BJCMR Brazilian Journal of Clinical Medicine and Review

PCAA PUBLICAÇÕES CIENTÍFICAS DE ACESSO ABERTO

Original Research

Biological Age and its Relationship with Mortality of Elderly People with COVID-19 in a Public Hospital in Northeastern Brazil

Isaura Romero Peixoto [1, 2, *], Alicia Rafaela Martinez Accioly [1, 3], Silvana Maria de Morais Campos [4], Eduarda Erika Ursulino Mattos [4], Elias Germano de Oliveira Júnior [4]

[1] Clinics Hospital of Pernambuco, Federal University of Pernambuco, Recife, PE, Brazil.
[2] Post-Graduate Program in Tropical Medicine, Federal University of Pernambuco, Recife, PE, Brazil.
[3] Post-Graduate Program in Neuropsychiatry and Behavioral Sciences, Universidade Federal de Pernambuco, Recife, PE, Brazil.
[4] Afya Faculty of Medical Sciences, Jaboatão, PB, Brazil.

* Correspondence: isaura.peixoto@ufpe.br.

Abstract: To estimate the biological age of elderly people hospitalized with a confirmed diagnosis of COVID-19, and its relationship with mortality. A retrospective and quantitative cohort study, carried out in a public hospital in the city of Recife-PE, from April 2020 to April 2021, with 115 elderly people of both sexes. The biological age of the participants was estimated by a calculator that uses nine laboratory blood tests and mortality was analyzed. Of the 115 elderly people hospitalized in a public referral hospital for COVID-19, the predominant gender was male, age ≥ 70 years, black/brown skin color, illiterate/low education, with a partner. Arterial hypertension and diabetes were the most common comorbidities in the study population. Regarding ICU admission, use of mechanical ventilation, length of ICU stays and mortality, there was a significant association with premature aging (p-value = 0.009, 0.009, 0.042 and 0.009 respectively). The biological Age was able to predict clinical outcomes, proving to be superior to Chronological Age.

Keywords: Covid-19; Elderly person; Biological age; Mortality; Premature aging.

Citation: Peixoto IR, Accioly AR M, Campos SMM, Mattos EEU, Oliveira Júnior EG. Biological Age and its Relationship with Mortality of Elderly People with COVID-19 in a Public Hospital in Northeastern Brazil. Brazilian Journal of Clinical Medicine and Review. 2025:Jan-Dec;03(1):bjcmr19.

https://doi.org/10.52600/2763-583X.bjcmr.2025.3.1.bjcmr19

Received: 13 August 2024
Accept: 16 October 2024
Published: 31 October 2024

1. Introduction

Throughout human history, pandemics have occurred numerous times, but the COVID-19 (Coronavirus disease 2019) pandemic is unique in that it is the first pandemic in a post-industrial society. In its early days, COVID-19 was recognized as a gerolavic infection (from the Greek géros "old" and epilavis, "harmful"). In China, in March 2020, elderly people aged 60 and over accounted for 81% of deaths from COVID-19, with a risk of death 23 times higher than that of non-elderly people [1].

Aging is a continuous process that limits resilience to adverse events, such as COVID-19 infection. Hypothetical reasons for the greater susceptibility of elderly people to COVID-19 include the coexistence of comorbidities and immunosenescence. These events occur and develop gradually and at different speeds among people, due to genetic background, environmental factors, and lifestyle. Thus, diseases and mortality related to aging occur in different ways among elderly people of the same chronological age, and this may reflect biological age. Due to the rate at which aging varies, chronological age may not be the best resource for quantifying this long-term decline in coping capacity [2,3].

There are still many gaps in the complete understanding of the dangers of this pathology for elderly people, including at the molecular level. The consensus, however, is that age represents the most important risk factor for the outcome of death from COVID-19. In this scenario, biological age emerges as a more robust biomarker than chronological age for expressing aging. Biological age is a metric capable of quantifying the impact of health problems associated with aging. There are resources called aging clocks that estimate biological age based on biodata analyzed by artificial intelligence. People with a biological age greater than their actual chronological age show accelerated aging [4,5].

Biological age has contributed significantly to mortality due to COVID-19. The first aging clocks were more difficult to implement, however, we now have tools that use routine clinical blood tests. Several studies have shown that accelerated biological aging is associated with a shorter life expectancy, early menopause, onset of cardiovascular and metabolic diseases, cancer, etc. Therefore, establishing the biological age of the elderly person is increasingly important for an accurate prediction of the evolution of the infection. Furthermore, it is believed that the effect of biological age on the course of the disease may be more relevant than that of chronological age. To date, we do not have a single universal biomarker for estimating health and the probability of longevity. Furthermore, there is still no consensus on the concept of aging and how to assess it. In everyday life, doctors use indicators that can be biomarkers of biological aging [6].

Epigenetic clocks predict biological age based on DNA methylation levels. In 2018, an epigenetic biomarker of aging was developed, calculating phenotypic age from nine clinical markers most significantly associated with mortality (albumin, creatinine, serum glucose, C-reactive protein, lymphocyte percentage, mean corpuscular volume, RDW, and alkaline phosphatase) and chronological age. Therefore, epigenetic clocks are among the most promising biomarkers of biological age and powerful predictors of life expectancy [7].

Accelerated biological aging has been shown to be associated with shorter life expectancy, raising the possibility that biological age has a greater effect on the course of COVID-19 than chronological age. The present study hypothesizes that biological age, estimated through phenotypic biomarkers, represents a more accurate predictor of unfavorable outcomes in elderly people with COVID-19, when compared to chronological age.

2. Method

A retrospective, quantitative cohort study was conducted in a public referral hospital for the treatment of COVID-19, in the city of Recife, Northeastern Brazil. The study included all (100%) individuals aged 60 years or older, with a positive diagnosis for COVID-19 by polymerase chain reaction in an oropharyngeal swab, according to the WHO-2019 criteria [8], admitted to the service between April 2020 and April 2021, totaling 115 elderly individuals.

Pre-hospital and hospital circumstances were investigated. The pre-hospital variables considered were sociodemographic (chronological age, sex, education, skin color, and marital status), comorbidities (type 2 diabetes mellitus, systemic arterial hypertension, heart failure, chronic obstructive pulmonary disease, asthma, dementia, cancer, chronic kidney disease), and smoking. The hospital variables included the need for admission to the Intensive Care Unit, use of invasive ventilatory support, length of hospital stay and mortality. Data collection took place at the Medical and Statistical Archiving Service (SAME), with research into patient records and application of the research inclusion criteria. Data from the physical and virtual medical records made available by SAME were collected by a team of properly trained researchers, through the application of a structured instrument composed of sociodemographic, clinical and laboratory variables.

To estimate biological age, we used the online phenotypic calculator Ageless Rx calculate [9], which uses nine main blood markers (albumin, creatinine, glucose, C-reactive protein, lymphocytes, mean corpuscular volume, RDW (Red cell distribution width), alkaline phosphatase and leukocytes), participants' birth dates and laboratory test results.

This tool was selected because its calculation relies on easily accessible blood tests already performed in clinical practice, in addition to having been validated in previous studies [7] as a better prognostic tool than chronological age.

To analyze the data, a database was created in Excel and the SPSS 25.0 (Statistical Package for the Social Sciences) for Windows and Excel 365 software were used. A 95% confidence interval was applied to all tests. Chi-square and Fisher's exact tests were used for categorical variables, due to the nature of the variables and the need to evaluate associations between clinical outcomes and sociodemographic characteristics. The results are presented in table form with their respective absolute and relative frequencies.

3. Results

A total of 115 elderly individuals participated in the study, of which 60 (52.1%) were men. Fifty-six (48.7%) were between 60 and 69 years old and 59 (51.3%) were 70 years old or older. It was found that 103 (89.6%) patients presented premature aging. 71.3% of the sample declared themselves black/brown, 25.2% were illiterate, while 30.4% had a low level of education, with up to 5 years of formal schooling. In this population studied, 52.1% had a partner.

Table 1 shows the sociodemographic characteristics according to the presence or absence of premature aging. Premature aging was equally prevalent between the two chronological age groups (60 to 69 and 70 years or older). Characteristics such as sex, education, skin color, and marital status were not different between the groups with and without premature aging.

Table 1. Sociodemographic characteristics and their association with premature aging in elderly patients hospitalized with COVID-19.

	Premature aging				
Variables	**Yes (n, %)**	**No (n, %)**	**PR**	**CI 95% PR**	**p-value**
Chronological age					
60 a 69	50 (89,3)	6 (10,7)	1,00	---	0,924 *
70 or +	53 (89,9)	6 (10,2)	1,01	0,89 – 1,14	
Sex					
Male	55 (91,7)	5 (8,3)	1,00	---	0,441 *
Female	48 (87,3)	7 (12,7)	0,95	0,84 – 1,08	
Education					
Illiterate	26 (89,7)	3 (10,3)	1,00	0,82 – 1,22	1,000 **
1-5 years	32 (91,4)	3 (8,6)	1,02	0,85 – 1,23	
6-9 years	21 (91,3)	2 (8,7)	1,02	0,84 – 1,25	
> 9 years	17 (89,5)	2 (10,5)	1,00	---	
Skin color					
Black / Brown	74 (90,2)	8 (9,8)	1,03	0,87 – 1,22	0,709 **
Others	21 (87,5)	3 (12,5)	1,00	---	
Conjugality					
With partner	55 (91,7)	5 (8,3)	1,00	---	0,726 **
Without partner	47 (94,0)	3 (6,0)	1,03	0,92 – 1,14	

(*) Chi-square (**) Fisher's exact test.

The study population presented several comorbidities, as shown in Table 2, with high blood pressure, diabetes mellitus and cancer being the most prevalent. In the group with

premature aging, comorbidities were more frequent, but without statistical significance. Smoking was of low prevalence. Regarding the outcome of death, a significant association with premature aging was observed (p-value = 0.009).

Table 2. Clinical characterization, smoking, mortality and premature aging in elderly people hospitalized with COVID-19.

	Premature aging				
Variables	**Yes (n, %)**	**No (n, %)**	**PR**	**CI 95% PR**	**p-value**
Diabetes mellitus					
Yes	45 (84,9)	8 (15,1)	0,91	0,80 – 1,03	0,131 *
No	58 (93,5)	4 (6,5)	1,00	---	
Hypertension					
Yes	72 (91,1)	7 (8,9)	1,06	0,91 – 1,23	0,512 **
No	31 (86,1)	5 (13,9)	1,00	---	
Heart failure					
Yes	15 (93,8)	1 (6,3)	1,05	0,91 – 1,22	1,000 **
No	88 (88,9)	11 (11,1)	1,00	---	
COPD					
Yes	9 (90,0)	1 (10,0)	1,01	0,81 – 1,25	1,000 **
No	94 (89,5)	11 (10,5)	1,00	---	
Asthma					
Yes	2 (100,0)	0 (0,0)	1,12	1,05 – 1,19	1,000 **
No	101 (89,4)	12 (10,6)	1,00	---	
Dementia					
Yes	6 (100,0)	0 (0,0)	1,12	1,05 – 1,20	1,000 **
No	97 (89,0)	12 (11,0)	1,00	---	
Cancer					
Yes	18 (94,7)	1 (5,3)	1,07	0,94 – 1,22	0,687 **
No	85 (88,5)	11 (11,5)	1,00	---	
Chronic kidney disease					
Yes	15 (93,8)	1 (6,3)	1,05	0,91 – 1,22	1,000 **
No	88 (88,9)	11 (11,1)	1,00	---	
Smoking					
Active	8 (80,0)	2 (20,0)	0,90	0,64 – 1,25	0,709 **
Inactive	43 (89,6)	5 (10,4)	1,00	0,85 – 1,18	
Never smoked	25 (89,3)	3 (10,7)	1,00	---	
Death					
Yes	37 (100,0)	0 (0,0)	1,18	1,08 – 1,30	0,009 **
No	66 (84,6)	12 (15,4)	1,00	---	

(*) Chi-square (**) Fisher's exact test.

Regarding ICU admission, use of mechanical ventilation assistance and length of ICU stay, Table 3 shows a significant association with premature aging (p-value = 0.009, 0.009 and 0.042, respectively). Regarding the accumulation of comorbidities, there was no statistical significance.

Table 3. ICU admission, use of invasive mechanical ventilation assistance, length of ICU stays, number of comorbidities and premature aging in elderly people hospitalized with COVID-19.

	Premature aging				
Variable	**Yes (n, %)**	**No (n, %)**	**PR**	**CI 95% PR**	**p-value**
ICU admission					
Yes	58 (96,7)	2 (3,3)	1,18	1,03 – 1,35	0,009 *
No	45 (81,8)	10 (18,2)	1,00	---	
Use of mechanical ventilation					
Yes	75 (94,9)	4 (5,1)	1,22	1,02 – 1,46	0,009 **
No	28 (77,8)	8 (22,2)	1,00	---	
	Median (P25; P75)	Median (P25; P75)			
Hospitalization time	11,0 (6,0 – 20,0)	6,0 (4,3 – 7,0)	---	---	0,042 ***
Number of comorbidities	2,0 (1,0 – 3,0)	2,0 (1,0 – 2,0)	---	---	0,268 ***

(*) Chi-square (**) Fisher's exact (***) Mann-Whitney.

4. Discussion

This study shows that the group of elderly patients identified as prematurely aging based on their biological age had a greater need for ICU care, use of ventilatory support, longer hospital stays, and a higher mortality rate due to COVID-19. It is important to clarify that the number of elderly individuals who required ventilatory support exceeded the number of individuals admitted to the ICU because many received ventilatory support in the ward, since there were insufficient ICU beds to meet demand in that pandemic scenario.

In the context of the pandemic, the severity criteria were based on the chronological age and hemodynamic instability of hospitalized patients. However, studies have indicated that chronological age is not a reliable marker of an individual's health conditions. Bakakos et. al [10] evaluated the impact of chronological age and other clinical markers on the 60-day survival of elderly individuals hospitalized for COVID-19 in the ICU. Despite the lower survival rate for those aged ≥65 years (58%) compared to those aged <65 years (89.3% and p-value <0.001), multivariate analysis demonstrated that the presence of sepsis and a higher Charlson comorbidity index were independent predictors of mortality, whereas Chronological Age was not, suggesting the need to search for a set of clinical markers that better predict outcomes in COVID-19.

Initial studies with Biological Age sought to predict Chronological Age from DNA methylation biomarkers in blood or other tissues. However, it was observed that the effect size of these clocks in correlating with age-related diseases and conditions was small to moderate [11,12]. Thus, the study by Levine et al. [7] sought to develop the PhenoAge calculator, based on the prediction of a new age - the phenotypic age - that would be able to predict the risk of morbidity and mortality among individuals of the same age. The phenotypic age, created from routine blood tests, predicted clinical outcomes - all-cause mortality, mortality from specific causes, count of coexisting diseases and physical functionality. From this new composite of clinical measures, these researchers identified new DNA methylation groups that had not been observed in studies targeting Chronological Age, and that are possibly the result of age-related diseases and conditions. In this way,

PhenoAge would be able to capture changes in the number of years lived as well as other clinical conditions that differ among individuals of the same Chronological Age. Thus, the calculation of Biological Age by PhenoAge was able to predict clinical outcomes due to COVID-19 in our study.

Research by Kuo et al. [13] demonstrated the potential of phenotypic age in predicting complications from COVID-19. In this study, Biological Age was measured by PhenoAge prior to the pandemic, through exams collected between 2006 and 2010, and they observed an association with COVID-19 severity results, and the association was partially explained by prevalent chronic diseases close to the time of infection. In contrast, our study calculated Biological Age at hospital admission for COVID-19, which may have been able to encompass the baseline health conditions of patients at the time they contracted COVID-19 infection, which predispose them to a state of greater vulnerability to infectious complications. Both studies corroborate the potential of Biological Age as a measure that more accurately measures the real physiological state of organs, systems or the organism as a whole and is more capable of predicting clinical complications.

Cao et. al. [14] calculated Biological Age in people with COVID-19 using five different epigenetic clocks, one of which was PhenoAge. Acceleration of epigenetic age was found for patients with severe and non-severe COVID-19 compared to healthy individuals, across all timescales. In particular, the study also explored the dynamic changes in epigenetic age throughout the course of the disease in six individuals with COVID-19 compared to healthy individuals. A progressive increase in Biological Age was observed in the early and critical phases of COVID-19, which was partially reversed in the late phases of the disease across all timescales. This result corroborates the present study in capturing the acceleration of Biological Age at the time of admission for COVID-19, and may be useful as a prognostic marker.

In agreement with previous literature, the current research presents Biological Age as a prognostic tool that best responds to the dichotomy between survival and mortality in patients affected by COVID-19 infection, to the detriment of Chronological Age. It is noteworthy that data on sociodemographic characteristics, such as sex and Chronological Age, and underlying diseases did not contribute to the prediction of mortality in the present study. Possibly, analyzing such attributes individually does not allow us to understand the complex and interdependent process of health and disease in patients, translated into the form of risk of complications from COVID-19. However, it is noteworthy that Chronological Age is one of the variables that feeds the PhenoAge calculator, incorporating it into the Biological Age compound together with the other nine blood test variables.

It is important to highlight that PhenoAge was constructed from 42 laboratory variables and Chronological Age. Using the Cox penalized regression model, the ten variables most associated with the clinical outcomes studied were selected, one of which was Chronological Age. The selected tests represent measures of liver function (albumin and alkaline phosphatase), kidney function (creatinine), metabolic function (glucose), immune function (percentage of lymphocytes, MCV, RDW and leukocytes) and inflammatory status (CRP). According to the authors, these variables and Chronological Age express the physiological dysregulation caused by endogenous, exogenous and age-related factors, which in turn promote imbalance in the various organic systems, producing pathogenesis and consequently molecular alterations. Together, the combination of variables makes up the phenotypic age constructed from clinical risk markers, such as mortality [9].

The use of a tool, available free of charge via the internet - Ageless Rx calculate - and which uses resources that are easy to collect in a controlled hospital environment - date of birth and the results of laboratory tests - to compose the Biological Age makes it an accessible and practical tool in clinical settings. In contrast, previous studies have measured Biological Age using more complex methods, such as genetic and epigenetic markers – telomere shortening and DNA methylation [15-17], however, such methods are difficult to access in routine clinical practice.

Some limitations stand out in this study. This is a retrospective study and, therefore, there is a need for future prospective longitudinal studies to investigate the contribution of these variables to biological aging and vulnerability to SARS-CoV-2 infection in the elderly population. Our sample consisted of 103 elderly people with premature aging and only 12 with normal aging. Since our study was carried out in a hospital setting, the sample consisted of all elderly people with severe COVID-19 requiring hospitalization, and the Biological Age tool may have captured this group of greater clinical severity in the form of premature aging. A larger sample would be interesting to include more patients with normal aging to allow greater robustness in comparisons between the groups and possible generalization of the results. A study with a larger sample of healthy individuals could result in greater statistical difference between the groups.

However, it is important to note that our analysis is based on the spectrum of the Brazilian population, which has multiple health inequalities and lacks a measurement of severity that is based on the availability of health resources. However, future studies are needed with larger sample sizes and including populations from other regions of Brazil, since the country has great demographic diversity and health conditions, which may influence the outcomes related to COVID-19.

This research, therefore, adds to the previous literature to corroborate the potential of Biological Age from routine blood samples as a prognostic tool and brings as a differential its applicability in the COVID-19 scenario. The recognition of Biological Age as a better prognostic tool can help in clinical practice to identify patients at higher risk, improving care, reducing unfavorable outcomes and enabling the optimization of health resource management, especially in the public setting and in extreme situations, such as the pandemic.

5. Conclusion

This study sought to assess whether Biological Age, measured through laboratory blood tests, would be able to predict the risk of severity and mortality due to COVID-19 in elderly patients hospitalized. The group of patients identified as having premature aging by Biological Age had a higher mortality rate, need for MVA, and length of hospital stay. These results demonstrate the prognostic value of Biological Age for outcomes in elderly patients with COVID-19, using a free, easily accessible tool and based on common blood tests in daily clinical practice.

Funding: None.

Research Ethics Committee Approval: The present research respects the basic ethical principles of bioethics (autonomy, non-maleficence, beneficence and justice), in accordance with resolution number 466/12, under CAEE 44881321.7.0000.5208. As this is a study with secondary data, the use of the Free and Informed Consent Form is not required.

Acknowledgments: None.

Conflicts of Interest: The authors declare no conflict of interest.

Supplementary Materials: None.

References

1. Galkin F, Parish A, Bischof E, Zhang J, Mamoshina P, Zhavoronkov A. Increased Pace of Aging in COVID-Related Mortality. Life (Basel). 2021 Jul 22;11(8):730. doi: 10.3390/life11080730. PMID: 34440474; PMCID: PMC8401657.
2. Mueller AL, McNamara MS, Sinclair DA. Why does COVID-19 disproportionately affect older people? Aging (Albany NY). 2020 May 29;12(10):9959-9981. doi: 10.18632/aging.103344. Epub 2020 May 29. PMID: 32470948; PMCID: PMC7288963.
3. Cao X, Li W, Wang T, Ran D, Davalos V, Planas-Serra L, Pujol A, Esteller M, Wang X, Yu H. Accelerated biological aging in COVID-19 patients. Nat Commun. 2022 Apr 19;13(1):2135. doi: 10.1038/s41467-022-29801-8. PMID: 35440567; PMCID: PMC9018863.

4. Zhavoronkov A, Li R, Ma C, Mamoshina P. Deep biomarkers of aging and longevity: from research to applications. Aging (Albany NY). 2019 Nov 25;11(22):10771-10780. doi: 10.18632/aging.102475. Epub 2019 Nov 25. PMID: 31767810; PMCID: PMC6914424.
5. Galkin F, Mamoshina P, Aliper A, de Magalhães JP, Gladyshev VN, Zhavoronkov A. Biohorology and biomarkers of aging: Current state-of-the-art, challenges and opportunities. Ageing Res Rev. 2020 Jul;60:101050. doi: 10.1016/j.arr.2020.101050. Epub 2020 Apr 6. PMID: 32272169.
6. Erema VV, Yakovchik AY, Kashtanova DA, Bochkaeva ZV, Ivanov MV, Sosin DV, Matkava LR, Yudin VS, Makarov VV, Keskinov AA, et al. Biological Age Predictors: The Status Quo and Future Trends. Int J Mol Sci. 2022;23(23):15103. doi: 10.3390/ijms232315103.
7. Levine ME, Lu AT, Quach A, Chen BH, Assimes TL, Bandinelli S, Hou L, Baccarelli AA, Stewart JD, Li Y, Whitsel EA, Wilson JG, Reiner AP, Aviv A, Lohman K, Liu Y, Ferrucci L, Horvath S. An epigenetic biomarker of aging for lifespan and healthspan. Aging (Albany NY). 2018 Apr 18;10(4):573-591. doi: 10.18632/aging.101414. PMID: 29676998; PMCID: PMC5940111.
8. World Health Organization. Laboratory testing for COVID-19 in suspected human cases. WHO; 2020.
9. Liu Z, Kuo PL, Horvath S, Crimmins E, Ferrucci L, Levine M. A new aging measure captures morbidity and mortality risk across diverse subpopulations from NHANES IV: A cohort study. PLoS Med. 2018 Dec 31;15(12). doi: 10.1371/journal.pmed.1002718. Erratum in: PLoS Med. 2019 Feb 25;16(2). doi: 10.1371/journal.pmed.1002760. PMID: 30596641; PMCID: PMC6312200.
10. Bakakos A, Koukaki E, Ampelioti S, Ioannidou I, Papaioannou AI, Loverdos K, Koutsoukou A, Rovina N. The Real Impact of Age on Mortality in Critically Ill COVID-19 Patients. J Pers Med. 2023 May 29;13(6):908. doi: 10.3390/jpm13060908. PMID: 37373897; PMCID: PMC10303099.
11. Maierhofer A, Flunkert J, Oshima J, Martin GM, Haaf T, Horvath S. Accelerated epigenetic aging in Werner syndrome. Aging (Albany NY). 2017 Apr;9(4):1143-1152. doi: 10.18632/aging.101217. PMID: 28377537; PMCID: PMC5425119.
12. Horvath S, Erhart W, Brosch M, Ammerpohl O, von Schönfels W, Ahrens M, Heits N, Bell JT, Tsai PC, Spector TD, Deloukas P, Siebert R, Sipos B, Becker T, Röcken C, Schafmayer C, Hampe J. Obesity accelerates epigenetic aging of human liver. Proc Natl Acad Sci U S A. 2014 Oct 28;111(43):15538-43. doi: 10.1073/pnas.1412759111. Epub 2014 Oct 13. PMID: 25313081; PMCID: PMC4217403.
13. Kuo CL, Pilling LC, Atkins JL, Masoli JAH, Delgado J, Tignanelli C, Kuchel GA, Melzer D, Beckman KB, Levine ME. Biological Aging Predicts Vulnerability to COVID-19 Severity in UK Biobank Participants. J Gerontol A Biol Sci Med Sci. 2021 Jul 13;76(8). doi: 10.1093/gerona/glab060. PMID: 33684206; PMCID: PMC7989601.
14. Cao X, Li W, Wang T, Ran D, Davalos V, Planas-Serra L, Pujol A, Esteller M, Wang X, Yu H. Accelerated biological aging in COVID-19 patients. Nat Commun. 2022 Apr 19;13(1):2135. doi: 10.1038/s41467-022-29801-8. PMID: 35440567; PMCID: PMC9018863.
15. Mongelli A, Barbi V, Gottardi Zamperla M, Atlante S, Forleo L, Nesta M, Massetti M, Pontecorvi A, Nanni S, Farsetti A, Catalano O, Bussotti M, Dalla Vecchia LA, Bachetti T, Martelli F, La Rovere MT, Gaetano C. Evidence for Biological Age Acceleration and Telomere Shortening in COVID-19 Survivors. Int J Mol Sci. 2021 Jun 7;22(11):6151. doi: 10.3390/ijms22116151. PMID: 34200325; PMCID: PMC8201243.
16. Erema VV, Yakovchik AY, Kashtanova DA, Bochkaeva ZV, Ivanov MV, Sosin DV, Matkava LR, Yudin VS, Makarov VV, Keskinov AA, et al. Biological age predictors: the status quo and future trends. Int J Mol Sci. 2022;23(23):15103. doi: 10.3390/ijms232315103.
17. Jylhävä J, Pedersen NL, Hägg S. Biological Age Predictors. EBioMedicine. 2017 Jul;21:29-36. doi: 10.1016/j.ebiom.2017.03.046. Epub 2017 Apr 1. PMID: 28396265; PMCID: PMC5514388.