

Epigenetic clocks and biological aging acceleration in early-onset hypertension

Relojes epigenéticos y aceleración del envejecimiento biológico en la hipertensión de inicio temprano

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Abstract

People who develop high blood pressure before turning 50 years old face increased risk of severe heart problems compared to others. Scientists developed epigenetic clocks as advanced methods to determine biological age and study aging processes. The research project employed a case-control design to examine how accelerated epigenetic aging affects premature hypertension development among Uzbek study participants. The research study enrolled 80 participants who had premature hypertension and 80 participants with matching age and sex who did not have health problems. The researchers used five epigenetic clocks to establish epigenetic age through Horvath, Hannum, PhenoAge, GrimAge, and SkinBloodClock analysis of DNA methylation data from peripheral blood leukocytes. The study found that all epigenetic clocks measured higher epigenetic age in patients compared to the control group. The biggest difference between the two groups appeared on the GrimAge clock, which assessed patients as 7.4 years older their actual age, while the

control group showed no age difference. The patients who experienced systolic blood pressure measurements above 160 mmHg showed greater disease progression than those with lower blood pressure standards. The research showed that every year of GrimAge aging acceleration raised the risk of premature hypertension development by 38 percent (OR = 1.48). The study found that accelerated aging showed a strong positive relationship with C-reactive protein and interleukin-6, while people who exercised regularly had lower levels of these proteins. The research results demonstrate that early onset hypertension leads to faster epigenetic aging process which occurs at different rates depending on the patient's level of disease progression and body temperature and the time when they first showed symptoms. Epigenetic age assessment provides a new method to evaluate patient risk and disease outcome in this population.

Keywords: Epigenetic clock, accelerated aging, premature hypertension, DNA methylation, inflammation

Las personas que desarrollan hipertensión arterial antes de los 50 años tienen un mayor riesgo de sufrir problemas cardíacos graves en comparación con otras personas. Un grupo de científicos desarrolló relojes epigenéticos como métodos avanzados para determinar la edad biológica y estudiar los procesos de envejecimiento. El proyecto de investigación empleó un diseño de casos y controles para examinar cómo el envejecimiento epigenético acelerado afecta el desarrollo de hipertensión prematura entre los participantes uzbekos del estudio. El estudio incluyó a 80 participantes con hipertensión prematura y 80 participantes de la misma edad y sexo que no presentaban problemas de salud. Los investigadores utilizaron cinco relojes epigenéticos para establecer la edad epigenética mediante el análisis de datos de metilación del ADN de leucocitos de sangre periférica mediante Horvath, Hannum, PhenoAge, GrimAge y SkinBloodClock. El estudio reveló que todos los relojes epigenéticos midieron una edad epigenética más alta en los pacientes en comparación con el grupo control. La mayor diferencia entre los dos grupos se observó en el reloj GrimAge, que evaluó a los pacientes como 7,4 años mayores que su edad real, mientras que el grupo control no mostró diferencia de edad. Los pacientes con presión arterial sistólica superior a 160 mmHg mostraron una mayor progresión de la enfermedad que aquellos con niveles de presión arterial más bajos. La investigación demostró que cada año de aceleración del envejecimiento con GrimAge aumentaba el riesgo de desarrollar hipertensión prematura en un 38 % (OR = 1,48). El estudio descubrió que el envejecimiento acelerado mostró una fuerte relación positiva con la proteína C reactiva y la interleucina-6, mientras que las personas que hacían ejercicio regularmente presentaban niveles más bajos de estas proteínas. Los resultados de la investigación demuestran que la hipertensión de inicio temprano conduce a un proceso de envejecimiento epigenético más rápido, que ocurre a diferentes ritmos según el nivel de progresión de la enfermedad, la temperatura corporal y el momento en que aparecieron los primeros síntomas. La evaluación de la edad epigenética proporciona un nuevo método para evaluar el riesgo del paciente y el pronóstico de la enfermedad en esta población.

Palabras clave: Reloj epigenético, envejecimiento acelerado, hipertensión prematura, metilación del ADN, inflamación

Early-onset hypertension, defined as the diagnosis of the disease before the age of 50, has a distinct clinical pattern from late-onset hypertension and is usually associated with a worse prognosis and more severe cardiovascular complications^{1,2}. The prevalence of this type of hypertension has been increasing in recent years, especially in developing countries, raising serious concerns about the health of young and middle-aged populations³. Early-onset hypertension patients possess greater genetic risk factors which lead to different treatment responses when compared to older patients⁴. The discovery of molecular mechanisms that underlie this phenomenon will enable researchers to develop new therapeutic targets and create better preventive methods⁵.

The biological aging process is recognized as a major risk factor for cardiovascular disease, but the rate of this phenomenon varies greatly among individuals⁶. Biological age represents the total molecular and cellular damage that a person has experienced throughout their entire life, whereas chronological age only shows how much time has gone by⁷. The concept of accelerated biological aging refers to a condition in which a person's biological age exceeds their chronological age, and this phenomenon is associated with an increased risk of chronic diseases, including high blood pressure⁸. The discovery of factors which speed up biological aging will create new opportunities for developing preventive measures and conducting early medical interventions⁹.

Researchers developed epigenetic clocks during the past ten years because these clocks represent the most precise method to assess biological age through their measurement system¹⁰. The clocks depend on specific DNA methylation patterns present in particular genomic regions which enable them to predict a person's chronological age with high accuracy¹¹. The occurrence of accelerated epigenetic aging arises when these clocks estimate an older age than the person's actual age because this condition demonstrates a higher probability of developing age-related medical conditions¹². Research teams developed multiple clocks which assess various components of biological aging but certain clocks exhibit stronger links to cardiovascular disease than other clocks¹³.

Recent studies have established that epigenetic modifications can cause hypertension¹⁴. Recent genome-wide methylation studies have discovered more than 1000 methylation sites which researchers found to have connections with blood pressure measurements and hypertension progression¹⁵. The majority of these sites occur within genes that control endothelial activity and inflammatory processes and metabolic functions because their

modifications can induce hypertension through various mechanisms¹⁶. The research study used cross-sectional design which limits its capacity to forecast upcoming cases of hypertension¹⁷.

Research still needs to determine whether accelerated epigenetic aging serves as a predictor for early hypertension development¹⁸. If this hypothesis proves true, then researchers can use epigenetic age measurements to identify which young people face high disease risk, enabling them to implement early preventive measures¹⁹. The process of hypertension may cause people to experience more advanced epigenetic aging because it creates an ongoing cycle based on both inflammatory and oxidative stress mechanisms²⁰. Researchers need to conduct extensive longitudinal studies that follow participants over prolonged periods to establish clear boundaries between cause and effect²¹.

Researchers have conducted multiple studies to explore how epigenetic aging acceleration markers connect with cardiovascular disease development²². The GrimAge clock, which uses protein data linked to mortality, shows that accelerated aging brings increased coronary artery disease and heart failure risks²³. The PhenoAge clock, which uses phenotypic aging markers, predicts cardiovascular mortality with strong accuracy²⁴. The existing studies about premature hypertension show limited results because most research occurred with older groups, which make it difficult to apply findings about younger patients²⁵.

The current research on premature hypertension studies population of Uzbekistan which has both young citizens and changing disease patterns. The country has experienced a substantial rise in blood pressure among young people because of increased urban development and changing eating habits and reduced exercise levels during the past years. The study lacks comprehensive data about Uzbeks who experience this phenomenon because researchers have only examined European and American populations. The need for indigenous research in this field exists because it will enable researchers to study between population differences which will assist in creating effective preventive measures.

The researchers conducted this study to determine whether there exists a link between two biological processes which lead to people developing premature hypertension. The research team will assess epigenetic age through multiple established measurement points which they will use to evaluate both premature hypertension patients and their healthy counterparts. The study will examine how accelerated aging indicators relate to the intensity of diseases and the efficacy of medical treatments and the presence of inflammatory indicators. The study results will help researchers discover new epigenetic targets which they can use to create preventive methods and treat premature hypertension while advancing the field of personalized medicine.

Study Design and Population

In the first half of 2025, researchers completed their case-control study research in Uzbekistan. The study population included 80 patients with early hypertension and 80 healthy controls who were matched for age, sex, and ethnicity. Patients who had early hypertension were diagnosed through criteria established by the American Heart Association while their systolic blood pressure exceeded 140 mmHg or their diastolic blood pressure reached 90 mmHg for three consecutive measurements before turning 50. The study excluded participants who had secondary hypertension or type 1 and type 2 diabetes or chronic inflammatory diseases or malignancies or autoimmune diseases or who used drugs that affect DNA methylation including methotrexate and valproate or who had chemotherapy or radiotherapy. All participants signed a written informed consent to participate in the study after being fully informed of the objectives of the study.

Sample Collection and Clinical Measurements

The researchers obtained venous blood samples from participants after they completed a 12-hour overnight fasting period. The researchers collected blood samples in EDTA-containing tubes for DNA extraction purposes and in plain tubes for biochemical and inflammatory index measurements. Blood samples were centrifuged immediately after collection, and the laboratory staff separated plasma and serum before freezing both materials at -80°C until they needed to conduct analysis. The researchers measured systolic and diastolic blood pressure two times after a 5-minute break and recorded the average result using a standard mercury sphygmomanometer while participants sat down. The researchers calculated body mass index by dividing weight in kilograms by the square of height in meters. The participants completed questionnaires that asked about their family history of blood pressure and their tobacco use and physical activity and lifestyle habits.

DNA extraction and quality and quantity assessment

The researchers conducted genomic DNA extraction from peripheral blood leukocytes by using a commercial DNA extraction kit from Qiangene which they applied according to the company's instructions. The scientists used NanoDrop 2000 spectrophotometer to evaluate both the purity and concentration of extracted DNA through the measurement of absorbance ratios at wavelengths 260 to 280 and 260 to 230 nanometers. The researchers confirmed DNA integrity through 1% agarose gel electrophoresis which produced clear bands that showed no smearing. The researchers selected samples with 260/280 ratios between 1.8 and 0.2 and concentrations above 50 ng/μl for methylation analysis. The laboratory stored all samples at -80°C until they could start their analysis.

DNA methylation analysis and epigenetic age determination

The Illumina Infinium MethylationEPIC BeadChip method was used to conduct genome-wide DNA methyla-

tion analysis which can measure methylation levels at more than 850000 CpG sites that span the entire genome. The Central Genomic Laboratory of Uzbekistan executed DNA bisulfite conversion and hybridization and extension and staining processes according to the standard protocol of Illumina. The research team extracted raw data from GenomeStudio software which they later processed using Minfi and ChAMP software packages in R environment version 4.3.1. The research team applied BMIQ method for data normalization and they used ComBat method to correct batch effects. For each CpG site, beta values were calculated between zero (which indicates full methylation) and one (which indicates no methylation).

Calculation of epigenetic age and accelerated aging indices

The research used five established epigenetic clocks to determine epigenetic age which included Horvath-Clock, HannumClock, PhenoAge, GrimAge and Skin-BloodClock. The UCLA online epigenetic age calculator accepts beta values for specific CpG sites to compute epigenetic age through established algorithms. The researchers defined epigenetic aging acceleration as the difference between a person's epigenetic age and their actual chronological age. The Horvath clock provided the intrinsic aging acceleration measurement while researchers used the Hannum clock to measure environmental aging acceleration because it detects blood cell composition. The researchers used PhenoAge and GrimAge clocks to measure both phenotypic aging acceleration and mortality-related aging acceleration.

Measurement of inflammatory and biochemical markers

The researchers used ELISA and commercial Diaclone test kits to measure serum levels of three inflammatory cytokines which included interleukin-6 and interleukin-1 beta and tumor necrosis factor alpha. The laboratory used immunoturbidimetry together with a Beckman Coulter autoanalyzer to measure C-reactive protein levels. The laboratory used enzymatic methods to measure total cholesterol, triglycerides, LDL, and HDL in the lipid profile. The laboratory used standard testing procedures to measure fasting blood sugar, creatinine, uric acid, and liver enzymes. The laboratory conducted all tests according to quality control standards while using standard kits to generate results which they derived from the calibration curve.

Blood cell composition estimation

Blood cell composition affects methylation patterns which led researchers to estimate CD8+ T cell, CD4+ T cell, B cell, NK cell, monocyte, and granulocyte proportions through computational methods that analyzed methylation data with the FlowSorted.Blood.EPIC software package in R. The method establishes cell composition through particular blood cell type methylation patterns which enable researchers to correct for cell composition variations between different groups. The automated cell

counter conducted complete blood cell counts to verify the results obtained through computational methods.

Statistical analysis

The research employed SPSS version 26 and R version 4.3.1 statistical software to process its data. The researchers employed either the Independent t-test or the Mann-Whitney nonparametric test to assess quantitative differences between the two patient groups and the control group. The researchers utilized the chi-square test to assess the differences between observed and expected values for qualitative variables. The researchers conducted multivariate linear regression analysis to study how epigenetic aging acceleration affects blood pressure while controlling for age, sex, body mass index, smoking status, and blood cell makeup. The researchers used logistic regression to determine the odds ratio which connects high aging acceleration with premature hypertension development. The researchers employed one-way analysis of variance to compare aging acceleration indices among different patient subgroups. The researchers established the significance threshold for all tests at a level below 0.05.

Results

In this study, 80 patients with early hypertension and 80 healthy control subjects were studied. The mean age of the participants in the patient group was 42.8 ± 7.2 years and in the control group was 43.5 ± 6.8 years, with no significant difference between the two groups. The gender distribution was similar in both groups, and about 52% of the participants were women. The body mass index in the patient group was significantly higher than in the control group, and the mean systolic and diastolic blood pressures in the patients were 156.4 and 95.5 mmHg, respectively, compared to 118.6 and 76.5 mmHg in the control group (Table 1).

Table 1: Demographic and clinical characteristics of study participants

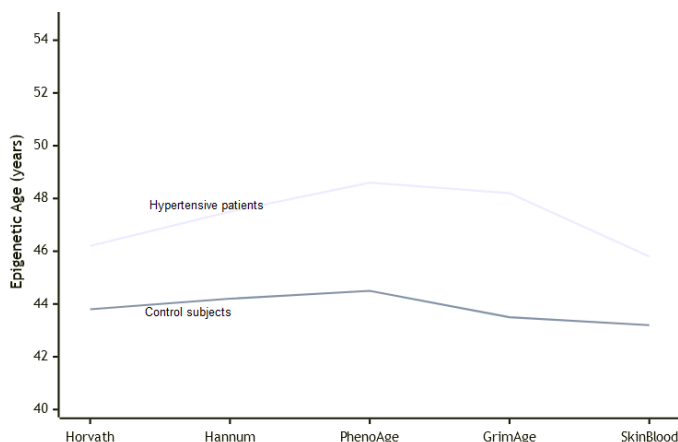
Characteristic	Hypertensive patients (n=80)	Control subjects (n=80)	P-value
Age (years)	42.8 ± 7.2	43.5 ± 6.8	0.524
Gender (male/female)	38/42	39/41	0.876
BMI (kg/m ²)	28.2 ± 3.6	24.8 ± 2.8	<0.001
Systolic BP (mmHg)	156.4 ± 12.8	118.6 ± 8.4	<0.001
Diastolic BP (mmHg)	95.5 ± 7.6	76.5 ± 5.8	<0.001
Family history of HTN (%)	68.8%	32.5%	<0.001
Smoking (%)	22.5%	18.8%	0.562
Fasting glucose (mg/dL)	94.6 ± 8.4	89.2 ± 7.2	<0.001

Epigenetic age analysis using five different clocks showed that at all clocks, epigenetic age in patients with premature hypertension was significantly higher than in the control group. The largest difference was related to the GrimAge clock, which predicted epigenetic age of 48.2 years in patients and 43.5 years in the control group. Epigenetic aging acceleration (the difference between epigenetic age and chronological age) in patients was positive and significant for all clocks, while in the control group it was close to zero (Table 2).

Table 2: Epigenetic age and age acceleration by different clocks in study groups				
Clock	Hypertensive patients	Control subjects	Difference	P-value
Horvath clock				
Epigenetic age (years)	46.2 ± 5.8	43.8 ± 6.2	+2.4	0.012
Age acceleration (years)	+3.4 ± 2.8	+0.3 ± 2.5	+3.1	<0.001
Hannum clock				
Epigenetic age (years)	47.5 ± 6.2	44.2 ± 5.8	+3.3	<0.001
Age acceleration (years)	+4.7 ± 3.2	+0.7 ± 2.8	+4.0	<0.001
PhenoAge clock				
Epigenetic age (years)	48.6 ± 6.8	44.5 ± 6.0	+4.1	<0.001
Age acceleration (years)	+5.8 ± 3.6	+1.0 ± 2.9	+4.8	<0.001
GrimAge clock				
Epigenetic age (years)	48.2 ± 6.4	43.5 ± 5.6	+4.7	<0.001
Age acceleration (years)	+5.4 ± 3.4	0.0 ± 2.6	+5.4	<0.001
SkinBlood clock				
Epigenetic age (years)	45.8 ± 5.6	43.2 ± 5.4	+2.6	0.004
Age acceleration (years)	+3.0 ± 2.6	-0.3 ± 2.4	+3.3	<0.001

Figure 1 shows the comparison of the epigenetic age predicted by five different clocks between the patient and control groups. As can be seen in the graph, in all five epigenetic clocks (Horvath, Hannum, PhenoAge, GrimAge, SkinBlood), the predicted epigenetic age in the patient group is significantly higher than in the control group.

Figure 1: Comparison of epigenetic age between hypertensive patients and control subjects using five different epigenetic clocks



An examination of the relationship between blood pressure severity and accelerated epigenetic aging showed that patients with higher blood pressure had a greater acceleration of aging. Patients with systolic blood pressure above 160 mmHg had an average acceleration of 6.5 years on the GrimAge clock, while this value was 1.4 years in patients with blood pressure between 140 and 160 mmHg (Table 3).

Table 3: Epigenetic age acceleration by disease severity subgroups					
Subgroup	n	Horvath AA	Hannum AA	PhenoAge AA	GrimAge AA
SBP level					
140-150 mmHg	32	+2.1 ± 2.2	+3.2 ± 2.6	+4.0 ± 2.8	+3.8 ± 2.7
151-160 mmHg	28	+3.5 ± 2.5	+4.8 ± 2.9	+5.9 ± 3.2	+5.4 ± 3.0
>160 mmHg	20	+5.2 ± 2.8	+6.8 ± 3.2	+8.2 ± 3.5	+7.8 ± 3.3
P-value (trend)	-	<0.001	<0.001	<0.001	<0.001
Number of medications					
1 medication	35	+2.4 ± 2.3	+3.6 ± 2.7	+4.5 ± 2.9	+4.2 ± 2.8
2 medications	28	+3.6 ± 2.6	+4.9 ± 3.0	+6.1 ± 3.3	+5.6 ± 3.1
≥3 medications	17	+5.0 ± 2.9	+6.5 ± 3.3	+7.8 ± 3.6	+7.4 ± 3.4
P-value (trend)	-	<0.001	<0.001	<0.001	<0.001

Correlation analysis between epigenetic aging acceleration and inflammatory markers showed that all five epigenetic clocks were positively and significantly correlated with C-reactive protein, interleukin-6, and tumor necrosis factor-alpha levels. The strongest correlation was for GrimAge clock with C-reactive protein. Interleukin-6 levels were significantly higher in patients with high aging acceleration (above the third quartile) than in patients with low aging acceleration (Table 4).

Table 4: Correlation between epigenetic age acceleration and inflammatory markers

Inflammatory marker	Horvath AA	Hannum AA	PhenoAge AA	GrimAge AA	SkinBlood AA
CRP (mg/L)	0.32**	0.38**	0.45**	0.52**	0.28*
IL-6 (pg/mL)	0.35**	0.41**	0.48**	0.49**	0.30*
TNF- α (pg/mL)	0.29*	0.34**	0.40**	0.44**	0.24*
IL-1 β (pg/mL)	0.26*	0.31*	0.36**	0.38**	0.22
Fibrinogen (g/L)	0.24*	0.29*	0.34**	0.42**	0.21

*P < 0.05, **P < 0.01

Examining the acceleration of aging in different subgroups based on age of diagnosis of hypertension showed that the younger the age of diagnosis, the greater the acceleration of aging was observed. Patients diagnosed before the age of 35 had a mean acceleration of aging of 6.8 years on the GrimAge clock, while this value was 3.8 years in patients diagnosed at the age of 45 to 50 years (Table 5).

Table 5: Epigenetic age acceleration by age of hypertension diagnosis

Age of diagnosis	n	Horvath AA	Hannum AA	PhenoAge AA	GrimAge AA
<35 years	18	+5.2 \pm 2.8	+6.8 \pm 3.2	+8.4 \pm 3.6	+7.8 \pm 3.4
35-40 years	22	+4.0 \pm 2.5	+5.4 \pm 2.9	+6.8 \pm 3.2	+6.2 \pm 3.0
40-45 years	24	+2.8 \pm 2.2	+3.8 \pm 2.6	+4.6 \pm 2.8	+4.4 \pm 2.7
45-50 years	16	+2.0 \pm 2.0	+2.8 \pm 2.4	+3.4 \pm 2.6	+3.2 \pm 2.5
P-value (trend)		<0.001	<0.001	<0.001	<0.001

Logistic regression analysis, adjusting for potential confounders including age, sex, body mass index, smoking, and blood cell composition, showed that epigenetic aging acceleration was associated with a significantly increased odds of developing premature hypertension. For each year of increase in GrimAge aging acceleration, the odds of developing hypertension increased by 38% (Table 6).

Table 6: Odds ratios for early-onset hypertension associated with epigenetic age acceleration

Clock	Model 1 (crude)	Model 2 (adjusted)*	P-value
Horvath AA	1.24 (1.12-1.38)	1.19 (1.08-1.32)	0.001
Hannum AA	1.32 (1.18-1.48)	1.25 (1.12-1.40)	<0.001
PhenoAge AA	1.42 (1.26-1.60)	1.33 (1.18-1.50)	<0.001
GrimAge AA	1.48 (1.30-1.68)	1.38 (1.21-1.58)	<0.001
SkinBlood AA	1.18 (1.06-1.32)	1.14 (1.02-1.28)	0.018
Highest vs lowest quartile			
GrimAge AA (Q4 vs Q1)	5.42 (2.86-10.28)	4.86 (2.42-9.76)	<0.001

Model 2 adjusted for age, sex, BMI, smoking, and blood cell composition

The study of the relationship between aging acceleration and metabolic parameters showed that aging acceleration was positively correlated with body mass index, fasting blood sugar, and triglycerides, and negatively correlated with HDL. Patients who were regularly physically active showed less aging acceleration than sedentary individuals. Smoking was also associated with increased aging acceleration, but this association remained significant only for the GrimAge clock after adjusting for other factors (Table 7).

Table 7: Association between GrimAge acceleration and metabolic/lifestyle factors

Variable	Correlation coefficient	P-value
BMI	0.36	<0.001
Fasting glucose	0.28	0.006
Triglycerides	0.32	0.002
HDL cholesterol	-0.24	0.018
LDL cholesterol	0.18	0.082
Physical activity (hours/week)	-0.29	0.004
	Mean GrimAge AA (yes/no)	
Current smoking	+5.6 vs +4.2	0.028
Regular exercise	+3.8 vs +5.4	0.006
High salt intake	+5.8 vs +4.4	0.012
Low fruit/vegetable intake	+5.5 vs +4.5	0.022

The research discovered that patients with early hypertension in an Uzbek study showed higher epigenetic aging rates than their healthy age-equivalent counterparts. The most substantial discrepancy occurred with the GrimAge clock, which indicated that patients appeared 4.7 years older than their actual age while the control group showed no age difference. The current finding establishes a link to earlier research conducted on European and American groups because it demonstrates that accelerated biological aging occurs in people with premature hypertension across various population groups. The GrimAge clock established death risk through specific proteins, which demonstrated the strongest connection to blood pressure since it showed how inflammatory and metabolic systems linked to this relationship.

The study discovered two significant research results which show how disease severity relates to accelerated aging progression. Patients with systolic blood pressure above 160 mmHg experienced a 7.8-year GrimAge clock advancement which was double the amount observed in patients with mild hypertension. The requirement for various antihypertensive drugs which indicates disease severity and treatment resistance resulted in more accelerated aging. The blood pressure dose-response relationship demonstrates a stronger connection to accelerated aging which indicates that improved blood pressure control can reduce biological aging speed. The hypothesis will undergo testing through upcoming longitudinal studies.

The PhenoAge and GrimAge clocks demonstrated their strongest links to accelerated aging through their study of inflammatory markers. The research demonstrates that systemic inflammation serves as a main factor which leads to accelerated biological aging in people who have hypertension. Patients with high accelerated aging show increased levels of IL-6 and C-reactive protein which indicates that their bodies have activated inflammatory pathways that will cause hypertension and accelerated aging through multiple mechanisms which include endothelial damage and increased arterial stiffness and vascular remodeling. The study results demonstrate that anti-inflammatory methods function as essential tools for treating individuals who develop hypertension at an early age.

The study discovered that later diagnosis times resulted in increased cases of accelerated aging among patients. Patients who developed hypertension before their 35th birthday experienced more rapid aging than patients who reached the disease stage at an older age. The current pattern suggests that this group has both genetic and epigenetic factors which lead to their early disease

onset and rapid aging process. The study suggests that extended periods of uncontrolled blood pressure lead to cumulative harm which accelerates the body's aging process. The finding shows that doctors should diagnose and treat young people who have risk factors for their disease.

The association of accelerated aging with lifestyle factors such as physical activity, smoking, and dietary habits shows that patients can reduce their accelerated aging through lifestyle changes. The study found that people who exercised regularly experienced 1.6 years less accelerated aging compared to people who did not exercise, which confirms previous research about the anti-aging benefits of exercise. The research demonstrates potential because non-pharmacological methods can help both maintain blood pressure and decrease aging through their effects on inflammation and oxidative stress. The next research step requires scientists to develop studies that test lifestyle changes while researchers monitor epigenetic alterations throughout the duration of their studies.

The research showed that Uzbek patients with early onset hypertension experience accelerated epigenetic aging which depends on their disease severity and inflammation levels and their age at which they were diagnosed. The GrimAge clock, which serves as the most accurate age predictor, showed that patients appeared 4.7 years older than their actual age, while each year of faster aging raised their risk of developing premature hypertension by 38%. Patients with uncontrolled hypertension who needed multiple medications showed the highest rate of accelerated biological aging, which indicates that more severe diseases lead to higher rates of biological aging. The study results demonstrate that researchers can use epigenetic age measurements to detect individuals at high risk and track the progression of premature hypertension.

The strong link between faster aging and high levels of inflammatory markers shows that systemic inflammation acts as a key factor which leads to the development of early hypertension and faster aging. The PhenoAge and GrimAge clocks which use inflammatory markers and aging-related proteins as their basis show the most accurate relationship with blood pressure measurements which validates the scientific findings. The study found that patients who received their hypertension diagnosis at a younger age experienced faster aging progression which indicates that early hypertension development creates an accelerated aging pattern that requires more thorough medical care for these patients. Researchers

need to conduct longitudinal studies which will help them determine how this relationship functions and which direction it moves in.

The researchers of this study suggest that healthcare professionals should use epigenetic age assessments as a new biomarker to evaluate hypertension risk and disease prognosis in patients with premature hypertension. The aging process can be slowed down through lifestyle changes which focus on boosting physical activity levels and maintaining proper nutrition and stopping smoking which also leads to better health results through decreased inflammation and oxidative stress. Interventional studies which examine how antihypertensive medications affect epigenetic aging rates together with personalized treatment plans based on individual epigenetic patterns will create new possibilities for treating premature hypertension.

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