Low serum albumin, aspartate aminotransferase, and body mass are risk factors for frailty in elderly people with diabetes: possible mechanistic role of dehydroepiandrosterone sulfate – a cross-sectional study

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Abstract

Background: Relatively low dehydroepiandrosterone sulfate (DHEA-S) and high cortisol/DHEA ratio have been suggested to be associated with frailty, evaluated using a physical scale. However, the significance of these two hormones for frailty in elderly patients with type 2 diabetes mellitus (T2DM) has not been assessed using a wider range of measures of frailty, including physical, mental, and social indices.

Methods: We performed a cross-sectional study to investigate the significance of these two hormones for frailty in elderly T2DM patients (n=148; ≥65 years), using a broad assessment, the clinical frailty scale, and to reevaluate the risk factors for frailty in elderly T2DM patients. We compared parameters between the non-frail and frail groups using the unpaired t and Mann-Whitney U tests. The Jonckheere-Therpstra test was used to identify relationships with the severity of frailty and risk factors were identified using binary regression analysis.

Results: Simple regression analysis identified a number of significant risk factors for frailty, including DHEAS <70 μg/dL and cortisol/DHEA-S ratio ≥0.2. Multiple regression analysis showed that low albumin (<4.0 g/dl) (odds ratio [OR]=5.79, p <0.001), low aspartate aminotransferase (AST) activity (<25 IU/L) (OR=4.34, p =0.009), and low body mass (BM) (<53 kg) (OR=3.85, p =0.012) were independent risk factors for frailty. A significant decrease in DHEA-S and a significant increase in the cortisol/DHEA-S ratio occurred alongside increases in the severity of frailty. DHEA-S concentration positively correlated with both serum albumin and BM.

Conclusions: Hypoalbuminemia, low AST, and low BM are independent risk factors for frailty in elderly T2DM patients, strongly implying relative malnutrition in these frail patients. DHEA-S may be important for the maintenance of liver function and BM. A decrease in DHEA-S and an increase in the cortisol/DHEAS ratio may be involved in the mechanism of the effect of malnutrition in elderly T2DM patients.

Introduction

In Japan both men and women have long life expectancies. The aging population of Japan includes 10 million people with diabetes, and 50% of diabetes patients are elderly. Furthermore, it is predicted that the proportion of diabetes patients that are elderly will increase further in the future. Elderly people also frequently develop a geriatric syndrome that includes frailty. Frailty is a state of vulnerability and a consequence of cumulative decline in multiple physiologic systems over a lifespan, and is associated with a number of adverse outcomes, including falls, disability, hospitalization, care home admission, and mortality [1,2]. Therefore, interventions are important for the achievement of optimal life expectancy. However, the risk factors for frailty have not been fully characterized.

The Clinical Frailty Scale (CFS) is thought be the most suitable index for the quantification of frailty in elderly people, because it includes physical, mental, and social scales [3]. We have previously shown, on basis of a diagnosis of frailty made using the CFS, that 42% of 132 elderly patients with type 2 diabetes

(T2DM) were frail, and that aging and low circulating concentrations of albumin, high-density lipoprotein-cholesterol (HDL-C), systolic blood pressure (SBP), HbAlc, and total cholesterol were risk factors for frailty [4, 5]. Thus, the traditional risk factors for metabolic syndrome and/or cardiovascular disease in middle-aged people may shift from being deleterious to beneficial in old age. This shift, which is associated with malnutrition and chronic inflammation in elderly people, has been termed “reverse metabolism” [6, 7].

Sarcopenia is considered to be a risk factor for frailty in elderly people, and in our previous study of 108 T2DM patients of more than 65 years of age, we found that 35% had sarcopenia [8]. Serum DHEA-S increases adrenarche, peaks in a person’s 20 s, and then decreases linearly with age to a concentration 10–20% of that of a young person [9, 10], suggesting that there might be an association between DHEA-S and the geriatric syndrome that includes sarcopenia and frailty. In our previous study, the elderly T2DM patients with sarcopenia had high serum cortisol concentrations and very low serum DHEA-S concentrations, presumably reflecting chronic stress. Furthermore, we showed that a cortisol/DHEA-S ratio of ≥ 0.2 is the strongest independent risk factor for sarcopenia [8].

In a cross-sectional study (mean age ± SD : 84.9 ± 9.6 years [11], 74.6 ± 7.7 years [12]) and a longitudinal study [13, 14, 15] (mean age ± SD at the start of study: 66.9 ± 2.2 years [13], 59 ± 11 years [14]) that used Fried’s method[2], which only involves assessment of the physical characteristics of the frailty, it was found that elderly people with relatively high DHEA-S have a relatively low risk of frailty. It has also been reported that elderly people classified as frail on the basis of the Fried method have high cortisol/DHEA-S ratios [13]. However, a broader assessment of frailty, like the CFS, has not been used to assess the roles of cortisol and DHEA-S in the frail elderly.

In our previous study of frailty in elderly T2DM patients [4], the roles of cortisol and DHEA-S were not investigated. Therefore, we performed the present study to determine the significance of these hormones for frailty in elderly T2DM patients, using the CFS. In addition, we aimed to re-evaluate the risk factors for frailty in elderly T2DM patients.

Materials And Methods

Participants

We retrospectively reviewed the data from 148 consecutive elderly T2DM patients aged more than 65 years (63 men and 85 women; 65–95 years) who were being treated as outpatients or were hospitalized at Muta Hospital between October 2016 and September 2017. Patients taking glucocorticoids orally or by inhalation were excluded, because glucocorticoid administration affects the serum concentrations of cortisol and DHEA-S. None of the included patients was taking drugs to treat mental illness or was affected by alcoholism. T2DM was diagnosed using the criteria proposed by the Japan Diabetes Society [16] or because of a history of administering insulin or oral hypoglycemic agents. Data regarding age, blood test results, general physical assessments, and medication were obtained from

the patients' medical records. The duration of T2DM was recorded as the time from the initial identification of hyperglycemia. This study was approved by the Institutional Ethics Committee (29 – 0001, May 15, 2017) and registered with UMIN (number 000031357).

Hematology and hormone measurements

Blood samples were obtained in the morning between 0900 and 1200 h and used to measure HbA1c, red blood cell count (RBC), hemoglobin concentration (Hb), serum albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, uric acid, HDL-C, low-density lipoprotein-cholesterol (LDL-C), triglycerides, and corrected calcium. The estimated glomerular filtration rate (eGFR) was calculated using the serum creatinine concentration. We also collected height, body mass (BM), and body mass index (BMI) data. BMI was calculated as the BM in kilograms divided by the height in meters, squared. SBP and diastolic blood pressure (DBP) were measured using a mercury sphygmomanometer, with the patient at rest and in a sitting position. Serum cortisol concentration was measured using a chemiluminescence enzyme immunoassay kit [17] (Abbott Japan, Tokyo, Japan). Serum DHEA-S concentration was measured by chemiluminescence enzyme immunoassay using an Access DHEA-S kit [18] (Beckman Coulter, Tokyo, Japan). The detection limits for cortisol and DHEA-S were 0.8 μg/dL and 2.0 μg/dL, respectively. The intra-assay coefficients of variance for cortisol and DHEA-S were both 10%. The cortisol (μg/dL)/ DHEA-S (μg/dL) ratio was then calculated.

Evaluation of frailty

The CFS [3] was used to evaluate frailty, as previously described [4,8]. The CFS consists of nine stages (1, very fit; 2, well; 3, managing; 4, vulnerable; 5, mildly frail; 6, moderately frail; 7, severely frail; 8, very severely frail; and 9, terminally ill). Patients classified with CFS grades 1 to 4 are defined as not being frail, because they can live independently, whereas patients with CFS grades 5 to 9 are defined as frail, because they require assistance with daily activities. The CFS grades of the participants ranged from 1 to 7, with 18 having CFS1, 17 having CFS2, 27 having CFS3, 29 having CFS4, 15 having CFS5, 28 having CFS6, and 14 having CFS7.

Statistical analysis

Comparison of the non-frail and frail groups were made using the unpaired t-test and the Mann-Whitney U test. The Jonckheere-Therpstra test was used to determine the relationships of other parameters with the severity of frailty. The risk factors for frailty were identified using binary regression analysis, odds ratios (ORs), simple regression analysis, and multiple binary regression analysis. Receiver operating characteristic (ROC) analysis was performed and appropriate cut-off value were estimated for each risk factor. A p-value < 0.05 was considered significant.

Results

Of the 148 elderly T2DM patients, 57 were frail (38.5%; 20 men and 37 women; CFS 5–7) and 91 (43 men and 48 women; CFS 1–4) were not frail.

Table 1 shows a comparison of the characteristics of the frail and non-frail elderly T2DM patients. Compared with the non-frail group, the frail group was significantly older ($p < 0.001$) and had lower BM ($p < 0.001$), BMI ($p = 0.029$), SBP ($p = 0.013$), DBP ($p = 0.047$), RBC ($p = 0.005$), Hb ($p = 0.001$), albumin (Alb) ($p < 0.001$), AST ($p = 0.047$), ALT ($p = 0.017$), eGFR ($p = 0.007$), HDL-C ($p = 0.002$), and Calcium ($p = 0.011$). Furthermore, compared with the non-frail group, the frail group had a significantly lower serum concentration of DHEA-S ($p = 0.002$) and significantly higher serum cortisol concentration ($p = 0.022$). As a result, the cortisol/DHEA-S ratio was significantly higher in the frail group than the non-frail group ($p < 0.001$).

Table 1

Characteristics of the elderly patients with diabetes, categorized according to frailty status

	All cases N = 148	Non Frailty N = 91	Frailty * N = 57	P values
Age, years	76.9 ± 7.4	75.1 ± 6.8	79.8 ± 7.5	< 0.001 [1)]
Male, n (%)	63 (42.6)	43 (47.3)	20 (35.1)	0.173 [2)]
Body mass, kg	57.4 ± 11.1	61.8 ± 9.6	49.1 ± 8.5	< 0.001 [1)]
BMI, kg/m^2	23.2 ± 3.7	23.7 ± 3.5	22.3 ± 3.8	0.029 [1)]
SBP, mmHg	135.5 ± 19.0	138.5 ± 18.8	130.6 ± 18.4	0.013 [1)]
DBP, mmHg	72.4 ± 12.1	74.0 ± 12.2	69.9 ± 11.6	0.047 [1)]
RBC, ×10^4/∝L	413 ± 58	424 ± 55	396 ± 59	0.005 [1)]
Hemoglobin, g/dL	12.7 ± 1.7	13.1 ± 1.7	12.1 ± 1.6	0.001 [1)]
Albumin, g/dL	3.95 ± 0.51	4.15 ± 0.32	3.63 ± 0.60	< 0.001 [1)]
AST, IU/L	25.3 ± 10.7	26.7 ± 10.9	23.1 ±10.3	0.047 [1)]
ALT, IU/L	16.5 [12.0-25.3]	19.0 [13.0–27.0]	15.0 [10.0–22.0]	0.017 [3)]
HbA_{1c}, %	6.92 ± 0.84	6.99 ± 0.79	6.80 ± 0.90	0.171 [1)]
S-Creatinine, mg/dL	0.70 [0.60-1.00]	0.70 [0.60–0.90]	0.80 [0.60–1.10]	0.125 [3)]
eGFR, mL/min/1.73 m^2	59.5 [40.0-73.4]	65.4 [52.3–74.4]	54.9 [38.4–69.1]	0.007 [3)]
Uric acid, mg/dL	5.16 ± 1.43	5.06 ± 1.33	5.33 ± 1.57	0.265 [1)]
Triglycerides, mg/dL	140 ± 77	139 ± 74	141 ± 82	0.911 [1)]
LDL-C, mg/dL	101 ± 31	102 ± 31	99 ± 31	0.623 [1)]
HDL-C, mg/dL	53.2 ± 14.3	56.0 ± 14.3	48.6 ± 13.4	0.002 [1)]

Data are expressed as means ± SD or medians [25–75% values] or numbers (%).

* Frailty was defined using the clinical frailty score (≥5). P values were determined using [1)] the unpaired t-test, [2)] Fisher's exact test [3)] Mann-Whitney test. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; DHEA-S, dehydroepiandrosterone sulfate; HT; hypertension; DL, dyslipidemia.

	All cases N = 148	Non Frailty N = 91	Frailty * N = 57	P values
Calcium, mg/dL	9.35 ± 0.49	9.27 ± 0.36	9.48 ± 0.63	0.011 [1)]
DHEA-S, ∝g/dL	57.5 [39.0–89.0]	66.0 [44.5–106.0]	48.0 [33.0–68.0]	0.002 [3)]
Cortisol, ∝g/dL	9.50 ± 2.79	9.09 ± 2.77	10.16 ± 2.71	0.022 [1)]
Ratio Cortisol/ DHEA-S	0.16 [0.10–0.25]	0.13 [0.09–0.22]	0.20 [0.14–0.34]	< 0.001 [3)]
Anti-HT drug use, n (%)	87 (58.8)	51 (56.0)	36 (63.2)	0.493 [2)]
Anti-DL drug use, n (%)	72 (48.6)	44 (48.4)	28 (49.1)	0.999 [2)]
Data are expressed as means ± SD or medians [25–75% values] or numbers (%).				
* Frailty was defined using the clinical frailty score (≥5). P values were determined using [1)] the unpaired t-test, [2)] Fisher's exact test [3)] Mann-Whitney test. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; DHEA-S, dehydroepiandrosterone sulfate; HT; hypertension; DL, dyslipidemia.				

To clarify the risk factors for frailty, simple regression analysis and multiple regression analysis using binary logistic regression were performed and ORs were calculated (Table 2). Simple regression analysis revealed that the significant risk factors for frailty were age ≥75 years ($p = 0.005$), BM < 53 kg ($p = 0.002$), RBC < 400×10^4/μL ($p = 0.037$), Hb < 13 g/dL ($p = 0.003$), Alb < 4.0 g/dL ($p < 0.001$), AST activity < 25 IU/L ($p = 0.016$), eGFR < 60 ml/min/1.73 m^2 ($p = 0.002$), HDL-C < 40 mg/dL ($p = 0.005$), DHEA-S < 70 μg/dL ($p = 0.007$), and cortisol/DHEAS ratio ≥0.2 ($p = 0.008$). Multiple regression analysis showed that low Alb (< 4.0 g/dL) (OR = 5.79, $p < 0.001$), low AST activity (< 25 IU/L) (OR = 4.34, $p = 0.009$), and low BM (< 53 kg) (OR = 3.85, $p = 0.012$) were independent risk factors for frailty.

Table 2

Risk factors for frailty, determined using binary logistic regression analysis

Variables	Before adjustment		After adjustment	
	OR (95%CI)	P values	OR (95%CI)	P values
Age ≥75 years	2.74 (1.35–5.56)	0.005	0.97 (0.36–2.63)	0.956
Body mass < 53 kg	3.03 (1.52–6.05)	0.002	3.85 (1.35–10.99)	0.012
SBP ≥135 mmHg	0.69 (0.35–1.34)	0.270	0.56 (0.23–1.32)	0.184
RBC < 400×10^4/∝L	2.06 (1.04–4.08)	0.037	0.28 (0.08–1.03)	0.055
Hemoglobin < 13 g/dL*	2.87 (1.42–5.79)	0.003	2.72 (0.76–9.67)	0.122
Albumin < 4.0 g/dL *	6.50 (3.10-13.59)	< 0.001	5.79 (2.20-15.26)	<0.001
AST < 25 IU/L *	2.40 (1.18–4.88)	0.016	4.34 (1.43–13.17)	0.009
ALT < 22 IU/L *	1.46 (0.71–2.99)	0.304	0.38 (0.12–1.27)	0.188
eGFR < 60 mL/min/1.73 m^2	5.06 (1.83–13.98)	0.002	2.92 (0.83–10.27)	0.094
HDL-C < 40 mg/dL	3.44 (1.45–8.20)	0.005	0.97 (0.86–8.83)	0.089
Calcium ≥9.4 mg/dL *	1.25 (0.64–2.45)	0.515	1.00 (0.41–2.45)	0.996
DHEA-S < 70 ∝g/dL *	2.78 (1.33–5.71)	0.007	2.19 (0.91–5.22)	0.081
Cortisol ≥9.5 ∝g/dL *	1.75 (0.90–3.42)	0.100	1.75 (0.90–3.42)	0.100
Ratio Cortisol / DHEA-S ≥0.2	2.55 (1.27–5.10)	0.008	Not apply	

The chi-square value was 9.917 for the Hosmer-Lemeshow test (p = 0.271). * The mean value was used. OR, odds ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein-cholesterol; DHEA-S, dehydroepiandrosterone sulfate.

Next, ROC analysis was performed to determine appropriate cut-off values for the prediction of frailty (Table 3). The cut-off values calculated were 4.0 g/dL for Alb, 0.15 for cortisol/DHEA-S, 57 μg/dL for DHEA-S, 53 kg for BM, and 20 IU/L for AST. The AUC was highest for Alb (0.787), followed by cortisol/DHEA-S ratio (0.697), DHEA-S (0.653), BM (0.645), and AST (0.634).

Table 3
AUC for each predictor, determined using ROCs

Predictors	Cut-off values	AUC (95%CI)	P values
Body mass	53 kg	0.645 (0.549–0.741)	0.003
Albumin	4.0 g/dL	0.787 (0.710–0.864)	< 0.001
AST	20 IU/L	0.634 (0.541–0.728)	0.006
Ratio Cortisol / DHEA-S	0.15	0.697 (0.611–0.782)	< 0.001
DHEA-S	57 ∝g/dL	0.653 (0.584–0.741)	0.002

AUC, area under the curve; ROC, receiver-operating characteristic; CI, confidence interval; DHEA-S, dehydroepiandrosterone sulfate.

The relationships between these predictive variables and the CFS are shown in Fig. 1. Significant reductions in Alb ($p < 0.001$) and DHEA-S ($p < 0.001$); and increases in age ($p < 0.001$), cortisol ($p < 0.001$), and cortisol/DHEA-S ratio ($p < 0.001$) occurred alongside an increase in the severity of frailty. In addition, BM was significantly decreased with an increase in the severity of CFS (Fig. l).

We also analyzed the relationships of serum log DHEA-S and cortisol concentrations with age, serum Alb and BM (Fig. 2). Serum log DHEA-S significantly decreased ($r = -0.216$, $p = 0.008$) and serum cortisol concentration significantly increased ($r = 0.194$, $p = 0.018$) with age. Serum Alb concentration significantly positively correlated with serum DHEA-S ($r = 0.240$, $p = 0.003$), but did not correlate with serum cortisol concentration (data not shown). BM significantly positively correlated with serum log DHEA-S ($r = 0.230$, $p = 0.005$) and significantly negatively correlated with serum cortisol ($r = -0.330$, $p < 0.001$).

Discussion

In the present study, we have identified independent risk factors for frailty, defined using the CFS, in 148 elderly T2DM patients, using multiple logistic regression analysis. These were serum Alb < 4.0 g/dl ($p < 0.001$), AST activity < 25 IU/L ($p = 0.009$), and BM < 53 kg ($p = 0.012$). In our previous study of 132 elderly T2DM patients, multiple regression analysis revealed that advanced age, and low albumin, HDL-C, SBP, HbA1c, and BM were risk factors for frailty, quantified using CFS, of which albumin was the most potent [4].

Low albumin was also identified to be the most potent risk factor for frailty in the present study. Therefore, we recommended that the serum albumin concentration of elderly people is maintained at ≥ 4.0 g/dL to prevent frailty. In Japan, protein intake is low in the elderly, which is likely to cause frailty. Furthermore, mortality in hospitalized patients is associated with hypoalbuminemia, and hypoalbuminemia has been shown to increase mortality [19].

In the present study, low Alb concentration and BM were shown to be independent risk factors for frailty, as shown previously, but HDL-C, SBP, and HbA1c were not. This is probably because the participants and sample size differed from those in the previous study, even though there was an overlap in the participants in each study (the number were 74 of 148 cases). However, although the list of risk factors differed between the studies, the common factors suggest that malnutrition or a related condition may be the most important cause of frailty in elderly T2DM patients. Malnutrition may be a constitutional syndrome or may be the result of strict dietary control imposed by the individual or their doctor. However, a number of endocrine factors may also be involved in malnutrition [5], as discussed below.

Interestingly, in the present study, the ALT and AST activities were significantly lower in the frail group than in the non-frail group, and AST < 25 IU/L was shown to be an independent risk factor for frailty. Recently, low serum ALT activity has been shown to be associated with higher mortality, and higher prevalence of sarcopenia and frailty in the elderly [20, 21]. However, there is no explanation for these associations. Low serum ALT and AST activities occur secondary to low serum concentrations of vitamin B6, because AST, and especially ALT, require vitamin B6 as a cofactor [22]. Furthermore, vitamin B6 deficiency has been shown to be associated with low activity and low serum albumin in elderly nursing home residents [23]. Thus, one plausible explanation for the low transaminase activities in frail T2DM patients may be relative vitamin B6 deficiency, resulting from malnutrition.

Although serum cortisol, DHEA-S and cortisol/DHEA-S ratio were not found to be independent risk factors in the multiple regression analysis, there is evidence that they contribute to frailty in elderly T2DM patients. In the present study, while log serum DHEA-S decreased significantly with age, even in the range of 65–95 years old, serum cortisol increased significantly. Serum DHEAS < 70 μg/dL was found to be a risk factor for frailty in simple regression analysis, but no significant relationship was identified between serum cortisol and frailty. Serum cortisol significantly increased, while serum DHEA-S significantly decreased with increasing CFS, between grades 1 and 7. As a result, a cortisol/DHEAS ratio ≥0.2 was a significant risk factor for frailty in simple regression analysis. As for elderly T2DM patients with sarcopenia [8], frail T2DM patients are thought to be under stress. Whereas cortisol is as catabolic hormone, DHEA-S is anabolic and antagonizes cortisol. Therefore, the relative cortisol overactivity may disrupt homeostasis, resulting in frailty and sarcopenia.

Interestingly, serum albumin concentration positively correlated with serum DHEA-S concentration ($r = 0.240$), suggesting that DHEA-S may have an anabolic effect in the liver. DHEA has also been suggested to reduce urinary albumin excretion in the kidney [24], which may also contribute to the maintenance of the serum albumin concentration. A protective action of DHEA-S in the liver has been also suggested by other studies: the serum DHEA-S concentration is low in non-alcoholic fatty liver disease (NAFLD) [25, 26] and DHEA reduces liver fat deposition in obese (fa/fa) Zucker rats [27]. The underlying molecular mechanism for the protective effect of DHEA-S in liver may involve the induction of CYP4A, which removes harmful substances. Alternatively the dihydrotestosterone, ΔAdiol, and 3b-Adiol generated from DHEA-S may promote miR-21 production, leading to the proliferation of hepatocytes [28]. Therefore, it may be that the

low serum DHEA-S in frail T2DM patients identified in the present study may lead to an impairment in liver function, illustrated by the altered serum Alb concentration and transaminase activities.

As discussed above, BM < 53 kg ($p = 0.012$) was also identified to be an independent risk factor for frailty in the present study, and as the severity of frailty worsened (for CFS grades 1 to 7), BM decreased. Usually, adipose tissue and fat deposition are necessary for growth in adolescence [29, 30]. However, in middle age, metabolic syndrome is characterized by visceral fat deposition and an inverse relationship between DHEA-S concentration and BMI [31]. An anti-obesity effect of DHEA has been shown in both humans and animals [27, 32, 33], which involves the inhibition of 11β-hydroxysteroid dehydrogenase type 1 [34] and the activation of dual-specificity protein phosphatase [35], a target gene of DHEA [36]. Although the apparently paradoxical effect of DHEA in middle-aged and elderly people remain to be explained, DHEA-S is thought to play a role in maintaining homeostasis by controlling fat deposition, but in a manner that is dependent on life stage.

In conclusion, hypoalbuminemia, low AST activity, and low BM were found to be independent risk factors for frailty in elderly T2DM patients, strongly suggesting relative malnutrition in this group. In addition, DHEA-S may be important for the maintenance of liver function and BM. The reduction in DHEA-S and the increase in the cortisol/DHEAS ratio may be involved in the mechanism of the effects of malnutrition in elderly T2DM patients.

A List Of Abbreviations:

The Clinical Frailty Scale (CFS),type 2 diabetes (T2DM)high-density lipoprotein-cholesterol (HDL-C), systolic blood pressure (SBP), red blood cell count (RBC), hemoglobin concentration (Hb), aspartate aminotransferase (AST), alanine aminotransferase (ALT), low-density lipoprotein-cholesterol (LDL-C), estimated glomerular filtration rate (eGFR), body mass (BM), body mass index (BMI), diastolic blood pressure (DBP), odds ratios (ORs), receiver operating characteristic (ROC), albumin (Alb), non-alcoholic fatty liver disease (NAFLD)

Declarations

- Ethics approval and consent to participate

The research ethics committee of Muta Hospital approved the present study (date of approval: 15th May 2017, approval number: 29-001), and the study conformed to the Helsinki Declaration, as revised in 2013. The present study was also registered in the UMIN (ID: 000031357). We obtained informed consent by publishing an opt-out option on the homepage of Muta Hospital.

- Consent for publication

Not applicable

- Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

- Competing interests

The authors declare that they have no competing interests.

- Funding

There were no grants or fellowships.

- Authors' contributions

IY, YF, CI and MH analyzed and interpreted the patient data. IY was a major contributor in writing the manuscript. YK and MT became the conductor and TI, TE, NY, YK, MY and MH evaluated frailty of the patients. YT and HA collected and organized the patient data. SY, EA, TY, HN and KM interpreted the results and advised IY about how to compile this article. HN and TY have collaborated with each other to complete this work and to write manuscript. HN and TY have actual responsibilities for this manuscript.

All authors read and approved the final manuscript.

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Figures

Figure1

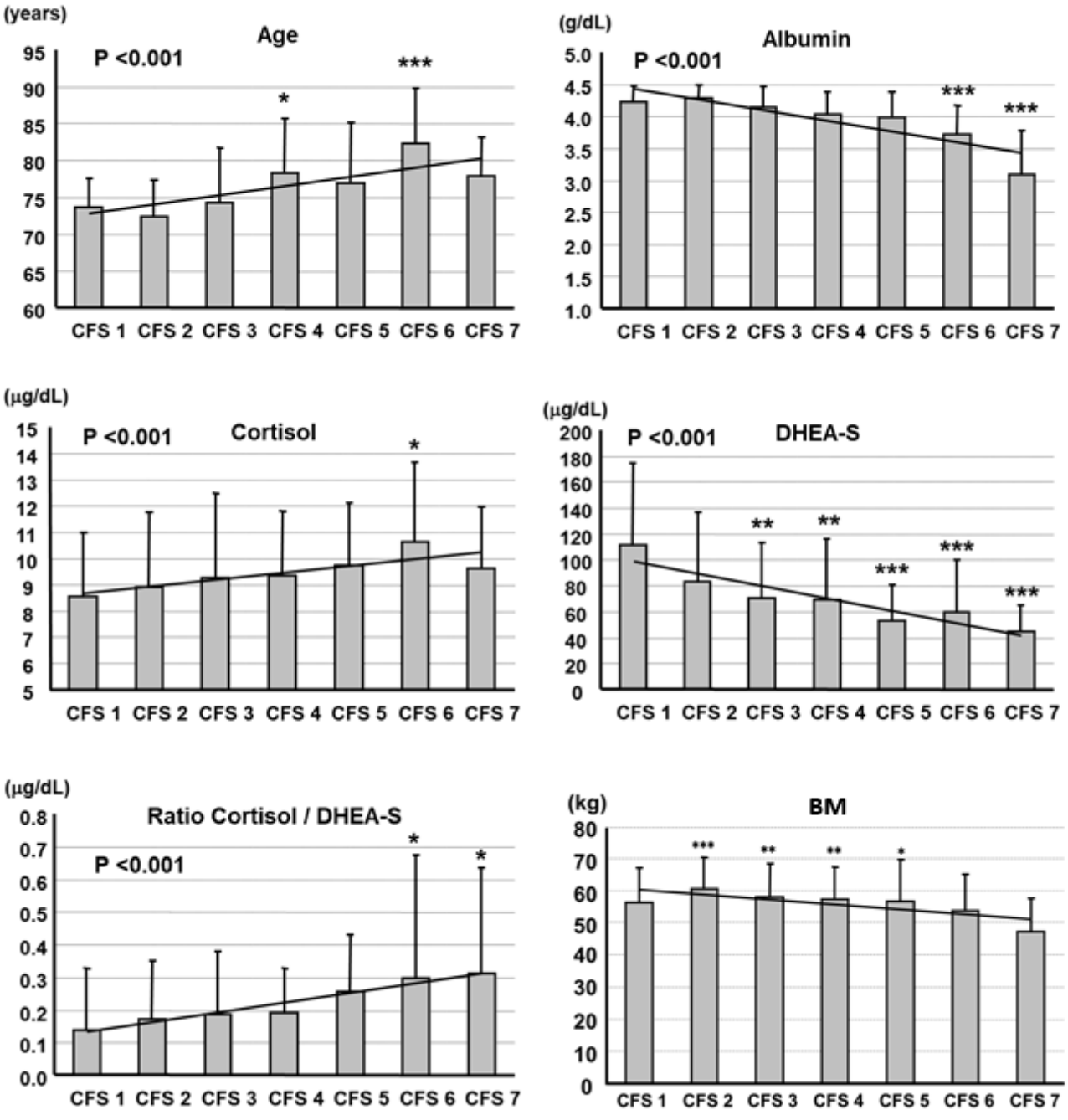

Figure 1

Predictive variables, classified using the Clinical Frailty Scale (CFS). Data are means + standard deviation (SD). P values for linear regressions were determined using the Jonckheere-Terpstra test. * p<0.05, ** p<0.01, *** p<0.001 vs. CFS1, determined by multiple comparison using Fisher's LSD test, following analysis of variance (ANOVA). For body mass, * p<0.05, ** p<0.01, *** p<0.001 vs. CFS7, determined using Fisher's LSD multiple comparison method, following ANOVA (p=0.025)

Figure2

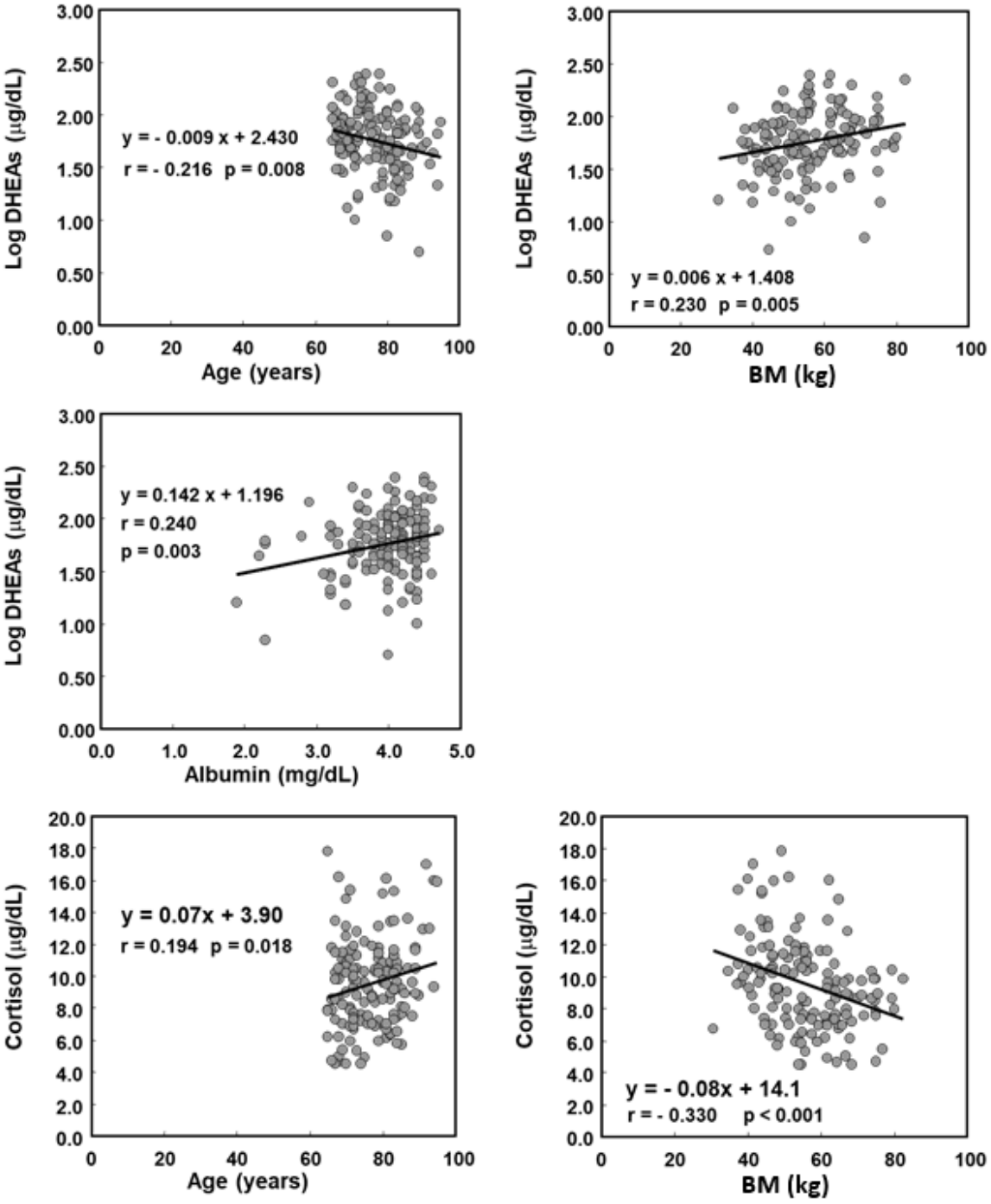

Figure 2

Relationships of log DHEA-S and cortisol concentrations with patient characteristics