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ORIGINAL ARTICLE

Epidemiological study for personal risk factors and quality of life related to Dupuytren's disease in a mountain village of Japan

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Abstract
Background This study investigated the etiology, personal risk factors, and quality of life related to Dupuytren's disease among residents of a mountain village in Japan.
Methods Medical examinations were conducted of 401 adult residents (163 men, 238 women; average age of 66.7 years, range 40–92) of a mountain village in Japan. All had completed a self-administered questionnaire including items for gender, weight, height, dominant hand, occupation, history of diabetes mellitus, and frequency of smoking tobacco and drinking alcohol, in addition to EuroQol-5-Dimensions-3-level Japanese version. Blood samples were collected and assessed for biochemical markers related to Dupuytren's disease. The Dupuytren's disease diagnosis was based on clinical signs. Meyerding's classification was used to ascertain the disease severity. After examining background data and physical examination data related to Dupuytren's disease, we evaluated the association of Dupuytren's disease with those factors using univariate and logistic regression analysis.
Results Dupuytren's disease was diagnosed in 28 subjects (7.0 %). Univariate analysis revealed associations of age, male gender, occupation, history of diabetes mellitus, and alcohol intake with Dupuytren's disease. Logistic regression analysis after adjustment for age revealed a significant association between Dupuytren's disease and male gender, occupation, and history of alcohol intake. No significant difference was found between Dupuytren's disease patients and participants without this disease in the scoring and visual analog scale of EuroQol. No relation was found in scoring, the visual analog scale of EuroQol, or grading of Meyerding's classification in participants with Dupuytren's disease.
Conclusion This cross-sectional study revealed Dupuytren's disease in 7.0 % of 401 subjects among the general population of a mountain village in Japan. The prevalence is higher with age and is apparently associated with male gender, occupation and alcohol intake. Risk factors associated with Dupuytren's disease were identified as age, male gender, occupation, and alcohol consumption habits.

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Introduction

Dupuytren's disease, a fibromatous disorder of the palmar fascia causing chronic contracture of the fingers, especially of the fourth and fifth fingers, reportedly has much higher prevalence among Europeans than among people of other races [1–3]. It is regarded as one of the most commonly inherited connective-tissue disorders affecting the Caucasian of northern European geneology. The prevalence of Dupuytren's disease is more than 4 % among the male population in England [3], with an incidence of more than 40 % in Icelandic men older than 70 years [1]. Conventional treatments for Dupuytren's disease include surgical correction by fasciectomy or fasciotomy including skin grafting. The disease is linked to many environmental factors including diabetes mellitus, alcohol consumption, epilepsy, smoking, manual labor, and high levels of cholesterol and triglycerides [1, 4–7]. Few reports of epidemiological studies of Dupuytren's disease describe analyses of the general population in Asia [8].

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Health-related quality of life (QOL) has become an important indicator to inform patient therapeutic management. The EuroQol-5-Dimensions, a recently developed self-report measure of health-related QOL [9], is a questionnaire for collecting information related to pain, mobility, self-care, activity, and anxiety in addition to providing a patient global assessment (VAS) of 0–100, where 100 is indicative of the best imaginable health state. Previous studies related to the association between musculoskeletal disorder and health-related QOL exist [10], but few reported studies have examined QOL of patients affected by Dupuytren's disease. The present study was conducted to estimate the prevalence of Dupuytren's disease and to evaluate risk factors and QOL effects related to the disease in the general population of a mountain village in Japan.

Materials and methods

Local medical examinations intended for early detection of cancer and for prevention of lifestyle-related diseases were conducted for residents of a mountain village in Japan, where agroforestry and tourism are the main industries. The total number of local medical examination examinees was 1,080 people, including 500 men and 580 women aged 39–92 years. The participants in this study, whom we randomly selected, were 401 people (163 men, 238 women, average age 66.7 years, range 40–92) (Table 1). They had been informed that their data would be published. They gave their consent to participate in this study. Each had completed a self-administered questionnaire with items related to gender, dominant hand, occupation, smoking and drinking habits and history, and history of diabetes mellitus, in addition to the EuroQol-5-Dimensions-3-Levels Japanese version (EQ-5D-3L) and EuroQol-VAS Japanese version (EQ-VAS) to assess health-related QOL. The EuroQol-5D-3L (Japanese version) was validated by Tsuchiya et al. [11] as having evaluation capacity equivalent to the original version. Blood samples were collected for medical examinations to assess hemoglobin A1c, (HbA1c) asparate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyltranspeptidase (γ-GTP), low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, and triglycerides. Height, weight, and blood pressure were measured at arrival.

The Dupuytren's disease diagnosis was based on clinical signs. Diagnostic criteria for Dupuytren's disease were thickening of the palmar fascia and/or flexion contracture in the phalanx of the hand. Physical examinations were performed by an orthopedic surgeon with more than 13 years of experience, whose subspecialty was hand surgery. Meyerding's classification was used to assess the Dupuytren's disease severity [12]. It was graded into five stages: stage 0, at which there were only palpable nodules in the palm and no flexion contracture of digits; stage 1, with only one digit exhibiting flexion contracture; stage 2, with plural digits with flexion contracture and less than 60° total contracture of the metacarpo-phalangeal and interphalangeal joint; stage 3, with 60° or greater contractures of digits; and stage 4, with all digits with flexion contracture, except for the thumb. We investigated Dupuytren's diathesis (plantar aponeurosis fibrosis, Peyronie's disease, knuckle pads) of all patients. Moreover, we checked up the medical history of those in whom Dupuytren's disease was found. Thereby, we verified the history of their parents or distant relatives and their history of immigration from Europe.

We examined their background data and physical examinations related to Dupuytren's disease and evaluated the association between the prevalence of Dupuytren's disease and background factors and assessed Health-related QOL in people with Dupuytren's disease.

Statistical analysis

Univariate analysis with age adjustment was used to evaluate statistical significance. Spearman's correlation

Table 1 Prevalence of Dupuytren's disease for each by gender and generation

	Men			Women			Total Prevalence (%)
	Total examined number	Dupuytren's disease (+) number	Prevalence (%)	Total examined number	Dupuytren's disease (+) number	Prevalence (%)	
Age							
40–49	11	0	0	20	0	0	0
50–59	26	2	7.7	43	2	4.7	5.8
60–69	52	5	9.6	59	2	3.4	6.3
70–79	53	10	18.9	91	2	2.2	8.3
≥80	22	2	9.1	25	3	12	10.6
All ages	163	19	11.7	238	9	3.8	7

coefficient by rank testing was used to correlate the grade of Meyerding's classification in the participants with Dupuytren's disease. The EQ-5D-3L score and EQ-VAS were useful in evaluating health-related QOL. Mann–Whitney U tests were used to compare the EQ-5D-3L score and EQ-VAS among participants with Dupuytren's disease and participants without this disease. Multivariate logistic regression was used in the analysis of personal risk factors for Dupuytren's disease in this general population, using the following factors as explanatory variables: age, gender, occupation, history of diabetes mellitus, and alcohol consumption. A p value of <0.05 was regarded as statistically significant. This study was approved by the regional ethics board. Informed consent was obtained from all participants.

Results

Among the 401 individuals, Dupuytren's disease was found in the hands of 19 men and 9 women; the disease prevalence was 7.0 %. Both hands were affected in seven cases (25 %). Plural digits were affected in four cases (14.3 %). Dupuytren's disease was detected in 39 finger rays. The ring finger ray was affected with the highest frequency (79.7 %). There were 25 cases (89.3 %) of nodules without finger contracture (stage 0). One digit with flexion contracture (stage 2) was found in three cases (10.7 %). No association was found between the dominant hand and the affected side ($p = 0.13$). The average age of subjects with Dupuytren's disease was 66.7 years. The prevalence of the disease increased with age: it was highest in subjects older than 80 years (7/47 subjects, 10.6 %). The prevalence of Dupuytren's disease was significantly higher among men than among women in univariate analysis [$p = 0.0037$, OR 3.99, 95 % confidence interval (CI) 1.48–7.76] and in age-adjusted analysis ($p = 0.0045$, OR 3.30 95 % CI 1.45–7.52). Among Dupuytren's patients, no information indicated a relation to medical history affected by Dupuytren's disease of their parents or distant relatives or a history of immigration from Europe. No patient was complicated by plantar aponeurosis fibrosis or Peyronie's disease, knuckle pads. Weight, height, body mass index, and blood pressure were not statistically associated with Dupuytren's disease (Table 2).

Significant association was found between diabetes mellitus and Dupuytren's disease in univariate analysis ($p = 0.04$, OR 3.03, 95 % CI 1.06–8.64) (Table 2). However, no association was found between diabetes mellitus and the disease after adjustment for age ($p = 0.13$, OR 2.41, 95 % CI 0.77–7.56). The value of HbA1c was not associated significantly with Dupuytren's disease (Table 3).

No significant difference in the prevalence of Dupuytren's disease was found between smokers (ever smoked) and non-smokers in univariate analysis ($p = 0.5$, OR 0.79, 95 % CI 0.23–2.73), or with age-adjusted analysis ($p = 0.25$, OR 0.3, 95 % CI 0.04–2.34) (Table 2).

Alcohol intake was associated significantly with Dupuytren's disease in both univariate analysis ($p = 0.003$, OR 3.15, 95 % CI 1.44–6.87) and age-adjusted analysis ($p = 0.01$, OR 2.87, 95 % CI 1.27–6.48) (Table 2). However, regarding biochemical parameters, AST, ALT, LDL-

Table 2 Clinical status of study participants

Clinical status	Dupuytrer's disease (+) ($n = 28$)	Dupuytrer's disease (−) ($n = 373$)	Crude OR (95 % CI)	p value	Age-adjusted OR (95 % CI)	p value
Mean age (years)	70.8 (9.7)	66.4 (10.8)			1.04 (1.0013–1.08)	0.04*
Weight (kg)	60.2 (9.0)	58.0 (10.8)	1.02 (0.98–1.05)	0.3	1.03 (0.99–1.07)	0.14
Height (cm)	157.4 (10.2)	155.6 (9.1)	1.02 (0.98–1.06)	0.32	1.04 (0.99–1.09)	0.06
Body mass index	24.1 (1.8)	23.8 (1.3)	1.03 (0.92–1.16)	0.63	1.02 (0.91–1.15)	0.7
Systolic blood pressure (mmHg)	136.7 (13)	133.0 (15.2)	1.02 (0.99–1.04)	0.21	1.01 (0.99–1.04)	0.42
Diastolic blood pressure (mmHg)	79.1 (9.7)	80.8 (9.2)	0.98 (0.94–1.02)	0.35	0.98 (0.94–1.03)	0.41
Diabetes mellitus (%)	17.9	6.7	3.03 (1.06-8.64)	0.04*	2.41 (0.77-7.56)	0.13
Smoking (current and former) (%)	10.7	13.1	0.79 (0.23–2.73)	0.5	1.01 (0.29–3.56)	0.98
Alcohol (current and former) (%)	57.1	34	3.15 (1.44–6.87)	0.003*	2.87 (1.27–6.48)	0.01*

Mean values are shown with the standard deviation in parentheses. Odds ratios were calculated using univariate and age-adjusted analysis. A one-unit change in the explanation variable increases the odds of having Dupuytren's disease by a factor of odds ratio

CI confidence interval, *OR* odds ratio

* $p < 0.05$

Table 3 Serum biochemical markers of study participants

Biochemical markers	Dupuytren's disease (+) ($n = 28$)	Dupuytren's disease (−) ($n = 373$)	Odds ratio (95 % CI)	p value
Hemoglobin A1c (%)	5.35 (1.05)	5.21 (0.68)	1.24 (0.88–1.88)	0.31
Asparate aminotransferase (IU/1)	26.0 (8.5)	25.3 (11.4)	1.0049 (0.9975–1.0038)	0.74
Alanine aminotransferase (IU/1)	19.4 (9.3)	19.6 (12.5)	0.99 (0.97–1.03)	0.91
γ-glutamyltranspeptidase (IU/dl)	40.1 (35.9)	30.8 (35.8)	1.0043 (0.9974–1.0112)	0.22
Low-density lipoprotein-cholesterol (mg/dl)	121 (39.1)	123.0 (31.3)	0.9986 (0.9865–1.0108)	0.82
High-density lipoprotein-cholesterol (mg/dl)	63.4 (14.0)	64.5 (14.6)	0.9945 (0.9681–1.0217)	0.69
Triglyceride (mg/dl)	138.2 (85.7)	125.6 (74.6)	1.0091 (0.9975–1.0063)	0.39

Mean values are shown with the standard deviation in parentheses. Odds ratios were calculated using univariate analysis. A one-unit change in the explanation variable increases the odds of having Dupuytren's disease by a factor of odds ratio

CI confidence interval

Table 4 Comparison of occupational categories

Occupation	Dupuytren's disease (+) ($n = 28$)	Dupuytren's disease (−) ($n = 373$)	Crude OR (95 % CI)	p value	Age-adjusted OR (95 % CI)	p value
Housework	1	71	1		1	
Tertiary sector of industry	10	136	5.22 (0.66–41.6)	0.08	4.57 (0.57–36.7)	0.15
Farmer	13	150	6.15 (0.79–48.0)	0.12	5.07 (0.64–40.0)	0.12
Manual labor	3	12	16.4 (1.58–170)	0.02*	13.8 (1.31–146.0)	0.03*
Factory worker	1	4	23.7 (1.17–476.7)	0.04*	20.3 (0.99–419.1)	0.051

Odds ratios were calculated with univariate and age-adjusted analysis

CI confidence interval, *OR* odds ratio

* $p < 0.05$

cholesterol, HDL-cholesterol and triglycerides were not related with Dupuytren's disease (Table 3). In terms of occupational category, manual workers in occupations such as carpentry, forestry worker, and factory workers were associated significantly with Dupuytren's disease in univariate analysis (manual workers; $p = 0.02$, OR 16.4, 95 % CI 1.58–170, factory workers; $p = 0.04$, OR 23.7, 95 % CI 1.17–476.7). In age-adjusted analysis, manual workers were associated significantly with Dupuytren's disease ($p = 0.03$, OR 13.8, 95 % CI 1.31–146) (Table 4).

The median (the first and third quartile) of the EQ-5D-3L single index and VAS was 0.80 (0.79, 1.00) and 70.0 (51.5, 81.5) in participants with Dupuytren's disease. No significant difference was found between participants with Dupuytren's disease and those without this disease in the EQ-5D-3L single index and VAS (Table 5). The EQ-5D-3L single index was positively correlated with VAS in participants with the disease ($p = 0.02$, $r = 0.44$). The EQ-5D-3L single index and VAS were not correlated with the grade of Meyerding's classification in participants with the disease (EQ-5D-3L, $p = 0.33$, $r = 0.19$; VAS, $p = 0.07$, $r = 0.34$).

Discussion

This cross-sectional study revealed that 7.0 % of 401 subjects had Dupuytren's disease among the general population residing in a mountain village in Japan. Our result was lower than that found for European countries [1–3]. McFarlane reported that the origin and spread of Dupuytren's disease was presumably from Northern Europe and that the Dupuytren's disease gene might have spread with its migrating population [13]. However, no information was found to suggest a relation to the medical history of Dupuytren's disease and a history of immigration from Europe among the parents and distant relatives of the participants with the disease in this study. Cases with Dupuytren's disease found in this study might also have been affected by environmental factors.

Results show that 16.7 % of male participants and 3.8 % of women were affected by Dupuytren's disease. The prevalence of Dupuytren's disease was significantly higher among men than among women. Pagnotta et al. [14] reported that cells from Dupuytren's disease patients had a higher expression of androgen receptors, and that, when

Table 5 EuroQOL index score and VAS of study participants

	Dupuytren's disease (+) ($n = 28$)	Dupuytren's disease (−) ($n = 373$)	p value
EuroQOL index score	0.80 (0.79, 1.00)	0.80 (0.79, 1.00)	0.63
EuroQOL VAS	70.0 (51.5, 81.5)	70.0 (50.0, 81.0)	0.43

Values are shown as median (the first and third quartile)

stimulated with 5α-dihydrotestosterone, they showed higher rates of myofibroblast proliferation. Androgen function might account for the male prevalence of Dupuytren's disease development. Dupuytren's disease was more common among older people than young people. Egawa et al. reported a 14 % incidence rate in elderly men and 8 % in elderly women who were Japanese nursing home residents. That result appears to be significantly higher than among other Asian people [8]. Gudmundsson et al. [1] reported that the prevalence of the condition increased with age. In this study, logistic regression analysis results also revealed a significant association between Dupuytren's disease and age. We sought to investigate the age onset of Dupuytren's disease for participants of our study but we were unable to obtain data because many participants had no memory of the onset. Properly speaking, the age of onset of this disease should be investigated to elucidate the disease etiology.

This study found no association with the dominant hand and the affected side in participants with Dupuytren's disease. Nevertheless, it is conceivable that the dominant hand is closely linked with frequency of use in manual work. Reportedly, high cumulative work exposure is associated with Dupuytren's disease [6]. Gudmundsson et al. found that Dupuytren's disease was common among manual laborers. It was almost 3 times more common among manual laborers than those with occupations demanding higher education [1]. Furthermore, Descatha et al. [15] found that occupational exposure including both vibration exposure and heavy manual work without significant vibration exposure was associated with Dupuytren's disease. We found a highly significant association between Dupuytren's disease and manual workers such as those who worked in carpentry and forestry. Vibrating tools are often used in such work. Our results support the relation between vibration exposure and Dupuytren's disease. However, we were unable to investigate the work careers and related information of manual laborers among the participants of this study. Further research must be undertaken to clarify the relation with the dominant hand, working conditions, and Dupuytren's disease.

Diabetes mellitus was significantly more common among participants with Dupuytren's disease than among participants without this disease, but no association between Dupuytren's disease and diabetes mellitus was found using aged-adjusted analysis. In our study, the serum level of HbA1c was measured to evaluate the average glucose level condition. No significant difference in the serum level of HbA1c was found among participants with Dupuytren's disease and participants without this disease. This result might reflect the influence of conditions of people undergoing medical treatment for diabetes mellitus. Geoghegan et al. [16] reported diabetes mellitus as a significant risk factor, particularly insulin-controlled diabetes mellitus. Fifty percent of participants with diabetes mellitus (20 % participants with Dupuytren's disease and 60 % participants without Dupuytren's disease) were medicated in this study. However, no significant difference was found in the prevalence of Dupuytren's disease between medicated patients with diabetes mellitus and non-medicated patients with diabetes mellitus in our study ($p = 0.16$). Shaw et al. [17] reported that diabetes mellitus might trigger the onset of Dupuytren's disease, and it might be true that microvascular change encourages local hypoxia, which can provoke Dupuytren's disease.

It has been suggested that high values of cholesterol and triglycerides are related to Dupuytren's disease [7]. Hypercholesterolemia and hyperlipidemia cause arteriosclerosis, inducing microvascular changes that might trigger the onset of Dupuytren's disease. Our study revealed no association of this disease with the serum level of LDL-cholesterol, HDL-cholesterol, or triglycerides. We evaluated the relation with Dupuytren's disease and hypertension as a degenerative disease related to arteriosclerosis. However, no correlation was found with these diseases, as reported also in results of another study [1].

We found a significant association between Dupuytren's disease and drinking in both univariate and age-adjusted analysis. Godtfredsen et al. [5] found alcohol to be a strong independent risk factor for development of Dupuytren's disease. In addition, Bertrand et al. [18] reported that incidence among a group of alcoholic people with liver disease was higher than among controls, but Dupuytren's disease was not found to be associated with liver disease in another study [19]. Pan et al. [20] reported that alcohol might damage liver tissue, thereby provoking a fibrotic response. We checked the serum concentrations of ALT, AST, and γ-GTP to evaluate the liver function of the study participants. Results show that Dupuytren's disease was not significantly related with the serum level of ALT, AST, or γ-GTP. Future research should be undertaken to investigate the mechanism between Dupuytren's disease and alcohol.

Several reports have described that smoking is significantly associated with Dupuytren's disease and that it might be related to microvascular changes with hypoxic

conditions [5]. Godtfredsen et al. [5] reported that prevalence of Dupuytren's disease was higher in relation to smoking frequency. However, no significant relation was found between smoking and Dupuytren's disease in our study. Dupuytren's disease might be related to other factors related to blood flow aside from smoking, such as cold stimulation.

A few reported studies have examined QOL in patients with Dupuytren's disease. Trybus et al. [21] reported the Dupuytren Disease Scale of Subjective Wellbeing of Patients, a 12-item questionnaire covering four subscales consisting of self-esteem, family life, occupational life, and social life to evaluate QOL of the patients with Dupuytren's disease. We used the EQ-5D to assess and compare QOL between the patients with Dupuytren's disease and the subjects without the disorder. The EQ-5D is a non-disease specific instrument for evaluating health-related QOL. In the EQ-5D-3L index score and VAS, no significant difference was found between Dupuytren's disease patients and participants without Dupuytren's disease. Furthermore, no correlation was found with the EQ-5D-3L index score and VAS and grade of Meyerding's classification in Dupuytren's disease patients. The result might reflect the reason why 89.2 % (25/28) of the patients fell out of grade 0 of Meyerding's classification. Only palpable nodules in the palm without flexion contracture of digits might not degrade ADL and QOL in patients with Dupuytren's disease. However, responsiveness of the EQ-5D-3L has not been evaluated for patients with Dupuytren's disease. Responsiveness is related to an instrument's ability to capture clinically important change [22]. Further work is necessary to compare the EQ-5D-3L to other patient-related outcome measures and to evaluate responsiveness of the EQ-5D-3L for patients with Dupuytren's disease. Valid reproducible, responsive Dupuytren's disease-specific measures should be developed.

In conclusion, this cross-sectional study showed that 7.0 % of 401 subjects in the general population residing in a mountain village in Japan had Dupuytren's disease. Dupuytren's disease is less common in Japan than in northern European countries. The prevalence is higher with age and is apparently associated with male gender, occupations such as carpentry and forestry, and alcohol intake. The risk factors involved in the presence of Dupuytren's disease were identified as age, occupations such as carpentry and forestry, and alcohol intake. Our report described a small subpopulation in a limited area in Japan. More consideration of whether the EQ-5D-3L is the most sensitive and relevant self-reported outcome measure in Dupuytren's disease patients will be required. Additional large-scale research is necessary to assess the incidence data in order to confirm the relationships between exposures and Dupuytren's disease and to evaluate health-related QOL in people with Dupuytren's disease.

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Conflict of interest The authors declare that they have no conflict of interest.

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