

University of Groningen

Association of Cardiovascular Health Score Trajectory With Incident Myocardial Infarction in Hypertensive Patients

Huang, Zegui; Chen, Zekai; Wang, Xianxuan; Ding, Xiong; Cai, Zefeng; Li, Weijian; Cai, Zhiwei; Lan, Yulong; Chen, Guanzhi; Fang, Wei

Published in:
Hypertension

DOI:
[10.1161/HYPERTENSIONAHA.122.19633](https://doi.org/10.1161/HYPERTENSIONAHA.122.19633)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2022

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Huang, Z., Chen, Z., Wang, X., Ding, X., Cai, Z., Li, W., Cai, Z., Lan, Y., Chen, G., Fang, W., Wu, S., & Chen, Y. (2022). Association of Cardiovascular Health Score Trajectory With Incident Myocardial Infarction in Hypertensive Patients. *Hypertension*, 79(11), 2622-2630. <https://doi.org/10.1161/HYPERTENSIONAHA.122.19633>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

ORIGINAL ARTICLE

Association of Cardiovascular Health Score Trajectory With Incident Myocardial Infarction in Hypertensive Patients

Zegui Huang¹, Zekai Chen², Xianxuan Wang, Xiong Ding, Zefeng Cai, Weijian Li¹, Zhiwei Cai¹, Yulong Lan¹, Guanzhi Chen, Wei Fang, Shouling Wu¹, Youren Chen¹

BACKGROUND: The association between changes in cardiovascular health score (CHS) over time and myocardial infarction (MI) risk in hypertensive patients remains unclear.

METHOD: This was a prospective study comprising 17 374 hypertensive patients from the Kailuan study cohort who underwent 3 surveys and were identified to be free of MI, stroke, or cancer from 2006 to 2010. CHS consisted of 7 cardiovascular health metrics (plasma glucose, total cholesterol, blood pressure, smoking, body mass index, physical activity, salt intake), ranging from 0 (worst) to 13 (best) in the study. CHS trajectories were developed during 2006 to 2010 to predict the MI risk from 2010 to 2020. Additionally, the Cox proportional hazard model was established to calculate the hazard ratio and 95% CI of incident MI in different trajectory groups.

RESULT: This study identified the 5 CHS trajectories from 2006 to 2010: low-stable (n=1161; range, 4.7–4.5), moderate-decreasing (n=3928; decreased from 6.9 to 6.0), moderate-increasing (n=1014; increased from 5.6 to 7.8), high-stable I (n=7940; range, 8.1–8.2), and high-stable II (n=3331; range, 9.2–9.7). During the median follow-up of 10.04 years, 288 incident MI cases were identified. After adjusting for potential confounders, compared with low-stable group, the hazard ratio and 95% CI of MI were 0.24 (0.15–0.40) for high-stable II, 0.36 (0.24–0.54) for high-stable I, 0.46 (0.25–0.83) for moderate-increasing, and 0.61 (0.41–0.90) for moderate-decreasing, respectively.

CONCLUSIONS: In hypertensive patients, high-stable CHS or improvement in CHS is associated with a lower risk of incident MI, when compared with low-stable CHS trajectory over time. (*Hypertension*. 2022;79:2622–2630. DOI: 10.1161/HYPERTENSIONAHA.122.19633.) • [Supplemental Material](#)

Key Words: cardiovascular diseases ■ cohort studies ■ hypertension ■ myocardial infarction

Cardiovascular disease (CVD) is the leading cause of mortality and disability worldwide, accounting for 18.6 million deaths and 34.4 million years lived with disability in 2019.¹ As the most severe subtype of CVD, myocardial infarction (MI) contributed to >2.4 million deaths in America and > 4 million deaths in Europe and northern Asia annually.² Concordantly, the economic burden of MI is tremendous, which resulted in high US hospitalization costs amounting to around

14.3 billion dollars for 662 000 hospital stays in 2017.³ Patients with MI are often found to have a history of hypertension when they are screened. There is a high prevalence of hypertension among patients with MI, with 30% to 40% in ST-elevation MI and 70% to 75% in non-ST elevation acute myocardial infarction.⁴ Hypertension, as the main risk factor for MI, combined with 8 other modifiable risk factors, accounts for over 90% of the risk for MI.⁵ Meanwhile, hypertension is

Correspondence to: Shouling Wu, Department of Cardiology, Kailuan General Hospital, 57 Xinhua East RD, Tangshan, 063000, China, Email drwusl@163.com or Youren Chen, Department of Cardiology, Second Affiliated Hospital of Shantou University Medical College, 69 Dongxia North RD., Shantou 515000, China, Email yrchen3@stu.edu.cn

*Z. Huang and Z. Chen contributed equally.

Supplemental Material is available at <https://www.ahajournals.org/doi/suppl/10.1161/HYPERTENSIONAHA.122.19633>.

© 2022 American Heart Association, Inc.

Hypertension is available at www.ahajournals.org/journal/hyp

NOVELTY AND RELEVANCE

What Is New?

This is the first large prospective study with 10 years follow-up to examine the association of cardiovascular health score trajectory and myocardial infarction risk in hypertensive patients.

What Is Relevant?

Five distinct cardiovascular health score trajectory during 2006 to 2010 were identified to predict myocardial

infarction risk from 2010 to 2020 among hypertensive patients.

Clinical/Pathophysiological Implications

High-stable or improvement in cardiovascular health score is associated with a lower risk of myocardial infarction in hypertensive patients. These findings highlight the importance of taking primordial approaches to promote and maintain long-term healthy cardiovascular status in hypertensive patients.

Nonstandard Abbreviations and Acronyms

ARIC	Atherosclerosis Risk in Communities
BP	blood pressure
CHS	cardiovascular health score
CVD	cardiovascular disease
HR	hazard ratio
MI	myocardial infarction

independently associated with adverse cardiac outcomes followed by acute MI.^{6,7} Therefore, compared with the normal population, hypertensive population should be more mindful of the risks of MI. The prevention of MI in the hypertensive population has also gained increasing attention.

Previous studies have found that in addition to controlling blood pressure,⁸ healthy lifestyle behaviors such as quitting smoking, physical activities, and losing weight also reduce the occurrence of incident MI in hypertensive patients.^{9,10} In 2010, the American Heart Association proposed 7 cardiovascular health metrics to promote the primordial prevention of CVD. The cardiovascular health metrics consists of 4 cardiovascular risk modifiable health behaviors (smoking, body mass index, physical activities, and diet) and 3 biological factors (blood pressure, fasting plasma glucose, and total cholesterol).¹¹ The cardiovascular health scores (CHSs) were created according to the individual level (ideal, intermediate, or poor) of each health metric to assess the cardiovascular status of the population.¹² Plenty of evidence has proved that higher CHS was associated with a lower risk of MI in both the general population and hypertensive patients.^{13–15} However, the past studies only stressed the association between single CHS and MI risk while the longitudinal association between changes in CHS over time and MI risk in hypertensive patients was not examined.

We hypothesize that the maintenance of high CHS over time reduces MI risk in individuals with hypertension

and changes in CHS could alter MI risk. Based on this hypothesis, we used CHS trajectory patterns collected over 4 years from the Kailuan study cohort (Registration Number: CHICTR-TNRC-11001489) to investigate the association between the trajectory of CHS and MI risk in hypertensive patients.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Availability of Data and Materials

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

Ethics Approval and Consent to Participate

The study was performed according to the guidelines of the Helsinki Declaration and was approved by the Ethics Committee of Kailuan General Hospital (Approval Number: 2006-05) All participants were agreed to take part in the study and provided informed written consent.

Study Design and Participants

The Kailuan study is a community-based, prospective cohort study conducted in Tangshan, China. The specific study design and methodology have been introduced previously.^{16,17} From 2006 to 2007, the retiree and employee of the Kailuan Group were recruited to participate in the baseline survey and were with a follow-up every 2 years thereafter. Comprehensive health evaluations were conducted and questionnaires were used to collect demographic attributes, medication history, and lifestyle habits (eg, salt consumption, smoking, drinking status, and physical exercises). We enrolled 57 914 participants who consecutively participated in the 2006 to 2007, 2008 to 2009, and 2010 to 2011 surveys of the Kailuan study. Among them, 23 057 hypertensive individuals were identified in the baseline survey (2006–2007). In addition, hypertensive patients with missing CHS data, or with MI, stroke or cancer in the 2006, 2008, or 2010 surveys were excluded. The flowchart about the process of selecting participants was shown in Figure 1.

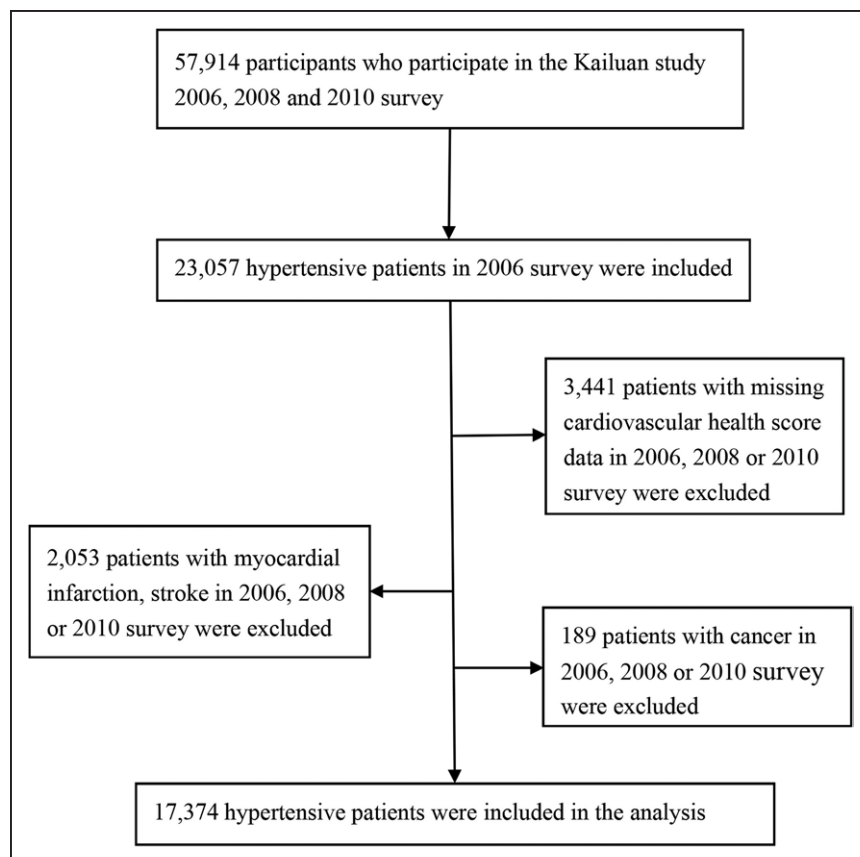


Figure 1. Flow chart of inclusion and exclusion.

The flowchart of 17 374 hypertensive patients included in the final analysis.

The trajectories were established using the consecutive and complete CHS data from 2006 to 2010. With follow-up starting in 2010, we observed and collected the incidence of MI in hypertensive patients until 2020. This study was carried out following the Declaration of Helsinki and was approved by the Ethics Committee of Kailuan General Hospital. All participants offered written informed consent.

Data Collection

All participants underwent baseline and follow-up health assessments in 11 hospitals in the Kailuan community. Height and weight data were collected in the physical examination. A standard right-angle device was used to measure the height to the nearest 1 cm, and weight was measured to the nearest 0.1 kg with a spring balance, with participants shoeless and wearing light clothes. Body mass index was calculated with the formula of weight/height² (kg/m²). Blood samples were collected from the antecubital vein in the morning after an overnight fast. The biochemical indicators, such as total cholesterol, fasting plasma glucose, and hs-CRP (high-sensitivity C-reactive protein) were evaluated with an automatic analyzer (Hitachi 747, Tokyo, Japan) located in the central laboratory of the hospital.

Definition of Hypertension

According to the recommendations of the Seventh Report of the Joint National Committee, the criteria for diagnosis of hypertension are blood pressure (BP) measurement of $\geq 140/90$ mmHg, self-reported physician diagnosis or the use of antihypertensive medication.¹⁸ BP measurements and

questionnaires were conducted by trained physicians. In a seated posture, the BP of participants was measured at least twice in the right upper arm with a calibrated mercury sphygmomanometer. BP was then measured again if the difference between the 2 measurements was ≥ 5 mmHg. The average value of the BP measurements was applied for hypertension diagnosis.

Assessment of the CHS

The cardiovascular health metrics adopted in this study were similar to those proposed by the American Heart Association¹¹ but with some modifications added according to the specific circumstances of the Kailuan study. Owing to the lack of healthy diet data in the early stage of Kailuan study and considering the strong association between salt intake and risk of hypertension and CVD in Chinese population,^{19,20} salt intake was applied as a surrogate measure for a healthy diet. We assessed salt intake by asking participants to rate their habitual daily salt intake as low, moderate, or high in the questionnaire. Low was defined as <6 g/d, moderate as 6 to 10 g/d, and high as >10 g/d, as described previously.²¹ Regarding the BP component, we assigned a BP score equal to 1 in the controlled group and a BP score of 0 in the uncontrolled group, depending on whether BP was controlled or not. The classification of poor (0 points), intermediate (1 point), and ideal (2 points) were assigned to each component of the other cardiovascular health metrics, as shown in Table S1. The CHS was on a 14-point scale in the general population, but the total CHS varied from 0 (worst) to 13 (best) in this study since all participants had hypertension.

Outcome Assessment: Myocardial Infarction

The primary outcome of this study is the first occurrence of MI. The ICD-10 revision codes were applied to confirm MI (I21).^{22,23} MI diagnosis data were retrieved from 11 hospital discharge registers and municipal social insurance institutions of the Kailuan Group. Annual discharge records were collected and reviewed by an expert team of 3 experienced physicians and were updated annually during the follow-up period. MI was diagnosed by the presence of clinical symptoms, ECG and dynamic changes of cardiac enzymes in patients in accordance with the WHO diagnostic criteria.²⁴ Follow-up was conducted with all participants until incident MI diagnosis, death or December 31, 2020, whichever came first.

Statistical Analysis

The CHS trajectories from 2006 to 2010 in hypertensive patients were identified using the latent mixture modeling within the PROC TRAJ procedure, as mentioned previously.^{25,26} The number of participants in each trajectory (>5% of the overall population) and the Bayesian information criterion were used to assess the model fit. The model with 5 patterns was identified as the best fit.

Continuous, normally distributed variables were shown as the mean±SD, and continuous variables with a skewed distribution were considered to be the median with an interquartile range (25%–75%). Number and percentage (%) were used to describe categorical variables. The Kruskal-Wallis test or the ANOVA was conducted to contrast the continuous variables based on the distribution while the χ^2 test was conducted to analyze the categorical variables. The incidence rate was calculated by dividing the number of events by the total person-years of follow-up and presented as events per 1000 person-years. Furthermore, with the proportional hazard assumption was satisfied, the Cox proportional hazard models were developed to analyze the hazard ratio and 95% CI of incident MI of other trajectories groups in contrast with the low-stable group. Model 1 was adjusted for sex and age, while further adjustments were made for heart rate, hs-CRP, education level (elementary school or below, high school, or college or above), drinking status (never, past, or current), and antihypertensive drugs in Model 2. Moreover, multiple imputations by chained equations²⁷ were utilized to impute the missing value of covariates, and the details of the missing covariates were shown in Table S2. Additionally, subgroup analyses were stratified by sex and age (<65 versus ≥65 years).

The robustness of the results was evaluated by conducting several sensitivity analyses. First, additional adjustments were made for CHS in 2006 and CHS in 2010, respectively to evaluate whether this relationship can be interpreted by a single CHS during the follow-up. Second, taking account of the influence of reverse causality, MI events that occur in the first year of follow-up were excluded. Third, we repeated the analysis without multiple imputation of covariates given that the impact of imputed data on the results. Finally, considering that salt intake was a substitute for a healthy diet, and its effect on results, we conducted a sensitivity analysis of excluding the salt intake from the component of the CHS score. SAS 9.4 (SAS Institute, Inc, Cary, NC) software was used in this study to perform statistical analysis, where $P<0.05$ (2-sided test) was deemed to have statistical significance.

RESULTS

Baseline Characteristics

A total of 17 374 hypertensive participants were included in the analyses. The mean (SD) age of the population was 56.11 ± 11.01 years with 14 362 (82.66%) male and 3012 (17.34%) female participants. In the current study, 5 distinct trajectory patterns were confirmed by latent mixture modeling according to the CHS changes from 2006 to 2010 (Figure 2): Low-stable ($n=1161$; mean CHS range, 4.7–4.5 during 2006–2010), moderate-decreasing ($n=3928$; mean CHS decreased from 6.9 in 2006 to 6.0 in 2010), moderate-increasing ($n=1014$; mean CHS increased from 5.6 in 2006 to 7.8 in 2010), high-stable I ($n=7940$; mean CHS range, 8.1–8.2 during 2006–2010), and high-stable II ($n=3331$; mean CHS range, 9.2–9.7 during 2006–2010). The basic characteristics of 17 374 hypertensive patients based on the trajectories of CHS from 2006 to 2010 are shown in Table 1. The patients in the high-stable II group are featured with a lower proportion of current drinking and the use of antihypertensive drugs, a lower systolic blood pressure, diastolic blood pressure, heart rate, and hs-CRP as well as a high education level than the others.

Incident Myocardial Infarction

Within the median follow-up of 10.04 years, 288 cases with incident MI were identified. The incidence rate of MI is illustrated in Table 2. After adjusted for potential confounders, the hazard ratio and 95% CI of MI in the high-stable II was 0.24 (0.15–0.40), 0.36 (0.24–0.54) for high-stable I, 0.46 (0.25–0.83) for moderate-increasing, and 0.61 (0.41–0.90) for moderate-decreasing, respectively, when compared with low-stable group.

Subgroup and Sensitivity Analysis

The results from the subgroup analysis were presented in Table 3. There was no significant interaction between the CHS trajectories and age and sex. However, in the age ≥65 years old or male group, the associations between subsequent MI risk and CHS trajectories seemed to be more distinct. After making additional adjustment for the CHS in 2006 or 2010, the results did not change substantially (Tables S3 and S4). Moreover, the results obtained after eliminating MI events of the first year of follow-up were similar to the main results (Table S5). In addition, the results from analyses that did not perform multiple imputation for covariates, or excluded salt intake from the components of CHS, were still consistent with those of the primary analysis (Table S6 and S7).

DISCUSSION

In this prospective study of 17 374 hypertensive participants, we identified 5 distinct CHS patterns that

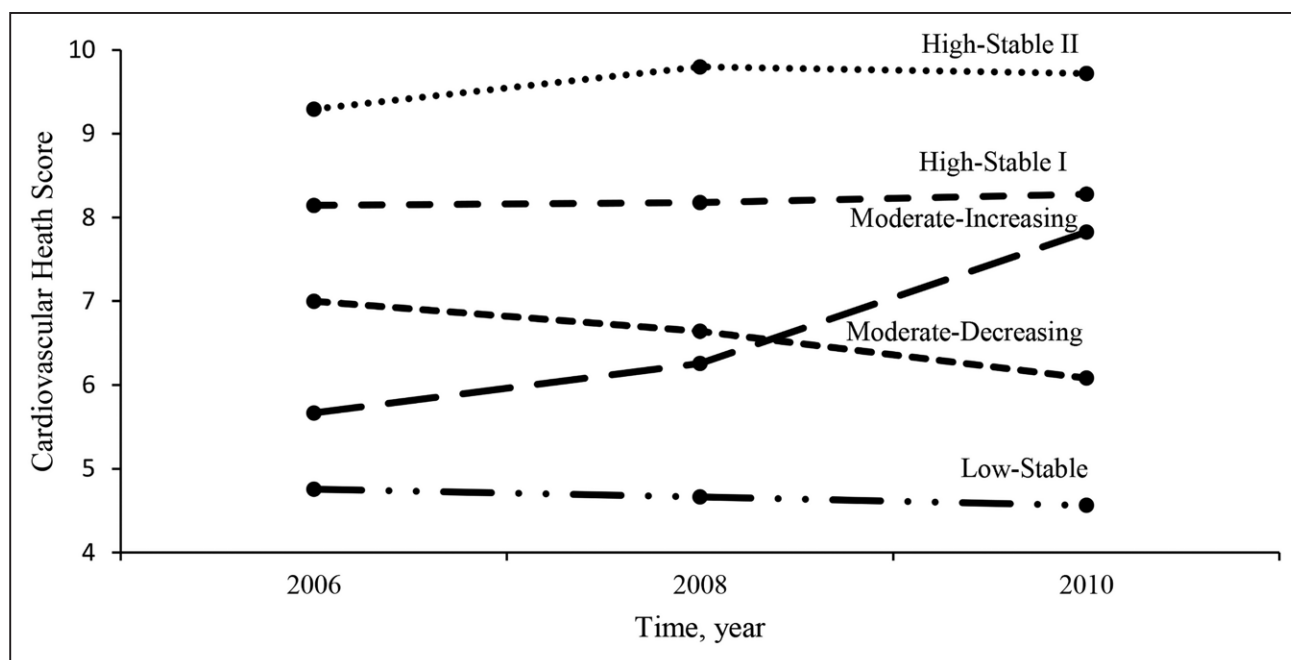


Figure 2. Mean Cardiovascular Health Score in 2006, 2008, and 2010 in Hypertensive Patients, according to 5 Cardiovascular Health Score Trajectory Patterns.

correlated to altered MI risk by using trajectory modeling. The primary results showed that as compared with the low-stable CHS, hypertensive patients with the highest CHS over 4 years had a 76% lower risk of incident MI, independent of the baseline CHS. In addition, the improvement in CHS over time was also associated with a lower MI risk in hypertensive patients. These findings were robust among the subgroup and sensitivity analyses.

To the best of our knowledge, there are currently no studies that evaluated the relationship between changes in CHS and the risk of MI in individuals with hypertension. A nationwide prospective cohort study conducted across mainland China reported that hypertensive patients with more ideal cardiovascular health metrics have significantly reduced incidents of CVD.¹⁵ In another prospective study with the participation of 5488 hypertensive patients, Ying et al²⁸ found that an increased number of ideal cardiovascular health metrics was inversely related to the risk of ischemic stroke in participants with hypertension. However, only the baseline cardiovascular health metrics was regarded as exposure of interest and the subsequent changes in cardiovascular status were ignored in their studies. In contrast to previous studies, the CHS trajectory over 4 years was used to represent changes in cardiovascular status, indicating that hypertensive patients who maintained high CHS had a lower risk of MI incidence, relative to those with a consistently low CHS. In the general population, Danielle et al²⁹ utilized data from the Framingham Offspring Study to demonstrate the odd ratios

of CVD in the low-low CHS group, which is 1.90 (1.51–2.39) when compared with the high-high CHS group. The report from the ARIC (Atherosclerosis Risk in Communities) study has also found that the hazard ratio of CVD was 0.26 (0.20–0.34) in those with ideal cardiovascular status at both measures³⁰ in contrast with individuals with poor cardiovascular status at both visits, indirectly supporting our findings in hypertensive patients.

We also observed that hypertensive patients who started with low CHS but have an improved CHS over time, have a lower risk of MI when compared with low-stable CHS. Using the data from the ARIC study, Amil et al³¹ reported that improvements in ideal CV health throughout mid- to late-life were associated with lower CVD prevalence when reaching elderly age. Bamba et al³⁰ showed that improving from poor to intermediate/ideal cardiovascular status has an association with a lower risk of CVD in the general population. These results are in line with the findings in hypertensive patients, suggesting that if the cardiovascular status is poor in the beginning but improves later, is associated with a lower risk of MI. Higher CHS is associated with higher levels of cardioprotective biomarkers but lower concentrations of pro-atherosclerotic, neurohormonal, and cardiac stress biomarkers.³² Furthermore, the improvements in the CHS are also greatly related to the lower atherosclerosis progression and greater cardiovascular structure and function.^{31,33} These observations may reveal potential biological mechanisms showing the relationship between the CHS change and MI risk.

Table 1. Baseline Characteristics of 17 374 Hypertensive Patients According to the Trajectories of CHS From 2006 to 2010

Variables	Low-stable	Moderate-decreasing	Moderate-increasing	High-stable I	High-stable II	P Value
Participants n (%)	1161 (6.68)	3928 (22.61)	1014 (5.84)	7940 (45.70)	3331 (19.17)	...
Age, y	52.22±8.91	55.02±10.27	53.95±9.99	56.76±11.08	57.87±11.99	<0.01
Male n (%)	1120 (96.47)	3463 (88.16)	970 (95.66)	6496 (81.82)	2313 (69.44)	<0.01
Heart rate, beats/min	78.72±11.71	76.37±11.33	75.26±11.13	74.27±10.93	72.96±10.56	<0.01
SBP, mm/Hg	145.83±18.64	145.34±18.55	139.70±19.03	141.17±19.19	135.17±18.72	<0.01
DBP, mm/Hg	93.62±11.07	91.89±10.80	89.15±10.45	89.30±10.53	85.42±10.13	<0.01
hs-CRP, mmol/L	1.70 (0.90–3.80)	1.44 (0.66–3.40)	1.30 (0.60–3.17)	1.08 (0.36–2.65)	0.90 (0.30–2.08)	<0.01
Education n (%)						<0.01
Elementary school or below	105 (9.04)	391 (9.95)	73 (7.20)	652 (8.21)	270 (8.11)	
High school	987 (85.01)	3307 (84.19)	899 (88.66)	6844 (86.20)	2832 (85.02)	
College or above	69 (5.94)	230 (5.86)	42 (4.14)	444 (5.59)	229 (6.87)	
Drinking status n (%)						<0.01
Never	389 (33.51)	1911 (48.65)	665 (65.58)	5597 (70.49)	2816 (84.54)	
Past	6 (0.52)	29 (0.74)	6 (0.59)	51 (0.64)	12 (0.36)	
Current	766 (65.98)	1988 (50.61)	343 (33.83)	2292 (28.87)	503 (15.10)	
Antihypertensive drugs n (%)	388 (33.42)	1139 (29.01)	183 (18.05)	1458 (18.36)	519 (15.58)	<0.01
CHS at 2006	4.60±1.23	6.89±1.18	5.35±1.16	8.12±1.16	9.39±1.04	<0.01
CHS at 2010	4.45±1.30	6.01±1.06	8.09±0.98	8.27±1.19	9.97±1.05	<0.01

CHS indicates cardiovascular health score; DBP, diastolic blood pressure; hs-CRP, high-sensitivity C-reactive protein; and SBP, systolic blood pressure.

The significance of this study is to contribute to the current database with evidence that maintaining a high CHS or an improvement in CHS has an inverse association with the MI risk in the hypertensive population. Although the mortality rate caused by MI has decreased due to the development of modern medicine, it is still a major contributor to global death and disability.³⁴ The reports from the Chinese Health Examination Database³⁵ and the National Health and Nutrition Examination Survey³⁶ have discovered that only a few people have achieved ideal cardiovascular health metrics whereas most people have poor cardiovascular statuses. It is noteworthy that the cardiovascular status of people with hypertension is poorer than the general population, potentially leading to a higher incidence of MI. Health interventions such as losing weight, quitting smoking, and staying physically active are associated with lower risk of MI in individuals with hypertension.^{9,10} However, the

effective prevention of MI requires long-term maintenance of a healthy cardiovascular state.³⁷ Our previous work showed that the incidence rate of MI in the general population was 1.15/1000 person-years.³⁸ In this study, we found that the incidence rates of MI decreased from 3.27/1000 person-years in the low-stable CHS group to 1.09/1000 person-years in the high-stable II group in hypertensive patients. The above indicated that if hypertensive patients maintain an ideal cardiovascular status for a long time, they may even obtain a lower incidence rate of MI than general people. In light of this, our findings provided new evidence regarding the control and management of MI risk in hypertensive patients.

STRENGTHS AND LIMITATIONS

This is the first large prospective study with a duration of follow-up to 10 years exploring the association

Table 2. The HRs of Myocardial Infarction in Hypertensive Patients According to Trajectories of CHS From 2006 to 2010

	Low-stable	Moderate-decreasing	Moderate-increasing	High-stable I	High-stable II
Case/total	36/1161	85/3928	17/1014	115/7940	35/3331
IR	3.27	2.28	1.75	1.52	1.09
Model 1	1 (reference)	0.62 (0.40–0.91)	0.49 (0.28–0.87)	0.37 (0.25–0.57)	0.27 (0.16–0.42)
Model 2	1 (reference)	0.61 (0.41–0.90)	0.46 (0.25–0.83)	0.36 (0.24–0.54)	0.24 (0.15–0.40)

Model 1 adjusted for age, sex; Model 2 adjusted for heart rate, hs-CRP, drinking status, education level, anti-hypertensive drugs on the basis of model 1. CHS indicates cardiovascular health score; hs-CRP, high-sensitivity C-reactive protein; and IR, incidence rate (per 1000 person-years).

Table 3. The HR of Myocardial Infarction in Hypertensive Patients According to Trajectories of CHS From 2006 to 2010, Stratified by Sex or Age

	Low-stable	Moderate-decreasing	Moderate-increasing	High-stable I	High-stable II	P Value for interaction
Sex						
Male						
Case/total	35/1120	73/3463	15/970	98/6496	31/2313	
	1 (reference)	0.59 (0.39–0.89)	0.42 (0.22–0.78)	0.36 (0.24–0.55)	0.28 (0.17–0.47)	
Female						
Case/total	1/41	12/465	2/44	17/1444	4/1018	
	1 (reference)	1.14 (0.14–9.13)	1.88 (0.16–21.92)	0.51 (0.07–4.11)	0.18 (0.02–1.78)	
Age						
<65 y						
Case/total	29/1073	67/3291	12/878	74/6185	17/2436	
	1 (reference)	0.71 (0.46–1.11)	0.45 (0.22–0.89)	0.40 (0.25–0.63)	0.24 (0.12–0.45)	
≥65 y						
Case/total	7/88	18/637	5/136	41/1755	18/895	
	1 (reference)	0.34 (0.14–0.83)	0.42 (0.13–1.33)	0.26 (0.12–0.60)	0.22 (0.09–0.53)	

Adjusted for age, sex, heart rate, hs-CRP, drinking status, education level, and antihypertensive drugs. CHS indicates cardiovascular health score; HR, hazard ratio; and hs-CRP, high-sensitivity C-reactive protein.

between the trajectory of CHS and MI risk in hypertensive patients, contributing to one of the study's strengths. The trajectory was used to present the CHS change patterns over 4 years to observe its long-term effect on the risk of MI. Furthermore, the Kailuan study cohort was followed up strictly by biennial physical examinations, and the whole research population was also relatively stable, hence the occurrence of primary outcomes can be monitored fully. However, several limitations need to be considered. First, we used salt intake as a surrogate for the healthy diet score because the data about other components (eg, fruits, vegetables, fish) of the healthy diet score were not available until 2014. We were aware that salt intake could only reflect one aspect of the healthy diet score, but our previous work has found a strong association between higher salt intake and lower healthy diet scores by using the dietary data in 2014.³⁸ Meanwhile, given that excessive salt intake is a common dietary habit in China³⁹ and is strongly associated with the development of hypertension and CVD,^{19,20} salt intake was applied as a surrogate of diet quality in this study. Moreover, removing the salt intake from the component of the CHS did not substantially change the results. Nevertheless, our results should be interpreted cautiously. Second, we acknowledged being underpowered for interaction analyses because we have a relatively small population of female (17.34%). Therefore, it caused certain categories had only single-digit events in female group. Additionally, the cohort only consisted of Chinese adults from the Kailuan community in Tangshan, hence the generalization of the results was limited to a certain extent. Finally, although the fitting values of CHS trajectories were close to the

real values in this study, these trajectories identified by the latent mixture modeling may still be overfitting, thus, our results require external validation.

PERSPECTIVES

Hypertensive patients who maintain a prolonged high CHS, which is presented by the ideal healthy cardiovascular status, would have a lower risk of MI. Improvement in the CHS might also provide protective benefits against the incident of MI. Therefore, these results emphasize the significance of taking primordial approaches to promote and maintain a healthy cardiovascular status to prevent the incidence of MI events among patients with hypertension. Further studies, with multiple regions and larger sample sizes, particularly those with detailed dietary data are still warranted to verify our results.

ARTICLE INFORMATION

Received May 1, 2022; accepted August 21, 2022.

Affiliations

Shantou University Medical College, China (Z.H., X.W., Zhiwei Cai, W.F.). Department of Cardiology, Second Affiliated Hospital of Shantou University Medical College, China (Z.H., X.W., Zefeng Cai, Y.L., W.F., Y.C.). Department of Epidemiology, University Medical Center Groningen, University of Groningen, the Netherlands (Z. Chen). School of Public Health, Wuhan University, China (X.D.). Department of Cardiology, Shenzhen Luohu People's Hospital, China (W.L.). China Medical University, Shenyang, China (G.C.). Department of Cardiology, Kailuan General Hospital, Tangshan, China (S.W.).

Acknowledgments

We sincerely express our gratitude to all parties in the Kailuan Study, as well as members of Kailuan General Hospital and its affiliated hospitals. Authors' contributions

The study idea was designed by ZGH, SLW and YRC; ZGH, ZKC, XXW, XD and ZFC analyzed and interpreted the data; ZGH, ZKC, GZC, WJL, YLL, WF and

ZWC were responsible for drafting the article. The article was reviewed by SLW and YRC. All authors have read and approved the final article.

Sources of Funding

This work has been supported by the National Natural Science Foundation of China (No. 81870312). Zekai Chen is supported by a joint fellowship from the China Scholarship Council and University Medical Center Groningen (no. 202008440344).

Disclosures

None.

REFERENCES

- Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, Barengo NC, Beaton AZ, Benjamin EJ, Benziger CP, et al. global burden of cardiovascular diseases and risk factors, 1990-2019: update from the GBD 2019 study [published correction appears in *J Am Coll Cardiol*. 2021 Apr 20;77(15):1958-1959]. *J Am Coll Cardiol*. 2020;76:2982-3021. doi: 10.1016/j.jacc.2020.11.010
- Reed GW, Rossi JE, Cannon CP. Acute myocardial infarction. *Lancet*. 2017;389:197-210. doi: 10.1016/S0140-6736(16)30677-8
- Liang L, Moore B, Soni A. *National Inpatient Hospital Costs: The Most Expensive Conditions by Payer*. HCUP. 2017.
- Picariello C, Lazerri C, Attanà P, Chiostrì M, Gensini GF, Valente S. The impact of hypertension on patients with acute coronary syndromes. *Int J Hypertens*. 2011;2011:563657. doi: 10.4061/2011/563657
- Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004;364:937-952. doi: 10.1016/S0140-6736(04)17018-9
- Thune JJ, Signorovitch J, Kober L, Velazquez EJ, McMurray JJ, Califf RM, Maggioni AP, Rouleau JL, Howlett J, Zelenkofske S, et al. Effect of antecedent hypertension and follow-up blood pressure on outcomes after high-risk myocardial infarction. *Hypertension*. 2008;51:48-54. doi: 10.1161/HYPERTENSIONAHA.107.093682
- Chen G, Hemmelgarn B, Alhaider S, Quan H, Campbell N, Rabi D. Meta-analysis of adverse cardiovascular outcomes associated with antecedent hypertension after myocardial infarction. *Am J Cardiol*. 2009;104:141-147. doi: 10.1016/j.amjcard.2009.02.048
- Zhang W, Zhang S, Deng Y, Wu S, Ren J, Sun G, Yang J, Jiang Y, Xu X, Wang TD, et al. Trial of intensive blood-pressure control in older patients with hypertension. *N Engl J Med*. 2021;385:1268-1279. doi: 10.1056/NEJMoa2111437
- Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, Ramirez A, Schlaich M, Stergiou GS, Tomaszewski M, et al. 2020 International Society of Hypertension global hypertension practice guidelines. *J Hypertens*. 2020;38:982-1004. doi: 10.1097/HJH.0000000000002453
- Arija V, Villalobos F, Pedret R, Vinuesa A, Jovani D, Pascual G, Basora J. Physical activity, cardiovascular health, quality of life and blood pressure control in hypertensive subjects: randomized clinical trial. *Health Qual Life Outcomes*. 2018;16:184. doi: 10.1186/s12955-018-1008-6
- Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, Greenlund K, Daniels S, Nichol G, Tomaselli GF, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation*. 2010;121:586-613. doi: 10.1161/CIRCULATIONAHA.109.192703
- Huffman MD, Capewell S, Ning H, Shay CM, Ford ES, Lloyd-Jones DM. Cardiovascular health behavior and health factor changes (1988-2008) and projections to 2020: results from the National Health and Nutrition Examination Surveys. *Circulation*. 2012;125:2595-2602. doi: 10.1161/CIRCULATIONAHA.111.070722
- Isiozor NM, Kunutsor SK, Voutilainen A, Kurl S, Kauhanen J, Laukkanen JA. Ideal cardiovascular health and risk of acute myocardial infarction among Finnish men. *Atherosclerosis*. 2019;289:126-131. doi: 10.1016/j.atherosclerosis.2019.08.024
- Wilsgaard T, Loehr LR, Mathiesen EB, Løchen ML, Bønaa KH, Njølstad I, Heiss G. Cardiovascular health and the modifiable burden of incident myocardial infarction: the Tromsø Study. *BMC Public Health*. 2015;15:221. doi: 10.1186/s12889-015-1573-0
- Wu S, Xu Y, Zheng R, Lu J, Li M, Chen L, Huo Y, Xu M, Wang T, Zhao Z, et al. Hypertension defined by 2017 ACC/AHA guideline, ideal cardiovascular health metrics, and risk of cardiovascular disease: a nationwide prospective cohort study. *Lancet Reg Health West Pac*. 2022;20:100350. Published 2022 Jan 8. doi: 10.1016/j.lanwpc.2021.100350
- Wu Z, Jin C, Vaidya A, Jin W, Huang Z, Wu S, Gao X. Longitudinal patterns of blood pressure, incident cardiovascular events, and all-cause mortality in normotensive diabetic people. *Hypertension*. 2016;68:71-77. doi: 10.1161/HYPERTENSIONAHA.116.07381
- Wu S, Huang Z, Yang X, Zhou Y, Wang A, Chen L, Zhao H, Ruan C, Wu Y, Xin A, et al. Prevalence of ideal cardiovascular health and its relationship with the 4-year cardiovascular events in a northern Chinese industrial city. *Circ Cardiovasc Qual Outcomes*. 2012;5:487-493. doi: 10.1161/CIRCOUTCOMES.111.963694
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA*. 2003;289:2560-2572. doi: 10.1001/jama.289.19.2560
- Aaron KJ, Sanders PW. Role of dietary salt and potassium intake in cardiovascular health and disease: a review of the evidence. *Mayo Clin Proc*. 2013;88:987-995. doi: 10.1016/j.mayocp.2013.06.005
- Cook NR, Cutler JA, Obarzanek E, Buring JE, Rexrode KM, Kumanyika SK, Appel LJ, Whelton PK. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). *BMJ*. 2007;334:885-888. doi: 10.1136/bmj.39147.604896.55
- Li Y, Huang Z, Jin C, Xing A, Liu Y, Huangfu C, Lichtenstein AH, Tucker KL, Wu S, Gao X. Longitudinal change of perceived salt intake and stroke risk in a chinese population. *Stroke*. 2018;49:1332-1339. doi: 10.1161/STROKEAHA.117.020277
- Jin C, Chen S, Vaidya A, Wu Y, Wu Z, Hu FB, Kris-Etherton P, Wu S, Gao X. Longitudinal change in fasting blood glucose and myocardial infarction risk in a population without diabetes. *Diabetes Care*. 2017;40:1565-1572. doi: 10.2337/dc17-0610
- Li W, Jin C, Vaidya A, Wu Y, Rexrode K, Zheng X, Gurol ME, Ma C, Wu S, Gao X. Blood pressure trajectories and the risk of intracerebral hemorrhage and cerebral infarction: a prospective study. *Hypertension*. 2017;70:508-514. doi: 10.1161/HYPERTENSIONAHA.117.09479
- Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation*. 1994;90:583-612. doi: 10.1161/01.cir.90.1.583
- Jones BL, Nagin DS, Roeder K. A SAS procedure based on mixture models for estimating developmental trajectories. *Social Methods Res*. 2001;29:374-393. DOI:10.1177/0049124101029003005
- Jones BL, Nagin DS. Advances in group-based trajectory modeling and an SAS procedure for estimating them. *Social Methods Res*. 2007;35:542-571. DOI:10.1177/0049124106292364
- Sterne JA, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, Wood AM, Carpenter JR. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ*. 2009;338:b2393. doi: 10.1136/bmj.b2393
- Ying Y, Lin S, Kong F, Li Y, Xu S, Liang X, Wang C, Han L. Corrigendum: ideal cardiovascular health metrics and incidence of ischemic stroke among hypertensive patients: a prospective cohort study. *Front Cardiovasc Med*. 2021;8:829078. doi: 10.3389/fcvm.2021.829078
- Enserro DM, Vasan RS, Xanthakis V. Twenty-year trends in the american heart association cardiovascular health score and impact on sub-clinical and clinical cardiovascular disease: the Framingham Offspring Study. *J Am Heart Assoc*. 2018;7:e008741. doi: 10.1161/JAHA.118.008741
- Gaye B, Tajeu GS, Vasan RS, Lassale C, Allen NB, Singh-Manoux A, Jouven X. Association of changes in cardiovascular health metrics and risk of subsequent cardiovascular disease and mortality. *J Am Heart Assoc*. 2020;9:e017458. doi: 10.1161/JAHA.120.017458
- Shah AM, Claggett B, Folsom AR, Lutsey PL, Ballantyne CM, Heiss G, Solomon SD. Ideal cardiovascular health during adult life and cardiovascular structure and function among the elderly. *Circulation*. 2015;132:1979-1989. doi: 10.1161/CIRCULATIONAHA.115.017882
- Xanthakis V, Enserro DM, Murabito JM, Polak JF, Wollert KC, Januzzi JL, Wang TJ, Tofler G, Vasan RS. Ideal cardiovascular health: associations with biomarkers and subclinical disease and impact on

- incidence of cardiovascular disease in the Framingham Offspring Study. *Circulation*. 2014;130:1676–1683. doi: 10.1161/CIRCULATIONAHA.114.009273
33. Gao J, Bao M, Liu Y, Shi J, Huang Z, Xing A, Wang Y, An S, Cai J, Wu S, et al. Changes in cardiovascular health score and atherosclerosis progression in middle-aged and older persons in China: a cohort study. *BMJ Open*. 2015;5:e007547. doi: 10.1136/bmjopen-2014-007547
34. Krumholz HM, Normand SL, Wang Y. Trends in hospitalizations and outcomes for acute cardiovascular disease and stroke, 1999–2011. *Circulation*. 2014;130:966–975. doi: 10.1161/CIRCULATIONAHA.113.007787
35. Wu HY, Sun ZH, Cao DP, Wu LX, Zeng Q. Cardiovascular health status in Chinese adults in urban areas: analysis of the Chinese Health Examination Database 2010. *Int J Cardiol*. 2013;168:760–764. doi: 10.1016/j.ijcard.2012.09.235
36. Yang Q, Cogswell ME, Flanders WD, Hong Y, Zhang Z, Loustalot F, Gillespie C, Merritt R, Hu FB. Trends in cardiovascular health metrics and associations with all-cause and CVD mortality among US adults. *JAMA*. 2012;307:1273–1283. doi: 10.1001/jama.2012.339
37. Karmali KN, Lloyd-Jones DM. Adding a life-course perspective to cardiovascular-risk communication. *Nat Rev Cardiol*. 2013;10:111–115. doi: 10.1038/nrcardio.2012.185
38. Wu S, An S, Li W, Lichtenstein AH, Gao J, Kris-Etherton PM, Wu Y, Jin C, Huang S, Hu FB, et al. Association of trajectory of cardiovascular health score and incident cardiovascular disease. *JAMA Netw Open*. 2019;2:e194758. doi: 10.1001/jamanetworkopen.2019.4758
39. He FJ, Brown M, Tan M, MacGregor GA. Reducing population salt intake—an update on latest evidence and global action. *J Clin Hypertens (Greenwich)*. 2019;21:1596–1601. doi: 10.1111/jch.13664