Atherogenic Index of Plasma as Predictor for Cardiovascular Events and Cardiometabolic Diseases: The Pamela Study

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Article

Atherogenic Index of Plasma as Predictor for Cardiovascular Events and Cardiometabolic Diseases: The Pamela Study

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Abstract

The Atherogenic Index of Plasma (AIP), ratio between triglycerides and high-density lipoprotein cholesterol, has been associated with cardiovascular (CV) events, metabolic syndrome and hypertension (HT)-related vascular organ damage. However, the majority of the published studies suffer from important limitations, such as the cross-sectional or retrospective nature and the performance in selected Asian populations only. To overcome these limitations, we performed an analysis of the data collected in the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study, providing longitudinal information on the relationships between AIP, diabetes mellitus (DM), HT and left ventricular hypertrophy LVH) in a western european general population. At the study entry baseline data were collected in 2035 subjects, while longitudinal data were obtained in 1412 subjects examined for a median follow-up time amounting to 10.7 years. 50.6% of the subjects were males. aged 50.9±13.7 (mean±SD) years. During the follow-up AIP did not significantly change (from -0.11±0.3 to -0.12±0.29 a.u., *P*=NS), while systolic BP and plasma glucose significantly increased with a significant relationship with HT, DM and LVH development (*P* <0.0001). At multivariable analysis, AIP significantly and independently predicted all the above-mentioned outcomes, with the exception of HT development based on home BP. The same significant association was detected for fatal and non-fatal CV events. These data provide evidence that in a general European population characterized by a low CV risk AIP significantly and independently predicts HT, DM and LVH development and is significantly associated with the composite outcome of CV morbidity and mortality.

Keywords: atherogenic index of plasma; cardiovascular mortality; cardiovascular events; hypertension; diabetes; left ventricular hypertrophy

1. Introduction

The Atherogenic Index of Plasma (AIP) is a log-transformed biomarker predicting cardiovascular disease (CVD), atherosclerosis, and metabolic syndrome risk, calculated as $\log_{10}$ (triglycerides/HDL cholesterol) [1–5]. The majority of information on the predictive value of AIP on cardiovascular morbidity and mortality, however, are based on data collected almost invariably in cross-sectional or retrospective studies, the published studies investigating these associations in a longitudinal fashion in diabetes mellitus or in hypertension being few and performed in eastern Asian populations [6–12]. In addition, AIP has ben also associated with some markers of hypertension-mediated organ damage, such as the wall stiffness of the large and medium size arteries and the intima-media thickness at the level of the carotid arteries [13–18]. However, the information on the association between AIP and the most clinically relevant hypertension-related marker of

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cardiac organ damage, such as left ventricular hypertrophy (LVH), appear to be so scanty as to remain almost anecdotical [19].

With this background in mind, we performed in the present paper an analysis of the longitudinal data collected in the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study [20], in order to obtain information in a general western European population on the association between (1) AIP and CV morbidity and mortality and (2) AIP and development during the years of follow-up of diabetes mellitus, hypertension and LVH. The unique feature of the study was the long-term follow-up, whose temporal duration amounted to more than ten years.

2. Methods

2.1. Study Population

The methods used in the PAMELA study have been reported in detail elsewhere [5,20]. Briefly, 3200 residents in Monza (a town located in the northeast outskirts of Milan, Italy) were randomly selected, stratified for gender and age decades, to be representative of the general population. They were aged between 25 and 74 years and the initial evaluation was carried out between 1990 and 1993. The participation rate in this first study was 64%, allowing to collect data in 2051 individuals. The demographic and clinical characteristics of participants and nonparticipants were assessed by phone interviews without any significant difference.

Survivors (n=1412) were then reassessed with the same evaluation carried out in the same hospital and with the same methods after 10 years (2002-2003). Median time from baseline to follow-up examination was 10.7 years (I-III quartiles 10.2-11.1 years). In the present study subjects with missing variables needed to calculate AIP (n=16) were excluded from the analysis, resulting in a final sample size amounting to 2035 individuals. In both the surveys medical visits took place at the outpatient sector of the Saint Gerardo Hospital (Monza, Italy), during the morning of a working day, asking to the patients to follow an overnight fast and abstinence from alcohol and cigarette smoking. The study protocol complied with the Declaration of Helsinki, and it was approved by the Ethics Committee of the Institution involved. All participants provided informed written consent after being informed of the study nature and purpose.

2.2. Measured Variables

In each enrolled subject a medical history was collected, and a physical examination was carried out. Office blood pressure (BP) was taken three times in the sitting position using a mercury sphygmomanometer and the average value was used for the analyses. 24-hour ambulatory BP monitoring (ABPM) was performed (Spacelabs 90207, Issaquah, WA, USA) [5,20] and set to obtain automated oscillometric BP and heart rate readings every 20 minutes over the 24-hour period. During the monitoring period indications were given to the subjects to perform their normal activities and to hold the arm still at time of the BP readings, going to bed not later than 11.00 p.m. and waking up not before 7.00 a.m. Furthermore, participating subjects self-measured BP at home, with a validated semiautomatic oscillometric device (Model HP 5331, Philips, Amsterdam, The Netherlands), with a cuff size appropriate to each individual's arm circumference, at 7.00 a.m. and 7.00 p.m., using the arm contralateral to the one used for ABPM.

Height and weight were measured, and body mass index (BMI) and body surface area (BSA) were calculated. Laboratory analyses were performed in the subject's fasting state and included glucose, total and HDL cholesterol, serum triglycerides and serum creatinine. Glomerular filtration rate was estimated via the Modification of Diet in Renal Disease equation, while low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation. AIP was calculated as the base-10 logarithm of ratio of serum triglycerides (mmol/l) to HDL cholesterol (mmol/l) and expressed as arbitrary units (a.u.). Previous CV events were collected including coronary revascularization, myocardial infarction, stroke or transient cerebral ischemic attack. Use of CV drugs

 doi:10.20944/preprints202603.1135.v1

was assessed in all the enrolled subjects, with a specific attention to the administration of antihypertensive drugs and statins treatment.

2.3. Echocardiographic Evaluation

Transthoracic echocardiographic examination was performed (Acuson 128 CF, Computer Sonography, Samsung Medison EKO 7, Seoul, South Korea), with specific interest in left ventricular mass (LVM) assessment and detection of the presence of LVH. To use the Devereux formulae to calculate LVM, left ventricular end-diastolic diameter (LVEDD), interventricular septal thickness and posterior wall thickness were measured off-line from two-dimensionally guided M-mode tracings recorded at 50-100 cm/s speed, during at least three consecutive cardiac cycles. LVM was estimated via the following formulae: 0.8 x 1.04 x [(LVEDD + septal thickness + posterior wall thickness) ^{3} - LVEDD^3] + 0.6. It was then indexed both for height elevated at 2.7 factor ($h^{2.7}$) and body surface area (m^2) calculated via the DuBois formulae: 0.007184 x height (cm)^0.725 multiplied by weight (kg)^0.425. Echocardiographic tracings were collected by two skilled operators and read off-line by a third expert cardiologist. The intra-observer coefficient of variation was 0.6% for LVEDD, 3.1% for interventricular septal wall and 3.2% for the posterior wall thickness.

2.4. Surrogate and Hard Endpoints

Hypertension was defined based on the detection of BP greater than the normal values at the follow-up evaluation. The cut-off used amounted to 140/90 mmHg for office BP, 135/85 mmHg for home BP and 130/80 mmHg for ABPM [5,20]. Diabetes mellitus was defined as the occurrence of fasting glycemic values >126 mg/dl or the presence of insulin therapy or antidiabetic drugs at the follow-up examination [5,20]. As far as LVH development is concerned, the cut-off used were 95 and 115 g/m^2 (for females and males, respectively) for BSA indexing and 47 and 50 g/$height^{2.7}$ (for females and males, respectively) indexed to $height^{2.7}$ [5,20].

The hard endpoints included fatal (CV deaths) and non-fatal CV events (atrial fibrillation, myocardial infarction, myocardial revascularization, chronic heart failure and stroke) and all-cause mortality. Follow-up was carried out in 2004 (mean follow-up time 13.0 years, I-III quartile 12.6-13.5 years) and CV events were defined according to the International Classification of Diseases code obtained from discharge letter from the regional healthcare system.

2.5. Data Analysis

Analysis of CV morbidity and mortality was conducted on the entire dataset (n=2035), while analyses regarding hypertension, LVH and diabetes mellitus development were conducted on patients with available follow-up data (n=1392, 21 patients excluded due to the lack of data necessary to calculate AIP) and without the relative pathological condition already detected at study entry (n= 566, 437 and 41, respectively). Continuous variables were reported as means ± standard deviations, while, for categorical variables, percentages were reported. Paired T-test and McNemar test were used to compare baseline to follow-up characteristics. The association of AIP with the development of hypertension, diabetes mellitus and LVH was firstly assessed by univariable logistic regression model. Then, three multivariable logistic models (with development of hypertension, diabetes mellitus and LVH as dependent variables) were performed. Covariates in the models were: gender, age, BMI, baseline 24-hour SBP, antihypertensive drug treatment, fasting glucose, LDL cholesterol, previous CV events and estimated glomerular filtration rate. BMI was removed from the LVH development model (due to collinearity reasons), while baseline LVM indexed by BSA or $height^{2.7}$ was added. Similarly, antihypertensive therapy was removed from the hypertension development multivariable models.

Cox proportional hazards regression models were applied to assess the association between AIP and the risk of all-cause mortality and CV events, including both fatal and non-fatal outcomes. AIP was modelled both as a continuous variable and as quartiles, with the lowest quartile used as

 doi:10.20944/preprints202603.1135.v1

reference category. Both unadjusted and multivariable-adjusted models were fitted, with adjustment for age, gender, previous CV events, antihypertensive pharmacological treatment, 24-hour BP, LDL cholesterol, serum glucose, BMI and estimated glomerular filtration rate. Event-free survival across AIP quartiles was compared using Kaplan-Meier survival curves, and differences between groups were evaluated using the log-rank test. All analyses were carried out using SAS 9.4 software (SAS Institute, Cary, NC, USA) and R (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria). A *P* value <0.05 was considered statistically significant.

3. Results

3.1. Characteristics of the Whole Population Sample

As shown in Table 1, left column, the whole population included 2035 subjects, of which 50.6% were males, with a mean age of 50.9±13.7 years. As far as CV risk factors are concerned, 46.2% of the subjects displayed arterial hypertension, while 3.5% diabetes mellitus and 4.2% reported a previous CV event. Biochemical variables showed LDL cholesterol amounting to 145.4±39.1 mg/dl, mean glucose to 90.8±21.1 mg/dl and mean creatinine to 0.88±0.19 mg/dl (corresponding to an estimated glomerular filtration rate of 87.5±16.4 ml/min). Mean HDL and triglycerides value were 55.5±15.5 mg/dl and 116.0±76.7 mg/dl respectively, resulting in a mean AIP amounting to -0.09±0.3 (Figure 1, panel A). Finally, as far as hypertension-mediated cardiac organ damage is concerned, mean LVM indexed to BSA was 86.7±21.1 g/m^2, with a LVH prevalence amounting to 15.9%.

Table 1. Population characteristics.

Variable	Whole population	Patients with follow-up evaluation		P value
		Baseline	Follow-up	
Demographic data				
Number	2035	1392	1392	
Age, years	50.9±13.7	48.6±13	59.2±12.6	-
Male, %	1030 (50.6%)	711 (51.1%)	711 (51.1%)	-
Cardiovascular risk factors				
Arterial hypertension, %	937 (46.2%)	564 (40.6%)	847 (60.8%)	<.0001
Office SBP, mmHg	132.9±21.3	129.9±19.8	137.7±22.8	<.0001
Office DBP, mmHg	83.9±10.6	83.3±10.3	83.6±10.8	0.2227
Home SBP, mmHg	124.6±19.2	122±17.4	125.3±16.5	<.0001
Home DBP, mmHg	76.5±10.6	75.7±10.2	74.7±8.9	0.0066
24h SBP, mmHg	120.3±11.9	119.3±11.2	123.6±11.9	<.0001
24h DBP, mmHg	74.4±7.6	74.3±7.2	74.6±7.8	0.1123
BMI, kg/m^2	25.6±4.4	25.3±4.3	26.7±4.4	<.0001

 doi:10.20944/preprints202603.1135.v1

Diabetes mellitus, %	71 (3.5%)	40 (2.9%)	82 (5.9%)	<.0001
Previous CV events, %	85 (4.2%)	38 (2.7%)	-	-
Cardiovascular drugs				
Antihypertensive drugs, %	393 (19.4%)	214 (15.4%)	474 (34.1%)	<.0001
Statins, %	61 (3.0%)	42 (3.0%)	96 (6.9%)	<.0001
Biochemical data				
Total cholesterol, mg/dl	224.1±42.8	221.9±42.2	205.3±36.9	<.0001
HDL cholesterol, mg/d	55.5±15.5	56.0±15.7	60.3±15.3	<.0001
Triglycerides, mg/dl	116.0±76.7	110.9±67.7	116.4±71.9	0.0018
LDL cholesterol, mg/dl	145.4±39.1	143.7±38.9	121.7±32.5	<.0001
Fasting glucose, mg/dl	90.8±21.1	89.7±19.4	94.4±24.1	<.0001
Creatinine, mg/dl	0.88±0.19	0.87±0.16	0.91±0.22	<.0001
Glomerular filtration rate, ml/min	87.5±16.4	89.2±15.2	83±18.5	<.0001
AIP (a.u.)	-0.09±0.3	-0.11±0.3	-0.12±0.29	0.0547
Cardiac organ damage				
LVMI (BSA), g/m^2	86.7±21.1	84.8±19.5	98.9±26.9	<.0001
LVH (BSA), %	271 (15.9%)	152 (13.0%)	452 (34.4%)	<.0001
Outcomes				
All causes mortality, %	231 (11.4%)	-	-	-
CV mortality, %	69 (3.4%)	-	-	-
CV events, %	176 (8.6%)	-	-	-

Abbreviations: SBP = Systolic blood pressure; DBP = Diastolic blood pressure; BMI = Body mass index; CV = cardiovascular; HDL = High density lipoprotein; LDL = Low density lipoprotein; AIP = Atherogenic index of plasma; LVMI = Left ventricular mass index; BSA = Body mass Index; LVH = Left ventricular hypertrophy.

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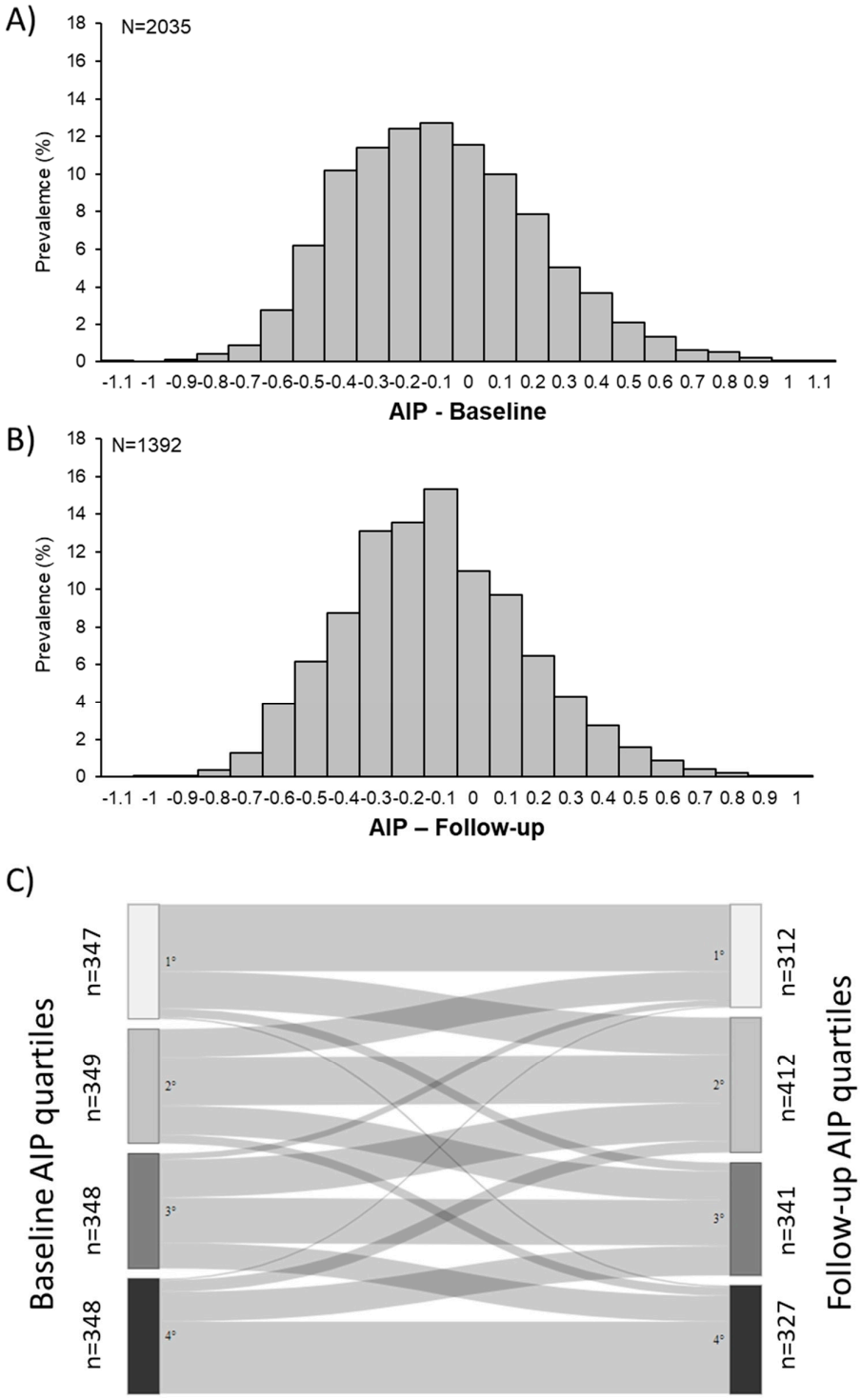

Figure 1. Distribution of the values of the Atherogenic Index of Plasma (AIP) in 2025 subjects of the PAMELA study evaluated at baseline (panel A), and in 1392 subjects examined during the 10-year follow-up (panel B). Changes in the quartiles distribution of AIP values are shown in Panel C.

3.2. Characteristics of the Population Sample with Follow-Up Data

Table 1, central and right columns show the data collected in 1392 subjects evaluated longitudinally in the first and in the second PAMELA study. During the median follow-up time of 10.7 years, systolic BP values, as well as plasma glucose, were significantly increased, corresponding

 doi:10.20944/preprints202603.1135.v1

respectively to a significant increase in the prevalence of hypertension (from 40.6 to 60.8%, P<0.0001), use of antihypertensive drugs (from 15.4 to 34.1%, P<0.0001) and diabetes mellitus (from 2.9 to 5.9%, P<0.0001) as well. Plasma creatinine, HDL plasma cholesterol and triglycerides also significantly increased, while no significant variation was detected for AIP values (Figure 1, panel B and C). Finally, LVM indexed for BSA increased during the follow-up from 84.8±19.5 to 98.9±26.9 kg/m^2, with a corresponding increase in LVH prevalence from 13.0% to 34.4%. Both these increases were highly statistically significant (P<0.0001).

3.3. Hypertension, Diabetes and LVH Development

During 338. and 257 subjects developed office and ABPM hypertension, respectively, the corresponding values for diabetes mellitus and LVH development amounting to 52 and 249, respectively. Figure 2 shows the unadjusted and adjusted data related to the associations between AIP and development of hypertension, diabetes mellitus and LVH. All the evaluated parameters displayed a highly significant relationship with AIP both at unadjusted and adjusted analysis, with the exclusion only of hypertension development when home BP values were considered (Odds Ratio 1.79; 95% Confidence Interval: 0.88,3.65; *P*=0.1084). The association with the highest estimate variable was related to diabetes mellitus development (Odds Ratio 3.57; 95% Confidence Interval:1.23,10.38; *P*=0.0193).

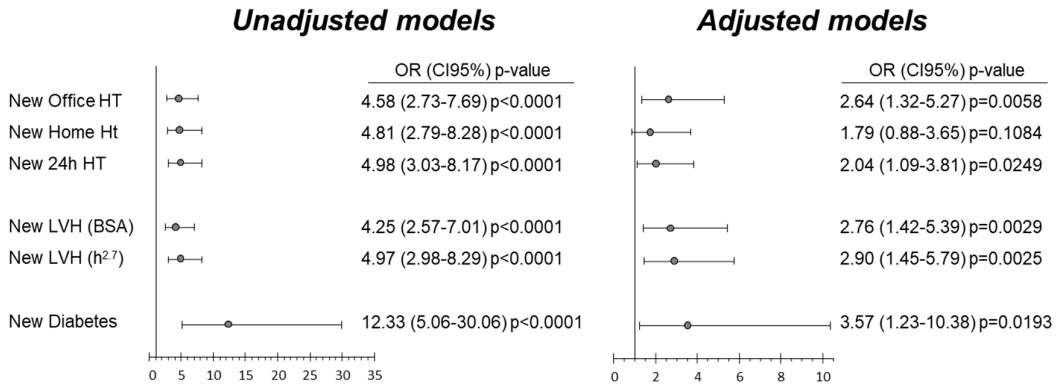

Figure 2. Unadjusted and adjusted association between Atherogenic Index of Plasma and development during the 10 years follow up of hypertension (HT), diagnosed via office, home or 24-hour blood pressure measurement, left ventricular hypertrophy (LVH) and diabetes mellitus. BSA: body surface area, OD: odds ratio.

3.4. CV Events, CV Mortality and All-Cause Mortality

During the follow-up 231 (11.4%) all-cause fatal events and 176 (8.6%) fatal and non-fatal CV events were observed. As shown in Table 2 and in Figure 3, panel A, AIP showed a significant association with the composite end-point of CV events and CV mortality at the full adjusted model, both when considered as a continuous variable (hazard ratio 1.913; 95% confidence interval:1.093, 3.347; *P*=0.0232) and when expressed as quartiles (Q4 vs reference hazard ratio 2.045;95% confidence interval:1.091,3.832; *P*=0.0255). On the other hand, no significant association was detected with all-cause mortality at adjusted analyses, both when AIP was expressed as a continuous variable and when expressed as quartiles (Table 2, Figure 3, panel B).

 doi:10.20944/preprints202603.1135.v1

Table 2. Unadjusted associations and multivariable model data of the association between atherogenic index of plasma (AIP), cardiovascular events and mortality.

		CV Mortality and Events			All-cause Mortality		
		HR	**95% CI**	**p-value**	**HR**	**95% CI**	***P*-value**
AIP as a continuous variable							
Not adjusted	**AIP, for 1 unit**	6.494	4.193-10.057	<.0001	3.337	2.245-4.959	<.0001
Age and sex adjusted	**AIP, for 1 unit**	2.995	1.796-4.994	<.0001	1.402	0.885-2.22	0.15
Full adjusted	**AIP, for 1 unit**	1.913	1.093-3.347	0.0232	1.106	0.67-1.826	0.6938
AIP quartiles							
Not adjusted	**AIP, 1Q**	1	Ref		1	Ref	0
	AIP, 2Q	2.833	1.499-5.354	0.0013	1.751	1.106-2.771	0.0168
	AIP, 3Q	3.672	1.981-6.807	<.0001	2.29	1.475-3.556	0.0002
	AIP, 4Q	7.259	4.046-13.025	<.0001	3.381	2.225-5.139	<.0001
Age and sex adjused	**AIP, 1Q**	1	Ref		1	Ref	0
	AIP, 2Q	1.892	0.999-3.586	0.0505	1.193	0.752-1.894	0.4528
	AIP, 3Q	1.747	0.935-3.264	0.0804	1.149	0.734-1.798	0.543
	AIP, 4Q	2.794	1.534-5.09	0.0008	1.41	0.914-2.175	0.1207
Full adjusted	**AIP, 1Q**	1	Ref		1	Ref	
	AIP, 2Q	1.712	0.894-3.28	0.1048	1.108	0.684-1.795	0.6757
	AIP, 3Q	1.481	0.783-2.799	0.2271	1.147	0.719-1.83	0.5652
	AIP, 4Q	2.045	1.091-3.832	0.0255	1.257	0.784-2.015	0.3426

AIP = Atherogenic Index of Plasma; CV: Cardiovascular; Q: Quartiles; HR: Hazard Ratio. Full adjusted model includes as covariates age, sex, previous CV event, antihypertensive treatment, 24-hour systolic blood pressure, LDL cholesterol, serum glucose, body mass index and estimated glomerular filtration rate.

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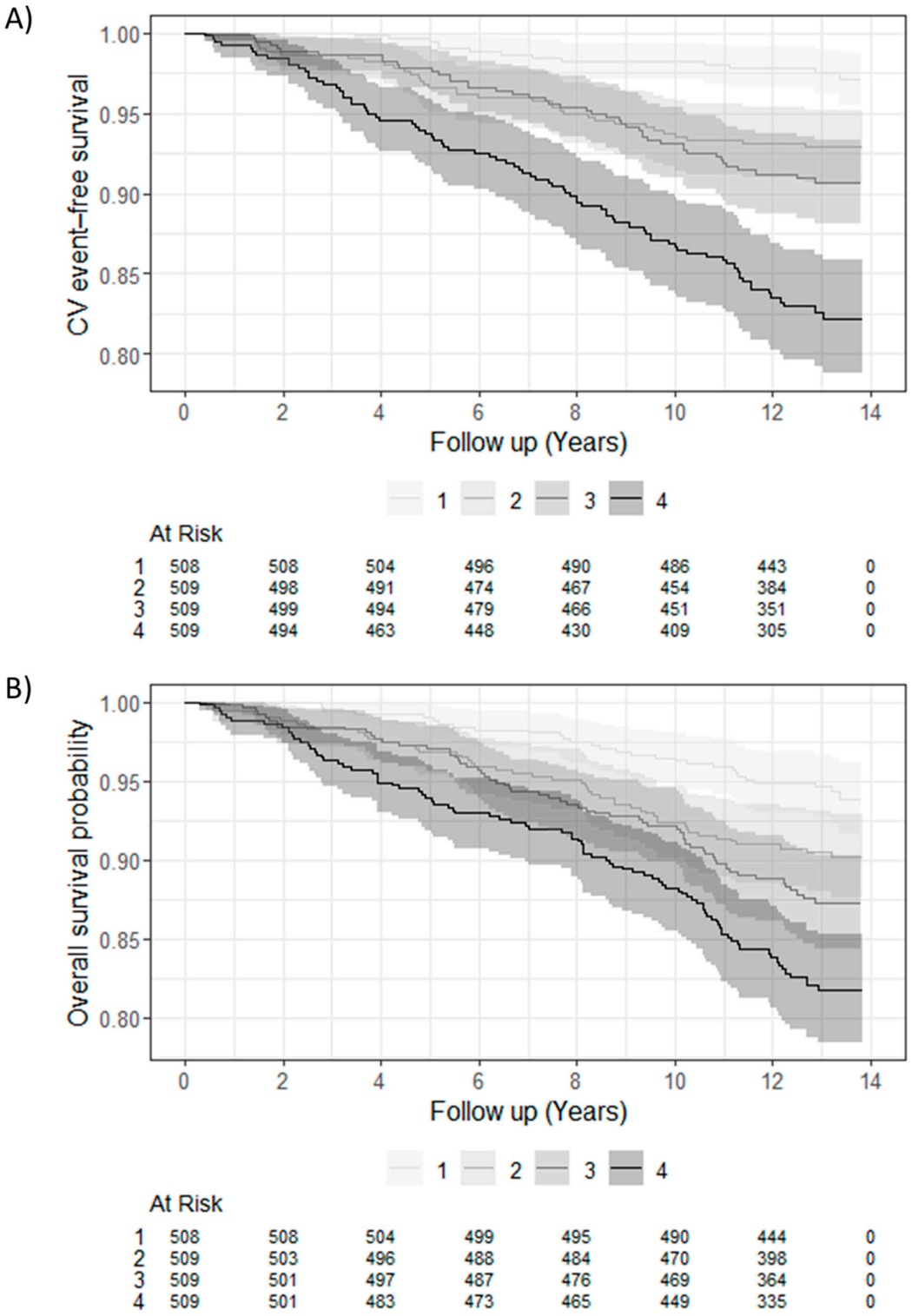

Figure 3. Kaplan-Maier survival curves for fatal and nonfatal cardiovascular events (panel A) and all-cause mortality (panel B) in the study population subdivided in different AIP quartiles. Note the progressive survival reduction for cardiovascular events in the subjects belonging to the higher AIP quartiles. For abbreviations see legend of Figure 1.

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4. Discussion

Two are the major results of the present study. The first result refers to the finding that in a general population characterized by a low CV risk profile, such as the one examined in the PAMELA study, AIP represents an independent prognostic marker of fatal and non-fatal CV events. Thus, the present study confirms the evidence provided, although not homogeneously, by previous investigations on the relationship between AIP, CV events and CV mortality [21–23]. The second new finding of our study concerns the evidence that AIP is significantly and independently associated with the future development of cardiometabolic disease, such as hypertension and diabetes mellitus, and with the occurrence of hypertension-related cardiac organ damage. An additional result of our study refers to the evidence that assessment of AIP in the longitudinal follow-up documents its stability throughout years without any significant temporal variation in its values. This finding has relevance for the evidence, provided in the ELSA cohort study [24] that a highly stable AIP values has the strongest relationship with the increased risk of CV events.

The results of a recent study have shown the highest hazard ratio characterizing the association between AIP and CV mortality, as compared to other anthropometric and atherogenic indices [25]. The mechanisms underlying this association are mainly related to the atherogenic potential of high triglycerides and low HDL (and thus to elevated AIP). In fact, AIP has been associated with the detection of coronary artery atherosclerosis and its severity [26]. Other non-mutually excluded mechanisms may participate, however. These include the vascular inflammatory process, the oxidative stress and the endothelial dysfunction as well. They also include the relationships with hypertension, diabetes mellitus and LVH. Indeed, as previously mentioned, AIP is also associated with the development of CV risk factors and hypertension-mediated organ damage. However, only few studies performed these analyses in a longitudinal fashion and data have been almost selectively obtained in Asian population, limiting the generalizability to the European ancestry.

Four longitudinal studies have been focused on diabetes mellitus development, all showing a significant association with AIP [8,10,27,28]. In 2 studies also the association between AIP changes over time and the subsequent diabetes mellitus development was evaluated [8,9]. In the first one [8], in 14968 subjects, AIP changes during the 5-years follow-up predicted the 10-years occurrence of new diabetes mellitus diagnosis. Subjects in which AIP increased (14.8%), when compared to subjects in which AIP remained stable (29.6%), displayed a hazard ratio of 1.18 (95% CI 1.00, 1.40) for diabetes development. On the contrary, subjects in which AIP decreased (14.8%) showed a significant risk reduction (HR 0.80, 95% CI 0.67, 0.95) [8]. Similar results were obtained in 42850 participants with an average follow-up of 4 years [10]. AIP mainly remained stable in the individuals in which greater levels were maintained, displaying a hazard ratio of 2.50 (95% CI 2.06, 3.03) for the development of diabetes mellitus, when compared to subjects in which AIP remains at lower levels [10].

To the best of our knowledge, only two studies report data on the association between AIP and hypertension development [27,28]. In these two papers, after multivariable adjustment, individuals with high AIP displayed an elevated risk of new-onset hypertension (hazard ratio close to 1.5). The mechanisms through which AIP could contribute to diabetes mellitus and hypertension development are far from being completely elucidated. They are likely to be related to the lipid's alterations evaluated by this ratio. In particular, elevated triglycerides are stored in visceral adipose tissue leading to the occurrence of insulin resistance, the primary pathological determinant of diabetes mellitus. Furthermore, insulin resistance reduces nitric oxide availability and increases oxidative stress, inflammation and sympathetic cardiovascular drive [29,30]. This will lead to the occurrence of an endothelial dysfunction and an arterial stiffening process [31], which both concur to HT development.

Finally, AIP has been documented to be associated with some measurements of hypertension-mediated organ damage, with the same limitations above mentioned. Focusing on LVH, some of the AIP associations studies were conducted in pediatric population [32,33], while data collected in adults are scanty [19,34–36]. None of them, however, followed a longitudinal design as we did in the present study.

 doi:10.20944/preprints202603.1135.v1

Our study has some strengths but also some limitations. The strengths include the long follow-up (median 10.7 years) allowing to assess the development throughout the years of hypertension, diabetes and LVH as well. Furthermore, in the present study HT development has been evaluated by three different methods to assess BP (office, home and ABPM), an approach which has never been performed in previous published investigations. Similarly, also LVH was defined by used criteria (BSA and height$^{2.7}$). Moreover, while most of the studies on surrogate end-points were carried out in Asian population, our study provide data in the European setting. Finally, since diabetes mellitus, hypertension and LVH could influence one another, in our study multivariable models for surrogate end-point were corrected in-between them (i.e., LVH development models was corrected for BP and glucose and anti-hypertensive therapies).

As above mentioned, the present investigation displays also some limitations. First, our study was conducted in a single center, which may limit generalizability to different context or populations. Furthermore, the absence of a long hard events follow-up in a sufficient number of patients after the second PAMELA study doesn't allow us to perform analysis on the association of evaluated parameters with AIP changes over a very prolonged time period. A further limitation is that no information was available regarding the use of anti-diabetic drugs in the PAMELA study, affecting the results of the diabetes mellitus development analysis. Finally, in the multifactorial context linking AIP and evaluated surrogate and hard endpoints it was impossible to assess all parameters potentially involved in the above-mentioned relationship. This was the case for factors such as diet, physical activity, and alcohol consumption, which were not analyzed in details, despite their potential impact on lipid and metabolic profile.

5. Conclusions

In conclusion, the data discussed in the present paper provide longitudinal prognostic information on the independent predictability of AIP for the development of cardiometabolic disease and related cardiac organ damage in a European population characterized by a low cardiovascular risk. Inclusion of AIP in prognostic models may thus allow to improve cardiometabolic risk stratification.

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Conflicts of Interest: Authors declare they have no conflict of interest.

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