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Investigate Nutrition-related Risks and Activities of Daily Living in Diabetes Patients with Severe Hypoglycemia

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ABSTRACT

Aims/Introduction: *This study aimed to investigate a nutritional index score and activities of daily living (ADLs) in diabetes patients with severe hypoglycemia.*

Materials and Methods: *Fifty-four diabetes patients who were admitted to a regional hospital for severe hypoglycemia were retrospectively enrolled in the present study. Nutrition-related risk was assessed using the Geriatric Nutritional Risk Index (GNRI). ADLs were assessed using the Barthel Index (BI) at discharge. Intergroup comparisons of clinical characteristics were performed by type of diabetes, age, and GNRI class.*

Results: *Eight, 44, and two patients had type 1, type 2, and pancreatic diabetes, respectively. Compared with patients with type 1 diabetes, those with type 2 diabetes had a significantly higher age ($P < 0.01$) and significantly lower GNRI and BI scores (both $P < 0.05$). GNRI scores were low/moderate/high-risk for one (12.5%) patient with type 1 diabetes and 42 (95.5%) patients with type 2 diabetes. Of type 2 diabetes patients with severe hypoglycemia, 39.5% had a BI score ≤ 70 at discharge, and 88.2% of those were patients aged 65 years or older. In patients with type 2 diabetes, the odds of a BI score ≤ 70 at discharge were significantly higher if inappropriate diet or sick day management preceded hypoglycemia, with an adjusted odds ratio of 10.4 (95% confidence interval: 2.1–51.7, $P = 0.004$).*

Conclusions: *Patients with type 2 diabetes and severe hypoglycemia are at nutritional risk, according to GNRI scores. Nutritional assessment using the GNRI may prevent severe hypoglycemia and impairment of ADLs.*

Keywords
Activities of daily living, Hypoglycemia, Nutritional index.

Introduction
In the treatment of diabetes, strict glycemic control delays the onset and progression of diabetic microvascular disease and reduces long-term complications and total mortality [1-3]. However, treatments that aid strict glycemic control also carry a risk of hypoglycemia [4]. Severe hypoglycemia is associated not only with acute symptoms, but also with an increased risk of cardiovascular disease and death, and the disruption of many everyday activities [5-7].

The Geriatric Nutritional Risk Index (GNRI) is used as an index to stratify the risk of morbidity and mortality in older hospitalized patients [8]; however, it has since been applied as a prognostic determinant of clinical outcomes in chronic heart failure [9] and hemodialysis [10] patients. In addition, low GNRI affects activities of daily living (ADLs) at discharge in older hospitalized patients

with heart failure [9,11]. In older patients with type 2 diabetes, low GNRI is also associated with sarcopenia [12]. In addition, the GNRI is a useful predictor of hypoglycemia in hospitalized older patients with diabetes [13].

There have been few reports on the use of the GNRI in patients with severe hypoglycemia. To investigate the GNRI and ADLs in patients with severe hypoglycemia, we compared clinical data of diabetes patients hospitalized with severe hypoglycemia by diabetes type, age, and GNRI classification.

Materials and Methods

Study design and Patients

This study was conducted at a regional referral hospital, the Kagoshima City Hospital, Kagoshima, Japan, between January 2014 and March 2024. This was a retrospective, cross-sectional study using medical record information. Eligibility criteria were patients who were admitted to the hospital after an emergency transport due to impaired consciousness caused by hypoglycemia and aged ≥ 18 years old. Of the 60 patients, 54 (24 women and 30 men) participated in the current study after excluded six patients from the study for the following reasons: two patients had unmeasured serum albumin concentrations and four had attempted suicide. Of the 54 included patients, four patients had been hospitalized twice for severe hypoglycemia. Routine biochemical and hematological tests and screening for diabetic complications were carried out for all patients. In addition, the following variables were investigated: glycemic control agent use, factors preceding severe hypoglycemia onset, timing of severe hypoglycemia onset, presence or absence of a severe hypoglycemia-associated fall, length of hospital stay, and prognosis. Severe hypoglycemia was defined as severe cognitive impairment requiring assistance from another person for recovery [14]. This study involving human participants was reviewed and approved by the Kagoshima City Hospital Ethics Committee (approval no: 2023–21). Written informed consent was waived owing to the retrospective observational design of the study. All data were collected from historical hospital records.

Nutritional assessment using the GNRI

Nutrition-related risks were assessed using the GNRI, which was calculated from patients' height, body weight, and serum albumin concentration at hospital admission using the following formula [10]: GNRI = 14.89 × serum albumin (g/dL) + 41.7 × (body weight/ideal body weight). If the patient's body weight was greater than the ideal body weight, body weight/ideal body weight was set to 1. The ideal body weight was calculated from patients' height and a body mass index of 22 kg/m^2. Based on the original study [10], patients were categorized into four nutrition-related risk groups as follows: high risk (GNRI < 82), moderate risk (GNRI ≥ 82 and < 92), low risk (GNRI ≥ 92 and ≤ 98), and no risk (GNRI > 98). On the basis of these grades, we divided the patients into two GNRI subgroups for analysis: a no/low/moderate-risk group and a high-risk group.

Assessment of ADLs

ADLs were assessed using the Barthel Index (BI) [15]. This 100-point clinical rating index includes 10 items related to self-care ability: feeding (0, 5), bathing (0, 5), grooming (0, 5), dressing (0, 5, 10), bladder control (0, 5, 10), bowel control (0, 5, 10), toilet use (0, 5, 10), chair transfer (0, 5, 10, 15), mobility (0, 5, 10, 15), and stair climbing (0, 5, 10). The BI score ranges from 0 (total dependence) to 100 points (total independence). The evaluation was conducted by trained nurses at discharge. There are various cutoff values used for the BI, but according to previous definitions [16], BI scores were classified as follows: moderate or severe dependence (below 70 points), mild dependence (75–95 points), and total independence (100 points).

Statistical analyses

Calculated data are expressed as the mean ± standard deviation. Data were analyzed by one-way analysis of variance, and group differences in numeric variables were calculated using Student's *t*-tests or Mann–Whitney *U* tests. Factor analysis was carried out to assess factors related to a low BI score at discharge using multivariate logistic regression analysis. The results of the regression modeling are presented as the odds ratio (OR) and 95% confidence interval (CI). All statistical analyses were performed using Excel 2021 (Microsoft, Redmond, WA, USA) with the add-in software Statcel 3 (OMS, Tokyo, Japan) and EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [17]. A P-value < 0.05 was considered statistically significant.

Results

The demographic data of the 54 participants are listed in Table 1. The distribution of patients across diabetes types was as follows: eight patients had type 1 diabetes, 44 patients had type 2 diabetes, and two patients had pancreatic diabetes. The mean age of the patients was 73.2 ± 11.2 years, with a mean duration of diabetes of 22.0 ± 12.9 years. The mean glucose level at presentation (before treatment) was 32.1 ± 12.5 mg/dL. The mean glycosylated hemoglobin (HbA1c) level at the onset of severe hypoglycemia was 6.7% ± 1.2%. Nutrition-related risk assessed using the GNRI was low for 17 (31.5%) patients, moderate for 12 (22.2%) patients, high for 16 (29.6%) patients, and zero for nine (16.7%) patients. Severe hypoglycemia was noted irrespective of the progression of diabetic retinopathy and nephropathy. Cardiovascular disease was prevalent in 40.7% of patients. Antidiabetic agents used in patients with severe hypoglycemia included insulin treatment for 24 patients (44.4%) and sulfonylureas for 27 patients (50.0%). The main factors that affected the onset of severe hypoglycemia included drug overdose or incorrect drug use (55.5%) and inappropriate dietary or sick day management (31.5%); other factors accounted for the remaining cases (13%). There was no particular trend in the timing of severe hypoglycemia onset. Falls resulting from hypoglycemia occurred in 9.3% of patients. The mean length of hospital stay was 11.9 ± 9.4 days. The distribution of BI scores at discharge was as follows: 35.2% of patients had moderate or severe dependence, 20.3% had mild dependence, and 42.5% had total independence. Subsequent central nervous system sequelae were observed in 3.7% of patients, and death occurred in 1.9% of patients.

Table 1: Clinical characteristics of patients

	Total patients (n = 54)
Type of diabetes; type 1/type 2/pancreatic (n)	8/44/2
Sex (% male)	55.6
Age (years)	73.2 ± 11.2
Diabetes duration (years) (n = 45)	22.0 ± 12.9
BMI (kg/m^2)	22.8 ± 3.8
Blood glucose (mg/dL)	32.1 ± 12.5
HbA1c (%)	6.7 ± 1.2
Total protein (g/dL)	6.5 ± 0.7
Total lymphocyte (/mm^3) (n = 49)	1096 ± 602
Hemoglobin (g/dL)	11.4 ± 1.9
Total cholesterol (mg/dL) (n = 38)	171 ± 47
BUN to creatinine ratio	19.1 ± 8.7
eGFR (mL/min/1.73 m^2)	44.5 ± 32.2
GNRI	89.3 ± 10.3
GNRI class; no/low/moderate/high (%)	16.7/31.5/22.2/29.6
Retinopathy; none/SDR/PPDR//PDR (%) (n = 27)	14.8/7.4/9.3/18.5
Nephropathy; stage 1/2/3/4/5 (%) (n = 48)	22.2/14.8/13.0/29.6/9.3
Cardiovascular disease (%)	40.7
Glycemic control agents; insulin/SU/other (%)	44.4/50.0/5.6
Hypoglycemia factors; drugs/diet or sick days/other (%)	55.5/31.5/13.0
Timing of severe hypoglycemia onset; 06:00–18:00/18:00–06:00 (%)	48.1/51.9
Hypoglycemia-associated fall (%)	9.3
Duration of hospitalization (days)	11.9 ± 9.4
BI score at discharge (n = 53)	73.5 ± 33.4
Prognosis; recovery/CNS sequelae/death (%)	94.6/3.7/1.9

Data are expressed as mean ± standard deviation or number (percentage). BMI, body mass index; HbA1c, glycosylated hemoglobin; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; GNRI, Geriatric Nutritional Risk Index; SDR, simple diabetic retinopathy; PPDR, preproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; SU, sulfonylurea; BI, Barthel Index; CNS, central nervous system.

Table 2 presents factors associated with severe hypoglycemia by diabetes type. Patients with type 2 diabetes were significantly older than those with type 1 diabetes ($P < 0.01$). Hemoglobin concentrations and GNRI scores of patients with type 2 diabetes were significantly lower than those of patients with type 1 diabetes (both $P < 0.01$). GNRI risk was high/moderate/low for one (12.5%) patient with type 1 diabetes and 42 (95.5%) patients with type 2 diabetes. Compared with patients with type 1 diabetes, patients with type 2 diabetes had significantly fewer occurrences of severe hypoglycemia onset from 6:00 p.m. to 6:00 a.m. ($P < 0.05$). Additionally, patients with type 2 diabetes had a significantly longer length of hospital stay ($P < 0.01$) and significantly lower BI scores at discharge ($P < 0.05$) than those with type 1 diabetes.

Table 2: Comparison of patient clinical characteristics by diabetes type.

	Type 1 diabetes (n = 8)	Type 2 diabetes (n = 44)	P
Sex (% male)	75.0	52.3	0.238
Age (years)	62.9 ± 7.7	74.3 ± 10.6	0.005
Diabetes duration (years) (n = 45)	28.0 ± 10.2	21.1 ± 13.1 (n = 37)	0.172
BMI (kg/m^2)	22.2 ± 3.4	23.0 ± 3.8	0.576
Blood glucose (mg/dL)	34.8 ± 18.2	31.0 ± 11.0	0.428
HbA1c (%)	7.0 ± 0.4	6.6 ± 1.1	0.309
Total protein (g/dL)	6.9 ± 0.6	6.4 ± 0.7	0.120
Total lymphocyte (/mm^3) (n = 49)	1140 ± 541	1075 ± 629 (n = 41)	0.786
Hemoglobin (g/dL)	13.2 ± 0.9	11.1 ± 1.8	0.003
Total cholesterol (mg/dL) (n = 38)	177 ± 48 (n = 7)	170 ± 49 (n = 31)	0.726
BUN to creatinine ratio	17.1 ± 10.9	19.2 ± 8.4	0.539
eGFR (mL/min/1.73 m^2)	60.9 ± 44.3	40.5 ± 29.2	0.100
GNRI	100.7 ± 12.6	87.3 ± 8.7	< 0.001
GNRI class; no/low/moderate/high (%)	87.5/0/0/12.5	4.5/36.4/27.3/31.8	< 0.001
Retinopathy; none/SDR/PPDR//PDR (%) (n = 26)	25.0/12.5/25.0/12.5 (n = 6)	11.4/6.8/6.8/20.5 (n = 20)	0.373
Nephropathy; stage 1/2/3/4/5 (%) (n = 46)	25.0/25.0/0/0/37.5 (n = 7)	20.5/13.6/13.6/36.4/4.5 (n = 39)	0.740
Cardiovascular disease (%)	12.5	47.7	0.066
Glycemic control agents			
insulin (%)	100	31.8	< 0.001
SU (%)	0	61.4	0.002
Hypoglycemia factors			
drug overdose or incorrect drug use (%)	62.5	56.8	0.767
inappropriate dietary or sick day management (%)	25.0	34.1	0.618
other (%)	12.5	9.1	0.766
Timing of severe hypoglycemia onset			
06:00–18:00/18:00–06:00 (%)	12.5/87.5	54.5/45.5	0.030
Hypoglycemia-associated fall (%)	0	11.4	0.321
Duration of hospitalization (days)	5.9 ± 4.5	13.0 ± 9.8	0.004
BI score at discharge (n = 51)	88.1 ± 33.6	70.8 ± 33.6 (n = 43)	0.035
Prognosis; recovery/CNS sequelae/death (%)	100/0/0	93.2/4.5/2.3	0.451

Data are expressed as mean ± standard deviation or number (percentage). BMI, body mass index; HbA1c, glycosylated hemoglobin; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; GNRI, Geriatric Nutritional Risk Index; SDR, simple diabetic retinopathy; PPDR, preproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; SU, sulfonylurea; BI, Barthel Index; CNS, central nervous system.

Table 3 presents factors associated with severe hypoglycemia by age in patients with type 2 diabetes. Prior to the onset of severe hypoglycemia, inadequate dietary or sick day management was significantly more prevalent among patients aged 65 and older than among patients younger than 65 ($P < 0.05$). Compared with patients under 65 years old, patients aged 65 years or older had a significantly higher prevalence of cardiovascular disease and significantly lower BI scores at discharge (both $P < 0.05$). Sulfonylurea use tended to be higher in patients aged 65 years or older than in those under 65 years old, but this was not significantly different ($P = 0.056$).

Table 3: Comparison of patient clinical characteristics by age in patients with type 2 diabetes

	Age < 65 years (n = 9)	Age ≥ 65 years (n = 35)	P
Sex (% male)	55.6	50	0.827
Diabetes duration (years) (n = 33)	17.1 ± 2.0 (n = 8)	22.2 ± 14.6 (n = 29)	0.336
BMI (kg/m^2)	21.8 ± 2.9	23.3 ± 4.1	0.298
Blood glucose (mg/dL)	28.6 ± 10.5	31.6 ± 11.2	0.466
HbA1c (%)	6.8 ± 1.2	6.5 ± 1.0	0.364
Total protein (g/dL)	6.4 ± 0.8	6.4 ± 0.7	0.950
Total lymphocyte (/mm^3) (n = 41)	1153 ± 719 (n = 8)	1056 ± 616 (n = 33)	0.703
Hemoglobin (g/dL)	11.4 ± 1.0	11.0 ± 2.0	0.604
Total cholesterol (mg/dL) (n = 31)	182 ± 29 (n = 8)	166 ± 54 (n = 23)	0.446
BUN to creatinine ratio	21.0 ± 9.7	18.7 ± 8.2	0.463
eGFR (mL/min/1.73 m^2)	44.1 ± 33.9	39.5 ± 28.4	0.681
GNRI	88.8 ± 9.3	86.9 ± 8.6	0.577
GNRI class; no/low/moderate/high (%)	11.1/33.3/22.2/33.3	2.9/37.1/28.6/31.4	0.806
Retinopathy; none/SDR/PPDR//PDR (%) (n = 20)	33.3/0/22.2/33.3 (n = 8)	5.7/8.6/2.9/17.1 (n = 12)	0.567
Nephropathy; stage 1/2/3/4/5 (%) (n = 38)	33.3/0/11.1/33.3/11.1 (n = 8)	17.1/17.1/14.3/37.1/2.9 (n = 30)	0.985
Cardiovascular disease (%)	11.1	57.1	0.015
Glycemic control agents			
insulin (%)	66.7	22.9	0.013
SU (%)	33.3	68.6	0.056
Hypoglycemia factors			
drug overdose or incorrect drug use (%)	77.8	51.4	0.159
inappropriate dietary or sick day management (%)	0	42.9	0.017
other (%)	22.2	5.7	0.129
Timing of severe hypoglycemia onset			
06:00–18:00/18:00–06:00 (%)	66.7/33.3	51.4/48.6	0.418
Hypoglycemia-associated fall (%)	11.1	11.4	0.979
Duration of hospitalization (days)	9.8 ± 9.2	13.8 ± 9.9	0.282
BI score at discharge (n = 43)	84.4 ± 34.3	67.2 ± 33.0 (n = 34)	0.043
Prognosis; recovery/CNS sequelae/death (%)	88.9/11.1/0	94.2/2.9/2.9	0.594

Data are expressed as mean ± standard deviation or number (percentage). BMI, body mass index; HbA1c, glycosylated hemoglobin; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; GNRI, Geriatric Nutritional Risk Index; SDR, simple diabetic retinopathy; PPDR, preproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; SU, sulfonylurea; BI, Barthel Index; CNS, central nervous system.

Table 4 presents factors associated with severe hypoglycemia by GNRI class in patients with type 2 diabetes. Compared with the findings in the moderate/low/no-risk group, in the high-risk group, significantly fewer patients used sulfonylureas, and a significantly more prevalent of inappropriate dietary or sick day management instances were recorded (both $P < 0.05$). Total protein was significantly lower in the high-risk group than in the moderate/low/no-risk group ($P < 0.01$). There were no significant differences in total lymphocyte count, hemoglobin concentration, total cholesterol concentration, blood urea nitrogen-to-creatinine ratio, or estimated glomerular filtration rate between the two subgroups. There was no significant difference in factors affecting the onset of severe hypoglycemia between a GNRI high/moderate-risk group and a low/no-risk group.

In the age-based comparison of patients with type 2 diabetes, significant differences were found not only in BI scores at discharge, but also in instances of inappropriate dietary or sick day management and the prevalence of cardiovascular disease; therefore, these variables were included in the multivariate analyses. In patients with type 2 diabetes, the odds of a BI score ≤ 70 at discharge were calculated as an OR after adjustment for the potential confounding roles of age and the presence of cardiovascular disease (Table 5). Instances of inappropriate dietary or sick day management preceding severe hypoglycemia onset were associated with higher odds of a BI score ≤ 70 at discharge with an adjusted OR of 10.4 (95% CI: 2.100–51.700, $P = 0.004$). Age and presence of cardiovascular disease were not associated with the odds of a BI score ≤ 70 at discharge.

Discussion

This study investigated nutrition-related risks and ADLs in patients with severe hypoglycemia. We found that 95.5% of type 2 diabetes patients with severe hypoglycemia were at nutritional risk (GNRI score ≤ 98). In particular, people with type 2 diabetes had increased odds of impaired ADLs on discharge because of inappropriate dietary or sick day management prior to hospital admission for severe hypoglycemia. Although the GNRI is not an index of malnutrition, GNRI scores are correlated with nutritional status-related complications, which means it can be used as a nutrition-related risk index [10]. Our results suggest that nutrition-related risk is associated with impaired ADLs in patients with severe hypoglycemia.

The characteristics of patients with severe hypoglycemia were similar to those of participants from large-scale surveys in Japan: there was no difference in the male-to-female ratio, and many patients had had diabetes for more than 20 years [4]. Severe hypoglycemia was observed in patients with type 1 diabetes across age brackets; however, hypoglycemia was observed more

Table 4: Comparison of patient clinical characteristics by Geriatric Nutritional Risk Index (GNRI) class in patients with type 2 diabetes

	GNRI		
	< 82 (high risk; n = 14)	≥ 82 (moderate/low/no risk; n = 30)	P
Sex (% male)	57.1	50.0	0.662
Age (years)	75.4 ± 10.8	73.8 ± 10.7	0.641
Diabetes duration (years) (n = 37)	24.4 ± 14.5 (n = 11)	19.8 ± 12.5 (n = 26)	0.337
BMI (kg/m^2)	22.2 ± 3.5	23.3 ± 4.0	0.390
Blood glucose (mg/dL)	33.9 ± 10.5	29.6 ± 11.1	0.241
HbA1c (%)	6.6 ± 0.8	6.5 ± 1.2	0.782
Total protein (g/dL)	5.9 ± 0.7	6.7 ± 0.6	< 0.001
Total lymphocyte (/mm^3) (n = 41)	854 ± 441	1190 ± 686 (n = 27)	0.106
Hemoglobin (g/dL)	10.9 ± 1.4	11.1 ± 2.1	0.767
Total cholesterol (mg/dL) (n = 31)	194 ± 64 (n = 9)	160 ± 38 (n = 22)	0.081
BUN to creatinine ratio	17.1 ± 10.9	20.1 ± 7.0	0.263
eGFR (mL/min/1.73 m^2)	44.9 ± 35.0	38.4 ± 26.6	0.500
Retinopathy; none/SDR/PPDR//PDR (%) (n = 20)	7.1/0/7.1/28.6 (n = 6)	13.3/10.0/6.7/16.7 (n = 14)	0.221
Nephropathy; stage 1/2/3/4/5 (%) (n = 39)	21.4/14.3/21.4/28.6/7.1 (n = 13)	20.0/13.3/10.0/40.0/3.3 (n = 26)	0.803
Cardiovascular disease (%)	50.0	46.7	0.838
Glycemic control agents			
insulin (%)	50.0	23.3	0.080
SU (%)	35.7	73.3	0.018
Hypoglycemia factors			
drug overdose or incorrect drug use (%)	28.6	70.0	0.011
inappropriate dietary or sick day management (%)	57.1	23.3	0.029
other (%)	14.3	6.7	0.418
Timing of severe hypoglycemia onset			
06:00–18:00/18:00–06:00 (%)	35.7/64.3	50.0/50.0	0.381
Hypoglycemia-associated fall (%)	14.3	10.0	0.680
Duration of hospitalization (days)	12.0 ± 8.5	13.4 ± 10.5	0.665
BI score at discharge (n = 43)	59.3 ± 42.0	76.4 ± 27.9 (n = 29)	0.358
Prognosis; recovery/CNS sequelae/death (%)	92.9/7.1/0	93.3/3.3/3.3	0.977

Data are expressed as mean ± standard deviation or number (percentage). GNRI, Geriatric Nutritional Risk Index, BMI, body mass index; HbA1c, glycosylated hemoglobin; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; SDR, simple diabetic retinopathy; PPDR, preproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; SU, sulfonylurea; BI, Barthel Index; CNS, central nervous system.

Table 5: Odds of a Barthel Index (BI) score ≤ 70 at discharge for patients with type 2 diabetes according to a multivariate logistic regression analysis

Factor	Multivariate analysis		
	Odds ratio	95% CI	P
BI score ≤ 70 at discharge			
Age (years)	0.981	0.904–1.070	0.656
Cardiovascular disease	3.610	0.671–19.400	0.135
Inappropriate dietary or sick day management	10.400	2.100–51.700	0.004

CI, confidence interval; BI, Barthel Index.

frequently in patients with type 2 diabetes, who tended to be older (median age, 74.3 years; participants ≥ 65 years old, 79.5%). Compared with people with type 2 diabetes, those with type 1 diabetes had a higher frequency of nocturnal hypoglycemia; this is supported by results that suggest autonomic responses to hypoglycemia may be reduced during sleep in patients with type 1 diabetes [18,19]. Although age and the timing of severe hypoglycemia onset varied by diabetes type, there was no difference in HbA1c levels, with values of 7% or lower and 7.5% or lower observed in 68.5% and 77.8% of patients with type 1 and type 2 diabetes, respectively. Severe hypoglycemia did not occur in patients with an HbA1c of 9% or higher. Of the antidiabetic drugs used in patients with type 2 diabetes, sulfonylureas were most commonly used (61.4%) followed by insulin (31.8%), which, together, accounted for 93% of all drugs used. These results align with previous reports in Japan, which also show a high rate of sulfonylurea use [20]. In 6.8% of patients with type 2 diabetes and severe hypoglycemia, neither sulfonylureas nor insulin were used; instead, 4.5% and 6.8% of patients used glinides and dipeptidyl peptidase-4 inhibitors, respectively. All of these patients had stage 3 or higher nephropathy, and insulin secretory agents are to be used judiciously in nephropathy patients, depending on disease progression. The most common factors that affected the onset of severe hypoglycemia were drug overdose or incorrect drug use and inappropriate dietary or sick day management; others included excessive exercise, bathing, and the presence of an insulin ball. In the majority of cases, severe hypoglycemia could have been avoided through appropriate treatment selection and patient guidance. In this study, 9.3% of patients who developed hypoglycemia fell; the Atherosclerosis Risk in Communities study in the United States found that severe hypoglycemia was associated with a more than twofold higher risk of falls (hazard ratio: 2.23, 95% CI: 1.61–3.07)

[21]. The mechanism by which hypoglycemia directly increases the risk of falls has not yet been clarified; however, because 80% of the falls in this study were in people aged 80 and over, frailty and sarcopenia may have been involved.

Diabetes interacts with frailty and sarcopenia through insulin dysfunction and hyperglycemia, which form a vicious cycle [22]. Risk factors for sarcopenia in patients with diabetes include advanced age, low body mass index, low bone mineral content, low serum albumin levels, and poor glycemic control [23,24]. Although the association between hypoglycemia and sarcopenia in patients with diabetes is unclear, a U-shaped association between hypoglycemia and frailty has been reported, which suggests that in addition to high glucose levels, low glucose levels may also be tied to greater frailty risk [25]. Indeed, there is a dose–response relationship between hypoglycemic episodes and frailty risk among patients with diabetes [26]. In a study of older people without sarcopenia at hospital admission, 14.7% developed sarcopenia during their average 10.2 days in the acute care hospital [27]. Hospitalization due to severe hypoglycemia can also lead to further deteriorations in physical function, which can increase the risk of mobility disabilities [28]. In fact, in the present study, 39.5% of type 2 diabetes patients with severe hypoglycemia had a BI score ≤ 70 at discharge, and 88.2% of those were patients aged 65 years or older. In this way, hypoglycemia was associated with impaired ADLs; furthermore, multivariate regression analyses showed that nutritional risk in the form of inappropriate dietary or sick day management may have been involved in this association. In particular, older people tend to have unstable food intake in their daily lives, which means they need to be vigilant about hypoglycemia [29].

As hypoglycemia is a risk factor for frailty and the need for nursing care in older people, it is particularly important to avoid hypoglycemia in the management of older patients with diabetes. Indeed, fewer patients are receiving drugs associated with severe hypoglycemia in clinical practice, which might reflect recent treatment strategies to avoid hypoglycemia in older patients [30]. The International Conference of Frailty & Sarcopenia Research has proposed a practical decision-making approach for older people with diabetes and frailty: they emphasize preventing hypoglycemia, avoiding rest due to hospitalization, providing basic education and training on hypoglycemia for patients and their cares, and relaxing the HbA1c target to 7.5%–8.5% in moderate-to-severe frailty [31]. Providing adequate amounts of energy and protein is important to prevent frailty. The European Society for Clinical Nutrition and Metabolism guidelines recommend that energy intake in older persons should be approximately 30 kcal/kg body weight/day, and protein intake should be at least 1 g/kg body weight/day [32]. Nutritional assessment using the GNRI is a possible way to identify patients at high risk of severe hypoglycemia and impaired ADLs. This could allow early medical intervention, such as appropriate nutritional management and guidance on care during illness, and may contribute to the prevention of frailty and impaired ADLs. However, the GNRI should be used for nutritional screening and assessment only after fully understanding the characteristics of the patient.

This study has several limitations. First, it was designed as a single-center trial, and the sample size was relatively small. Patients in the high-risk group tended to have lower BI scores at discharge than those in the moderate/low/no-risk group, but this was not significantly different. This may have been caused by the low statistical power due to the small sample size. A comparison between a high/moderate/low-risk group and the no-risk group was not possible because of the small number of cases in the no-risk group. Therefore, the generalizability of these survey results may be limited. Further investigations using a large sample size are required to determine the relevance of our findings to a larger population. Second, ADL scores at discharge were affected by those at admission. For this reason, we also considered using the change in ADL score during hospitalization as an outcome indicator. However, ADL scores at admission may have been affected by severe hypoglycemia, while the BI was assessed based on interviews with the patient or their family rather than by trained nurses. Consequently, only BI scores at discharge were used for the assessment of ADLs.

Conclusion

Patients with type 2 diabetes and severe hypoglycemia are at nutritional risk, according to the GNRI. Interventions for patients identified as being at risk may help to avoid severe hypoglycemia and prevent impaired ADLs. These findings could be used to form treatment guidelines for older patients with diabetes and frailty.

References

1. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy: the Epidemiology of Diabetes Interventions and Complications (EDIC) study. JAMA. 2003; 290: 2159-2167.
2. Holman RR, Paul SK, Bethel MA, et al. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008; 359: 1577-1589.
3. Shichiri M, Kishikawa H, Ohkubo Y, et al. Long-term results of the Kumamoto Study on optimal diabetes control in type 2 diabetic patients. Diabetes Care. 2000; 23: B21-B29.
4. Namba M, Iwakura T, Nishimura R, et al. The current status of treatment-related severe hypoglycemia in Japanese patients with diabetes mellitus: A report from the committee on a survey of severe hypoglycemia in the Japan Diabetes Society. J Diabetes Investig. 2018; 9: 642-656.
5. Frier BM. Hypoglycaemia in diabetes mellitus: epidemiology and clinical implications. Nat Rev Endocrinol. 2014; 10: 711-722.
6. Seaquist ER, Anderson J, Childs B, et al. Hypoglycemia and diabetes: a report of a workgroup of the American Diabetes Association and the Endocrine Society. Diabetes Care. 2013; 36: 1384-1395.

7. Bonds DE, Miller ME, Bergenstal RM, et al. The association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study. BMJ. 2010; 340: b4909.
8. Bouillanne O, Morineau G, Dupont C, et al. Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. Am J Clin Nutr. 2005; 82: 777-783.
9. Kinugasa Y, Kato M, Sugihara S, et al. Geriatric nutritional risk index predicts functional dependency and mortality in patients with heart failure with preserved ejection fraction. Cir J. 2013; 77: 705-711.
10. Kobayashi I, Ishimura E, Kato Y, et al. Geriatric Nutritional Risk Index, a simplified nutritional screening index, is a significant predictor of mortality in chronic dialysis patients. Nephrol Dial Transplant. 2010; 25: 3361-3365.
11. Kitamura M, Izawa KP, Yaekura M, et al. Differences in nutritional status and activities of daily living and mobility in elderly hospitalized patients with heart failure. ESC Heart Fail. 2019; 6: 344-350.
12. Matsuura S, Shibazaki K, Uchida R, et al. Sarcopenia is associated with the Geriatric Nutritional Risk Index in elderly patients with poorly controlled type 2 diabetes mellitus. J Diabetes Investig. 2022; 13: 1366-1373.
13. Kimura Y, Kimura N, Akazawa M. Increased nutrition-related risk as an independent predictor of the incidence of hypoglycemia in the hospitalized older individuals with type 2 diabetes: a single-center cohort study. Diabetol Int. 2021; 12: 420-429.
14. American Diabetes Association. 6. Glycemic Targets. Diabetes Care. 2017; 40: S48-S56.
15. Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. Md State Med J. 1965; 14: 61-65.
16. Balu S. Differences in psychometric properties, cut-off scores, and outcomes between the Barthel Index and Modified Rankin Scale in pharmacotherapy-based stroke trials: systematic literature review. Curr Med Res Opin. 2009; 25: 1329-1341.
17. Kanda Y. Investigation of the freely available easy-to-use software EZR for medical statistics. Bone Marrow Transplant. 2013; 48: 452-458.
18. Jones TW, Porter P, Sherwin RS, et al. Decreased epinephrine responses to hypoglycemia during sleep. N Engl J Med. 1998; 338: 1657-1662.
19. Banarer S, Cryer PE. Sleep-related hypoglycemia-associated autonomic failure in type 1 diabetes: reduced awakening from sleep during hypoglycemia. Diabetes. 2003; 52: 1195-1203.
20. Iwakura T, Sasaki S, Fujiwara Y, et al. Clinical analysis of 135 type 2 diabetes patients with severe drug-induced hypoglycemia. J Japan Diab Soc. 2012; 55: 857-865.
21. Lee AK, Juraschek SP, Windham BG, et al. Severe hypoglycemia and risk of falls in type 2 diabetes: the Atherosclerosis Risk in Communities (ARIC) study. Diabetes Care. 2020; 43: 2060-2065.
22. Landi F, Onder G, Bernabei R. Sarcopenia and diabetes: two sides of the same coin. J Am Med Dir Assoc. 2013; 14: 540-541.
23. Fukuoka Y, Narita T, Fujita H, et al. Importance of physical evaluation using skeletal muscle mass index and body fat percentage to prevent sarcopenia in elderly Japanese diabetes patients. J Diabetes Investig. 2019; 10: 322-330.
24. Sugimoto K, Tabara Y, Ikegami H, et al. Hyperglycemia in non-obese patients with type 2 diabetes is associated with low muscle mass: The Multicenter Study for Clarifying Evidence for Sarcopenia in Patients with Diabetes Mellitus. J Diabetes Investig. 2019; 10: 1471-1479.
25. Zaslavsky O, Walker RL, Crane PK, et al. Glucose levels and risk of frailty. J Gerontol A Biol Sci Med Sci. 2016; 71: 1223-1229.
26. Chao CT, Wang J, Huang JW, et al. Hypoglycemic episodes are associated with an increased risk of incident frailty among new onset diabetic patients. J Diabetes Complications. 2020; 34: 107492.
27. Martone AM, Bianchi L, Abete P, et al. The incidence of sarcopenia among hospitalized older patients: results from the Glisten study. J Cachexia Sarcopenia Muscle. 2017; 8: 907-914.
28. Abdelhafiz AH, McNicholas E, Sinclair AJ. Hypoglycemia, frailty and dementia in older people with diabetes: Reciprocal relations and clinical implications. J Diabetes Complications. 2016; 30: 1548-1554.
29. Ikeda K, Takahara S, Son C, et al. Drug-induced hypoglycemia in 50 patients with type 2 diabetes mellitus necessitating emergency treatment. J Japan Diab Soc. 2007; 50: 129-135.
30. Sugimoto T, Noma H, Kuroda Y, et al. Time trends (2012-2020) in glycated hemoglobin and adherence to the glycemic targets recommended for elderly patients by the Japan Diabetes Society/Japan Geriatrics Society Joint Committee among memory clinic patients with diabetes mellitus. J Diabetes Investig. 2022; 13: 2038-2046.
31. Sinclair A, Abdelhafiz A, Dunning T, et al. An International Position Statement on the Management of Frailty in Diabetes Mellitus: Summary of Recommendations 2017. J Frailty Aging. 2018; 7: 10-20.
32. Volkert D, Beck AM, Cederholm T, et al. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr. 2019; 38: 10-47.