JIM Original Article

doi: 10.1111/joim.20082

Chest x-ray aortic size and risk of death and cardiovascular disease in older Chinese: Guangzhou biobank cohort study

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Abstract. Sun L, Tian W, Wang J, Wu T, Liu X, Jin Y, et al. Chest x-ray aortic size and risk of death and cardiovascular disease in older Chinese: Guangzhou biobank cohort study. *J Intern Med.* 2025;543–55.

Background. Chest radiograph can independently predict adverse outcomes in outpatients. We examined the associations of aortic knob width (AKW), ascending aortic length (AAL), and ascending aortic width (AAW) from chest x-ray with death and cardiovascular events in adults aged 50 and above.

Methods. Participants without cardiovascular disease were included from the Guangzhou Biobank Cohort Study (2003–2008). AKW, AAL, and AAW were indexed by body surface area. Aortic enlargement was defined using sex- and age-specific thresholds, calculated as the average value plus 1.96 multiplied by the standard deviation (SD). The associations of AKW, AAL, and AAW indices with all-cause and cause-specific mortality (cardiovascular and cancer), and incident nonfatal and fatal cardiovascular events, were examined through multivariate Cox regressions. Logistic regressions were performed to determine risk factors for aortic enlargement.

Results. Among 27,047 participants (mean age 62 years ± 7 years SD), there were 6977 deaths and 6478 cardiovascular events over an average follow-up period of 16.3 years. Each SD increase in AKW index was associated with a higher risk of all-cause mortality, cardiovascular mortality, and cardiovascular events, with hazard ratios (95% confidence interval [CI]) of 1.13 (1.11–1.16), 1.20 (1.15–1.25), and 1.11 (1.08–1.14), respectively. Similar findings were observed regarding the AAL and AAW indices. Hypertension was a strong risk factor for enlarged AKW (odds ratio 2.52, 95% CI 2.17–2.93), AAL (1.95, 1.63–2.32), and AAW (1.80, 1.56–2.09), respectively.

Conclusions. Thoracic aortic parameters measured through an accessible, cheap, and safe chest radiograph were associated with higher risks of death and cardiovascular events. Hypertension should be managed.

Keywords: aorta, cardiovascular disease, chest x ray, hypertension, thoracic

Introduction

Chest radiograph is one of the most widely used diagnostic imaging test and can be available in both community and hospital settings. Although its primary role is the diagnosis of lung diseases, additional abnormalities identified on chest x-rays have been shown to independently predict the risks for death, biological age, acute stroke, and myocardial infarction in outpatients [1–3]. However, outpatients are likely at higher risk than the general population, and it is unknown that whether chest x-ray parameters can predict risks for mortality and cardiovascular events in general population.

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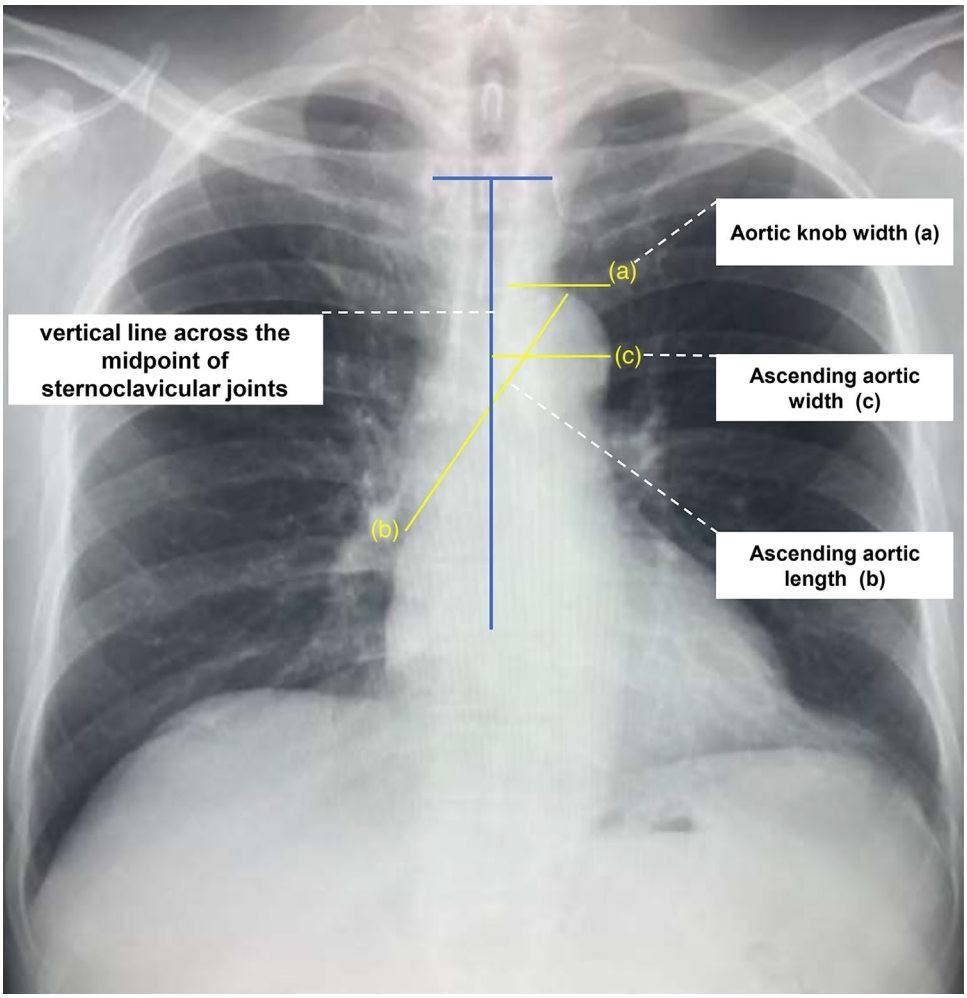

Fig. 1 *The measurement of thoracic aortic parameters in chest x-ray. (a) Aortic knob width (AKW) was measured as the distance from the right margin of the aortic arch to the left margin of that. (b) Ascending aortic length (AAL) was measured as the distance from the indentation at the right margin of the heart to the apex of the aorta. (c) Ascending aortic width (AAW) was measured as the distance from the leftmost margin of the aorta to the vertical line across the midpoint of the sternoclavicular joints.*

The aortic knob, a radiographic structure on chest x-ray, represents a portion of the descending aorta and the foreshortened aortic arch (Fig. 1). It reflects the extent of aortic dilation and tortuosity of the aortic arch [4]. Previous studies have reported an association between aortic knob width (AKW) and the severity of arterial stiffness and atherosclerotic disease in patients with hypertension and obstructive sleep apnea [5–7]. AKW was also found to be associated with metabolic syndrome, left ventricular remodeling, and dysfunction, all of which contribute to an increased risk of cardiovascular disease [4, 8]. However, no studies have investigated the associations of AKW or other thoracic aortic parameters, such as ascending aortic length (AAL) and width (AAW), measured by chest x-ray with mortality and cardiovascular events in the general population.

In this study, we explored the associations of AKW, AAL, and AAW as assessed by chest x-ray with mortality and cardiovascular events in a Chinese population aged 50 or older, using data from the Guangzhou Biobank Cohort Study (GBCS). These findings may have significant implications for clinical practice, offering the potential to incorporate

readily available chest x-ray measurements into cardiovascular health assessments.

Methods

Study participants

At the baseline of the GBCS, 30,430 people aged 50 and above were recruited between 2003 and 2008. Details of GBCS can be found in previous publication [9]. Briefly, this study represents a collaboration involving the Guangzhou Twelfth People's Hospital, the Universities of Hong Kong and Birmingham, with participants sourced from the "Guangzhou Health and Happiness Association for the Respectable Elders" (GHHARE), a community social welfare organization that offers affordable membership (4 RMB per month, ≈50 US cents) to local residents. With branches across Guangzhou, GHHARE engaged approximately 7% of Guangzhou residents aged 50 and above. Participants within the same sex and age group had comparable levels of chronic diseases like hypertension and diabetes compared to national urban Chinese samples [9]. Of those invited to participate through the GHHARE, approximately 9 out of 10 agreed to take part, with very few declining participation. This study was approved by the Guangzhou Medical Ethics Committee (No. 2020044), and written informed consent was obtained from each participant prior to their involvement. All procedures adhered to the Declaration of Helsinki.

Chest-x-ray and thoracic aortic parameters

AKW, AAL, and AAW were assessed through plain chest x-ray (Toshiba KSO-15R machine) examination. Participants underwent chest x-ray imaging in an upright posteroanterior stance, maintaining a deep inspiratory breath-hold during the procedure [10]. AKW was defined as the horizontal distance from the lateral edge of the trachea to the left lateral wall of the aortic knob [7, 8]. AAL was measured as the distance from the indentation at the right cardiac border to the apex of the aorta. AAW was defined as the distance from the leftmost margin of the aorta to the vertical line passing through the midpoint of the sternoclavicular joints. Fig. 1 shows the visualization of these measurements. To minimize potential errors due to patient misalignment, we ensured consistent positioning during imaging by aligning the spinal processes and the midpoint of the sternoclavicular joints using defined anatomical reference points. All measurements were conducted separately by two experienced radiologists following a standardized protocol. Prior to undertaking these evaluations, the radiologists underwent specific training to ensure consistency and accuracy in identifying anatomical landmarks, such as the left margin of the aortic arch and the indentation at the right margin of the heart. Nevertheless, we recognize that challenges in identifying certain anatomical landmarks, such as the left margin of the aortic arch and the indentation at the right margin of the heart, may introduce variability in measurements. These limitations are inherent to the use of plain chest x-rays and should be considered when interpreting the findings. Inter-observer agreement for thoracic aortic measurements has been previously validated, demonstrating an agreement rate of 85% and moderate consistency (Kappa value 0.68, $p < 0.001$) [10].

To enable normalization of these values across a diverse population and to distinguish between normal variations in size attributable to body stature and those indicative of pathology, these parameters were indexed for body surface area (BSA), using the ratio of aortic parameter to BSA (mm/m^2) to obtain aortic parameter index (AKW index, AAL index, and AAW index) [11]. The Mosteller formula was used to calculate BSA [12]. Because aortic parameters vary greatly between sex and age groups, sex- and age-specific aortic parameter indices were categorized into normal and enlarged categories based on their upper limits of normality, defined as the mean plus 1.96 standard deviations (SD) (Table S1).

Outcomes

Outcomes included all-cause mortality and cause-specific (cardiovascular and cancer) mortality, as well as incident nonfatal and fatal cardiovascular events. Trained clinical coding officers coded death causes and cardiovascular events based on the International Classification of Diseases, 10th Revision. Cardiovascular events included any hospital admission or death due to coronary heart disease (CHD) (I20–I25), heart failure (HF) (I50), stroke (I60–I69), and peripheral artery disease (I73). Information on the incidence of cardiovascular events and underlying causes of deaths were followed up to December 2020 and November 21, 2023, respectively. Details on the data sources [10] and follow-up methods [13, 14] have been reported previously.

Potential confounders

Potential confounders considered were sex, age (continuous), occupation (manual, non-manual, other), household annual income (<30,000 RMB/year, ≥30,000 RMB/year, unknown), education (primary, middle school, college), physical activity (inactive, moderate, active), smoking status (never, former, current), alcohol use (never, former, current), hypertension, left ventricular hypertrophy (LVH), aortic calcification (yes, no), diabetes, waist circumference, triglyceride, and white blood cell counts. Confounders such as physical activity, blood pressure, biochemical parameters, and LVH were evaluated using established methods, with specific measurement details provided in the Supporting Information section.

Statistical analysis

Analysis of variance, Kruskal–Wallis test, and chi-square tests were employed to compare baseline characteristics based on the presence of an enlarged AKW index. Associations of the aortic parameter index with mortality and cardiovascular events were examined using Cox proportional hazards regression, with methods for nonlinear analyses and survival curves described in our previous publication [10, 15]. To investigate whether some potential effect modifiers (sex, age [<65/≥65 years], hypertension [no/yes], diabetes [no/yes], and LVH [no/yes]) modified the associations between each SD increase in aortic size and adverse outcomes, likelihood ratio tests were performed to assess whether including interaction terms improved the model fit. The risk factors for aortic enlargement were determined using logistic regression. In sensitivity analyses, we divided the follow-up period into different intervals (<5 years, 5–<10 years, 10–<15 years, and ≥15 years) to examine whether the associations of each SD increase in AKW, AAL, and AAW indices with adverse outcomes persisted across these time intervals. With only 6% of the data missing across all variables, complete-case analysis was used for this research. Statistical analyses were done using R (version 4.4.1) and STATA/MP (version 18.0). Statistical significance was defined as a two-sided p value less than 0.05.

Results

Of the 30,430 participants, 3383 were excluded in the present study because they reported having a history of cardiovascular disease, including CHD, myocardial infarction, angina, HF, stroke, peripheral vascular disease, and congenital heart disease (n = 2709), had an unknown vital status due to being lost to follow-up (n = 372), or had incomplete information on thoracic aortic parameters due to the absence of these measurements (n = 302), resulting in 27,047 participants in this study.

Baseline characteristics

Table 1 shows that participants with enlarged AKW index were older, had a higher proportion of manual jobs, lower levels of household income, and education, and a lower proportion of current alcohol use compared to those with normal AKW index ($p < 0.05$). Those with enlarged AKW index had higher proportions of hypertension, LVH and the presence of aortic calcification, higher levels of systolic blood pressure, diastolic blood pressure, and high-density lipoprotein cholesterol, but a lower proportion of diabetes, lower levels of waist circumference, BSA, body mass index, triglycerides, total cholesterol, and low-density lipoprotein cholesterol ($p < 0.05$).

Associations of AKW index with death and cardiovascular events

There were 6977 deaths and 6478 cardiovascular events over an average follow-up period of 16.3 (SD 3.9) years. Kaplan–Meier analyses showed that participants with enlarged AKW index had greater risks of all-cause mortality (Fig. 2a), cardiovascular mortality (Fig. 2b), and cardiovascular events (Fig. 2d) than those with normal AKW index (all p for log-rank test <0.001); however, no increased risk of death due to cancer was observed (p for log-rank test 0.20) (Fig. 2c). In contrast, an enlarged AAL index was associated only with a higher risk of all-cause mortality (Fig. S1), whereas the findings for the enlarged AAW index were consistent with those for the enlarged AKW index (Fig. S2).

Table 2 shows the associations of AKW index with adverse outcomes. After adjusting for 15 potential confounding factors, enlarged AKW index was associated with higher risks of all-cause mortality, cardiovascular mortality, cardiovascular events, CHD, stroke, hemorrhagic stroke, and ischemic stroke. Additionally, for each SD increase in the AKW index, significant associations remained not only with these adverse outcomes but also with specific cardiovascular events, with adjusted HRs (95% confidence intervals [CIs]) of 1.13 (1.11–1.16)

Table 1. *Baseline characteristics of participants with and without enlarged aortic knob width index on chest x-ray.*

	All participants	Normal	Enlarged	*p* value
Number (%)	27,047 (100.0)	26,014 (96.5)	955 (3.5)	–
Sex, men (%)	7499 (27.8)	7240 (27.8)	259 (27.1)	0.63
Age, years[a]	61.8 (7.1)	61.8 (7.1)	62.3 (7.4)	0.03
Occupation (%)				<0.001
Manual	16,559 (61.7)	15,906 (61.5)	653 (68.5)	
Non-manual	6217 (23.2)	6046 (23.4)	171 (17.9)	
Other	4049 (15.1)	3920 (15.2)	129 (13.5)	
Household income, RMB (%)				<0.001
<30,000	10,228 (38.0)	9816 (37.8)	412 (43.2)	
≥30,000	10,305 (38.3)	10,020 (38.6)	285 (29.9)	
unknown	6402 (23.8)	6145 (23.7)	257 (26.9)	
Education (%)				<0.001
≤Primary	11,588 (43.0)	11,053 (42.5)	535 (56.0)	
Middle school	13,049 (48.4)	12,681 (48.8)	368 (38.5)	
≥College	2321 (8.6)	2269 (8.7)	52 (5.4)	
Physical activity (%)				0.45
Inactive	2242 (8.3)	2152 (8.3)	90 (9.4)	
Moderate	11,001 (40.8)	10,617 (40.8)	384 (40.2)	
Active	13,726 (50.9)	13,245 (50.9)	481 (50.4)	
Smoking status (%)				0.13
Never	21,717 (80.8)	20,960 (80.8)	757 (79.5)	
Former	2410 (9.0)	2331 (9.0)	79 (8.3)	
Current	2767 (10.3)	2651 (10.2)	116 (12.2)	
Alcohol use (%)				<0.001
Never	16,718 (67.2)	16,144 (67.2)	574 (67.1)	
Former	625 (2.5)	584 (2.4)	41 (4.8)	
Current	7520 (30.3)	7279 (30.3)	241 (28.2)	
Hypertension, yes (%)	10,973 (40.7)	10,453 (40.2)	520 (54.5)	<0.001
Left ventricular hypertrophy, yes (%)	496 (1.8)	458 (1.8)	38 (4.0)	<0.001
Aortic calcification, yes (%)	9070 (27.0)	8713 (33.5)	357 (37.4)	0.01
Diabetes, yes (%)	3275 (12.2)	3194 (12.3)	81 (8.6)	0.001
Waist circumference, cm[a]	78.63 (9.0)	78.8 (8.9)	74.6 (9.1)	<0.001
Body surface area, m^2	1.59 (0.2)	1.6 (0.2)	1.5 (0.2)	<0.001
Body mass index, kg/m^2	23.72 (3.3)	23.8 (3.3)	22.0 (3.4)	<0.001
Systolic blood pressure, mmHg[a]	130 (22)	130 (22)	137 (24)	<0.001
Diastolic blood pressure, mmHg[a]	74 (11)	73 (11)	78 (13)	<0.001
Triglycerides, mmol/L[b]	1.4 (1.0–2.0)	1.4 (1.0–2.0)	1.2 (0.9–1.8)	<0.001
Total cholesterol, mmol/L[a]	5.9 (1.1)	5.9 (1.1)	5.7 (1.1)	<0.001
Low-density lipoprotein-cholesterol, mmol/L[a]	3.3 (0.7)	3.3 (0.7)	3.2 (0.7)	<0.001
High density lipoprotein-cholesterol, mmol/L[a]	1.62 (0.41)	1.62 (0.41)	1.63 (0.42)	0.03
White blood cell counts, $10^9/L$[a]	6.3 (1.6)	6.3 (1.6)	6.4 (1.7)	0.25

Note: *p* values were calculated using the chi-square test, analysis of variance, or Kruskal–Wallis test.
[a]Data were expressed as mean (standard deviation).
[b]Data were expressed as median (interquartile range).

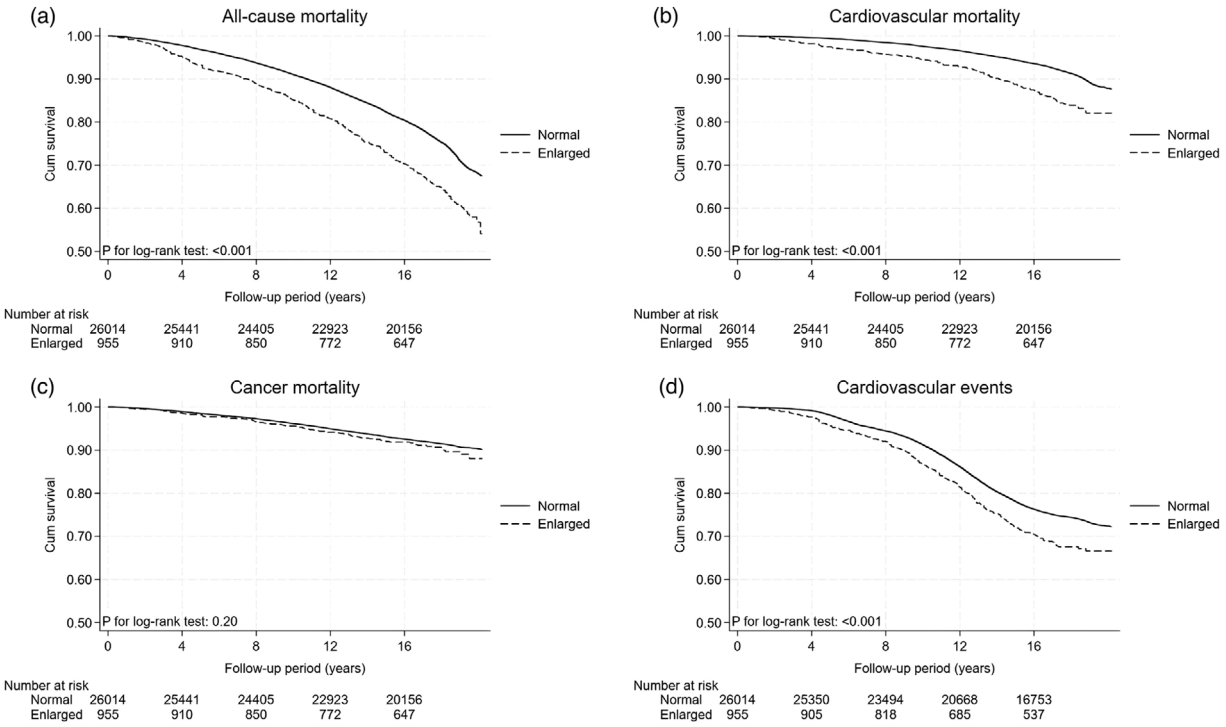

Fig. 2 *Kaplan–Meier survival curve by the presence of enlarged aortic knob width index for all-cause mortality (a), cardiovascular mortality (b), cancer mortality (c), and cardiovascular events (d). Note: Values below 0.50 on the y-axis are omitted to emphasize the relevant range of cumulative survival.*

for all-cause mortality, 1.20 (1.15–1.25) for cardiovascular mortality, 1.11 (1.08–1.14) for cardiovascular events, 1.09 (1.05–1.14) for CHD, 1.11 (1.04–1.19) for myocardial infarction, 1.17 (1.03–1.32) for HF, 1.12 (1.08–1.16) for stroke, 1.19 (1.08–1.31) for hemorrhagic stroke, and 1.14 (1.09–1.19) for ischemic stroke. Each SD increase in the AAL and AAW indices was also significantly associated with the above adverse outcomes but did not include ischemic stroke (Table S2).

The nonlinearity assumptions of AKW index with all-cause mortality (Fig. 3a), cardiovascular mortality (Fig. 3b), cancer mortality (Fig. 3c), and cardiovascular events (Fig. 3d) were not supported (all p for nonlinearity >0.05). For AAL and AAW indices, similar results were also observed (Figs. S3 and S4). Only the association of the AAL index with all-cause mortality appeared to demonstrate nonlinearity (p for nonlinearity 0.001, Fig. S3A). None of the AKW (Table 2 and Fig. 3c), AAL (Table S2 and Fig. S3C), or AAW indices (Table S2 and Fig. S4C) were associated with cancer mortality.

Sensitivity analysis

In the sensitivity analysis, Fig. S5 shows that the adjusted HRs of all-cause mortality, cause-specific mortality (cardiovascular and cancer), cardiovascular events, and specific cardiovascular event for AKW, AAL, and AAW indices remained relatively stable across different follow-up intervals.

Interaction analysis of aortic enlargement and outcomes

Table S3 shows that the association between each SD increase in the AKW index and the risk of all-cause mortality (HR 1.20 [1.15–1.26] vs. HR 1.10 [1.07–1.13]) appeared to be stronger in participants aged below 65 years than in those aged above 65 years (p for interaction 0.001). Stratified by diabetes status, the associations of each SD increase in the AKW index with all-cause mortality (HR 1.16 [1.12–1.19]; p for interaction <0.001), cardiovascular mortality (HR 1.24 [1.18–1.30]; p for interaction <0.001), and cardiovascular events (HR 1.11 [1.09–1.15]; p for interaction 0.03) were statistically significant. However, among participants with diabetes, these associations were not

Table 2. *Adjusted HRs (95% confidence intervals [CIs]) of all-cause, cardiovascular and cancer mortality, cardiovascular events, and specific cardiovascular event for the enlarged aortic knob width index and each standard deviation increase in chest x-ray in GBCS from 2003 to 2008 and followed up until November 21, 2023.*

	Count of deaths/events (Incidence rate, per 1000 person-years)		Enlarged vs. Normal		Each SD (2.97 mm/m^2)	
	Normal	Enlarged	Crude HR (95% CI)	Adjusted HR (95% CI)[a]	Crude HR (95% CI)	Adjusted HR (95% CI)[a]
All-cause mortality	6604 (15.56)	340 (23.40)	1.56 (1.40–1.74)***	1.41 (1.25–1.59)***	1.39 (1.37–1.42)***	1.13 (1.11–1.16)***
Cardiovascular mortality	2115 (4.98)	130 (8.95)	1.88 (1.58–2.25)***	1.62 (1.33–1.97)***	1.48 (1.44–1.52)***	1.20 (1.15–1.25)***
Cancer mortality	2077 (4.89)	81 (5.57)	1.16 (0.93–1.44)	1.12 (0.89–1.42)	1.20 (1.15–1.25)***	1.04 (0.99–1.09)
Cardiovascular events	6177 (15.59)	273 (20.15)	1.33 (1.18–1.50)***	1.22 (1.07–1.39)**	1.31 (1.28–1.34)***	1.11 (1.08–1.14)***
Coronary heart disease	2695 (6.53)	121 (8.56)	1.34 (1.12–1.61)**	1.23 (1.00–1.50)*	1.29 (1.25–1.33)***	1.09 (1.05–1.14)***
Myocardial infarction	1093 (2.60)	47 (3.26)	1.28 (0.96–1.71)	1.25 (0.91–1.71)	1.30 (1.23–1.36)***	1.11 (1.04–1.19)**
Heart failure	281 (0.66)	12 (0.83)	1.29 (0.72–2.30)	0.97 (0.48–1.96)	1.43 (1.31–1.55)***	1.17 (1.03–1.32)*
Stroke	3510 (8.61)	154 (11.05)	1.31 (1.11–1.54)**	1.23 (1.04–1.47)*	1.32 (1.28–1.35)***	1.12 (1.08–1.16)***
Hemorrhagic stroke	415 (0.98)	35 (2.42)	2.48 (1.76–3.51)***	1.72 (1.14–2.59)**	1.49 (1.40–1.58)***	1.19 (1.08–1.31)***
Ischemic stroke	2403 (5.68)	90 (6.22)	1.25 (1.01–1.54)*	1.72 (1.14–2.59)**	1.26 (1.22–1.31)***	1.14 (1.09–1.19)***

Abbreviations: CI, confidence interval; GBCS, Guangzhou Biobank Cohort Study; HRs, hazard ratios; SD, standard deviation.

[a]HRs were adjusted for sex, age, occupation, household annual income, education, physical activity, smoking status, alcohol use, hypertension, left ventricular hypertrophy, aortic calcification, diabetes, waist circumference, total cholesterol, and white blood cell counts.

*$p < 0.05$.

**$p < 0.01$.

***$p < 0.001$.

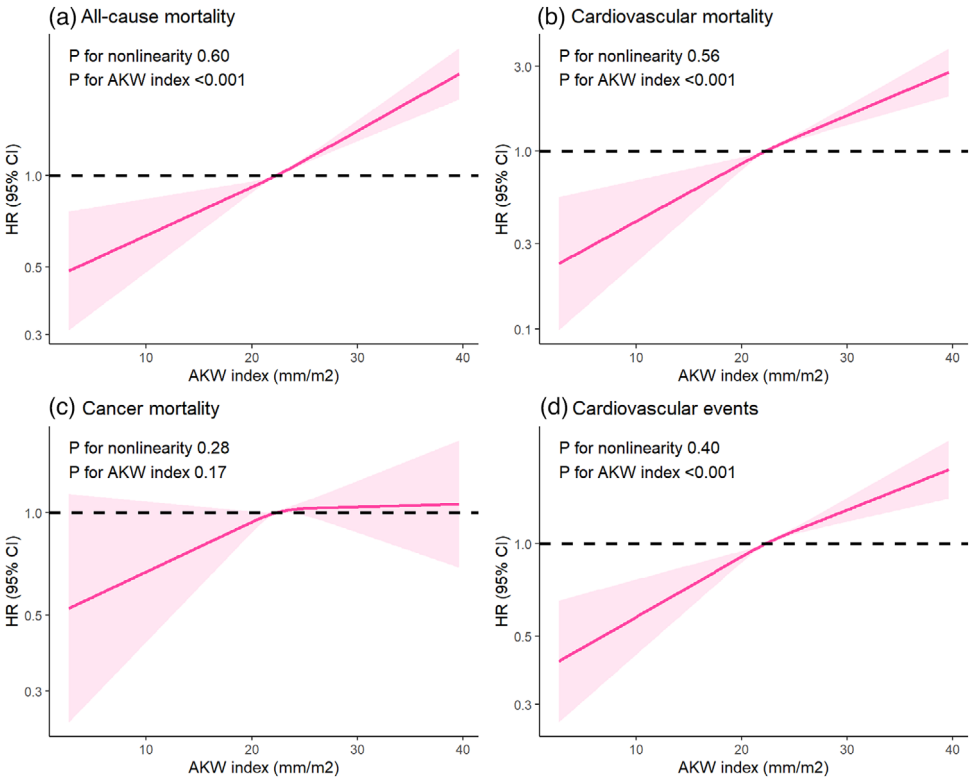

Fig. 3 *Association of AKW index with all-cause mortality (a), cardiovascular mortality (b), cancer mortality (c), and cardiovascular events (d) in Guangzhou Biobank Cohort Study (GBCS) from 2003 to 2008 and followed up until November 21, 2023. HRs were adjusted for sex, age, occupation, household annual income, education, physical activity, smoking status, alcohol use, hypertension, left ventricular hypertrophy, aortic calcification, diabetes, waist circumference, total cholesterol, and white blood cell counts. AKW, aortic knob width; CI, confidence interval; HR, hazard ratio.*

significant. In addition, the participants with LVH showed stronger associations with all-cause mortality (HR 1.36 [1.18–1.57] vs. 1.13 [1.10–1.16]; *p* for interaction 0.02) and cardiovascular mortality (HR 1.46 [1.18–1.82] vs. 1.19 [1.14–1.24]; *p* for interaction 0.03) than those without LVH. Furthermore, similar interactions by age and diabetes status were observed for AAL and AAW indices.

Risk factors for aortic enlargement

Table 3 shows that hypertension was a risk factor for aortic enlargement, whereas a higher level of education was a protective factor. However, several other cardiovascular risk factors, including diabetes, body mass index, triglycerides, and low-density lipoprotein cholesterol, had inverse associations with enlarged aortic parameter indices. Hypertension was significantly associated with enlarged AKW, AAL, and AAW indices, the odds ratios (95% CIs) were 2.52 (2.17–2.93) for AKW, 1.95 (1.63–2.32) for AAL, and 1.80 (1.56–2.09) for AAW.

Discussion

This study showed that thoracic aortic parameters, particularly AKW, measured through chest x-ray, were significantly associated with higher risks of all-cause mortality, cardiovascular mortality, and cardiovascular events in individuals aged 50 or older. Hypertension was found to be a key risk factor for aortic enlargement, underscoring the importance of managing blood pressure. Given the widespread availability, affordability, and safety of chest x-rays, our findings provide new insights into the potential utility of simple radiographic measurements in cardiovascular risk assessment. Although we do not advocate for their immediate incorporation into routine screening programs, our

Table 3. *Adjusted ORs (95% confidence interval [CI]) of risk factors for aortic enlargement.*

	Enlarged AKW index	Enlarged AAL index	Enlarged AAW index
Age, years	0.98 (0.977–0.99)***	0.98 (0.97–0.99)**	0.98 (0.97–0.99)**
Sex men			
Women	1.00	1.00	1.00
Men	0.93 (0.744–1.117)	0.91 (0.71–1.17)	1.06 (0.85–1.31)
Occupation			
Manual	1.00	1.00	1.00
Non-manual	0.88 (0.71–1.08)	0.84 (0.67–1.05)	1.12 (0.93–1.36)
Other	0.94 (0.76–1.16)	1.02 (0.81–1.29)	0.94 (0.76–1.16)
Education			
≤Primary	1.00	1.00	1.00
Middle school	0.60 (0.51–0.71)***	0.81 (0.67–0.97)*	0.66 (0.56–0.78)***
≥College	0.55 (0.39–0.77)***	0.71 (0.49–1.01)	0.43 (0.30–0.60)***
Physical activity			
Inactive	1.00	1.00	1.00
Moderate	0.96 (0.73–1.27)	0.87 (0.65–1.16)	0.82 (0.64–1.06)
Active	0.90 (0.68–1.18)	0.96 (0.72–1.28)	0.78 (0.61–1.00)
Smoking status			
Never	1.00	1.00	1.00
Former	0.95 (0.70–1.28)	0.71 (0.49–1.03)	0.86 (0.64–1.14)
Current	0.96 (0.73–1.27)	1.43 (1.08–1.89)*	1.00 (0.76–1.30)
Alcohol use			
Never	1.00	1.00	1.00
Former	1.92 (1.35–2.74)***	1.04 (0.63–1.70)	1.06 (0.70–1.60)
Current	1.12 (0.95–1.33)	0.91 (0.76–1.10)	0.86 (0.72–1.01)
Hypertension, yes	2.52 (2.17–2.93)***	1.95 (1.63–2.32)***	1.80 (1.56–2.09)***
Diabetes, yes	0.69 (0.54–0.89)**	0.43 (0.29–0.64)***	0.90 (0.73–1.12)
Body mass index, kg/m^2	0.81 (0.79–0.83)***	0.56 (0.54–0.58)***	0.95 (0.93–0.97)***
Triglyceride, mmol/L	0.99 (0.92–1.06)	0.76 (0.66–0.88)***	0.98 (0.91–1.04)
Low-density lipoprotein cholesterol, mmol/L	0.81 (0.72–0.92)**	0.83 (0.73–0.95)**	0.77 (0.68–0.86)***
High-density lipoprotein cholesterol, mmol/L	1.00 (0.82–1.22)	1.11 (0.90–1.36)	1.02 (0.84–1.24)
White blood cell counts, 10^9/L	1.04 (0.99–1.09)	1.00 (0.95–1.05)	0.99 (0.95–1.04)

Abbreviations: AAL, ascending aortic length; AAW, ascending aortic width; AKW, aortic knob width; CI, confidence interval; ORs, odd ratios.
*$p < 0.05$.
**$p < 0.01$.
***$p < 0.001$.

results highlight the need for further investigation and standardization to assess their application in clinical practice.

The aortic knob visible on a chest x-ray is formed by the foreshortened aortic arch. A prospective study of 3026 Framingham Heart Study Offspring and Third Generation Cohort Participants found that aortic arch width measured through CT and above the 90th percentile was associated with cardiovascular events (HR 1.55 [1.04–2.30]) [16]. Although current guidelines recommend advanced imaging techniques such as CT and MRI for detailed assessment of aortic dimensions [17], their high cost, limited accessibility, and radiation concerns, particularly with CT, make them less suitable for

routine use [18]. Although less precise, chest x-ray can still provide valuable insights into thoracic aortic parameters, making it a practical tool for cardiovascular risk assessment in large populations, especially in resource-limited settings.

Previous research has demonstrated the association of AKW with atherosclerosis in individuals with hypertension [5, 6]. Additionally, some studies also reported that AKW was associated with metabolic syndrome [4], left ventricular dysfunction [8], and obstructive sleep apnea syndrome [19], all of which contribute to cardiovascular disease. Currently, only one study involving 103 hemodialysis patients has shown the association of AKW with a higher risk of death [20]. We showed that AKW is associated with higher risks of all-cause mortality, cardiovascular mortality, and cardiovascular events in adults aged 50 and above. These findings were consistent across different follow-up periods, suggesting that reverse causation is less likely to explain the observed associations. Additionally, several studies showed the association of AKW with LVH in patients with hypertension [8] or myocardial perfusion [21], our study first highlights the modifying effect of LVH on the associations of AKW with mortality from all causes and cardiovascular issues. Thus, more emphasis should be put on people who have both LVH and aortic knob enlargement.

The observed associations may be explained by age-related vascular remodeling, characterized by reduced elastin fibers, increased collagen deposition, and calcification, which is associated with increased aortic stiffness [22]. Some studies reported that AKW may be an indicator of subclinical atherosclerosis [5–7]. Thus, this could explain why the AKW index was associated with higher risks of many specific cardiovascular events. We also found that AAL and AAW indices were associated with hemorrhagic stroke, and AKW index was associated with both hemorrhagic and ischemic stroke. This distinction could be attributed to atherosclerotic changes in the aortic arch, including unstable plaques that increase the risk of thromboembolism and subsequent ischemic stroke [23–25]. Unlike the AKW and AAW indices, the AAL index may be more sensitive to variations in thoracic anatomy or physiological factors that differ across the population. Additional studies are needed to explore potential explanations and their implications for risk prediction.

Hypertension was strongly associated with aortic enlargement in our study, consistent with prior evidence linking elevated blood pressure to vascular remodeling. However, results from previous studies have been inconsistent, possibly due to differences in aortic measurement sites and study designs. Although cross-sectional studies have shown variable associations depending on aortic segments [26–29], longitudinal data and Mendelian randomization analyses provide stronger evidence supporting the causal role of hypertension in aortic dilation and related complications [30–32]. These findings underscore the importance of managing hypertension to prevent aortic diseases.

Additionally, some cardiovascular risk factors showed inverse associations with aortic enlargement. Low-density lipoprotein cholesterol and diabetes exhibited inverse associations with aortic enlargement, consistent with previous observational studies and Mendelian randomization studies [27, 28, 33, 34]. The inverse association between low-density lipoprotein cholesterol and aortic enlargement points to the possibility of an anti-atherogenic lipid profile influencing aortic dilatation, requiring additional research for confirmation [35]. The use of statins may affect the accuracy of the outcome. For diabetes, this inverse association may be related to metabolic changes, which lead to collagen deposition and other structural changes in the aortic wall, making it stiffer and potentially limiting its expansion [28]. The inverse association was also observed between BMI and aortic enlargement. A possible explanation for this is that increased body mass index contributes to arterial stiffness, which reduces vascular elasticity and restricts aortic dilation [36]. However, these mechanisms remain complex and warrant further investigation.

Our study had some limitations. First, this study involved a group of relatively healthy people from Guangzhou. Although the cohort is broadly comparable to nationally representative urban samples in terms of chronic disease prevalence (e.g., hypertension and diabetes), there may still be selection bias related to occupation, income, and other sociodemographic factors. Survivor bias could also have influenced the findings, potentially underestimating the HRs. These factors should be considered when generalizing the findings to different populations. Second, this is an observational study, and despite our efforts to adjust for 15 confounding factors, some residual confounding

may still exist. Third, the analysis of risk factors for aortic enlargement was based on a cross-sectional design, which cannot establish causality. For example, we observed inverse associations between aortic enlargement and several cardiovascular risk factors, including low-density lipoprotein cholesterol, triglycerides, and diabetes. Although similar observations have been reported in earlier research, the biological mechanisms underlying these associations remain unclear. Survival bias or competing risks may also have contributed to these findings. Further longitudinal studies are needed to confirm these findings. Fourth, there are differences between the carefully standardized methods used in the present study and the routinely performed chest x-rays in clinical practice. Further studies and validation are required to determine whether thoracic parameters could be incorporated into routine clinical or screening settings. Finally, our participants were urban Chinese, which could restrict the generalizability of the results to the wider population. It remains uncertain whether these findings can be extended to other ethnic groups and settings.

In conclusion, we have shown a significant dose-response relationship of thoracic aortic parameters measured through chest x-ray with greater risks of all-cause mortality, cardiovascular mortality, and cardiovascular events in Chinese adults aged 50 or older, particularly with AKW. Given the widespread use of chest x-ray radiography, the results indicate additional clinical utility for this imaging modality. We advocate for the measurement of thoracic aortic parameters from existing chest x-ray images for cardiovascular risk assessment, which may support the decision on whether additional imaging procedures CT are needed.

Author contributions

Linye Sun: Writing—original draft; validation; software. **Wenbo Tian**: Writing—original draft; writing—review and editing. **Jiao Wang**: Resources; supervision; formal analysis. **Tianqiong Wu**: Methodology; formal analysis; validation; visualization; resources; writing—original draft. **Xiangyi Liu**: Data curation; supervision; validation; writing—original draft. **Yali Jin**: Writing—original draft; writing—review and editing; methodology; resources. **Taihing Lam**: Conceptualization; investigation; funding acquisition; writing—original draft; writing—review and editing; methodology; validation; visualization; supervision; project administration. **Karkeung Cheng**: Conceptualization; investigation; funding acquisition; writing—original draft; methodology; validation; writing—review and editing; visualization; project administration; supervision. **Weisen Zhang**: Funding acquisition; writing—original draft; writing—review and editing; methodology; supervision. **Lin Xu**: Data curation; supervision; resources; funding acquisition; writing—review and editing; investigation; conceptualization; writing—original draft; methodology; validation; visualization; formal analysis; project administration; software.

Acknowledgments

This work was funded by the National Natural Science Foundation of China [grant number 82373661]. The study's sponsor or funder did not participate in designing the study, collecting, analyzing, or interpreting data, writing the report, or placing any limitations on the report's publication of the report.

Conflict of interest statement

The authors declare no conflicts of interest.

Funding information

National Natural Science Foundation of China, Grant Number 82373661

Data availability statement

The corresponding author can provide the data supporting findings upon request. Due to privacy or ethical concerns, the data are not publicly accessible.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1: Cutoff points for sex-specific aortic enlargement.

Table S2: Adjusted HRs (95% CIs) of all-cause, cardiovascular and cancer mortality, cardiovascular events and specific cardiovascular event for the enlarged ascending aortic length index and each standard deviation increase in chest X-ray in GBCS from 2003 to 2008 and followed up until 21st Nov 2023.

Table S3: Associations of each standard deviation increase in aortic parameters with mortality from all-cause, cardiovascular and cancer, and cardiovascular events by sex, age, diabetes, hypertension and left ventricular hypertrophy.

Figure S1: Kaplan-Meier survival curve by the presence of enlarged ascending aortic length index for all-cause mortality, cardiovascular mortality, cancer mortality and cardiovascular events.

Figure S2: Kaplan-Meier survival curve by the presence of enlarged ascending aortic width index for all-cause mortality, cardiovascular mortality, cancer mortality and cardiovascular events. Note: Values below 0.50 on the y-axis are omitted to emphasize the relevant range of cumulative survival.

Figure S3: Association of AAL index with all-cause mortality, cardiovascular mortality, cancer mortality and cardiovascular events in GBCS from 2003 to 2008 and followed up until 21st Nov 2023.

Figure S4: Association of AAW index with all-cause mortality, cardiovascular mortality, cancer mortality and cardiovascular events in GBCS from 2003 to 2008 and followed up until 21st Nov 2023.

Figure S5: Associations of each standard deviation increase in aortic parameters with mortality from all-cause, cardiovascular and cancer, and cardiovascular events across different follow-up time intervals.