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ARTICLE

Frequency of early vascular aging and associated risk factors among an adult population in Latin America: the OPTIMO study

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Abstract

The main objective was to estimate the frequency of early vascular aging (EVA) in a sample of subjects from Latin America, with emphasis in young adults. We included 1416 subjects from 12 countries in Latin America who provided information about lifestyle, cardiovascular risk factors (CVRF), and anthropometrics. We measured pulse wave velocity (PWV) as a marker of arterial stiffness, and blood pressure (BP) using an oscillometric device (Mobil-O-Graph). To determine the frequency of EVA, we used multiple linear regression to estimate each subject's PWV expected for his/her age and systolic BP, and compared with observed values to obtain standardized residuals (z-scores). We defined EVA when z-score was ≥1.96. Finally, a multivariable logistic regression analysis was performed to determine baseline characteristics associated with EVA. Mean age was 49.9 ± 15.5 years, male gender was 50.3%. Mean PWV was 7.52 m/s (SD 1.97), mean systolic BP was 125.3 mmHg (SD 16.7) and mean diastolic BP was 78.9 mmHg (SD 12.2). The frequency of EVA was 5.7% in the total population, 9.8% in adults of 40 years or less and 18.7% in those 30 years or less. In these young adults, multiple logistic regression analyses demonstrated that dyslipidemia and hypertension showed an independent association with EVA, and smoking a borderline association ($p = 0.07$). In conclusion, the frequency of EVA in a sample from Latin America was around 6%, with higher rates in young adults. These results would support the search of CVRF and EVA during early adulthood.

Introduction

Arteriosclerosis develops throughout the life-course starting at very early stages (i.e., in utero and during childhood) and is influenced by genetic and environmental cardiovascular risk factors (CVRF), even though the clinical expression appears decades later [1–3]. This phenomenon has fostered the adoption of a life-course approach to reduce CVRF and cardiometabolic disease [4].

First described in 2008 by Nilsson PM et al., the "early (or accelerated) vascular aging" (EVA) is a growing clinical concept that mainly refers to the observation of an increased arterial stiffness (arteriosclerosis) in either susceptible individuals under the influence of CVRF, when compared with the expected arterial stiffness according to their chronological age [1, 5].

Carotid to femoral pulse wave velocity (c-f PWV) measurement represents the propagation velocity of the pulse wave and is currently regarded as the gold standard for the assessment of arterial stiffness [6, 7]. Despite being strongly correlated with age, blood pressure (BP), and metabolic factors [8–14], c-f PWV represents an independent predictor of coronary heart disease, stroke, cognitive decline, and cardiovascular death, after adjusting for the established CVRF [15, 16]. Therefore, c-f PWV plays a central role in the EVA definition, but given the lack of an operational definition (threshold values), it has been

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proposed to define EVA when PWV values are above the 97.5th percentile of the age-adjusted z-score, using as a normal reference cohort the Reference Values for Arterial Stiffness Collaboration [7, 17]

The OPTIMO study was designed to evaluate lifestyle predictors of healthy arteries in a population sample from Latin America. In the present analysis, our primary objective was to determine the frequency of EVA focused on the detection of subjects with a true increase in the arterial stiffness (i.e., elevation of estimated PWV) independently of the effect of age and BP. Since higher PWV values characterize older people, we sought to investigate the existence of EVA with emphasis on young adults (age range between 20 and 40 years), when both EVA and subclinical arteriosclerosis reach a high prevalence [17, 18]. Second, we evaluated the relationship of baseline variables with EVA.

Materials and methods

The OPTIMO study design is based on an international prospective cohort of adults aged 20 years or more from 12 Latin American countries (Argentina, Brazil, Chile, Colombia, Costa Rica, Guatemala, Honduras, México, Nicaragua, Panamá, Dominican Republic, and El Salvador). The present report is based on a cross-sectional analysis of the baseline information collected over 1 year, from October 2014 to October 2015.

Individuals from public and private general and cardiovascular health facilities, and also from public places (i.e., shopping malls) and working areas (i.e., factory or laboratory employees) were asked to voluntarily participate, after signing an informed consent. The protocol required a consecutive recruitment during the time of collaboration. There was no formal invitation, therefore each investigator offered participation to subjects following local strategies and ethics rules.

All participants provided information about their *lifestyle* (dietary habits, alcohol intake, smoking, and physical activity), *demographic* (age and gender), *anthropometric* and *socio-economic* variables (education, occupation, and marital status), and *medical history*, by completing the WHO STEPS surveillance questionnaire [19]. Although this is a self-administered survey, research staff helped individuals to complete it adequately. As blood samples were drawn only in one-fourth of the cases, such results are not included in this analysis.

Nutrition was tabulated using the unit "days per week" (d/w) as a continuous variable for consumption of fruits, vegetables, fish, seeds/nuts, and alcohol. Regular alcohol intake was also defined as 3 or more d/w, regular fish consumption as 2 or more d/w, and regular exercise 3 or more d/w. Regarding medical history, diagnosis of hypertension (HTN), dyslipidemia, or diabetes were considered present if the subject reported use of any drug medication for the condition or if he/she referred that it was previously diagnosed by a physician. Overweight and obesity were defined as a body mass index of ≥25 kg/m^2 and ≥30 kg/m^2, respectively. Prior atherosclerotic cardiovascular disease (ASCVD) was defined as coronary heart disease, myocardial infarction, stroke, or peripheral arterial disease.

Noninvasive measurements of systolic BP (SBP) and diastolic BP (DBP), heart rate, and an estimated value of PWV were determined using the Mobil-O-Graph® (IEM, Stolberg, Germany), a commercially available brachial oscillometric BP monitor validated by the European Society of Hypertension [20]. The device includes the ARCSolver® method (Austrian Institute of Technology, Vienna) that generates the aortic pulse wave using a proprietary transfer function after checking for signal quality. Estimated PWV using this technology has been successfully compared with tonometric reference devices [13, 21–24]. A regular brachial cuff adjusted to the circumference of the left arm in each individual was applied and measurements were performed after 5 min of rest in a sitting position. During the assessment, speaking was not allowed. The monitor protocol includes a first brachial BP measurement, then a 30-s pause, followed by a second measurement. The first is automatically discarded and the second one is reported. Measurement was repeated only in the case of a poor or regular quality according to the quality checking. Monitor application and evaluation was performed by physicians previously trained with the method for use in clinical practice. The OPTIMO protocol did not instruct about the presence or not of the person who operated the device. Actually, the operator was usually present. Patients with atrial fibrillation or frequent premature cardiac beat contractions and those who consumed food or smoked in the prior 2 h were excluded.

The study protocol was approved by the research ethics board at every screening site. Informed consent was obtained from each participating individual.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation unless otherwise specified, and categorical variables are expressed as percentages. Estimated PWV and BP results according to the age are described in decades of life.

We developed a multiple linear regression model among the whole population to estimate each subject's PWV expected for his/her age and SBP registered during the examination. We checked for linearity and model fitting by comparing the observed PWV and the PWV predicted by the model. Then, we performed a standardized residuals

Table 1 Baseline characteristics of the total OPTIMO study population ($n = 1416$)

Variable	Result
Age, mean (SD)	49.9 (15.5)
Male gender (%)	50.3
Height, cm (SD)	168.4 (9.8)
Weight, kg (SD)	75.9 (17.3)
Education level (%)	
<7 years (no or incomplete primary)	1.8
7 years (complete primary)	4.2
12 years (complete secondary)	23.3
>12 years (tertiary, no university)	22.7
>12 years (university or post-degree)	48
Cardiovascular risk factors (%)	
Current smoking	12.2
Dyslipidemia	58.3
Hypertension	41.2
Diabetes	11.6
Overweight	34.9
Obesity	24.4
Prior ASCVD event (%)	6.3
Aspirin treatment (%)	15.6
Antihypertensive drugs use (%)	39.2
Lipid-lowering drugs use (%)	48
Any statin	41
Regular alcohol intake (%)	61.3
Alcohol intake, days per week (SD)	3.7 (1.9)
Fruits, days per week (SD)	4.8 (2.2)
Vegetables, days per week (SD)	5 (2)
Fish, days per week (SD)	1.1 (0.9)
Seeds/nuts, days per week (SD)	1.4 (1.9)
Regular exercise (%)	60.2
Exercise, days per week (SD)	2.2 (1.9)

ASCVD atherosclerotic cardiovascular disease

analysis (z-scores) to determine EVA frequency using the function "Observed PWV–Predicted PWV/SD Predicted PWV". EVA was determined when z-score exceeded +1.96 (equivalent to 97.5th percentile). Further, low PWV was defined by a z-score lower than −1.96 and normal PWV when z-score was in between. We determined the frequency of EVA in the general population, as well as in young adults under 40 years and under 30 years.

As the primary objective of the present analysis was to describe the distribution of the predicted value of PWV adjusted for age and SBP in a general population sample, based on prior information [17] we expected a frequency of EVA around 10% (95% confidence interval (CI): 8–12%). Taking into account, an alpha error of 0.05 and a power of 90% we estimated a target sample size of 1100 individuals.

Table 2 Age, PWV, SBP, and DBP values ($n = 1416$)

	Mean (SD)	Min-max	Percentiles				
			10%	25%	50%	75%	90%
Age, years	49.9 (15.5)	20–91	27	38	51	61	70
PWV, m/s	7.5 (1.9)	2.1–15	5.1	6.0	7.3	8.7	10.1
SBP, mmHg	125.3 (16.7)	87–198	105	114	123.5	135.5	145
DBP, mmHg	78.9 (12.2)	49–118	65	72	79	86	92

PWV pulse wave velocity, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

We also evaluated independent baseline characteristics associated with EVA using multiple logistic regression models based on the whole population and further in subjects under 40 years, after excluding those with prior ASCVD events. We reported adjusted odds ratios (OR) 95% CIs and associated p-values to three decimals. For all tests, a p-value < 0.05 was considered significant. All analyses were performed using STATA version 14 (StataCorp, USA).

Results

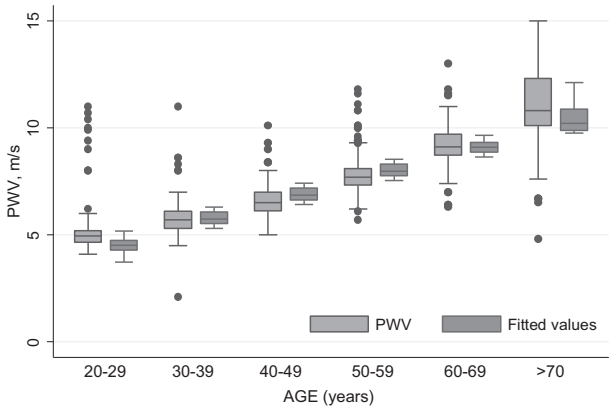
We recruited a total of 1511 subjects, of whom 1416 were included in the present report after excluding those with incomplete data (3.3%) or measurement failure (3%). Distribution per country was mostly in Argentina (76%), followed by México (7%), Brazil (5%), Colombia (5%), and the remaining countries (7%). Mean age was 49.9 (SD 15.5) years and male gender was 50.3%. Ninety-four percent reported completion of secondary school or had reached a higher educational level. The frequency of classic CVRF in the overall population was: current smokers 12.2%, dyslipidemia 58.3%, HTN 41.2%, diabetes 11.6%, overweight 34.9%, and obesity 24.4%. Regular exercise was reported by 60% of participants. Table 1 shows intake of alcohol, fruits, vegetables, fish, and nuts.

During the evaluation, 25% of the total population had HTN (of these 65% had prior HTN). Among those with prior HTN, 40% showed values >140 and/or >90 mmHg. Among those without prior HTN, 15% showed BP elevated values. Table 2 describes the distribution of age, PWV, SBP, and DBP in the total population. Mean PWV was 7.5 m/s (SD 1.9), with a 90th percentile of 10.1 m/s. We found 159 (11.2%) cases with PWV >10 m/s. Mean SBP was 125.3 mmHg (SD 16.7) and mean DBP was 78.9 mmHg

Table 3 Mean PWV according to age categories in the total population and in healthy subjects with neither cardiovascular risk factors nor prior ASCVD events

Age (years)	Total population ($n = 1416$)		Healthy subjects ($n = 455$)	
	n	Mean PWV (SD), m/s	*n*	Mean PWV (SD), m/s
<30	160	5.20 (1.18)	105	4.98 (0.91)
30–39	216	5.77 (0.79)	110	5.65 (0.73)
40–49	261	6.54 (0.70)	87	6.35 (0.78)
50–59	272	7.79 (0.81)	75	7.55 (0.77)
60–69	264	9.14 (0.86)	49	8.93 (0.99)
70–79	102	10.37 (1.36)	19	9.93 (1.86)
>79	41	12.35 (1.86)	---	---

PWV pulse wave velocity, *ASCVD* atherosclerotic cardiovascular disease



PWV: pulse wave velocity

SBP: systolic blood pressure

Fig. 1 Boxplots of PWV values predicted by the model and the observed PWV values adjusted for age and SBP. (Colour figure online)

(SD 12.2). Regarding young adults (<40 years), actual BP values showed systolic and/or diastolic HTN in 43 of 376 (11.4%), categorized as follows: isolated systolic HTN in 24 (6.4%), isolated diastolic HTN in 11 (2.9%), and combined systolic and diastolic HTN in 8 (2.1%).

Table 3 shows mean PWV per decade of life in the total population, and in the subgroup of healthy subjects with neither CVRF nor prior ASCVD events ($n = 455$). As expected, the observed PWV was lower in the healthy subgroup of each age category compared with the whole population.

In Supplemental Table 1, we present PWV means and SD according to decades and BP categories. Individuals <30 years with BP <120/80 mmHg showed the lowest PWV with a mean value of 4.8 m/s and individuals >80 years with BP >140/90 mmHg showed a mean PWV almost three times higher, with a value of 13.2 m/s.

Frequency of EVA

Multiple linear regression analyses with PWV as dependent variable was applied in a final model that included age, quadratic age (age^2), and SBP, showing for each variable a significant association with PWV. Supplemental Fig. 1 shows model development and the final model with, as expected, a very good linear prediction of PWV. Supplemental Fig. 2 shows the linear relationship of predicted and observed PWV values by age as a continuous variable, and Supplemental Figure 3 shows boxplots of the observed PWV across age categories, where some outliers stand out, such as high PWV values in young subjects and low PWV in elders. Boxplots in Fig. 1 indicate a very good correlation between PWV values predicted by the model and the observed PWV values across age categories, after adjusting for age and SBP. The PWV outliers described before remain after including SBP in the model.

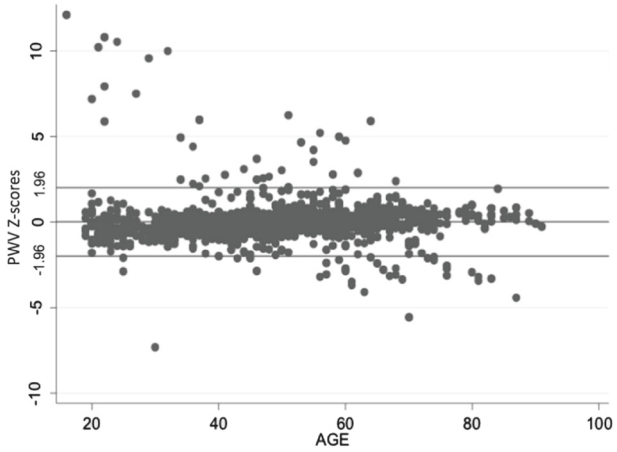
Finally, Fig. 2 shows a scatter-plot of PWV z-scores distribution according to age and SBP (standardized analysis). PWV z-score values higher than those predicted by the model (z-score higher than +1.96) persist in younger subjects. They complied with the EVA definition and represent 5.7% (81/1416) of the total sample. Additionally, PWV z-score values lower than those predicted by the model (z-score lower than −1.96) depict older subjects with the healthier arteries, who represent 4.5% (63/1416) of total population.

EVA frequency was also determined in the subgroup of young adults: we found 9.8% (37/376) in subjects <40 years and 18.7% (30/160) in those <30 years.

Variables associated with EVA

Multiple logistic regression analysis performed in the whole population, after exclusion of 90 individuals with prior ASCVD, and adjusted for alcohol intake and smoking, showed that variables significantly associated with EVA were age, OR 0.92 (95% CI: 0.90–0.94, $p < 0.001$), dyslipidemia, OR 2.36 (95% CI: 1.31–4.23, $p = 0.004$), and aspirin intake, OR 4.28 (95% CI: 1.84–9.97, $p = 0.001$) (Supplemental Figure 4a).

A similar analysis restricted to subjects aged 40 years or less determined that baseline characteristics significantly associated with EVA were age, OR 0.78 (95% CI: 0.72–0.85, $p < 0.001$), dyslipidemia, OR 6.88 (95% CI: 2.79–16.99, $p < 0.001$), history of HTN, OR 3.29 (95% CI: 1.02–10.55, $p = 0.045$), and regular alcohol intake, OR 0.27 (95% CI: 0.10–0.73, $p = 0.011$). Smoking showed a borderline significance, OR 2.32 (95% CI: 0.91–5.85, $p = 0.075$) (Supplemental Figure 4b).



PWV: pulse wave velocity
SBP: systolic blood pressure

Fig. 2 Scatter plots of the distribution of PWV z-scores according to age and SBP. (Colour figure online)

We further explored the association between alcohol intake and EVA after increasing the sample by including subjects <50 years but we did not find a significant association, OR 0.57 (95% CI: 0.24–1.30, $p = 0.18$).

Discussion

We found an overall frequency of EVA of around 6% in a mixed population sample from 12 countries in Latin America using a simple, practical, and affordable oscillometric device on the brachial artery, which estimates PWV as a surrogate of arterial stiffness. Interestingly, the EVA frequency was particularly elevated in young adults under 40 years (9.8%), and even higher in subjects under 30 years (18.7%).

According to our standardized analysis, including age and SBP determined simultaneously with PWV, z-scores suggested that EVA has a low frequency after the age of 60 years because PWV values are mostly predicted by older age and SBP. Interestingly, in this age subgroup we also recorded a frequency of 4.5% of individuals with a very low PWV that represent elderly subjects with the healthiest arteries.

We further described PWV means (and SD) in the total population stratified by age decades and BP categories. To separate healthy arteries and EVA in our sample, the percentiles 2.5th and 97.5th can be calculated by applying the formula PWV ± 1.96 SD to the values showed in Supplemental Table 1.

Finally, our study suggests that in young adults between 20 and 40 years the presence of dyslipidemia and HTN, and probably smoking, may contribute to the early development of arterial stiffness, or EVA, starting even in the early twenties when medical care is less often requested.

We also wanted to put our study results in perspective of previous studies with similar aims. The Guimaràes/Vizela Study [17] included 2542 randomly sampled subjects over 18 years from Northern Portugal. The authors applied an EVA definition based upon the age-adjusted normal European population of the Reference Values for Arterial Stiffness Collaboration, after measurements with a tonometric device (Sphygmocor) [7]. Therefore, a PWV ≥ 97.5th percentile of z-score for mean PWV values adjusted for age was considered as a practical definition of EVA. Consequently, they reported a 12.5% overall prevalence of EVA, with a 19.3% in subjects <40 years and 26.1% in those <30 years. Z-scores analyses in OPTIMO study, using its own sample z-scores as a normal reference, demonstrated a lower frequency of EVA (overall 5.7%, but 9.8% in subjects <40 years and 18.7% in <30 years).

The OPTIMO study design included a convenience sampling that probably reflects a more selected population if we take into account, for example, a high average educational level, which allows better lifestyle, nutrition, and healthcare, and also a higher use of lipid-lowering drugs, compared with the Guimaràes/Vizela Study (48% vs. 17.7%). Anyway, both studies found an elevated frequency of EVA in young adults.

We believe that the observed low frequency of EVA after 60 years reflects the fact that PWV is supposed to be a surrogate marker of arterial stiffness, which attempts to identify vascular damage at earlier stages of life than expected, but loses diagnostic precision with advanced age and higher SBP values [15]. Accordingly, multiple logistic regression analysis determined that age had an inverse independent relationship with EVA (OR 0.93) implying a stronger association in younger subjects than in older. This evidence does not argue against the elevated prevalence rate of PWV in the elderly and its independent prognostic value in this subgroup. However, to the best of our knowledge, the OPTIMO and the Guimaràes/Vizela studies [17] are the only screening studies that have reported a high frequency of EVA in younger adults.

Existing evidence reinforces the importance of EVA diagnosis in youth. Among 2849 elderly individuals, the Rotterdam study established that PWV added to the Framingham score allowed for a limited risk reclassification and did not provide a significant clinical utility to predict cardiovascular events during 8 years of follow-up [25]. Furthermore, an individual participant meta-analysis that included 17,635 subjects, determined that the predictive power of PWV for future ASCVD events and mortality was stronger in younger and middle-aged subjects than in older people [15].

Regarding the PWV cut-off value of 10 m/s proposed by a consensus document [26], we believe that using fix thresholds regardless of age and BP, whichever the

measurement technique applied, does not work for our operational definition of EVA, and probably it also represents an imperfect marker of subclinical organ damage, particularly in the older. In OPTIMO study, we found 11.2% individuals with PWV over the proposed limit that does not necessarily match with cases of EVA. Actually, EVA cases in young adults are mostly below PWV of 10 m/s (see outliers in Fig. 1).

Regarding the use of a similar oscillometric device in a general population, Nunan et al. [27] performed an interesting study estimating PWV with Mobil-O-Graph in 1794 subjects from a community setting ("real world") in Vienna, Austria. As we did in OPTIMO study, they adjusted PWV for age and BP levels, but also for gender. PWV results were quite similar in both studies, with mild differences around 0.65 m/s on average in subgroups <70 years, probably due to population samples features. Between subgroups 70 and 79 years old, there was a higher difference of 1 m/s (11.4 m/s in Nunan et al. vs. 10.37 m/s in OPTIMO study). However, in those elderly subjects with BP <140/90 mmHg, both studies reported a similar PWV (10.6 and 10.5 m/s, respectively). A possible explanation is that in the first study the rate of elevated BP >140/90 mmHg was higher compared with OPTIMO study (60% vs. 30%, respectively), probably due to a higher proportion of pharmacologically treated subjects in our sample (95% of those with prior HTN).

To the best of our knowledge, this is the first study determining EVA frequency in a sample from Latin America. There exists some regional reports from population-based studies on normal/reference PWV values according to age and BP categories in healthy individuals, mostly performed with tonometric methods [22, 28–30]. They provide a basis for diagnosis of vascular aging but, however, they do not report EVA prevalence, neither in the general nor in the young adult population.

Analyses of the baseline characteristics of young adults under 40 years in our OPTIMO study suggest that EVA is associated with biological determinants, such as history of HTN, dyslipidemia, and smoking. Similarly, the Amsterdam Growth and Health Longitudinal Study (AGAHLS) described that the same CVRF during adolescence and young adulthood anticipated the development of arterial stiffness at the age of 36 years [31]. Both arteriosclerosis and EVA reach a high prevalence in youth, relatively speaking [17, 18]. Therefore, in spite of the lack of data related to ASCVD outcomes in young populations, these findings support the aim of promoting cardiovascular prevention during childhood or adolescence, that is, through healthy lifestyle in order to prevent arterial stiffening during the following years and thereby potentially reducing the risk of future ASCVD events and increasing survival [32, 33].

A potential biased finding in the OPTIMO study was the observation of a beneficial relationship between regular alcohol intake and EVA in young adults. The INTERHEART Study demonstrated that regular alcohol intake, defined as three or more times per week, was an independent "protector" for myocardial infarction adjusted by age, sex, and smoking (OR 0.79, 95% CI: 0.73–0.86), but not when other CVRFs were added to the model [34]. Furthermore, a subgroup analysis demonstrated that regular alcohol intake was not significantly associated to risk of myocardial infarction in subjects <45 years (OR 0.94, 95% CI: 0.81–1.11) [35]. Our data showed a benefit of regular alcohol intake on PWV in young adults <40 years, however, the effect disappeared by expanding the subgroup sample size to subjects <50 years. The risk of EVA for aspirin users could reflect another observational bias, because subjects with elevated cardiovascular risk are more expected to be treated or self-medicated with aspirin.

Strengths and limitations

The prospective cohort design included a diverse ethnic population from many countries of Latin America. However, a high proportion of participants were included in one country. Therefore, the lack of a representative sample limits us to refer to frequency of EVA instead of prevalence.

Importantly, data collection was performed using a standardized questionnaire with predetermined definitions, and PWV, as well as BP were determined in all subjects using the same type of device and measurement protocol. In spite of the lack of a direct measurement of PWV, the oscillometric device Mobil-O-Graph has been satisfactorily compared with the applanation tonometry (SphygmoCor) and other devices [13, 21–24]. Furthermore, it is easy to use with a simple training and is relatively inexpensive.

Luzardo et al. [22] compared Mobil-O-Graph measurements with a tonometric device (SphygmoCor) in a volunteers sample from Uruguay. In the substudy performed at rest in the laboratory, they found no significant differences in observed results, reporting a mean PWV of 7.3 (SD 1.9) m/s with tonometry and 7.0 (SD 2.2) m/s ($p = 0.11$) with oscillometry. They found a statistically significant difference in PWV (7.9 m/s, SD 2.1, vs. 7.4 m/s, SD 1.6) but only in the substudy performed with Mobil-O-Graph "ambulatory" monitoring during 24 h, a different condition compared with our OPTIMO evaluation at rest. Anyway, tonometric methods represent the gold standard for PWV and large prospective studies are still needed to validate oscillometric devices.

Increasing age is a strong marker of arterial stiffness, and SBP is a surrogate of it, particularly in older people [8, 9, 11–13]. Therefore, we believe that our proposed methodology to predict PWV based on a multiple linear

regression model adjusted for age and SBP, followed by a standardized residuals analysis, allowed us to determine a realistic frequency of EVA in our sample. We also adjusted the analyses for treatment with lipid-lowering and antihypertensive drugs.

Our limited study population sample size is insufficient to generate firm conclusions on frequencies, particularly in some categories of age and BP distribution including a small number of participants, as well as some associations between baseline characteristics and EVA. Furthermore, our sample is biased due to the convenience sampling design performed at some private medical centers or shopping areas where educated and health-conscious people predominate, instead of recruiting a random population sample. As previously mentioned, an increased use of lipid-lowering (48%) and antihypertensive drugs (40%), a high rate of self-reported regular exercise (60%), and dominance of participants with high educational levels, support the existence of this potential bias. The cross-sectional design only allows us to determine associations, but not causality. Finally, the lack of an independent comparative cohort in Latin America for derivation of cut-off levels for EVA to be used in OPTIMO study is regretful, but as the OPTIMO study is the first on the continent other screening studies will probably follow.

In recent years, arterial stiffness has emerged as an independent predictor of cardiovascular risk and represent a core component of the novel EVA syndrome along with other changes of the arterial wall [1, 5]. Measurement of PWV is currently accepted as the most simple, noninvasive, and reproducible method to determine arterial stiffness [6]. An individual participant meta-analysis of 17,635 subjects has demonstrated its independent prognostic value to predict future ASCVD events and mortality, even after adjusting for classic CVRF, and allows reclassification of risk categories, particularly in young people [15].

In spite of attempts to standardize reference values of PWV obtained by different techniques (i.e., tonometric, oscillometric, ultrasound, magnetic resonance imaging) [7], the EVA syndrome represents a "proof of concept" still without an exact established definition [36]. However, we believe that searching for EVA based on PWV values from any validated method at this stage represents a step forward in cardiovascular prevention. In this direction, the OPTIMO study represents a multicenter experience from Latin America setting the basis of EVA prevalence and encourages future clinical work and research in the field.

Young adulthood (age between 20 and 40 years) represents the healthiest period of life, and therefore cardiovascular health promotion is usually scarce in this age group. Accumulated evidence calls for attention and debate regarding the age of initiation of cardiovascular screening for subclinical arteriosclerosis and atherosclerosis. The "Progression of Early Subclinical Atherosclerosis" (PESA) study [18] included 40–54 years asymptomatic participants and determined the existence of 63% of subclinical atherosclerosis in any of the carotid, abdominal aortic, iliofemoral, or coronary territories. The authors of PESA reported that among subjects with a low 10-year risk calculated with the Framingham risk score, 58% had subclinical disease. If we consider, for example, that in the United States [37], the mean age of ST-elevation myocardial infarction is 64 (SD 13) years, therefore 34% (1 SD) occur between 51 and 64 years and 14% (2 SD) between 38 and 51 years. Consequently, strategies to prevent these ASCVD events in young people should start 10–15 years earlier. We believe that detecting an EVA syndrome before the age of 40 and even 30 years represents a contemporaneous challenge for cardiovascular prevention.

Conclusion

The OPTIMO study shows a frequency of EVA around 6% among a population sample from Latin America, with a higher rate in young adults. Baseline variables associated with EVA in the former subgroup were well-known CVRF, such as HTN, dyslipidemia, and smoking. Our results are consistent with those from others, and call for a debate about the search for CVRF and subclinical atherosclerosis during early adulthood. In this regard, determination of arterial stiffness (EVA) using measurements of PWV with simple and inexpensive devices might help to select subjects from these age groups at increased cardiovascular risk who deserve a more intense preventive intervention and follow-up.

Summary Table

What is known about this topic?

- EVA is a growing clinical concept that refers to an increased arterial stiffness (arteriosclerosis) when compared with the expected level of arterial stiffness according to the chronological age.
- There is no data about EVA prevalence and its characteristics obtained from a population sample in Latin America.
- Little is known about determinants of EVA in young adults.

What this study adds?

- We found an overall frequency of EVA of around 6% using a simple oscillometric device on the brachial artery, which calculates the PWV as a marker of arterial stiffness.

- EVA frequency was higher in young adults under 40 years (9.8%), and even higher in subjects under 30 years (18.7%).
- In young adults, the presence of dyslipidemia and hypertension, and probably smoking, may contribute to the early development of EVA.

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Compliance with ethical standards

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