Coffee is one of the most widely consumed beverages in the world, and it has been considered to have beneficial capacities to one's health. Accumulating evidence suggests that coffee intake has numerous potential pharmacological benefits, such as antioxidant (Sato et al., 2011), antitumor (Franco, 2008), anti-diabetic (Ong et al., 2012), and anti-inflammatory effects (Chang et al., 2010; Shen et al., 2010).

Since the above effects of coffee might have the potential to improve sarcopenia and the functions of satellite cells (Macaluso and De Vito, 2004; Meng and Yu, 2010; Schaap et al., 2006; Sriram et al., 2011; Strasser et al., 2007), we hypothesized that coffee intake might have a beneficial effect on the prevention of sarcopenia. Furthermore, we hypothesized that this effect might involve inflammation. To the best of our knowledge, few studies have examined the effect of coffee intake on muscles in aged people or aged animals, or the relationship between coffee intake and pro-inflammatory mediator levels. Thus, in the present study, we examined the effects of coffee treatment on muscle weight, muscle strength, satellite cell functions, regenerating capacity of the skeletal muscles in vivo and in vitro, and the involvement of pro-inflammatory mediators in an animal model using aged mice.

2. Material and methods

2.1. Mice and drink treatment

Male C57BL/6 mice were obtained from Clea Japan (Tokyo, Japan) and maintained under specific pathogen-free conditions with unrestricted access to food and water. Experiments were carried out in accordance with the guidelines established by the Tohoku University Committee on Animal Research. At the age of 27-months, mice were divided into 2 groups according to the beverages provided for each group and maintained for the next 4 weeks, with 12 mice in each group. The 2 groups were: normal water (controls) and coffee. Ready-to-drink coffee (Clear®) was purchased from Nescafe (Sizuoka, Japan) and diluted with distilled water at 1:2 dilutions. In this study, all of the coffee products were from the same lot number. Japan Food Research Laboratories (Tokyo, Japan) analyzed the main components of the coffee. The coffee used in this study contained: coffee bean, ≈2.5 g/100 ml; chlorogenic acid, 0.07 mg/ml; anhydrous caffeine, 0.45 mg/ml; polyphenols, 1.4 mg/ml; specific gravity, 1.005 (at 20 °C). The water and coffee were changed every day. The mice had unrestricted access to food and water. Two mice in the control and one mouse in the treatment group died of natural causes during the treatment period. After 4 weeks of treatment, 4 mice from the control group and 5 mice from the coffee group were anesthetized, sacrificed, their sera were collected, and the weights of the hind limb muscles were measured. The hind limb muscles included the tibialis anterior muscle (TA), triceps surae muscle, quadriceps muscle, biceps femoris muscle, gluteus maximus muscle, and iliopsoas muscle. For evaluation of the myogenic progenitor proliferation and differentiation and fusion capacity of injured skeletal muscles, mice were sacrificed 3 or 5 days after the injury, respectively, 3 mice in each group.

2.2. Isolation and culture conditions of satellite cells and cell proliferation assay

Satellite cells were isolated from untreated, 28-month-old mice according to our previous study (Niu et al., 2013). Briefly, the hind limb muscles including the TA, triceps surae muscle, quadriceps muscle, biceps femoris muscle, gluteus maximus muscle, and iliopsoas muscle were isolated, non-muscle tissues were removed, and then the muscles were subjected to enzymatic dissociation with 0.2% collagenase type II (Worthington Biochemical Corporation, Lakewood, NJ, USA) for 60 min, then with 0.04 U/ml dispase (Gibco BRL, Grand Island, NY, USA) for 45 min. The cell suspension was filtered through a cell strainer (BD Bioscience, Franklin Lakes, NJ, USA), incubated with anti-mouse CD16/CD32 monoclonal antibody (mAb, 2.4G2, BD Bioscience) to block Fc receptors, then with the following antibodies: FITC-labeled anti-CD31, anti-CD45 (BD Bioscience), anti-CD11b, and anti-Sca-1 antibodies (eBioscience, San Diego, CA, USA); PE-labeled anti-Integrin α7 (MBL, Nagoya, Japan); Alexa 647-labeled anti-CD34 (BD Bioscience). The cells were sorted by a FACSAria™ II flow cytometer (BD Bioscience) as previously described (Niu et al., 2013).

Sorted satellite cells were cultured in growth medium containing high-glucose Dulbecco's modified Eagle's medium (HG-DMEM) with 20% fetal bovine serum (FBS) (MP Biomedicals, Morgan Irvine, CA, USA), 2.5 ng/ml basic fibroblast growth factor (bFGF, Invitrogen, Eugene, OR, USA), 100 U/ml penicillin, and 100 μg/ml streptomycin (Sigma, St. Louis, MO, USA). Satellite cells under 8 passages were used in this study. Diluted coffee solution was sterilized by a filter then added to the culture medium at the following concentrations: 10, 30, 50, or 100 μg/ml. The cells were cultured for 72 h, and the number of cells was determined by a water-soluble tetrazolium-8 (WST-8, DOJINDO, Tokyo, Japan) assay using a cell counting kit (Okazaki et al., 2008).

2.3. Locomotor activity recordings

Freely moving locomotor activity was recorded by an infrared ray sensor system (SUPERMEX®; Muromachi-Kikai, Tokyo, Japan) that consisted of 12 small compartments divided by walls on a large shelf. Each compartment (width: 40 cm × depth: 50 cm × height: 35 cm) was equipped with a ceiling sensor that can detect heat energy radiated from a mouse. The system detected mouse movement by recording changes in heat energy in the covered field. Mice were individually placed in a plastic cage (width: 19 cm × depth: 27.5 cm × height: 17 cm) and then put into the system shelf. Counts were measured every 10 min (Inoue et al., 1996). Locomotor activity was consecutively measured on days 0–1, 5–6, 10–11, and 19–20.

2.4. Grip strength test

Grip strength was measured by an electronic grip strength meter (MK-380; Muromachi Kikai). Mice were put on the fence and pulled back slowly. The point at which mice released the fence was determined as the grip strength. The measurements were repeated 3 times and maximal readings were taken (Arai et al., 2001). The grip strength was measured twice a week.

2.5. Cell-cycle analysis by flow cytometry

DNA synthesis in cells was evaluated by measuring BrdU incorporation (BrdU Flow Kits; BD Biosciences, San Jose, CA, USA) by flow cytometry. Briefly, 5×10^5 cells were cultured overnight. Then, the cells were stimulated for the next 72 h with 10, 30, 50, or 100 μg/ml coffee bean extract sterilized with a 0.22 μm filter. The cells were labeled with BrdU during the final 2 h of stimulation. The cells were then permeabilized, fixed, and stained with an anti-BrdU antibody coupled with FITC according to the manufacturer's protocol. Flow cytometry data were collected using a logarithmic scale, and the percentage of BrdU-positive cells was determined (Niu et al., 2012).

2.6. Muscle injury model

After 4 weeks of the coffee treatment, the mice were anesthetized and cardiotoxin from Naja mossambica mossambica (Sigma) dissolved in 100 μl phosphate-buffered saline (PBS) (10 μM) was injected into the TA. Three or five days later, the mice were sacrificed, the TA muscles were isolated, frozen in 2-methylbutane precooled in liquid nitrogen, and stored at −80 °C for the following histological analysis (Uezumi et al., 2010).

2.7. Immunohistochemistry and immunocytochemistry

Frozen muscle tissues were sectioned from a region approximately 3 mm from the top of the TA (8 μm in thickness) using a cryostat. For embryonic myosin heavy chain (eMyHC) staining, frozen sections were fixed with acetone/methanol (50%/50%) for 30 s at −20 °C. Specimens were blocked with 1% BSA, 0.1% Triton X-100 in PBS at room temperature for 45 min, then incubated with anti-eMyHC antibody (F1.652, DSHB, Iowa City, IA, USA) at a 1:2 dilution at 4 °C overnight, followed by Rodamine conjugated-secondary antibody staining (Chemicon International, Temecula, CA, USA) at room temperature in the dark for 1 h. Finally, the sections were mounted in Vectashield Mounting Medium with 4′,6-diamidino-2-phenylindole (DAPI) (Vector labs, Burlingame, CA, USA). In vivo, the regenerating capacity of the injured skeletal muscles was evaluated by quantifying the percentage of eMyHc-immunoreactive area per field (Fukada et al., 2012). Ten randomly selected fields at ×200 magnification were measured in each sample. ImageJ software was used to quantify the eMyHC-immunoreactive areas per field. For ki-67 staining, after quenching endogenous peroxidase with 3% H_2O_2 in PBS for 15 min, the sections were incubated with primary antibodies at 4 °C overnight (anti-ki67 antibody, 1:40 dilution; DAKO, Tokyo, Japan), followed by incubation with biotinylated anti-rabbit immunoglobulin G antibody using Histofine (Max-PO (Multi), Nichirei Bioscience, Osaka, Japan) according to the manufacturer's instructions. Then, the antibody complex was visualized with 3,30-diaminobenzidine tetrahydrochloride (MERCK, Darmstadt, Germany) (Niu et al., 2012). Images were taken using a phase-contrast and fluorescence microscope BZ9000 (Keyence, Osaka, Japan) (Asada et al., 2009).

2.8. Western blot analysis

Akt and phosphorylated-Akt (phospho-Akt) proteins of the satellite cells were detected by western blot analysis. Some cells were serum-starved overnight, then stimulated with 10 nM insulin (Sigma), which is a potent activator of Akt, for 5 min as a positive control. Western blot analysis was performed with a SDS-PAGE Electrophoresis System as describe previously (Yamanda et al., 2009). In brief, the cells were rinsed twice with ice-cold PBS and lysed using RIPA Lysis Buffer (Upstate, Temecula, CA, USA). The extracted protein fraction was electrophoresed in a sodium dodecyl sulphate-10% polyacrylamide gel and then transferred onto an Immobilon transfer membrane (Millipore, Bedford, MA, USA). The amount of protein loaded onto the gels was 36 μg per well. The membranes were immunoblotted with the primary antibodies to Akt and phospho-Akt (Cell Signaling, Boston, MA, USA) at 1:1000 dilutions. Then the membranes were incubated with horseradish peroxidase-conjugated anti-rabbit immunoglobulin G (Cell Signaling) at 1:25,000 dilution and the protein bands were detected with an enhanced chemiluminescence detection kit (Amersham, Buckinghamshire, UK) (Yamanda et al., 2009).

2.9. Enzyme-Linked Immunosorbent Assay (ELISA)

Sera were isolated from the inferior vena cava of the mice (Okazaki et al., 2007). The serum levels of IL-1α, IL-1β, IL-6, TNF-α, and IGF-1 were measured using a specific ELISA kit (R&D Systems) according to the manufacturer's instructions, respectively (Okazaki et al., 2007). The minimum detectable levels were 2.5, 3.0, 1.6, 5.1, and 3.5 pg/ml for IL-1α, IL-1β, IL-6, TNF-α, and IGF-1, respectively.

2.10. Statistical analysis

To determine the sample size, a power analysis was performed based on the results of previously performed research (Niu et al., 2013) and a preliminary experiment. The mean hind limb muscle-weight divided by the body weight of 28-month-old mice was 0.009. We estimated ≥20% (standard deviation: 0.0005) difference between the control and coffee groups in the hind limb muscle-weight divided by the body weight. Assuming an alpha error of 0.05 with a power of 0.90, we calculated a necessary sample size of 3 to show a significant effect. Based on this calculation and to ensure reasonable data, we increased the sample size to 4 or 5 in this study. The same calculation was applied to determine the sample size of myogenic progenitor proliferation and regenerating capacity test in vivo. Based on previously performed research (Niu et al., 2013) and a preliminary experiment, we estimated ≥30% (mean Ki67-positive cell number per field in control group ≈ 40 cells, SD ≈ 3.5) and ≥70% (mean relative eMyHc positive area in control group ≈ 9%, SD ≈ 1.8) difference in the myogenic progenitor proliferation and regenerating capacity test, respectively, between the control and coffee treatment groups. Assuming an alpha error of 0.05 with a power of 0.90 we calculated a necessary sample size of 3 to show a significant effect both in the myogenic progenitor proliferation and regenerating capacity test.

Data were presented as mean ± standard error (SE). Differences were analyzed by one-way analysis of variance (ANOVA) test (Post hoc, Tukey). The Spearman correlation coefficient (r) was calculated to evaluate the relationship between two continuous variables. All the tests for statistical significance were 2 sided, and $p < 0.05$ was considered statistically significant. All in vitro experiments were repeated at least 3 times. In this study, the main experiments such as grip strength measurement, cardiotoxin injection, and histological quantifications were blindly carried out.

3. Results

3.1. Coffee-treated mice had greater muscle weight and grip strength than controls

To examine the effects of coffee treatment on aged mice in vivo, we divided 27-month-old mice into 2 groups and treated them with either normal water (controls) or coffee for 4 weeks. Two mice in the control and one mouse in the treatment group died of natural causes during the treatment period. These mice were excluded from the analysis. During the intervention period, the body weight changed similarly in the coffee-treated and control groups (Fig. 1A) (p value > 0.89). The amounts of daily diet intake and drink were not different between the groups (Fig. 1B and C). We also examined the effect of coffee on locomotor activity in the aged mice. Experiments were performed under light: dark cycles of 12 h:12 h. Locomotor activity was not different between the groups (Fig. 1D). A previous study compared hind limb muscles-weight divided by body weight between 2, 8, and 24 month old mice and showed progressive loss of hind limb muscles-weight / body weight with aging, suggesting the progression of sarcopenia with aging (Niu et al., 2013). The hind limb muscles included the TA, triceps surae, quadriceps, biceps femoris, gluteus maximus, and iliopsoas muscles. Coffee treatment significantly increased the hind limb muscle-weight compared to controls (Fig. 1E). Similarly, we measured the weight of the bilateral hind limb muscles and divided by the body weight. Coffee treatment increased the weight of the hind limb muscles per body weight compared to control by 13.1% (0.011 ± 0.0005 for the coffee treatment group vs 0.0098 ± 0.0007 for the control group, mean ± SE, Fig. 1F). To examine the effect of coffee on the muscle strength, we performed the grip strength test. Consistent with the effect of coffee on the muscle mass, the coffee group had greater grip strength than the controls, suggesting that coffee improved the grip strength (Fig. 1G). Furthermore, a comparison between before and after the treatment period within the controls showed that grip strength decreased after the treatment period compared to before, suggesting the progression of age-related atrophy in muscle function during this period. In contrast, no significant changes were observed within the coffee group during the treatment period. These data suggested that coffee

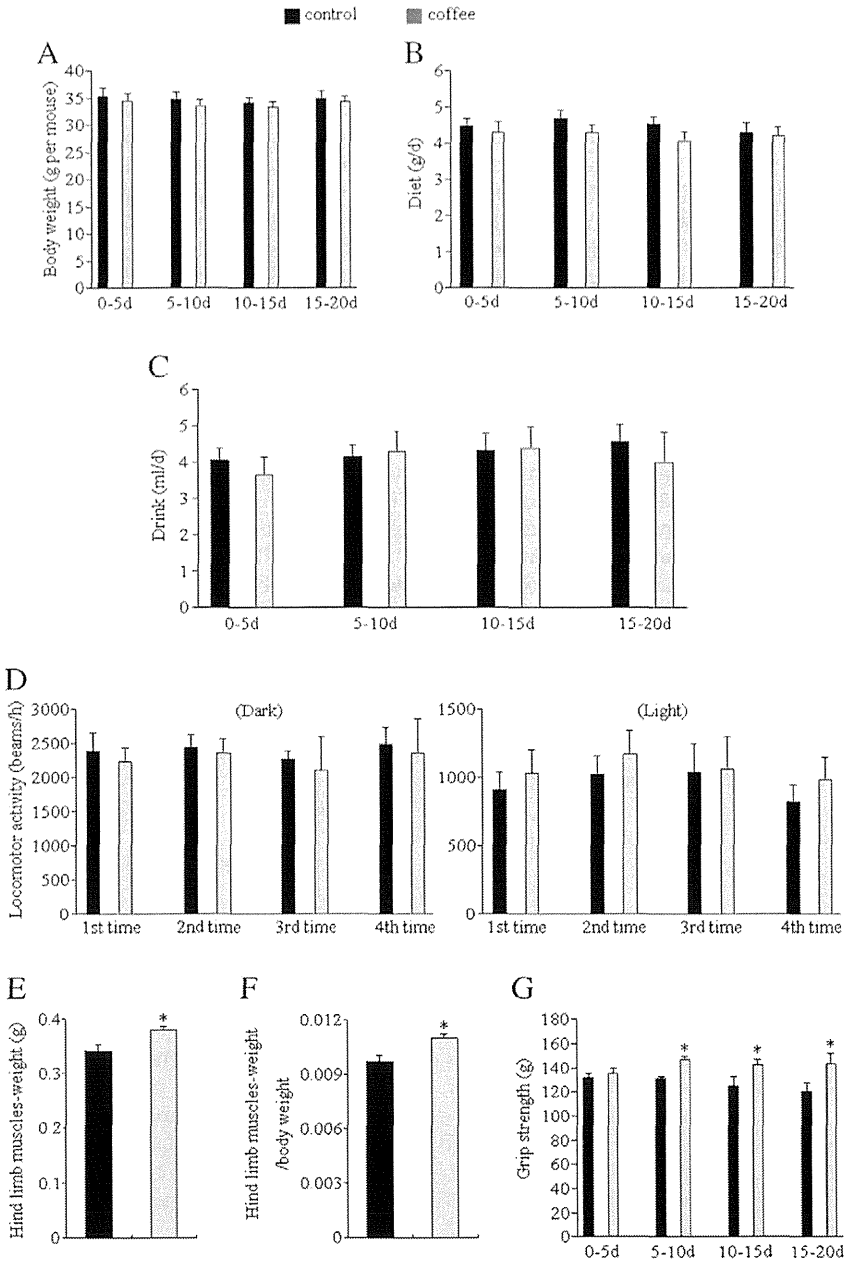

Fig. 1. Effects of coffee treatment on aged mice in vivo. Twenty-seven month-old mice were treated with coffee for 4 weeks. (A–C) Coffee treatment did not change body weight (A), the amount of the daily diet intake (B), or the volume of water intake (C). (D) Coffee did not change the daily locomotor activity levels. (E) The coffee-treated group had greater hind limb muscle-weight than the controls. (F) The coffee-treated group had greater hind limb muscles-weight per body weight than the controls. (G) The coffee-treated group had greater grip strength than controls. Columns are mean ± SE, n ≥ 4 in each group. *$p < 0.05$ compared with control.

treatment prevented the progression of atrophy in muscle weight and function in the aged mice.

3.2. Coffee treatment accelerated the regeneration of injured skeletal muscles

We next examined the effect of coffee treatment on the regenerating capacity of the skeletal muscles in aged mice in vivo by injuring the TA muscles with cardiotoxin injection and observed their regeneration. We isolated the muscles 3 or 5 days after the cardiotoxin injection. To determine the effect of coffee on the cell proliferation rate, we immunohistochemically stained muscle tissues for the cell proliferation marker Ki67 three days after the injury (Fig. 2A, left panels). The number of Ki67 immunoreactive cells was greater in the coffee group than that in controls, suggesting a greater cell proliferation rate in the coffee group (Fig. 2A, right panel). To confirm the regenerating capacity of the skeletal muscles, we immunohistochemically stained the muscle tissues for eMyHc, which is a marker of immature myotubes including regenerating muscles, 5 days after the injury (Fig. 2B, left panels). Quantification of the eMyHc immunoreactive area showed greater immunoreactive areas in the coffee group than in the controls (Fig. 2B, right panel). These results suggested that coffee treatment accelerated the regeneration of the injured skeletal muscles.

3.3. Coffee treatment decreased serum pro-inflammatory mediator levels

Since coffee has been suggested to have an anti-inflammatory effect, we examined the effect of coffee treatment on serum pro-inflammatory mediator levels in the aged mice. We chose IL-1α, IL-1β, IL-6, and TNF-α as pro-inflammatory mediators (Okazaki et al., 2003, 2009), and

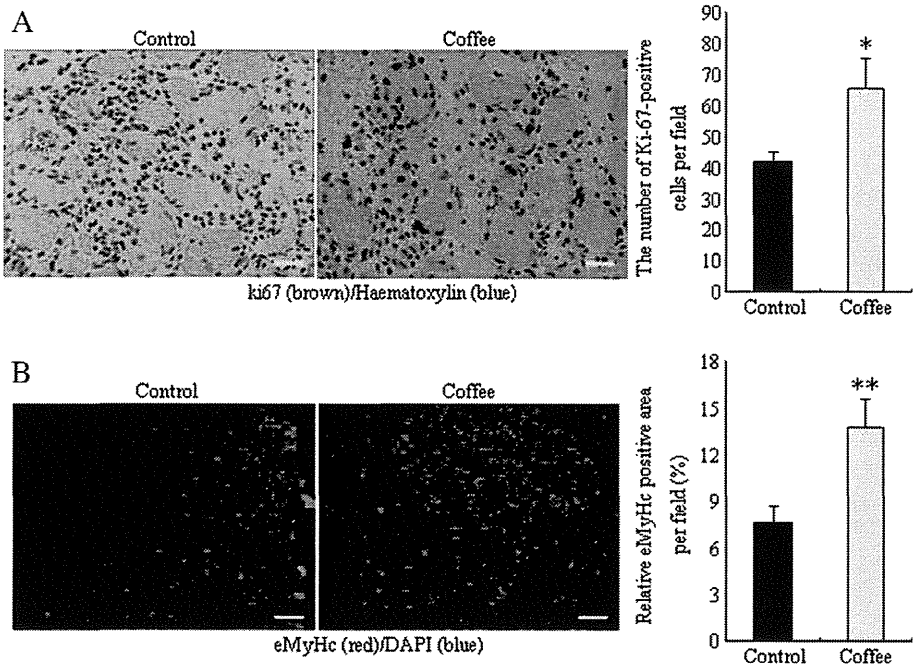

Fig. 2. Coffee treatment accelerated the regeneration of the injured skeletal muscles in aged mice. After 4 weeks of coffee treatment, we injected cardiotoxin into the tibialis anterior muscles of the mice to injure the muscles and isolated them 3 days later for (A) or 5 days later for (B). (A) The left panels are immunohistochemical staining for ki67 of the injured tibialis anterior muscles. The right graph is quantification of the number of ki-67 positive cells per visual microscopic field for each group (10 randomly selected fields at ×200 magnification per sample were quantified). (B) The left panels are immunohistochemical staining for eMyHC and DAPI of the injured tibialis anterior muscles. The right graph is quantification of the percentage of eMyHc-immunoreactive area per field for each group (10 randomly selected fields at ×200 magnification per sample). Scale bars, 100 μm. Columns are mean ± SE, n = 3 in each group. $^{*}p < 0.05$ and $^{**}p < 0.01$ compared with controls.

measured their levels in the serum. The levels of IL-1α, IL-6, and TNF-α were decreased in coffee treated group compared to controls (Fig. 3A). The correlation coefficients suggested a relationship between the serum pro-inflammatory mediator levels and the grip strength ($r = -0.38$, $r = -0.34$, $r = -0.42$, and $r = -0.36$ for IL-1α, IL-1β, IL-6, and TNF-α, respectively [$p < 0.05$ for all]). The correlation coefficients also suggested a significant relationship between several serum pro-inflammatory mediator levels and the muscle weight ($r = -0.52$, $r = -0.39$, $r = -0.69$, and $r = -0.63$ for IL-1α, IL-1β, IL-6, and TNF-α, respectively [$p < 0.05$ for IL-6 and TNF-α]). Since IGF-1 plays a central role in stimulating satellite cells, we also measured the serum levels of IGF-1. The serum levels of IGF-1 were not different (Fig. 3B).

3.4. Effects of coffee on the satellite cells of the aged mice in vitro

To examine the effect of coffee on the proliferation rate of the satellite cells of the aged mice in vitro, we isolated satellite cells from aged mice and stimulated them with coffee in growth medium for 72 h (Fig. 4A). Under the growing condition, coffee treatment increased the number of proliferating satellite cells compared to controls in a dose-dependent manner in vitro. Next, to examine the effect of coffee on the cell cycles of the satellite cells, we cultured the satellite cells for 72 h with coffee and measured DNA synthesis by BrdU incorporation using flow cytometry (Fig. 4B). The coffee-treated group had a greater BrdU incorporation rate than the controls (Fig. 4C). These results suggested that coffee enhanced the DNA synthesis of the proliferating satellite cells of the aged mice. The Akt signaling pathway plays a key role in the proliferation and cell cycle progression of the satellite cells (Giovannini et al., 2008; Kandarian and Jackman, 2006). Therefore, we next examined the activation level of Akt by western blot for Akt and the activated form of Akt, phosphorylated Akt. Coffee treatment increased the intensity of the bands of phosphorylated Akt compared to controls, which suggests that coffee treatment increased the activation

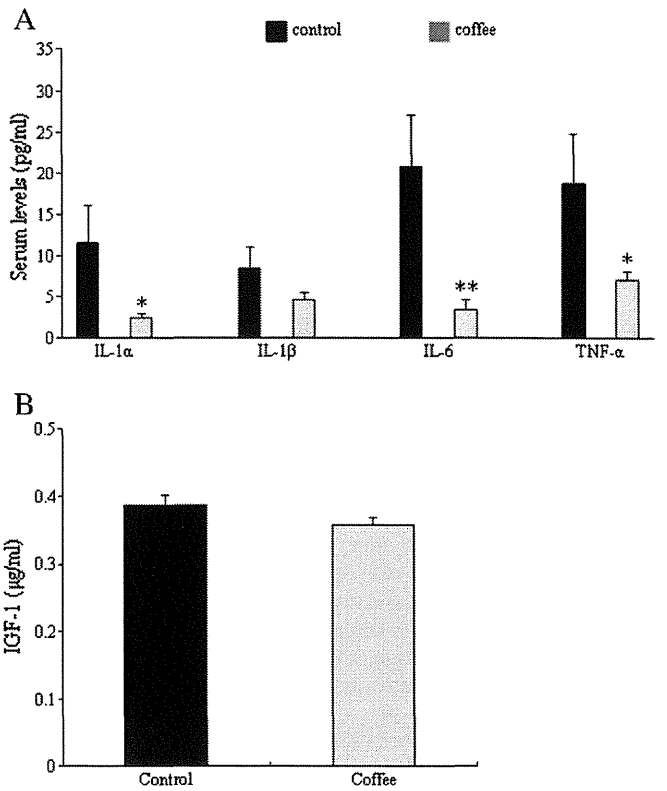

Fig. 3. Coffee treatment decreased the serum pro-inflammatory mediator levels, but did not affect the serum IGF-1 levels. ELISA determined serum levels of pro-inflammatory mediators and IGF-1 in aged mice treated with coffee for 4 weeks. (A) Coffee treatment significantly decreased the serum levels of IL-1α, IL-6, and TNF-α compared to controls. (B) Coffee treatment did not change the serum levels of the IGF-1 levels. Columns are mean ± SE, ≥4 in each group. $^{*}p < 0.05$, and $^{**}p < 0.01$ compared with control.

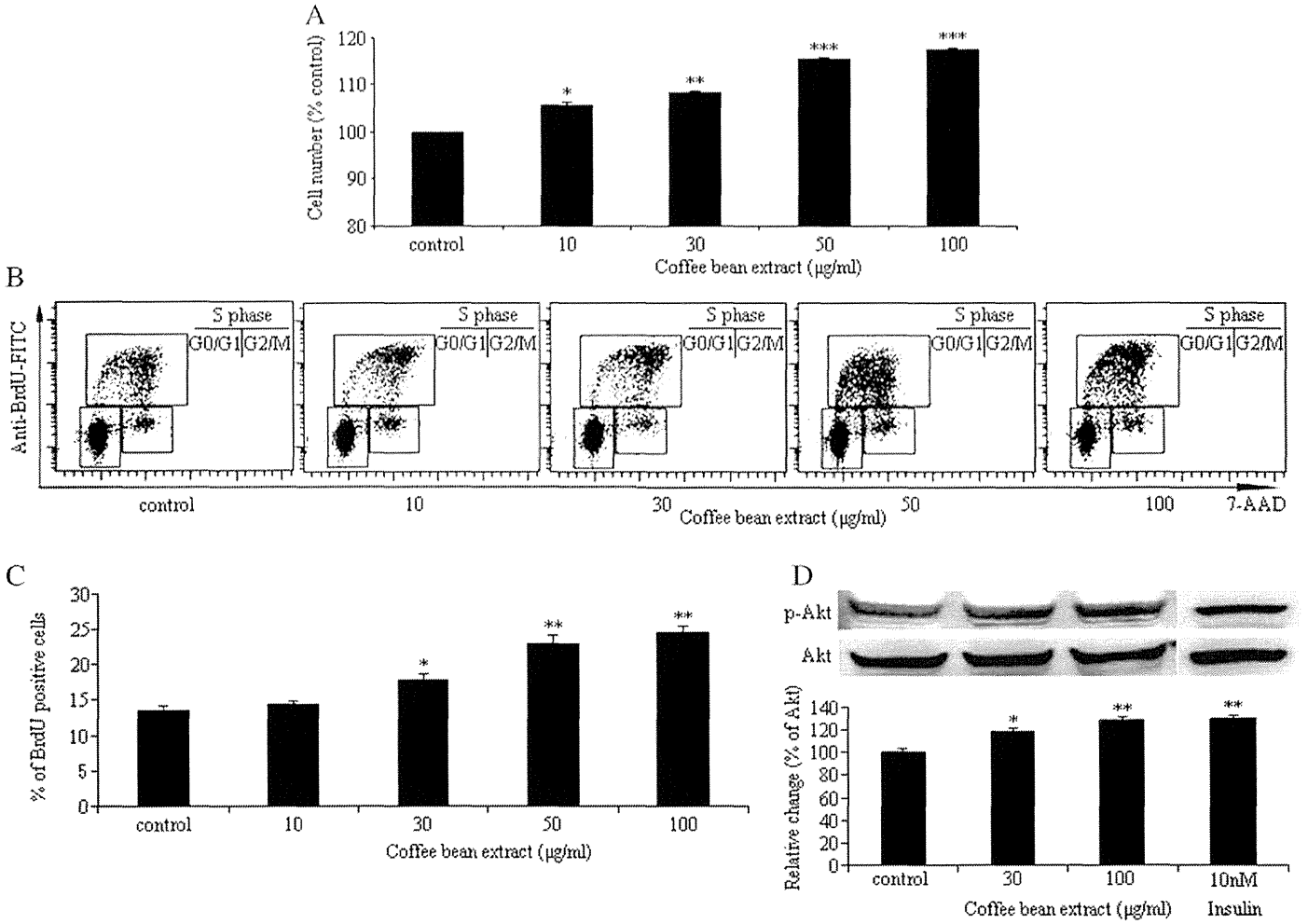

Fig. 4. Effects of coffee on the satellite cells of aged mice in vitro. (A) The satellite cells of aged mice were treated with the indicated concentrations of coffee bean extract for 72 h and the cell proliferation rate was measured. (B) Bromodeoxyuridine (BrdU)/7-AAD incorporation was evaluated by flow cytometry after stimulating the cells with water or indicated concentrations of coffee for 72 h. The regions were set on the G0/G1, S phase and G2/M populations. Representative data are shown. (C) The satellite cells of aged mice were cultured for 72 h with or without the indicated concentrations of coffee, and BrdU-positive percentages were calculated. (D) The satellite cells of aged mice were pretreated with coffee for 72 h, then the western blot analysis detected activated form of Akt (phospho-Akt) and total Akt. The densitometry quantified the band intensities. The graph shows the phospho-Akt band intensities normalized to the Akt band intensities. Representative of 3 independent experiments. Columns are mean ± SE. $^{*}p < 0.05$, $^{**}p < 0.01$, and $^{***}p < 0.0001$, compared with control.

level of Akt (Fig. 4D). As a positive control, we activated Akt in satellite cells with insulin (Fig. 4D). These results suggested that coffee treatment increased the proliferation rate and augmented DNA synthesis through the Akt signaling pathway in the satellite cells isolated from aged mice in vitro.

4. Discussion

In this study, using aged mice, we showed that coffee treatment increased the skeletal muscle weight, grip strength, regenerating capacity of injured skeletal muscles, and decreased the serum pro-inflammatory mediator levels compared to controls in vivo. In vitro, coffee treatment increased the cell proliferation rate, augmented DNA synthesis, and activated the Akt signaling pathway compared to controls in the satellite cells of aged mice.

Coffee treatment increased the number of proliferating satellite cells isolated from aged mice and augmented their cell cycle compared to controls, which could be the mechanism responsible for the increase in the skeletal muscle weight and grip strength, and accelerated the regeneration of injured skeletal muscles compared to controls. Since these effects possibly antagonized the loss of muscle mass and strength, the results suggested that coffee treatment might improve sarcopenia in aged mice. The coffee-treated group had greater grip strength than the controls. However, comparison between before and after the treatment period within the same groups showed that the grip strength did not change in the coffee-treated groups, whereas the grip strength decreased after the same period in the controls. This result suggested that coffee treatment did not improve but rather attenuated the progression of the decrease in muscle strength. Therefore, the effects of coffee on skeletal muscles might be attenuating the atrophy rather than improving the muscle mass and strength in aged mice. Satellite cells play an essential role in the regeneration of skeletal muscles (Lepper et al., 2011). Although skeletal muscle has the capacity to regenerate itself, this process is not activated in the gradual age-related loss of muscle fibers. The endocrine, autocrine, and paracrine environment in old muscle is less supportive of the activation, proliferation, and differentiation of satellite cells than in young muscle (Welle, 2002). The current results showed that coffee treatment increased the number of proliferating satellite cells, augmented their cell cycle in vivo and in vitro, and accelerated the differentiation and regeneration in vivo. These results suggested that coffee augmented the satellite cell activation. The decreased inflammatory levels by coffee treatment may contribute to the prevention of sarcopenia, as well. The combination of augmented satellite cell activation and decreased inflammatory levels by coffee treatment might antagonize the degenerative environment in old muscles and might prevent the sarcopenia.

Inflammation plays an important role in age-related sarcopenia (Beyer et al., 2012; Jensen, 2008). Therefore, the decreased serum levels of pro-inflammatory mediators after coffee treatment might be one of the mechanisms of the effects of coffee. Results from several experimental studies showed that coffee extracts inhibited inflammation in animal models (J.Y. Kim et al., 2006; Paur et al., 2010). A human clinical trial also demonstrated that coffee intake had beneficial effects on subclinical inflammation (Kempf et al., 2010). Our findings are consistent with these observations. Coffee contains many components and some of them have immunomodulatory effects. For example, a component of coffee, kahweol, inhibited the effect of TNF-α-induced protein and mRNA expression of the adhesion molecules, vascular cell adhesion molecule 1 and intercellular adhesion molecule 1, in human endothelial cells in vitro (H.G. Kim et al., 2006). Kahweol also inhibited the inflammatory response induced by carrageenan in a rat using an acute air pouch inflammation model (J.Y. Kim et al., 2006). These results strongly suggested that some components in coffee have significant anti-inflammatory effects in vitro and in vivo. Moreover, accumulating evidence suggests that coffee is a good source of antioxidant (Svilaas et al., 2004). Because oxidative stress causes inflammation (Butt and Sultan, 2011), the decrease in inflammation by coffee may be partly mediated through the antioxidant mechanism. Furthermore, some studies also reported that caffeine can increase skeletal muscle contractions by increasing calcium ion release (Olorunshola and Achie, 2011). Since this is a study of a complex product, we could not evaluate the effect of each component in the prevention of sarcopenia. However, the results suggested that whole coffee improved sarcopenia in aged mice. Further studies are required to evaluate the effects and mechanisms of the components of coffee on sarcopenia.

In vitro, coffee activated the Akt signaling pathway in satellite cells isolated from aged mice. Since coffee contains a wide variety of components, it is not clear which component(s) activated Akt. However, the effect of coffee on Akt activation is controversial. In several types of cancer cells, coffee decreased the Akt activation level (Choi et al., 2011; Oh et al., 2009). In contrast, in the cells of a Parkinson's disease model, coffee activated Akt and prevented apoptotic cell death (Nakaso et al., 2008). Combined with previous studies, our results suggested that the effect of coffee on Akt activation level might depend on the cell type. Since most satellite cells in aged animals are in a quiescent state, coffee might not activate Akt in vivo. However, satellite cells are activated by increased muscle loading and some of these cells fuse with apparently undamaged myofibers as part of the hypertrophy process (Adams, 2006). Furthermore, a recent study identified apoptotic cells as a new promoter of myoblast fusion (Hochreiter-Hufford et al., 2013). Therefore, some satellite cells might be in an active state in aged animals and coffee treatment might augment their Akt activation in vivo.

Several studies showed that exercise alone did not affect muscle function in aged animal models (Derbre et al., 2012; Leiter et al., 2011, 2012). A previous study indicated that the systemic environment of old animals is a crucial factor for maintaining and improving the function of satellite cells (Brack et al., 2007). In fact, another study suggested that nitric oxide and exercise together promoted muscle function in aged mice (Leiter et al., 2012). Therefore, the effect of exercise on muscle function in aged mice may depend on systemic and/or muscle environments. The decreased systemic inflammatory levels of the aged mice by coffee treatment may be one reason for the discrepancy in the effects on muscle function between exercise and coffee treatment.

Previous studies suggested that caffeine intake increased physical activity and energy metabolism, and decreased body weight (Magkos and Kavouras, 2004). However, in the present study, coffee intake did not change these parameters. The difference in age might partly explain this discrepancy.

A limitation of this study was that we could not clearly rule out whether caffeine, a major biological active component of coffee, or whole coffee itself produced stimulatory effects on proliferation in satellite cells. Several studies have shown that caffeine affected the proliferation rate and activation levels of Akt and inhibited reactive oxygen species in other cell types including epithelial, neuronal, cancer, and vascular smooth muscle cells (Mercer et al., 2012; Miwa et al., 2011, 2013; Nakaso et al., 2008; Sahu et al., 2013; Sarobo et al., 2012). Further study is required to clarify the exact effects and mechanisms of caffeine or other coffee components on the functions of satellite cells isolated from aged mice.

In conclusion, in vivo, coffee treatment increased the muscle weight, grip strength, regenerating capacity of injured muscles, and decreased serum pro-inflammatory mediator levels compared to controls in aged mice. In vitro, coffee increased the cell proliferation rate, augmented the cell cycle, and increased the activation level of the Akt signaling pathway compared to controls in satellite cells isolated from aged mice. These findings suggested that coffee treatment might have a beneficial effect on the prevention of age-related sarcopenia through decreasing the systemic inflammation and activating the Akt signaling pathway in satellite cells.

Conflict of interests

All the authors declare no conflicts of interest to disclose.

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TMJ

One-leg standing time with eyes open: comparison between the mouth-opened and mouth-closed conditions

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Objective: Many studies report a significant relationship between the one-leg standing time with the eyes open and the occlusal relationship. To determine the association between proprioception (the periodontal membrane vs muscle spindle) to the one-leg standing time, the authors compared the one-leg standing time with eyes open between mouth-opened and mouth-closed conditions.
Methods: The study participants were 107 healthy, elderly patients. The authors measured the one-leg standing time with eyes open between mouth-opened and mouth-closed conditions.
Results: The one-leg standing time was significantly shorter with the mouth opened (21.1±19.1 seconds) than with the mouth closed (25.1±21.4 seconds). Patients whose one-leg standing time was equal or shorter with the mouth opened than with the mouth closed were not different from the other patients with regard to age, handgrip strength, BMI, and the number of remaining teeth.
Discussion: The vertical mandibular position may affect body balance.

Keywords: Handgrip strength, One leg standing time with eyes open, Remaining teeth

Introduction

In today's aging society, a variety of initiatives have been proposed to address a major focus in primary care: falls and fractures prevention. The World Health Organization (WHO) declared the 2000–2010 decade as the Bone and Joint Decade.[1] In response, Japan has taken active steps towards preventing primary nursing care and nursing care risks due to locomotive difficulty. This is fueled by new concepts of the locomotive syndrome. A method of assessing the risk of falling is the one-leg standing time with the eyes open.[2] Several reports suggest that this standing time is significantly related to the number of remaining teeth and the occlusal relationship.[3–6] However, the causal relationship between these factors is not yet fully understood, and it is assumed that the connection lies between the proprioception of muscle spindles (e.g. the periodontal membrane or the masseter muscle).[7] Some researchers have examined the relationship between body posture and the mandibular position by using a stabilometer in young subjects, and they concluded that the foot center of pressure is not influenced by asymmetric malocclusion or by different dental positions.[8–10] This may indicate a need to focus on the effects of extreme mandibular positions in the elderly population to reveal this relationship.

If the proprioception of the periodontal membrane and muscle spindle affect the one-leg standing time with eyes open, a difference between one-leg standing times with the mouth opened and mouth closed would be expected. Therefore, to determine whether such a difference existed, the authors measured and compared the one-leg standing times with the eyes open and the mouth opened and mouth closed in community-dwelling elderly people.

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Table 1 Comparison between the sexes in age, grip strength, body mass index, number of remaining teeth, and normal one-leg standing time with eyes open (mouth closed)

Physical Indices	Sexes		
	Male	Female	*P*
Age (years)	75.9±5.1	75.4±5.1	0.650^{NS}
Hand grip strength (kg)	33.0±6.5	19.5±4.5	0.000*
BMI (kg/m^2)	24.4±2.5	24.6±3.2	0.903^{NS}
Number of remaining teeth	22.4±8.0	19.0±9.6	0.932^{NS}
Normal one-leg standing time (seconds)	25.3±22.3	25.0±21.2	0.071^{NS}

Note: BMI=body mass index; NS=no significant difference.
*P<0.05, based on the Mann–Whitney U test.

Methods

Healthy elderly residents (32 men and 75 women) aged 65–89 years (average age, 75.6±5.1 years) from the Yahatahigashi Ward of Kitakyushu City, Japan were selected for the study. All participants came to the research area (i.e. a community center) voluntarily. Brief medical interviews were performed. Patients with bone and joint disease, neuromuscular diseases, or temporomandibular disorders were excluded as subjects. The study was approved by the Saiseikai Yahata General Hospital Ethics Committee and was conducted with assistance from the Saiseikai Yahata General Hospital in Kokura, Japan.

The authors measured physical indices such as height, weight, and grip strength in the dominant hand and the one-leg standing times with the eyes open. Body mass index (BMI) was calculated by weight/height^2. For the one-leg standing time with eyes open, the authors measured the length of time with the mouth closed (i.e. 'normal') and with the mouth wide open—each for a maximum of 60 seconds. The authors randomized the order of measurements (i.e. open versus close) and waited a minimum of 1 minute between measurements. A dentist confirmed the number of remaining teeth through an intraoral examination: wisdom teeth were included in the measurement, but roots were excluded.

The statistical software PASWver.18 (IBM, Tokyo, Japan) was used for the analysis. These physical indices were compared by nonparametric analysis because one-leg standing times were counted up to 60 seconds. Spearman's rank correlation coefficient was assessed between the normal one-leg standing times and the age, grip strength, BMI and number of remaining teeth. Using the Wilcoxon signed-rank test, one-leg standing times with the mouth closed were compared to one-leg standing times with the mouth opened. Furthermore, subjects were divided into two subgroups: (1) patients whose one-leg standing times were equal or shorter with the mouth opened than with the mouth closed and (2) patients whose one-leg standing times were prolonged with the mouth opened. Physical indices of these subgroups were compared using the Mann–Whitney U test. The significance level was set at 0.05.

Results

The mean number of remaining teeth was 20.1±9.2. Everyone who had lost molar teeth contacts on both sides was wearing removable dentures. There was no difference between the sexes for all physical indices examined, except for grip strength (Table 1). Therefore, all variables were compared between both sexes. A significant correlation was observed between normal one-leg standing time with eyes open and age, handgrip strength, BMI, and the number of remaining teeth (Table 2).

The average one-leg standing times with the mouth closed and with the mouth opened were 24.84±21.33 and 21.55±19.24 seconds, respectively. The time was significantly shorter with the mouth opened than with the mouth closed. The shortened group patients, whose standing time was equal or shortened with the mouth opened than with the mouth closed, consisted of 19 males and 46 females. The prolonged group patients, whose time with the mouth opened was prolonged, consisted of 13 males and 29 females. There were no significant differences between the two

Table 2 Comparison between the normal one-leg standing time with eyes open (mouth closed) and the age, grip strength, BMI, and number of remaining teeth

		Age	Grip strength	Body mass index	Number of remaining teeth
Normal one-leg standing time	Correlation coefficient	−0.376	0.193	−0.194	0.316
	P	0.000*	0.047*	0.045*	0.001*

Note: *P<0.05, based on Spearman's rank correlation coefficient.

subgroups in age, handgrip strength, BMI, or the number of remaining teeth (Table 3).

Discussion

The results of the current study confirmed previous findings that a significant correlation exists between the one-leg standing time with eyes open and the number of remaining teeth. Furthermore, the authors found that the one-leg standing time was significantly shorter with the mouth opened than with the mouth closed. It may be concluded that the vertical mandibular position affects the one-leg standing time.

Gangloff and Perrin[11] report that body swaying increases when conduction anesthesia is performed on the mandibular foramen in young, healthy subjects, and they also indicate that the center of gravity changes, depending on experimentally conferred mandibular positions.[12] Both studies support the possibility that the periodontal membrane functions as a proprioceptor that governs body balance.

On the other hand, Perinetti *et al.*[13] found no evidence of changes to the center of gravity in patients with malocclusion, and concluded that postural control is not different in the closed-mouth state, which includes mandibular rest and the intercuspidation positions.[14]

Based on the authors' hypothesis that muscle spindles are more important than the periodontal membrane for postural control, the one-leg standing times with the mouth opened and with the mouth closed were compared. Bracco *et al.*[15] report that the myocentric position determined by muscle contractions lead to smaller differences in the center of gravity, compared to the rest position of the mandibular joints and centric occlusion. In addition, Sforza *et al.*[16] found that changes to the center of gravity can be stabilized with equivalent muscular activity from the right and left masseter muscles during sprinting. Previous studies by the authors indicate that edentulous patients with an unstable lower jaw are more prone to shifts of their centers of gravity and that the number of falls can be reduced in patients with dementia who wear dentures.[4,17] These observations suggest that mandibular stability is important for postural control, and the results of the current study support this conclusion.

However, many methods are available for measuring the one-leg standing time, and researchers select the method.[18] It remains to be seen whether the methods used in this study (e.g. one measurement lasting up to 60 seconds) were appropriate. To gain further insights into the role of the mandibular position on postural control, the authors believe that a more detailed investigation employing a stabilometer will be necessary.

Table 3 Comparison between the 'shortened' and 'prolonged' subgroups

	Subgroup		
Physical indices	Shortened	Prolonged	*P*
Age (years)	75.5±5.4	75.7±4.5	0.896^{NS}
Hand grip strength (kg)	23.5±8.6	23.6±7.2	0.592^{NS}
BMI	24.2±2.9	25.1±3.1	0.237^{NS}
Number of remaining teeth	20.9±8.9	18.6±9.6	0.266^{NS}

Note: NS=No significant differences (at $P=0.05$, based on the Mann–Whitney *U* test).
In the 'shortened' group patients, the one-leg standing time was equal or shortened with the mouth open than with the mouth closed. In the 'prolonged' group patients, the one-leg standing time was prolonged with the mouth open.

Conclusion

In this study, the authors found that the one-leg standing time with the mouth opened was significantly shorter than the time with the mouth closed. This may be because the proprioception of the periodontal membrane and muscle spindles becomes functional in the mouth-closed condition. The authors conclude that the vertical mandibular position may affect body posture.

Disclaimer Statements

Contributors MY has contributed in conceiving and designing the study, and writing the article in whole; YK has contributed in collecting the data; YO has contributed in collecting the data and obtaining ethics approval; YI has contributed in collecting the data and analysing the data; TF has contributed in collecting the data and revising the article; TK has contributed in obtaining funding.

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Prognosis-related factors concerning oral and general conditions for homebound older adults in Japan

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Purpose: The present study examined the relationship between oral function, such as eating/swallowing, and life prognosis among a homebound elderly population, considering physical and mental function.

Methods: The participants were 511 homebound older adults aged 65 years or older living in four Japanese prefectures. Sex, age, activities of daily living (ADL), cognitive function, underlying disease, nutritional status as Mini-Nutritional Assessment-Short Form (MNA®-SF), swallowing function, dietary modification and occlusal status were examined at baseline. Participants were categorized into poor outcome (died or admitted to hospital or nursing home) and good outcome (still under home care) groups at 1-year follow up, and significant related baseline factors were analyzed. In addition, these groups were compared by the ADL subgroup divided into <60 (lower) and ≥60 (higher) by Barthel Index.

Results: In total, 473 participants were followed up (poor outcome group 177 [37.4%], good outcome group 296 [62.6%]). Sex, age, ADL, MNA®-SF, swallowing function, dietary modification and occlusal support were significantly different between these groups. Logistic regression analysis showed that sex and MNA®-SF score were significantly related to prognosis in the lower ADL group, and sex, age, Charlson Comorbidity Index and occlusal support were significantly related in the higher ADL group.

Conclusions: ADL was strongly correlated with life prognosis in homebound older adults. Within the higher ADL participants, occlusal support was related to this outcome. **Geriatr Gerontol Int 2014; ••: ••–••.**

Keywords: activities of daily living, elderly, nutrition, occlusion, prognosis.

Introduction

Among the elderly population, malnutrition induces decreased immune competence[1] and sarcopenia.[2] As decreased immune competence increases the risk of infections and sarcopenia impairs physical function, malnutrition is important as a factor causing health disorders in these older people. It was reported that more than half of Japanese older adults requiring home care were malnourished or at risk of malnutrition.[3] Malnutrition occurred under these conditions as: (i) chronic diseases, such as cancer, chronic cardiac failure, chronic renal failure and chronic obstructive pulmonary disease; (ii) acute diseases or wounds, such as surgery, acute infection and multiple trauma; and (iii) starvation as a result of insufficient ingestion of energy and protein.[4] Among these, the risk of malnutrition as a result of (iii) is high in older adults, as dietary intake decreases with aging.[5] The risk of malnutrition becomes higher when older adults require long-term care, because these factors are combined with difficulty in oral ingestion as a result of impaired eating/swallowing functions.[6]

It has been reported that malnutrition is directly linked to longevity;[7,8] however, it has not been shown that impaired eating/swallowing function that causes malnutrition[9] is related to life expectancy. The aim of

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the present study was to clarify the relationship between oral function, such as eating/swallowing, and life prognosis among a homebound elderly population, considering physical and mental function.

Methods

We examined 716 homebound older adults aged 65 years or older living in four prefectures of Japan (Tokyo, Kanagawa, Niigata and Fukuoka) from October to December in 2010.[10] Among these participants, 511 participants were followed up 1 year later (162 men, 349 women, mean age 84.2 ± 7.6 years). This study was approved by the ethics committee of Nippon Dental University. All the patients and/or their families gave written informed consent before study participation.

At baseline, sex, age, basic activities of daily living (ADL), cognitive function, underlying disease, nutritional status, swallowing function, dietary modification and occlusal status were examined. The present living status was determined at 1-year follow up by interviewing care managers and physicians of the participants.

ADL

ADL was evaluated using the Barthel Index, which is a widely used index.[11] The participants with a Barthel Index score of ≥60 points (those whose basic actions in daily life were almost independent[12]) were classified as the higher ADL group, and participants with a Barthel Index score of <60 points were classified as the lower ADL group.

Cognitive function

Cognitive function was evaluated using Washington University Clinical Dementia Rating (CDR), an observational method that is widely used to evaluate the severity of dementia throughout the world.[13] Participants with a score of zero and 0.5 were classified as "absence of dementia", and participants with a score of ≥1 were classified as "presence of dementia".

Underlying disease

The underlying disease in each participant was obtained based on the diagnosis of the physician in charge and evaluated using the Charlson Comorbidity Index (concomitant underlying disease index), a concomitant disease index for prognostic evaluation.[14]

Nutritional status

The nutritional status was evaluated using Mini-Nutritional Assessment-Short Form (MNA®-SF) consisting of six screening items in the first step of MNA®, a simple evaluation method for older adults.[15]

Swallowing function

Swallowing function was evaluated according to the neck auscultation method by Zenner *et al.*[16] Each participant was made to ingest 3 mL of water from a glass and the swallowing status was evaluated by neck auscultation.[17] At this time, when a symptom such as choking, respiratory distress or wheezing occurred or the water was swallowed in multiple portions, "presence of swallowing disorder" was judged, and otherwise "absence of swallowing disorder" was judged. The dentist in charge of the test was instructed about the neck auscultation method in advance of the test.

Dietary modification

The interview showed whether the dietary modification, such as puree and nectar, was used or not in the every day diet. Drinking thickened water was also included in the dietary modification.

Occlusal status

A dentist carried out an oral examination at home, and depending on the occlusion status in the molar region, the participants were classified as follows. Participants with occlusion of the molar region with natural teeth or denture(s) at one or more sites were classified as "presence of occlusal support", whereas those with no molar region occlusion with either natural teeth or denture(s) were classified as "absence of occlusal support".

Statistical analysis

According to the follow-up examination, the participants were classified into two groups: (i) participants still receiving home care in the same manner as 1 year ago; and (ii) participants who were admitted to hospital or a nursing home, or died during the last 1-year period. Participants in group (i) were handled as the "good outcome group", and participants in group (ii) were handled as the "poor outcome group." These two groups were compared by the χ^2-test and Mann–Whitney *U*-test. Furthermore, multicollinearity was investigated with Spearman's rank correlation coefficient and Cramer's coefficient of association (Cramer's V). In addition, the participants were divided by Barthel Index score, and the influence of each factor ($P < 0.10$) was investigated by logistic regression analysis in each ADL subgroup. In statistical analysis, PASW Statistics 18 (IBM, Tokyo, Japan) was used, and the level of statistical significance was set at 95%.

Results

Excluding 38 participants (7.4%) in whom the follow-up investigation was not possible as the nursing-care service provided had changed or consent was not obtained, 473 participants (145 men, 328 women, mean age 84.1 ± 7.6 years) were followed up. The good outcome group consisted of 296 participants (75 men, 221 women, mean age 83.5 ± 7.7 years). The poor outcome group consisted of 177 participants (70 men, 107 women, mean age 85.1 ± 7.4 years). Among the poor outcome group, 119 participants (25.2%) were admitted to a hospital or nursing home. The reason for this admission was orthopedic disease in 19, pneumonia in 18, cerebrovascular disease in six, malignant neoplasm in five, cardiac disease in five, other in 30 and unclear in 36. Deceased participants accounted for 58 (12.3%), and the cause of death was pneumonia in 12, senile deterioration in 12, cardiac disease in eight, malignant neoplasm in seven, cerebrovascular disease in three, other in 10 and unclear in six.

The items that showed a significant difference between the good outcome group and poor outcome group were sex, age, ADL, MNA®-SF, swallowing function, dietary modification and occlusal support (Table 1).

Looking at the inter-item correlation, a strong correlation ($P < 0.001$) was detected between Barthel Index and other items, as shown in Table 2. Then, the participants were divided into the following two ADL subgroups for analysis. The lower ADL group with a Barthel Index score of <60 points consisted of 211 participants (67 men, 144 women, mean age 84.5 ± 8.0 years), and the higher ADL group with a Barthel Index score of ≥60 points consisted of 262 participants (78 men, 184 women, mean age 83.8 ± 7.3 years).

Comparing the good outcome group and poor outcome group in each ADL subgroup, a significant difference was recognized for MNA®-SF in the lower ADL group, and for sex, age, Charlson Comorbidity Index, swallowing function and occlusal support in the higher ADL group (Table 3). In addition, the stepwise logistic regression analysis showed that sex and MNA®-SF were identified as prognostic factors ($P < 0.05$) in the lower ADL group, and sex, age, Charlson Comorbidity Index and occlusal support were identified as prognostic factors ($P < 0.05$) in the higher ADL group (Table 4).

Table 1 Comparison between good outcome group and poor outcome group

	Prognosis		Odds ratio (95% CI)	*P*-value
	Good outcome group (n = 296)	Poor outcome group (n = 177)		
Men, n (%)	75 (25.3)	70 (39.5)	0.519 (0.348–0.773)	0.001
Age, mean (SD)†	83.5 (7.7)	85.1 (7.4)		0.034
ADL (Barthel Index), mean (SD)†	64.2 (26.7)	51.1 (29.0)		<0.001
CDR not less than 1, n (%)	157 (53.0)	105 (59.3)	1.291 (0.886–1.882)	0.184
Charlson Comorbidity Index, mean (SD)†	1.3 (1.2)	1.6 (1.4)		0.052
MNA®-SF, mean (SD)†	10.4 (2.3)	9.5 (2.3)		<0.001
Presence of swallowing disorder, n (%)	73 (24.7)	73 (41.2)	2.144 (1.438–3.196)	<0.001
Dietary modification, n (%)	70 (23.6)	69 (39.0)	2.063 (1.377–3.089)	<0.001
Absence of occlusal support, n (%)	26 (8.8)	31 (17.5)	2.205 (1.261–3.855)	0.005

†Mann–Whitney U-test, others: χ^2 test. ADL, activities of daily living; CDR, Clinical Dementia Rating; CI, confidence interval; MNA®-SF, Mini-Nutritional Assessment-Short Form.

Table 2 Correlation between activities of daily living (Barthel Index) and each examination item

	Sex	Age	CDR	Charlson Comorbidity Index	MNA®-SF	Swallowing disorder	Dietary modification	Occlusal support
Correlation coefficient	0.233†	−0.069	−0.205	−0.194	0.519	−0.261	−0.489	−0.116
P-value	0.178	0.134	<0.001	<0.001	<0.001	<0.001	<0.001	0.011

†Cramer's coefficient of association (Cramer's V). ADL, activities of daily living; CDR, Clinical Dementia Rating; MNA®-SF, Mini-Nutritional Assessment-Short Form.

Table 3 Comparison between good outcome group and poor outcome group in lower and higher activities of daily living group

	Lower ADL group				Higher ADL group			
	Outcome		Odds ratio (95% CI)	*P*-value	Outcome		Odds ratio (95% CI)	*P*-value
	Good outcome group (n = 109)	Poor outcome group (n = 102)			Good outcome group (n = 187)	Poor outcome group (n = 75)		
Men, n (%)	28 (25.7)	39 (38.2)	0.558 (0.311–1.004)	0.050	47 (25.1)	31 (41.3)	0.476 (0.271–0.839)	0.010
Age, mean (SD)†	84.2 (8.4)	84.8 (7.5)		0.714	83.1 (7.2)	85.5 (7.2)		0.008
CDR not less than 1, n (%)	66 (60.6)	71 (69.6)	1.492 (0.843–2.640)	0.168	91 (48.7)	34 (45.3)	0.875 (0.511–1.497)	0.626
Charlson Comorbidity Index, mean (SD)†	1.7 (1.5)	1.6 (1.4)		0.992	1.2 (1.0)	1.6 (1.4)		0.040
MNA®-SF, mean (SD)†	9.3 (2.2)	8.6 (2.2)		0.013	11.1 (2.1)	10.8 (1.8)		0.128
Swallowing disorder, n (%)	41 (37.6)	49 (48.0)	1.533 (0.886–2.654)	0.126	32 (17.1)	24 (32.0)	2.279 (1.230–4.223)	0.008
Dietary modification, n (%)	49 (45.0)	57 (55.9)	1.551 (0.901–2.670)	0.113	21 (11.2)	12 (16.0)	1.506 (0.700–3.240)	0.293
Absence of occlusal support, n (%)	13 (11.9)	19 (18.6)	1.690 (0.787–3.630)	0.175	13 (7.0)	12 (16.0)	2.549 (1.105–5.881)	0.024

†Mann–Whitney U-test, others: χ^2-test. ADL, activities of daily living; CDR, Clinical Dementia Rating; CI, confidence of interval; MNA®-SF, Mini-Nutritional Assessment-Short Form.

Table 4 Results of stepwise logistic regression analysis in lower and higher activities of daily living group

	B	Standard deviation	Wald test	*P*-value	Exp (B)	95% CI
Lower ADL group						
Sex	−0.657	0.307	4.588	0.032	0.518	0.284–0.946
MNA®-SF	−0.174	0.067	6.875	0.009	0.840	0.737–0.957
Constant	2.605	0.849	9.429	0.002	13.537	
Higher ADL group						
Sex	−0.896	0.326	7.534	0.006	0.408	0.215–0.774
Age	0.085	0.023	13.356	0.000	1.089	1.040–1.140
Charlson Comorbidity Index	0.417	0.142	8.631	0.003	1.518	1.149–2.004
Occlusal support	1.039	0.453	5.254	0.022	2.826	1.163–6.870
Constant	−8.306	2.076	16.012	0.000	0.000	

ADL, activities of daily living; B, partial regression coefficient; Exp (B), exponential function (partial regression coefficient); MNA®-SF, Mini-Nutritional Assessment-Short Form.

Discussion

The results of the present study suggested that occlusal support could be related to life prognosis in homebound older adults whose ADL is relatively maintained.

Regarding the correlation between nutritional status and outcome, low body mass index and hypoalbuminemia were handled as poor-prognostic factors in homebound older adults.[18] In addition, Tsai *et al.* reported that MNA® is a factor capable of predicting the nutritional status and outcome in older adults admitted to a nursing home.[19]

The Barthel Index is a globally used tool for ADL evaluation, and it was reported that the level of independence is high with a Barthel Index score of ≥60 points, severe disability is seen with a score of <40 points and total aid is necessary with a score of <20 points.[12] In the present study, a strong correlation was recognized between ADL and other examination items. Then, in order to avoid multicollinearity, the participants were divided into lower ADL group with a Barthel Index score of <60 points and higher ADL group with a Barthel Index score of ≥60 points for statistical analysis. As a result, in the lower ADL group, a significant correlation was recognized between malnutrition risk and life prognosis, the same as in previous studies.[18,19]

In contrast, in the higher ADL group, nutritional status was not related to life expectancy. In the higher ADL group, the items that showed a significant correlation with life prognosis were underlying disease and occlusal support, as well as sex and age. It could indicate that someone who has maintained relatively high ADL is admitted into the hospital or nursing home suddenly because of deterioration of their underlying medical problems. Furthermore, a significant correlation was recognized between occlusal support and prognosis, so we speculate that loss of occlusal support resulted in a chewing disorder and caused an eating disorder leading to malnutrition.

Many studies have shown that teeth, occlusal support and chewing ability were correlated with nutritional status in older adults, and it is concluded that the presence of occlusal support and chewing ability are favorable factors for nutritional status.[20–22] Chewing ability was produced by occlusal support as well as oral function including tongue, cheek and lips movement,[23] and oral function was significantly related to ADL.[24] It could be quite reasonable in the lower ADL group that oral function had already decreased in the same manner as general physical function, and eating/swallowing disorder and malnutrition were caused by the chewing disorder. In contrast, oral movement for chewing could be maintained in the higher ADL group, so that the existence of occlusal support might be directly involved in maintenance of chewing and eating function.

In the present study, the reason for admission to hospital or a nursing home did not focus on the underlying disease status, so further studies will be required to show that occlusal support is related to life prognosis in homebound older adults whose ADL is relatively maintained. Furthermore, as malnutrition accompanying loss of occlusal support was the cause of sudden worsening of outcome among the relatively ADL maintained group, we should investigate the possibility that recovery of chewing function by restoring occlusal support with denture(s) might improve eating function, leading to improvement of nutritional status and further to improvement of life expectancy.

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Disclosure statement

The authors declare no conflict of interest.

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徹底解説！訪問歯科診療

寝たきりでも快適な生活を送るための訪問歯科

高齢化社会を迎えた日本では、各方面で高齢者の健康と暮らしを守る取り組みが行われています。体が不自由になって歯科に通院できない高齢者のために、口腔ケアを中心とした「訪問歯科診療」のシステムが地道に取り組まれ、注目を集めています。

文／信夫京子　イラスト／塩浦信太郎　写真提供／菊谷 武

歯科医に通院できない人を支える訪問歯科診療

すでに"超高齢化社会"に入った日本では、高齢者の生活をどう支えていくかが大きな課題となっています。平均寿命は男女ともに延び続け、平成22年には男性は79・55歳、女性は86・30歳にまで達しており、世界でも有数の長寿国です。しかし、平均寿命は延びても、高齢者が健康で自立した状態にある"健康寿命"が同様に延びている訳ではありません。さらに要介護人口は年々増加し、寝たきりの高齢者も増加の一途をたどっています。

若く元気な時は意識することの少ない「口の健康」ですが、高齢者にとっては口の状態が心身に大きく影響を与えます。しかし、寝たきりなどになると、歯医者に通って治療を受けることができなくなり、口の不具合をそのまま放置する場合も多くなるようです。日本歯科大学口腔リハビリテーション多摩クリニックの院長、菊谷武先生に高齢者の口のトラブルについて伺いました。

「口の状態が悪化し、食べる、話すといった口の機能が衰えると、全身にさまざまな弊害が起きてきます。食が細くなって体力や免疫力が低下したり、唾液の分泌が低下して口の汚れが残りやすくなり、むし歯や歯肉炎などにもなりやすくなります。さらに状態が悪化すれば、糖尿病や心臓病のリスクが高くなり、認知症の加速にも繋がりかねません。」

このような状態を改善するために、訪問歯科診療が行われているといいます。医者の往診と同じように、自宅またはホームなどの施設、歯科の無い入院施設などに歯科医や歯科衛生士が訪れ、治療や口腔ケアを実施します。診察の対象となるのは、寝たきりの高齢者だけでなく、通院の難しい重度の障害を持つ人や認知症の人などです。

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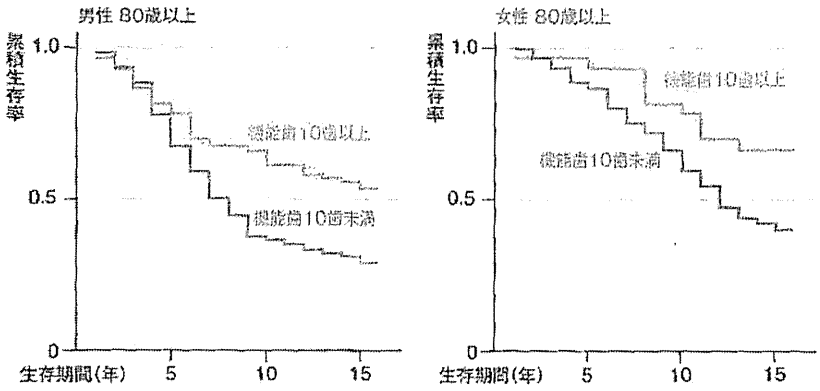
専門は高齢者の摂食・嚥下障害に対するリハビリテーション、口腔癌病患者の術後機能回復、口腔ケア。日本歯科大学歯学部卒業。現在、岡山大学、広島大学、徳島大学、九州歯科大学、琉球大学の非常勤講師を務める。『基礎から学ぶ口腔ケア』（学研）など一般にもわかりやすい著書など多数。

訪問歯科診療が必要な患者とは?

・身体的に1人で外出や移動が困難な人
寝たきりまたはそれに近い状態の高齢者、重度の障害を持つ人など。
・認知症で外出や診察室での診療が困難な人
・精神障害などで外出や診察室での診療が困難な人

歯の本数が多いほど寿命がのびる!

機能歯数(10歯未満/10歯以上)と生存曲線



Fukai K et al.,Geriatr Gerontol 7:314-347,2007

※特定の40歳以上の住民5,730名を15年間継続した調査の中で、80歳以上の高齢者は男女ともに機能歯数(噛める歯の数)と生命予後(生存年数)との間に関連があることが認められた。

高齢者の健康を守る基本は口腔ケア

噛むことができる歯の本数が多い高齢者ほど、寿命がのびる傾向にあることは調査で確認されています。しかし、体が自由に動かない、認知症があるなどで、歯磨きやうがい、歯垢除去などの口腔ケアが行き届かなくなると、口の中には細菌が繁殖し、むし歯や歯肉炎、歯槽膿漏などで噛める歯が少なくなり、症状がひどくなると歯を失うことも多いようです。

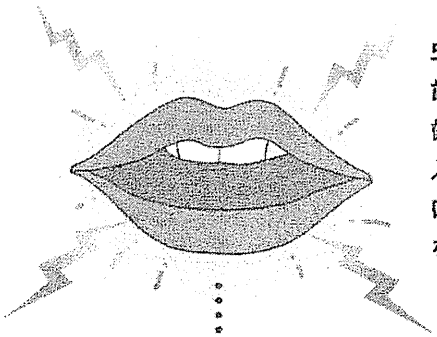
また、口の中の細菌が増えることは、誤嚥性肺炎の危険も増加するそうです。

高齢になると食べ物や唾液が誤って気管に入る「誤嚥」が起きやすくなり、口内で増殖した大量の細菌が肺に流入するためだといいます。

特別養護老人ホームの入所者を対象にした2年間の調査では、きちんとした口腔ケアを行うことで口中の細菌数が減り、肺炎の発症が4割、死亡が5割減少したという結果も出ています。さらに、口腔ケアの刺激によって口腔内の機能が回復し、誤嚥しにくくなるという効果も認められました。

誤嚥性肺炎のように、口のトラブルが命に関わることもあります。また、これ以外にも左図のようにいろいろな悪影響が考えられ、寝たきりの高齢者が安全に暮らし、生活の質を高めるには、適切な口腔ケアと口のトラブル改善が重要になってきます。

高齢者の口のトラブルによる悪影響



虫歯
歯肉炎
歯周病
入れ歯の不具合
口の機能低下
を放置すると…

誤嚥性肺炎の危険

咀嚼や嚥下が上手くできなくなり、細菌を含んだ唾液や食べ物を誤嚥してしまうことを繰り返すと肺炎を起こしやすくなる。

認知機能の低下

歯や口の機能にトラブルがあって、口から食べることが少なくなると、脳への刺激がなくなる。また、「食事」という楽しみがなくなることで、気持の張りがなくなり、認知機能にも影響する。

糖尿病や心臓病のリスク

歯周病があると、糖尿病や心臓病のリスクが格段にあがることがわかってきた。

転倒の危険

歯(奥歯)の咬み合わせが悪かったり、入れ歯を装着していないか合っていない場合、上下の歯がしっかりと噛み合っていないために重心が定まらず、転びやすくなる。

低栄養の危険

口の機能にトラブルがあると食べられるものが限られるなどして、栄養状態が悪くなりやすい。

インフルエンザの危険

口の中が汚れて雑菌が繁殖すると、細菌のだす酵素によってのどの粘膜が荒れてしまい、インフルエンザのウイルスが体内に入り込みやすくなる。

訪問歯科医療の役割

訪問歯科治療に詳しい菊谷武先生に訪問歯科診療について伺いました。

「訪問歯科診療は、寝たきりで歯科に通えない人にとっては大切なシステムです。しかし、設備の整った診療室ではなく、患者さんの枕元で行う治療には自ずと限界があることは知っておいてください。危険性のない治療範囲としては、軽度のむし歯や歯肉炎などです。むしろ、患者さんの口腔機能を最善に保つため、入れ歯の調整や口腔の清掃、機能の回復・維持のための指導などが重要な役割になってきます」

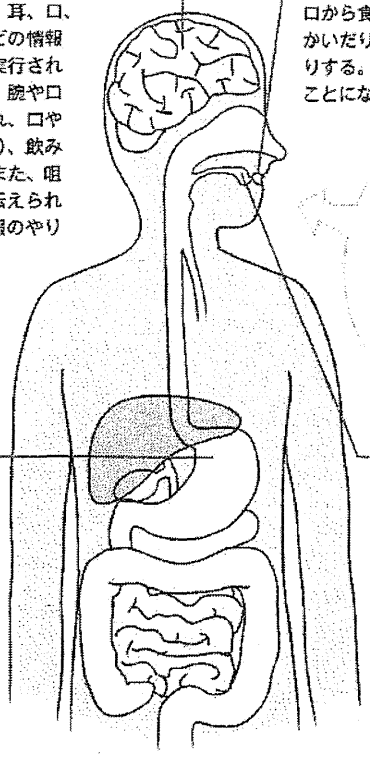
高齢者の訪問歯科医療では、患者さんの体調やほかの疾病を考慮しながら、患者さん自身が持つ力を最大限に発揮できるように咀嚼や嚥下などの"口腔機能"を管理することが役割となります。

治療内容としては、むし歯や歯肉炎、歯周病の治療に、入れ歯の調整や修理、口腔ケアになりますが、重点が置かれるのは口腔ケアになります。

訪問歯科診療では、実際に高齢者の介護をするヘルパーや訪問看護師などのスタッフとコミュニケーションをとり、日常の口腔ケアを指導することも大切な役割になるといいます。また、左図のように口から食べることにはいろいろなメリットがあるので、患者さんの状態に合わせて適切な食事指導も行うそうです。

よく噛めるようにと入れ歯にこだわる方が多いのですが、よく噛めるかどうかは、歯も大事ですが、実は口が動くかどうかの方が影響は大きいそうです。口の筋肉や舌を上手く使って、口に入って来た食べ物の動きをうまくコントロールできないと、噛んだり飲み込んだりはできないのです。咀嚼や嚥下が上手くいかなくなったら、患者さんの状態に合わせた口の体操やマッサージなどの指導もおこないます。

口やのどを使って食べるメリット



脳の活性化

食べ物を前にすると、目、鼻、耳、口、手を介して臭いや手ざわりなどの情報が脳に伝わる。食べる動作が実行される場合、脳から命令が出され、腕や口唇が動いて食べ物が取り込まれ、口やのどの筋肉が働いて噛み(咀嚼)、飲み込む(嚥下)動作が行われる。また、咀嚼や嚥下による刺激は、脳に伝えられる。このようにさまざまな情報のやり取りされ、脳は活性化する。

意識レベルの向上

口から食べることで、食べ物の匂いをかいだり、食感を感じたり、味わったりする。このことで五感が刺激されることになり、意識レベルが保たれる。

消化器の活性

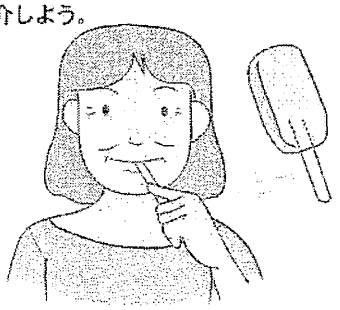
口から食べることで五感が刺激され、脳に情報が伝えられることで消化器官も活動を始める。胃、腸、肝臓など各器官が活動を始め、消化の準備を整える。

唾液の分泌向上

口の中で咀嚼することにより、唾液腺が刺激され、唾液の分泌が促進される。唾液によって初期消化が行われるとともに、唾液の持つ自浄作用や抗菌作用の働きで口内の清潔な環境を保つ。

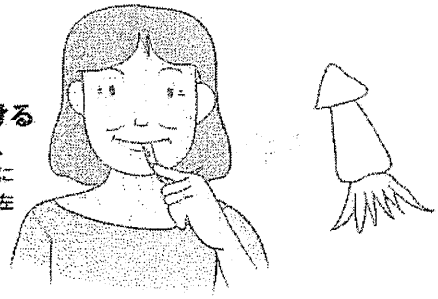
訪問歯科診療で教わる簡単"お口体操"

口の中の食べ物を噛み砕くには、歯や口の筋肉の複雑な動きがスムーズに行われる必要がある。食べるためには歯以外にくちびる、頬、舌、下顎などを使って、食べ物を巧みにまとめて歯の上に移動し、すり潰す動きを行なわなければいけない。噛む力や巧みさが低下している人が気軽にできる体操を紹介しよう。



噛む力(パワー)をつける

口にアイスキャンデーの棒などをくわえ、グッと噛みしめる。



噛む巧みさをつける

するめを片側の歯で噛み、手を使わずに反対側の歯に移動させて噛む。これを左右繰り返しておこなう。