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ORIGINAL RESEARCH

Association of Chronotype with Hypertension and Metabolic Parameters in Middle-Aged and Older Adults: A Cross-Sectional Study

Ming-Jun Hu[1,*], Wen-Wen Hu[2,*], Bei Yao[1], Xiao-Min Dong[1], Xue-Li Wang[1], Dan Su[1], Gui-Qi Song[2,3], Yong-Liang Zhang[1]

[1]Department of Health Management Center, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, People's Republic of China; [2]School of Nursing, Bengbu Medical University, Bengbu, Anhui, People's Republic of China; [3]Department of Education, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, People's Republic of China

*These authors contributed equally to this work

Correspondence: Gui-Qi Song, School of Nursing, Bengbu Medical University, Bengbu, Anhui, People's Republic of China, Email songguiqi66@sina.com; Yong-Liang Zhang, Department of Health Management Center, the First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, People's Republic of China, Tel +86 0551 62284719, Email zyl2020@ustc.edu.cn

Purpose: Chronotype can be used to describe individual's circadian preference in behavioral and circadian rhythm, representing the preferences for earlier or later sleep times. This study aimed to investigate the association of chronotype with hypertension and metabolic parameters in middle-aged and older adults.

Patients and Methods: A total of 945 participants were recruited from December 2023 to December 2024 at First Affiliated Hospital of University of Science and Technology of China. Chronotype was determined using the full Morningness-Eveningness Questionnaire, with higher scores indicating preference for morning chronotype. Chronotype was dichotomized at the median score in current cohort, classifying 447 participants as morning chronotypes and 498 as evening chronotypes. Anthropometric measurements and biochemical analyses were also conducted. Multivariable logistic, linear regression, and restricted cubic spline (RCS) analyses were employed to evaluate association between chronotype, metabolic parameters, and hypertension.

Results: After adjustment for covariates, evening chronotype was significantly associated with hypertension risk (OR = 1.60, 95% CI: 1.17−2.17), compared with morning chronotype. The RCS analysis suggested a significant nonlinearity association between chronotype score and hypertension (P for nonlinear = 0.047). Furthermore, higher chronotype score was significantly associated with decreased levels of total cholesterol [TC, β (95% CI): −0.12 (−0.19, −0.04)], low-density lipoprotein-cholesterol [LDL-C, β (95% CI): −0.21 (−0.33, −0.08)] and serum uric acid [SUA, β (95% CI): −0.09 (−0.18, −0.01)], but with increased levels of aspartate aminotransferase [AST, β (95% CI): 0.16 (0.05, 0.27)]. In discrimination model, chronotype was associated with hypertension independently of TC, SUA, alanine transaminase, and alkaline phosphatase, with model's AUC of 0.779 (95% CI: 0.749–0.808).

Conclusion: In middle-aged and older adults, preference for morning chronotype was associated with decreased levels of TC, LDL-C, and SUA, but with increased levels of AST. Moreover, evening chronotype was significantly independently associated with increased risk of hypertension.

Keywords: sleep, chronotype, metabolic parameters, hypertension, risk factors

Introduction

Hypertension is still a common chronic disease worldwide, affecting an estimated 1.28 billion adults globally (World Health Organization 2023). According to the findings from Chinese national survey, approximately 274 million adults aged 18–69 years in China had hypertension in 2018, with a prevalence of 38.1%, and 240 million of them had inadequately controlled blood pressure, with a control rate of only 13.2%.[1] In addition, hypertension is more common among the older population in China, with a total prevalence of 47%.[2] Hypertension-related cardiovascular disease in adults is one of the leading causes of premature death. Therefore, in today's ageing population, it is important to pay attention to blood pressure changes in middle-aged and older adults to prevent hypertension and subsequent cardiovascular diseases.

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Chronotype can be used to describe individual's circadian preference in behavioral and circadian rhythm, which allows people to be categorized as either morning or evening chronotype, representing the preferences for earlier or later sleep times.[3,4] In 1976, Horne and Ostberg developed the Morningness-Eveningness Questionnaire (MEQ) to assess this circadian preference, which has been widely translated and used.[5] Chronotype is partly regulated by the timing of endogenous biological clock rhythms, that is the internal central clock located in suprachiasmatic nucleus of the hypothalamus.[6] However, people's circadian preferences are increasingly influenced by factors such as artificial light, work pressure, and more frequency of late dinner timing in today's society. More evening chronotype can cause a mismatch between the internal circadian rhythm and 24-hour external environmental and behavioral cycle time.[7] Evening chronotype has been reported to differ from morning chronotype in terms of body temperature regulation, nervous and endocrine system activity, and hormone levels (eg, melatonin secretion).[8] Previous studies suggested that evening chronotype was linked to risk of obesity, type 2 diabetes, cancer, and depression.[9–12] However, the evidence linking chronotype to hypertension is limited, and existing conclusions remain inconsistent. For example, evening chronotype was reportedly associated with higher risk of hypertension in Finnish adults.[13] Nevertheless, another cross-sectional study did not observe this significant risk association.[14] It is necessary to further investigate the association between chronotype and hypertension.

Usually, the individuals with evening chronotype exhibit later behavioral timing and more unhealthy lifestyle habits, including late dinner timing, less physical activity, late sleep onset, and more smoking and drinking.[3,15] These factors may directly affect multiple metabolic parameters levels. Several previous studies have investigated the association of chronotype with metabolic parameters, but their focus is mostly on glycolipid metabolism.[3] The association between chronotype and key indicators of liver and kidney function remains unclear. In addition, it is unclear whether chronotype influences the occurrence and development of hypertension independently of metabolic parameters.

Against this background, the primary aim of current cross-sectional study was to investigate association of chronotype with hypertension in middle-aged and older adults. The secondary aim was to investigate association of chronotype with multiple metabolic parameters. To further clarify whether chronotype was independently associated with hypertension, we performed multivariable logistic regression to simultaneously assess the association of chronotype and metabolic parameters with hypertension.

Materials and Methods

Study Population

From December 2023 to December 2024, the individuals who received annual health examinations at the Health Management Center of the First Affiliated Hospital of University of Science and Technology of China (USTC) were recruited to participate in the current cross-sectional study. All participants were aged 40 years or older and had no prior history of diabetes or cancer. Participants with a history of diabetes or cancer were defined as those who had been previously diagnosed with I/II diabetes and any cancer by a doctor before participating in this study. We also excluded the individuals with a history of serious diseases in the cardiovascular, liver, kidney, and gastrointestinal system, such as coronary heart disease, heart failure, hepatic cirrhosis, acute hepatic failure, end-stage renal disease, acute kidney injury, gastric ulcer, and bowel obstruction. Finally, a total of 945 participants were included in current study. This study followed the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of USTC (NO. 2023KY-459 and 2023KY-483). All participants provided written informed consent prior to their inclusion in the study.

Chronotype Assessment

All participants were interviewed face to face by the trained interviewer using a structured questionnaire, including information on demographic characteristics (including age, sex, and education level), lifestyle and behavior habits (including smoking and drinking status, physical activity, sleep duration, and sleep quality), and personal disease history (including disease of hypertension, thyroid gland, liver, kidney, and gastrointestinal tract, as well as the malignancies). Chronotype was assessed with the full Morningness-Eveningness Questionnaire (MEQ), which consists of 19 items, to accurately determine the individual's preference for morning or evening. The chronotype score was presented continuously and ranged from 16 to 86, with higher scores indicating the preference for morning chronotype.[16] The Chinese version of MEQ was proven to be a trustworthy and valid tool.[17] We had obtained the license to use the MEQ from Mapi Research Trust (https://eprovide.mapi-trust.org). To promote the interpretation and potential of future clinical applications, the chronotype was further dichotomized into binary variable, namely more evening (≤61) and more morning (>61) chronotype, according to its median score in all participants.[16]

Anthropometric Measurement and Hypertension Diagnosis

Anthropometric measurements of all participants were determined by the trained nurses. For current height and weight, all participants were instructed to take off their shoes and wear light clothing before the measurement. During the measurement, all participants were asked to stand firmly and straight and to look horizontally in front of them. All measurements were required to be recorded to one decimal place, including nearest 0.1 kg for weight and 0.1 cm for height. The BMI (kg/m^2) was calculated by using weight in kilograms divided by the height in meters squared.

Seated blood pressure was measured with a sphygmomanometer and standard protocols in the quiet environment. Before measuring blood pressure, all participants were instructed to sit still for more than 5 minutes. During the measurement, participants were instructed to relax and keep the heart at roughly the same level as the cuff position, and the mean of their two readings was recorded. According to the ESC/ESH Guidelines for the management of hypertension, hypertension was defined as either: (i) the individuals with systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg, or (ii) the individuals were previously diagnosed with hypertension by a doctor, or (iii) use of antihypertensive medication. In this study, 153 participants were previously diagnosed with hypertension, with 115 of them currently taking antihypertensive medications, and 183 individuals were newly identified to have hypertension.

Metabolic Parameters and Serologic Examinations

Overnight fasting blood specimens were collected from all subjects, and serum specimens were centrifuged and separated for biochemical assay. Serum levels of fasting blood glucose (FBG), triglyceride (TG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), γ-glutamyltransferase (GGT), uric acid (SUA), creatinine (sCr), and blood urea nitrogen were determined by fully automatic biochemistry analyzer using standard protocols. The manufacturer's reagents and calibrators were used to quality control all indicators during testing.

Statistical Analysis

To estimate sample size, we employed the epidemiological formula [$n = (z_\alpha)^2 \times p(1-p)/d^2$, where p denoted the expected prevalence rate, d was the permissible error] for cross-sectional study design. According to data from Chinese national survey,[1] the estimated prevalence of hypertension in the middle-aged and older adults was 38%. Here $d = 0.1 \times p$, and $\alpha = 0.05$, the target sample size for this study was calculated to be at least n = 653.

Data was double-entered into EpiData version 3.1. In descriptive analyses, continuous variables were presented as mean ± standard deviation (SD) for normal distributed variable, median (interquartile range, IQR) for skewed distributed variable, and frequency (proportion, %) for categorical variables. Differences between two groups were compared by using the Student's *t*-test, Wilcoxon rank sum test (for continuous variables), and Pearson's Chi-square test (for categorical variables). Chronotype score and metabolic parameters levels were natural-log (ln) transformed to meet normal distribution and perform subsequent regression analysis.

Logistic regression model was employed to investigate the odds ratio (OR) and 95% confidence intervals (CI) for the association between chronotype and hypertension. To explore the potential nonlinearity in the association between hypertension and continuously chronotype score, we used restricted cubic spline regression (RCS) in the logistic regression model, with predefined three knots at the 5th, 50th, and 95th percentiles in RCS model and that the reference value was set at the 50th percentiles.[18] We also used linear regression model to assess association of chronotype score with multiple metabolic parameters.

To further clarify whether chronotype was independently associated with hypertension, we also performed multivariable logistic regression model to simultaneously assess the association of chronotype and metabolic parameters with hypertension. Depending on whether metabolic parameters variables were included, we created the basic and full variable regression models with hypertension as the outcome, respectively. We employed the backward elimination procedure and set alpha at 0.1 for variables to be retained in the final regression model.[19] The receiver operator characteristic (ROC) curve was used to evaluate the capability of the final multivariable logistic regression model for discriminating hypertension.

In addition, we performed the subgroup analyses stratified by strongly related factors, including age, sex, and BMI. All analyses were performed using R software (version 4.4.1, R Core Team). All tests of statistical significance were two-sided, and P value < 0.05 was considered statistically significant.

Results

Characteristics of Study Participants

A total of 945 middle-aged and older adults were included in this study, of whom 336 (35.6%) were diagnosed with hypertension. Compared with normotension group, hypertension group was older and more likely to be men, smokers, and drinkers (Table 1). Hypertension patients might exhibit higher serum levels of FBG, ALT, AST, ALP, GGT, SUA, and sCr (all P-value < 0.001). The median (IQR) of chronotype score for all participants was 61.0 (11.0), and there was no significant difference in chronotype score between two groups (P = 0.428).

Table 1 Description of General Characteristics for Study Population

	Total (n = 945)	**Normotension (n = 609)**	**Hypertension (n = 336)**	***P*-value**
Age (years), mean ± SD	55.3 ± 7.5	54.1 ± 7.3	57.6 ± 7.3	< 0.001
BMI (kg/m^2), mean ± SD	24.7 ± 3.1	24.0 ± 2.9	26.00 ± 3.1	< 0.001
Sex, n (%)				< 0.001
Men	514 (54.4)	280 (46.0)	234 (69.6)	
Women	431 (45.6)	329 (54.0)	102 (30.4)	
Education, n (%)				0.164
Less than high school	173 (18.3)	108 (17.7)	65 (19.3)	
High school and equivalent	147 (15.6)	86 (14.1)	61 (18.2)	
College and above	625 (66.1)	415 (68.2)	210 (62.5)	
Smoking status, n (%)				0.001
Never	652 (69.0)	444 (72.9)	208 (61.9)	
Ever	293 (31.0)	165 (27.1)	128 (38.1)	
Drinking status, n (%)				< 0.001
No	674 (71.3)	468 (76.8)	206 (61.3)	
Yes	271 (28.7)	141 (23.2)	130 (38.7)	
Physical activity, n (%)				0.360
Inactive	428 (45.3)	280 (46.0)	148 (44.1)	
Moderate	209 (22.1)	140 (23.0)	69 (20.5)	
Active	308 (32.6)	189 (31.0)	119 (35.4)	
Sleep duration (hours), median (IQR)	6.5 (1.5)	6.5 (1.5)	6.5 (1.5)	0.676
Sleep quality, n (%)				0.084
Poor	101 (10.7)	55 (9.0)	46 (13.7)	
General	323 (34.2)	211 (34.7)	112 (33.3)	
Good	521 (55.1)	343 (56.3)	178 (53.0)	
Chronotype score, median (IQR)	61.0 (11.0)	61.0 (11.0)	61.0 (10.0)	0.428
Chronotype, n (%)				0.592
Morning	447 (47.3)	292 (47.9)	155 (46.1)	
Evening	498 (52.7)	317 (52.1)	181 (53.9)	

(*Continued*)

Table 1 (Continued).

	Total (n = 945)	Normotension (n = 609)	Hypertension (n = 336)	*P*-value
Metabolic parameters, median (IQR)				
FBG (mmol/L)	5.3 (0.7)	5.2 (0.6)	5.3 (0.8)	< 0.001
TG (mmol/L)	1.3 (0.9)	1.2 (0.9)	1.5 (1.0)	< 0.001
TC (mmol/L)	5.2 (1.2)	5.3 (1.2)	5.0 (1.1)	< 0.001
LDL-C (mmol/L)	3.1 (1.1)	3.2 (1.1)	3.1 (1.0)	0.006
HDL-C (mmol/L)	1.2 (0.4)	1.3 (0.5)	1.1 (0.3)	< 0.001
ALT (U/L)	21.0 (11.0)	20.0 (10.0)	24.5 (14.0)	< 0.001
AST (U/L)	24.0 (7.0)	23.0 (7.0)	25.0 (7.0)	< 0.001
ALP (U/L)	74.0 (25.0)	72.0 (26.0)	76.0 (26.0)	< 0.001
GGT (U/L)	24.0 (18.0)	22.0 (15.8)	26.3 (20.6)	< 0.001
SUA (umol/L)	333.0 (116.0)	318.0 (106.0)	364.5 (110.8)	< 0.001
sCr (umol/L)	63.0 (21.0)	61.0 (18.0)	66.5 (23.0)	< 0.001
Urea (mmol/L)	5.3 (1.6)	5.3 (1.4)	5.3 (1.8)	0.591

Notes: *P*-values (two-sided) were calculated by using the Student's *t*-test, Wilcoxon rank sum test (for continuous variables) or Chi-squared test (for categorical variables).
Abbreviations: SD, standard deviation; BMI, body mass index; IQR, interquartile range; FBG, fasting blood glucose; TG, triglyceride; TC, total cholesterol; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; ALT, alanine transaminase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, γ-glutamyltransferase; SUA, serum uric acid; sCr, creatinine.

Chronotype and Hypertension

Table 2 presents the multivariable adjusted association between chronotype and hypertension. Among all participants, those with evening chronotype had a higher risk of hypertension in model 2 (OR = 1.60, 95% CI: 1.17–2.17), compared

Table 2 Odds Ratios and 95% Confidence Intervals for the Association Between Chronotype and Hypertension

	Total (n)	Hypertension (n)	Model 1		Model 2	
			OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Overall						
Morning	447	155	1.0 (Ref.)		1.0 (Ref.)	
Evening	498	181	1.08 (0.82, 1.41)	0.592	1.60 (1.17, 2.17)	0.003
Ages 40–59						
Morning	290	85	1.0 (Ref.)		1.0 (Ref.)	
Evening	369	114	1.08 (0.77, 1.51)	0.660	1.46 (0.99, 2.14)	0.057
Ages ≥ 60						
Morning	157	70	1.0 (Ref.)		1.0 (Ref.)	
Evening	129	67	1.34 (0.84, 2.14)		1.95 (1.15, 3.32)	0.014
Men						
Morning	251	104	1.0 (Ref.)		1.0 (Ref.)	
Evening	263	130	1.38 (0.98, 1.96)	0.069	1.97 (1.33, 2.93)	0.001
Women						
Morning	196	51	1.0 (Ref.)		1.0 (Ref.)	
Evening	235	51	0.79 (0.51, 1.23)	0.294	1.01 (0.61, 1.67)	0.970
BMI at or below median (≤ 24.4 kg/m^2)						
Morning	217	44	1.0 (Ref.)		1.0 (Ref.)	
Evening	254	61	1.24 (0.80, 1.93)	0.332	1.69 (1.05, 2.73)	0.033
BMI above median (> 24.4 kg/m^2)						
Morning	230	111	1.0 (Ref.)		1.0 (Ref.)	
Evening	244	120	1.04 (0.72, 1.49)	0.841	1.54 (1.03, 2.31)	0.037

Notes: Model 1 was unadjusted. Model 2 was adjusted for age, sex, body mass index, smoking status, and drinking status.
Abbreviations: OR, odds ratio; CI, confidence interval; Ref., reference.

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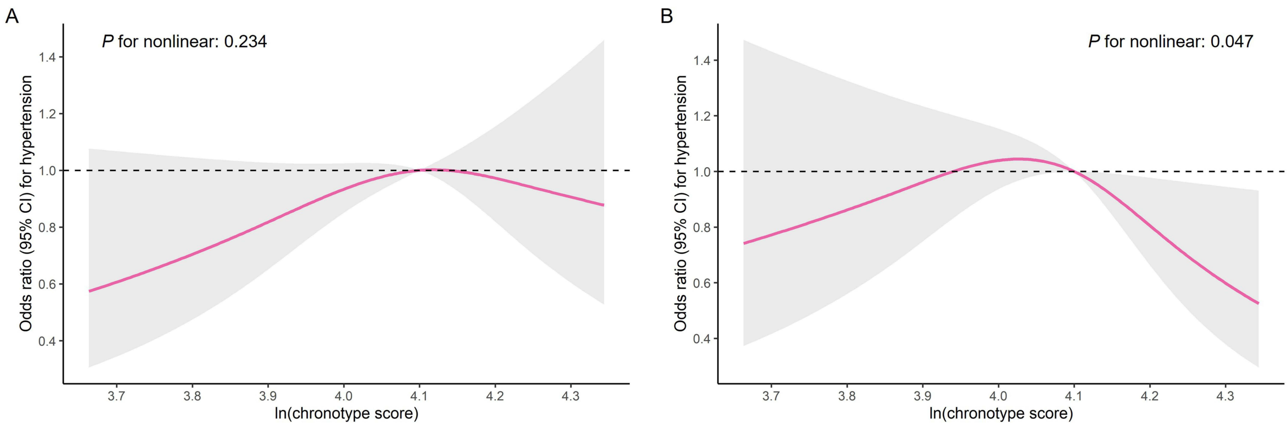

Figure 1 The restricted cubic spline (RCS) for the association of hypertension risk with chronotype score. The line with shade represented adjusted odds ratios (95% confidence interval (CI)) based on RCS for the natural-log (ln) transformed levels of chronotype score in the logistic regression model. Knots were placed at the 5th, 50th, and 95th percentiles of the chronotype score distribution, and the reference value was set at the 50th percentile. (**A**) The unadjusted OR (95% CI). (**B**) Adjusted for age, sex, body mass index, smoking status, and drinking status.

to those with morning chronotype. In subgroup analyses, the results showed similar trends. Additionally, the RCS analyses with chronotype score as continuous variables suggested a significant nonlinearity association between chronotype and hypertension (*P* for nonlinear = 0.047, Figure 1).

Chronotype and Metabolic Parameters

Figure 2 shows the multivariable adjusted association of chronotype with metabolic parameters in linear regression models. Among all participants, higher chronotype score was significantly associated with the decreased levels of TC [β (95% CI): −0.12 (−0.19, −0.04)], LDL-C [β (95% CI): −0.21 (−0.33, −0.08)], and SUA [β (95% CI): −0.09 (−0.18, −0.01)], but with the increased levels of AST [β (95% CI): 0.16 (0.05, 0.27)] after adjustment for covariates. When subgroup analyses were conducted according to age (Supplementary Table S1), sex (Supplementary Table S2), and BMI (Supplementary Table S3), we also observed that higher chronotype score was negatively associated with GGT in men [β (95% CI): −0.37 (−0.72, −0.03)] and the participants with BMI above median (>24.4 kg/m^2) [β (95% CI): −0.44 (−0.80, −0.10)], respectively.

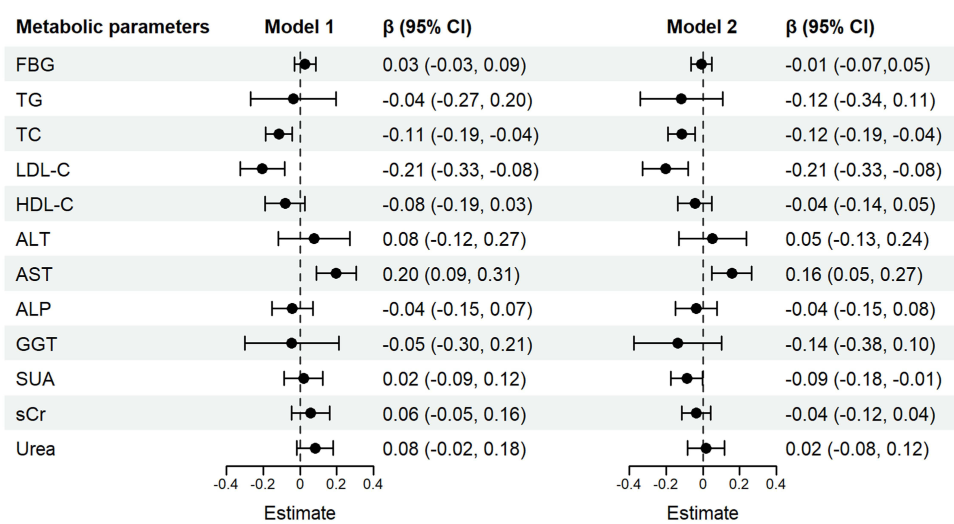

Figure 2 Forest plot for the association between chronotype score and metabolic parameters calculated using linear regression model. The chronotype score and metabolic parameters concentration were natural-log (ln) transformed. Model 1 was unadjusted. Model 2 was adjusted for age, sex, body mass index, smoking status, drinking status, and physical activity.

Table 3 Retained Variables in the Final Multivariable Logistic Regression Model for Hypertension Risk

Variables	Basic Variable Regression Model			Full Variable Regression Model		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Age	1.09	1.07–1.11	< 0.001	1.09	1.06–1.11	< 0.001
Sex (women vs men)	0.47	0.35–0.65	< 0.001	0.60	0.42–0.86	0.006
BMI	1.27	1.21–1.34	< 0.001	1.22	1.16–1.30	< 0.001
Chronotype (evening vs morning)	1.54	1.34–2.08	0.006	1.61	1.18–2.20	0.003
TC				0.26	0.10–0.62	0.003
ALT				1.57	1.10–2.26	0.014
ALP				3.01	1.65–5.47	< 0.001
SUA				2.36	1.10–5.05	0.027

Notes: All metabolic parameters concentrations were natural-log (ln) transformed. Basic variable regression model initially included the following variables: age, sex, BMI, smoking status, drinking status, and chronotype. Full variable regression model initially additionally included the following variables: FBG, TG, TC, LDL-C, HDL-C, ALT, AST, ALP, GGT, SUA, and sCr.

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; FBG, fasting blood glucose; TG, triglyceride; TC, total cholesterol; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; ALT, alanine transaminase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, γ-glutamyltransferase; SUA, serum uric acid; sCr, creatinine.

Multivariable Logistic Regression Model for Discriminating Hypertension

To explore the independent factors related to hypertension, we included all factors potentially associated with hypertension in univariate analyses to construct multivariable logistic regression model. Firstly, we only included the basic variables of study population to construct a basic variable regression model. The basic variable regression model ultimately retained four strongly related factors: age, sex, BMI, and chronotype (Table 3). ROC curve was used to assess the discriminative value of model, and the AUC was 0.757 (95% CI: 0.725–0.788) for basic variable regression model (Figure 3). Subsequently, we further included metabolic parameters to construct a fully variable regression model. The chronotype was still retained in the final regression model (Table 3), and this model's AUC was 0.779 (95% CI: 0.749–0.808). These results suggested that chronotype was associated with hypertension independently of TC, ALT, ALP, and SUA.

Discussion

In this cross-sectional study, we investigated the association of chronotype with hypertension and multiple metabolic parameters among middle-aged and older adults. Current results suggested that evening chronotype was significantly independently associated with hypertension. Furthermore, higher chronotype score, namely the preference for morning chronotype, was associated with decreased levels of TC, LDL-C, and SUA, but with increased levels of AST.

To date, the association between chronotype and hypertension remains clarified. A cross-sectional study among 811 middle-aged community residents found no significant association between chronotype and hypertension.[14] Another study conducted in 506 American women aged 20–79 years also did not observe the association.[20] However, a large cross-sectional study using a brief chronotype questionnaire (MEQ-5) presented that individuals with evening chronotype had a higher risk of hypertension.[13] Recently, Huang et al conducted the MEQ survey in 442 subjects aged 23–70 years, and found that chronotype scores were weakly positively correlated with systolic blood pressure ($r = 0.099$, $P = 0.038$) and diastolic blood pressure ($r = 0.096$, $P = 0.044$).[21] In current study, we used clinically diagnosed hypertension as the primary outcome and observed a significant association between evening chronotype and hypertension in middle-aged and older adults. Differences between these results might be related to study populations' age, ethnicity, and the categorization of chronotype. Some studies categorized the chronotype into evening, intermediate, and morning groups, according to the empirical cut-off of MEQ.[14,20] Consistent with categorization of previous studies, the median categorization of chronotype had more universal and clinical applications, although it did not represent the original morning and evening types of MEQ.[3,16] In addition, our dose–response analysis showed that participants with higher chronotype score had a lower risk of hypertension. Therefore, large and longitudinal studies were necessary to confirm association of hypertension with chronotype, including the fact that chronotype was categorized differently.

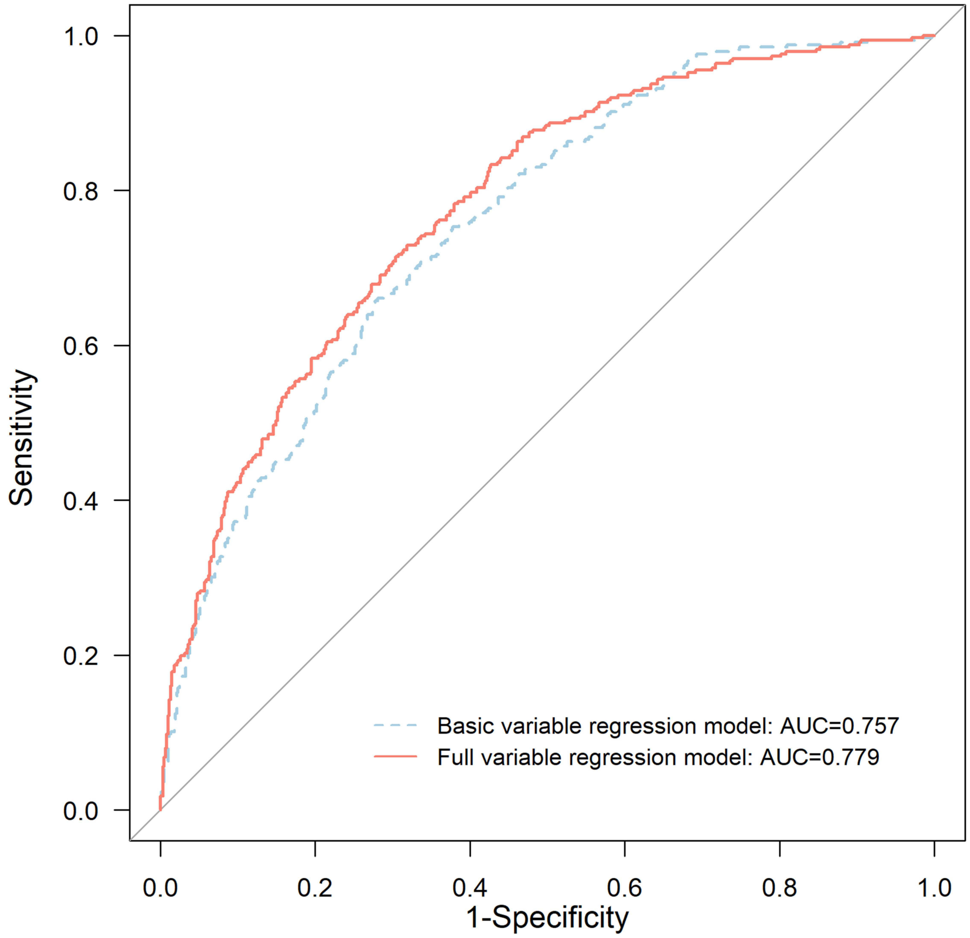

Figure 3 ROC curve generated by the multivariable logistic regression model for discriminating hypertension. The blue dotted line represented the basic variable regression model, which ultimately retained factors in the multivariable regression model including age, sex, BMI, and chronotype. The Orange solid line represented the full variable regression model, which ultimately retained factors in the multivariable regression model including age, sex BMI, chronotype, TC, ALT, ALP, and SUA. The AUC was 0.757 (95% CI: 0.725–0.788) for basic variable regression model and 0.779 (95% CI: 0.749–0.808) for full variable regression model. **Abbreviations**: ROC, receiver operator characteristic curve; BMI, body mass index; TC, total cholesterol; ALT, alanine transaminase; ALP, alkaline phosphatase; SUA, serum uric acid; AUC, area under the ROC curve.

Recent studies have linked evening chronotype to several metabolic conditions, including obesity, type 2 diabetes, and female metabolic syndrome.[22,23] A cross-sectional study of Korean adults found that evening chronotype was associated with higher levels of TC, TG, LDL-C, and non-HDL cholesterol.[24] Huang et al reported that, compared to evening chronotype, subjects with morning chronotype had higher AST levels but showed no significant differences in other metabolic parameters.[21] These results were partially consistent with our findings. We also observed that higher chronotype score was negatively associated with SUA levels, and positively associated with AST levels. However, little is known about the association of chronotype with the liver and kidney function. Association between chronotype and metabolic parameters might largely stem from different dietary patterns. For example, intake of carbohydrates, fish, and fruit differed between evening and morning chronotype.[16] Individuals with evening chronotype were inclined to eat late at night, consume more processed and ultra-processed foods, and frequently skip breakfast. In contrast, those with morning chronotype were inclined to eat early in the day and increase adherence to the Mediterranean diet, including more fresh and less processed foods.[25] Furthermore, diet-induced thermogenesis and insulin sensitivity were not the same across eating time in the morning, midday and evening, especially impaired during the evening.[26] Later dinner time might reduce postprandial lipolysis and fatty acid oxidation.[27] This might aggravate liver and kidney functions, which in turn could damage its metabolic indicators.

The effects of chronotype on hypertension and metabolic health might be also linked to circadian rhythm disruptions and more unhealthy behaviors.[28] Excessive evening chronotype could cause a mismatch between actual sleep time and internal central clock.[29] This evening chronotype preference could disrupt the normal circadian pattern of blood pressure, including shortening the duration of blood pressure decline during nighttime sleep. Circadian rhythms regulated cellular transcription, translation, and hormone synthesis within the cardiovascular system, such as enhancing higher synthesis and utilisation of adenosine triphosphate in cardiac myocytes during wakefulness and regulating mitochondrial function and apoptosis.[30] In modern society, circadian rhythm could be disturbed by artificial light exposure, late dinner time, irregular sleep schedules, and ever-changing work patterns.[31] Therefore, individuals with evening chronotype often engage in more adverse health behaviors during waking and activity periods, such as smoking, excessive drinking, mindless snacking, shorter sleep duration, and physical inactivity.[28] These unhealthy lifestyles might trigger mechanisms contributing to hypertension and metabolic disorders, including insulin resistance, inflammatory reaction, oxidative stress, elevated sodium retention, endothelial function alterations, lowered baroreflex and chemoreflex cardiovascular control, and excitement of sympathetic activity.[32,33] Additionally, the effect of chronotype on hypertension onset might also vary depending on the changes in blood pressure. Microvasculature played a crucial role in hypertension progression by regulating vascular tone to match tissue metabolic demands. Evening chronotype was reportedly associated with cardiometabolic risk factors.[34] Then, evening chronotype might have adverse effects on microvascular endothelium through the cardiometabolic risk, particularly in individuals with probable hypertension or at risk of hypertension. Because microvascular changes could occur early in the pathogenesis of hypertension, and this association was established even at a young age.[35] In hypertension patients, microvascular damage also occurred in the renal microcirculation. At this time, evening chronotype might cause abnormal renal stress-natriuretic mechanisms and renal tubular interstitial damage by increasing the metabolic burden on renal function.[36] Afterwards, this might further induce long-term hypertensive damage to the kidneys and cause persistent high blood pressure.

Of note, to further clarify whether chronotype was independently associated with hypertension, we performed multivariable logistic regression model to simultaneously assess the association of chronotype and metabolic parameters with hypertension. Regardless of the inclusion of metabolic parameters, the final regression model all retained the chronotype variable, and models' AUC was >0.75. This indicated that chronotype might be an independently related-factor of hypertension. The predictive effect of chronotype in hypertension should be further explored in future studies, and attempts should be made to establish and validate the performance of hypertension risk prediction models that include chronotype. This has important public health implications for uncovering and managing the modifiable risk factors for hypertension.

To the best of our knowledge, this study is the first to investigate association between chronotype, key indicators of liver and kidney function, and hypertension risk. To avoid the impact of potential covariates, we conducted multivariable models and subgroup analyses to observe more specific association. However, several limitations should be mentioned. First, the cross-sectional nature of current study limited causal inference, which could only evaluate the association. Second, chronotype was determined using the MEQ rather than objective measures, which could cause the self-report bias and measurement errors. Although the MEQ was most extensively studied and validated for assessing chronotype,[22] the use of accelerometry or other wrist actigraphy in future studies would be appreciated. Finally, this study was conducted at a single center, and the diagnosis of some hypertensive patients was based on a single measurement. The results were necessary to be validated in more regions and larger sample populations.

Conclusion

In middle-aged and older adults, the preference for morning chronotype was associated with decreased levels of TC, LDL-C, and SUA, but associated with increased levels of AST. Moreover, the evening chronotype was significantly independently associated with increased risk of hypertension. However, further studies are needed to confirm these findings. Especially, external validation and longitudinal studies are warranted before chronotype can be incorporated into risk-prediction tools.

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Data Sharing Statement

The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the First Affiliated Hospital of USTC (NO. 2023KY-459 and 2023KY-483). Informed consent was obtained from all individual participants included in the study.

Author Contributions

Ming-Jun Hu: Conceptualization, Formal analysis, Investigation, Funding acquisition, Writing – original draft. Wen-Wen Hu: Investigation, Data curation, Formal analysis, Writing – original draft. Bei Yao: Investigation, Writing – review & editing. Xiao-Min Dong: Investigation, Writing – review & editing. Xue-Li Wang: Investigation, Writing – review & editing. Dan Su: Investigation, Writing – review & editing. Gui-Qi Song: Conceptualization, Methodology, Writing – review & editing. Yong-Liang Zhang: Methodology, Data curation, Supervision, Writing – review & editing.

All authors agreed on the journal to which the article was submitted, reviewed and approved all versions of the manuscript prior to submission, during revision, and the final version accepted for publication. They also agreed to take responsibility and be accountable for the contents of the article, including any significant changes introduced during the proofing stage. All authors have drafted or written, or substantially revised or critically reviewed the article.

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Disclosure

The author(s) report no conflicts of interest in this work.

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