

Is Biological Age a Better Indicator than Chronological Age for Metabolic Health?

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Abstract

Our earlier studies have shown more advanced biological age than chronological age in obese women ≥ 40 years of age and particularly with greater visceral obesity. Advancement of age was also seen in women with Polycystic Ovarian Syndrome. Both obesity and Polycystic Ovarian Syndrome patients are known to be associated with metabolic dysfunction with underlying insulin resistance. Since metabolic syndrome is highly prevalent in Indian population, there is a pressing need for in-depth studies about how advancement of biological age over chronological age impacts health and longevity. In this article, we limit the review to the definition, dimensions, markers and predictors of biological aging.

Keywords: Biological age, Chronological age, HOMA IR, Metabolic syndrome, PCOS

Introduction

Health and well being are crucial for each individual to have a good quality of life. Chronological age (CA) is the time elapsed since birth- the primary way people define age. Aging is a major risk factor for impairment of bodily functions, chronic diseases and mortality. However, there is a great heterogeneity in the health outcomes of older individuals. Some persons who are in their seventies may be frail and require assistance in daily living. Others who are in the same age group or are even older may be able to function independently without assistance. Given the increase in the aging population globally, it would be worthwhile to have good understanding of the temporal process of aging verses biological determinants of accelerated aging.

Currently the concept of biological age (BA) has emerged as a marker of functional health status of an individual. BA and CA are differentiated by multiple biomarkers; these markers are influenced by lifestyle,

nutrition, antioxidant defence, immunity and chronic diseases. In a gerontological research, the concept of BA and specific markers of its estimation have gained significant importance. The fact that different people age differently and some retain youthful health have intrigued scientist for long.

Dimensions of Aging

Three interesting dimensions of aging are (i) prediction of survival and mortality, in other words relating aging to longevity as an outcome, (ii) aging as a process in relation to the ability to function. This becomes of great relevance when the ability to function independently is associated with aging and (iii) to evaluate therapies and interventions to improve health and to extend lifespan in a meaningful way.^[1] Yoo *et al.* in 2017, observed that death rate increased significantly as biological age increased more than chronological.^[2] A Korean study of 557,940 subjects aged 20-93 years reported 13106 cases of death. The authors reported that the average BA of living subjects was almost the

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same as the average CA, whereas for those who were deceased, the BA was greater than the CA. These investigators noted that BA can be a valid proxy for aging and that biological aging could be related to frailty and physical fitness.^[3]

It is well known that energy metabolism slows down as a person ages. Energy expenditure by the body is assessed by measuring the resting metabolic rate. Also, physical activity of individuals decreases with age. However, the decline in resting metabolic rate with CA has been shown to manifest differently depending on the individual's BA.^[1] Characteristically, with aging there is insulin resistance, physiological decline in growth hormone as well as change in body composition. Proinflammatory cytokines that interfere with the action of insulin also increase. These cytokines are associated with visceral /abdominal fat and along with the increasing number of senescent cells, there is also a loss of mitochondrial function in many tissues including skeletal muscle.^[4]

Markers of Biological Age

In aging research, several clinical and other biomarkers have been studied. Aging affects the levels of proteins, metabolites, and other biomolecules in body fluids.^[5] Some of these are molecular e.g. based on DNA or RNA, others have looked at clinical markers like lipid levels, creatinine, grip strength etc.^[1] Biomarkers that are known to influence aging process have been for evaluation of BA. Markers of metabolic, cardiac, kidney, lung and liver functions which correlate with CA have also been found to be correlated with estimated BA. Some of the markers that have been studied include uric acid, IL-6, urea, albumin, muscle strength, blood pressure, lipids, glucose, BMI, smoking fibrinogen, HbA1c, BMI, lung function and hip bone mineral density. While many have sought to determine the risk of death, it would be more important/meaningful to reflect the true metabolic and physiological state (of aging) as a determinant of morbidity in order to improve early detection and facilitate appropriate intervention.^[5]

We at our institution, conducted a study on a group of women with Polycystic ovarian syndrome (PCOS), which is also considered as metabolic syndrome with underlying insulin resistance and chronic inflammation.^[6,7] We compared them to metabolically healthy women. The question we sought an answer to was whether women with PCOS are rapidly advancing in age. We used bioelectrical impedance tool for assessing BA. Advance body age, i.e. the difference be-

tween chronological age and body age, in these 41 patients, ranged from 8 to 40 years. Our study showed that in the participants who had PCOS, advanced body age significantly correlated with body mass index, total percent body fat as well as the percent visceral fat, whereas chronological age did not show any correlation. Advanced body age also correlated significantly with HOMA-IR, the marker of insulin resistance, in patients with PCOS.

In a study of 954 young adults, Belsky *et al.* (2015) tracked multiple biomarkers that assessed pulmonary, periodontal, cardiovascular, renal, hepatic, and immune function across three time points spanning into the third and fourth decades of the participants and determined biological aging.^[8] Before midlife itself, they observed that some individuals were aging more rapidly and these individuals were less physically able, showed cognitive decline, brain aging, self-reported worse health and looked older. "BA predictor could be defined as a biomarker correlated with chronological age, which brings additive information in the risk assessments for age-related conditions on top of chronological age".^[9] "Aging is now understood as a gradual and progressive deterioration of integrity across multiple organ systems".^[10] In the same age group/age band, BA would reflect the heterogeneity in functional status and vulnerability to disease which cannot be assessed by chronological age.

Thus, age-related physiological changes; chronic inflammatory disorders which affect organ systems can be effectively evaluated on the basis of body age. BA would be a useful assessment tool to provide meaningful information in order to improve health status using preventive, promotive or therapeutic approaches. Hsu has mooted "effective health age" that can be potentially changed with appropriate life style alterations that can lead to improvements in metabolic condition.^[11]

Predictors of Biological Age

Earls *et al.* in 2019 investigated biological aging in 3,558 individuals, in a longitudinal study.^[12] They found that measures of metabolic health, inflammation, and toxin bioaccumulation were strong predictors of BA. Among 43 health conditions, they noted that obesity, hypertension, high cholesterol, lung infection, type 2 diabetes (T2D), and breast cancer were associated with increased age. Using, modelling studies, they found that type 2 diabetes mellitus had the greatest increase with age. Among the biomarkers studied, glycated haemoglobin was the strongest positive pre-

dicator of BA independent of sex and overall metabolic health. Inflammation and bioaccumulation of toxins were found to be the most strongly related to BA. In men, creatinine was observed to be a strong predictor of biological aging. These authors also observed that those persons who were participating in a wellness programme showed a significantly lower rate of change than the expected ~1 year per year. These data clearly suggest that appropriate interventions might be useful in stabilizing or perhaps reducing the pace of biological aging. Bae *et al.* investigated and examined the data of 16,518,532 subjects (8,671,838 males and 7,846,694 females) who completed a validated health survey of the National Health Insurance Service of the Republic of Korea (2014–2015). This data was analyzed to develop a BA model for metabolic syndrome.^[13] These authors found that smoking influenced visible signs of aging, particularly among women. A similar sex-specific effect was found with alcohol consumption. On the other hand, regular physical activity was found to be beneficial, and that a high level of physical activity was associated with lower values for BA in both males and females. The authors have pointed out that several other research groups have found that BA increased with decreased physical activity, and that physiological improvement can reduce the rate of aging. In active, middle-aged men, who did endurance exercise regularly, the average BA was 4.7 years lower than their CA.^[14]

Conclusion

In summary, CA basically reflects the time that has flown or elapsed after birth and it has limitations in terms of being able to reflect the decline in physiological functions and the health and aging status of the individual. BA, on the other hand, is a better indicator of the health status of an individual. BA has been studied by researchers since the 1970's and mostly in several Western countries. It would be worthwhile to examine the potential for using BA in the Indian context and to identify individuals who have advanced BA vis-à-vis the CA for intervention therapies, and not particularly to predict lifespan or risk of mortality. It would be very worthwhile to test therapies or health-inducive behaviours and to monitor how the BA per se and the extent of change in the BA.^[3] There is a need to study the effectiveness of various Indian traditional practices such as fasting or phytoactives or plant materials/formulations recommended in the Ayurvedic texts for their ability to modulate advances in biological aging. Even a N=1 study would be immensely useful to begin with followed by more detailed and in-depth studies designed to enable application of the findings at pop-

ulation level.

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