Beyond *Heart Rate*

Cardiovascular Age Unlocks
New Dimensions of Health

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Foreword

As a physician deeply committed to precision medicine, I am fascinated by the interface of technology, biosensors, and biomarkers and how specific metrics can accelerate behavior change and activate health. Oura Ring stands at the forefront of this revolution, offering novel insights like Cardiovascular Age, which is described in this white paper. Recent technology enables us to monitor and manage science-based wellness with accuracy previously unattainable, aligning closely with my philosophy of personalized health solutions.

The interplay between technology and biology, detailed in this white paper as the basis for Oura's Cardiovascular Age feature, provides a disruptive approach to personalized health. By harnessing data from daily life, Oura offers a precision map to help create, improve, and support the highest expression of health, mirroring the principles of precision medicine that I advocate and practice.

The potential for Oura to detect early signs of health issues, track recovery progress, and even help a clinician anticipate future health challenges is a potent testament to the role of technology like Oura in our evolving healthcare ecosystem.

I am optimistic about the potential of technology like Oura to empower individuals in their health journeys, transforming the way we approach disease prevention, detection, and management. The integration of wearables into our daily lives signifies a leap towards a future where healthcare is no longer reactive but rather proactive, predictive, participatory, and preventive. This white paper contributes to our understanding and utilization of such technologies, heralding a new era of health and well-being.

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Key Terms

Arterial stiffness Rigidity of the arterial wall.[1]

Carotid-femoral pulse wave velocity (cfPWV) Measure of aortic stiffness and an established measure of vascular aging.[2] cfPWV is an estimation of the speed at which pulse pressure waves travel through the aorta to the leg, indirectly measured by capturing the wave's counterpart at the carotid artery in the neck.

Diastolic blood pressure Lowest arterial blood pressure of a cardiac cycle occurring during diastole (relaxation and dilation of the chambers of the heart, specifically the ventricles during which they fill with blood) of the heart. [3, 4]

Heart failure Condition in which the heart is unable to pump blood at an adequate volume.[5]

Myocardium Middle muscular layer of the heart wall.[6]

Photoplethysmography (PPG) Optical technique that can be used to detect blood volume changes in the vascular bed.[7]

Systolic blood pressure Highest arterial blood pressure of a cardiac cycle occurring immediately after systole (the contraction of the heart by which the blood is forced out of the chambers and into the aorta and pulmonary artery) of the left ventricle of the heart.[8, 9]

Executive Summary

- Oura has introduced a pioneering approach to understanding and managing cardiovascular health with advanced analysis of estimated arterial stiffness. The Cardiovascular Age feature builds upon the rich data collected during periods of rest and sleep, offering members insights into the aging of their cardiovascular system.
- Oura Ring utilizes photoplethysmography (PPG) technology to estimate arterial stiffness and cardiovascular age, providing a deeper understanding of vascular health and aging.
- Oura offers members actionable insights into how lifestyle factors influence their vascular health, emphasizing the role of physical exercise, dietary habits, and lifestyle choices in maintaining cardiovascular health – and Cardiovascular Age provides a novel composite metric of a personalized, proactive health future.
- This feature complements existing Oura features, such as sleep, activity, stress and resilience, and heart rate tracking, providing a more holistic view of the member's health and well-being.
- The Cardiovascular Age feature represents a significant advancement in personal health monitoring, empowering Oura members to take control of their vascular health, make informed decisions, and take data-informed action to improve their overall health and longevity.

Introduction

The human heart is a tireless pump ensuring all parts of the body receive the oxygen and nutrients required to function. As the heart moves blood, the pumping motion generates pulsatile pressure waves. The larger conduit arteries of the body act as shock absorbers that dampen and slow down the pulsatile forces generated by the heart. This ensures that the smaller, more sensitive microcirculation receives a laminar flow of blood and steady tissue perfusion. Over time, large arteries can stiffen and lose elasticity, a condition called large artery stiffening (LAS). During this process, larger arteries lose the ability to cushion pulsatile forces. This stiffening can lead to numerous health problems affecting blood vessels, the heart, and other organs.[10]

While aging is an inevitable and unmodifiable cause of LAS, it can be exacerbated by lifestyle-related factors such as obesity, smoking, insulin resistance, and high cholesterol. Eventually, LAS leads to a self-reinforcing loop of increasing blood pressure and risk of target-organ damage. Fortunately, physical exercise has been found to slow down, and in some cases even reverse, arterial stiffness.[11]

The main mechanisms of adverse clinical manifestations of LAS are threefold: isolated hypertension, impaired coronary artery circulation with increasing myocardial strain, and facilitation of a greater influx of pulsatile force into sensitive microvasculature. These factors lead to not only a significant loss in quality of life but also a significant decrease in years of life.[12]

Cardiovascular age carries significance beyond its effects on vascular health, extending to broader implications for overall well-being, lifespan, and healthspan. It stands as a crucial biomarker, providing nuanced insights into an individual's health status. With an understanding of cardiovascular age, individuals can take a proactive and personalized role in their health and make decisions related to lifestyle modifications for improved health outcomes. Thus, the concept of cardiovascular age offers actionable opportunities to shape health trajectories, fostering long-term health.

The Cardiovascular Age (CVA) feature from Oura provides an estimate of cardiovascular age and is an advancement that marks a significant departure from traditional methods used to approximate this metric. Oura gauges CVA by analyzing age-related observations within the photoplethysmograph (PPG) signal, which carries information about estimated arterial stiffness and pulse wave velocity (PWV). Carotid-femoral pulse-wave velocity (cfPWV) is also estimated by analyzing the PPG signal collected by Oura Ring during sleep and is a metric for measuring arterial stiffness and vascular aging. In the Oura App, both are shown as continuous variables accompanied by educational content and insights on improving one's CVA.

Background and *Research*

Arterial stiffness, mortality, and *cardiovascular outcomes*

A large body of literature shows that arterial stiffness, as measured by PWV (with cfPWV as the accepted standard) is a strong predictor of total, and cardiovascular, mortality, even after adjusting for multiple traditional risk factors, such as age, BMI, smoking history, and blood lipids.

In a meta-analysis of 17 studies (15,877 subjects combined, mean follow-up 7.7 years), Vlachopolous et. al. used a study-specific classification of high vs. low PWV and reported adjusted risk ratios (RRs) of 2.26, 2.02 and 1.90 for all cardiovascular events, cardiovascular mortality, and all-cause mortality, respectively.[13] These correspond to 226%, 202%, and 90% higher relative risks.

In a more granular analysis, the authors report that each incremental 1 m/s in PWV was associated with a 14% higher relative risk of any cardiovascular event. The same incremental increase was also associated with a 15% higher relative risk of cardiovascular and all-cause death. To put this into context, the normal reference values for PWV according to age groups have been established as follows (adopted from European Heart Journal):[14]

Figure 1. Distribution of pulse wave velocity (m/s) according to the age category in the normal values population (1455 subjects)[14]

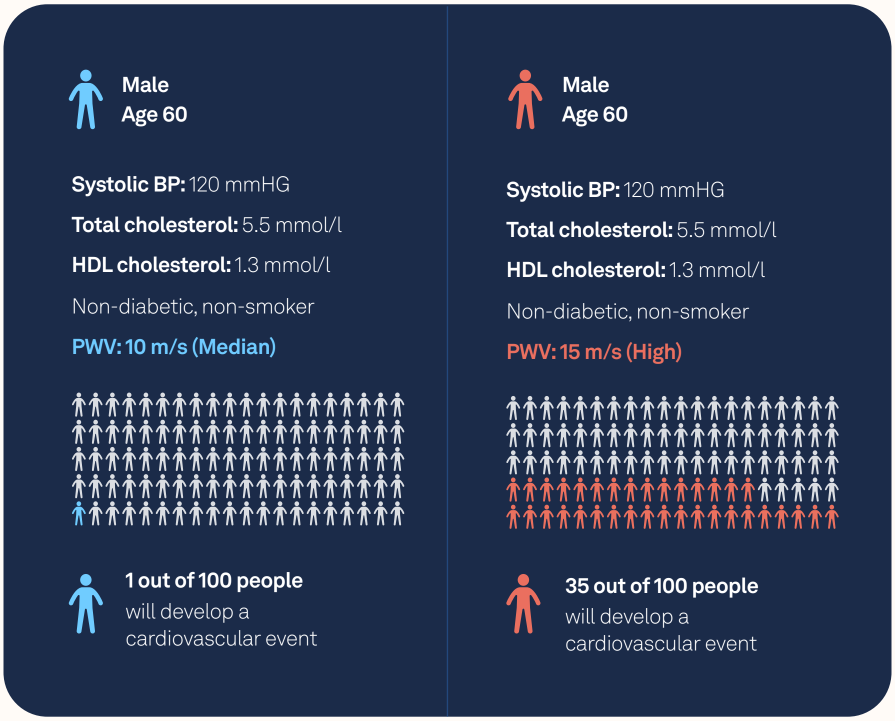
Age category (years)	Mean (±2 SD)	Median (10-90 pc)
<30	6.2 (4.7—7.6)	6.1 (5.3—7.1)
30-39	6.5 (3.8—9.2)	6.4 (5.2—8.0)
40-49	7.2 (4.6—9.8)	6.9 (5.9—8.6)
50-59	8.3 (4.5—12.1)	8.1 (6.3—10.0)
60-69	10.3 (5.5—15.0)	9.7 (7.9—13.1)
≥70	10.9 (5.5—16.3)	10.6 (8.0—14.6)

SD, standard deviation; 10 pc, the upper limit of the 10th percentile; 90 pc, the lower limit of the 90th percentile.

As the study by Vlachopolous et. al. was based on summary statistics and underpowered to study the associations within various subgroups, a subsequent meta-analysis by [Ben-Shlomo et al.](#) used individual-level data and a larger data set to confirm the predictive value, even when the population was stratified according to sex, presence of hypertension, or diabetes. [15]

As a practical example, Ben-Shlomo et. al. demonstrate that in an otherwise healthy 60-year-old man (non-smoking, non-diabetic, optimal blood lipids and blood pressure), a 1 m/s higher PWV is associated with a fully-adjusted 7% higher relative risk of cardiovascular events (visual illustration of this is depicted in Figure 2).

Figure 2. Visual illustration of the relative cardiovascular event risk associated with increased pulse-wave velocity. Data adopted from Ben-Shlomo et al and assuming linear increase of 7% relative risk per 1 m/s pulse wave velocity.



Understanding Cardiovascular Age: *Making sense of risk factors*

To understand the evaluation of heart disease risk via the measurement of blood lipids and glucose, consider how one monitors traffic to estimate its impact on local infrastructure. Observing the volume and type of traffic can infer impacts on roads during peak times and the effect of different vehicles. Similarly, single health metrics provide snapshots of risk factors for cardiovascular health. Directly examining road conditions, such as potholes, offers a picture of cumulative damage, much like assessing vascular stiffness reveals the overall health impact on arteries, serving as a direct indicator of cardiovascular health.

Arterial stiffness and *target-organ damage*

Arterial stiffness affects the entire arterial system and all of the organs connected to it. This can be viewed as a central, upstream contributor to a range of chronic conditions. Organs are affected differently based on their anatomical location and individual hemodynamic requirements. The most important organs impacted by increased pulsatile stress are the heart itself, the brain, and the kidneys.[16]

The heart is a particular organ of interest with regard to the effect of arterial stiffening. In a normal physiologic state, the coronary arteries are in part perfused by pulse wave reflections during the cardiac cycle. As the heart contracts (systole), the pulse wave is ejected into the peripheral system. When arteries are elastic (low stiffness), the main pressure wave travels relatively slowly, reflects back, and arrives when the heart is dilated (diastole). In a diastolic state, the coronary arteries are also dilated and the returning wave contributes to coronary blood flow. With advanced arterial stiffness, the pulse wave travels faster, and the reflected wave reaches the heart already during systole when the coronary arteries are also in a more contracted state. This hampers the coronary blood flow and increases pressure on the left cardiac ventricle. This means the heart has to do more work with less oxygen, hence why arterial stiffness is a strong predictor of heart failure.[17,18,19]

The kidneys are a central organ for regulating blood pressure. They're also subject to some of the largest blood volume flows in the entire body and contain very sensitive vasculature. This makes the kidneys highly vulnerable to increased pulsatile forces caused by both high blood pressure and arterial stiffness. In hypertensive patients, arterial stiffness is an independent marker of kidney damage, and in chronic kidney disease patients, arterial stiffness predicts cardiovascular mortality.[20,21] Due to the unique role of the kidneys in blood pressure regulation, it is a target of a vicious cycle where increasing blood pressure induces kidney damage, which in turn disrupts blood pressure regulation further.

The brain shares similar hemodynamic requirements to the kidneys, in the sense that they both rely on steady, laminar flow of blood and are poorly shielded against strong pulsatile forces.[22] Hence, much like the kidneys, the brain is also at a significantly higher risk of adverse outcomes as arterial stiffness increases. For example, compared to the lowest tertile of PWV, the hazard ratio of stroke increases by 22% (second tertile) and 228% (highest tertile) after adjusting for traditional risk factors and potential confounders.[23] Increased PWV is also associated with the pathological features of Alzheimer's disease, such as the deposition of amyloid plaque.[24]

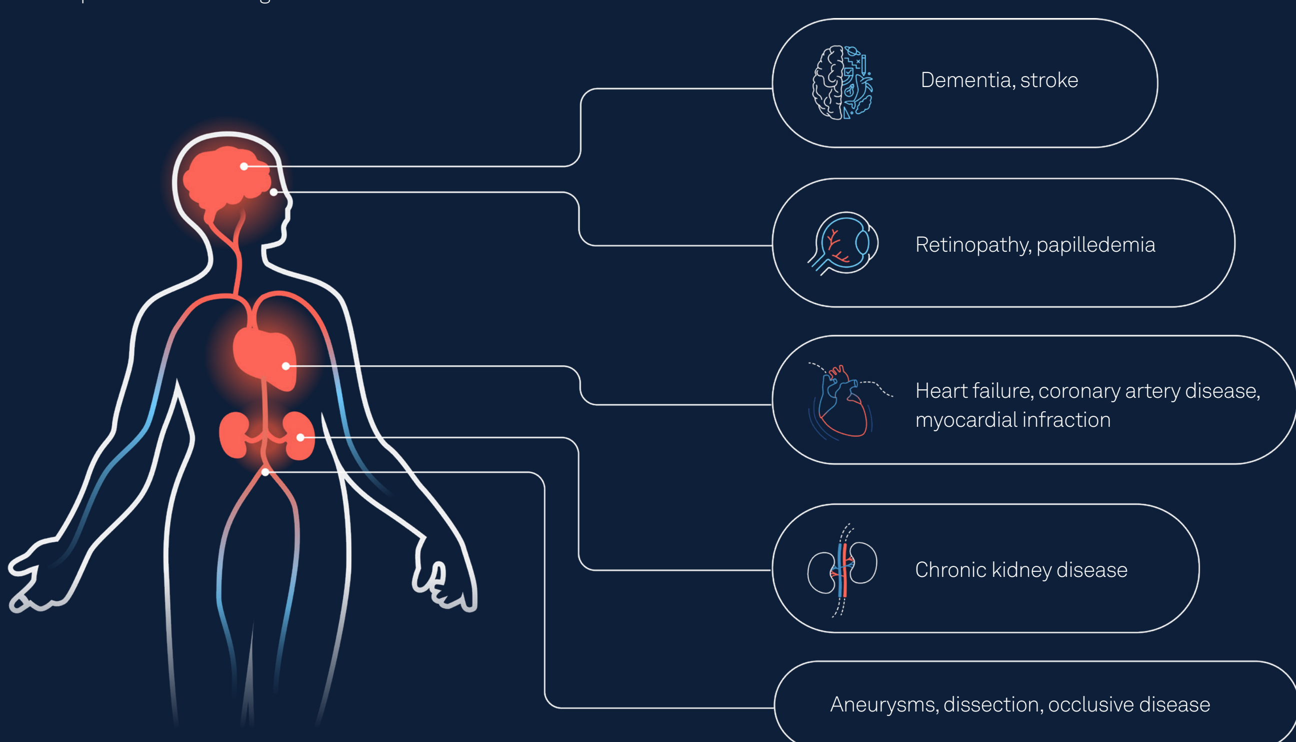
Figure 3. Adverse consequences of high arterial stiffness.

CVA = Low

Large arteries function as shock absorbers, protecting sensitive organs from pulsatile forces

CVA = High

Large arteries stiff and unable to protect sensitive organs



Mitigating *arterial stiffness*

As a systemic, structural phenomenon, arterial stiffness is not specifically susceptible to targeted interventions with pharmacological treatments; there are no approved drugs targeting the structural changes taking place in arterial walls. Some blood pressure drugs do lower PWV, but their effects vary across mechanisms of action.[25] Vasodilating agents may also have a beneficial effect, but many other drug classes (e.g. targeting inflammation, lipids, etc.) remain equivocal.[26, 27] The common feature about targeting arterial stiffness with any pharmacological treatment is that there continues to be a lack of evidence regarding its clinical utility. In other words, rigorous evidence is needed to demonstrate that treatments specifically targeting arterial stiffness provide clinical benefit beyond the current treatment targets (e.g. blood pressure).

While future studies are needed to evaluate the benefit of drugs, arterial stiffness has been shown to be supported by healthy lifestyle factors that also provide a wide range of other health benefits. For example, multiple randomized controlled trials have shown that aerobic exercise can reduce PWV.[28,29] In a particularly in-depth study, Bhuva et al. showed that participants who started training for their first-ever marathon reduced arterial stiffness as measured by magnetic resonance distensibility. The authors also reported an average 4-year reduction in a custom "biologic aortic age" metric, which was defined specifically for this study at various parts of the aorta.[30] The benefits were greatest in the older study participants, indicating that reversing the course of arterial stiffness may be possible even later in life.

Other lifestyle interventions that have been shown to lower PWV include weight loss and dietary sodium restriction.[31,32] Interestingly, in the latter case, the exact mechanisms of sodium restriction continue to be debated. Based on the close relationship between arterial stiffness and blood pressure, it would be plausible that the effects of sodium restriction are mediated by blood pressure lowering, but some studies suggest blood pressure-independent effects.[33,34]

While arterial stiffness has been a recognized physiological phenomenon for decades, early vascular aging (EVA) is a relatively new medical concept introduced in the late 2000s.[35,36] Conceptually it has been used to describe a situation where relatively young people present with typical vascular features usually encountered in significantly older people. The concept of EVA has been linked to multiple lifestyle factors, with arterial stiffness being one of the key clinical features. In recent years, the concept has evolved to encompass molecular markers of aging (such as telomere length), and the clinical connection to longevity and disease prevention is becoming widely recognized.[37,38]

Measuring *Cardiovascular Age*

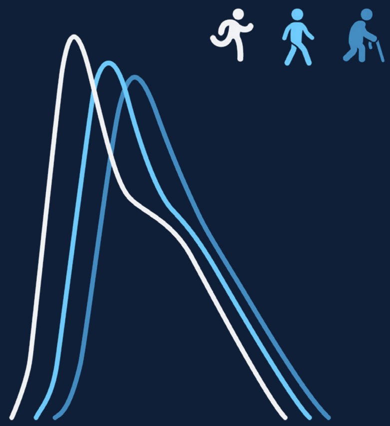
Indicators of cardiovascular aging are increasingly acknowledged in the research community as an important metric of cardiovascular health.[39] Representing the aging of an individual's cardiovascular system, cardiovascular age considers several influencing factors including arterial stiffness and blood pressure.

Typically, blood pressure is measured in mmHg whereas cfPWV is measured in m/s. PWV indicates the velocity of the pulse wave on large arteries for each heartbeat. While blood pressure is straightforward to measure at home, PWV normally requires a trained professional to conduct the measurement in a clinical setting. In addition to the assessments of blood pressure and cfPWV, the evaluation of an individual's cardiovascular system can be complemented through specialized clinical measures. These advanced diagnostics go deeper into the nuances of cardiovascular health, offering a more detailed understanding of the system's status.[40]

Oura Ring provides continuous monitoring of cardiovascular health and personalized health insights, enabling the identification and contextualization of changes in aging trends.

This information, together with other metrics and insights provided by Oura, can be used to make informed lifestyle choices to improve one's cardiovascular health.

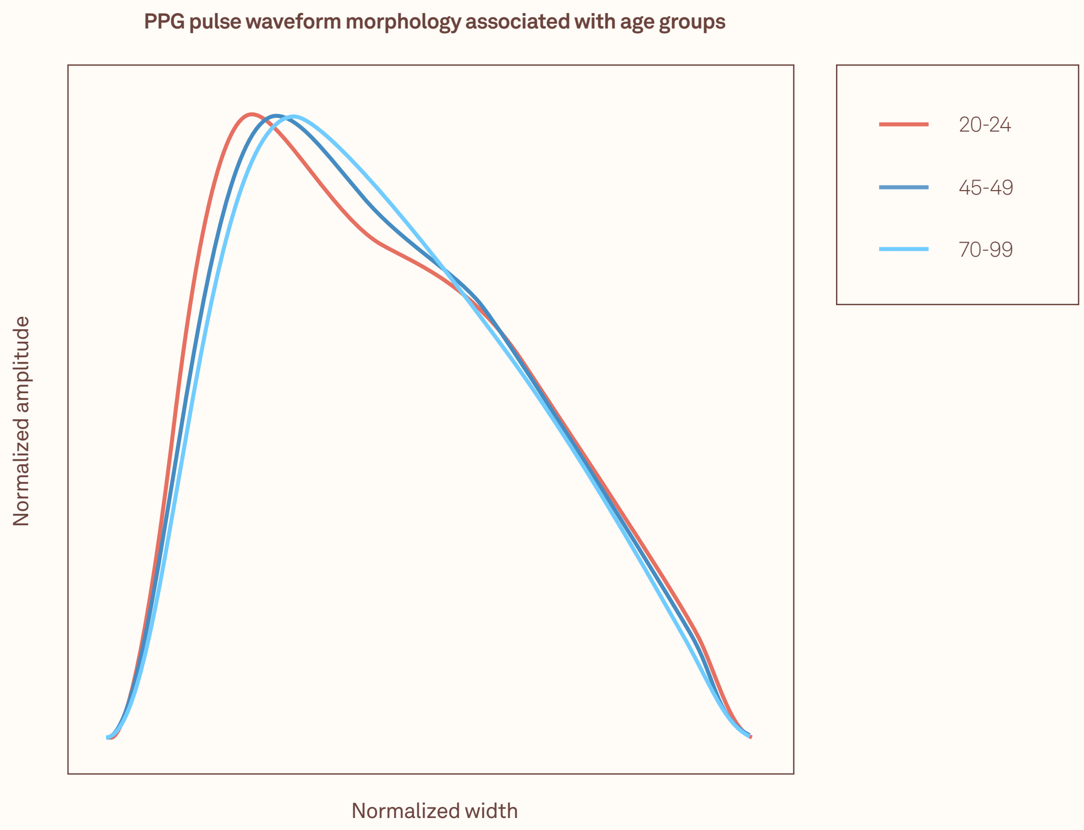
Cardiovascular Age *Algorithm*



The CVA algorithm developed by Oura offers insights into the overall condition of an individual's cardiovascular system. Using Pulse Wave Analysis (PWA) on the high-resolution PPG signal, the algorithm estimates CVA and PWV.

As shown in Figure 4, age-related changes in the shape of the PPG pulse wave enable assessment of cardiovascular age.

Figure 4. PPG pulse waveforms morphology associated with age groups. Each age group consists of 10,000 individuals with equal number of both females and males.

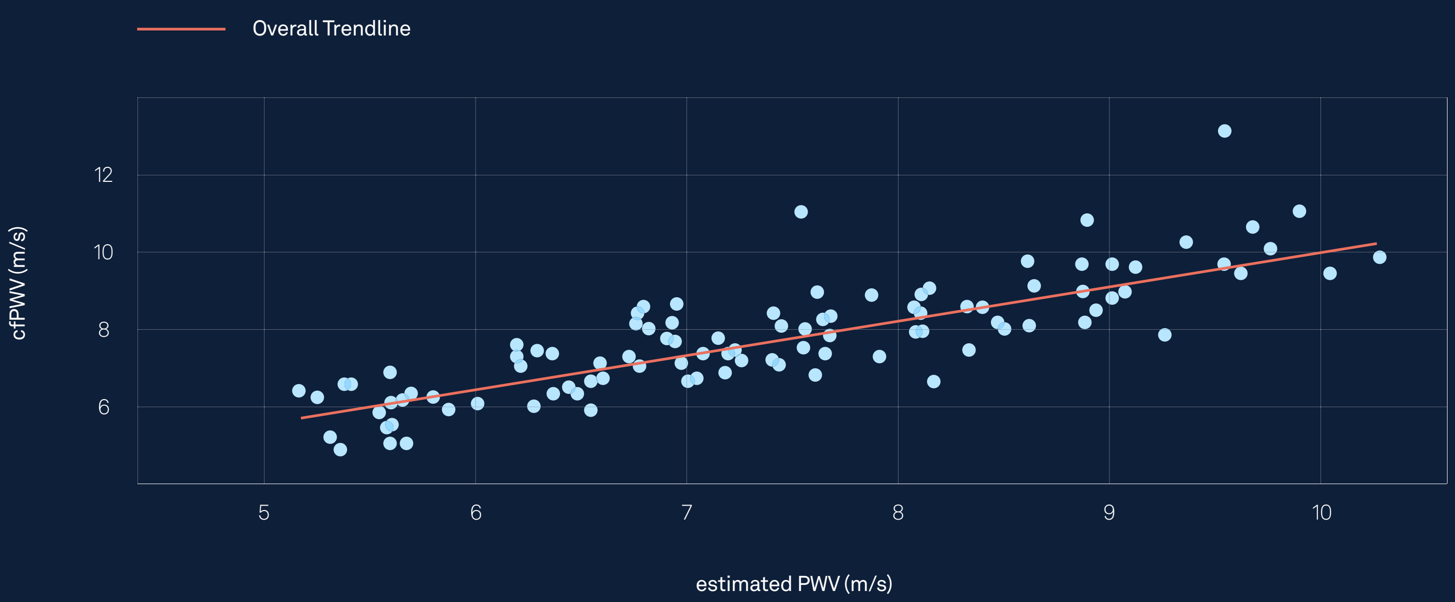


The algorithm takes into account the impact of individual demographics, providing personalized estimates of an individual's cardiovascular age. It has been validated against cfPWV, in internal study, achieving a strong correlation between cfPWV and CVA, and acceptable accuracy for PWV estimate based on the recent guidelines.[41]

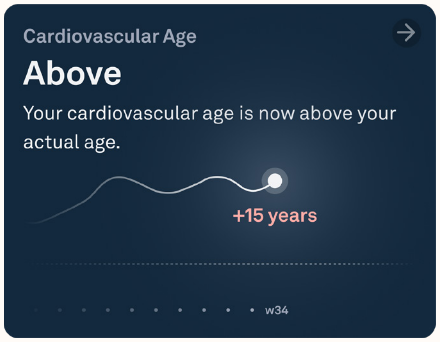
Figure 5. Correlation of Oura's estimated PWV with carotid-femoral PWV in healthy individuals (r=0.83).

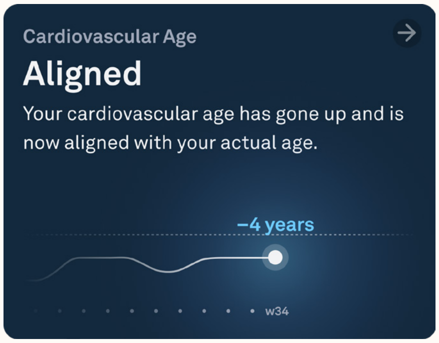
Subjects N=99 (36 males and 63 females)

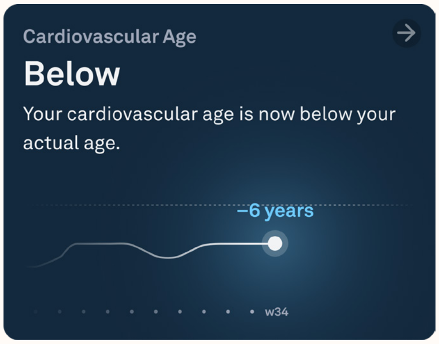
Item	Mean ± SD
Age (year)	46.60 ± 16.58
BMI (kg/m²)	26.29 ± 4.83
cfPWV (m/s)	7.77 ± 1.49



An Oura member's estimated CVA is shown relative to their chronological age. This comparison results in the categorization into one of three levels: **Above, Aligned, and Below:**







Above: When a member's estimated cardiovascular age exceeds the chronological age by six years or more, it is categorized as 'Above.' This difference indicates that various factors have potentially accelerated the cardiovascular aging process.

Aligned: Members whose estimated cardiovascular age falls within a five-year range above or below their actual age are considered 'Aligned.' This category follows a normal pace of cardiovascular aging.

Below: The 'Below' category includes those whose estimated cardiovascular age is at least six years younger than their chronological age. Achieving this level typically reflects the positive impact of long-term healthy lifestyle choices and/or an advantageous genetic background.

Limitations – Cardiovascular Age

To ensure accuracy, Oura Ring collects the requisite data for CVA during rest and sleep, when physical motion is minimal. 14 days and nights of data over the previous 30 days are needed to generate a CVA.

These scenarios might prevent the CVA measurement:

- Absence of rest and sleep: An individual needs to be resting or sleeping to initiate the measurement.
- Motion detection: Measurement is not initiated if physical movement was detected recently. For example, restless sleepers might not get an estimate because of excessive movement.
- Insufficient battery: Measurement cannot be conducted due to low battery.

These scenarios might prevent the CVA measurement:

- Poor signal quality: Factors such as cold hands, wearing a ring that is rotated, or a loose ring fit may interfere with Oura Ring signal quality, potentially impacting measurement accuracy.
- Incorrect demographic information: Demographic information is used to provide an accurate estimate of CVA. If the provided demographics are incorrect, it might affect the estimation accuracy.

Conclusion

Arterial stiffness has been shown to be a significant and independent predictor of a range of adverse health outcomes, mortality, and morbidity. While it is a systemic physiological phenomenon that inevitably progresses with chronological age, it can be considered a distinct form of biological aging. The key difference to chronological aging is that arterial stiffness, and therefore cardiovascular aging, can be slowed down considerably, and in some cases, reversed. Key methods for mitigation are aerobic exercise, maintaining healthy body weight, and consuming a blood-pressure-lowering diet.

Traditionally the measurement of arterial stiffness has been difficult and available only at specialized clinics. Now, Oura Ring offers a novel feature able to accurately estimate an individual's cardiovascular aging through continuous monitoring of arterial stiffness. This is a revolutionary and convenient new method to observe the effects of various lifestyle changes on cardiovascular health.

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[4] Diastole

[5] Heart failure

[6] Myocardium

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[8] Systolic blood pressure

[9] Systole

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[11] Chapter 52 - Effect of exercise training and weight loss on arterial stiffness and pulsatile hemodynamics

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[13] Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis

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[19] Pulsatile arterial haemodynamics in heart failure

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[33] High sodium intake and arterial stiffness

[34] Chapter 53 - Dietary salt and arterial stiffness

[35] Recommendations for Improving and Standardizing Vascular Research on Arterial Stiffness

[36] Early vascular aging (EVA): consequences and prevention

[37] Cardiovascular Aging and Longevity: JACC State-of-the-Art Review

[38] Biological Versus Chronological Aging: JACC Focus Seminar

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This paper was reviewed by Sara Szal Gottfried, MD, a paid Oura Medical Advisor

Note: Oura Ring is not a medical device and is not intended to diagnose, treat, cure, monitor, or prevent medical conditions or illnesses.