

The Association Between Estimated Pulse Wave Velocity and Cancer Risk in Middle-Aged and Older Adults

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Research Article

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Abstract

Objective

This study aimed to investigate the association between arterial stiffness, as characterised by estimated pulse wave velocity (ePWV), and the risk of cancer in middle-aged and older adults. Subgroup analyses were conducted to assess the role of ePWV in predicting cancer risk across different subgroups. We also explored the association between ePWV and the risk of cancer across different organ systems.

Methods

A cohort study design was employed. We enrolled 11,648 middle-aged and older adults aged 45 years and above, newly recruited to the China Health and Retirement Longitudinal Study (CHARLS) between 2011 and 2015. Cancer incidence during the 2013–2018 follow-up period was defined as the outcome event. The median follow-up duration was 7.00 years. Using X-tile software, ePWV was categorised into two groups: Low-level (Low, < 8.84) and High-level (High, ≥ 8.84). Descriptive analysis was used to compare baseline characteristics. Univariate and multivariate Cox proportional hazards models were employed to analyse the association between ePWV and cancer risk. Subgroup analyses assessed effect differences across populations, and explored the association between ePWV and cancers of different organ systems.

Results

There were 215 cancer cases during follow-up. Cancer incidence was significantly higher in the high ePWV group than in the low ePWV group (68.84% vs 31.16%, $P = 0.010$). After adjusting for age, sex and other confounders in the multivariable Cox regression model, high ePWV was independently associated with an increased cancer risk (HR = 1.48, 95% CI: 1.07–2.06, $P = 0.020$). All variables had variance inflation factors (VIF) < 5 , indicating no multicollinearity. Subgroup analysis showed high ePWV was a significant risk factor for increased cancer incidence in individuals aged < 65 years, males, rural residents, alcohol consumers, those sleeping ≥ 6 hours per night, those with a BMI < 24 kg/m², and those with a comorbidity index ≤ 2 . Site-specific analysis indicated high ePWV was associated with head cancer (HR = 3.77, 95% CI: 1.31–10.84, $P = 0.014$), respiratory cancers (HR = 2.67, 95% CI: 1.07–6.65, $P = 0.035$), and cancers of other systems (HR = 2.27, 95% CI: 1.04–4.95, $P = 0.040$).

Conclusion

This study demonstrates that arterial stiffness, as characterised by ePWV, is significantly associated with increased cancer risk in middle-aged and older adults. This association is more pronounced in certain subgroups. Furthermore, ePWV is closely associated with the risk of head, respiratory, and other

system cancers, and may serve as a potential indicator for identifying high-risk groups for cancer in middle-aged and older adults.

1 Introduction

Cancer is the second leading cause of death globally after cardiovascular disease. According to the latest epidemiological survey from the Global Burden of Disease (GBD) study, there were approximately 18.5 million new cancer cases and 10.4 million cancer deaths worldwide in 2023. Furthermore, both incidence and mortality rates show a significant upward trend with increasing age, making cancer a major contributor to the global burden of disease^{1,2}. The active identification of risk factors for cancer is of significant public health importance for early screening, prevention and the reduction of the disease burden.

Arteriosclerosis, as a core marker of impaired vascular function and structure, involves multiple pathophysiological processes such as inflammatory responses, immune cell dysfunction, and extracellular matrix remodelling^{3,4}. Interestingly, these processes also play a key role in the onset and progression of cancer, suggesting a potential biological link between arterial stiffness and cancer risk. Existing cohort studies have confirmed that arterial stiffness, as characterised by brachial-ankle pulse wave velocity (baPWV), is significantly associated with the risk of cancer incidence and mortality in Chinese adults^{5,6}. The estimated pulse wave velocity (ePWV) serves as a simplified alternative measure of arterial stiffness calculated based on age and blood pressure, requiring no specialized equipment for measurement. In predicting cardiovascular disease (CVD) and all-cause mortality risk, ePWV demonstrates performance comparable to or even superior to baPWV and carotid-femoral PWV (cfPWV)⁷⁻⁹. Recent studies have found that high ePWV is associated with an increased risk of gynaecological cancer and higher mortality rates in the US population¹⁰; however, there is currently a lack of longitudinal studies examining the association between ePWV and cancer incidence, and there is a dearth of large-scale evidence specifically targeting middle-aged and older adults, a population at high risk of cancer.

This study, based on the large-scale CHARLS community cohort, included 11,648 middle-aged and older adults aged 45 years and above. Through a 7-year longitudinal follow-up, we analysed the association between ePWV and the risk of cancer incidence, assessed subgroup differences across populations with varying demographic and clinical characteristics, and explored the association patterns between ePWV and cancers of different systems. The aim is to provide evidence-based support for the identification of high-risk groups for cancer among middle-aged and older adults, as well as for their health management and research into the mechanisms of disease onset.

2 Materials and Methods

2.1 Study Design and Participants

This study is a dynamic cohort study, with data sourced from the China Health and Retirement Longitudinal Study (CHARLS). This study is a household interview survey conducted by the National School of Development at Peking University, designed to investigate the socio-economic and health status of community residents aged 45 years and older across 28 provinces, municipalities and autonomous regions in China¹¹. The CHARLS national baseline survey was launched in 2011, employing a multi-stage stratified cluster sampling method to complete the baseline survey among over 17,000 participants across 150 county-level units in 28 provinces and municipalities nationwide. Three rounds of follow-up surveys were subsequently conducted in 2013, 2015 and 2018, to collect data on socio-demographic characteristics, physical examinations, biological indicators and health-related outcomes.

This study included participants newly enrolled in the CHARLS database between 2011 and 2015. A multi-stage stratified cluster sampling method was again employed. The study population consisted of Chinese community residents aged 45 years and older who completed follow-up surveys in 2013, 2015, and 2018. Data were collected on socio-demographic characteristics, physical examinations, biological indicators, and health-related outcomes. All data used in this study were obtained from the CHARLS public database. The study was approved by the Biomedical Ethics Review Committee of Peking University (Approval No. : IRB00001052-11015), and all participants provided written informed consent.

Inclusion criteria: Participants aged 45 years and older who were newly enrolled in the CHARLS database between 2011 and 2015. Exclusion criteria: (1) Diagnosed with cancer at baseline; (2) Missing data for ePWV assessment; (3) No data on cancer outcomes during the follow-up period. A total of 11,648 participants were ultimately included in the analysis.(Fig. 1.)

2.2 Follow-up Methods and Definition of Outcomes

With 2011–2015 as the baseline, stratified follow-up was conducted according to the time of enrolment: The first cohort of participants enrolled in 2011 underwent three follow-up surveys in 2013, 2015 and 2018; the second cohort enrolled in 2013 underwent two follow-up surveys in 2015 and 2018; and the third cohort enrolled in 2015 underwent a single follow-up survey in 2018. The follow-up period ended upon the occurrence of cancer between 2013 and 2018 or upon the last follow-up visit during this period, whichever occurred first; the median follow-up duration was 7.00 (7.00, 7.00) years.

Outcome variables: Cancer incidence, assessed based on the combined evaluation of cancer diagnoses from the CHARLS database using DA007, ZDA007_4, DA007_w2_1_4 and DA007_w2_2_4; Cancer site was classified according to the DA017 record, including head cancers (brain, thyroid), respiratory system cancers (larynx, other pharynx, lung), digestive system cancers (oral cavity, oesophagus, stomach, liver, pancreas), urogenital system cancers (kidney, bladder, prostate, etc.), breast cancer, and cancers of other systems (skin, other organs, non-Hodgkin's lymphoma, leukaemia, etc.).

2.3 Key Study Factors and Variable Definitions

2.3.1 Estimated Pulse Wave Velocity (ePWV)

- The formula for ePWV is: $ePWV = 9.587 - 0.402 \times \text{age} + 4.560 \times 10^{-3} \times \text{age}^2 - 2.621 \times 10^{-5} \times \text{age}^2 \times \text{mean arterial pressure (MBP)} + 3.176 \times 10^{-3} \times \text{age} \times \text{MBP} - 1.832 \times 10^{-2} \times \text{MBP}$; where $\text{MBP} = \text{diastolic blood pressure (DBP)} + 0.4 \times (\text{systolic blood pressure (SBP)} - \text{DBP})^{12}$. Using the X-tile software, ePWV was categorised into a low-level group (Low, < 8.84) and a high-level group (High, ≥ 8.84)¹³.

2.3.2 Covariates

Based on the literature and clinical practice, the included covariates comprised socio-demographic characteristics (age, gender, educational attainment, marital status, residential area), lifestyle factors (physical activity, smoking, alcohol consumption, sleep duration), anthropometric measures (body mass index, BMI) and clinical indicators (SBP, DBP, MBP, comorbidity index). Specifically: BMI can be treated as a categorical variable, with $\geq 24 \text{ kg/m}^2$ indicating overweight/obesity; Night-time sleep duration is extracted from DA049, with < 6 hours classified as short sleep; Physical activity can be converted into energy expenditure, calculated based on the activity level reported in DA051¹⁴: we transformed the time range by taking the middle value. That is, “ $\geq 10 \text{ min}$ and $< 30 \text{ min}$ ” was recorded as 20 min, “ $\geq 30 \text{ min}$ and $< 2 \text{ h}$ ” was recorded as 75 min, “ $\geq 2 \text{ h}$ and $< 4 \text{ h}$ ” was recorded as 180 min, and “ $\geq 4 \text{ h}$ ” was recorded as 240 min. Weekly energy expenditure = $8.0 \times \text{weekly vigorous physical activity duration} + 4.0 \times \text{weekly moderate physical activity duration} + 3.3 \times \text{weekly low-intensity physical activity duration (walking)}$; physical activity $\geq 600 \text{ MET} \cdot \text{min/week}$ is defined as sufficient physical activity¹⁵; Smoking status: Determined based on DA059 and DA063; whether the individual smokes; Alcohol consumption status: Determined based on DA067, DA072, DA074 and DA076; whether the individual consumes alcohol. The comorbidity index is constructed from comorbidities such as Hypertension, Dyslipidaemia, Diabetes, Liver Diseases, Heart Disease, Stroke, Chronic Lung Diseases, CKD, Stomach, Emotional Disorders, Arthritis and Asthma. A score of 1 is assigned for the presence of a condition and 0 for its absence; the total comorbidity index score is 12 points. The presence of comorbidities is determined based on the chronic conditions reported in DA007, with diabetes, hypertension and chronic kidney disease assessed using a combination of laboratory tests and self-reports. The laboratory diagnostic criteria for diabetes are fasting blood glucose $\geq 7.0 \text{ mmol/L}$ or HbA1c $\geq 6.5\%$, or self-reported diabetes, or receipt of antidiabetic treatment; hypertension is defined as self-reported hypertension, receipt of antidiabetic treatment, or systolic blood pressure $\geq 140 \text{ mmHg}$ or diastolic blood pressure $\geq 90 \text{ mmHg}$; Chronic kidney disease is defined as self-reported kidney disease (excluding tumours or cancer) or an eGFR $\text{CKD-EPI} < 60 \text{ mL/min/1.73 m}^2$; a response of “heart disease (heart attack, coronary heart disease, angina, congestive heart failure, or other heart problem)” indicates the presence of heart disease. $eGFR_{\text{CKD-EPI}} = 142 \times \min(\text{Scr}/\kappa, 1)^\alpha \times \max(\text{Scr}/\kappa, 1)^{-1.200}$

$\times 0.9938^{\text{age}} \times 1.012$ (if female), κ is 0.7 for females and 0.9 for males, α is -0.241 for females and -0.302 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1. Scr is expressed in mg/dL ¹⁶.

2.4 Data Processing and Missing Value Management

There were a small number of missing values for the variables smoking status, educational attainment, gender, place of residence, weight, height, sleep duration and alcohol consumption; the proportion of missing values for the alcohol consumption variable was 13.03%. This study employed the Multivariate Imputation by Chained Equations (MICE) method, which completes the imputation of missing values through iterative sampling of the conditional distributions of multiple variables. (**Supplementary Table 1.**) The effectiveness of the imputation was verified through sensitivity analysis; the results showed no significant differences in the distributions of the variables before and after imputation (all $P > 0.05$), indicating that the method for handling missing values is reliable. (**Supplementary Table 2.**)

2.5 Statistical Analysis Methods

R software version 4.5.1 (2025-06-13 ucrt) was used for data extraction and all subsequent analyses, with a significance level of $\alpha = 0.05$.

2.5.1 Descriptive Analysis

Quantitative data were tested for normality using skewness and kurtosis. Following Levene's test for homogeneity of variances, normally distributed data were presented as mean $\pm$ standard deviation (Mean $\pm$ SD). For data with homogeneous variances, t-tests were used for between-group comparisons; for heterogeneous variances, Satterthwaite's t-test was employed. Non-normally distributed data were expressed as the median and interquartile range [M (Q₁, Q₃)], and comparisons between groups were performed using the Wilcoxon rank-sum test. Categorical data were presented as counts and proportions (n, %), and comparisons between groups were performed using the chi-square test or Fisher's exact test.

2.5.2 Univariate Cox Proportional Hazards Model

All variables were included in a univariate Cox proportional hazards model to estimate the hazard ratio (HR) of ePWV exposure for cancer, thereby verifying the association between each variable and cancer outcomes. All variables with $P < 0.05$ were selected as covariates for the adjusted Model 2. The covariates in Model 2 for this study were: Residence, BMI, and Comorbidity index.

2.5.3 Multivariate Cox Proportional Hazards Model

Three models were constructed to analyse the association between ePWV and the risk of cancer incidence: Model 1 was an unadjusted model; Model 2 adjusted for residence, BMI and comorbidity index; and Model 3 adjusted for all confounding factors; Hazard ratios (HR) and 95% confidence intervals (CI) were calculated, and multicollinearity within the models was assessed using the variance inflation factor (VIF); a VIF < 5 was considered indicative of no multicollinearity.

2.5.4 Subgroup Analysis

Stratification was performed according to characteristics such as age, sex, residential area and lifestyle to assess the predictive role of ePWV in cancer risk across different subgroups.

2.5.5 Site-specific analysis

The association between ePWV and the risk of cancer in different systems was analysed separately, using a multivariable Cox proportional hazards model to adjust for all confounding factors.

3 Results

3.1 Baseline Characteristics of the Study Population

This study included a total of 11,648 participants, with 215 cases of cancer occurring during the follow-up period, representing a cancer incidence rate of 1.84%. When grouped by cancer outcome, statistically significant differences were observed between the two groups in terms of physical activity, BMI, comorbidity index, ePWV classification and duration of follow-up (all $P < 0.05$); whereas there were no significant differences in the distribution of age, gender, educational attainment, marital status, residential area, smoking, alcohol consumption, sleep duration, and blood pressure indicators (SBP, DBP, MBP) (all $P > 0.05$). Notably, the proportion of participants with high ePWV in the cancer group (68.84%) was significantly higher than in the non-cancer group (59.94%); the proportion of overweight/obese individuals (48.37%) and the mean comorbidity index (1.93 ± 1.35) in the cancer group were significantly higher than those in the non-cancer group (40.17%, 1.69 ± 1.26) (Table 1.).

Table 1
Comparison of baseline characteristics

Variables	Total (N = 11648)	Cancer = No (N = 11433)	Cancer = Yes (N = 215)	Statistics	P
Age, years, n (%)				$\chi^2 = 0.000$	0.994
<65	8422 (72.30)	8266 (72.30)	156 (72.56)		
≥65	3226 (27.70)	3167 (27.70)	59 (27.44)		
Gender, n (%)				$\chi^2 = 0.849$	0.357
Male	5536 (47.53)	5441 (47.59)	95 (44.19)		
Female	6112 (52.47)	5992 (52.41)	120 (55.81)		
Education, n (%)				$\chi^2 = 0.471$	0.492
High School Below	10426 (89.51)	10230 (89.48)	196 (91.16)		
High School and Above	1222 (10.49)	1203 (10.52)	19 (8.84)		
Marital status, n (%)				$\chi^2 = 0.006$	0.936
Married	10233 (87.85)	10045 (87.86)	188 (87.44)		
No married	1415 (12.15)	1388 (12.14)	27 (12.56)		
Residence, n (%)				$\chi^2 = 2.683$	0.101
Village	10395 (89.24)	10211 (89.31)	184 (85.58)		
Town/City	1253 (10.76)	1222 (10.69)	31 (14.42)		
Physical activity, n (%)				$\chi^2 = 6.297$	0.043
Insufficient	860 (7.38)	845 (7.39)	15 (6.98)		
Sufficient	4050 (34.77)	3958 (34.62)	92 (42.79)		
Unknown	6738 (57.85)	6630 (57.99)	108 (50.23)		
Table caption: SD: Standard Deviation; M: Median; Q ₁ : 1st Quartile; Q ₃ : 3st Quartile					

Variables	Total (N = 11648)	Cancer = No (N = 11433)	Cancer = Yes (N = 215)	Statistics	P
Smoking, n (%)				$\chi^2 = 0.185$	0.667
No	7019 (60.26)	6893 (60.29)	126 (58.60)		
Yes	4629 (39.74)	4540 (39.71)	89 (41.40)		
Drinking, n (%)				$\chi^2 = 2.887$	0.089
No	8885 (76.28)	8710 (76.18)	175 (81.40)		
Yes	2763 (23.72)	2723 (23.82)	40 (18.60)		
Sleeping duration, n (%)				$\chi^2 = 1.983$	0.159
<6	3423 (29.39)	3350 (29.30)	73 (33.95)		
≥6	8225 (70.61)	8083 (70.70)	142 (66.05)		
BMI, n (%)				$\chi^2 = 5.559$	0.018
<24	6951 (59.68)	6840 (59.83)	111 (51.63)		
≥24	4697 (40.32)	4593 (40.17)	104 (48.37)		
Comorbidity index, score, Mean (± SD)	1.69 (± 1.26)	1.69 (± 1.26)	1.93 (± 1.35)	t = -2.753	0.006
SBP, mmHg, Mean (± SD)	130.80 (± 21.23)	130.79 (± 21.26)	131.08 (± 20.02)	t = -0.194	0.846
DBP, mmHg, Mean (± SD)	75.95 (± 11.89)	75.95 (± 11.89)	75.66 (± 11.79)	t = 0.363	0.717
MBP, mmHg, Mean (± SD)	97.89 (± 14.51)	97.89 (± 14.52)	97.82 (± 13.86)	t = 0.065	0.948
ePWV, Mean (± SD)	9.60 (± 1.92)	9.60 (± 1.92)	9.70 (± 1.80)	t' = -0.819	0.414
ePWV, n (%)				$\chi^2 = 6.600$	0.010
Low	4647 (39.90)	4580 (40.06)	67 (31.16)		
High	7001 (60.10)	6853 (59.94)	148 (68.84)		
Follow time, years, Mean (± SD)	6.19 (± 1.83)	6.21 (± 1.82)	5.18 (± 2.05)	t' = 7.313	< 0.001
Table caption: SD: Standard Deviation; M: Median; Q ₁ : 1st Quartile; Q ₃ : 3st Quartile					

Variables	Total (N = 11648)	Cancer = No (N = 11433)	Cancer = Yes (N = 215)	Statistics	P
Head cancer, n (%)				-	< 0.001
No	11627 (99.82)	11433 (100.00)	194 (90.23)		
Yes	21 (0.18)	0 (0.00)	21 (9.77)		
Respiratory system cancer, n (%)				-	< 0.001
No	11612 (99.69)	11433 (100.00)	179 (83.26)		
Yes	36 (0.31)	0 (0.00)	36 (16.74)		
Digestive system cancer, n (%)				-	< 0.001
No	11571 (99.34)	11433 (100.00)	138 (64.19)		
Yes	77 (0.66)	0 (0.00)	77 (35.81)		
Urogenital system cancer, n (%)				-	< 0.001
No	11595 (99.54)	11433 (100.00)	162 (75.35)		
Yes	53 (0.46)	0 (0.00)	53 (24.65)		
Breast cancer, n (%)				-	< 0.001
No	11629 (99.84)	11433 (100.00)	196 (91.16)		
Yes	19 (0.16)	0 (0.00)	19 (8.84)		
Other system cancer, n (%)				-	< 0.001
No	11604 (99.62)	11433 (100.00)	171 (79.53)		
Yes	44 (0.38)	0 (0.00)	44 (20.47)		
Table caption: SD: Standard Deviation; M: Median; Q ₁ : 1st Quartile; Q ₃ : 3st Quartile					

t: Student's t test; t': Satterthwaite t test; W: Wilcoxon rank sum test; χ^2 : Chi-square test; -: Fisher's exact test.

3.2 Univariate Cox proportional hazards model analysis

Results from the univariate Cox proportional hazards model showed that place of residence (urban vs rural: HR = 1.53, 95% CI: 1.04–2.23, P = 0.030), BMI (≥ 24 vs < 24 : HR = 1.35, 95% CI: 1.03–1.76, P = 0.028), and comorbidity index (HR = 1.22, 95% CI: 1.08–1.39, P = 0.002) were significantly associated with the risk of cancer incidence; these variables were included as adjusting covariates in Model 2; other variables such as age, sex and educational attainment were not significantly associated with the risk of cancer (all P > 0.05) (Table 2.).

Table 2
Univariate Cox proportional hazards regression model

Variables	HR (95% CI)	P
Age		
<65	Ref	
≥65	1.15 (0.85–1.55)	0.365
Gender		
Male	Ref	
Female	1.10 (0.84–1.44)	0.479
Education		
High School Below	Ref	
High School and Above	0.83 (0.52–1.32)	0.427
Marital status		
Married	Ref	
No married	1.17 (0.78–1.75)	0.449
Residence		
Village	Ref	
Town/City	1.53 (1.04–2.23)	0.030
Physical activity		
Insufficient	Ref	
Sufficient	1.18 (0.68–2.04)	0.549
Unknown	0.85 (0.49–1.45)	0.548
Smoking		
No	Ref	
Yes	1.11 (0.85–1.46)	0.440
Drinking		
No	Ref	
Yes	0.74 (0.52–1.04)	0.080
Sleeping duration		
Table caption: HR: Hazard ratio; CI: Confidence intervals; Ref: reference		

Variables	HR (95% CI)	P
<6	Ref	
≥6	0.79 (0.60–1.05)	0.101
BMI		
<24	Ref	
≥24	1.35 (1.03–1.76)	0.028
Comorbidity index	1.22 (1.08–1.39)	0.002
Table caption: HR: Hazard ratio; CI: Confidence intervals; Ref: reference		

3.3 Association between ePWV and cancer risk

Results from the multivariable Cox proportional hazards model showed that, in the unadjusted model, the risk of cancer incidence in the high ePWV group was 1.59 times that of the low ePWV group (HR = 1.59, 95% CI: 1.19–2.13, P = 0.002); after adjusting for residential area, BMI and comorbidity index, the association remained significant (HR = 1.45, 95% CI: 1.07–1.96, P = 0.016); following further adjustment for all confounding factors, high ePWV levels remained an independent risk factor for cancer incidence (Table 3.) (HR = 1.48, 95% CI: 1.07–2.06, P = 0.020). The VIF test results for the model showed that the VIF values for all variables were < 5, indicating no multicollinearity (Table 4.).

Table 3
Association of ePWV exposure with cancer outcomes

Variables	Model 1		Model 2		Model 3	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
ePWV	1.14 (1.00-1.31)	0.056	1.08 (0.93–1.24)	0.328	1.07 (0.88–1.30)	0.502
ePWV						
Low	Ref		Ref		Ref	
High	1.59 (1.19–2.13)	0.002	1.45 (1.07–1.96)	0.016	1.48 (1.07–2.06)	0.020
Table caption: HR: Hazard ratio; CI: Confidence intervals; Ref: reference						

Model 1 Unadjusted model without any covariate adjustment;

Model 2 The model was adjusted for: Residence; BMI; Comorbidity index;

Model 3 The model was adjusted for: Age; Gender; Education; Marital status; Residence; Physical activity; Smoking; Drinking; Sleeping duration; BMI; Comorbidity index.

Table 4
VIF values of the multivariate Cox proportional hazards model for ePWV exposure and cancer

Variables	VIF
Age ≥ 65	1.127
GenderFemale	2.0652
EducationHigh School and Above	1.0401
Marital statusNo married	1.0932
ResidenceTown/City	1.0342
Physical activitySufficient	4.1237
Physical activityUnknown	4.1169
SmokingYes	1.8989
DrinkingYes	1.2706
Sleeping duration ≥ 6	1.033
BMI ≥ 24	1.1065
Comorbidity index	1.0951

The restricted cubic spline (RCS) curve demonstrated a consistently rising trend in risk with increasing ePWV exposure levels. Prior to the cut-off value of 8.84, the HR for cancer incidence approached 1, thereafter moving further away from 1, indicating an increasing risk of occurrence. Due to the extremely low number of cancer events at higher ePWV levels, the trend of the RCS curve reversed somewhat, and the 95% CI of the RCS curve widened significantly (Fig. 2A.); The Kaplan-Meier survival curves show that, during the 2013–2018 follow-up period, the probability of cancer events in the High group was higher than in the Low group, and this difference passed the Log-rank test ($P = 0.001$) (Fig. 2B.)

3.4 Results of Subgroup Analysis

Subgroup analysis revealed that in subgroups comprising individuals aged < 65 years, males, rural residents, alcohol consumers, those with sleep duration ≥ 6 hours, BMI < 24 kg/m², and a comorbidity index ≤ 2 , ePWV exposure levels were significant risk factors for increased cancer incidence (Fig. 3.).

3.5 Association between ePWV and the risk of cancer in different systems

After adjusting for all confounding factors, site-specific analyses revealed that ePWV was a significant risk factor for increased cancer incidence in the head, respiratory system and other sites; high ePWV

levels were associated with an increased risk of cancer in these sites: ☐ Head cancers: the risk in the high ePWV group was 3.77 times that of the low ePWV group (HR = 3.77, 95% CI: 1.31–10.84, P = 0.014); ☐ Respiratory cancers: the risk in the high ePWV group was 2.67 times that of the low ePWV group (HR = 2.67, 95% CI: 1.07–6.65, P = 0.035); ☐ Cancers of other systems: the risk in the high ePWV group was 2.27 times that of the low ePWV group (HR = 2.27, 95% CI: 1.04–4.95, P = 0.040). However, ePWV was not significantly associated with the risk of gastrointestinal cancers, genitourinary cancers or breast cancer (P > 0.05 for all) (Table 5.).

Table 5
Association between ePWV and the risk of cancer incidence in different systems

Cancer	Model 1			Model 2		Model 3	
	Variables	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Head cancer	ePWV	0.81 (0.51–1.31)	0.400	0.74 (0.44–1.24)	0.255	1.21 (0.63–2.33)	0.564
	ePWV						
	Low	Ref		Ref		Ref	
	High	2.29 (0.84–6.27)	0.105	2.22 (0.78–6.27)	0.133	3.77 (1.31–10.84)	0.014
Respiratory system cancer	ePWV	1.28 (0.93–1.76)	0.132	1.18 (0.84–1.66)	0.331	1.06 (0.66–1.70)	0.808
	ePWV						
	Low	Ref		Ref		Ref	
	High	2.97 (1.30–6.78)	0.010	2.72 (1.16–6.36)	0.021	2.67 (1.07–6.65)	0.035
Digestive system cancer	ePWV	1.21 (0.97–1.51)	0.091	1.24 (0.98–1.56)	0.075	1.14 (0.82–1.59)	0.428
	ePWV						
	Low	Ref		Ref		Ref	
	High	1.50 (0.93–2.42)	0.096	1.57 (0.96–2.59)	0.074	1.28 (0.73–2.25)	0.387
Urogenital system cancer	ePWV	0.90 (0.67–1.21)	0.496	0.78 (0.56–1.07)	0.121	0.77 (0.51–1.15)	0.203
	ePWV						
	Low	Ref		Ref		Ref	
	High	1.10 (0.63–1.91)	0.736	0.88 (0.49–1.56)	0.655	0.99 (0.53–1.86)	0.985
Table caption: HR: Hazard ratio; CI: Confidence intervals; Ref: reference							

Cancer	Model 1			Model 2		Model 3	
	Variables	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Breast cancer	ePWV	0.84 (0.51–1.37)	0.476	0.85 (0.50–1.46)	0.561	0.78 (0.39–1.58)	0.495
	ePWV						
	Low	Ref		Ref		Ref	
	High	0.98 (0.39–2.43)	0.962	1.05 (0.40–2.72)	0.927	1.20 (0.40–3.60)	0.745
Other system cancer	ePWV	1.41 (1.06–1.88)	0.018	1.28 (0.94–1.74)	0.116	1.49 (0.98–2.27)	0.063
	ePWV						
	Low	Ref		Ref		Ref	
	High	2.46 (1.22–4.98)	0.012	2.02 (0.97–4.18)	0.059	2.27 (1.04–4.95)	0.040
Table caption: HR: Hazard ratio; CI: Confidence intervals; Ref: reference							

Model 1 Unadjusted model without any covariate adjustment;

Model 2 The model was adjusted for: Residence; BMI; Comorbidity index;

Model 3 The model was adjusted for: Age; Gender; Education; Marital status; Residence; Physical activity; Smoking; Drinking; Sleeping duration; BMI; Comorbidity index.

4 Discussion

Based on the large-scale longitudinal CHARLS cohort, this study is the first to demonstrate that arterial stiffness, as characterised by ePWV, is significantly associated with an increased risk of cancer in middle-aged and older adults, and that high ePWV levels constitute an independent risk factor for cancer; subgroup analyses revealed that this association was more pronounced in specific populations, such as those aged < 65 years, males, and rural residents; simultaneously, ePWV is closely associated with the risk of developing cancers of the head, respiratory system and other systems, providing a new potential indicator for identifying high-risk groups for cancer among middle-aged and older adults.

The association between arterial stiffness and cancer risk may stem from shared pathophysiological mechanisms^{6,17}. The core pathological processes of atherosclerosis include chronic low-grade

inflammation, oxidative stress, endothelial dysfunction and immune dysregulation^{3,4}, and these processes are also key drivers of cancer initiation and progression: chronic inflammation can accelerate tumourigenesis by promoting cell proliferation, inhibiting apoptosis and inducing angiogenesis¹⁸; oxidative stress can cause DNA damage and induce genetic mutations¹⁹ and impaired endothelial function disrupts the vascular barrier, creating conditions conducive to tumour cell invasion and metastasis. As a simple indicator of arterial stiffness²⁰, an elevated ePWV reflects the extent of vascular structural and functional damage²¹ and may indirectly represent a state of systemic pathophysiological dysregulation, thereby correlating with cancer risk. Furthermore, as ePWV is calculated based on age and blood pressure—both of which are risk factors for cancer²²—ePWV may integrate the risk effects of both, serving as a more comprehensive risk assessment indicator.

This study found that ePWV was significantly associated with cancers of the head and respiratory system, but showed no significant association with cancers of the digestive or urogenital systems, suggesting that the risk profile of ePWV for cancer may exhibit site-specificity. This phenomenon may be related to differences in the pathogenesis of cancers across different systems: organs of the head and respiratory system are in direct contact with the external environment and are susceptible to inflammation and oxidative stress²³, whilst vascular pathological changes associated with arterial stiffness may further exacerbate damage to these organs through local microcirculatory impairment and the release of inflammatory factors, thereby increasing the risk of cancer; in contrast, the development of cancers of the digestive and urogenital systems is more closely linked to factors such as diet, metabolism and hormone levels, with the influence of arterial stiffness being relatively weaker^{24,25}. Furthermore, the small number of cases for certain types of cancer in this study may have compromised the statistical power of the association analysis, necessitating validation through studies with larger sample sizes.

Subgroup analyses revealed that the association between ePWV and cancer was more pronounced in individuals aged < 65 years, males, and those with a BMI < 24 kg/m². This finding provides insights for the targeted screening of high-risk populations for cancer. Although the incidence of cancer is lower in middle-aged and older adults aged < 65 years compared to the elderly, early increases in arterial stiffness may serve as a warning sign for cancer development, and timely intervention can effectively reduce subsequent risks; The association was more pronounced in men, which may be related to higher exposure rates to risk factors such as smoking and alcohol consumption, as well as more severe vascular damage and inflammatory responses⁵; meanwhile, the significant association in those with a BMI < 24 kg/m² may suggest that overweight/obesity acts as an independent risk factor for cancer, whose effects may mask the role of arterial stiffness, indicating the presence of an effect-modifying relationship.

The strengths of this study lie in: ☐ its use of the large-scale CHARLS community cohort, which features a large sample size and long follow-up duration, ensuring good representativeness and generalisability of the results; ☐ it is the first longitudinal study to investigate the association between ePWV and cancer

incidence risk in middle-aged and older adults, filling a research gap in this field; ④ a multidimensional adjustment model was constructed, controlling for various confounding factors such as socio-demographic characteristics, lifestyle, and clinical indicators, and multicollinearity was ruled out via VIF testing, ensuring high reliability of the results; ⑤ subgroup and site-specific analyses were conducted, providing detailed evidence-based grounds for precise prevention and control.

However, this study also has certain limitations: ① Although the sample size was large, the incidence of cancer in the community population is low, and the number of cases for certain organ-specific cancers was small, which may have affected the statistical power of the site-specific analyses, making it impossible to accurately identify the actual impact of ePWV on specific organ-specific cancers; ② as this is an observational study, it cannot establish a causal relationship between ePWV and cancer incidence; further prospective cohort studies and mechanistic research are required for validation; ③ the study did not include information on tumour staging or histological types, making it impossible to analyse the association between ePWV and cancer severity or prognosis; ④ as the study population consisted solely of middle-aged and elderly Chinese individuals, caution is required when extrapolating the results to other populations.

5 Conclusions

Arterial stiffness, as characterised by ePWV, is significantly associated with an increased risk of cancer in middle-aged and elderly individuals. High ePWV levels constitute an independent risk factor for cancer in this population, with the association being more pronounced in specific subgroups such as those aged < 65 years, males, and rural residents. Furthermore, ePWV is closely associated with the risk of cancers of the head, respiratory system, and other systems. As a simple, non-invasive indicator of arterial stiffness, ePWV may serve as a potential tool for identifying high-risk groups for cancer in middle-aged and elderly individuals, offering new insights for early cancer screening and health management. Future studies involving larger, multicentre cohort studies are required to validate these findings and to further explore the pathophysiological mechanisms linking arterial stiffness to cancer incidence, thereby providing a basis for the development of targeted prevention and control strategies.

Declarations

Ethics approval and consent to participate

The study was approved by the Biomedical Ethics Review Committee of Peking University (Approval No.: IRB00001052-11015), and all participants provided written informed consent.

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Author Contribution

L. and X. were responsible for the overall conceptualization of the manuscript. W. conducted data collection and processing, and drafted the original manuscript.

Data Availability

The datasets analyzed during the current study are available in the CHARLS repository, Data | CHARLS

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Figures

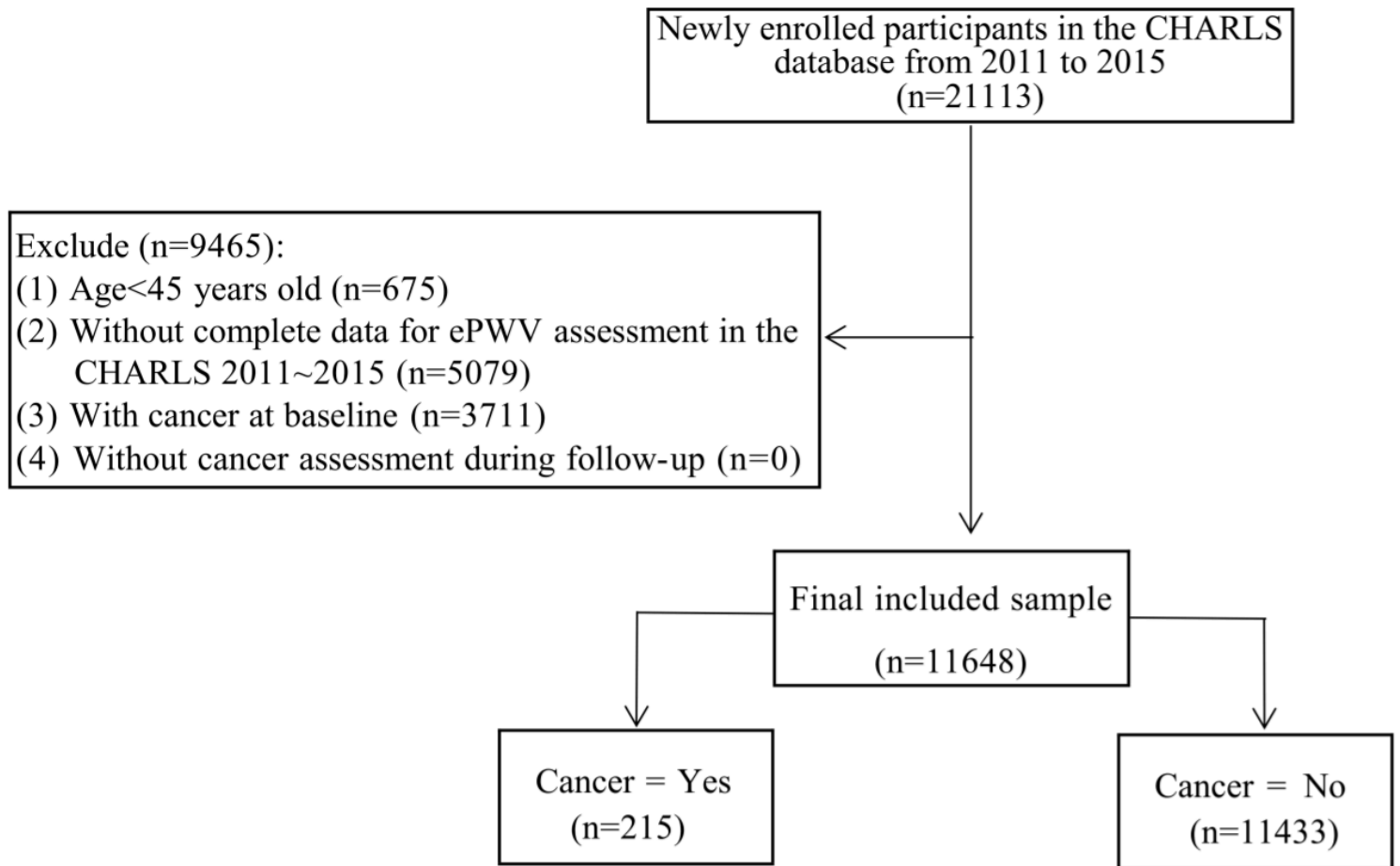


Figure 1

Flowchart of study participants.

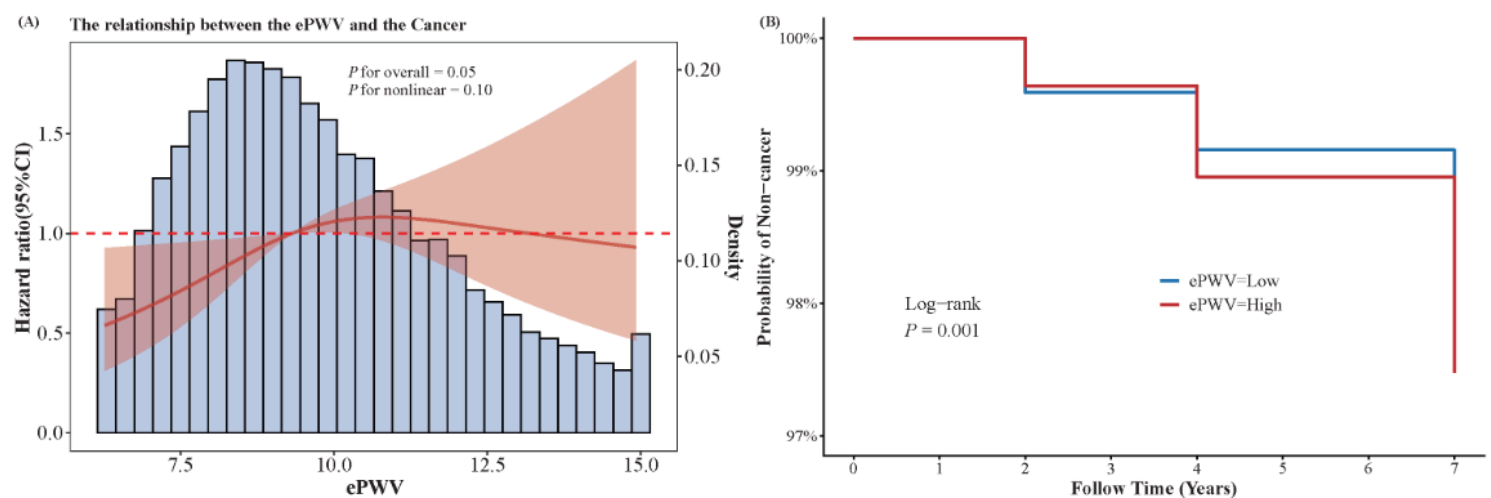


Figure 2

Relationship between ePWV exposure levels and cancer outcomes. (A) HRs for cancer risk across subgroups; (B) ORs for site-specific cancer risk.

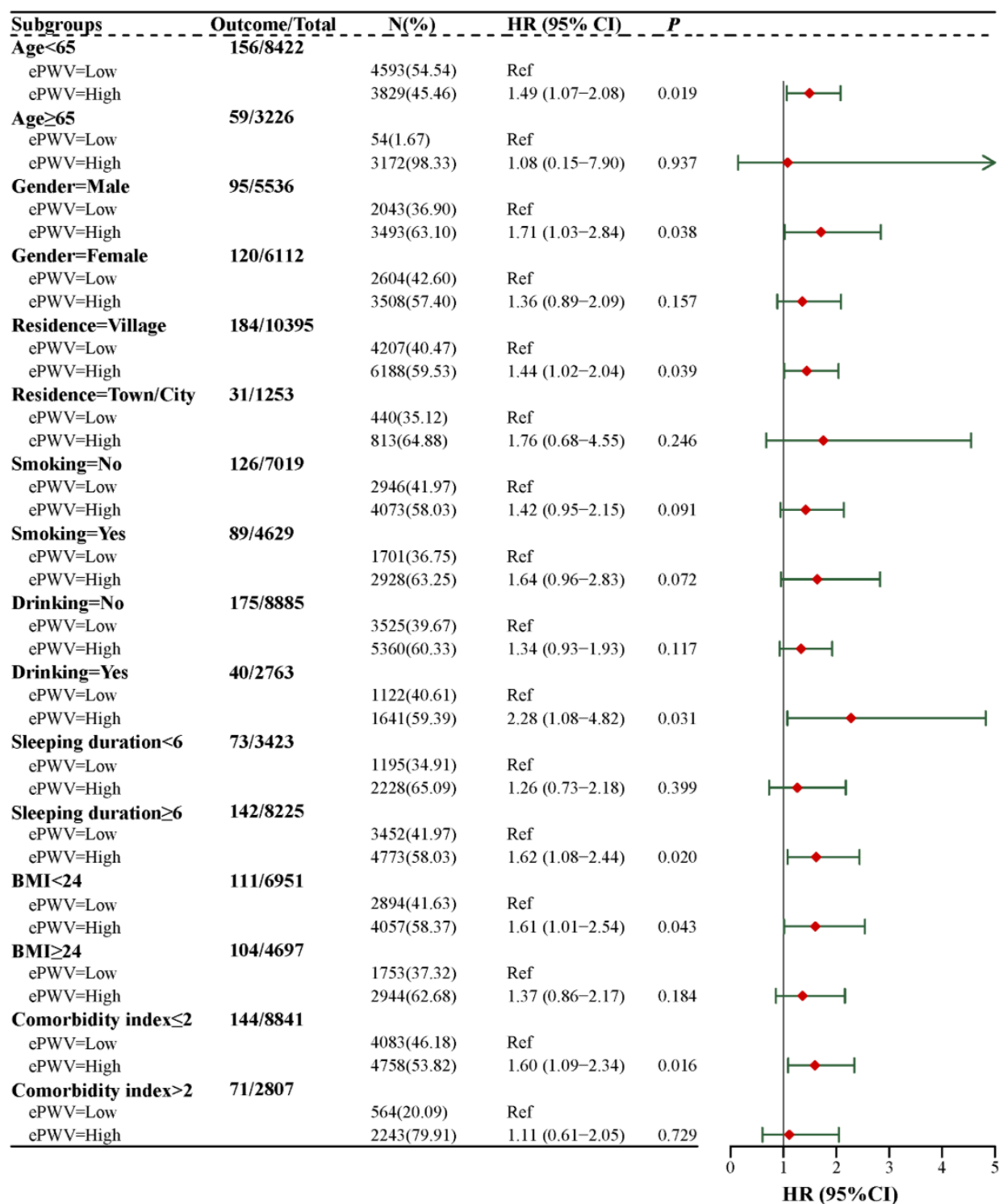


Figure 3

Subgroup analysis of the association between ePWV and cancer risk in middle-aged and older adults.