No	376 (91.04)	1.17 (1.09 ~ 1.25)	<.001	
Yes	37 (8.96)	1.06 (0.89 ~ 1.25)	0.524	
K				<.001
<3.5mmol/L	68 (16.46)	1.50 (1.19 ~ 1.90)	<.001	
≥3.5mmol/L	345 (83.54)	1.07 (0.99 ~ 1.15)	0.106	
Urinary Na				0.490
Q1	136 (32.93)	1.21 (1.08 ~ 1.34)	<.001	
Q2	141 (34.14)	1.13 (1.01 ~ 1.26)	0.039	
Q3	136 (32.93)	1.11 (1.00 ~ 1.23)	0.048	
Age				0.475
<60 years	345 (83.54)	1.17 (1.10 ~ 1.25)	<.001	
≥60 years	68 (16.46)	1.09 (0.92 ~ 1.30)	0.307	

OR: Odds Ratio, CI: Confidence Interval

Table2.Subgroup analysis. A logistic regression model was used to calculate the HR of the relative risk of the primary outcome and the associated 95% CI in the two groups.

Conclusion:

① The sandwich CLIA shows good consistency with LC-MS/MS, and may serve as a clinical alternative to mass spectrometry, reducing detection costs.

② UAL has certain value in the screening of PA, with better screening performance in males, people with hypokalemia, and those under 60 years of age.

Key words: primary alsteronism, screening, urinary aldosterone

论文 ID：653

Ethnic Differences in All-Cause and Cardiovascular Mortality Among Hypertensive Patients: Findings from a Multi-ethnic Cohort Study in China

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Background: Studies in Western countries showed significant racial and ethnic differences in hypertension and cardiovascular adverse outcomes. However, in China, this information is lacking.

Methods: This cohort study encompassed 55,940 primary hypertensive patients aged ³ 35 years, including Han Chinese, Yi, Zhuang, Dai, and Tibetan ethnic groups, who participated in the China Basic Public Health Service Program in 2018 and followed up until November 30, 2023. Differences in all-cause and CVD mortality between ethnic groups were analyzed using Cox proportional hazards regression models with adjustment for demographic, socio-economic status, lifestyle, clinical risk factors, and residential altitude. The percent reduction in the β estimate (log-hazard ratio [HR]) for ethnic groups quantified the contribution of each factor group to ethnic differences in all-cause and CVD mortality.

Results: A total of 55,940 hypertensive patients were included. During 268,738 person years of follow-up, 12.3% of participants (n=6906) died, of which 7.8% (n=4337) died from CVD. After full model adjustment, the risk of for all-cause mortality increased by 50% for Dai (HR, 1.50; 95% CI, 1.37-1.63), and 42% for Tibetan participants (HR, 1.42; 95% CI, 1.13-1.79), respectively, compared with Han participants, while the risk of all-cause mortality was further reduced for Zhuang participants (HR, 0.60; 95% CI, 0.54-0.67), with no significant difference observed among Yi participants. Among Yi and Tibetan participants, adjusting for socioeconomic factors (108% and 137%) and altitude of residence (58% and 195%)

resulted in the greatest reduction in β estimates for ethnicity. Similar trends were also seen for CVD mortality.

Conclusion: The study highlights differences in all-cause and CVD mortality between different ethnic groups in China, which are contribution in part to social determinants of health and residential altitude.

Key words: Hypertension; Ethnicity; Cardiovascular disease; Mortality; Disparity

论文 ID：660

Association of Weight-adjusted Waist Index with Hypertension Plus Hyperuricemia among Middle-aged and Older Adults in China: A Cross-sectional Analysis

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Background: The weight-adjusted waist index (WWI) is a novel indicator that could estimate body fat and muscle mass. This study aimed to investigate the relationship between WWI and hypertension plus hyperuricemia (HTN-HUA).

Methods: The data were drawn from the China Health and Retirement Longitudinal Study. Logistic regression analyses were used to explore the association between WWI with HTN-HUA, hypertension (HTN) alone, and hyperuricemia (HUA) alone. Restricted cubic spline (RCS) analyses were employed to examine potential nonlinear associations. Receiver operating characteristic (ROC) curves were utilized to assess the predictive ability of WWI.

Results: A total of 9,801 participants were included, among whom 756 (8%) were diagnosed with HTN-HUA, 4,381 (45%) with HTN alone, and 1,236 (13%) with HUA alone. WWI was significantly associated with HTN-HUA, HTN alone, and HUA alone after adjusting for potential confounders. Compared to the lowest quartiles of WWI, the odds ratios of the

highest quartiles were 3.04 (95% confidence interval [CI]: 2.35-3.94) for HTN-HUA, 1.53 (95%CI: 1.34-1.74) for HTN alone, and 1.93 (95%CI: 1.42-2.61) for HUA alone. RCS analyses demonstrated a nonlinear association between WWI with HTN-HUA. The fully adjusted model, which included WWI, exhibited a moderate predictive ability for HTN-HUA (area under the curve: 0.753, 95%CI 0.736-0.771). The association between WWI and HTN-HUA was more prominent among individuals between 45-59 years and those without diabetes.

Conclusion: The study suggested that a significant and nonlinear association between WWI and HTN-HUA. WWI had the potential to facilitate the early detection of HTN-HUA.

Key words：Weight-adjusted waist index, hypertension, hyperuricemia

论文 ID：671

Global Pattern of Cardiovascular Diseases Caused by Hypertension in 1990-2021

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Background：Cardiovascular diseases caused by hypertension pose a serious threat to global health. This study analyzed trends and future projections of hypertension-related cardiovascular diseases burden using Global Burden of Disease 2021 data.

Methods: We estimated mortality and disability-adjusted life years (DALYs) via DisMod-MR 2.1, analyzed regional disparities by socio-demographic index (SDI), and projected trends to 2060 using the Bayesian age-period-cohort model. Health inequalities were evaluated via the slope index of inequality and concentration index.

Results: Globally, the number of DALYs and deaths due to cardiovascular diseases caused by hypertension increased in 2021, reaching 214,518,341 (95% uncertainty interval [UI]: 180,418,055-247,570,720) and 10,376,441 (95% UI: 8,784,052-12,032,762) respectively, while the age-standardized DALYs rate (ASDR) and age-standardized mortality rate (ASMR) decreased. In high SDI regions, the number of DALYs and deaths decreased, while in the remaining

regions, they increased. However, the ASDR and ASMR in all SDI regions decreased. In 21 major regions, the number of DALYs and deaths increased. East Asia had the highest values, and Oceania had the lowest. Only in Southern Sub-Saharan Africa did the ASDR and ASMR increase. Regarding age, DALYs rates increased with age from 15-74 years, and mortality increased with age from 15-84 years, and decreased after 75 and 85 years, respectively. It is predicted that DALYs rates and mortality continue to decline and stabilize by 2060.

Conclusion: Hypertension-related cardiovascular diseases burden is unevenly distributed, with socio-economic development strongly associated with outcomes. Tailored prevention strategies are critical to address this evolving public health crisis.

Key words: Cardiovascular diseases; Hypertension; Health inequality analysis; Bayesian age-period-cohort; GBD

论文 ID：674

Sleep Disorders as a Causal Factor for Hypertension Risk: Evidence from NHANES and Mendelian Randomization

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Background: Hypertension is a leading cause of chronic cardiovascular disease, with its incidence exceeding 60% in individuals over 60. While adequate sleep is essential for health, the causal relationship between sleep disorders and hypertension remains unclear. This study aims to explore this relationship using data from the National Health and Nutrition Examination Survey (NHANES) and Mendelian Randomization (MR) analysis.

Methods: We utilized data from the 2006-2014 NHANES cycles and genome-wide association study (GWAS) data from the MR-Base database. Hypertension data were derived from three GWAS databases, and sleep disorder data were sourced from the FinnGen study. Multivariable-

adjusted logistic regression was used to evaluate the observational relationship between sleep disorders and hypertension. For the MR analysis, single nucleotide polymorphisms (SNPs) associated with sleep disorders were used as instrumental variables to assess the causal effect on hypertension.

Results: The NHANES analysis included 17,001 participants, with 16,176 classified as having sleep disorders. The incidence of hypertension was significantly higher in participants with sleep disorders compared to those without (79.5% vs. 61.7%). Multivariable-adjusted models showed a strong association between sleep disorders and increased risk of hypertension (OR = 1.516, 95% CI 1.103 - 2.083, P = 0.011 in the fully adjusted model). MR analysis supported a causal relationship between sleep disorders and hypertension.

Conclusions: This study provides evidence supporting a causal relationship between sleep disorders and an increased risk of hypertension. The findings highlight the importance of addressing sleep disorders in the prevention and management of hypertension, suggesting that improving sleep health may be an effective strategy to reduce hypertension incidence and its associated health burden.

Key words: Mendelian randomization; causality; hypertension; sleep disorders; NHANES.

论文 ID：678

Association between the Estimated Pulse Wave Velocity and Stroke: a Population Based Cross-sectional Study

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Aims: Pulse wave velocity (PWV) is a well-established measure of arterial stiffness which has been linked to cardiovascular disease. In recognition of the challenges associated with measuring PWV, researchers have developed an alternative method by

equations rely on age and mean arterial pressure (ePWV). However, whether this parameter is indeed associated with stroke, has not been fully verified.

Methods: The current study was a branch of the ChinaHEART cohort in middle China that involved a total of 6860 community-dwelling adults. We examine the association between ePWV and stroke in a cross-sectional survey.

Results: According to restricted cubic spline analysis, the odds of stroke was increased in individuals with a higher level of ePWV; ROC analysis indicated that ePWV had good discriminatory power for stroke (AUC=0.746 in the adjusted model); according to logistic regression, the OR of each 1 m/s increase of ePWV was 1.26 (1.14-1.39, P<0.001), and the high ePWV group (≥10 m/s) had 2.22 (1.54-3.21, P<0.001) times risk of incident stroke.

Conclusions: This study demonstrates that ePWV is independently linked to stroke. These findings support the use of vascular aging markers in the fight against stroke.

Key words: ePWV, stroke, population study, cross-sectional study

论文 ID：679

Association Between Knee Cartilage Degradation and Cardiac Remodeling: A Cross-Sectional Analysis in a Community-Based Cohort

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Objective : Osteoarthritis (OA), a leading cause of disability, has been epidemiologically linked to cardiovascular disease (CVD), yet the relationship between structural cartilage degeneration and cardiac remodeling remains poorly characterized. This cross-sectional study investigates whether knee cartilage degradation, quantified via ultrasonography, correlates with echocardiographic markers of subclinical cardiovascular dysfunction.

Methods: Middle-aged and elderly people aged 35-75 years who met the inclusion criteria were enrolled. Knee cartilage degradation was scored (0-3 per side) using ultrasound, with total scores categorized as Normal (0-3, n=1041) or Degraded (≥4, n=430). Cardiac structure and function parameters, including left ventricular ejection fraction (LVEF), left atrial volume index (LAVI), left ventricular mass index (LVMI), and diastolic function (mitral valve e' and E/e' ratio), were measured by echocardiography. Group comparison, logistic regression, subgroup and sensitivity analyses and XGBoost machine learning were used to assess associations and feature importance.

Results: Participants with degraded cartilage were older (median age 64 vs. 58 years, P<0.001) and had a lower male proportion (31% vs. 45%, P<0.001). The Degraded group exhibited a significantly higher median LAVI (29 vs. 27 mL/m², P<0.001). Subgroup and sensitivity analyses confirmed the association with LAVI was robust. XGBoost analysis identified cartilage degradation as an important contributor to LAVI (standardized gain value 4.89%, ranking 10th among 24 variables).

Conclusion: Knee cartilage degeneration is associated with left atrial enlargement. These findings underscore the potential role of OA-related structural joint damage in subclinical cardiac remodeling, offering a foundation for future exploration of comprehensive care strategies.

Key words: Osteoarthritis; Knee cartilage degeneration; Cardiac remodeling; Population study; Left atrial volume index;

论文 ID：680

Association of Aldosterone Levels with Left Ventricular Hypertrophy in Primary Hypertension: Evidence from Young and Middle-Aged Hospitalized Patients

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Objective: To investigate the demographic and clinical characteristics, etiological classification of hypertension, and prevalence of target organ damage among hospitalized Chinese patients aged 12–50 years, and to identify risk factors for target organ damage.

Methods: We retrospectively reviewed medical records of patients aged 12–50 years who were admitted to the Hypertension Unit of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, from 2015 to 2019 for etiological evaluation of hypertension. Demographic data, medical history, and laboratory results were collected. Hypertension etiology was determined based on clinical and diagnostic findings. Left ventricular mass index (LVMI) was calculated, and left ventricular hypertrophy (LVH) was defined according to 2024 Chinese guidelines for the management of hypertension. Logistic regression and mediation analyses were performed to evaluate factors associated with LVH.

Results: A total of 1,802 patients were included, with a mean age of 36.5 ± 9.9 years; 65.3% (n=1,177) were male. Secondary hypertension was diagnosed in 641 patients (35.6%), predominantly endocrine hypertension (n=439, 68.4%) and renovascular hypertension (n=134, 20.9%). The prevalence of LVH was significantly higher in secondary hypertension than in primary hypertension (30.4% vs. 17.0%, $P<0.001$), with the highest rate observed in patients with renal parenchymal hypertension (47.2%). After adjusting for ambulatory blood pressure levels and potential confounders, basal plasma aldosterone, orthostatic plasma aldosterone, and 24-hour urinary aldosterone were all independently associated with LVH ($P<0.013$). Subgroup analyses showed that in primary hypertension, baseline plasma aldosterone was significantly associated with LVMI, whereas this association was not observed in secondary hypertension ($P_{interaction}=0.011$). Similar results were found for upright plasma aldosterone ($P_{interaction}=0.019$).

Conclusion: Among hospitalized hypertensive patients aged 12–50 years, the majority were male and had primary hypertension. Nevertheless, elevated aldosterone levels in primary hypertension were independently associated with LVH, underscoring the importance of early aldosterone assessment to prevent target organ damage.

Key words: Aldosterone; left ventricular hypertrophy; primary hypertension

论文 ID：697

Prognostic Value of Left Atrial Stiffness Index for Incident Heart Failure in Paroxysmal Atrial Fibrillation: A Prospective Cohort Study

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Aims: Approximately 20-30% of paroxysmal atrial fibrillation (PAF) may progress into heart failure (HF). Identifying specific PAF characteristics predisposing to HF is crucial for enabling precise interventions.

Methods and results: A cross-sectional study first evaluated subclinical cardiac dysfunction in PAF (n=142) versus controls (n=63), employing echocardiography to assess noninvasive left ventricular myocardial work (LVMW), left atrial (LA) remodeling, and LA strain. Subsequently, a prospective cohort study within the PAF group identified echocardiography predictors for incident HF using multivariable logistic regression analysis (adjusted for confounding; Stata 15.0, R 4.1). Compared with the controls, PAF had significantly elevated global wasted work (GWW), impaired global work efficiency (GWE), increased peak strain dispersion (PSD), enlarged LA volume index (LAVI), decreased LA ejection fraction (LAEF), impaired LA strain and increased LA stiffness index (LASI) (0.69±0.51vs 0.41±0.18, $p<0.001$). Increased LA stiffness index was correlated with increased PSD, impaired E/e', enlarged LAVImin, decreased LAEF and impaired LA strain in PAF. During a median follow-up of 40.5 months, incident HF occurred in 9.86% of PAF participants. Increased LASI (OR:16.4, 95%CI 1.44-186.72, p=0.02) was significantly associated with incident HF, with a value greater than 1.24 maximizing predictive accuracy (AUC=0.77, 95%CI 0.61-0.93) in non-alation subgroup.

Conclusions: Subclinical cardiac dysfunction of PAF includes elevated GWW, reduced GWE, increased LASI, and impaired LA strain. The cardiac dysfunction of PAF may originate in LA dysfunction. Increased LASI could predict incident HF independently and PAF with LASI greater than 1.24 should be strongly proposed for early sinus rhythm restoring strategy to prevent incident HF.

Key words: Key words: Paroxysmal Atrial Fibrillation, Noninvasive Left Ventricle Myocardial Work, Left Atrial Remodeling, Left Atrial Strain, Left Atrial Stiffness Index, Incident Heart Failure

论文 ID：709

Associations of Serum Folate Levels with Hypertension Among Middle-Aged and Elderly Population in Eastern China

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Background: Although B vitamins are implicated in cardiovascular regulation, the associations between serum folate (vitamin B9) and hypertension remain unclear, particularly regarding discrepancies in this association across different genders and BMI subgroups. This study aimed to investigate relationships between serum folate levels and hypertension among middle-aged and elderly population in eastern China.

Methods: A community-based cross-sectional study was conducted among 3278 participants aged 45–69 years in Zhejiang Province, China. Serum folate levels were quantified using liquid chromatography tandem mass spectrometry (LC-MS/MS). Hypertension was defined as measured blood pressure ≥ 140/90 mmHg, or current use of antihypertensive medications. Multivariate logistic regression models were used to assess associations of folate with hypertension prevalence. Dose–response relationships were evaluated using restricted cubic splines (RCSs).

Results: Higher serum folate levels were significantly associated with reduced hypertension prevalence (adjusted OR per SD increase: 0.90; 95%CI: 0.84, 0.98), with RCSs confirming linear dose–response (p-overall < 0.05, p-nonlinearity > 0.05). Compared with the lowest tertile, participants in the highest folate tertile had a 20% lower hypertension

risk. This association was statistically significant in females and in overweight/obese subgroups, but was not observed in males or in individuals with normal and low BMI.

Conclusions: Serum folate is inversely associated with hypertension prevalence in middle-aged and elderly population. This study supports the potential of serum folate as a modifiable biomarker in hypertension prevention strategies, particularly among females and among overweight/obese individuals within middle-aged and elderly population.

Key words: hypertension, serum folate, vitamin B9, blood pressure

论文 ID：717

Association between Cumulative Atherogenic Index of Plasma and new-onset Stroke among Middle-aged and Elderly Chinese patients with stage 0-3 Cardiovascular-Kidney-Metabolic syndrome: A Longitudinal Cohort Study

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Background: The clinical characteristics of Cardiovascular-kidney-metabolic syndrome (CKM) syndrome are characterized by the interplay between chronic kidney disease, cardiovascular disease, and metabolic disorders. The relationship between the cumulative atherogenic index of plasma (CumAIP) and the risk of stroke in patients with CKM syndrome remains unclear.

Methods: We acquired data from the China Health and Retirement Longitudinal Study (CHARLS). In total, 4,674 subjects were categorized into quartiles according to their CumAIP score and stratified by CKM syndrome stages (0–3). Using multivariable Cox regression models, we assessed the link between CumAIP and stroke risk, while restricted cubic spline (RCS) assessment was performed to evaluate potential non-linear associations.

Subgroup analyses examined the modifying effects of age, sex, smoking, drinking, hypertension, and diabetes status.

Results: During follow-up, 261 (5.6%) stroke events occurred, with incidence rising from 2.5% in CKM stages 0-1 to 6.3% in stages 2-3. After correccting for various potential confouders, each unit increase in CumAIP was linked to a 149% higher stroke risk (HR = 2.49, 95% CI: 1.69-3.65). Participants in the highest CumAIP quartile had a 144% greater risk than those in the lowest quartile (HR = 2.44, 95% CI: 1.61-3.7). RCS analysis indicated a linear relationship (P for non-linearity = 0.182).

Conclusion: Elevated CumAIP is strongly linked to enhanced stroke risk, particularly among patients with advanced CKM stages and high-risk subgroups such as older adults, smokers, and individuals with diabetes.

Key words: cumulative atherogenic index of plasma, atherogenic index of plasma, stroke, cardiovascular-kidney-metabolic, CHARLS

论文 ID：719

Association of Anemia with All-cause, Cardiovascular and Cancer Mortality in Hospitalized Patients Aged 85 Years and Older:

A 13-year Retrospective Cohort Study

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Background: This research sought to explore the relationships between anemia and mortality outcomes, including all-cause, cardiovascular, and cancer-related deaths, in individuals aged 85 years or older.

Methods: A total of 377 patients aged 85 and above were enrolled from the geriatric department of the General Hospital of Northern Theater Command between September 1, 2011,

and December 1, 2024. Participants were categorized into anemia (n=238) and non-anemia (n=139) groups using hemoglobin (Hb) levels at admission, with anemia defined by WHO standards. The primary endpoint was all-cause mortality, while secondary endpoints included cardiovascular and cancer mortality. Cox proportional hazards models and Kaplan-Meier survival analyses were employed to evaluate these associations.

Results: Over the follow-up period, 40.3% (n=152) of patients died from all causes, 25.5% (n=96) from cardiovascular events, and 14.9% (n=56) from cancer. Cox regression indicated a significant inverse relationship between Hb levels and all-cause mortality (HR=0.99, 95% CI: 0.98-0.99, P=0.001). Patients in the highest Hb quartile exhibited a 51% reduced risk of all-cause mortality compared to the lowest quartile (HR=0.49, 95% CI: 0.29-0.83). Additionally, higher Hb levels were linked to significantly lower cancer mortality (HR=0.26, 95% CI: 0.10-0.68, P=0.006), though no significant association was found with cardiovascular mortality (P=0.084). Kaplan-Meier analysis demonstrated notable survival differences among Hb quartiles (P=0.000680). Subgroup analyses revealed consistent results across diverse populations.

Conclusion: Among super-elderly patients, anemia significantly correlates with increased all-cause and cancer-related mortality risks, emphasizing the importance of effective anemia management in this population.

Key words: Anemia, All-cause Mortality, Cardiovascular Mortality, Cancer Mortality, older adults

论文 ID：724

Comparison of Brachial and Central Blood Pressure in a Young Population Based on the "CONNEQT Pulse" Device

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Objective: To describe blood pressure (BP) patterns of Shanghai youth using "CONNEQT Pulse" (Cardiex).

Methods: 359 participants (18-35 years) were enrolled, with measurements including heart rate (HR), brachial BP (bBP), central aortic BP (cBP), augmentation pressure (AP), index (AIx), and subendocardial viability ratio (SEVR). Systolic amplification = brachial systolic BP (bSBP) - central systolic BP (cSBP); pulse pressure (PP) amplification = brachial PP (bPP)/central PP (cPP). Brachial hypertension: bSBP/brachial diastolic BP (bDBP)≥140/90 mmHg; prehypertension 120-139/80-89 mmHg. Central hypertension: cSBP/central diastolic BP (cDBP)≥130/90 mmHg. ANCOVA controlled confounders; ROC curve determined cSBP cut-off.

Results: 359 participants (173 males, 48.2%): age 20.9±2.3 years, BMI 22.2±3.5 kg/m². Key metrics (mean±SD): bSBP 117.6±14.6 mmHg, cSBP 105.6±12.8 mmHg, SEVR 142.1±26.9%. Males vs. females: higher bSBP (124.0±14.1 vs. 111.6±12.3 mmHg), cSBP (110.0±13.0 vs. 101.4±11.1 mmHg), SEVR (148.1±27.7% vs. 136.6±25.0%) (all P<0.001). Lower AIx in males (10.5±10.8% vs. 13.7±13.2%, P<0.05); AP similar (P=0.711). Males had greater systolic amplification (14.0±4.48 vs. 10.2±3.6 mmHg) and PP amplification (both P<0.05), significant after adjusting for age, BMI, HR (P<0.01). Of 50 brachial hypertension cases (37 males), 49 (36 males) had central hypertension. Of 73 brachial prehypertension cases (35 males), 8 (3 males) had central hypertension. Optimal cSBP cut-off: 119.5 mmHg (sensitivity 100%, specificity 92.5%).

Conclusions: (1) Young males have higher bBP, cBP, SEVR, lower AIx. (2) Males show greater PP amplification. (3) Central BP enables more accurate monitoring. (4) Optimal cSBP cut-off for youth hypertension: 119.5 mmHg.

Key words: Blood Pressure, Pulse Pressure Amplification, Prehypertension

论文 ID：727

A Comparative Study of Endocardial Septal Radiofrequency Ablation and Ventricular Pacemaker Implantation on SAM Improvement in Patients with Left Ventricular Outflow Tract Obstruction

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Objective: To investigate the efficacy of intramyocardial septal radiofrequency ablation and ventricular pacemaker in the treatment of dynamic left ventricular outflow tract obstruction (LVOTO).

Methods: The 90 patients with dynamic LVOTO admitted to the Department of Cardiology of the Affiliated Hospital of Chengdu University from June 2017 to January 2025 were selected, and were divided into the observation group and the control group according to random number table method, with 45 cases in each group. The observation group was treated with intramyocardial septal radiofrequency ablation and the control group was treated with ventricular packing. The therapeutic effects of the two groups were compared one year after surgery.

Results: The differences of left ventricular end-diastolic diameter, left ventricular mass index, left ventricular outflow tract pressure gradient (LVOTPG) and LVOTPG on provocation before and after the operation in the observation group were higher than those in the control group ($P < 0.05$). The differences of the levels of N-terminal pro-B-type natriuretic peptide (NT_x0002_proBNP) and troponin Ⅰ (cTnⅠ) before and after the operation in the observation group were higher than those in the control group ($P < 0.05$). There was no significant difference between the observation group and the control group in the middle interventricular septal thickness, the basal interventricular septal thickness and the posterior wall thickness ($P > 0.05$). There was no significant difference in the overall incidence of complications between the observation group and the control group ($P > 0.05$).

Conclusion: For patients with dynamic LVOTO, both ventricular packing and intramyocardial septal radiofrequency ablation can improve cardiac function and levels of cTnI and NT-proBNP, with a low incidence of complications, making them worthy of being widely applied in clinical practice.

Key words: dynamic left ventricular outflow tract obstruction; endocardial septal radiofrequency ablation; ventricular pacemaker

论文 ID：730

Effect of Salt Reduction Interventions in Lowering Blood Pressure and Salt Intake in Zhejiang Province, China, 2017–2021 A Randomized Controlled Trial

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Background: Addressing high-salt diets in China through interventions can significantly reduce blood pressure (BP) and the associated health risks. Objective: This study aims to evaluate the effectiveness of a comprehensive salt reduction intervention implemented across counties in Zhejiang Province, focusing on system establishment, extensive publicity, and targeted population interventions.

Methods: The Salt Reduction and Hypertension Prevention Project was initiated in Zhejiang Province. Cross-sectional surveys were conducted before the intervention and after. The research commenced in 2017 with a baseline survey involving 7512 participants from five counties. Four counties were randomly selected for the intervention, implementing a multifaceted salt reduction strategy, while one county served as a reference without any intervention. The primary outcomes measured were changes in BP and 24 h urinary sodium and potassium excretion.

Results: Following the intervention, 24 h urinary potassium excretion experienced a significant increase, rising from 1441.3 (SD 681.9) to 1676.9 (SD 931.4) mg per day, $p < 0.001$. Utilizing a linear mixed-effects model, the adjusted net difference in urinary

sodium changes was calculated to be 394.1 mg per day (95% CI, 133.2 to 655.0) (p = 0.003). There was a notable reduction in systolic blood pressure (SBP) from 131.2 (SD 19.2) to 129.8 mmHg (SD 18.0), and diastolic blood pressure (DBP) also decreased from 80.8 (SD 10.8) to 78.9 mmHg (SD 10.2), p < 0.001. The adjusted net differences for SBP and DBP between the intervention and reference groups were 1.3 (95%CI, 0.5 to 2.1) and 1.4 mmHg (95%CI, 0.9 to 2.0), respectively, p < 0.001.

Conclusions: The findings indicate that a multi-sectoral approach, combined with extensive public awareness initiatives and precisely targeted interventions, can significantly increase urinary potassium excretion and reduce sodium and blood pressure.

Key words: community intervention; salt reduction; effect evaluation; sodium; blood pressure

论文 ID：738

The risk of cardiovascular disease in prediabetes among the hypertensions --Analysis from the UPPDATE STUDY

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Backgrounds: The concurrent of hypertension and type 2 diabetes (T2DM) host more than triple risks of developing cardiovascular disease (CVD). In addition to T2DM, whether hypertension with prediabetes(preDM) had the same risk of developing CVD remains unknown.

Methods: The UPPDATE study enrolled 8548 eligible hypertension subjects from 36 cities in China from 2017 to 2019. All enrolled hypertensives would undergo questionnaires and clinical assessments and they were required to provide biomedical reports within one-year from his/her enrollment. In the cross-sectional study, preDM was defined as no T2DM history but reported HbA1c ranged 5.7-6.4% or diagnosed impaired fasting glycaemia or impaired

glucose tolerance. The history of coronary artery disease (CAD), cerebral infarction (CI), peripheral arterial occlusive, heart failure (HF) and atrial fibrillation were recognized as CVD. Stata 15.0 was used for analyzing the association of preDM and CVD.

Results: 330, 63, 117 subjects were classified into preT2DM group using HbA1c, FPG, PG2h data, respectively. In all, 4005 subjects were included in the analysis, consisting of 41.9% with no T2DM (n=1678), 9.5% with preT2DM (n=382) and 48.6% with T2DM (n=1945). Of 8493, self-reported history of CAD, CI, PAD, AF, HF, PCI or CABG were 17.9%, 10.1%, 1.8%, 2.4%, 2.3% and 0.9%. Cumulative CVD proportion was 23.9%. Compared with no T2DM group, the odds ratio of CVD risk was 1.24 (95%CI 0.91-1.68, p=0.17) in preDM group, with significant risk in CAD (OR=1.35, 95%CI 1.01-1.90, p=0.046) and HF (OR=2.04, 95%CI 1.12-3.75, p=0.021), and 1.41 (95% 1.16-1.72, p=0.001) in the T2DM group in adjusted model with significant risk in CAD, CI and HF. Subgroup analysis revealed that preDM with LDL>2.6mmol/L and SBP >140mmHg may host significant risk of developing CVD.

Conclusions: Compared with the patients with no diabetes, hypertension patients with preDM were associated with higher risk of CVD. Blood pressure and LDL-C level need strictly controlled in preDM patients with hypertension to prevent CVD.

Key words: CVD, prediabetes, hypertension

论文 ID：746

Association between CKM Stages and Cognitive Function

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Background: China's rapidly aging population faces a significant burden of cognitive impairment, associated with individual cardiovascular and metabolic risk factors. The novel Cardiovascular-Kidney-Metabolic (CKM) syndrome framework integrates these interconnected

conditions into a progressive staging system, capturing cumulative multi-organ dysfunction. Its association with cognitive function in the Chinese population remains unexplored.

Objective: To investigate the cross-sectional and longitudinal associations between CKM stages and cognitive function in middle-aged and older Chinese adults.

Methods: This study utilized data from the nationally representative China Health and Retirement Longitudinal Study (CHARLS). Participants with complete data from the baseline wave (2011) and follow-up (2015) were included. CKM stages were defined per 2023 AHA criteria, adapted for Asian populations: Stage 0 (no risk factors); Stage 1 (overweight/obesity/prediabetes); Stage 2 (established metabolic risk factors [e.g., hypertension, diabetes] and/or moderate CKD); Stage 3 (subclinical CVD or advanced CKD). Cognitive function was assessed across five domains: Orientation, Attention, Visuoconstruction, Episodic Memory (immediate/delayed recall), and Mental Integrity (Total Score, sum of domains 0-31). Scores were Z-normalized. Covariates included gender, age (>60), education, marital status, smoking, alcohol, income, and depressive symptoms (CESD-10). Cross-sectional analysis (n=5,749, 2011) used linear regression to assess baseline CKM stage and cognitive scores. Longitudinal analysis (n=417 with baseline impairment) used logistic regression to assess baseline CKM stage and cognitive decline over 4 years. Models were sequentially adjusted.

Results: Men had higher cognitive scores (16.13 vs 15.04, $p<0.001$), lower depression (CESD 8.66 vs 10.22, $p<0.001$), lower abdominal obesity (32.1% vs 71.5%, $p<0.001$), and lower metabolic syndrome prevalence (23.8% vs 44.3%, $p<0.001$) than women. Women were more frequently classified in CKM Stage 2 (47.7% vs 17.1%), while men were more often in Stage 3 (58.8% vs 23.1%). Higher CKM stages were significantly associated with poorer overall cognitive performance ($p<0.001$), with the lowest scores in Stage 3. Episodic Memory showed the most pronounced decline. Linear regression confirmed a robust negative association between CKM stage and Total Cognitive Score, persisting after full adjustment (Model 4: $\beta = -2.128$, $p = 0.033$). Episodic Memory also showed a strong, consistent inverse association across all models (Model 4: $\beta = -2.731$, $p = 0.006$). Visuoconstruction showed a negative association only in the unadjusted model, which attenuated after adjustment. No significant adjusted associations were found for Orientation, Attention, or Mental Integrity. In unadjusted analysis, baseline CKM Stage 2 was associated with a significantly reduced risk of further cognitive decline over 4 years compared to Stage 0 (OR = 0.349, 95% CI: 0.155-0.787, $p = 0.011$). Stages 1 and 3 showed no significant effect. After adjustment for

covariates (Model 4), Stage 2 maintained a non-significant trend towards protection (OR = 0.483, 95% CI: 0.206-1.134, p = 0.096; overall model p=0.027). Stage 3 showed a non-significant trend towards increased risk (OR = 1.675, 95% CI: 0.876-3.203, p=0.117).Discussion: This study provides the first evidence in a large Chinese cohort that higher CKM stages are significantly associated with poorer cognitive function, particularly episodic memory, independent of demographic, lifestyle, and psychological factors. This underscores the value of the CKM framework in capturing cumulative systemic risk for cognitive decline. The potential protective association of Stage 2 against cognitive decline in individuals with existing impairment, though attenuated after adjustment, suggests a possible critical window for intervention before advanced subclinical CVD emerges. Pronounced gender differences in CKM stage distribution and risk profiles highlight the need for sex-specific approaches. The attenuation of the visuoconstruction association and lack of association with other domains suggests domain-specific vulnerabilities.

Conclusion: Higher CKM stages are significantly associated with worse cognitive function, especially episodic memory, in middle-aged and older Chinese adults. The CKM staging system effectively reflects the cumulative burden of multi-organ dysfunction impacting cognitive health. Stage 2 may represent a crucial, modifiable window for integrated management of metabolic, cardiovascular, and kidney health to delay cognitive decline, particularly in individuals showing early impairment. These findings emphasize the importance of holistic strategies targeting systemic health to mitigate cognitive aging in China's rapidly aging population. Further longitudinal and mechanistic studies are warranted.

Key words: CKM syndrome, cognitive function, CHARLS, aging, multi-organ dysfunction