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Prevalence and correlates of multimarker hypertension-mediated organ damage in Ghanaian adults: evidence from the Ghana Heart Study

Kwabena Oteng Agyapong

kwabenaoteng.agyapong@aya.yale.edu

Yale School of Public Health https://orcid.org/0000-0001-8184-7569

Esther Kyeremah

Columbia University Mailman School of Public Health

Aba Folson

University of Health and Allied Sciences

Francis Agyekum

University of Ghana Medical School

Kim Blenman

Yale University

Lambert Appiah

Kwame Nkrumah University of Science and Technology

Yaw Adu Boakye

Kwame Nkrumah University of Science and Technology

Isaac Owusu

Kwame Nkrumah University of Science and Technology

Article

Keywords: hypertension-mediated organ damage, arterial stiffness, baPWV, Ghana, sub-Saharan Africa, cardiovascular risk stratification, pulse wave velocity, left ventricular hypertrophy

Posted Date: November 12th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11444055/v1

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Additional Declarations: There is **NO** conflict of interest to disclose.

Prevalence and correlates of multimarker hypertension-mediated organ damage in Ghanaian adults: evidence from the Ghana Heart Study

Authors:

K. O. Agyapong, MD, MPH [1,2,8]; E. Kyeremah, MD, MPH [3]; A. A. Folson, MD [4,5]; F. Agyekum, MD [6]; K. R. M. Blenman, PhD, MS [8,9]; L. T. Appiah, MD [7]; Y. Adu-Boakye, MD [7]; I. K. Owusu, MD [7]

Affiliations:

[1]Yale School of Public Health, New Haven, CT, USA

[2]Department of Medicine, Greater Accra Regional Hospital, Ridge-Accra, Ghana

[3]Department of Epidemiology, Columbia University Mailman School of Public Health, New York, NY, USA

[4]Department of Internal Medicine and Therapeutics, School of Medicine, University of Health and Allied Sciences, Ho, Ghana

[5]Department of Internal Medicine, Ho Teaching Hospital, Ho, Ghana

[6]Department of Medicine, College of Health Sciences, University of Ghana Medical School, Accra, Ghana

[7]Department of Medicine, School of Medicine and Dentistry, College of Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

[8]Department of Internal Medicine, Section of Medical Oncology, Yale Cancer Center, New Haven, CT, USA

[9]Department of Computer Science, Yale School of Engineering and Applied Science, Yale University, New Haven, CT, USA

Corresponding Author:

Kwabena Oteng Agyapong, MD, MPH

Yale School of Public Health, 60 College Street, New Haven, CT 06510, USA

Telephone: +1 774 623 1145; Email: kwabenaoteng.agyapong@aya.yale.edu

Summary Table

What is known about the topic

- Single markers of hypertension-mediated organ damage (HMOD) have been described in African populations, but multi-organ assessment in West Africa populations is limited and understudied.
- Conventional cardiovascular risk stratification tools tend to correlate poorly with each other in Ghanaian adults.
- Brachial-ankle pulse wave velocity (baPWV) can be used to measure arterial stiffness and is a validated marker. Its value in detecting HMOD in sub-Saharan Africa remains undefined.

What this study adds

- One in five of the adults examined had HMOD diagnosed by multiple markers and one in six had two or more organs affected by HMOD.
- baPWV discriminates multimarker HMOD significantly better than the Pooled Cohort Equations (PCE) (AUC 0.807 vs 0.526).
- There was a significant rural penetration effect for multimarker HMOD with greatest effect at younger ages.

Abstract

Manifestations of hypertension-related organ damage have been described in several African populations. Yet a comprehensive characterization of hypertension-related damage to multiple organs and a comparison with conventionally calculated cardiovascular disease risk in a West African setting is lacking. We performed a secondary analysis of the Ghana Heart Study, which included 1 106 community-dwelling Ghanaian adults from 4 regions. Eight vascular, cardiac, and renal endpoints were determined. Multimarker HMOD (≥2 abnormal markers among participants with ≥6 measured components) was present in 20.7% and true multiorgan HMOD

(≥2 of three organ systems) in 16.2%. Prevalence rose from 8.6% at ages <45 years to 44.1% at ≥60 years. In an external- predictor model (n=1 044), age, systolic blood pressure, hypertension, and rural residence were independently associated with multimarker HMOD; Central region residence was inversely associated. Brachial-ankle pulse wave velocity (baPWV) showed the highest discrimination among continuous markers (AUC 0.832). Among 530 participants aged 40–74 years, baPWV alone (AUC 0.807) and baPWV plus the Pooled Cohort Equations (AUC 0.815) substantially outperformed the Pooled Cohort Equations alone (AUC 0.526), with improved net benefit across thresholds. Multimarker HMOD is common, strongly age- and blood pressure- dependent, and more frequent in rural settings at younger ages. baPWV may usefully complement conventional risk assessment; prospective studies are required to confirm whether baPWV-guided care improves outcomes.

Keywords: hypertension-mediated organ damage; arterial stiffness; baPWV; Ghana; sub-Saharan Africa; cardiovascular risk stratification; pulse wave velocity; left ventricular hypertrophy

Introduction

Cardiovascular disease remains the leading cause of death globally, with more than 80% of mortality from cardiovascular disease occurring in low- and middle-income countries. [1,2] Sub-Saharan Africa, including Ghana, is currently experiencing a rapid epidemiological transition caused by urbanization, dietary change, and physical inactivity, resulting in rising hypertension and its complications. [3–5] The Ghana Heart Study (2016–2017) assessed the cardiovascular disease risk factors of 1 106 adults from within the community. The study found high prevalence of obesity, hypertension, diabetes, and dyslipidemia, as well as several unhealthy behaviors. [6,7]

Hypertension is a major risk factor for cardiovascular disease. It causes a variety of changes, referred to as hypertension-mediated organ damage (HMOD), in the heart, arteries, and kidneys in the subclinical phase before clinical events occur. [8] These changes can be detected early, allowing for intensified prevention, and have often been found in single organs in previous studies. However, in many cases, chronic hypertension affects multiple organs, and thus HMOD is of a multi-domain nature. Prior analyses of the same data set found single-organ prevalence of Peripheral Artery Disease (10.1%), Carotid Thickening (8.3%), Left Ventricular Hypertrophy (4.1%), and chronic kidney disease (2.5%). [6].

Most imported atherosclerotic cardiovascular disease (ASCVD) risk calculators perform poorly in diagnosing cardiovascular diseases in Ghanaian adults. [9] The World Health Organization/International Society of Hypertension charts, recommended by national guidelines [10], classify many adults aged 40–74 years as low risk. In contrast, other tools assign far higher proportions to intermediate or high risk, creating uncertainty about treatment intensification thresholds. [9]

This secondary analysis of the Ghana Heart Study therefore aimed to: (1) determine the prevalence of multimarker and true multiorgan HMOD; (2) identify independent clinical correlates using predictors external to the outcome definition; (3) compare the discriminative performance of brachial-ankle pulse wave velocity (baPWV) with the ASCVD Pooled Cohort Equations (PCE); and (4) evaluate the incremental clinical utility of arterial stiffness measurement for risk stratification in this population.

Materials and Methods

Study design and population

This is a secondary analysis of the Ghana Heart Study, a community-based cross-sectional survey conducted between September 2016 and March 2017. A three-stage stratified random sampling strategy recruited 1 106 adults aged ≥18 years from eight communities (four urban, four rural) across Greater Accra, Ashanti, Central, and Northern regions. [6,7] Although half the sampled communities were rural, the final analytic sample was predominantly urban (80.4%), reflecting larger urban community sizes and differential response rates. Exclusion criteria comprised pregnancy, type 1 diabetes, established atherosclerotic cardiovascular disease, congenital heart disease, secondary hypertension, or refusal of consent. Ethical approval was obtained from the Committee on Human Research, Publications and Ethics of Kwame Nkrumah University of Science and Technology and Komfo Anokye Teaching Hospital (CHRPE/AP/415/16). Written informed consent was obtained from all participants. The study was registered at ChiCTR1800017374.

Data collection and definitions

All measurements followed a standardized protocol for data collection for demographics, lifestyle factors, anthropometry, and blood pressure. The blood pressure was measured with the arm at heart level in a quiet room after a 10-minute rest using an automated blood pressure monitor (OMRON M6, Omron Healthcare, Kyoto, Japan) [11] as per the European Society of Hypertension [11]. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, or current use of antihypertensive medication. Lipid, HbA1c, creatinine, and other relevant blood markers were measured from blood samples collected after a fasting period of at least 12 hours. Measurements of baPWV and the ankle-brachial index (ABI) were performed using a VP-2000 integral blood pressure monitor (Omron Healthcare, Kyoto, Japan) [12]. The presence of carotid plaque and intima-media thickness

(IMT) was assessed by ultrasound using a VibrantQ imaging platform (GE Healthcare, Horten, Norway). Left ventricular mass index, geometry and function were assessed by echocardiography using the same imaging platform and analyzed according to the guidelines for assessment of left ventricular and left atrial size, function and form [13,14] and assessment of diastolic function of the heart using a 12 lead electrocardiogram to assess for left ventricular hypertrophy by the Sokolow–Lyon criteria [15] or Cornell criteria [15] and chronic kidney disease (CKD) was assessed by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation to estimate glomerular filtration rate (eGFR) and defined as CKD stage ≥3, eGFR <60 mL/min/1.73 m², and albuminuria defined as a urine albumin-to-creatinine ratio ≥30 mg/g. [16]

Multimarker and multiorgan HMOD definitions

Eight markers were included in the composite: high baPWV, peripheral artery disease (PAD), defined by an ankle-brachial index (ABI) below 0.9, carotid plaque, electrocardiographic (ECG) left ventricular hypertrophy, echocardiographic left ventricular hypertrophy, diastolic dysfunction, chronic kidney disease stage ≥3, and albuminuria defined by a urine albumin-to-creatinine ratio ≥30 mg/g. The multimarker definition of HMOD was defined as ≥2 abnormal markers, measured in at least six of the eight components. A true multiorgan dysfunction phenotype was defined as involvement of ≥2 of the three organ systems, i.e., vascular (baPWV, PAD, carotid plaque), cardiac (ECG or echocardiographic evidence of left ventricular hypertrophy, diastolic dysfunction), and renal (chronic kidney disease, albuminuria). The cardiometabolic risk triad (CAT), central obesity + hypertension + dyslipidemia or diabetes, was used as a non-circular correlate.

Statistical analysis

Continuous variables are presented as mean (standard deviation), and categorical variables are presented as number of cases (percentages). The primary multivariable logistic regression model included variables that were external to the outcome (i.e., age, sex, systolic blood pressure, hypertension, body mass index, diabetes, dyslipidemia, smoking status, physical inactivity, region, and urban/rural residence). An interaction term for age and rural residence was tested. The Receiver Operating Characteristic curve assessed discrimination among the models, and the area under the curve (AUC) was compared using DeLong's test [17] on identical participant samples. To address the primary aim among adults aged 40-74 years with complete data (n=530), the performance of the PCE [18] model, the baPWV model, and the combined model was assessed. Bootstrap internal validation (1 000 resamples) and calibration, along with decision-curve analysis [19] across all thresholds (0.05-0.60), were performed to determine the added value of the baPWV over the PCE model. The continuous net reclassification improvement (NRI) [20] and integrated discrimination improvement (IDI) were used to quantify the incremental value of the baPWV model over the PCE model. Leave-one-domain-out (LODO) analyses were performed to assess the robustness of the primary results. All analyses were conducted in R version 4.3.3. A two-sided p-value <0.05 was considered statistically significant.

Results

Participant characteristics and HMOD prevalence

Mean age was 46.9 (17.2) years; 58.0% were women, and 80.4% resided in urban areas (Table 1). Multimarker HMOD was present in 229 participants (20.7%) and true multiorgan HMOD in 179 (16.2%). Prevalence increased steeply with age: 8.6% (<45 years), 19.0% (45–59 years), and 44.1% (≥60 years) (Figure 1). Every individual marker was substantially more

frequent among participants with multimarker HMOD (Table 2). Electrocardiographic left-ventricular hypertrophy was common even among participants without multimarker HMOD (32.7%), consistent with the known tendency of voltage criteria to overcall left-ventricular hypertrophy in African populations.

External-predictor model and rural–urban disparity

In the final model (n=1 044 complete cases), age (odds ratio [OR] 1.04 per year, 95% confidence interval [CI] 1.03–1.05), systolic blood pressure (OR 1.04 per mmHg, 95% CI 1.02–1.05), hypertension (OR 1.72, 95% CI 1.06–2.80) and rural residence (OR 1.99, 95% CI 1.29–3.08) were independently associated with multimarker HMOD; Central region residence was inversely associated (OR 0.53, 95% CI 0.29–0.95) (Table 3). A significant age × rural-residence interaction (OR 0.97 per year, 95% CI 0.95–0.99; p = 0.013) indicated that the rural excess was greatest at younger ages and attenuated thereafter; the main-effect rural OR of 1.99 should therefore be interpreted as the estimated association at the reference age and not as constant across the age range (Figure 2). The cardiometabolic risk triad was independently associated with multimarker HMOD (adjusted OR, 2.33; 95% CI, 1.54–3.53) (Table 3). External-predictor associations were largely stable in leave-one-domain-out analyses (Supplementary Table S2). The rural-residence association was strongest when high baPWV was removed (OR 2.685) and attenuated when echocardiographic LVH was removed (OR 1.344; p = 0.209), whereas the associations with age and systolic blood pressure were stable across all models.

Discriminative performance of baPWV versus the PCE

Among the continuous markers examined, baPWV showed the highest discrimination (AUC 0.832; 95% CI 0.798–0.865), although this estimate is partly inflated because high baPWV is itself an outcome component (Figure 3). In the matched age 40–74 sample (n=530), PCE alone

had poor discrimination (AUC 0.526, 95% CI 0.463–0.589), baPWV alone had good discrimination (AUC 0.807, 95% CI 0.764–0.849), and the combined model AUC 0.815 (95% CI 0.774–0.857; ΔAUC +0.289, DeLong $p=3.2\times10^{-15}$) (Table 4, Figure 4). Bootstrap internal validation (1 000 resamples) yielded optimism-corrected AUCs of 0.521 for PCE alone and 0.813 for the combined model. Calibration was imperfect for both models (Hosmer–Lemeshow $\chi^2=22.7$, $p=0.004$ for PCE alone; $\chi^2=27.8$, $p<0.001$ for the combined model). The combined model provided the highest net benefit across all thresholds tested (0.05–0.60), with a continuous NRI of 1.05 (95% CI 0.89–1.22) and an IDI of 0.227 (95% CI 0.183–0.270). In leave-one-domain-out analyses, removal of high baPWV reduced composite prevalence from 20.7% to 12.3%. It attenuated the baPWV association (OR 1.448, $p < 0.001$) in the reference model vs OR 1.075 ($p = 0.180$) when high baPWV was removed, consistent with partial circularity (Supplementary Table S1).

Discussion

In this multiregional Ghanaian community cohort, approximately one in five adults met a multimarker HMOD threshold, and one in six met a stricter true multiorgan definition. The burden of HMOD increased dramatically with age and BP burden and was independently higher in rural than in urban dwellers, particularly at younger ages. Comparing noninvasive vascular assessment with previously established clinical evaluation for prevalent HMOD, we found that baPWV substantially outperformed the PCE in defining multimarker HMOD and added incremental clinical value beyond the PCE in defining true multiorgan HMOD.

The gap between multimarker (20.7%) and true multiorgan (16.2%) prevalence underscores that composite scores can overstate genuine cross-system involvement; reporting both figures avoids overstatement. This distinction is methodologically important and should inform future

HMOD research that uses composite outcomes. The independent association of rural residence, modified by age, suggests that prevention efforts may need to be intensified among younger rural adults; the narrowing of the rural–urban gap at older ages (Figure 2) may reflect saturation of age-related risk in both settings. The inverse association with Central region residence (OR 0.53) is notable and may reflect regional differences in dietary patterns, physical activity, or access to care that warrant targeted investigation. The non-circular association of the cardiometabolic triad further supports a genuine clinical correlate of the phenotype.

Partial circularity in the vascular domain for baPWV is acknowledged: when high baPWV was removed from the composite, the baPWV association lost significance (OR 1.075, p = 0.180; Supplementary Table S1), and the composite prevalence fell from 20.7% to 12.3%. However, decision curve analysis was superior for the multimarker-defined HMOD phenotype across all tested thresholds. [19] PCE may not be the best marker for cross-sectional assessment of HMOD, as it was developed for a prospective assessment of ASCVD events; some degree of construct mismatch is expected. [18] Arterial stiffness, measured by baPWV, is a known predictor of cardiovascular disease across various populations [21–24], and this study demonstrates its applicability in a West African community-based setting.

Previous studies, such as the Ghana Heart Study [6] and data from the RODAM study [25], provided relevant single-marker information. Still, these are not directly comparable to the present study due to differences in outcome definitions, age distributions, and study designs/sampling frames. This study contributes to current knowledge by being among the first to use a multi-organ HMOD definition in a community-based study in a West African country, while addressing predictor-outcome circularity.

Limitations of this work are the cross-sectional nature of the data (i.e., no causal relationships can be defined), the use of a single blood pressure measurement as opposed to measurements taken over 24 hours or the use of other indirect means of determining central pressure, the relative lack of data from rural communities, incomplete information on urine albumin measurements, lack of information on the device used for measurement of baPWV in this study and its possible lack of validation in a West African setting, and the lack of information on ambulatory blood pressure monitoring (ABPM) and other arterial stiffness indices. As previously noted, electrocardiographic measures for left ventricular hypertrophy have been noted to overdiagnose in African populations. Thus, the high prevalence of left ventricular hypertrophy as defined by ECG (even in those without HMOD (32.7%)) could influence composite results. The rural-residence association was not fully robust to the exclusion of echocardiographic LVH (OR 1.344; $p = 0.209$; Supplementary Table S2), suggesting that part of the rural excess in multimarker HMOD is attributable to echo-LVH; this should be interpreted with caution. This work would thus primarily apply to similar multi-regional community studies in Ghana.

In conclusion, Multimarker HMOD is prevalent and strongly age- and blood pressure-dependent in a multiregional Ghanaian community-based cohort. The burden is higher in rural communities, especially at younger ages. Furthermore, there is value in using baPWV as a surrogate endpoint for cardiovascular disease and baPWV-guided assessment of HMOD in improving clinical outcomes in the West African population. A prospective study is required to prove this value.

Data Availability Statement

The datasets analyzed in this study form part of the Ghana Heart Study. De-identified participant-level data may be requested from the corresponding author, subject to institutional data governance requirements and applicable data transfer agreements.

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Acknowledgments

The authors thank the participants, community leaders, and field staff of the Ghana Heart Study. Technical and logistical support from the participating regional hospitals is gratefully acknowledged.

Author Contributions

K.O. Agyapong: Conceptualization, Methodology, Formal Analysis, Writing – Original Draft, Writing – Review & Editing. E. Kyeremah: Data Curation, Writing – Review & Editing. A.A. Folson: Resources, Data Curation, Writing – Review & Editing. F. Agyekum: Resources, Data Curation, Writing – Review & Editing. K.R.M. Blenman: Conceptualization, Writing – Review & Editing. L.T. Appiah: Data Curation, Writing – Review & Editing. Y. Adu-Boakye: Data Curation, Writing – Review & Editing. I.K. Owusu: Conceptualization, Resources, Supervision, Writing – Review & Editing.

Funding

Funding for the original Ghana Heart Study was provided by the Guangdong Academy of Medical Sciences and the China-Ghana West African Heart Center Cooperation Project. The present secondary analysis received no additional external funding. The funders had no role in the design, analysis, interpretation, or writing of this secondary analysis.

Ethical Approval

The study received ethical approval from the Committee on Human Research, Publications and Ethics of the Kwame Nkrumah University of Science and Technology and Komfo Anokye Teaching Hospital (CHRPE/AP/415/16). Written informed consent was obtained from all participants. The study was registered at the Chinese Clinical Trial Registry (ChiCTR1800017374).

Competing Interests

The authors declare no competing financial interests.

Figure Legends

Figure 1. Multimarker hypertension-mediated organ damage (HMOD) prevalence by age group among 1 106 Ghanaian adults. Bars show the proportion meeting the ≥2-of-8 marker composite within each age stratum; numbers above bars are counts with HMOD. The dashed horizontal line indicates overall cohort prevalence (20.7%).

Figure 2. Multimarker HMOD prevalence by age group and urban/rural residence. Prevalence was consistently higher among rural than urban participants, but the rural–urban gap narrowed with age: 15.8% vs 6.8% at ages <45 years (2.3×), 26.8% vs 17.2% at ages 45–59 years (1.6×), and 53.3% vs 41.7% at ages ≥60 years (1.3×). The age × residence interaction was significant (odds ratio 0.97 per year; 95% confidence interval 0.95–0.99; p=0.013).

Figure 3. Receiver operating characteristic (ROC) curves for continuous markers discriminating between participants with and without multimarker HMOD. Continuous measures underlying other outcome components (ankle-brachial index, left ventricular mass index, estimated glomerular filtration rate, and urine albumin-to-

creatinine ratio) and the composite itself are excluded. baPWV is shown but is partly circular, because high baPWV (≥14 m/s) is itself one of the eight outcome components. baPWV had the highest discrimination (AUC 0.832, 95% CI 0.798–0.865), followed by carotid intima-media thickness (IMT; AUC 0.717), average E/e′ ratio (AUC 0.671), high-sensitivity C-reactive protein (hs-CRP; AUC 0.593), right ventricular systolic pressure (RVSP; AUC 0.576), HbA1c (AUC 0.561), low-density lipoprotein cholesterol (LDL; AUC 0.543) and ejection fraction (EF; AUC 0.508). The ASCVD Pooled Cohort Equations (PCE), shown in black for reference, had an AUC of 0.468 in the full, non-age-restricted sample.

Figure 4. ROC curves comparing the ASCVD Pooled Cohort Equations (PCE) alone, baPWV alone, and the combined PCE + baPWV model in the age 40–74 years, complete-data sample (n=530). PCE alone AUC 0.526; baPWV alone AUC 0.807; combined AUC 0.815 (ΔAUC +0.289, DeLong $p=3.2\times10^{-15}$).

Tables

Table 1. Baseline characteristics of the analytic sample (N=1 106)

SD, standard deviation; BMI, body-mass index; BP, blood pressure; baPWV, brachial-ankle pulse wave velocity; HMOD, hypertension-mediated organ damage.

Table 2. Prevalence of individual HMOD markers by multimarker HMOD status

Component comparisons are descriptive. HMOD, hypertension-mediated organ damage; baPWV, brachial-ankle pulse wave velocity; ECG, electrocardiographic.

Table 3. External-predictor logistic model for multimarker HMOD (n=1 044)

OR, odds ratio; CI, confidence interval; BP, blood pressure; BMI, body mass index. Age × rural-residence interaction: OR 0.97 per year (95% CI 0.95–0.99), p=0.013. The main-effect rural OR should be interpreted at the reference age.

Table 4. Discrimination of baPWV versus PCE (matched age 40–74 years, n=530)

AUC, area under the receiver-operating-characteristic curve; PCE, Pooled Cohort Equations; baPWV, brachial-ankle pulse wave velocity; NRI, net reclassification improvement; IDI, integrated discrimination improvement. DeLong p for PCE vs combined =

3.2×10^{-15}. High baPWV (≥14 m/s) is one of the eight outcome components, so comparisons involving baPWV are partly circular. The combined model had the highest net benefit across all thresholds from 0.05 to 0.60.

Supplementary Information

Additional tables (distribution of the composite score, missing-data summary, leave-one-domain-out results, non-circular marker associations, sensitivity analyses) and figures (additional ROC curves, decision-curve analysis) are available as Supplementary Information.

Supplementary Table S1. Leave-one-domain-out sensitivity analysis of the composite outcome and baPWV association

baPWV, brachial-ankle pulse wave velocity; AUC, area under the receiver-operating-characteristic curve; OR, odds ratio; PAD, peripheral artery disease; ECG-LVH, electrocardiographic left-ventricular hypertrophy; Echo-LVH, echocardiographic left-ventricular hypertrophy; CKD, chronic kidney disease. Removal of high baPWV reduced composite prevalence from 20.7% to 12.3% and attenuated the baPWV association (OR 1.448 to 1.075, p=0.180), demonstrating partial circularity.

Supplementary Table S2. Leave-one-domain-out sensitivity analysis of the external-predictor model for multimarker HMOD

OR, odds ratio; SBP, systolic blood pressure; HTN, hypertension; PAD, peripheral artery disease; ECG-LVH, electrocardiographic left-ventricular hypertrophy; Echo-LVH, echocardiographic left-ventricular hypertrophy; CKD, chronic kidney disease. Associations between age and systolic blood pressure were stable. The rural-residence association rose when high baPWV was removed (OR 2.685) and attenuated when echocardiographic LVH was removed (OR 1.344, p=0.209).

Figure 1

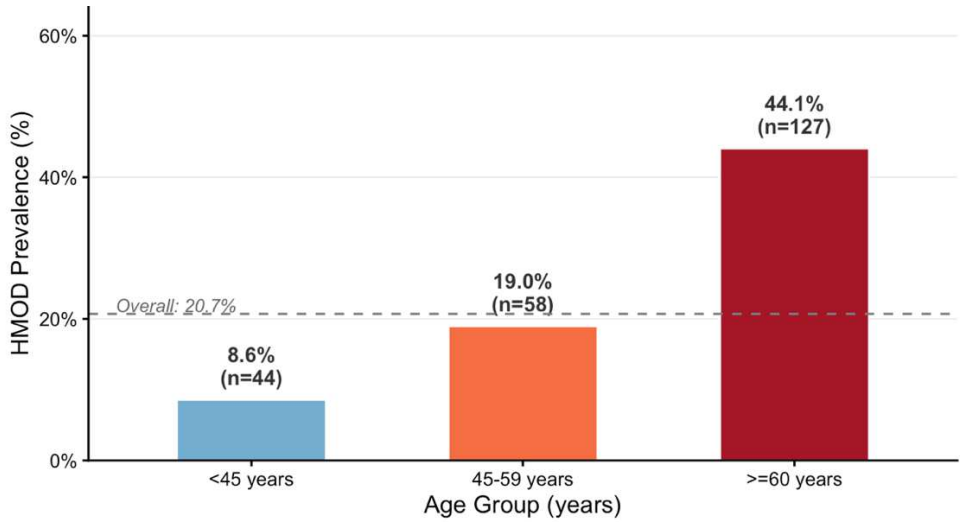


Figure 2

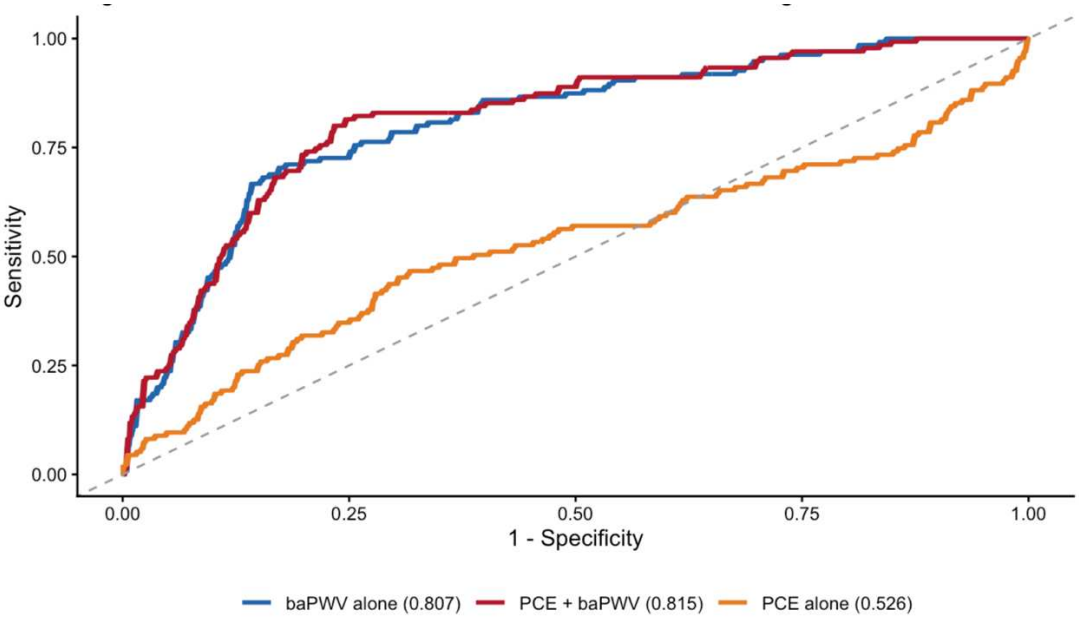


Figure 3

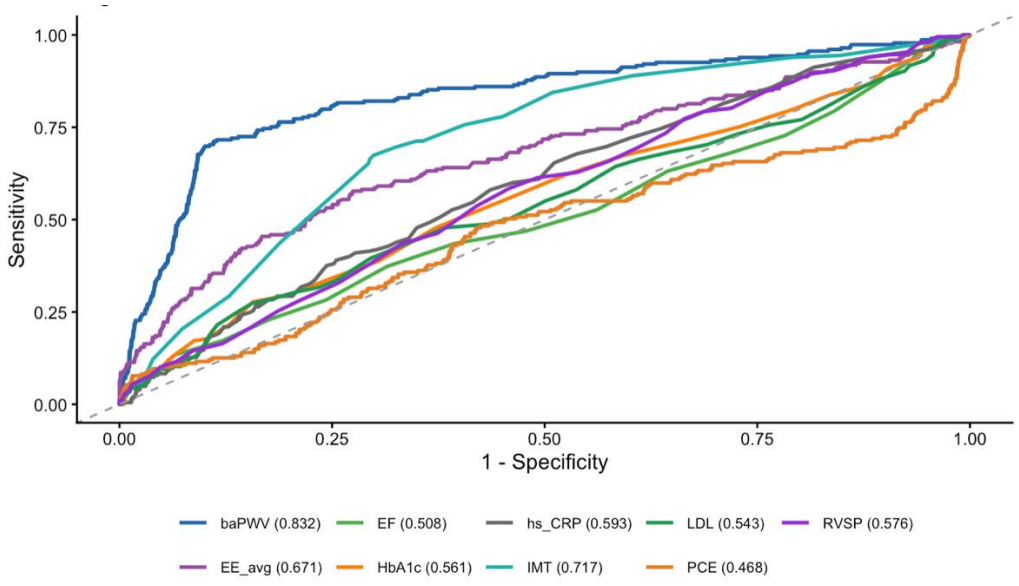
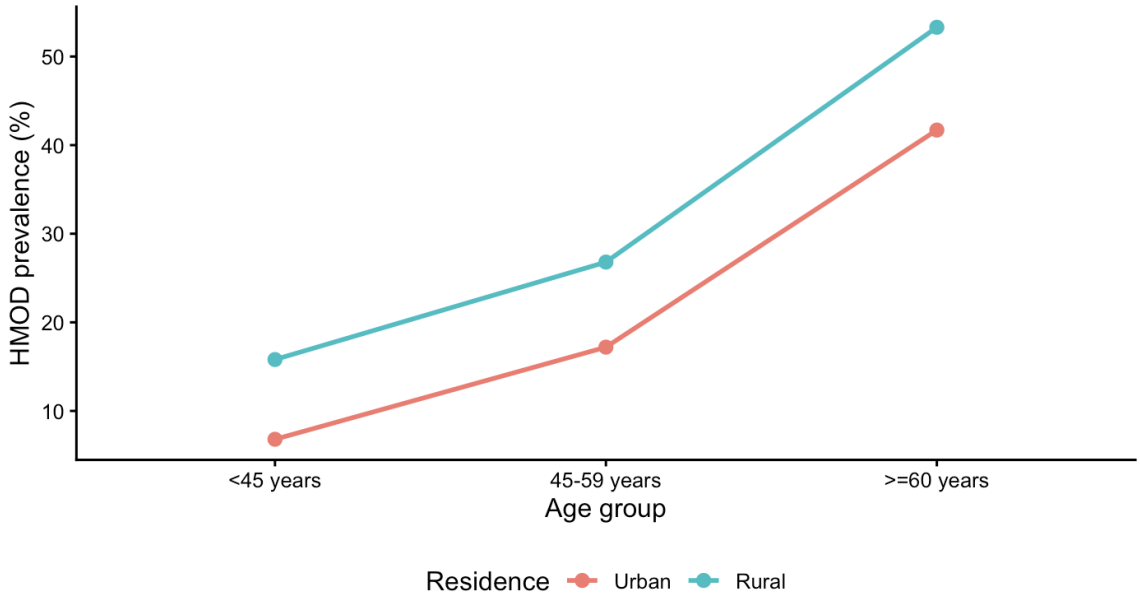


Figure 4

421


HMOD prevalence (%)
50
40
30
20
10
<45 years
45-59 years
>=60 years
Age group
Residence
Urban
Rural

422

423

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable.docx
- TablesJHH.docx