Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.0332-22
Intern Med 62: 1431-1439, 2023
http://internmed.jp

【 ORIGINAL ARTICLE 】

Association of Impaired Awareness of Hypoglycemia with Driving Safety and Hypoglycemia Problem-solving Abilities among Patients with Type 1 Diabetes in Japan: The PR-IAH Study

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Abstract:

Objective Patients with type 1 diabetes (T1D) and impaired awareness of hypoglycemia (IAH) are at an elevated risk of experiencing automobile accidents. We therefore investigated the association of IAH with driving safety and hypoglycemia problem-solving abilities in adults with T1D.

Methods This cross-sectional survey used Gold's method in adult patients with T1D at the National Hospital Organization (NHO) Hospital from February 14, 2020, to October 31, 2021. The participants were divided into control and IAH groups. The data included information on demographics, worries and distress regarding hypoglycemia, hypoglycemia problem-solving abilities, and adverse driving events.

Patients We enrolled 233 participants (mean age: 48.5±12.8 years old, mean hemoglobin A1c level: 7.6%±0.9%) from NHO collaborating centers in Japan.

Results Among a total of 233 participants (mean age: 48.5±12.8 years old, mean hemoglobin A1c level: 7.6%±0.9%), the prevalence rate of IAH was 11.6% [95% confidence interval (CI): 7.8-16.4%]. IAH was significantly associated with near-miss car accidents (odds ratio: 5.41; 95% CI:1.64-17.80). Diabetic peripheral neuropathy was associated with an increased risk of IAH, while treatment with continuous subcutaneous insulin infusion was not associated with a decreased risk of IAH. The average hypoglycemia problem-solving perception, detection control, and seeking preventive strategies scores in the IAH group were significantly reduced compared with those in the control group.

Conclusion IAH was associated with an increased risk of near-miss car accidents among adults with T1D. Furthermore, good hypoglycemia problem-solving abilities were associated with a decreased risk of IAH.

Key words: impaired hypoglycemia awareness, prevalence, type 1 diabetes, driving, near-miss traffic events

(Intern Med 62: 1431-1439, 2023)
(DOI: 10.2169/internalmedicine.0332-22)

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Received for publication May 20, 2022; Accepted for publication August 1, 2022

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Introduction

Type 1 diabetes (T1D) results from autoimmune destruction of insulin-producing beta cells in the pancreas (1). Intensive therapy reportedly reduces the hemoglobin A1c (HbA1c) level and diabetic microvascular and macrovascular complications but is associated with an increased risk of hypoglycemia (2).

In 2020, 2,839 individuals out of a population of approximately 125 million died on roads in Japan. Many traffic accidents caused by hypoglycemia, along with epilepsy and recurrent syncope, have been reported by the media in Japan. Hypoglycemia, particularly impaired awareness of hypoglycemia (IAH) and severe hypoglycemia (SH), impairs driving performance and causes traffic accidents in drivers with T1D (3-5). Accordingly, local regulations and recommendations should be followed for driving with T1D (6).

The Road Traffic Act, revised in Japan in 2001, resulted in the placement of certain restrictions on the acquisition and renewal of driver's licenses. The 2001 ordinance designated "asymptomatic hypoglycemia (excluding cases where blood glucose levels can be artificially adjusted)" as a disease causing episodes of disturbed consciousness or movement disorder (7). Driving is a complex process that places considerable demands on cognitive and physical functions. Many complications of diabetes can impair driving performance, including those affecting vision, cognition, and the peripheral neural function (8, 9). Technological improvements in continuous glucose monitoring (CGM) and continuous subcutaneous insulin infusion (CSII) help prevent hypoglycemia in patients with T1D (10). Many adults with T1D experience diabetes-related distress, such as negative emotional reactions specific to managing hypoglycemia. However, there has been no research on IAH in relation to safe driving and hypoglycemia problem-solving abilities.

We therefore assessed the prevalence rate of hypoglycemia-related driving accidents and explored the factors associated with near-miss driving accidents and actual driving accidents in patients with T1D.

Materials and Methods

This exploratory and cross-sectional study was approved by the National Hospital Organization (NHO) Central Research Ethics Committee (R2-0117002) and performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guideline.

Participants and settings

Between February 2020 and October 2021, we enrolled adult patients with IAH from the NHO collaborating centers in Japan. The following seven institutions participated in this study: NHO Mie Hospital, NHO Kyoto Medical Center, NHO Osaka National Hospital, NHO Himeji Medical Center, NHO Hyogo-Chuo National Hospital, NHO Okayama Medical Center, and NHO Kokura Medical Center. The participants were divided into IAH and non-IAH (control) groups.

The inclusion criteria were T1D (11), diabetes duration of ≥1 year, age ≥20 years old, and attending a collaborating center. The exclusion criteria were non-insulin therapy, antidementia drug use, and inappropriate cases judged by the research director or coordinators.

Diabetic complications

Diabetic retinopathy, nephropathy, and peripheral neuropathy (DPN) were treated by certified diabetologists according to the treatment guidelines for diabetes in 2018-2019.

Diabetic retinopathy was assessed by an ophthalmologist using retinal photography. Retinopathy was classified as absent, simple, pre-proliferative, or proliferative. Nephropathy was classified as stages 1 to 5 based on the estimated glomerular filtration rate, presence of albuminuria, or hemodialysis stage (12). DPN presence was considered based on meeting the relevant criteria after the diagnosis of diabetes was made and polyneuropathy was excluded (except for cases of diabetic polyneuropathy); it was determined to be positive in the presence of at least two of the following three criteria: 1) subjective symptoms (numbness, pain, or dysesthesia in the bilateral lower extremities); 2) decreased or absent bilateral Achilles tendon reflexes; and 3) diminished bilateral vibratory sensation at the malleolus medialis (<10 seconds using a tuning fork at 128 Hz) (13). The coefficient of variation of R-R intervals (CV-RR) was calculated automatically using a computed analyzer that collected 100 R-R intervals and divided the standard deviation by the mean value. A CV-RR of <3% was considered indicative of diabetic cardiac autonomic neuropathy (14). The mean corrected QT (QTc) interval was calculated using Bazett's formula, and a QTc interval of >440 ms was considered prolonged (15). Data on the HbA1c level, glycated hemoglobin (GA) level, liver enzyme (aspartate aminotransferase, alanine transaminase, and gamma-glutamyl transferase) levels, and lipid profiles were collected from medical records. Furthermore, the GA/HbA1c ratio, which reflects glucose variability, was calculated by dividing the GA level by the HbA1c level (16).

IAH and hypoglycemic symptoms

SH was defined as an event requiring assistance from another individual to actively administer carbohydrates or glucagon or take corrective action (17). IAH was determined using the gold-standard method (18). The Gold score constitutes a single question ("Are you aware when hypoglycemia is commencing?") rated on a 7-point Likert scale (from 1= "always aware" to 7="never aware"). In the gold-standard method, a score of ≥4 implied the presence of IAH. The detection threshold for hypoglycemia was also based on a single question ("What is the lowest blood glucose level you have reached before feeling symptoms of hypoglycemia?") and was categorized as follows: 60-69, 50-59, 40-49, and

<40 mg/dL.

Hypoglycemic symptoms were evaluated using the Edinburgh Hypoglycemia Scale (19, 20). This questionnaire comprises 11 key symptoms (sweating, palpitations, shaking, hunger, confusion, drowsiness, odd behavior, speech difficulty, incoordination, nausea, and headache), which are evaluated on a 7-point Likert scale (from 1="not at all" to 7 ="very severe") and divided into 3 domains (neuroglycopenic, autonomic, and general malaise). The self-reported number of SH episodes, defined as "hypoglycemia that you were unable to treat yourself," in the preceding year was also assessed.

Diabetes and driving safety screener

The diabetes and driving safety screener version 1 of the Diabetes Center, NHO Kyoto Medical Center was used. This screener includes the driver's license, driving mileage, purpose for driving, self-monitoring of blood glucose (SMBG) before driving, preparation for hypoglycemia during driving, near-miss accidents related to hypoglycemia during the past year, driving accidents during the past year, and accidents related to hypoglycemia during the past year. Driving mileages were divided into 5 categories: <3,000, 3,000-5,000, 5,000-10,000, 10,000-15,000, and ≥15,000 km. The purpose of driving was divided into three categories: family use, work use, and both. Responses to questions regarding measurement of the blood glucose level before driving were given on a 5-point scale ranging from "always" to "not at all." Responses to questions regarding preparation of snacks for hypoglycemia during driving were given on a 5-point scale ranging from "always" to "not at all."

Diabetes-related distress and hypoglycemia problem-solving abilities

Diabetes-related distress was assessed using the Problem Areas in Diabetes (PAID) questionnaire. Each item of the PAID questionnaire was scored from 0 ("no problem") to 4 ("serious problem"). All 20 scores were summed and multiplied by 1.25, resulting in a total score of 0-100 points. Higher scores indicate greater diabetes-related distress, and a cut-off score of ≥40 indicates high distress (21, 22).

Fear of hypoglycemia was assessed using the Hypoglycemia Fear Survey (HFS) adapted for use in Japan (23, 24). The HFS has two subscales: the HFS-B (behavior subscale) and HFS-W (worry subscale). The items are rated on a 5-point Likert scale ranging from 0 (never) to 4 (always). Higher scores indicate a greater fear of hypoglycemia.

The health-related quality of life was assessed, and the utility index was calculated using the European Quality of Life-5-Dimension (EQ-5D) questionnaire (25, 26). The EQ-5D questionnaire has five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. We used the EQ-5D-3 level, which assesses each dimension with three levels of severity in the answer options (e.g. "no problem," "some problems," or "unable").

Hypoglycemia problem-solving abilities were assessed using the Hypoglycemia Problem-Solving Scale (HPSS) (27). The HPSS has 24 items and 7 subscales, as follows: problem-solving perception, detection control, identifying problem attributes, setting problem-solving goals, seeking preventive strategies, evaluating strategies, and immediate management.

Lifestyle factors

Self-administered questionnaire data regarding lifestyle behaviors (current smoking, regular exercise, dietary habits, drinking habits, and sleeping habits) were collected using a standardized questionnaire from the Specific Health Check and Guidance System (28). Exercise habits included 3 items: 1) regular exercise (≥2 times/week of exercise of ≥4 METs/h), 2) active physical activity (≥23 METs×h/week), and 3) walking pace (rapid or not rapid), which is an indicator of physical fitness. Excessive drinking was defined based on the answers to questions concerning drinking habits of both "occasionally or every day" and "≥180 mL of sake (equivalent to ≥20 g of alcohol)." Sleep debt was defined as a difference between the self-reported total weekday and weekend sleep hours of at least 2 hours (29). Healthy lifestyle behaviors included the intake of fruits, fish, and milk; exercise; avoidance of smoking; moderate alcohol intake; and moderate sleep duration (30).

Data analyses

Qualitative variables were compared using Fisher's exact test. As the analyzed quantitative variables were not normally distributed, comparisons were conducted using the Mann-Whitney U test for two groups and the Kruskal-Wallis test for three or more groups. The normality of the variable distribution was verified using the Shapiro-Wilk test. Logistic regression was used to estimate the odds ratios (ORs) and their corresponding 95% confidence intervals (CIs). Statistical significance was set at $p<0.05$. Cronbach's alpha coefficient and mean interitem correlations were used to measure the internal consistency of the questionnaires. Cases with missing data were excluded from the analysis. Analyses was conducted using the R program version 4.1.2.

Results

Participants

The study included a total of 233 adults with T1D and IAH (mean age: 48.5±12.8 years old; proportion of men: 42.5%; diabetes duration: 17.3±11.3 years; mean HbA1c level: 7.6%±0.9%), who were divided into the control and IAH groups.

Diabetic complications, treatment, driving safety, lifestyle factors, and laboratory data

DPN was more prevalent in the IAH group than in the control group. Furthermore, the prescription rate of mecobalamin was higher in the IAH group than in the control

Table 1. Clinical Characteristics of the Patients with Driver's License in the Control and IAH Groups.

Variables	Control group (n=206)	IAH group (n=27)	p value
Age, years	48.5 (12.8)	48.6 (12.8)	0.975
Male sex, %	42.7	40.7	>0.999
Diabetes duration, years	17.2 (11.0)	18.0 (13.1)	0.752
BMI, kg/m^2	23.3 (3.6)	23.0 (3.5)	0.682
HbA1c, %	7.6 (0.9)	7.4 (1.0)	0.249
Diabetic complication			
Retinopathy, %			
NDR/SDR/PPDR/PDR	76.5/16.0/5.0/2.5	86.4/4.5/4.5/4.5	0.375
Photocoagulation	9.2	14.8	0.318
Nephropathy, %			
Stage 1/2/3/4/5	83.9/11.2/3.4/0/1.5	96.2/3.8/0/0/0	0.570
Peripheral neuropathy, %	11.3	30.4	0.019*
Severe hypoglycemia, % (≥1 episode)	6.9	22.2	0.018*
Treatment			
CSII, %	38.8	25.9	0.212
SAP, %	23.3	18.5	0.807
CGM, %	58.3	59.3	>0.999
isCGM	34.0	37.0	0.830
rtCGM	24.3	22.2	>0.999
TDD/BW, U/kg	0.64 (0.22)	0.65 (0.24)	0.818
Anti-hypertensive drug	22.3	14.8	0.462
Cholesterol-lowering drug	22.3	29.6	0.466
Mecobalamin	2.4	18.5	0.002*
ECG			
QTc interval (Bazett's formula), ms	414.7 (27.7)	418.3 (29.8)	0.684
>440 ms	11.4	18.2	0.621
CV-RR, %	3.6 (1.7)	3.1 (1.7)	0.460
<3%	41.7	62.5	0.288

*p<0.05.

IAH: impaired awareness of hypoglycemia, BMI: body mass index, HbA1c: hemoglobin A1c, NDR: non-diabetic retinopathy, SDR: simple diabetic retinopathy, PPDR: pre-proliferative diabetic retinopathy, PDR: proliferative diabetic retinopathy, CSII: continuous subcutaneous insulin infusion, SAP: sensor augmented pump, isCGM: intermittently scanned continuous glucose monitoring, rtCGM: real-time continuous glucose monitoring, ECG: electrocardiogram, QTc: corrected QT, CV-RR: coefficient of variation of R-R intervals

group. The prevalence rate of SH was higher in the IAH group than in the control group. There were no marked differences in the HbA1c level or other complications, except for DPN, between the groups. There was no marked difference in the rate of treatment with CSII or CGM between the groups (Table 1).

DPN was associated with an increased risk of IAH (OR: 3.44; 95% CI: 1.27-9.29; p=0.019), whereas treatment with CSII was not associated with a decreased risk of IAH (OR: 0.55; 95% CI: 0.22-1.36; p=0.212). There were no marked differences in the CV-RR or QTc interval between the groups. The SMBG before driving was less frequently reported in the IAH group than in the control group. There was no marked difference in driving accidents related to hypoglycemia between the groups, although near-miss accidents related to hypoglycemia were more prevalent in the IAH group than in the control group (Table 2). The prevalence rate of IAH in the patients with near-miss accidents was higher than that in the patients without near-miss accidents (20.8% and 4.6%, respectively; p=0.011). The average Gold score in the patients with near-miss accidents was higher than that in the patients without near-miss accidents (2.9±1.7 and 2.0±1.3, respectively; p=0.019). There was no marked difference in the healthy lifestyle score, sleep debt, or excessive drinking rate between the groups (Table 3). There was also no marked difference in the laboratory data, including the HbA1c level (7.6%±0.9% and 7.4%±1.0% in the IAH and control groups, respectively) and GA/HbA1c ratio.

Hypoglycemic symptoms, diabetes-related distress, and hypoglycemia problem-solving abilities

The palpitation and shaking scores in the IAH group were significantly lower than those in the control group. However,

Table 2. Diabetes and Driving Safety Screener among the Drivers with T1D in the Control and IAH Groups.

Variables	Control group	IAH group	p value
Purpose of driving			
Family use	72.9	65.2	
Work use	3.6	4.3	0.504
Both	23.4	30.4	
Mileage, %			
<3,000 km	51.0	52.0	
3,000-5,000 km	14.1	16.0	
5,000-10,000 km	15.2	24.0	0.543
10,000-15,000 km	11.6	8.0	
≥15,000 km	8.1	0	
SMBG before driving, %			
Always/almost	34.2	12.5	0.036*
Preparation of snacks or drinks for hypoglycemia during driving, %			
Always/almost	77.1	75.0	0.800
Near-miss accidents related to hypoglycemia during the past 1 year, %	4.6	20.8	0.011*
Driving accidents during the past 1 year, %	2.0	0	>0.999
Driving accidents related to hypoglycemia during the past 1 year, %	0	0	NA

*p<0.05.

T1D: type 1 diabetes, IAH: impaired awareness of hypoglycemia, SMBG: self-monitoring of blood glucose, NA: not applicable

Table 3. Lifestyle Factors of the Study Participants.

Variables	Control group	IAH group	p value
Lifestyle, %			
Skipping breakfast	10.2	14.8	0.506
Rapid eating	34.1	33.3	>0.999
Late-night dinner eating	29.3	33.3	0.659
Snack and sweetened beverage consumption	74.4	63.0	0.248
Milk intake of ≥1 per day	57.6	44.4	0.220
Fish intake of ≥1 per day	7.8	3.7	0.701
Vegetable dish intake of ≥5 per day	4.4	11.1	0.153
Exercise habit	32.7	33.3	>0.999
Physical activity	56.6	51.9	0.683
Rapid walking	47.8	44.4	0.839
Overworking	23.4	18.5	0.807
Current smoking	20.5	18.5	>0.999
Daily drinking	18.5	22.2	0.608
Excessive drinking	11.2	7.4	0.747
Healthy lifestyle score, points	4.3 (1.4)	3.9 (1.3)	0.181
Sleep			
Average sleep time, min	394 (56)	405 (115)	0.443
Sleep time during weekdays, min	378 (60)	392 (119)	0.305
Sleep time during weekend, min	435 (81)	435 (115)	0.987
Sleep debt, %	30.9	23.1	0.500
Non-restorative sleep, %	36.6	44.4	0.526

IAH: impaired awareness of hypoglycemia

there was no marked difference in the neuroglycopenic or general malaise scores between them (Table 4). The average HFS-W score and EQ-5D utility index in the IAH group were significantly higher than those in the control group. There were no marked differences in the average PAID, Patient Health Questionnaire Depression Scale-9, or HFS-B scores between the groups. The average hypoglycemia problem-solving perception, detection control, and seeking preventive strategies scores were significantly lower in the IAH group than in the control group. The OR (95% CI) threshold for detecting hypoglycemic symptoms (50-59, 40-49, and <40 mg/dL) compared with that for predicting SH

Table 4. Hypoglycemic Symptoms and Hypoglycemia Problem-solving Abilities of the Study Participants.

Variables	Control group	IAH group	p value
Autonomic, points			
Sweating	3.5 (1.9)	2.8 (1.9)	0.083
Palpitations	3.6 (1.7)	2.6 (1.7)	0.013*
Shaking	3.8 (1.8)	2.9 (1.8)	0.019*
Hunger	3.6 (1.9)	3.4 (1.8)	0.502
Neuroglycopenic, points			
Confusion	2.0 (1.6)	2.1 (1.8)	0.815
Drowsiness	2.2 (1.5)	2.4 (1.9)	0.512
Odd behavior	1.6 (1.2)	1.8 (1.5)	0.337
Speech difficulty	1.8 (1.4)	2.4 (2.0)	0.073
Incoordination	2.6 (1.7)	2.8 (1.8)	0.617
General malaise, points			
Headache	1.9 (1.5)	1.4 (1.3)	0.131
Nausea	1.7 (1.3)	1.4 (0.8)	0.195
Total score, points	27.8 (10.2)	24.8 (9.7)	0.146
Psychological, points			
PAID	29.0 (20.1)	31.8 (17.7)	0.501
PHQ-9	3.8 (4.0)	4.5 (4.7)	0.396
HFS-B	18.3 (6.3)	16.8 (4.9)	0.249
HFS-W	10.3 (9.2)	16.9 (12.0)	0.001*
EQ-5D utility index	0.92 (0.12)	0.87 (0.18)	0.043*
Hypoglycemia problem-solving abilities, points			
1. Problem-solving perception, four items	3.5 (0.6)	2.9 (1.1)	<0.001*
2. Detection control, two items	2.5 (1.2)	2.0 (1.1)	0.047*
3. Identifying problem attributes, five items	2.2 (1.1)	1.9 (1.2)	0.251
4. Setting problem-solving goals, three items	1.8 (1.1)	1.5 (1.0)	0.156
5. Seeking preventive strategies, four items	1.5 (0.9)	1.4 (1.1)	0.457
6. Evaluating strategies, four items	2.5 (0.9)	2.1 (0.8)	0.032*
7. Immediate management, two items	3.0 (1.0)	2.9 (1.0)	0.646
Total score, points	56.8 (15.3)	48.0 (15.6)	0.005*

*p<0.05.

IAH: impaired awareness of hypoglycemia, PAID: problem areas in diabetes, PHQ: patient health questionnaire depression scale, HFS-B: hypoglycemia fear survey (behavior subscale), HFS-W: hypoglycemia fear survey (worry subscale), EQ-5D: European quality of life-5-dimension

(60-69 mg/dL) was 1.45 (0.35-5.54), 9.04 (2.15-37.64), and 17.51 (1.12-274.91), respectively.

Discussion

This is the first study to evaluate the association of IAH with driving safety and hypoglycemia problem-solving abilities in Japanese patients with T1D. Lohan et al. reported that 19% of 233 insulin-treated drivers self-reported at least 1 episode of hypoglycemia while driving in the preceding year (31). The prevalence rate of near-miss accidents related to hypoglycemia and actual traffic accidents was lower than that in our previous study of 133 adults with T1D (32). Recent advances in diabetes treatment and autonomous driving to avoid accidents may explain this phenomenon. With a stepped hypoglycemic insulin clamp, the proportion of patients judging that they could drive safely decreased as the serum glucose level decreased from 70% at 120 mg/dL to 22% at 40 mg/dL (33). In a prospective study of 109 Brazilian adults with T1D, the best predictor for new traffic accidents due to hypoglycemia was a history of episodes of hypoglycemia while driving (34). Forty-two percent of patients reported checking their blood glucose level rarely or never within 30 minutes before driving (35). However, most drivers rely on symptoms to detect hypoglycemia while driving and seldom test their blood glucose level before driving (36). In this study, the SMBG implementation rate before driving was lower, but the HFS-W score and rate of near-miss accidents related to hypoglycemia were higher in the IAH group than in the control group. There's a problem with self-management behaviors in the IAH group. Adults with IAH may avoid SMBG because of potential diabetes distress. Diabetes doctors and healthcare professionals should therefore counsel their patients regarding the risk of driving with hypoglycemia and the importance of measuring the blood glucose level before driving, especially for long distances.

In this study, treatment with CSII or CGM was not asso-

ciated with an increased risk of IAH. New technologies, including CGM, aim to improve awareness of hypoglycemia. However, several studies have suggested that IAH persists even with CGM. Reddy et al. reported that real-time CGM (rtCGM; Dexcom G5; Dexcom, San Diego, USA) more effectively reduces the time spent in a hypoglycemic status at 8 weeks than does intermittently scanned CGM (Abbott Freestyle Libre; Abbott Diabetes Care, Witney, UK) in 40 adults with T1D and IAH using an MDI regimen (37). Furthermore, rtCGM systems reduce unawareness of hypoglycemia in children, adolescents, and adults with T1D (38). Further examinations including rtCGM and large samples will be required to confirm these issues, as the rtCGM rate was low in the present study. rtCGM may be useful in reducing unawareness and improving driving safety (39). Conversely, treatment with CSII may be useful in reducing awareness of hypoglycemia in adults with T1D. The clinical statement for the management of problematic hypoglycemia (2015) recommended the following: 1) structured education regarding MDIs of an insulin analog or hypoglycemia-specific education; 2) CSII or MDI with rtCGM; 3) use of a sensor-augmented pump with or without a low-glucose suspension feature or very frequent contact (weekly for 3-4 months); and 4) pancreatic islet transplantation (40). Observational studies based on these guidelines are required to confirm these findings.

The strength of the study is that it employed a validated self-administered questionnaire using Gold's method. However, our study has some limitations, including the lack of a driving simulator. This study employed a cross-sectional design to make causal inferences. DPN was estimated according to its presence or absence; therefore, the severity of peripheral neuropathy was not evaluated. Further examinations including nerve conduction studies and sympathetic skin responses are required to confirm these issues.

IAH is prevalent among adults with T1D. Careful attention should be paid to safe driving in patients with T1D and IAH. IAH can be easily identified using validated questionnaire-based methods, namely Gold's methods. Furthermore, if the lowest blood glucose level before feeling the symptoms of hypoglycemia is reported to be 40-49 or <40 mg/dL, the risk of SH is high. This simple parameter is useful in predicting SH.

We also identified the protective factors for IAH, such as treatment with CSII and the problem-solving perception in the HPSS. CSII or structured education should be considered in adults with T1D and IAH. Problem solving, which is defined as a self-directed cognitive-behavioral process by which individuals attempt to cope with a difficult situation, is a behavioral strategy in diabetes management. It refers to a mental process that involves discovering, analyzing, and solving problems. The problem-solving perception explained most of the variance among the seven factors. This subscale consists of four reverse items: discouraged due to failure to prevent hypoglycemia, feeling depressed or angry because of difficulties in preventing hypoglycemia, worrying about how to prevent hypoglycemia but not taking any action, and reduced self-esteem. Acceptance and commitment therapy-based interventions for diabetes-related distress (41) may help improve the problem-solving perception of patients. The detection control subscale consists of two items: knowing how to handle hypoglycemia, persisting when the initial attempt effectively prevents hypoglycemia failure, and believing that the best approach will be found to solve it. Resilience or the capacity to recover rapidly from difficulties may improve detection control. Interventions based on the HPSS effectively improved the HbA1c level and hypoglycemia problem-solving abilities in individuals with hypoglycemia (42). We should recommend that patients speak to their families, diabetes doctors, and health care professionals regarding preventive strategies. An educational program promoting an increased problem-solving ability in adults with T 1D and IAH should be considered.

In conclusion, we found that IAH is associated with an increased risk of near-miss car accidents in adults with T1D. Furthermore, treatment with CSII and improved hypoglycemia problem-solving abilities are associated with a decreased risk of IAH. The survey by the Japan Diabetes Society highlights the need to implement preventive measures against hypoglycemia through education on hypoglycemia for patients at a high risk of developing SH (43). This information may help prevent hypoglycemia-related traffic accidents in patients with T1D.

Approval of the research protocol: This study was approved by the National Hospital Organization Central Review Board (NHOCRB/ R2-0117002, R3-0614027).

Informed consent or a substitute for it was obtained from all patients for inclusion in the study.

Approval date of Registry and the Registration No. of the study/trial: Trial registration number: University hospital Medical Information Network (UMIN) Center: UMIN000039475), Approval date 13 February 2020

The authors state that they have no Conflict of Interest (COI).

Financial Support

The PR-IAH study with funding from the National Hospital Organization Clinical research (NHO) (Grant number: H31-NHO (Endocrinology and Nephrology)-01).

Acknowledgement

The authors are grateful to the NHO Diabetology group.

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