

**Vascular age in patients admitted for coronary syndrome with ST segment elevation**

**Abstract:**

**Background:** Vascular age is an emerging health indicator and predictor of vital organ damage (heart, brain, and kidneys). Arterial stiffness is the most widely used measure for predicting vascular aging status. For a very long time, specific risk calculation algorithms were used for each cardiovascular disease, but they were not used to approximate vascular age and therefore to give an idea of the risk of all cardiovascular complications. A review of all epidemiological studies is therefore necessary to allow a global and multimodal evaluation of the different determinants of vascular age and the association of vascular aging with cardiovascular events.

**Methods and results:** We are conducting a retrospective descriptive and analytical study of 284 patients admitted to the cardiology department for STEMI. The mean chronological age of our patients was 60.89 years, while the vascular age was much higher, up to 75 years. The vascular age of STEMI patients is 14 years higher than the chronological age. The definition of the early vascular age, normal VA and Supernova profiles was based on the calculation of the difference between chronological age and vascular age, then the different clinical and paraclinical parameters of the 3 categories were studied allowing to conclude after a multivariate analysis that: diabetes (OR=9.25, [3.52; 24.36],  $p < 0.0001$ ) and smoking (OR=12.01, [4.56; 31.62],  $p < 0.0001$ ) were associated with higher rates of EVA, while hypertension (OR=1.35, [0.58; 3.1],  $p = 0.485$ ) is a neutral factor. Also, age (OR=1.23, [1.11; 1.38],  $p = 0.0002$ ), age range between 40 and 54 years old (OR=42.53, [7.04; 256.82],  $p < 0.0001$ ) promotes the EVA phenotype while advanced age is a confounding factor. Regarding gender, female (OR=0.35, [0.13; 0.96],  $p = 0.041$ ) is a protective factor.

From this analytical study we observe that there is a large difference between chronological and vascular age. This is due to the interaction between the different risk factors and each one potentiates the other. More the patient has risk factors, the more his vessels are sick and the more he risks having fatal events. And this has an impact on the overall management of the patient.

**Keywords:**

Chronological age, vascular age, aging, cardiovascular risk factors, cardiovascular diseases, early vascular age, SUPERNOVA.

## **I. Introduction:**

Cardiovascular diseases are a multisystemic damage that affects different organs and tissues. They correspond to a disease related to age. Most cardiovascular risk estimates are strongly influenced by chronological age and, starting from 50 years, age turns out to be the predominant cardiovascular risk factor. In fact, aging is a physiological process characterized by a deterioration of the function and composition of the different tissues and therefore is a cause of multimorbidity [1]. This same process applies to arteries, arteries are very sensitive to the variation of the internal environment that can be secondary to aging and different CVRF, especially those of medium and large size. This is why it is necessary to introduce a new concept including the different angles to estimate the vascular age of the patient and from all this we classify the patients in early (EVA) and abnormal aging (SUPERNOVA).

## **II. Methods:**

We conducted a retrospective, descriptive and analytical study of 284 patients admitted to the cardiology department of Mohammed IV University Hospital of Marrakech for STEMI over a period of 1 year from December 2021 to December 2022. We excluded from our study any incomplete file. The examination of the files made it possible to obtain the information necessary for our studies, ranging from the patient's socio-demographic variables, sex, cardiovascular risk factors, the patient's clinical history to the clinical examination and the results of biological tests. The levels of total cholesterol, LDL and HDL cholesterol in serum were determined by standardized enzymatic methods. The calculation of vascular age was done according to the Framingham model using the version of the French committee for the fight against hypertension (CFLHTA), variables included in the model were age, sex, total cholesterol, HDL cholesterol, systolic blood pressure, use of antihypertensive medications, current smoking, and diabetic status.

Age ranges 1, 2 and 3 represent respectively the age ranges 40-54 years, 55-69 years, and 70-84 years. The  $\Delta$ -age was calculated as the chronological age minus the vascular age. The 10th and 90th percentiles of  $\Delta$ -age were used as cutoffs to define the EVA and SUPERNOVA.

The quantitative variables were represented in mean standard deviation and extreme, and qualitative variables were represented in number and percentage using excel Microsoft office 2016.

The Easymed Stat software version 3.21.5 was used for the multivariate analysis by logistic regression with as independent variable vascular age (VA) compared to the dependent variable: chronological age, age range, sex, hypertension, diabetes, and smoking. Data were checked for multicollinearity with the Belsley-Kuh-Welsch technique. Heteroskedasticity and normality of residuals were assessed respectively by the White test and the Shapiro-Wilk test. A p-value < 0.05 was considered statistically significant.

Patients' anonymity was respected.

## **III. Results**

### III.1. Demographic characteristics

The study population for the calculation of vascular age was selected from a pool of patients admitted to cardiology department for STEMI.

The characteristics in terms of the different ages studied are summarized in table 1. The average chronological age of our patients was 60,89 years with extremes ranging from 40 to 82 years, while the vascular age was much higher, up to 75 years, which allowed us to have a  $\Delta$ -age of -14, a negative value since the chronological age is lower than the vascular age.

### III.2. Clinical characteristics

The clinical characteristics and risk factors of the entire study population are presented in table 2. There is a clear male predominance with a percentage of 76,1%. The age range 2 represents the largest portion (57,36%), followed by the range 1 (26,06%) while the older subjects represented by the range 3 represent only 16,55%.

41,95% of the population was constituted of hypertensive patients and 46,02% of patients with diabetes mellitus, while smokers are more numerous and represent 52,8% of which 68,44% are still active.

The results of the blood pressure measurement and the lipid balance represented in mean and standard deviation are summarized in table 3.

$\Delta$ -age was calculated as the difference between chronological age and vascular age, and the 10th and 90th percentile of the  $\Delta$ -age distribution was used as thresholds to define EVA and SUPERNOVA, respectively. Indeed, EVA was defined when vascular age was greater than chronological age by  $>5.7$  years ( $\Delta$ -age  $<-5.7$  years) and SUPERNOVA when vascular age was less than chronological age of 6.2 years or more ( $\Delta$ -age  $>6.2$  years). The clinical characteristics of the 3 VA categories (EVA, normal VA, and SUPERNOVA) are presented in Table 4.

### III.3. Characteristics of the population in bivariate analysis

In bivariate analysis, the median age was respectively  $59.75 \pm 8.59$  and  $65.97 \pm 12.29$  for patients whose normal VA (indicated by no in the Graph) and EVA (indicated by yes in the Graph) (difference: 5.0,  $p=0.008$ ) (Graph 1).

The EVA rates were 13.95%, respectively 10.61% for Male whose Gender is and Female patients ( $p=0.54$ ) (Graph 2).

The EVA (indicated by yes in the Graph) rate was 20.0% for diabetic patients versus only 4.76% for non-diabetic patients ( $p<0.001$ ) (Graph 3)

This same observation applies to smoking, since the EVA (indicated by yes in the Graph) rate of 22.9% was reported in smoking patients, compared to 4.67% in non-smoking patients ( $p<0.001$ ) (Graph 4).

Hypertension is considered a neutral factor since the rate of EVA was 12.35%, respectively 14.29% in hypertensive and non-hypertensive patients ( $p=0.767$ ) (Graph 5).

### III.4. Characteristics of the population in multivariate analysis

The logistic regressions allowing to study the relation between the vascular age and the different studied variables (age, age range, gender, hypertension, diabetes, and smoking) are represented in table 5. To be noted that only the EVA and normal VA were compared with the independent variables given the insufficient number of patients SUPERNOVA.

From these multivariate analyses we can conclude that diabetes (OR=9.25, [3.52; 24.36],  $p < 0.0001$ ) and smoking (OR=12.01, [4.56; 31.62],  $p < 0.0001$ ) were associated with higher rates of EVA, while hypertension (OR=1.35, [0.58; 3.1],  $p = 0.485$ ) is a neutral factor.

Likewise, age (OR=1.23, [1.11; 1.38],  $p = 0.0002$ ), age range 1 (OR=42.53, [7.04; 256.82],  $p < 0.0001$ ) promotes the EVA phenotype, while female gender (OR=0.35, [0.13; 0.96],  $p = 0.041$ ) is a protective factor.

Concerning the age ranges 2 and 3, they lend to a confusion factor, since the more one advances in age the more the chronological age approaches the vascular age and thus the delta-age will be falsely more reassuring.

### IV. Discussion:

Vascular aging is a new concept that tends to replace the classical assessment of cardiovascular risk factors and is characterized by its close link to CVRF, in fact, the cumulative effect of CVRF tends to accelerate this process. Alterations in endothelial function, the reduction of vascular elasticity and an increase in stiffness are its main effects [2]. As a result, the vessel wall stiffens and is less able to adapt to the pulsatility of blood pressure resulting in excessive blood pressure and pulsatility observed in the microvasculature of organs such as the brain, kidneys and heart, resulting in damage and sometimes irreversible failure of these organs [3].

Most of the studies done on cardiovascular risk factors have created specific risk algorithms for each CV disease, for example, that of coronary artery disease by Assmann and al [4], and the algorithm of Zhang [5]. This is not easy to apply routinely in the medical office, hence the need to bring out global risk tools for all CVD to guide both primary prevention and to select diseases for which measures should be intensified [6]. Therefore, vascular age takes place especially in young patients, in whom the classical risk of the 10-year risk is low and can give a misleading impression, so vascular age is particularly important. [7]. From this principle the Framingham score study originated as a study of a single multivariable risk function that predicts the risk of developing all cardiovascular diseases and its cardiovascular diseases and its components [6].

After studying our sample, we found that some patients are younger than their chronological age (supernova), but this phenomenon is not frequent and represents only 1% of our patients, unlike the majority who have a vascular age higher than their chronological age (EVA), so patients with a previous cardiovascular event (STEMI in our sample) are more likely to be high vascular age

patients. This same observation was reported by the study of Bruno and al. which concluded that patients with vascular age lower than 6 years chronological age have 40% less cardiovascular events [8] (figure 1).

So, for a substantially similar vascular age and cardiovascular (CV) risk profile, early vascular aging (EVA) individuals are significantly younger and supernormal vascular aging (SUPERNOVA) are significantly older than the normal vascular aging (VA) aging group. Consequently, SUPERNOVA subjects have the largest difference between chronological and vascular age ( $\Delta$ -age,); conversely, EVA subjects have negative  $\Delta$ -age. This translates into a lower rate of CV events in SUPERNOVA subjects, and a higher rate in EVA subjects; in other words,  $\Delta$ -age is inversely associated with CV events.

The male predominance in the EVA group was not consistent with Bruno's results and this is probably due to the underestimation of cardiovascular risk in women in our context and that women have both strokes and MI (whereas our series only includes STEMI) [8,11].

Our observation concerning the neutrality of the hypertension towards the 2 groups EVA and normal VA was also reported by Bruno [8] with similar percentage of hypertension in the 2 groups (60% Vs 60,7%). Similarly, in the cohort of the Malmö Diet and Cancer Study [12], the difference between the percentages of hypertension in the 2 categories of EVA and normal VA was not very important, respectively 76% and 62,4%.

On the other hand, as Bruno's study showed, mortality in the SUPERNOVA group was not low, and this can be explained by the fact that hypercholesterolemia and mild obesity, could paradoxically protect (reverse causality) against non-cardiovascular and all-cause mortality in the very old [8,9,10].

### **Conclusion:**

The vascular age of STEMI patients is 14 years higher than the chronological age. We have shown that vascular age and therefore the rate of cardiovascular events is closely related to age, male sex, diabetes, and smoking, while hypertension is a neutral factor. This is to identify people at premature risk of cardiovascular events and therefore who will undergo strict interventions to stop the evolution of atheromatous disease, and the SUPERNOVA phenotype, resistant to the deleterious effects of aging and western lifestyle on the cardiovascular system.

### **Declarations**

### **Abbreviations**

STEMI: ST elevation myocardial infarction

VA: Vascular age

OR : Odd ratio

CVRF: Cardiovascular risk factor

EVA: Early vascular age

LDL: Low density lipoprotein

HDL: High density lipoprotein

TC: Total cholestérol

BP : Blood pressure

CVD : Cardiovascular diseases

#### **Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### **consent for publication**

Not applicable

#### **ethical approval and consent to participate.**

The study protocol was in accordance with the 1975 declaration of Helsinki. The informed consent was cancelled by the ethics committee of the clinical research center of the Mohammed VI University Hospital of Marrakech due to the retrospective nature of our study.

#### **References:**

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**Table 1: Summary table of the different ages studied represented by mean and standard deviation.**

Variable	Moyenne ± ET
Age chronologique, an	60,89±9,36
Age vasculaire, an	75,1±9,24
Δ-age, an	-14,59±8,60

**Table 2: Summary of clinical characteristics of our sample**

Variable	Effectif	Pourcentage
Sexe masculin	216	76,1%
Tranche d'age		
1	74	26,06%
2	163	57,36%
3	47	16,55%
Tabagisme	150	52,8%
Tabagisme actif	102	68,44%
Hypertension	119	41,95%
Diabète	126	46,02%

**Table 3: Results of blood pressure and lipid profile in mean and standard deviation**

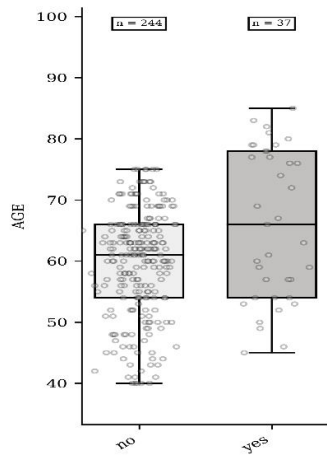
Variable	Moyenne± ET
Pression artérielle systolique, mmHg	131,70±20,63
Pression artérielle diastolique, mmHg	76,18±11,47
CT	1,80 ±0,44
HDL	0,42±0,10
LDL	1,12±0,40

**Table 4: Clinical characteristics and results of the different measurements of the 3 age categories vascular**

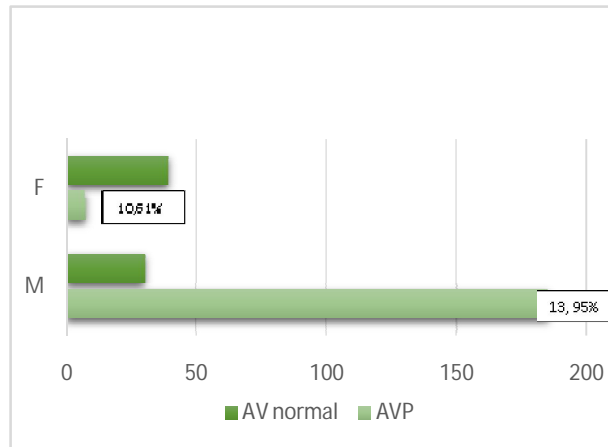
Variable	AVP ( $\Delta$ -age <-5.7 an, n=242)	Age vasculaire normal (-5.7 $\leq$ $\Delta$ -Age <6.2 an, n=37)	SUPERNOVA ( $\Delta$ -age >6.2 an, n=3)
Age chronologique, an	59,79	65,97	62
Age vasculaire, an	76,70	66,89	51,66
$\Delta$ -age, an	-17,08	-0,91	10,33
Sexe masculin (%)	76,13%(184)	81,08%(29)	33,33%(1)
Sexe féminin (%)	23,87%(58)	18,92%(8)	66,37%(2)
tabagisme(%)	58,8%(142)	18,9%(7)	0%
Tabagisme actif (%)	59,05%((83)	31% (2)	0%
Hypertension(%)	41,15% (99)	45,94%(17)	0%
Diabete (%)	48,97%(120)	16,2%(6)	0%
Pression artérielle systolique, mmHg	132,44	131,16	104,33
Pression artérielle diastolique, mmHg	76,69	73,2	60,66
Cholesterol total, g/L	1,76	1,83	1,52
HDL cholesterol, g/L	0,40	0,57	0,45
LDL cholesterol, g/L	1,09	1,07	0,80

Table 5: Regression coefficients and Odds Ratio of the different dependent variables compared to the independent variable, vascular age

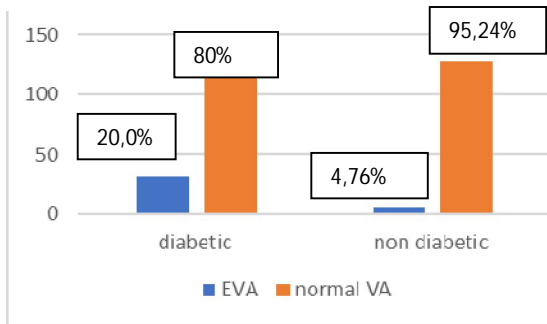
		Age vasculaire normal	AVP	p	OR
Diabetes	Oui	6 (16,21%)	31(83,79%)	<0,0001	9,5[3,52-24,36]
	Non	120(49,18%)	124(50,81%)		
Hypertension	Oui	17(45,97%)	20(54,03%)	0,485	1,35[0,585-3,1]
	Non	102(41,80%)	142(58,19%)		
tabagisme	Oui	7(18,91%)	30(81,09%)	<0,0001	12,01[4,56-31,62]
	Non	143(58,60%)	101(41,40%)		
Age (moyenne± ET)		59.75 ± 8.59	65.97 ± 12.29	<0,001	1,23[1,11-1,38]
Tranche d'age	1	11(6,79%)	151(93,21%)	<0,0001	42,53[7,04-256,82]
	2	10(13,69%)	63(86,31%)	<0,0001	0,0235[0,00389-0,142]
	3	30(65,21%)	16(34,79%)	0,00706	0,0219[0,00136-0,353]
sexe	M	30(13,95%)	185(86,04%)	0,041	2,86[1,04-7,84]
	F	7(10,60%)	59(89,40%)		



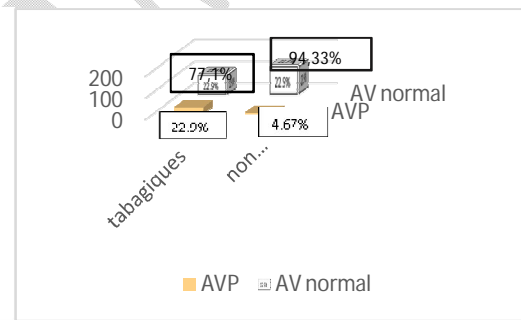
Graph 1: Median age of patients with VAS and normal VAS



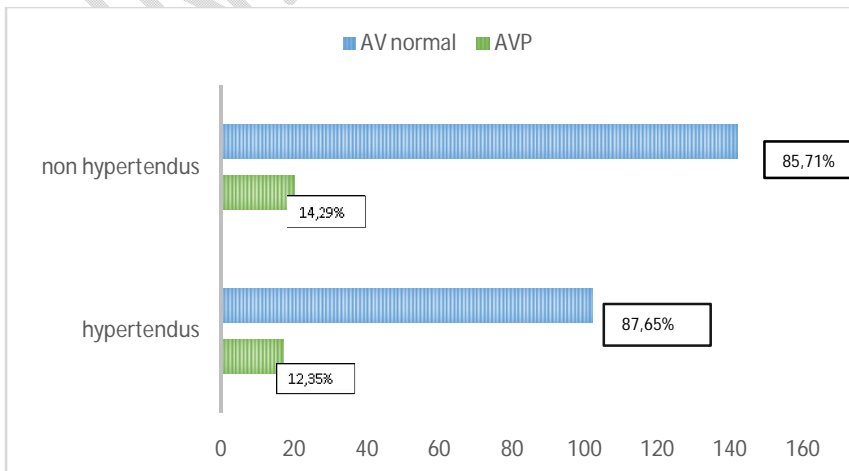
Graph 2: Percentage of AVP for women and men



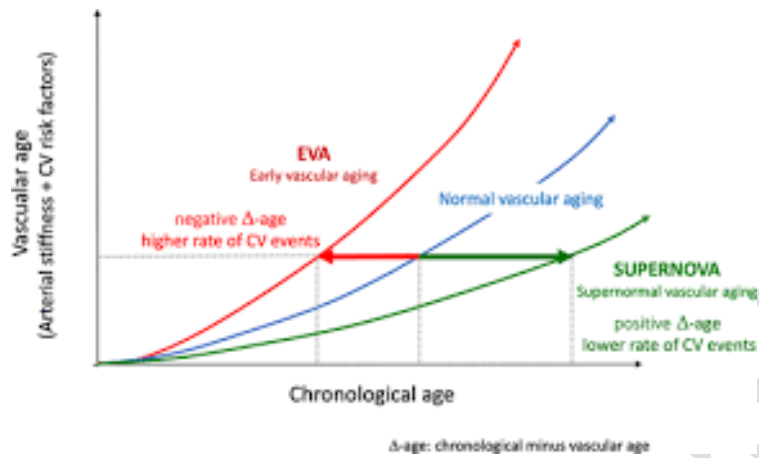
Graph 3: Percentage of AVP for diabetic patients



Graph 4: Percentage of AVP for patients who smoke



Graph 5: Percentage of AVP for hypertensive patients



**Figure 1: Figure showing that individuals with the greatest difference between chronological age and vascular age ( $\Delta$ -age) have the lowest rate of cardiovascular events, independent of conventional cardiovascular risk factors.[8]**