Original Article

Skin Accumulation of Advanced Glycation End Products and Lifestyle Behaviors in Japanese

Keitaro Nomoto 1), Masayuki Yagi 1,2), Seizaburo Arita 1,3), Mari Ogura 4), Yoshikazu Yonei 1)

1) Anti-Aging Medical Research Center, Graduate School of Life and Medical Sciences Doshisha University
2) Glycation Stress Research Center, Graduate School of Life and Medical Sciences Doshisha University
3) Medical Fuzzy Research Center, Graduate School of Life and Medical Sciences Doshisha University
4) Faculty of Human Life and Science, Doshisha Women’s College of Liberal Arts

Abstract

Purpose: Skin accumulation of advanced glycation end products (AGEs) was non-invasively detected as specific fluorescence and the relationship with lifestyle behaviors in younger and middle age Japanese was examined.

Method: Subjects were 244 Japanese aged 20-59 (82 men, mean age: 45.4±8.7 years old; 162 women, mean age: 43.4±8.8 years old). The intensity of skin Auto Fluorescence (AF) in the upper arms was measured by AGE Reader. Subjects were divided into 4 groups with a 10-year age interval: 20-29 (20s), 30-39 (30s), 40-49 (40s) and 50-59 (50s) and lifestyle behaviors, surveyed by Anti-Aging Common Questionnaire, were examined and grouped into a risk merger model in relation to the validation of skin AF.

Results: Smoking (r=0.255, p<0.001) and frequency of alcohol intake (r=0.210, p<0.001) were positively correlated with skin AF. Sleeping hours might be negatively correlated with skin AF (r=-0.124, p=0.054). After the cutoff value of these lifestyles was set up, subclass analysis was conducted. The skin AF of smoking risk (+) group was higher than that of smoking risk (-) group (p=0.002). The skin AF of drinking risk (+) group was higher than that of drinking risk (-) group (p=0.006), and the skin AF of sleeping risk (+) group might be higher than that of sleeping risk (-) group (p=0.060). Cumulative effects were observed in these three risk factors associated with increased skin AF.

Conclusion: Skin AF might reflect the AGEs accumulation promoted by bad lifestyle behaviors which are smoking, high frequency of alcohol drinking and lack of sleeping. So it was thought that skin AF would be one of effective index that subjects could check their glucose metabolic conditions even if they are not elder people.

KEY WORDS: advanced glycation end products, smoking, alcohol, sleep, fluorescence

Introduction

The incidence of lifestyle-related diseases has increased steadily in recent years, and has become a major social issue. The results of a national health and nutrition survey in 2008 indicated that one in two males and one in five females from the age of 40 to 74 years was at risk of developing metabolic syndrome 1). These diseases occur frequently in middle-aged and elderly persons. So lifestyle improvement from middle age or earlier is indispensable to prevent these. In addition, if the simple method of predicting the degree of the metabolic disorder by bad lifestyle behavior is developed, it would be effective as a motivation tool for lifestyle improvement for prevention.

Recent research has found that protein glycation (Maillard reaction) increases with age, and researchers have proposed the concept of glycation stress defined as the modification of cell proteins by non-enzymatic/irreversible reactions with reducing sugars 2,3). These reactions generate advanced glycation end products (AGEs) by a chain of various intermediate reactions that produce Schiff bases and Amadori products. It is known that AGEs were thought to have been implicated in the pathology of age-related diseases 4,5), and glycation has a strong relationship with lifestyle behaviors, such as diet or exercise. This is because sugar metabolic disorder might promote the reaction.

In addition, several AGEs have a characteristic fluorescence, which presents clinicians with a potential method of measuring cumulative AGE deposition in human skin non-invasively 6-8). Most of these researchers have pointed out the relationship between skin fluorescence and diseases such as diabetes mellitus 9,10). But for the prevention of lifestyle-related diseases, it is important to investigate healthy people's lifestyles and the relationship with AGE accumulation with aging. AGEs accumulate in skin partially by binding with collagen protein. Since glycation of collagen may also cause a loss of skin elasticity and wrinkle formation, skin AGEs might be an index of skin aging. In this study, we pay attention to the method of measuring AGE accumulation by skin fluorescence. We also tried to investigate the relationship with Japanese skin autofluorescence and lifestyle behavior, and the degree of glycation in the body by the cross sectional research.

Subjects and Methods

Subjects

Total of 244 Japanese men and women, aged 20 to 59 years Japanese (82 men, mean age: 45.4±8.7 years old; 162 women, mean age: 43.4±8.8 years old) who were admitted to the Anti-Aging Medical Research Center, Doshisha University were collected. From their lifestyle behaviors, surveyed by Anti-Aging Common Questionnaire, we selected “Smoking (Cigarettes/day),” “Alcohol intake (mL/day),” “Frequency of alcohol drinking (times/week),” “Frequency of exercise (days/week),” “Sleeping hours (hours/day).” In terms of smoking, even if the subject did not presently smoke, 44 subjects who had smoked in the past also included. Since the number of cigarettes of these 44 subjects was unknown, the number of cigarettes was used the data of the other 200 subjects. In terms of drinking, the intake of various types of alcohol was converted into the amount of pure alcohol using “Standard Tables of food composition in Japan Fifth Revised and Enlarged Edition” and the amount of intake(g/time) was computed.

Then, BMI (Body Mass Index), systolic blood pressure, and diastolic blood pressure were measured in 155 of subjects, and their blood samples were taken. Biochemical measurements for the following parameters were completed at the Mitsubishi Chemical Medicine Corporation (Minato-ku, Tokyo, Japan): high density lipoprotein-cholesterol (HDL-Cho) (mg/dL), low density lipoprotein-cholesterol (LDL-Cho), fasting blood glucose (FBG) (mg/dL), triglyceride (TG) (mg/dL), hemoglobin A1c (HbA1c) (%), immuno-reactive insulin (IRI) (μU/mL). All subjects had received medical checkup known as the “Anti-Aging Dock,” and we collected the data from the Anti-Aging Medical Research Center, Doshisha University.

Manner of grouping

A flow chart of the grouping and development of the model in this study are shown in Fig. 1. In order to carry out age adjustment, data from all 244 subjects were divided by ten year intervals into four age groups: (aged 20-29 [n = 20], 30-39 [n = 50], 40-49 [n = 102], 50-59 [n = 72] years).

Single correlation analysis with lifestyle behavior and skin AF were carried out, as the selection of the lifestyle behavior items that were important to accumulate AGEs using Pearson correlation coefficients.

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Fig. 1. Flow chart of the grouping and development of the model
To evaluate risk incurred by skin AGE accumulation based on lifestyle behavior, all subjects were assigned to one of two groups for behavior: if a subject had a bad lifestyle behavior, they were placed into a risk (+) group, whereas if they had a good lifestyle behavior, they were placed into a risk (−) group. Analysis was then carried out between these two groups per behavior category. In addition, to evaluate whether a merger of each bad lifestyle behavior accelerated accumulation of skin AGES, the lifestyle risks of all subjects were counted and grouped into a risk merger model.

Measurement of skin AF

The accumulation of AGEs in skin was evaluated with an AGE Reader™ (DiagnOptics, Groningen, Netherlands). This instrument was designed to non-invasively evaluate AGES accumulated in skin using the principle that several AGES emit a characteristic AF when excited by UV light. The AF of immune(−)-histochemical skin biopsies from patients with diabetes mellitus and nephropathy receiving dialysis is correlated with the level of accumulated AGEs, such as pentosidine or CML, although CML is a non-fluorescent AGE. Excitation light (wavelength 300-420 nm) is projected onto 1 cm² of the skin surface, and the intensity of any light (420-600 nm) emitted is measured with a spectrometer. Skin AF (in arbitrary units [AUs] × 100) is calculated from the mean value of the emitted light intensity divided by the excitation light intensity. Skin AF was measured from the inside of the upper arm approximately 10 cm above the elbow.

Analysis

Mean ± standard deviation for all data in each age group was calculated. A one-way analysis of variance (ANOVA) was calculated to compare the group mean skin AF, which were then evaluated by Tukey’s post-hoc test. The correlation analysis was carried out using Spearman’s rank correlation coefficient. In addition, partial correlation coefficients were calculated in order to examine the correlation when the data were age adjusted. A Mann-Whitney test was used for inter-group and subclass analysis. A Dunnett test was calculated to compare the lifestyle behavior risk number. The significance level was set at p<0.05. All statistical analyses were conducted using SPSS software (IBM Japan, Minato-ku, Tokyo, Japan).

Ethical considerations

The present study followed guidelines (‘The Ethical Principles Concerning Epidemiologic Study’) published by the Japanese Ministry of Health, Labour and Welfare, and the study protocol was approved by the Doshisha University Ethical Committee for Clinical Studies (approval number #0832). Data was not linked to subjects’ personal information.

Results

The data and profile of each age group

The mean skin AF of each age group increased from the 20s to 40s, but did not change from the 40s to 50s. (1.78±0.25 in 20s, 2.02±0.33 in 30s, 2.17±0.35 in 40s, and 2.16±0.31 in 50s) (Table 1 (a)) (Fig. 2). Then we found no correlation between age and skin AF in each age group. As for the lifestyle behaviors, frequency of alcohol drinking (r=0.164, p=0.010) and alcohol intake (r=0.135, p=0.034) were positively correlated with skin AF (Table 2).

Relationship between skin AF and lifestyle behaviors

Smoking (r=0.255, p<0.001) and frequency of alcohol drinking (r=0.210, p<0.001) were positively correlated with skin AF. Sleeping hours might be negatively correlated with skin AF (r=−0.124, p=0.054) (Table 2). Although age adjust were carried out by the partial correlation analysis, smoking (r=0.272, p<0.001) and frequency of alcohol drinking (r=0.164, p=0.010) were positively correlated with skin AF. And sleeping hours was negatively correlated with skin AF (r=−0.149, p=0.020). As for “smoking risk,” subjects who smoke or have smoked in the past were “smoking risk (+); Sm (+)” (subjects never having smoked were Sm (−)), and the average skin AF of Sm (+) group was higher than that of Sm (−) group (p=0.002) (Table 3(a)). As for “drinking risk,” subjects who drank 4 or more times a week were “Dr (+)” (subjects who drank less than 4 times a week were “Dr (−)”), and the average skin AF of Dr (+) group was higher than that of Dr (−) group (p=0.006) (Table 3(b)). As for “Sleeping risk,” subjects that slept 6 hours or less were “Sl (+)” (subjects that slept more than 6 hours were “Sl (−)”), and the average skin AF of Sl (+) group might be higher than that of Sl (−) group (p=0.060) (Table 3(c)). As for age each group analysis, the skin AF of Sm (+) group was higher than Sm (−) group in the 40s (p=0.037), and Sl (+) group might be higher than Sl (−) group in the 20s (p=0.013).

Influence of a Merger of a lifestyle risk

Two merger models for lifestyle behaviors were developed.

Case I: Smoking and drinking risk (Risk 0-2)

The skin AF of each age group, middle aged, and all the age groups were shown for each lifestyle risk (Table 4 (a)). An increase in the skin AF of all ages was observed with the risk increased (Risk 1 vs. Risk 0: p=0.010, Risk 2 vs. Risk 0: p<0.001) (Fig. 3 (a)). In middle age, an increase in skin AF between Risk 2 and Risk 0 was observed (p=0.018). As for each age group, some cases of an increase in skin AF in the 20s (Risk 2 vs. Risk 0: p=0.031), 30s (Risk 1 vs. Risk 0: p=0.041), and 40s (Risk 2 vs. Risk 0: p=0.042) were observed. In addition, aging curve was developed using the data of Table 4 (a) (Fig. 4 (a)).

Case II: Smoking, drinking, and sleeping risk (Risk 0-3)

An increase in the skin AF of all age was observed between Risk 2, 3 and Risk 0 (Risk 2 vs. Risk 0: p=0.001, Risk 3 vs. Risk 0: p<0.001) (Fig. 3 (b)). In middle age, an increase in skin AF between Risk 2, 3 and Risk 0 was also observed (Risk 2 vs. Risk 0: p=0.019, Risk 3 vs. Risk 0: p=0.004). As for each age group, some cases of increase in skin AF in the 30s (Risk 2 vs. Risk 0: p=0.011) and 40s (Risk 3 vs. Risk 0: p=0.006) were observed. In addition, an aging curve was developed using the data of Table 4 (b) (Fig. 4 (b)). Then skin AF reached the peak in the 40s and decreased in the 50s in Risk 3.
**Table 1(a)  Skin AF and lifestyle behaviors of subjects**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>20s</th>
<th>30s</th>
<th>40s</th>
<th>50s</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>20</td>
<td>50</td>
<td>102</td>
<td>72</td>
</tr>
<tr>
<td>Men : Women [%]</td>
<td>40.0:60.0</td>
<td>18.0:82.0</td>
<td>36.3:63.7</td>
<td>38.9:61.1</td>
</tr>
<tr>
<td>Age [years]</td>
<td>25.8 ± 2.1</td>
<td>35.6 ± 2.8</td>
<td>45.1 ± 2.7</td>
<td>53.6 ± 3.1</td>
</tr>
<tr>
<td>Skin AF [%]</td>
<td>1.78 ± 0.25</td>
<td>2.02 ± 0.33</td>
<td>2.17 ± 0.35</td>
<td>2.16 ± 0.31</td>
</tr>
<tr>
<td>Smoking [%]</td>
<td>45.0</td>
<td>28.0</td>
<td>91.1</td>
<td>37.5</td>
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<tr>
<td>Frequency of Drinking [times/week]</td>
<td>1.0 ± 2.3</td>
<td>1.2 ± 2.0</td>
<td>2.5 ± 2.7</td>
<td>1.9 ± 2.3</td>
</tr>
<tr>
<td>Daily Alcohol intake [g/times]</td>
<td>5.1 ± 9.3</td>
<td>18.4 ± 30.4</td>
<td>18.7 ± 22.7</td>
<td>13.2 ± 18.1</td>
</tr>
<tr>
<td>Sleeping time [h/day]</td>
<td>6.2 ± 0.9</td>
<td>6.4 ± 1.0</td>
<td>6.4 ± 0.9</td>
<td>6.2 ± 1.0</td>
</tr>
<tr>
<td>Frequency of Exercise [times/week]</td>
<td>1.0 ± 1.4</td>
<td>1.0 ± 1.7</td>
<td>1.1 ± 1.7</td>
<td>1.5 ± 2.1</td>
</tr>
</tbody>
</table>

Correlation (Skin AF vs Age) NS NS NS NS

**Table 1(b)  Profile of subjects**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>20s</th>
<th>30s</th>
<th>40s</th>
<th>50s</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>7</td>
<td>24</td>
<td>72</td>
<td>52</td>
</tr>
<tr>
<td>BMI [kg/m²]</td>
<td>19.9 ± 1.7</td>
<td>20.7 ± 2.6</td>
<td>24.1 ± 3.5</td>
<td>24.9 ± 2.8</td>
</tr>
<tr>
<td>Systolic blood pressure [mmHg]</td>
<td>103.1 ± 9.3</td>
<td>116.6 ± 14.1</td>
<td>122.3 ± 13.9</td>
<td>128.3 ± 15.6</td>
</tr>
<tr>
<td>Diastolic blood pressure [mmHg]</td>
<td>66.1 ± 5.6</td>
<td>68.5 ± 10.6</td>
<td>76.0 ± 10.8</td>
<td>80.3 ± 12.4</td>
</tr>
<tr>
<td>LDL-cho [mg/dl]</td>
<td>90.0 ± 27.8</td>
<td>110.9 ± 27.6</td>
<td>120.8 ± 33.3</td>
<td>140.9 ± 32.8</td>
</tr>
<tr>
<td>HDL-cho [mg/dl]</td>
<td>73.9 ± 14.4</td>
<td>72.8 ± 15.5</td>
<td>65.1 ± 15.8</td>
<td>59.4 ± 14.3</td>
</tr>
<tr>
<td>TG [mg/dl]</td>
<td>71.6 ± 39.6</td>
<td>69.5 ± 29.0</td>
<td>99.2 ± 52.3</td>
<td>146.0 ± 91.6</td>
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<tr>
<td>FBS [mg/dl]</td>
<td>85.6 ± 7.3</td>
<td>84.0 ± 10.1</td>
<td>85.6 ± 7.7</td>
<td>91.6 ± 13.5</td>
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<tr>
<td>HbA1c (JDS) [%]</td>
<td>4.9 ± 0.2</td>
<td>4.8 ± 0.2</td>
<td>5.0 ± 0.3</td>
<td>5.3 ± 0.6</td>
</tr>
<tr>
<td>IRI [μU/ml]</td>
<td>6.0 ± 2.4</td>
<td>4.2 ± 1.8</td>
<td>6.1 ± 3.4</td>
<td>6.2 ± 4.2</td>
</tr>
</tbody>
</table>

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**Fig. 2**  Skin AF with aging
AF, autofluorescence, closed circles, mean of skin AF ± standard deviation (SD), Tukey’s post-hoc test, * p < 0.05 vs. each neighboring age group.
Table 2  Single and partial correlation analysis

<table>
<thead>
<tr>
<th>Lifestyle behavior</th>
<th>vs Age</th>
<th>vs Skin AF</th>
<th>vs Skin AF (Age adjustment)</th>
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<tbody>
<tr>
<td></td>
<td>N</td>
<td>r</td>
<td>p-value</td>
</tr>
<tr>
<td>Smoking</td>
<td>200</td>
<td>0.049</td>
<td>0.489</td>
</tr>
<tr>
<td>Frequency of alcohol drinking</td>
<td>244</td>
<td>0.164</td>
<td>0.010*</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>244</td>
<td>0.135</td>
<td>0.034*</td>
</tr>
<tr>
<td>Frequency of exercise</td>
<td>244</td>
<td>0.106</td>
<td>0.098</td>
</tr>
<tr>
<td>Sleeping hours</td>
<td>244</td>
<td>-0.039</td>
<td>0.543</td>
</tr>
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Table 3(a) Existence or absence for smoking risk

<table>
<thead>
<tr>
<th>20s</th>
<th>30s</th>
<th>40s</th>
<th>50s</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking Risk (+)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin AF</td>
<td>1.85 ± 0.28</td>
<td>2.15 ± 0.36</td>
<td>2.27 ± 0.32</td>
<td>2.23 ± 0.31</td>
</tr>
<tr>
<td>N</td>
<td>9</td>
<td>14</td>
<td>44</td>
<td>27</td>
</tr>
<tr>
<td>Smoking Risk (-)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin AF</td>
<td>1.72 ± 0.22</td>
<td>1.97 ± 0.30</td>
<td>2.09 ± 0.35</td>
<td>2.13 ± 0.30</td>
</tr>
<tr>
<td>N</td>
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<td>36</td>
<td>58</td>
<td>45</td>
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Table 3(b) Existence or absence for drinking risk

<table>
<thead>
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<th>Average</th>
</tr>
</thead>
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<tr>
<td>Drinking Risk (+)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin AF</td>
<td>2.00 ± 0.26</td>
<td>2.24 ± 0.29</td>
<td>2.22 ± 0.33</td>
<td>2.23 ± 0.25</td>
</tr>
<tr>
<td>N</td>
<td>3</td>
<td>5</td>
<td>33</td>
<td>16</td>
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<tr>
<td>Drinking Risk (-)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin AF</td>
<td>1.74 ± 0.23</td>
<td>1.99 ± 0.32</td>
<td>2.14 ± 0.35</td>
<td>2.14 ± 0.32</td>
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<tr>
<td>N</td>
<td>17</td>
<td>45</td>
<td>69</td>
<td>56</td>
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</table>

Table 3(c) Existence or absence for sleeping risk

<table>
<thead>
<tr>
<th>20s</th>
<th>30s</th>
<th>40s</th>
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<th>Average</th>
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</thead>
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<tr>
<td>Sleeping Risk (+)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin AF</td>
<td>1.98 ± 0.23</td>
<td>1.92 ± 0.32</td>
<td>2.09 ± 0.34</td>
<td>2.10 ± 0.34</td>
</tr>
<tr>
<td>N</td>
<td>6</td>
<td>26</td>
<td>46</td>
<td>28</td>
</tr>
<tr>
<td>Sleeping Risk (-)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin AF</td>
<td>1.69 ± 0.21</td>
<td>2.12 ± 0.31</td>
<td>2.23 ± 0.34</td>
<td>2.20 ± 0.32</td>
</tr>
<tr>
<td>N</td>
<td>14</td>
<td>24</td>
<td>56</td>
<td>44</td>
</tr>
</tbody>
</table>

Spearman’s test
r: Spearman rank-correlation coefficient, *: p<0.05, **: p<0.001
r': Partial correlation coefficient, #: p<0.05, ##: p<0.001

Table 3(a) Existence or absence for smoking risk

Table 3(b) Existence or absence for drinking risk

Table 3(c) Existence or absence for sleeping risk

†: p<0.10, *: p<0.05
Mann-Whitney test
## Table 4(a) Case I: Skin AF in smoking and drinking risk

<table>
<thead>
<tr>
<th></th>
<th>Risk 0</th>
<th>Risk 1</th>
<th>Risk 2</th>
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<tbody>
<tr>
<td>20a</td>
<td>Skin AF</td>
<td>1.69 ± 0.21</td>
<td>1.88 ± 0.22</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.21</td>
<td>0.031*</td>
</tr>
<tr>
<td>30a</td>
<td>Skin AF</td>
<td>1.96 ± 0.31</td>
<td>2.23 ± 0.33</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>40</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.041#</td>
<td></td>
</tr>
<tr>
<td>40a</td>
<td>Skin AF</td>
<td>2.11 ± 0.33</td>
<td>2.20 ± 0.35</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>56</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.397</td>
<td>0.042*</td>
</tr>
<tr>
<td>50a</td>
<td>Skin AF</td>
<td>2.14 ± 0.30</td>
<td>2.19 ± 0.32</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>44</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.770</td>
<td>0.456</td>
</tr>
<tr>
<td>Middle aged</td>
<td>Skin AF</td>
<td>2.12 ± 0.32</td>
<td>2.20 ± 0.33</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>101</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.318</td>
<td>0.018*</td>
</tr>
<tr>
<td>Average</td>
<td>Skin AF</td>
<td>2.04 ± 0.33</td>
<td>2.18 ± 0.33</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>153</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.010*</td>
<td>&lt;0.001**</td>
</tr>
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### Table 4(b) Case II: Skin AF in smoking, drinking, and sleeping risk

<table>
<thead>
<tr>
<th></th>
<th>Risk 0</th>
<th>Risk 1</th>
<th>Risk 2</th>
<th>Risk 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>20a</td>
<td>Skin AF</td>
<td>1.83 ± 0.16</td>
<td>1.71 ± 0.26</td>
<td>1.69 ± 0.15</td>
</tr>
<tr>
<td></td>
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<td>30a</td>
<td>Skin AF</td>
<td>1.89 ± 0.33</td>
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<td>2.06 ± 0.25</td>
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<tr>
<td>40a</td>
<td>Skin AF</td>
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<td>2.18 ± 0.28</td>
<td>2.17 ± 0.28</td>
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<td>50a</td>
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<td>2.16 ± 0.32</td>
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<td>p-value</td>
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<td>Middle aged</td>
<td>Skin AF</td>
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<td>2.16 ± 0.29</td>
<td>2.24 ± 0.37</td>
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<td>p-value</td>
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<td>0.019*</td>
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<td>Average</td>
<td>Skin AF</td>
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<td>p-value</td>
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<td>0.001*</td>
<td>&lt;0.001**</td>
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Dunnett test (vs Risk 0)
*: p<0.05, **: p<0.001
Student t-test (vs Risk 0)
#: p<0.05
Fig. 3. Relationship of skin AF and lifestyle behavior risk number in merger model in all age groups
(a) Case I: Smoking and drinking risk (Risk 0-2), Case II: Smoking, drinking, and sleeping risk (Risk 0-3), AF, autofluorescence.
Dunnett test, * \( p < 0.05 \), ** \( p < 0.001 \) vs. Risk 0

Fig. 4. Aging curve for lifestyle behavior risk
(a) Case I: Smoking and drinking risk (Risk 0-2), Case II: Smoking, drinking, and sleeping risk (Risk 0-3), AF, autofluorescence.
Dunnett test, * \( p < 0.05 \), vs. Risk 0
Student \( t \)-test, \# \( p < 0.05 \), vs. Risk 0
Discussion

Meaning of skin AF, and change with aging

Studies thus far involving measurement of skin AF using an AGE Reader have mainly involved Caucasian subjects, with the relationship between skin AF and various diseases already well established for this ethnicity group. While an increasing amount of research has been conducted on Japanese subjects in recent years, the relationship between skin AF and aging has yet to be elucidated. We showed that the skin AF of Japanese people increased with aging. Simultaneously, in connection with aging, individual difference becomes large. So it is important to find the risk factors contributing to AGE accumulation and we paid attention to lifestyle behaviors. As a result of this study, the possibility that smoking and drinking risk can accelerate AGE accumulation was discovered. Although the skin AF of sleeping risk group might be higher, the data of sleeping hours surveyed by questionnaire was thought not to be reliable. So to discuss the possibility as a risk factor, two merger models were developed for the existence or absence of sleeping risk.

As for case I, an increase in the skin AF of all age was observed with the smoking and drinking risk increased (Table 4). On the other hand, only one risk couldn’t increase skin AF in case II. Therefore, only a lack of sleep was not always a strong risk factor, but might accelerate AGE accumulation with a merger of smoking and drinking risk.

Although age adjustment were carried out by the partial correlation analysis, smoking, high frequency of alcohol drinking, and lack of sleep were correlated with skin AF. Especially in the analysis of middle age, skin AF did not increase with age gradually, but it was suggested that lifestyle behaviors get involved in skin AF between 40 to 59 years old (Fig. 2). Then, as for risk 3 group in case II, from the 20s to 40s, skin AF increased as compared with risk 0-2, and it fell by the 50s.

The reason is that in this study, the subjects in the 40s had worth lifestyle behaviors in this study (Table 1). In addition, more healthy people who had not shown the symptoms of glycation in the skin in the 50s with risk 3 might have been investigated. The rate of lifestyle-related diseases including diabetes was known to increase with aging especially in middle age. On the other hand, our research might tend to admit more healthy people. According to our previous research, the average value of the skin AF of diabetics was around 2.5.

Limitations of the Aging curve model

This study tried to express the difference between morbid aging and normal aging by aging curves (Fig. 4 (a) (b)). In addition, several limitations to the present study warrant mention. The group division was made by the pattern of age group and lifestyle behavior, there were few subjects per group and a statistical significant difference was not able to be shown. In addition, since this study used designs that were cross-sectional studies, it required caution to not measure the same subject.

AGEs and Lifestyle behaviors

In this study, for skin AGE accumulation control, it is important not to form bad lifestyle behaviors, or to improve bad lifestyle behaviors if possible at an early age. Although we couldn’t find a relationship between exercise and skin AF, exercise habits are important to control glucose metabolism. The following is the glycation risk which is promoted by the bad lifestyle behaviors.

Conflict of interest statement

The authors declare no financial or other conflicts of interest in the writing of this paper.
References


