What does the Anti-Aging Medical Checkup show?: Data presentation

Yoshikazu YONEI¹ Wakako TAKABE¹ Masayuki YAGI¹

¹Anti-Aging Medical Research Center, Graduate School of Life and Medical Sciences, Doshisha University

ABSTRACT

In anti-aging medical check-ups, aging is evaluated by functional ages (muscle age, vascular age, neural age, hormone age, and bone age) and risk factors of aging (immune stress, oxidative stress, physical and mental stress, glycativ stress, and lifestyles) separately. Based on each measurement result, a medical treatment plan is implemented targeting the improvement of lifestyle habits including education about proper diet, nutrition, and physical exercise. In order to attain balance, we start with rectifying risk factors in descending order of seriousness by focusing on the most deteriorated parts of the body in terms of functionality. It enables the patient to prolong their years of healthy lifespan and to increase their average lifespan. We will show a practice example of the anti-aging medical check-up in occupational health care as well as elderly care. Among the college personnel, there are many who suffer from aging of their musculoskeletal system. Among those with metabolic syndrome, there are many who are weak in terms of the blood vessel systems.

It is shown that executives of big enterprises have a 15% younger bone age and IGF-I hormone compared to other males in the same generation. It is recommended that in the analysis of five months' intervention study on elderly patients, we should treat functional age adding 0.42 years which is equivalent to five months. In the anti-aging check-up, it is possible to attain information which cannot be recognized during an ordinary check-up. (HEP. 2017; 44: 600-605.)

Key words aging, functional age, occupational health, insulin-like growth factor-I (IGF-I), dehydroepiandrosterone (DHEA)

Introduction

Though the human body consists of various structures, parts, and organs, the aging process for them is not always the same. There are differences depending on each individual and each part. The risk factor to accelerate aging differs depending on the individual. In the latter part of 30s, the pathological degeneration due to aging begins to form on a part of the body, which can cause diseases that provide a negative impact on other healthy parts. Reviewing the examination results of centenarians who enjoy their life in a healthy state, it is seen that they have a well-balanced aging process of the whole body, and that they have few risk factors for aging. It will enable us to attain a healthy, long life to recognize early what our weaknesses are due to aging by having anti-aging medical check-ups, to attain balance of the whole body, and to rectify the risk factors for aging¹⁻³⁾. The anti-aging check-up was introduced as a means to measure aging^{1, 4)}, which we already mentioned in the previous report⁴⁾. This time, some practice examples of anti-aging check-ups will be shown.

Check-up items –Functional age and risk factors of aging–

Check-up items for aging are classified into two categories, functional age and risk factors in aging (Fig. 1)^{1, 4)}. In the anti-aging check-up, aging is measured by five items including muscle age, vascular age, neural age, hormone age, and bone age, while risk factors of aging are measured by five items, i.e. immune

Fig. 1 Evaluation of aging and risk factors.

Aging level is measured by dividing it to functional age and risk factors that accelerate aging. PWV: pulse wave velocity, CAVI: cardio-ankle vascular index, YAM: young adult mean, DEXA: dual energy x-ray absorptiometric scan, dROM/BAP • bOS/bAP: oxidative stress degree/anti-oxidant capacity (refer to Reference 7)), and AGE: advanced glycation end product. This figure was cited and modified from Reference 1).

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Corresponding author: Professor Yoshikazu Yonei, MD, PhD

¹Address: Anti-Aging Medical Research Center, Graduate School of Life and Medical Sciences, Doshisha University 1-3, Tatara Miyakodani, Kyotanabe, Kyoto 610-0394, Japan

TEL: +81-774-65-6394, FAX: +81-774-65-6394

E-mail: yyonei@mail.doshisha.ac.jp

Fig. 2 Law of Pirates.

There is a power law, the Pareto principle advocated by Italian economist Vilfredo Federico Damaso Pareto, which is not a verified law, but a rule of thumb. Law of Pirates is a variation of the Pareto principle. When the two indicators of aging including the most degenerated “functional age” and the largest “risk factor of aging” out of ten are rectified in advance, 80% of goals of medicine will be achieved. It is an important task for us health care providers to put a priority in education. Illustrations were produced through the courtesy of Medical Premier, Mainichi Shinbun.

stress, oxidative stress^{5, 6)}, physical and mental stress, glycativ stress⁷⁻⁹⁾, and lifestyles. When explaining the check-up result to examinees, it is easier for them to show it by functional age, rather than describing numerical values which might “increase or decrease”. Quantifying the risk factors, while showing which item is the biggest risk factor, enables clarification of the priority order in education. It is better to rectify the more important two items out of ten aging categories, that is, the most degenerated “functional age” along with the biggest “risk factor for aging” (Fig. 2).

There is no absolute evaluation method to measure functional age for the moment. Therefore, it is usual to use the curve evaluation, producing aging curves based on parameters in order to estimate the equivalent age. The target score for functional age is 80 percent of the actual age, while examined data is set by using the average value of age plus 0.5~1.0 standard deviation.

Measurement of functional age

• Muscle age

The skeletal muscle mass of the body decreases by one percent annually, unless some special load muscle training is implemented¹⁰⁾. Especially, the decrease in thigh muscles and trunk muscles is remarkable. The deterioration of muscle age leads to sarcopenia and locomotive syndromes which largely contribute to persons becoming bed-ridden (nursing care level five). The measurement of muscle mass is classified into the magnetic resonance imaging, e.g. MRI, the dual-energy X-ray absorptiometry: DEXA, and the bioelectrical impedance method. The bioelectrical impedance method is inferior in accuracy to the other methods but is sufficient as a screening method. By implementing some special load muscle training, it is possible to increase the skeletal muscle mass and to rejuvenate the muscle age.

• Vascular age

In order to measure the worsening level of arteriosclerosis, the finger plethysmogram test, the pulse wave velocity test (PWV),

and the cardio ankle vascular index test (CAVI) are used. The vascular age is nothing more than an indicator. An important aspect in anti-aging education is to evaluate risk factors for arteriosclerosis appropriately, one by one, and to rectify them in the descending order from the most serious factor. Diabetes, high blood pressure, hyperlipidemia, and smoking are considered to be the four biggest risk factors. Among them, diabetes and hyperlipidemia must be regarded as the status with high glycativ stress, while smoking must be regarded as the status with high oxidative stress. Other factors including high homocysteine values, physical and mental stress, and inflammation (hs-CRP, slightly positive) caused by immunity stress must be rectified appropriately.

• Neural age

The executive brain dysfunction includes attentiveness, frontal lobe function, perception function, cognitive function, impressibility, and other mental functions. The quantitative evaluation method for executive brain dysfunction is not exactly established and an examination of one item is not sufficient for evaluation. The Japan Brain Dock Society recommends that the Wisconsin card sorting test be implemented as a screening¹¹⁻¹³⁾.

• Hormone age

Growth hormone (GH) and IGF-I (insulin-like growth factor-I)

The secretion of GH, and its second messenger hormone IGF-I, starts decreasing around the age of 30 years old, and can be considered as a factor to predict the vital prognosis or the lowering of QOL. The deficiency of these hormones is called somatopause, which not only causes a delay of cell proliferation and protein synthesis, but is closely concerned with a lowering of neuropsychiatric function, reproductive function, digestive function, and also bone metabolism. Lifestyle-related diseases including fatty liver disease are also very concerning¹⁴⁾. Exercises are considered effective to increase the secretion of IGF-I¹⁵⁾.

DHEA (dehydroepiandrosterone sulfate)

DHEA-s is a steroid hormone secreted from the adrenal cortex. Using DHEA-s, more than 50 kinds of hormones including sex hormones and cortisol are produced¹⁾. The secretion of DHEA-s decreases as we grow old¹⁶⁾. The decrease of DHEA-s not only causes the lowering of immune function as well as resistance against mental stress, but also increases the risk of lifestyle-related diseases¹⁷⁾ such as metabolic syndrome, fatty liver disease, diabetes, high blood pressure, and osteoporosis. In the examination, the stabilized type of DHEA-s is measured. Exercises are considered effective to increase the secretion of DHEA-s¹⁵⁾.

• Bone age

The method to evaluate bone age is mainly divided into the DEXA method and the ultrasonic method. Although it is possible to measure bone density precisely by using the DEXA, there is a problem of equipment being very expensive. The measurement of lumbar vertebra tends to show comparatively higher values of bone density due to an adhesion or a compression fracture. It is better to evaluate bone age by the bone density of the femoral neck. In the case of patients who chronically lack sufficient walking habits, it is observed that the bone density of the femoral neck tends to decrease to more than that of the lumbar vertebra. The ultrasonic diagnostic equipment (A1000: Healthcare Japan) is

suitable for screening due to the comparatively reasonable price. The ultrasonic diagnostic equipment to measure bone stiffness of calcaneus is able to provide comparatively rich data to evaluate bone age.

Measurement of risk factors in aging

Here, we explain about two leading risk factors: oxidative stress and glycativ stress.

· Oxidative stress

The reactive oxygen species/free radical causes oxidative damage to the proteins, fats, and DNA that compose the human body⁵⁾. The factors that cause oxidative stress include smoking, ultraviolet exposure, mental and physical stress, and excessive intake of alcohols. There are various biomarkers provided for the measurement of oxidative stress. Based on the viewpoint of duplicability, accuracy and data storage, biomarkers including 8-OHdG (8-hydroxy-deoxyguanosine)/forming rate of isoprostane in urine, and lipid peroxides in blood/fixed quantity of ubiquinone (coenzyme q10)/oxidative stress degree (bOS/bAP) are used⁶⁾. 8-OHdG shows the degree of damage to the DNA, while isoprostane and fatty acid peroxides show the damage and degree of fat oxidation. Ubiquinone evaluates the total blood concentration and the oxidation rate each in oxidized form as well as the reduced form (oxidized/oxidized+reduced). When a more accurate checkup is necessary, fat-soluble antioxidants (vitamin A/E etc.), water-soluble antioxidants (vitamin C etc.) as well as oxidative precursors (Fe/cholesterol) must be measured. All of these enable us to provide measures to stop oxidative stress including a selection of antioxidants based on each result.

· Glycative stress

Glycative stress is a series of phenomena where an excessive intake of glucose, fructose, fats, and alcohols modify protein, fats, DNA base molecules, and amyloid in the body, resulting in the lowering of the function to form body waste including advanced glycation end products (AGEs) or degeneration of functional proteins^{7, 8)}. In the cases of diabetes, metabolic syndromes, lipid abnormalities, alcoholism, as well as chronic kidney diseases, glycative stress is kept so high as to cause a variety of diseases and regressive changes such as osteoporosis¹⁸⁾, dementia¹⁹⁾, skin aging⁷⁾, ovarian hypofunction²⁾, cataract/age-related macular degeneration²⁰⁾, and hair aging²¹⁾. To evaluate glycative stress, pentosidine in blood plasma or urine, carboxymethyllysine (CML) in blood serum/skin horny layer, and skin auto fluorescence of AGEs (AGE Reader, DiagnOptics) are measured⁹⁾. In order to reduce glycative stress, such measures as prevention/rectification of postprandial blood glucose level, generation inhibition of AGEs, and decomposition/renal discharge of AGEs should be taken.

Education based on results

For example, when the bone age of a 55 year-old male is close to the average bone age of 60 year-old people, his bone age is set as 60 years old. The functional age can be calculated in reference with the database. In preventive medicine, we put a priority on the primary prevention where the improvement of lifestyle habits

(dietary habit, exercise, and intellectual education) will be attempted, based on the anti-aging medical check-up. In this way, the risk factors of aging are rectified one by one. When necessary, medical treatments including drug therapy, hormone replacement therapy and regenerative medicine will be provided. In the process of education, motivations/behavior modification are important, which requires the capability of experts/instructors of anti-aging therapy (educational skill/knowledge/eagerness).

Examples of introducing anti-aging medical check-ups into enterprises

47 examples of anti-aging check-ups for male employees who engage themselves in light work are shown (Fig. 3)²²⁾. In their workplace, employee's functional age, on average, is very close to their actual age. Then, in which part do they suffer from aging? Observing the weaker part of the body due to aging, it was recognized that 53% were weak in vascular age, while 32% were weak in neural age. This means that industrial physicians are able to provide group educations to employees, dividing them by their weak points.

Then, examples of university employees including faculty members are shown (Fig. 4)²²⁾. Unlike employees engaged in light work, there are many who were weak in bone age and muscle age. What is remarkable is that there are quite few (5%) who were weak in neural age. It can be assumed that employees of universities tend to routinely engage themselves in intellectual work, and that they have many opportunities to contact young people, including students of colleges or graduate schools.

In some enterprises, anti-aging check-ups are implemented, targeting those who were diagnosed to suffer from metabolic syndromes (including pre-metabolic syndromes) (Fig. 5)²³⁾. As a result, it was clarified that half of the recipients of check-ups showed a weakness in vascular age. The result verified that those people with problems regarding girth of abdomen, blood pressure, triglycerides, and fasting blood sugar level have a high risk of arteriosclerosis.

Company T light workers (male n = 47, 42.7 ± 14.4 y.o.)

Fig. 3 Anti-aging medical check-ups in enterprises: employees engaged in light work (June, 2004).

Regarding office employees for light work, weakness due to aging is most seriously observed in vascular age, followed by neural function age. The results were expressed as average value ± standard deviation. This figure was cited and modified from Reference 22).

University D faculty and staffs(male: 445, female: 269, total: 714, 44.4 ± 26.9 y.o.) **Fig. 4** Anti-aging medical check-ups in enterprises: university staffs and faculty (October, 2006).

Regarding university staffs and faculty, weakness due to aging is most seriously observed in bone age, followed by muscle function age. There were few who have weakness due to aging in neural age. The results were expressed as average value $\pm$ standard deviation. This figure was cited and modified from Reference 22).

Company M MetS subjects (male: 18, 54.7 ± 7.3 y.o.) **Fig. 5** Anti-aging check-ups in enterprises: those who are diagnosed with metabolic syndromes (2009).

The half of those who were diagnosed with metabolic syndromes (MetS) in the special check-up had weakness due to the aging of vascular bones. The results were expressed as average value $\pm$ standard deviation. This figure was cited and modified from Reference 23).

The result of check-ups for ordinary males in the same generation as male executives of enterprises is shown in **Fig. 6**²⁴⁾. The executives showed higher serum cortisol values than the ordinary males, while their bone age was 5.3 years younger, and IGF-I hormone age was 5.0 years younger. It was assumed that they manage to complete the daily work causing physical and mental stress by their solid bone, and growth hormone/ IGF-I hormone activity.

So far, some examples of introducing anti-aging check-ups into the enterprises were shown. They provide curious information regarding which part of the body aging accelerates depending on the kinds of work or lifestyle habits, and what the differences were regarding those who were assigned as executives. Anti-aging check-ups, which are sure to keep employees young with improved health conditions, will reduce their absentee rate, enhance corporate productivity and achievement, prevent acci-

Company J executives(male: 49, 59.5 ± 5.6 y.o.) **Fig. 6** Anti-aging check-ups in enterprises: Officers of big enterprises (2004).

It was clarified that though officers of big enterprises were suffering from physical and mental stress considering that they showed high serum cortisol, they showed younger bone age and IGF-I hormone. D/C ratio: ratio of DHEA-s and cortisol. The results were expressed as average value $\pm$ standard deviation. The figure was revised based on Reference 24).

dents from occurring, and contribute to the cost reduction of the health insurance society. We hope many industrial doctors will participate in the program.

Examples of anti-aging medical check-ups for the elderly

We have been engaged in our research “Kenpo-juku” since 2008, targeting independent elderly people living in the Yurin area located in Shimokyo-ku, Kyoto^{25, 26)}. Our activity aims at encouraging the elderly to engage themselves in physical activities including walking. In our activity, college/graduate school students visit a community center in the area every month to collect data on physical activity meter which participants are supposed to wear, interview them, and distribute printed papers to them. It is not sufficient to only allot pedometers for participants to continue the programs. However, when we show monthly results to them through students who are in the same generation as the grand-children of participants, they became positively pressured, which led them to become motivated to continue physical activities.

Fig. 7 shows the results of anti-aging check-ups conducted both in December 2008, the beginning year of our research, and in April in 2009²⁵⁾. There was no significant difference between the two periods of time regarding functional age. However, considering that there was an increase of actual age by 0.42 years in five months, it can be confirmed that the program worked on the rejuvenation of functional age in the categories besides neural age.

In the previous report⁴⁾, we have already introduced the result²⁹⁾ of comparison between independent elderly residents in Yurin area²⁵⁾, those requiring nursing care who go to and from nursing care centers²⁷⁾, and those in the same category who live in geriatric health services facilities²⁸⁾. As a result, it was clarified that

Fig. 7 Intervention examples targeting independent elderly residents: Health promotion program using management system of waking steps.

a) Comparison of functional age. Independent elderly residents were made to wear pedometers. They were interviewed every month for the promotion of walking habits. Their functional age was compared before the program and after five months. No significant difference was found for functional age. The results were expressed as average value $\pm$ standard deviation. b) It must be considered that the actual age was 0.42 years higher after five months. Produced based on Reference 25).

degeneration of neural function plays an active role in preventing elderly residents from being independent, as an obstacle of activities of daily living (ADL). In order to increase the number of the independent elderly who are free from care, it is important to offer them early interventions so they can retain cognitive functions.

Conclusion

Anti-aging is a method to prevent aging and to rejuvenate functional age. In order to have more years of healthy living, it is necessary that our whole body become senescent in a well-balanced way. By measuring our functional age through anti-aging medical check-ups, we are able to obtain information which is impossible to acquire during ordinary check-ups.

I set-up a hypothesis as follows: it is possible to prolong the healthy life years if we are able to let our whole body become senescent in a well-balanced manner and to reduce the gap between the average lifespan and the healthy lifespan. In order to realize this, it is necessary to recognize early the body parts where functional age degenerates most seriously, as well as the largest risk factor for it, while trying to rectify them. This hypothesis will be verified by collecting the data of anti-aging medical check-ups held in each medical institution and by analyzing them as a data set. I sincerely hope that more and more medical institu-

tions will offer the opportunity of having anti-aging check-ups to the public.

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